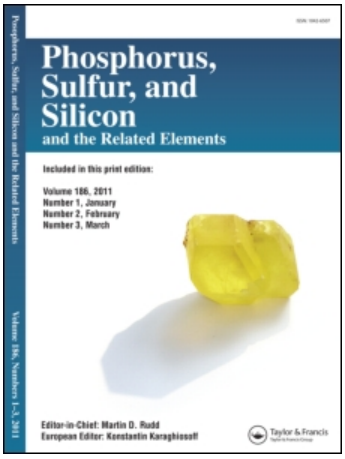



**Phosphorus, Sulfur, and Silicon and the Related Elements**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

# Phenylacetone as Building Blocks in Heterocyclic Synthesis: Synthesis of Polyfunctionally-Substituted Pyridines, and fused Pyridines

A. M. Hussein[a]; E. A. Ishak[a]; A. A. Atalla[a]; S. Abdel Hafiz[b]; M. H. Elnagdi[c]
[a] Department of Chemistry, Faculty of Science, Al Azhar University, Assiut, Egypt [b] Department of Chemistry, Faculty of Education, Suez Canal University, Al-Arish, Egypt [c] Department of Chemistry, Faculty of Science, Cairo University, Egypt

**To cite this Article** Hussein, A. M. , Ishak, E. A. , Atalla, A. A. , Hafiz, S. Abdel and Elnagdi, M. H.(2007) 'Phenylacetone as Building Blocks in Heterocyclic Synthesis: Synthesis of Polyfunctionally-Substituted Pyridines, and fused Pyridines', Phosphorus, Sulfur, and Silicon and the Related Elements, 182: 12, 2897 — 2917
**To link to this Article: DOI:** 10.1080/10426500701542858
**URL:** http://dx.doi.org/10.1080/10426500701542858

*Phosphorus, Sulfur, and Silicon*, 182:2897–2917, 2007

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500701542858



# Phenylacetone as Building Blocks in Heterocyclic Synthesis: Synthesis of Polyfunctionally-Substituted Pyridines, and fused Pyridines

**A. M. Hussein**
**E. A. Ishak**
**A. A. Atalla**
Department of Chemistry, Faculty of Science, Al Azhar University, Assiut, Egypt

**S. Abdel Hafiz**
Department of Chemistry, Faculty of Education, Suez Canal University, Al-Arish, Egypt

**M. H. Elnagdi**
Department of Chemistry, Faculty of Science, Cairo University, Egypt



*Many pyridinethiones are biologically active. In view of our interest in developing efficient syntheses of polyfunctionally substituted heteroaromatics utilizing the readily obtainable enaminone **3** as starting materials. So, treatment of enaminone **3** with cyanothioacetamide or cyanoacetamide afforded the pyridinethione **5a** and pyridone **5b.** compound **5a** reacted with α-halo- ketones in refluxing sodium ethoxide to give the thienopyridine derivatives **9a–e**. Compound **5a** reacted with methyl iodide to give 2-methylthiopyridine **10.** Condensation of pyridinethione **5a** with dimethylformamide-dimethylacetal gave the adduct **11** and with hydrazine hydrate afforded **12**. Compound **5a** reacted with arylidenemalonitrile to give styryl derivatives **14a–d**. Compound **14a–d** also prepared from the condensation of **5a** with the aromatic aldehydes under the same condition. Reflux of thienopyridine derivatives **9a–d** with triethylorthoformat, acetic anhydride, carbon disulfide and sodium nitrite to give compounds **19–23**, respectively. The aminopyrazole **12** reacted with dimethylaminopropiophenone hydrochloride **24** or enaminone **30** in refluxing DMF to yield compound **26a–d**. Treatment of **12** with **32** afforded **34**. Compound **34** can be also prepared from the reaction of **37** with aroylacetonitrile 31. Compound **12** reacted with DMF-DMA to give **37**, which reacted with compound **1** to give **38** prepared directly from reaction of **12** with enaminone **2**. Diazotization of **12** with nitrous acid followed by coupling with different active methylene reagents afforded the*

Received May 5, 2007; accepted June 5, 2007.
Address correspondence to M. Hussein, Department of Chemistry, Faculty of Science, Al Azhar University, Assiut Egypt. E-mail: abdelhaleemmh@yahoo.com

*pyridothienotriazines **42a,b**. Reaction of benzylideneacetophenone with **12** yielded the pyridopyrazolopyrimidine **44.** Also, compound **12** reacted directly with active methylene to give the pyridopyrazolopyrimidine derivatives **46a,b**.*

**Keywords** Pyrazolopyridines; pyridines; thienopyridines; Tria(Tetra)azafluorine

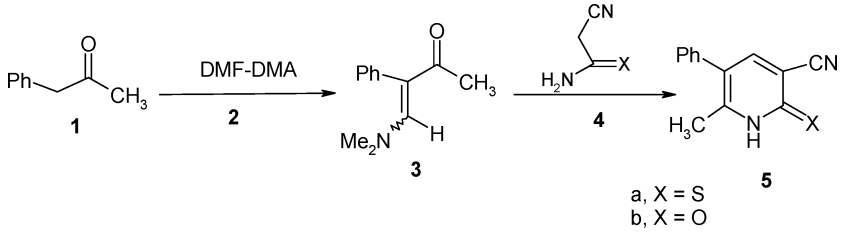


## INTRODUCTION

Certain functionally substituted pyridines are potent inhibitors of the human immunodeficiency virus,[1] most widely used calcium channel blockers.[2] They are also used for the treatment of congestive heart failure.[3,4] Also, many pyridinethiones are biologically active as bactericides[5,6] evaluated pharmacologically and it has been found that they show activity against diabetes mellitus, as analgesics and anti-inflammants.[7] In this concern, our interest is to develop efficient syntheses of polyfunctionally substituted heteroaromatics, utilizing the readily obtainable enaminone 1 as a starting material.[8–10] It is worthwhile to explore the potential utility of the syntheses of polyfunctionally substituted pyridines. We report herein synthesis and chemistry of some new derivatives of these compounds.

