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SYNTHESIS OF FUSED HETEROCYCLIC RING SYSTEMS RELATED TO 6-AMINO-1,4-DIHYDRO-3-METHYL-1-PHENYL-4-THIOXOTHIO-PYRANO[4,3-*c*]PYRAZOLE-7-CARBONITRILE[1]

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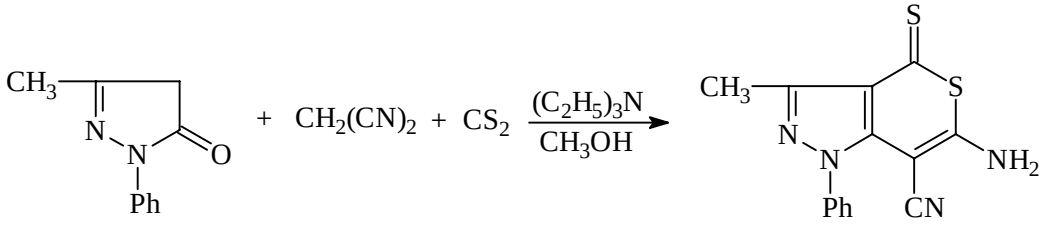
Abstract- The title compound **(1)** was prepared and reacted with some reagents e.g Ac_2O, $HC(OC_2H_5)_3$ to give thiopyrano[4,3-*c*]pyrazole derivatives (**2,10**); $PhNH_2$, NaOH, $AcONH_4$/AcOH, $H_2NNH_2.H_2O$ to afford pyrazolo[4,3-*c*]pyridine derivatives (**4,5,13,14**). Also **1** reacted with CS_2/CH_3I, PhNCS, CCl_3CN and $H_2NHNCSNH_2$ to provide the pyrazolo[3`,4`:4,5]thiopyrano[2,3-*d*]pyrimidine derivatives (**7,9,12**) and pyrazolo[4,3-*c*][1,2,4]triazolo[1,5-*a*]pyridine derivative **(8)**. On the other hand the *o*-diamino compound **(14)** was used for building up a third heterocyclic ring [eg. triazene **(15-17)**, triazole **(18,19)** and tetrazole **(20)**] through its interaction with some electrophilic reagents.

As a continuation of our studies on the synthesis of different heterocyclic ring systems related to pyrazolone ring[2-4] and their industrial and biological importance,[5-8] we report in this paper the synthesis and chemistry of the highly active 6-amino-1,4-dihydro-3-methyl-1-phenyl-4-thioxothiopyrano[4,3-*c*]pyrazole-7-carbonitrile (**1**) and its using as a precursors for the synthesis of a novel unreported linear and angular tricyclic ring systems. For this purpose, the target compound **(1)** was prepared by interaction of 3-methyl-1-phenyl-2-pyrazolin-5-one with malononitrile and carbon disulfide in the presence of triethylanime as a catalyst (Scheme 1).



1

Scheme 1

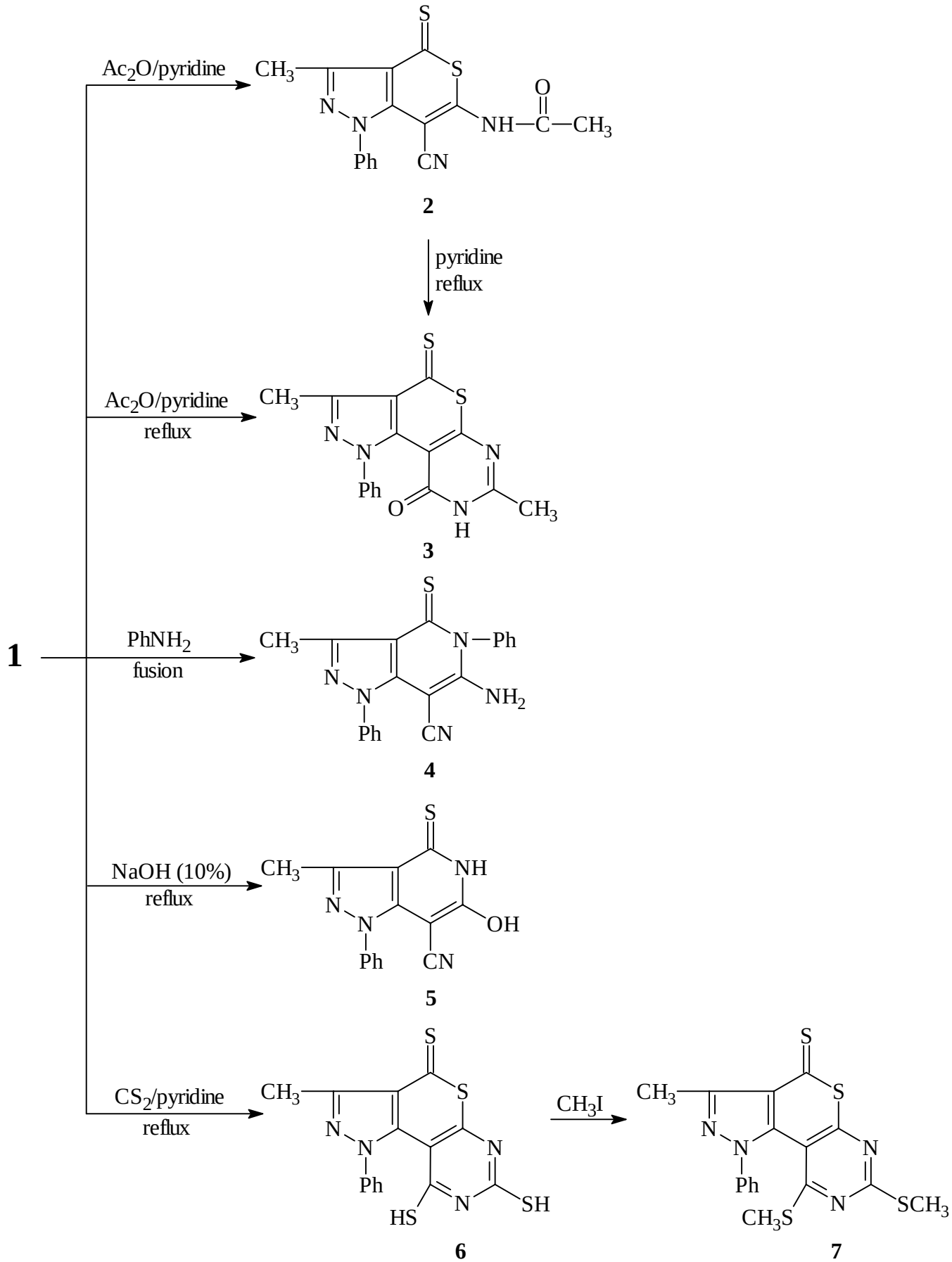
Thus, refluxing of **1** in acetic anhydride/pyridine for few minutes gave the acetamido derivative **(2)**, while on heating for long time (*cf.* experimental) it gave 4,8-dihydro-3,7-dimethyl-1-phenyl-4-thioxo-pyrazolo[3`,4`:4,5]thiopyrano[2,3-*d*]pyrimidin-9(1*H*)-one (**3**).[9] Fusion of **1** with aniline gave 6-amino-4,5-dihydro-3-methyl-1,5-diphenyl-4-thioxo-1*H*-pyrazolo[4,3-*c*]pyridine-7-carbonitrile (**4**), which was also

obtained by an alternative route on heating of 3-methyl-1-phenyl-2-pyrazolin-5-one with phenyl isothiocyante and malononitrile in DMF using $(C_2H_5)_3N$ as a catalyst. Compound **(1)** undergoes rearrangement on refluxing with 10% NaOH solution to afford 4,5-dihydro-6-hydroxy-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[4,3-*c*]pyridine-7-carbonitrile **(5)**. The interaction of **1** with carbon disulfide in pyridine proceeded through the addition of CS_2 on the amino group followed by cyclization *via* nucleophilic attack of the sulfur atom on the cyano group which underwent rearrangement to give pyrimidine dithiol derivative **(6)**.[10,11] Compound **(6)** reacted smoothly with methyl iodide in ethanol containing anhydrous sodium acetate to give bis(methylthio) derivative (**7**) (Scheme 2). Refluxing of **1** with thiosemicarbazide in dry ethanol in the presence of piperidine as a catalyst afforded 5-amino-2,3-dihydro-9-methyl-7-phenyl-2-thioxo-7*H*-pyrazolo[4,3-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carbonitrile **(8)** (Scheme 3).

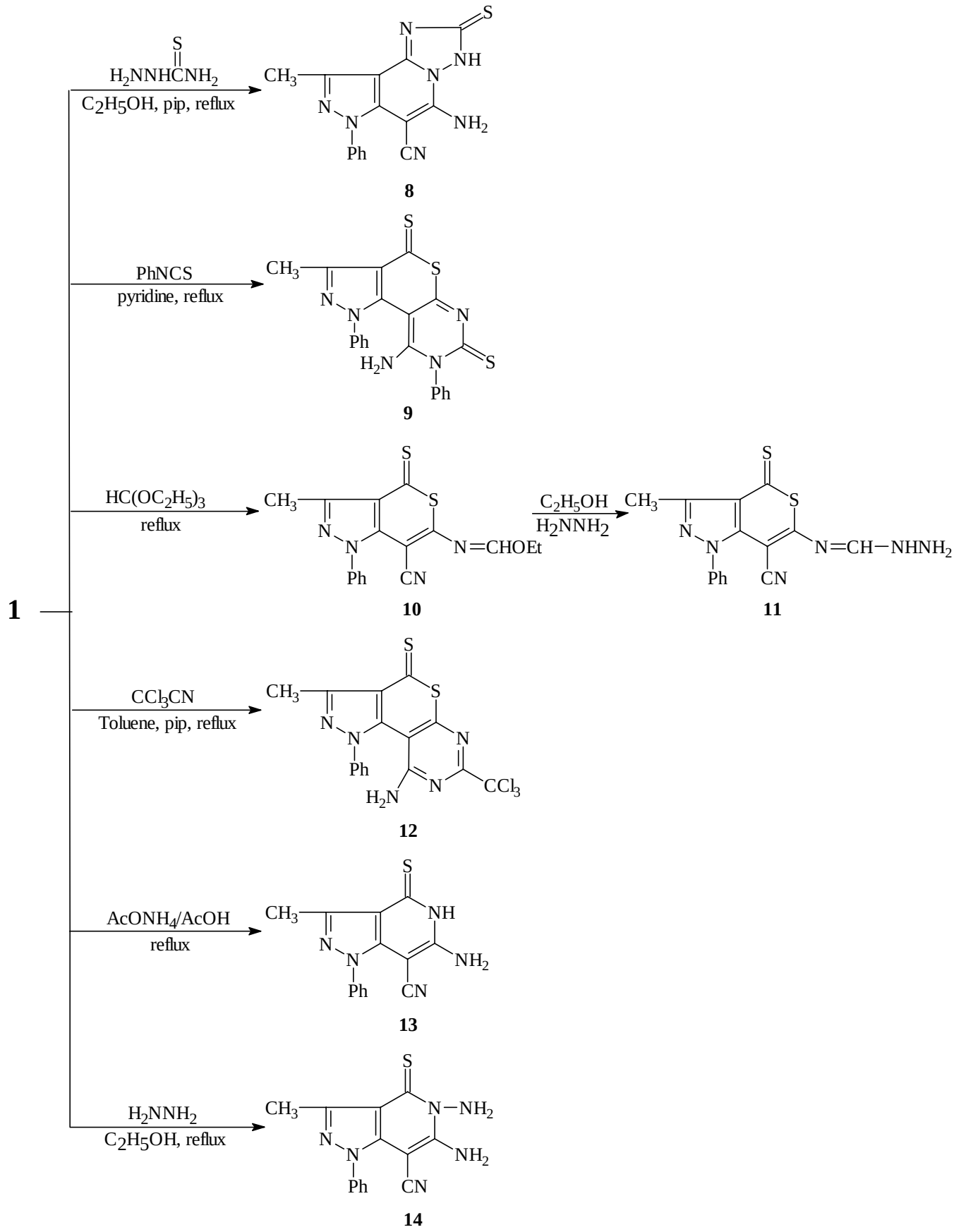
The reaction of **1** with PhNCS in refluxing pyridine produced 9-amino-1,4,7,8-tetrahydro-3-methyl-1,8-diphenylpyrazolo[3`,4`:4,5]thiopyrano[2,3-*d*]pyrimidine-4,7-dithione (**9**). Refluxing of **1** with triethyl orthoformate gave 6-ethoxymethyleneamino-1,4-dihydro-3-methyl-1-phenyl-4-thioxothiopyrano[4,3-*c*]-pyrazole-7-carbonitrile (**10**). Compound **(10)** further reacted with hydrazine hydrate to give 6-hydrazino-methyleneamino-1,4-dihydro-3-methyl-1-phenyl-4-thioxothiopyrano[4,3-*c*]pyrazole-7-carbonitrile (**11**). Reaction of trichloroacetonitrile with **1** in the presence of piperidine yields 9-amino-7-trichloromethyl-3-methyl-1-phenylpyrazolo[3`,4`:4,5]thiopyrano[2,3-*d*]pyrimidine-4(1*H*)-thione (**12**). Refluxing the thio-pyrano[4,3-*c*]pyrazole (**1**) with ammonium acetate in acetic acid produced 6-amino-4,5-dihydro-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[4,3-*c*]pyridine-7-carbonitrile(**13**). The reaction of **1** with hydrazine hydrate in boiling ethanol provided the corresponding 5,6-diamino-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[4,3-*c*]pyridine-7-carbonitrile (**14**) (Scheme 3).