## RESULTS AND DISCUSSION

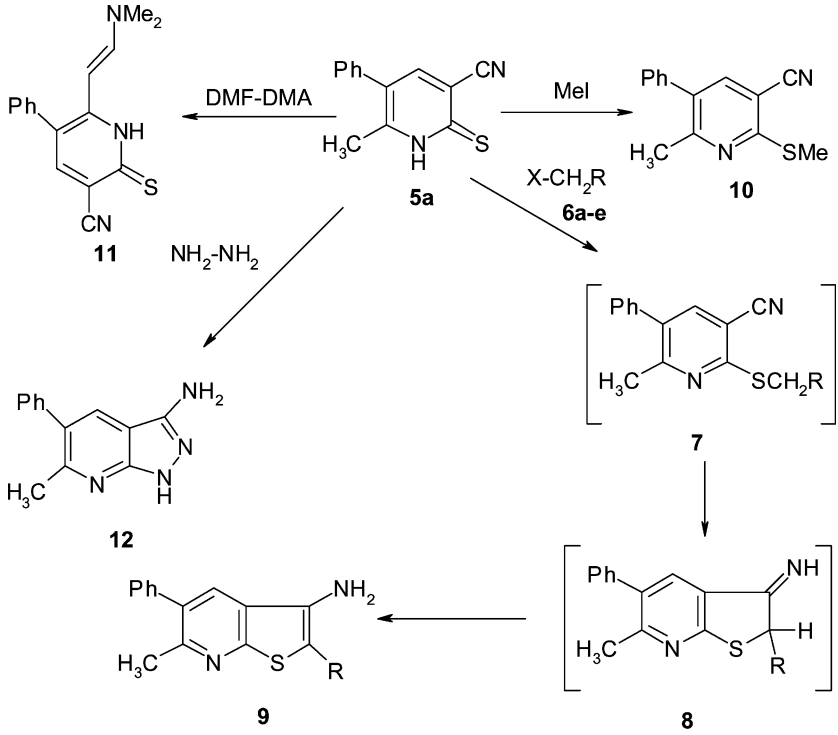
It has been found that phenylacetone **1** was condensed with N,N-dimethylformamide-dimethylacetal (DMF-DMA) in refluxing xylene to yield structure **3**. Compound **3** readily reacted with cyanothioacetamide **4** in refluxing ethanolic piperidine to yield 6-methyl-5-phenyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile **5a** and with cyanoacetamide to give pyridone 5b (Scheme 1).




**SCHEME 1**

With the aim of the preparing polyfunctionally substituted polycondensed pyridines, pyridinethione **5a** reacted with a variety of $\alpha$-haloketones **6a**–**e** in refluxing sodium ethoxide to give thienopyridine derivatives **9a**–**e** most likely via intermediacy of **7** and **8**. The structure

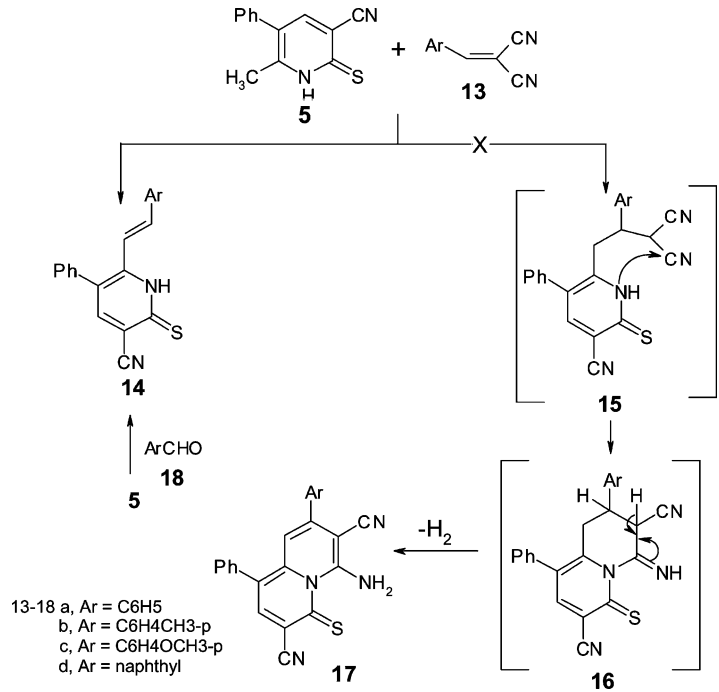
of this compound was confirmed with $^1$H NMR, which revealed the disappearance of methylene group and the appearance of $NH_2$ group. Alkylation of pyridinethione **5a** with methyl iodide gave **10** as a well-known reaction. Also, the reactivity of methyl function in **5a** toward DMF-DMA was also investigated. Thus, compound **5a** condensed with DMF-DMA to give the adduct 6-(2-dimethylamino-vinyl)-5-phenyl-2-thioxo-1,2-dihydro-pyridine-3-carbonitrile **11**. Condensation of pyridinethione **5a** with hydrazine hydrate afforded pyrazolopyridine **12**. Structure of compound **12** was confirmed by spectroscopic data. Thus, IR spectrum shows the appearance of $NH_2$group at $\upsilon$ $cm^{-1}$ 3433–3222. Also, the mass spectrum of **12** revealed a molecular ion peak at m/z = 224 ($M^+$) (Scheme 2).




**7-9** a, R = CONHPh
b, R = $CONHC_6H_4CH_3$-p
c, R = $CONHC_6H_4OCH_3$-p
d, R = $CONHC_6H_4COCH_3$-m
e, R = COPh

**SCHEME 2**

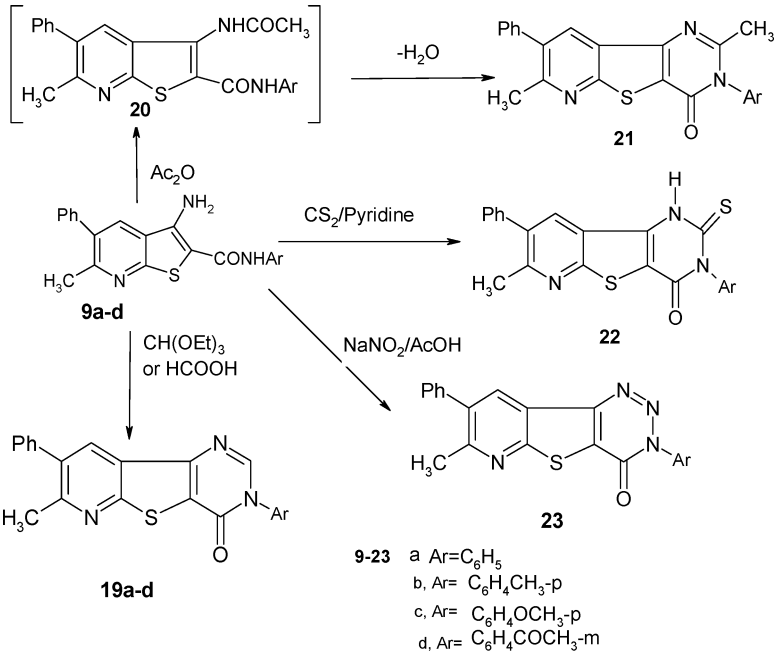
Attempted addition of arylidinemalononitriles **13a–d** to pyridinethione **5a** with the aim of preparing 4H-quinolizines **17** has resulted of formation of product condensation via malononitrile elimination to give styryl derivatives **14a–d**. This product also has been obtained by direct condensation of **5a** with aromatic aldehydes **18a–d**. Structure **14** has been assigned for this product based on $^1$H NMR that revealed existence tarns olefinic protons at $\delta$ 7.00 and 7.80 ppm.