The *o*-diamino compound **(14)** was used for building up a third angular heterocyclic ring through its interaction with some electrophilic reagents. Thus, reaction of **14** with *p*- substituted phenacyl bromides in refluxing ethanol furnished 8-aryl-1,4,6,7-tetrahydro-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[3`,4`:4,5]-pyrido[1,2-*b*][1,2,4]triazine-10-carbonitrile (**15a,b**).Treatment of **14** with the sodium salt of pyruvic acid in acetic acid gave1,4,8,9-tetrahydro-3,7-dimethyl-8-oxo-1-phenyl-4-thioxopyrazolo[3`,4`:4,5]pyrido[1,2-*b*]- [1,2,4]triazine-10-carbonitrile (**16**). Also, treatment of **14** with ethyl chloroacetate in boiling ethanol containing anhydrous sodium acetate gave 1,4,6,7,8,9-hexahydro-3-methyl-8-oxo-1-phenyl-4-thioxo-pyrazolo[3`,4`:4,5]pyrido[1,2-*b*][1,2,4]triazine-10-carbonitrile (**17**). The interaction of **14** with carbon disulfide in heating ethanolic potassium hydroxide solution produced 4,6,7,8-tetrahydro-3-methyl-1-phenyl-4,7-dithioxo-1*H*-pyrazolo[3,4-*d*][1,2,4]triazolo[1,5-*a*]pyridine-9-carbonitrile (**18**).

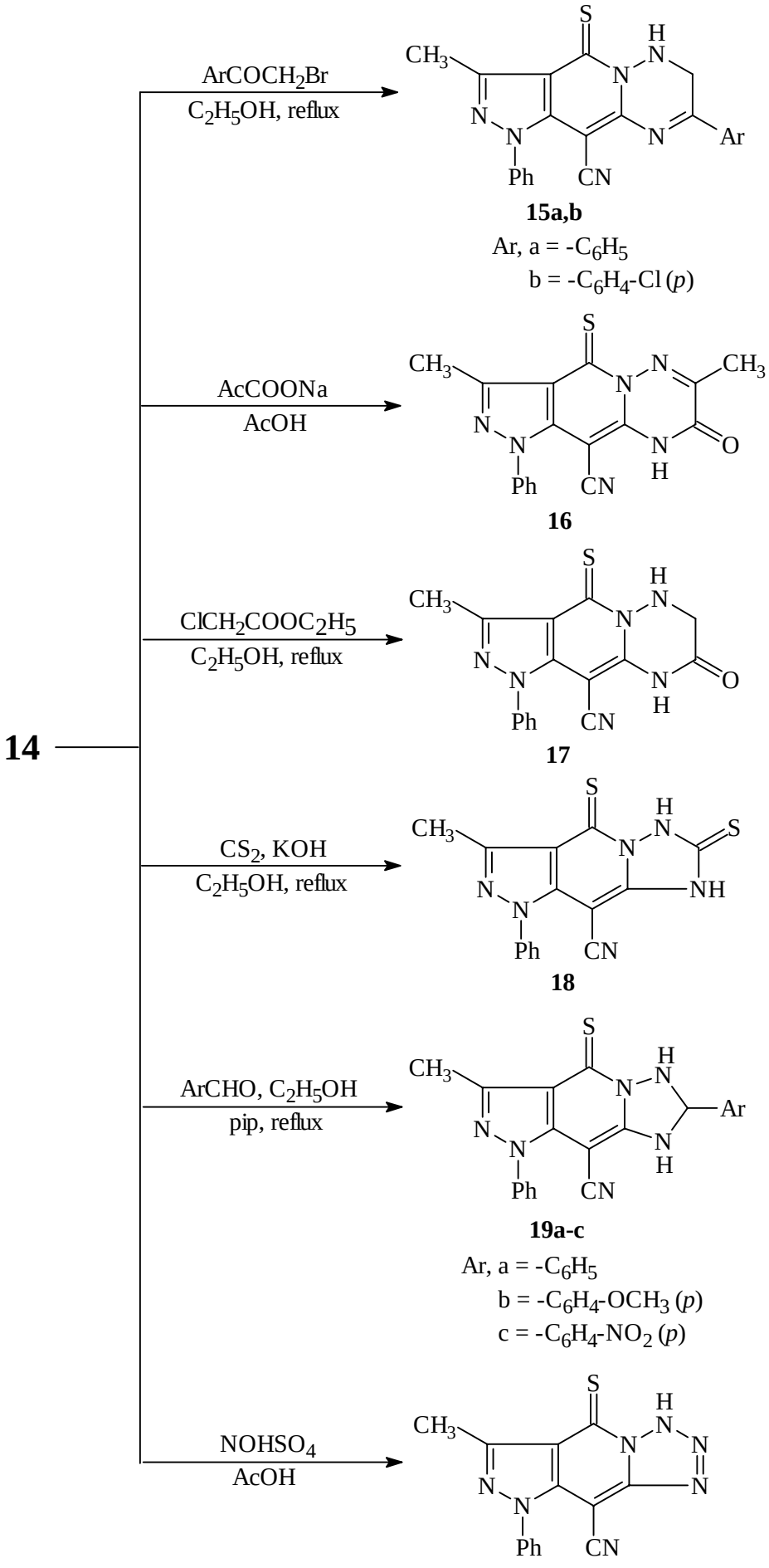
On the other hand, the reaction of compound (**14**) with aromatic aldehydes in dry ethanol in the presence of piperidine gave the 7-aryl-4,6,7,8-tetrahydro-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[3,4-*d*][1,2,4]-