**SCHEME 3**

Reactions of **9a–d** with triethylorthoformate in acetic acid gave the pyridothienopyrimidines **19a–d**. Also, compounds **9a–d** were acetylated with acetic anhydride to afford the pyridothienopyrimidines **21a–d**. The $^1$H NMR of compound **21a** shows the presence of two signals at $\delta$ 2.4 and 2.6 ppm corresponding to the methyl group of pyridine and pyrimidine moieties, respectively. Similarly, the reaction of **9a–d** with carbon disulfide in pyridine afforded **22a–d**. These compounds were confirmed by $^1$H NMR and elemental analysis. Also, the orthoamides have proved to be valuable for the synthesizing various heterocycles.

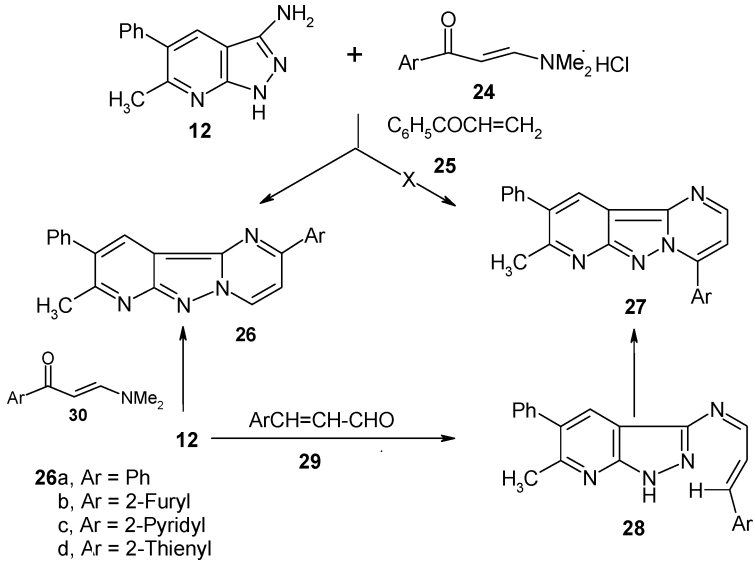
So, diazotization and self coupling of the aminoamides **9a–d** gave the pyidothienotriazine derivatives **23a–d** (Scheme 4).




**SCHEME 4**

In this part, we report synthesis of several new pyridopyrazolopyrimidines via reaction of aminopyrazolopyridine **12** with non-symmetrical double bond system and with different active methylene reagents. Thus, it has been found that the aminopyrazolopyridine **12** reacted with 3-dimethylaminopropiophenone hydrochloride **24** in refluxing DMF to yield product of condensation via elimination of water, dimethylamine hydrochloride and hydrogen. This product can thus be formulated as **26** or isomeric **27**. The structure **27** was ruled out on the bases of the preparation of **27** via condensation of **12** with cinnamaldehyde **29** and subsequent cyclization of resulting cinnamylidene derivative **28**. This product was proved to be different from product of reaction of **12** and **24**. Thus, structure **26** could be established for the later derivative. The formation of **26** was assumed to proceed by the addition of phenyl vinyl ketone **25**, resulting from elimination of dimethylamine hydrochloride from **24**, to ring nitrogen would afford intermediate which on cyclization via water elimination and aromatization would yield **26**. Compound **26** was also obtained on heating of aminopyrazole **12** with the enaminone

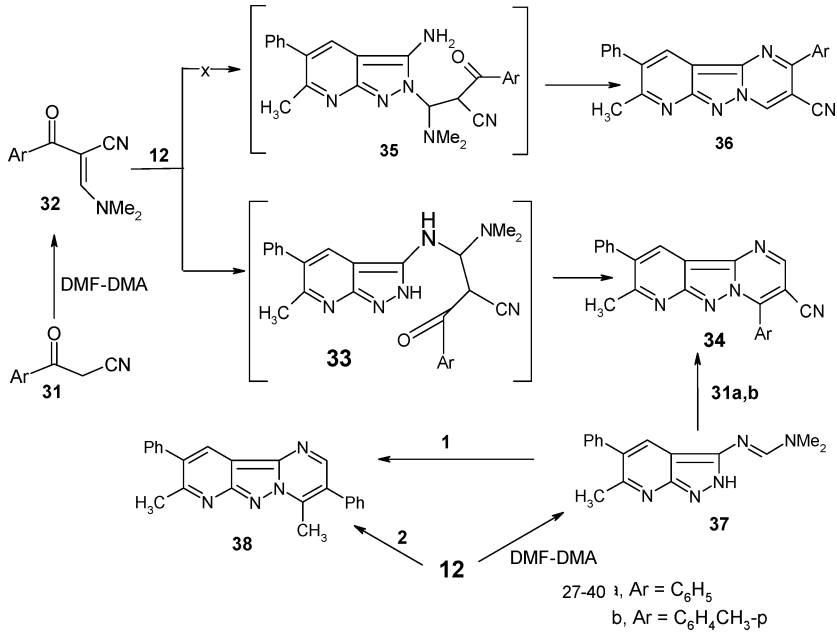
**30**. Moreover, this find parallelism to reported behavior of aminopyrazoles toward enaminone (Scheme 5).[11]




**SCHEME 5**

Treatment of 3-aryl-2-(*N*, *N*-dimethylamino)methylene-3-oxopropanenitriles **32a**,**b** prepared from the reaction of **31** with DMF-DMA according the literature[12] with the aminopyrazolopyridine **12** in ethanolic piperidine afforded products resulting the addition of both dimethylamine and water elimination. Several structures seemed possible for these products. Thus, initial formation of adduct **35** would lead to **36**, while the formation of adduct **33** can lead to **34**. Structure **36** was ruled out on the basis of $^1$H NMR spectra of the isolated product which revealed singlet signal in the range of $\delta$ 9.22 ppm which was assigned for the pyrimidine CH-4 in structure **34** and not CH-6 in structure **36.**[13] The latter structure was firmly established for the reaction product by the synthesis of the same product via condensing compound **12** with DMF-DMA and subsequent condensation of the so formed *N*, *N*-dimethyl-N′-(6-methyl-5-phenyl-2H-pyrazolo[3,4-b]pyridine-3-yl)-formamidine **37** with aroylacetonitrile **31** to afford products identical in all respects (m.p. and mixed m.p.) with those corresponding to compounds **34a**–**b**. Similarly, the aminopyrazole **12** reacted with enaminone **2** to yield the product of addition and both dimethylamine and water elimination **38**. This structure was firmly established for the reaction product by the synthesis of the same