1
Ac2O/pyridine
CH3
S
N
N
Ph
CN
NH—C—CH3
O
2
pyridine
reflux
Ac2O/pyridine
reflux
O
H
3
PhNH2
fusion
N—Ph
NH2
4
NaOH (10%)
reflux
NH
OH
5
CS2/pyridine
reflux
HS
SH
6
CH3I
CH3S
SCH3
7

Scheme 2


1
H2NNHCNH2
C2H5OH, pip, reflux
CH3
NH2
Ph
CN
8
PhNCS
pyridine, reflux
H2N
9
HC(OC2H5)3
reflux
N=CHOEt
10
C2H5OH
H2NNH2
N=CH−NHNH2
11
CCl3CN
Toluene, pip, reflux
CCl3
12
AcONH4/AcOH
reflux
13
H2NNH2
C2H5OH, reflux
N−NH2
14

Scheme 3


14
ArCOCH2Br
C2H5OH, reflux
15a,b
Ar, a = -C6H5
b = -C6H4-Cl (p)
AcCOONa
AcOH
16
ClCH2COOC2H5
C2H5OH, reflux
17
CS2, KOH
C2H5OH, reflux
18
ArCHO, C2H5OH
pip, reflux
19a-c
Ar, a = -C6H5
b = -C6H4-OCH3 (p)
c = -C6H4-NO2 (p)
NOHSO4
AcOH
20

Scheme 4

triazolo[1,5-*a*]pyridine-9-carbonitrile (**19a-c**). Treatment of **14** with nitrosyl sulfuric acid in cold acetic acid yielded 5,8-dihydro-6-methyl-8-phenyl-5-thioxo-1*H*-pyrido[3,4-*d*]tetrazolo[1,5-*a*]pyridine-9-carbonitrile (**20**) (Scheme 4).

EXPERIMENATAL

All melting points are uncorrected. The IR spectra were obtained on a Pye-Unicam SP 3-100 spectrophotometer using KBr disc technique (υ_{max} in cm^{-1}). ^{1}H-NMR spectra were recorded on a 90 MHz Varian NMR spectrometer in a suitable deuterated solvent using TMS as an internal standard, chemical shifts are given in δ scale. MS spectra were run on JEOL JMS 600 spectrometer. Yields, melting points and analytical data of all new compounds were given in Table 1.

6-Amino-1,4-dihYdro-3-methyl-1-phenyl-4-thioxothiopyrano[4,3-*c*]pyrazole-7-carbonitrile (1) .

To a mixture of malononitrile (6.6 g, 0.1 mol), 3-methyl-1-phenyl-2-pyrazolin-5-one (17.4 g, 0.1 mol), carbon disulfide (30 mL, 0.5 mol), methanol (30 mL), dimethylformamide (5 mL) was added triethylamine (6 mL, 0.043 mol) dropwise. The mixture was stirred at rt until a yellow product starts to precipitate. The reaction mixture was allowed to stand for 24 h. The solid product was then filtered off, washed with methanol and recrystallized from ethanol to give yellow crystals. IR (KBr): υ 3300, 3200 (NH_2), 2220 (CN), 1620 (C=C), 1505 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.43 (s, 3H, CH_3-Ar), 7.33-7.76 (m, 5H, Ph), 9.22 (s, 2H, NH_2); MS, m/z(%): 298 (M^+, 64.1), 282 (12.6), 251 (10.4), 223 (16.7), 207 (6.9), 195 (15.7), 149 (3.4), 131 (21.5), 115 (15.2), 111 (3.9), 193 (49.5), 77 (32.4), 57 (22.5), 41 (27.7), 29 (18.6).

N-(7-Cyano-1,4-dihydro-3-methyl-1-phenyl-4-thioxothiopyrano[4,3-*c*]pyrazol-6-yl)acetamide (2) .

A solution of **1** (2.98 g, 0.01 mol) in Ac_2O/pyridine mixture (30 mL, 2:1 v/v) was heated under reflux for 5 min, then cooled and poured into ice/water mixture. The precipitate thus formed was collected by filtration and washed several times with water, then recrystallized from ethanol to give buff crystals. IR (KBr): υ 3200 (NH), 2200 (CN), 1720 (C=O), 1520 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.22 (s, 3H, CH_3-CO-), 2.29 (s, 3H, CH_3-Ar), 7.43-7.87 (m, 5H, Ph), 10.72 (s, 1H, NH); MS, m/z(%): 340 (M^+, 10.4), 324 (100), 307 (24.6), 383 (4.5), 249.5 (1.7), 215.5 (6.4), 199.6 (8.8), 161.6 (2.5), 117.8 (1.7), 90.8 (7.9), 76.8 (15.1), 50.9 (4.0), 42.9 (6.1), 18 (2.0).

4,8-Dihydro-3,7-dimethyl-1-phenyl-4-thioxopyrazolo[3`,4`:4,5]thiopyrano[2,3-*d*]pyrimidin-9(1*H*)-one (3) .

A solution of **1** (2.98 g, 0.01 mol) in Ac_2O/pyridine mixture (30 mL, 2:1 v/v) was heated under reflux for 5 h, after cooling the reaction mixture, brownish red crystals were formed, filtered, and recrystallized from ethanol.IR (KBr): υ 3350 (NH),1680 (C=O),1520 (C=S);^{1}H-NMR (DMSO-d_6): δ 2.28 (s, 3H,CH_3 of pyrazolone), 2.69 (s, 3H, CH_3 attached to pyrimidine ring), 7.06-7.97 (m, 5H, Ph), 8.83 (s, 1H, NH); MS,

m/z(%): 340 (M^+, 14.4), 323 (100), 314 (2.0), 307 (24.6), 283 (4.5), 253 (1.3), 215.5 (6.4), 199.6 (8.8), 161.6 (2.5), 90.8 (7.9), 76.8 (15.1), 42.9 (6.1), 18 (2.0).