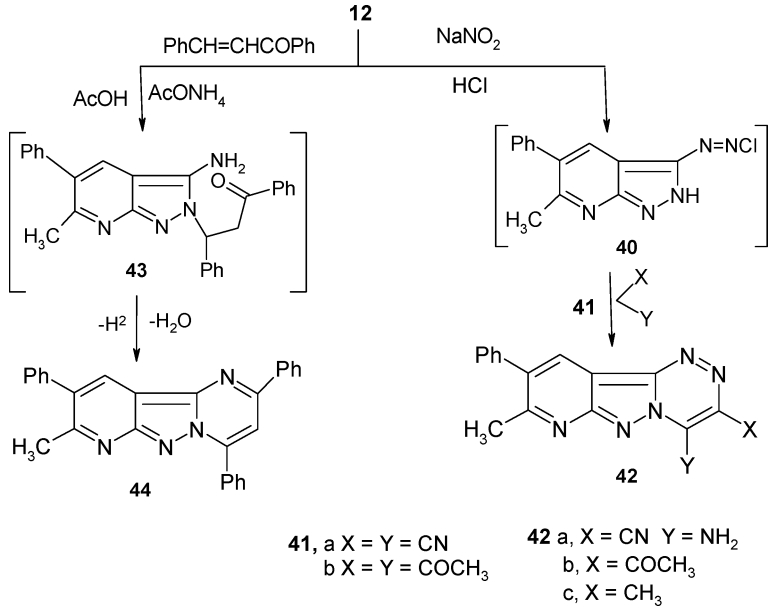
product via condensing compound **12** with DMF-DMA and subsequent condensation of the so formamidine **37** with phenylacetone **1** to afford product identical with corresponding to compound **38**. Also, structure of **38** was established with $^1$H NMR which revealed singlet signal at $\delta$ 2.32, 2.37 ppm for $2CH_3$, singlet at $\delta$ 7.73 ppm assigned for pyridine H-4 and singlet at $\delta$ 7.90 ppm assigned for pyrimidine H-4 (Scheme 6).[14]




**SCHEME 6**

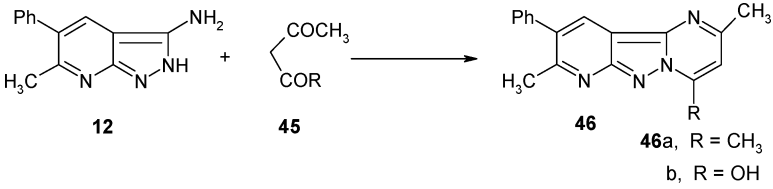
Diazotization and coupling of amino functional group in **12** by the action of sodium nitrite with different active methylene reagents **41a**,**b** namely malonoitrile and acetylacetone, gave the pyridopyrazolotriazine **42a**,**b.** Also, compound **12** reacted with benzylideneacetophenone to yield product condensation via elimination of water and hydrogen molecule. This was formulated as **44**. Formation of **44** is assumed to proceed via a Michael type addition on the most basic ring nitrogen in **12**, interamolecular cyclodehydration and spontaneous autoxidation under the reaction conditions. Similar autoxidations was reported previously.[15,16] It should be pointed out that the reaction of **12** with benzylideneacetophenone might involve the exocyclic amino group. However, the involvement of the endocyclic pyrazole-N was considered on the bases of literature reports which revealed that the ring

N in aminopyrazoles is the most reactive center in the molecule[17,18] (Scheme 7).




**SCHEME 7**

Also, aminopyrazole **12** reacted with active methylene reagents **45**, namely acetylacetone and ethyl acetoacetate to yield the pyridopyrazolopyrimidine derivatives **46a**,**b** (Scheme 8).[19]




**SCHEME 8**

## BIOLOGICAL ACTIVITIES

Most of the synthesized compounds have been tested against four different kinds of bacteria. The result of antimicrobial studies presented in Table I. It has been found that the prepared compound shows

**TABLE I Antimicrobial activity of some synthesized compounds and inhibition zones**

| No of compounds | A | B | C | D |
|---|---|---|---|---|
| 12 | ++ | ++++ | — | — |
| 19a | + | +++ | ++++ | ++ |
| 21b | ++++ | ++ | — | — |
| 22a | + | ++++ | ++ | +++ |
| 23d | ++++ | ++++ | +++ | ++ |
| 26a | +++ | + | ++++ | ++ |
| 26d | ++ | +++ | ++ | + |
| 34a | + | ++ | +++ | ++ |
| 46b | ++ | + | ++ | + |

Where: A = *Staphylococcus;* B = *Streptococcus;* C = *Esherichia coli*; D = *Nisseria sica;* — = Negative; + = Poor; ++ = Fair; +++ = Good; and ++++ = Very good.



antimicrobial activity against Staphylococcus aurous, Streptococcus mitor, Esherichia coli, and Nisseria sica.[20]

## CONCLUSION

The importance of the synthesized compounds as an intermediate for the synthesis of biologically active as antistaphylococcus, antisstreptococcus, antiesherichia coli, and antinNisseria sica.

## EXPERIMENTAL

All melting points are uncorrected and were determined on a Gellankap apparatus; IR (KBr) spectra were recorded on Schimadzu 470 spectrophotometer in potassium bromide discs; $^1$H NMR spectra were recorded on a Varian EM-390 (90 MHz) spectrophotometer using TMS as an internal standard; Mass spectrometer MS 30 (AEL) at 70 ev; Analytical data were obtained from the microanalytical data center at Cairo university.

### 4-Dimethylamino-3-phenyl-but-3-en-2-one (2)

A mixture of phenylacetone **1** (1.34 g, 10.0 mmol) and dimethylformamide-dimethylacetal (DMF-DMA) (1.19 g, 10.0 mmol) in dry xylene (30 ml), was refluxed for 6 h. After cooling, the solid product formed was collected by filtration and recrystallized from petroleum ether (40–60) as colorless crystals, yield 65%; m.p. 82°C. - IR (KBr) $\nu$ = 3049 (CH-aliphatic), 1673 (C = O) cm$^{-1}$; $^-$1H NMR (DMSO-d$_6$) $\delta$ = 2.05 (s, 6H, NMe$_2$), 2.49 (s, 3H, CH$_3$), 6.94–7.56 (m, 5H, Ar-H), 8.06 (s, 1H,

CH); $^{-}$MS (EI, 70 eV): m/z (%) = 189 [$M^+$]. Calcd for $C_{12}H_{15}NO$ (189.26): C 76.16; H 7.99; N 7.40. Found C 76.21; H 8.01; N 7.45.

## Preparation of Compounds 5a,b—General Procedure

A mixture of enaminone **2** (1.89 g, 10.0 mmol) and cyanothioacetamide or cyanoacetamide (10.0 mmol) in absolute ethanol (30 ml), was treated with few drops of piperidine and refluxed for 3 h. After cooling the solid product formed was collected by filtration and recrystallized from the proper solvent.

### *6-Methyl-5-phenyl-2-thioxo-1,2-dihydro-pyridine-3-carbonitrile (5a)*

Compound **5a** was obtained as yellow crystals from DMF/EtOH (1:3), yield 69%; m.p 265°C; IR (KBr) $\nu$ = 3225–3100 (NH), 2190 (CN), 1220 (C = S) $cm^{-1}$; $^1$H NMR (DMSO-$d_6$) $\delta$ = 2.38 (s, 3H, $CH_3$), 7.42–7.45 (m, 5H, Ar-H), 8.03 (s, 1H, pyridine-CH), 14.23 (s, 1H, NH); MS (EI,70 eV): m/z (%) = 226 [$M^+$]; $C_{13}H_{10}N_2S$ (226.30): Calcd for $C_{13}H_{10}N_2S$ (226.30): C, 69.00; H, 4.45; N, 12.38; S, 14.17. Found 69.12; H, 4.53; N, 12.42; S, 14.24.

### *6-Methyl-2-oxo-5-phenyl-1,2-dihydro-pyridine-3-carbonitrile (5b)*

Compound **5b** was obtained as white crystals from DMF/ethanol (1:3) as yield 67%; m.p. 210°C; IR (KBr) $\nu$ = 3332–3147 (NH), 2221 (CN), 1651 (C = O) $cm^{-1}$; $^1$H NMR (300 MHz, DMSO) $\delta$ = 2.26 (s, 3H, $CH_3$), 7.34–7.44 (m, 5H, Ar-H), 8.08 (s, 1H, pyridine-CH), 12.74 (s, 1H, NH); MS (EI,70 eV): m/z (%) = 210 [$M^+$]. Calcd for $^{-}C_{13}H_{10}N_2O$ (210.24): C, 74.27; H, 4.79; N, 13.32. Found C, 74.28; H, 4.82; N, 13.42.

## Preparation of Compounds (9a–e)— General Procedure

To a solution of compound **5a** (2.14 g, 10.0 mmol) in absolute ethanol (30 ml), the appropriate $\alpha$-halo compound (0.01 mol) was added. The reaction mixture was treated with a few drops of sodium ethoxide and refluxed for 3 h. The solid product so formed was filtered off and recrystallized from the appropriate solvent.

### *3-Amino-6-methyl-5-phenylthieno[2,3-b]pyridine-2-carboxylic Acid Phenylamide (9a)*

Compound **9a** was obtained as yellow crystals from DMF/ethanol in 52% yield; m.p. > 350°C; IR $\nu$ $cm^{-1}$ 3390–3225 ($NH_2$); 3225–3100 (NH); 1645 (CO); Calcd. for $C_{21}H_{17}N_3OS$: (359.45): C, 70.17; H, 4.77; N, 11.69: S, 8.92; Found: C, 70.20; H, 4.83; N, 11.71; S, 9.05.

### *3-Amino-6-methyl-5-phenylthieno[2,3-b]pyridine-2-carboxylic Acid P-Tolylamide (9b)*

This compound was obtained as yellow crystals from DMF/ethanol in 50% yield; m.p. 360°C; IR (KBr) $\nu$ $cm^{-1}$ 3390–3225 ($NH_2$); 3225–3100 (NH); 1651(CO); Calcd. for $C_{22}H_{19}N_3OS$ (373.48): C, 70.75; H, 5.13; N, 11.25; S, 8.58; Found: C, 70.82;H, 5.23; N, 11.34; S, 8.65.

### *3-Amino-6-methyl-5-phenylthieno[2,3-b]pyridine-2-carboxylic Acid (4-Methoxy-phenyl)amide (9c)*

This compound was obtained as yellow crystals from DMF/ethanol in 50% yield; m.p. >365°C; IR (KBr) $\nu$ $cm^{-1}$ 3390–3225 ($NH_2$); 3225–3100 (NH); 1649 (CO); $^1$H NMR (DMSO-$d_6$) $\delta = 2.50$ (s, 3H, $CH_3$); 3.76 (s, 3H, $OCH_3$); 6.89–6.93 (d, 2H, Ar-H); 7.35–7.51 (m, 5H, Ar-H); 7.56–7.60 (d, 2H, Ar-H); 8.37 (s, 1H, pyridine-CH); 9.36 (s, 1H, NH). Calcd. for $C_{22}H_{19}N_3O_2S$ (389.48):C, 67.85; H, 4.92; N, 10.79; S, 8.23. Found: C, 67.91; H, 5.08; N, 10.87; S, 8.36.

### *3-Amino-6-methyl-5-phenylthieno[2,3-b]pyridine-2-carboxylic Acid (3-Acetyl-phenyl)amide (9d)*

This compound was obtained as yellow crystals from DMF/ethanol in 50% yield; m.p. 348–350°C; IR (KBr) $\nu$ $cm^{-1}$ 3390–3225 ($NH_2$); 3225-3100 (NH); 1649 (CO); Calcd. for $C_{23}H_{19}N_3O_2S$ (401.49): C, 68.81; H, 4.77; N, 10.47; S, 7.99. Found: C, 68.96; H, 5.85; N, 10.44; S, 8.02.

### *3-Amino-6-methyl-5-phenylthieno[2,3-b]pyridin-2-yl)-phenyl-methanone(9e)*

This compound was obtained as yellow crystals from DMF/EtOH; yield 58%; m.p.178°C; IR (KBr) $\nu$ $cm^{-1}$ 3385–3016($NH_2$); 1674 (CO); $^1$H NMR (DMSO-$d_6$) $\delta = 2.38$ (s, 3H, $CH_3$); 7.44–7.83 (m, 12H, Ar-H and $NH_2$); 8.57 (s, 1H, pyridine-CH); Calcd. for $C_{21}H_{16}N_2OS$ (344.44): C, 73.23; H, 4.68; N, 8.13; S, 9.31. Found: C, 73.33; H, 4.75; N, 8.27; S, 9.49.

### *2-Methylthio-6-methyl-5-phenylpyridine-3-carbonitrile (10)*

To stirring suspension of compound **5a** (2.14 g, 10.0 mmol) in ethanol (50 ml) an aqueous sodium hydroxide (5 ml, 10 %) was added. The solution was stirred at room temperature for 10 min, then an excess of methyl iodide was added dropwise to a stirred solution. The stirring was continued for 15 min. The reaction mixture was poured into cold water and the solid product formed was collected by filtration, washed several times with water, dried and recrystallized from ethanol as yellow crystals; m.p. 289°C; IR (KBr) $\nu$ $cm^{-1}$ 2200 ( CN): $^1$H NMR (DMSO-$d_6$)

$\delta = 2.48$ (s, 3H, $CH_3$); 2.49 (s, 3H, $SCH_3$); 7.41–7.41 (m, 5H , Ar-H); 8.02 (s, 1H, pyridine-CH). Calcd. for $C_{14}H_{12}N_2S$ (240.33): C, 69.97; H, 5.03; N, 11.66; S, 13.34. Found: C, 70.03; H, 5.15; N, 11.72; S, 13.34.

### *6-(2-Dimethylamino-vinyl)-5-phenyl-thioxo-1,2-dihydro-pyridine-3-carbonitrile (11)*

A mixture of compound **5a** (2.14 g, 10.0 mmol) and (DMF-DMA) (2.26 g, 10.0 mmol) in xylene (50 ml), was refluxed for 12 h and left to stand. The solid product formed after dilution with ethanol was collected by filtration and recrystallized from ethanol in 43% yield; m.p. 355°C; IR (KBr) $\nu$ $cm^{-1}$ 2200 (CN). Calcd for $C_{16}H_{15}N_3S$ (281.38): C, 68.30; H, 5.37; N, 14.93; S, 11.40. Found: C, 68.43; H, 5.45; N, 14.99; S, 11.51.