6-Amino-4,5-dihydro-3-methyl-1,5-diphenyl-4-thioxo-1*H*-pyrazolo[4,3-*c*]pyridine-7-carbonitrile (4).
A mixture of **1** (2.98 g, 0.0l mol) and aniline (0.93 g, 0.01 mol) was heated in an oil bath at 200°C for 2 h, on cooling the reaction mixture a solid mass was formed, which on trituration with ethanol gave deep red precipitate. The product was filtered, collected and recrystallized from dioxane to give red crystals.
IR (KBr): υ 3400, 3300 (NH_2), 2200 (CN), 1520 (C=S), ^{1}H-NMR (DMSO-d_6): δ 2.07 (s, 3H, CH_3-Ar), 6.57 (s, 2H, NH_2), 7.01-8.00 (m, 10H, arom-H); MS, m/z(%): 357 (M^+, 20.3), 346.8 (10.2), 323 (4.1), 306 (10.1), 291 (23.6), 274 (28.8), 263 (3.2), 239 (1.3), 198.4 (8.6), 173.5 (13.7), 118.7 (3.7), 92.7 (35.8), 90.7 (18.6), 76.7 (25.7), 65.8 (9.8), 50.8 (7.0), 43.8 (29.5), 31.9 (8.5), 17.9 (100).

An alternative route for the synthesis of compound (4) .
A mixture of 3-methyl-1-phenyl-2-pyrazolin-5-one (1.74 g, 0.01 mol), phenyl isothiocyanate (1.35 g, 0.01 mol), dimethylformamide (1 mL), malononitrile (0.66 g, 0.01 mol) and triethylamine (0.5 mL, 0.0036 mol) was heated under reflux on a water bath for 3 h. The rection mixture was poured into cold water, acidified with acetic acid, the precipitate thus formed was isolated and recrystallized from dioxane to give deep red crystals. The compound that formed by this method was identical in all aspects (mp, mixed mp and spectral analysis) with that obtained by the previous one.

4,5-Dihydro-6-hydroxy-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[4,3-*c*]pyridine-7-carbonitrile (5) .
A solution of **1** (1.49 g, 0.005 mol) in aqueous sodium hydroxide solution (30 mL, 0.075 mol, 10%) was heated under reflux for 1 h. The reaction mixture was cooled and acidified with conc. HCl. The precipitated compound thus obtained was filtered off, washed several times with water and recrystallized from ethanol to give brown crystals. IR (KBr): υ 3450 (OH), 3300 (NH), 2200 (CN), 1520 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.59 (s, 3H, CH_3-Ar), 6.05 (s, 1H, OH), 7.35-7.76 (m, 5H, Ph), 8.09 (s, 1H, NH); MS, m/z(%): 282 (M^+, 40.6), 273 (11.3), 256 (15.6), 239 (86.6), 222 (39.7), 199 (31.7), 173 (36.6), 131 (8.4), 105 (20.9), 104 (7.3), 91 (48.9), 77 (100), 66 (21.8), 51 (48.0), 42 (22.5), 18 (25.4).

7,9-Dimercapto-3-methyl-1-phenylpyrazolo[3`,4`:4,5]thiopyrano[2,3-*d*]pyrimidine-4(1*H*)-thione (6).
A mixture of **1** (2.98 g, 0.01 mol) and carbon disulfide (5 mL, 0.1 mol) in pyridine (30 mL) was heated on a water bath for 8 h. The solid product thus formed was filtered off while hot, washed several times with ethanol and recrystallized from ethanol to give orange crystals. IR (KBr): υ 3450 (SH), 1620 (C=N), 1520 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.22 (s, 3H, CH_3-Ar), 4.70 (s, 2H, two SH), 7.11-7.94 (m, 5H, Ph); MS, m/z(%): 374 (M^+, 74.6).

7,9-Bis(methylthio)-3-methyl-1-phenylpyrazolo[3`,4`:4,5]thiopyrano[2,3-*d*]pyrimidine-4(1*H*)-thione (7) .

A mixture of **6** (0.374 g, 0.001 mol) and methyl iodide (2 mL, 0.048 mol) in ethanol (30 mL) in presence of anhydrous sodium acetate (2 g) was refluxed for 2 h. The reaction mixture was concentrated, poured into cold water, the solid product was collected by filtration and recrystallized from ethanol to give red crystals. IR (KBr): 1620 (C=N), 1510 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.26 (s, 3H, CH_3-Ar), 2.68 (s, 6H, two SCH_3), 7.07-7.71 (m, 5H, arom-H); MS: m/z(%): 402 (M^+, 23.0).

5-Amino-2,3-dihydro-9-methyl-7-phenyl-2-thioxo-7*H*-pyrazolo[4,3-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carbonitrile (8) .

A mixture of **1** (2.98 g, 0.01 mol) and thiosemicarbazide (0.91 g, 0.01 mol) in ethanol (30 mL) in presence of a catalytic amount of piperidine was refluxed for 8 h. The reaction mixture was concentrated to one have its volume and left to cool, a yellow crystalline compound was formed, which was isolated and recrystallized from ethanol to give yellow crystals. IR (KBr): υ 3400, 3300, 3200 (NH_2, NH), 2200 (CN), 1640 (C=C), 1610 (C=N), 1520 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.45 (s, 3H, CH_3-Ar), 4.47 (s, 2H, NH_2), 6.90-7.55 (m, 5H, arom-H), 8.62 (s, 1H, NH); MS, m/z(%): 321 (M^+, 40.2) 305.7 (1.8), 278.7 (5.2), 255.8 (22.4), 235 (3.5), 210.9 (2.1), 184.9 (7.1), 148.8 (28.4), 136.9 (15.1), 110.9 (15.5), 96.9 (23.6), 80.9 (33.8), 78 (4.3), 69 (62.2), 57 (40.8), 43 (34.9), 28 (10.2), 18 (100).

9-Amino-1,4,7,8-tetrahydro-3-methyl-1,8-diphenylpyrazolo[3`,4`:4,5]thiopyrano[2,3-*d*]pyrimidine-4,7-dithione (9) .