### *6-Methyl-5-phenyl-2H-pyrazolo[3,4-b]pyridin-3-ylamine (12)*

A solution of compound **5a** (2.14 g, 10.0 mmol) in ethanol (10 ml) was treated with an excess of hydrazine hydrate (30 ml). The reaction mixture was heated under reflux for 12 h and left to stand. It was poured into ice cold water and acidified with HCl. The solid product so formed was obtained by filtration and recrystallized from DMF/EtOH (1:3) as green crystals; yield 52%; m.p. 245°C; IR (KBr) $\nu$ $cm^{-1}$ 3433–3122 ($NH_2$-NH); $^1H$ NMR (DMSO-$d_6$) $\delta = 2.35$ (s, 3H, $CH_3$); 7.30–7.83 (m, 7H, Ar-H and $NH_2$); 8.25 (1H, pyridine-CH); 11.65 ( s.1 H, NH); Ms: m/z = 224($M^+$); Calcd. for $C_{13}H_{12}N_4$ (224.27): C, 69.62; H, 5.39; N, 24.98. Found: C, 69.73; H, 5.45; N, 25.07.



## Preparation of Compounds (14a–d)—General Procedure

### *Method (A)*

To a solution of compound **5a** (2.14 g, 10.0 mmol) in dry dioxan, the appropriate of arylidenemalononitrile **13a–e** (10.0 mmol) was added. The reaction mixture was treated with few drops of piperidine and refluxed for 4 h, poured on ice cold water and acidified with dilute HCl. The solid product so formed was filtered off, washed with water several times, dried, and recrystallized from the proper solvent.

### *Method (B)*

To a solution of compound **5a** (2.14 g, 10.0 mmol) in dry dioxan (20 ml.) the appropriate of aromatic aldehyde **18a–d** (10.0 mmol) was added. The reaction mixture was treated with little amount of trimethylamine and refluxed for 4 h. The solid product so formed was collected by filtration, washed with water several times, dried, and recrystallized from the proper solvent.

### *5-Phenyl-6-styryl-2-thioxo-1,2-dihydro-pyridine-3-carbonitrile (14a)*

Compound **14a** was obtained as yellow crystals from ethanol in 50% yield; m.p. 189°C; IR (KBr) $\nu$ $cm^{-1}$ 3225–3100 (NH); 2200 (CN); Ms: m/z = 314 ($M^+$); Calcd. for $C_{20}H_{14}N_2S$ (314.41): C, 76.40; H, 4.49; N, 8.91; S, 10.20. Found: C, 76.51; H, 4.53; N, 9.05; S, 10.17.

### *5-Phenyl-2-thioxo-6-(2-p-tolyl-vinyl)-1,2-dihydro-pyridine-3-carbonitrile (14b)*

Compound **14b** was obtained as yellow crystals from ethanol in 50% yield; m.p. 99–101°C; IR (KBr) $\nu$ $cm^{-1}$ 3431 (NH); 2206 (CN); $^1H$ NMR (DM50-$d_6$) $\delta$ = 2.41 (s, 3H, $CH_3$); 7.00–7.10 (d, 1H, CH); 7.33–7.47 (m, 4H, Ar-H); 7.86–7.90 (d, 1H, CH); 8.49 (s, 1H, pyridine-H); 14.20 (s, 1 H, NH); Calcd. for $C_{21}H_{16}N_2$ S (328.44): C, 76.80; H, 4.91; N, 8.53; S, 9.76. Found: 76.93; H, 4.94; N, 9.76; S, 9.82.

### *6-[2- (4-Methoxy-phenyl)-vinyl]5-phenyl-2-thioxo-1,2-dihydro–pyridine-3-carbonitrile (14c)*

This compound was obtained as yellow crystals from ethanol in 50% yield; m.p. 105–107°C; IR (KBr) $\nu$ $cm^{-1}$ 3433 (NH); 2205 (CN); Calcd. for $C_{21}H_{16}N_2OS$ (344.44): C, 73.23; H, 4.68; N, 8.13; S, 9.31. Found: C, 73.35; H, 4.72; N, 8.25; S, 9.43.

### *6-[2-(Napthalen-1-yl)-vinyl]-5-phenyl-2-thioxo-1,2-dihydro-pyridine-carbonitrile (14d)*

Compound **14d** was obtained as yellow crystals from ethanol in 50% yield; m.p. 115°C; IR (KBr) $\nu$ $cm^{-1}$ 3348 (NH); 2212 (CN); $^1H$ NMR (DM50-$d_6$) $\delta$ = 7.01–7.10 (d, 1H, CH); 7.46–7.55 (m, 12H, Ar-H); 7.87–7.96 (d, 1H, CH); 8.08 ( s, 1H, pyridine-H); 14.00 ( s, 1 H, NH); Calcd. for $C_{24}H_{16}N_2S$ (364.47): C, 79.09; H, 4.42; N, 7.69; S, 8.80. Found: C, 79.10; H, 4.52; N, 7.70; S, 8.89.

## Preparation of Compound (19a-d)—General Procedure

To a solution of compound **9a–d** (10.0 mmol) in acetic acid (30 ml), triethylorthoformate (3 ml) was added. The reaction mixture was refluxed for 3 h, then poured onto water and left to stand. The solid product formed was filtered off and recrystallized from the appropriate solvent.

### *2-Methyl-3,7-diphenyl-7H-a-thia-1,5,7-triaza-fluoren-8-one (19a)*

Compound **19a** was obtained as white crystals from dioxan; yield 66%; m.p. > 350°C; IR (KBr) $\nu$ $cm^{-1}$ 1660 ( CO); Calcd. for $C_{22}H_{15}N_3OS$ (369.45): C, 71.52; H, 4.09; N, 11.37; S, 8.68. Found: C, 71.62; H, 4.14; N, 11.46; S, 8.78.

### *2-Methyl-3-phenyl-7-p-tolyl-7H-a-thia-1,5,7-triaaza-fluoren-8-one (19b)*

Compound **19b** was obtained as grey crystals from dioxan; yield 65%; m.p. > 350°C; IR (KBr) $\nu$ $cm^{-1}$ 1673 (CO); $^1$H NMR (DM50-$d_6$) $\delta$ = 2.41 (s, 3H, $CH_3$); 2.61(s, 3H, $CH_3$); 7.37–7.52 (m, 9H, Ar-H); 8.27 (s.1H, pyridine-CH); 8.56 (s, 1H, pyrimidine-CH); Calcd. for $C_{23}H_{17}N_3OS$ (383.48): C, 72.04; H, 4.47; N, 10.96; S; 8.36. Found: C, 72.52; H, 4.53; N, 11.01; S, 8.45.



### *7-(4-Methoxy-phenyl)-2-methyl-3-phenyl-7H-a-thia-1,5,7-triaaza-fluoren-8-one (19c)*

Compound **19c** was obtained as yellow crystals from dioxan; yield 60%; m.p. >350°C; IR (KBr) $\nu$ $cm^{-1}$ 1640 (CO); Calcd. for $C_{23}H_{17}N_3OS$ (399.47): C, 69.15; H, 4.29; N, 10.52; S, 8.03. Found: 69.22; H, 4.34; N, 10.66; S, 8.18.