To a solution of **1** (2.98 g, 0.01 mol) in pyridine (20 mL) it was added phenyl isothiocyanate (1.19 mL, 0.01 mol) and then the mixture was refluxed for 10 h. After cooling, the reaction mixture was poured into cold water and the solid product thus formed was filtered off, washed several times with water and recrystallized from aqueous ethanol to give deep red crystals. IR (KBr): υ 3400, 3300 (NH_2), 1510 (C=S); ^{1}H-NMR ($CDCl_3$): δ 2.31 (s, 3H, CH_3-Ar), 4.65 (s, 2H, NH_2), 7.26-7.89 (m, 10H, arom-H), MS, m/z(%): 433 (M^+, 10.5), 388.6 (10.1), 366.8 (24.6), 354.6 (17.5), 310 (23.1), 279 (7.2), 235.3 (11.3), 194.3 (20.1), 193.3 (100), 170.4 (3.1), 166.3 (12.4), 92.7 (95.9), 76.7 (54.1), 65.8 (20.9), 40.9 (14.2), 27.9 (41.9), 17.9 (72.6).

6-Ethoxymethyleneamino-1,4-dihydro-3-methyl-1-phenyl-4-thioxothiopyrano[4,3-*c*]pyrazole-7-carbonitrile (10) .

A solution of **1** (2.98 g, 0.01 mol) in triethyl orthoformate (20 mL, 0.12 mol) was heated under reflux for 5 h. After cooling the precipitaled red crystalline product was filtered off, washed with cold ethanol and recrystallized from ethanol to give red crystals. IR (KBr): 2200 (CN), 1580 (CH=N), 1500 (C=S); ^{1}H NMR (DMSO-d_6): δ 1.66 (t, 3H, O-CH_2CH_3), 2.07 (s, 3H, CH_3-Ar), 3.82 (q, 2H, O-CH_2CH_3), 7.41-7.83 (m, 5H, arom-H), 8.53 (s, 1H, N=CH); MS, m/z(%): 354 (M^+, 10.1).

6-Hydrazinomethyleneamino-1,4-dihydro-3-methyl-1-phenyl-4-thioxothiopyrano[4,3-*c*]pyrazole-7-carbonitrile (11) .

A mixture of **10** (0.7 g, 0.002 mol) and excess hydrazine hydrate (2 mL, 0.04 mol) in dry ethanol (30 mL) was stirred at rt for 15 min. The precipitated product was collected by filtration and recrystallized from ethanol to give pale yellow crystals. IR (KBr): υ 3400, 3300, 3150 (NH, NH_2), 2200 (CN), 1580 (N=CH), 1500 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.24 (s, 3H, CH_3-Ar), 3.54 (s, 2H, NH_2), 6.95 (s, 1H, N=CH), 7.07-7.85 (m, 5H, arom-H), 7.96 (s, 1H, NH); MS: m/z(%): 340 (M^+, 20.4).

9-Amino-7-trichloromethyl-3-methyl-1-phenylpyrazolo[3`,4`:4,5]thiopyrano[2,3-*d*]pyrimidine-4(1*H*)-thione (12) .

To a solution of **1** (2.98 g, 0.01 mol) in dry toluene (30 mL) was added trichloroacetonitrile (1.44 g, 0.01 mol) and a catalytic amount of piperidine. The reaction mixture was then refluxed for 3 h, after cooling an orange precipitate was formed, collected by filtration and recrystallized from toluene to give orange crystals. IR (KBr): υ 3300, 3100 (NH_2), 1580 (C=N), 1500 (C=S), 750 (C-Cl); ^{1}H-NMR (DMSO-d_6): δ 2.35 (s, 3H, CH_3-Ar), 7.10-7.85 (m, 5H, arom-H), 11.83 (s, 2H, NH_2); MS, m/z(%): 442.8 (M^+, 10.0).

6-Amino-4,5-dihydro-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[4,3-*c*]pyridine-7-carbonitrile (13) .

A mixture of **1** (2.98 g, 0.01 mol), acetic acid (5 mL) and ammonium acetate (5 g, 0.06 mol) was heated under reflux until a clear solution was obtained, then the mixture was heated for additional 4 h. After cooling, the reaction mixture was poured into cold water, the formed orange precipitate was filtered off and recrystallized from ethanol to give red crystals. IR (KBr): υ 3400, 3300, 3200 (NH_2, NH),2200 (CN), 1640 (C=C), 1580 (C=N), 1500 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.39 (s, 3H, CH_3-Ar), 6.86 (s, 2H, NH_2), 7.07-7.51 (m, 5H, arom-H), 10.77 (s, 1H, NH); MS, m/z(%): 281 (M^+, 15.9), 264 (100), 247.2 (15.7), 221.3 (10.8), 193.4 (3.3), 152.5 (2.1), 117.6 (4.5), 89.7 (3.1), 76.8 (36.0), 62.8 (3.6), 50.8 (13.1), 42.9 (17.7), 27.9 (10.5), 17.9 (16.5).

5,6-Diamino-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[4,3-*c*]pyridine-7-carbonitrile (14) .

A mixture of **1** (2.98 g, 0.01 mol) and 90% hydrazine hydrate (2 mL, 0.04 mol) in dry ethanol (30 mL) was refluxed until evolution of H_2S gas ceased. The reaction mixture was cooled and the solid product thus formed was collected and recrystallized from ethanol to produce yellow needles. IR (KBr): υ 3300, 3200 (NH_2), 2200 (C≡N), 1600 (C=C), 1580 (C=N), 1500 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.23 (s, 3H, CH_3-Ar), 3.47 (s, 2H, N-NH_2), 5.67 (s, 2H, NH_2), 7.07-7.88 (m, 5H, arom-H); MS, m/z(%): 296 (M^+, 10.4), 280 (2.8), 279 (14.9), 269.2 (6.8), 261.4 (9.6), 237.3 (2.8), 222.4 (44), 206.5 (11.8), 205.5 (100), 190.5 (30.3), 188.5 (24.5), 182.6 (8.8), 173.6 (7.0), 146.6 (6.0), 115.84 (5.5), 93.8 (12.2), 76.8 (14.5), 56.9 (14.5), 92.9 (39), 35.9 (3.8), 27.9 (23), 18 (56).

8-Aryl-1,4,6,7-tetrahydro-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[3`,4`:4,5]pyrido[1,2-*b*][1,2,4]-triazine-10-carbonitrile (15a,b) .