### *7-(3-Acetyl-phenyl)-2-methyl-3-phenyl-7H-a-thia-1,5,7-triaaza-fluoren-8-one (19d)*

Compound **19d** was obtained as yellow crystals from dioxan; yield 60%; m.p. 358°C; IR (KBr) $\nu$ $cm^{-1}$ 1640 (CO); Calcd. for $C_{24}H_{17}N_3O_2S$ (411.49): C, 70.06; H, 4.16; N; 10.21; S, 7.79. Found: 70.11; H, 4.25; N, 10.35; S, 7.81.

## Preparation of Compounds (21a-d)—General Procedure

Compounds **21a**–**d** (2 g) were dissolved in acetic anhydride (20 ml) and refluxed for 3 h. The reaction mixture was poured onto ice water and left to stand for 12 h. The solid product formed was filtered off and recrystallized from the appropriate solvent.

### *2,6-Dimethyl-3,7-diphenyl-7H-a-thia-1,5,7-triaza-fluoren-8-one (21a)*

Compound **21a** was obtained as yellow crystals from DMF/dioxan; yield 50%; m.p. 355°C; IR (KBr) $\nu$ $cm^{-1}$ 3390–3225 ($NH_2$); 3225–3100 (NH); 2200 (CN); 1651 (CO); $^1$H NMR (DMSO-$d_6$) $\delta$ = 2.48 (s, 3H, $CH_3$);

2.62 (s, 3H, $CH_3$); 7.44–7.85 (m, 10H, Ar-H); 8.14 (s, 1H, pyridine-H); MS: m/z = 383 ($M^+$); Calcd. for $C_{23}H_{17}N_3OS$ (383.43): C, 72.04; H, 4.47; N, 10.96; S, 8.36. Found: C, 72.13; H, 4.51; N, 11.08; S, 8.47.

### *2,6-Dimethyl-3-phenyl-7-p-tolyl-7H-a-thia-1,5,7-triaza-fluoren-8-one (21b)*

Compound **21b** was obtained as yellow crystals from DMF/dioxan; yield 60; m.p. > 350°C; IR (KBr) $\nu$ $cm^{-1}$ 1673 (CO); Calcd. for $C_{24}H_{19}N_3OS$ (397.50): C, 72.52; H, 4.82; N, 10.57; S, 8.07. Found: C, 72.68; H, 4.96; N, 10.64; S, 8.12.

### *7-(4-Methoxy-phenyl)-2,6-dimethyl-3-phenyl-7H-a-thia-1,5,7-triaza-fluoren-8-one (21c)*

Compound **21c** was obtained as yellow crystals from DMF/dioxan (1:3) in yield 55%; m.p. 298°C; IR (KBr) $\nu$ $cm^{-1}$ 3430–3210 ($NH_2$); 2200 (CN); 1640 (CO); $^1$H NMR (DMSO-$d_6$) $\delta$ = 2.11 (s, 3H, $CH_3$); 2.49 (s, 3H, $CH_3$); 3.74 (s, 3H, $OCH_3$); 7.17–7.79 (m, 9H, Ar-H); 8.00 (s, 1H, pyridine-H); Calcd. for $C_{24}H_{19}N_3O_2S$ (413.50): C, 69.71; H, 4.63; N, 10.16; S, 7.75. Found: C, 69.82; H, 4.73; N, 10.21; S, 7.89.

### *7-(3-Acetyl-phenyl)-2,6-dimethyl-3-phenyl-7H-a-thia-1,5,7-triaza-fluoren-8-one (21d)*

Compound **21d** was obtained as yellow crystals from DMF/dioxan (1:3); yield 55%; m.p. 334°C; IR (KBr) $\nu$ $cm^{-1}$ 1665 (CO); 1640 (CO); Calcd. for $C_{25}H_{19}N_3O_2S$ (425.51): C, 70.57; H, 4.50; N, 9.88; S, 7.54. Found: C, 70.68; H, 4.66; N, 9.94; S, 7.62.



## Preparation of Compounds (22a–c)—General Procedure

A suspension of **9a**–**d** (10.0 mmol) in pyridine (50 ml) was treated with carbon disulfide (2 ml) and refluxed for 8 h. The reaction mixture was poured onto cold water and acidified with diluted HCl. The solid product so formed was collected by filtration and recrystallized from the appropriate solvent.

### *2-Methyl-3,7-diphenyl-6-thioxo-6,7-dihydro-5H-a-thia-1,5,7-triaza-fluoren-8-one (22a)*

Compound **22a** was obtained as yellow crystals from dioxan; yield 60%; m.p. 273°C; IR (KBr) $\nu$ $cm^{-1}$ 3425–3163 (NH); 1651 (CO); $^1$H NMR (DMSO-$d_6$) $\delta$ = 2.49 (s, 3H, $CH_3$), 7.04–7.98 (m,10H, Ar-H); 8.36 (s, 1H, pyridine-CH); 14.15 (s, 1H, NH); Calcd. for $C_{22}H_{15}N_3OS_2$ (401.51): C, 65.81; H, 3.77; N, 10.47; S, 15.97. Found: C, 66.31; H, 3.82; N, 10.54; S, 16.06.

### *2-Methyl-3,phenyl-6-thioxo-7-p-tolyl-6,7-dihydro-5H-a-thia-1,5,7-triaza-fluoren-8-one (22b)*

Compound **22b** was obtained as yellow crystals from dioxan; yield 65%; m.p. 277°C ; IR (KBr) $\nu$ $cm^{-1}$ 1650 (CO); Calcd. for $C_{23}H_{17}N_3OS_2$(415.54): C, 66.48; H, 4.12; N, 10.11; S, 15.43. Found: C, 66.52; H, 4.23; N, 10.22; S, 15.55.

### *7-(4-Methoxy-phenyl)-2-methyl-3-phenyl-6-thioxo-6,7-dihydro-5H-a-thia-1,5,7-triaza-fluoren-8-one (22c)*

Compound **22c** was obtained as yellow crystals from dioxan; yield 65%; m.p. 275°C; IR (KBr) $\nu$ $cm^{-1}$ 1650 (CO); Calcd. for $C_{23}H_{17}N_3O_2S_2$ (431.54): C, 64.02; H, 3.97, N, 9.74; S, 14.86. Found: C, 64.15; H, 4.07; N, 9.83; S, 14.93.

### *7-(3-Acetyl-phenyl)-2-methyl-3-phenyl-6-thioxo-6,7-dihydro-5H-a-thia-1,5,7-triaza-fluoren-8-one (22d)*

Compound **22d** was obtained as yellow crystals from dioxan; yield 65%; m.p. 282°C; IR (KBr) $\nu$ $cm^{-1}$ 1650 (CO); $^1$H NMR (DMSO-$d_6$) $\delta = 2.38$ (s, 3H, $CH_3$); 3.54 (s, 3H, $COCH_3$); 7.01–7.92 ( m, 9H, Ar-H); 8.03 (s, 1H, pyridine-CH) ); 14.02 (s, 1H, NH); Calcd. for $C_{24}H_{17}N_3O_2S_2$ (443.55): C, 64.99; H, 3.86, N, 9.47; S, 14.46. Found: C, 65.07; H, 3.98; N, 9.50; S, 14.53.