A mixture of **14** (2.96 g, 0.01 mol) and phenacyl bromide and its *p*-chloro derivative (0.01 mol) in ethanol (30 mL) was refluxed for 5 h. The reaction mixture was allowed to cool, the solid product was filtered off, and washed with 10% Na_2CO_3 solution. Compound **(15a)** was recrystallized from ethanol to give yellow crystals and **(15b)** was recrystallized from chloroform/pet ether (40-60°C) to give yellow crystals.

15a, IR (KBr): υ 3300 (NH), 2200 (CN), 1500 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.30 (s, 3H, CH_3-Ar), 3.00 (s, 2H, CH_2 of triazine), 7.24-7.94 (m, 10H, arom-H); MS, m/z(%): 396 (M^+, 3.3).

15b, IR (KBr): υ 3300 (NH), 2200 (CN), 1500 (C=S), 750 (C-Cl); ^{1}H-NMR (DMSO-d_6): δ 2.31 (s, 3H, CH_3-Ar), 3.00 (s, 2H, CH_2 of triazine), 7.18-7.88 (m, 10H, arom-H), 8.40 (s, 1H, NH); MS, m/z(%): 430.8 (M^+, 6.0), 414.9 (3.7), 329.9 (4.7), 292.9 (3.2), 280.9 (22.3), 280 (90.7), 250.9 (8.6), 222 (8.7), 182 (1.8), 85 (53), 84 (100), 77 (34), 56 (49.7), 42 (26.5), 28 (35.9), 18 (19.4).

1,4,8,9-Tetrahydro-3,7-dimethyl-8-oxo-1-phenyl-4-thioxopyrazolo[3`,4`:4,5]pyrido[1,2-*b*][1,2,4]-triazine-10-carbonitrile (16) .

To a solution of **14** (2.96 g, 0.01 mol) in acetic acid (10 mL), aqueous solution of sodium pyruvate (1.1 g , 0.01 mol) in 2 mL of H_2O was added. The mixture was stirred for 3 h, then refluxed for 1 h, and finally it was poured into cold water. The solid product was filtered off and recrystallized from aqueous ethanol to give yellow crystals. IR (KBr): υ 3300 (NH), 2200 (CN), 1710 (C=O), 1580 (C=N), 1500 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.07 (s, 3H, CH_3 of pyrazole ring), 2.43 (s, 3H, CH_3 of triazine ring), 4.00 (s, 1H, NH), 7.25-7.79 (m, 5H, arom-H); MS, m/z(%): 348 (M^+, 10.5), 323.4 (60.7), 322.4 (8.9), 307.3 (2.0), 282.2 (17.4), 281.2 (100), 252.3 (3.0), 224.2 (3.7), 198.2 (6.1), 189.2 (4.7), 167.2 (7.3), 148 (11.8), 133 (2.1), 118 (22.4), 105 (6.4), 91 (10.5), 77 (24.1), 67 (5.3), 51 (6.0), 44 (24.4), 31 (25.7), 28 (27.2), 18 (67.0).

1,4,6,7,8,9-Hexahydro-3-methyl-8-oxo-1-phenyl-4-thioxopyrazolo[3`,4`:4,5]pyrido[1,2-*b*][1,2,4]tri-azine-10-carbonitrile (17) .

To a solution of **14** (1.48 g, 0.005 mol) and ethyl chloroacetate (0.61 g, 0.005 mol) in ethanol (30 mL), sodium acetate (2 g) was added, the mixture was refluxed for 12 h, then allowed to cool. The precipitated product was collected by filtration, recrystallized from aqueous ethanol to give deep yellow crystals.

IR (KBr): υ 3300 (NH), 2200 (CN), 1720 (C=O), 1500 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.20 (s, 3H, CH_3-Ar), 3.79 (s, 2H, CH_2 of triazine ring), 5.88 (s, 1H, NH), 7.23-7.72 (m, 5H, arom-H); MS, m/z(%): 336 (M^+, 40).

4,6,7,8-Tetrahydro-3-methyl-1-phenyl-4,7-dithioxo-1*H*-pyrazolo[3,4-*d*][1,2,4]triazolo[1,5-*a*]pyridine-9-carbonitrile (18) .

To a mixture of **14** (2.96 g, 0.01 mol), and CS_2 (3.05 g, 2.4 mL, 0.04 mol) in ethanol (30 mL), potassium hydroxide solution (1 g in 2 mL H_2O) was added. The mixture was refluxed on a water bath for 5 h, then allowed to cool, and acidified by dil HCl (1:1, v/v). The solid product was collected and recrystallized from ethanol to give yellow crystals. IR (KBr): υ 3400 (NH), 2200 (CN), 1500 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.23 (s, 3H, CH_3-Ar), 7.24-7.94 (m, 5H, arom-H), 12.74 (s, 1H, NH), 13.41 (s, 1H, NH); MS, mz(%): 388 (M^+, 40.9), 281 (5.8), 257.7 (35.3), 255.7 (100), 223.8 (3.2), 191.8 (25.1), 161.8 (10.0), 199.8 (45.1), 127.9 (44.3), 95.9 (14.3), 77 (5.5), 73 (73.4), 63.9 (51.1), 44 (56.4), 18 (25.5).

7-Aryl-4,6,7,8-tetrahydro-3-methyl-1-phenyl-4-thioxo-1*H*-pyrazolo[3,4-*d*][1,2,4]triazolo[1,5-*a*]pyridine-9-carbonitrile (19a-c) .

***General procedure* .**

To a mixture of compound **(14)** (2.96 g, 0.01 mol) and aryl aldehyde (0.01 mol) in ethanol (30 mL), few drops of piperidine was added. The mixture was refluxed for 6 h, then allowed to cool. The solid product thus obtained was separated by filtration, washed by ethanol and recrystalized from the proper solvent.

19a, Yellow crystals from ethanol. IR (KBr): υ 3200 (NH), 2200 (CN), 1500 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.34 (s, 3H, CH_3-Ar), 7.24-7.94 (m, 10H, arom-H), 7.98 (s, 1H, CH of triazole ring), 8.13 (s, 1H, NH), 9.01 (s, 1H, NH); MS, m/z(%): 383 (M^+, 20.7), 368.6 (30), 368 (94.4), 353.7 (1.1), 290.7 (3.7), 279 (82.2), 264.7 (24.2), 258.8 (81.8), 250.7 (7.4), 234.7 (13.3), 214.8 (2.0), 180.8 (10.5), 156.8 (5.0), 127.9 (5.3), 114.9 (11.5), 90.9 (100), 76.9 (50.9), 64.9 (17.4), 93.9 (18.4), 28 (8.0), 18 (13.9).

19b, Yellow crystals from $CHCl_3$/pet. ether (40-60°C). IR (KBr): υ 3200 (NH), 2200 (CN), 1500 (C=S); ^{1}H-NMR ($CDCl_3$): δ 2.37 (s, 3H, CH_3-Ar), 3.83 (s, 3H, CH_3-O), 6.99-7.66 (m, 9H, arom-H), 7.84 (s, 1H, CH of triazole ring), 8.93 (s, 1H, NH), 9.87 (s, 1H, NH); MS: m/z(%): 414 (M^+, 26.0).

19c, Deep yellow crystals from ethanol. IR (KBr): υ 3250 (NH), 2200 (CN), 1520 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.30 (s, 3H, CH_3-Ar), 7.23-7.80 (m, 9H, arom-H), 7.94 (s, 1H, CH of triazole ring), 8.39 (s, 1H, NH), 9.23 (s, 1H, NH); MS: m/z(%): 429 (M^+, 19.4).

5,8-Dihydro-6-methyl-8-phenyl-5-thioxo-1*H*-pyrazolo[3,4-*d*]tetrazolo[1,5-*a*]pyridine-9-carbonitrile (20) .

To a solution of compound (**14**) (2.96 g, 0.01 mol) in acetic acid (15 mL), nitrosyl sulfuric acid (0.83 gm $NaNO_2$ in 1 mL of sulfuric acid, 0.012 mol) was added. The reaction mixture was stirred at rt until complete dissolution had occured. After standing for 5 h, the reaction mixture was poured into ice/water mixture. The resulting precipitate was filtered off, washed well with water and recrystallized from ethanol as orange

crystals. IR (KBr): υ 3200 (NH), 2200 (CN), 1620 (N=N), 1510 (C=S); ^{1}H-NMR (DMSO-d_6): δ 2.37 (s, 3H, CH_3-Ar), 3.75 (s, 1H, NH), 7.27-7.76 (m, 5H, arom-H); MS, m/z(%): 307 (M^+, 10.5).

Table 1 : Physical and Analytical Data of Compounds 1-20.

Compd No.	mp C°	Yield %	Molecular Formula	Analysis Calcd/Found				
				C%	H%	N%	S%	Cl%
1	315-316	10.5	$C_{14}H_{10}N_4S_2$	56.37 56.63	3.35 3.42	18.79 18.64	21.47 21.76	- -
2	274-275	92	$C_{16}H_{12}N_4OS_2$	56.47 56.69	3.52 3.62	16.47 16.26	18.82 19.13	- -
3	306-307	65	$C_{16}H_{12}N_4OS_2$	56.47 56.38	3.52 3.28	16.47 16.71	18.82 18.59	- -
4	201-202	71	$C_{20}H_{15}N_5S$	67.22 67.43	4.20 4.26	19.60 19.35	8.96 9.23	- -
5	281-282	90	$C_{14}H_{10}N_4OS$	59.57 59.64	3.54 3.33	19.85 19.91	11.34 11.28	- -
6	219-220	85	$C_{15}H_{10}N_4S_4$	48.12 47.86	2.67 2.55	14.97 15.22	34.22 34.36	- -
7	231-232	69	$C_{17}H_{14}N_4S_4$	50.79 50.55	3.48 3.64	13.93 14.13	31.84 31.65	- -
8	184-185	64	$C_{15}H_{11}N_7S$	56.07 56.33	3.42 3.57	30.52 30.35	9.96 9.85	- -
9	194-195	72	$C_{21}H_{15}N_5S_3$	58.19 58.07	3.46 3.33	16.16 16.31	22.17 22.37	- -
10	279-280	63	$C_{17}H_{14}N_4OS_2$	57.62 57.42	3.95 4.11	15.81 15.91	18.07 17.85	- -
11	237-238	77	$C_{15}H_{12}N_6S_2$	52.94 53.12	3.52 3.64	24.70 24.93	18.82 18.61	- -
12	244-245	61	$C_{16}H_{10}N_5Cl_3S_2$	43.38 43.29	2.25 2.43	15.81 15.64	14.46 14.69	24.06 24.28
13	323-324	64	$C_{14}H_{11}N_5S$	59.78 59.64	3.91 4.11	24.91 25.12	11.38 11.27	- -
14	> 350	72	$C_{14}H_{12}N_6S$	56.75 56.64	4.05 3.87	28.37 28.19	10.81 10.94	- -
15a	182-193	66	$C_{22}H_{16}N_6S$	66.66 66.47	4.04 3.88	21.21 21.33	8.08 7.86	- -
15_b	151-152	71	$C_{22}H_{15}N_6ClS$	61.32 61.49	3.48 3.62	19.51 19.75	7.43 7.27	8.24 8.12
16	174-175	67	$C_{17}H_{12}N_6OS$	58.62 58.82	3.44 3.27	24.13 24.31	9.19 9.34	- -

Table 1 : Continued.

Compd No.	mp C°	Yield %	Molecular Formula	Analysis Calcd./Found				
				C%	H%	N%	S%	Cl%
17	186-187	65	$C_{16}H_{12}N_6OS$	57.14 57.32	3.57 3.64	25.00 24.79	9.52 9.38	- -
18	158-159	73	$C_{15}H_{10}N_6S_2$	53.25 53.40	2.95 3.08	24.85 24.63	18.93 18.75	- -
19_a	194-195	64	$C_{21}H_{16}N_6S$	65.62 65.84	4.16 4.24	21.87 21.69	8.33 8.52	- -
19_b	180-181	75	$C_{22}H_{18}N_6OS$	63.76 63.57	4.34 4.18	20.28 20.52	7.72 7.83	- -
19_c	211-212	72	$C_{21}H_{15}N_7O_2S$	58.74 58.92	3.49 3.61	22.84 23.09	7.45 7.63	- -
20	196-197	62	$C_{14}H_9N_7S$	54.72 54.93	2.93 3.11	31.92 31.74	10.42 10.57	- -

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