## Preparation of Compounds (23a–d)—General Procedure

To a cold solution of compound **9a**–**d** (10.0 mmol) in acetic acid (30 ml), a cold solution of sodium nitrite (1 g in 2 ml $H_2O$) was added dropwise with stirring. The stirring was continued for 1 h and left to stand at room temperature for 1 h. The solid precipitate formed was collected by filtration and recrystallized from the appropriate solvent.

### *2-Methyl-3,7-diphenyl-7H-a-thia-1,5,6,7-tetraaza-fluoren-8-one (23a)*

Compound **23a** was obtained as red crystals from dioxan; yield 60%; m.p. 260°C; IR (KBr) $\nu$ $cm^{-1}$ 3395–3250 ( $NH_2$), 3250–3170 (NH); 2200 (CN); 1656 (CO); Calcd. for $C_{21}H_{14}N_4OS$ (370.44): C, 68.09; H, 3.81; N, 15.12; S, 8.66. Found: C, 68.13; H, 3.97; N, 15.21; S, 8.79.

### *2-Methyl-3-phenyl-p-tolyl-7H-a-thia-1,5,6,7-tetraaza-fluoren-8-one (23b)*

Compound **23b** was obtained as grey crystals from dioxan; yield 54%; m.p. >350°C; IR (KBr) $\nu$ $cm^{-1}$ 1667 (CO); $^1$H NMR (DMSO-$d_6$) $\delta = 2.49$ (s, 3H, $CH_3$); 2.65 (s, 3H, $CH_3$); 7.38–7.98 (m, 9H, Ar-H), 8.38 (s, 1H,

pyridine-CH); Calcd. for $C_{22}H_{16}N_4OS$ (384.46): C, 68.73; H, 4.19; N, 14.57; S, 8.34. Found: C, 68.86; H, 4.24; N, 14.65; S, 8.42.

### *7-(4-Methoxy-phenyl)-2-methyl-3-phenyl-7H-a-thia-1,5,6,7-tetraaza-fluoren-8-one (23c)*

Compound **23c** was obtained as white crystals from dioxan; yield 66%; m.p. > 350°C; IR (KBr) $\nu$ $cm^{-1}$ 1660 (CO); Calcd. for $C_{22}H_{16}N_4O_2S$ (400.46): C, 65.99; H, 4.03; N, 13.99; S, 8.01. Found: C, 68.15; H, 4.12; N, 14.13; S, 8.12.

### *7-(3-Acetyl-phenyl)-2-methyl-3-phenyl-7H-a-thia-1,5,6,7-tetraaza-fluoren-8-one (23d)*

Compound **23d** was obtained as white crystals from dioxan; yield 66%; m.p. > 350°C; IR (KBr) $\nu$ $cm^{-1}$ 1660 (CO); $^1$H NMR (DMSO-$d_6$) $\delta = 2.46$ (s, 3H, $CH_3$), 2.59 (s, 3H, $COCH_3$), 7.23–7.60 (m, 9H, Ar-H); 8.30 (s, 1H, pyridine-CH); Calcd. for $C_{23}H_{16}N_4O_2S$ (412.74): C, 66.98; H, 3.91; N, 13.58; S, 7.77. Found: C, 67.03; H, 3.99; N, 13.66; S, 7.87.

## Preparation of Compounds (26a–d)—General Procedure

To a solution of compound **12** (2.12 g, 10.0 mmol) in DMF (50 ml) dimthylaminopropiophenone hydrochloride **24a–c** (10.0 mmol) was added. The reaction mixture was refluxed for 3 h, and the solvent was concentrated until third volume under vacuo, then pour into ice-cold water. The solid product was obtained by filtration and recrystallized from the proper solvent.

### *2-Methyl-3,6-diphenyl-1,5,8a,9-tetraaza-fluorene (26a)*

This compound was obtained as yellow crystals from dioxane; yield 56%; m.p. 158°C; IR (KBr) $\nu$ $cm^{-1}$ 2995 (CH-aliphatic); $^1$H NMR (DMSO-$d_6$) $\delta = 2.46$ (s, 3H, $CH_3$); 7.45–7.90 (m,10H, Ar-H); 8.70 (s, 1H, pyridine-CH); Calcd. for $C_{22}H_{16}N_4$(336.40): C, 78.55; H, 4.79; N, 16.65. Found: C, 78.65; H, 4.83; N, 16.71.

### *6-(Furan-2-yl)-2-Methyl-3-phenyl-1,5,8a,9-tetraaza-flourene (26b)*

It was obtained as deep blue crystals from dioxan; yield 60%; m.p. 115°C; IR (KBr) $\nu$ $cm^{-1}$ 2905 (CH-aliphatic); Calcd. for $C_{20}H_{14}N_4O$ (326.36): C, 73.61; H, 4.32; N, 17.17. Found: C, 73.74; H; 4.43; N, 17.21.

### *2-Methyl-3-phenyl-6-(1H-pyrrol-2-yl)-1,5,8a,9-tetraaza-fluorene (26c)*

It was obtained as brown crystals from dioxane; yield 56%; m.p. 162°C; IR (KBr) $\nu$ $cm^{-1}$ 2995 (CH-aliphatic); Calcd. for

$C_{20}H_{15}N_5$(325.38): C, 73.83; H, 4.65; N, 21.52. Found C, 73.94; H, 4.75; N, 21.66.

### *2-Methyl-3-phenyl-6-(thiophene-2-yl)-1,5,8a,9-tetraaza-fluorene (26d)*

It was obtained as green crystals; yield 57%; m.p. 166°C; IR (KBr) $\nu$ $cm^{-1}$ 2995 (CH-aliphatic); $^1$H NMR (DMSO-$d_6$) $\delta = 2.48$ (s, 3H, $CH_3$); 7.37–7.98 (m, 10H, Ar-H and thiophene-H); 8.31 (s.1H, pyridine-CH); Calcd. for $C_{20}H_{14}N_4S$ (342.43): C, 70.15; H, 4.12; N, 16.36; S, 9.63. Found: C, 70.26; H, 4.23. N, 16.45; S, 9.47.

### *N,N-Dimethyl-N′-(6-methyl-5-phenyl-2H-pyrazolo[3,4-b]pyridin-3-yl)-formamidine (37)*

Dimethylformamide-dimethylacetyl (DMF-DMA) (119 g, 10.0 mmol) was added to a solution of compound **12** (2.12 g, 10.0 mmol) in dioxan (50 ml), and the reaction mixture was refluxed for 6 h. The removal of solvent under reduced pressure yielded the crude product which was crystallized from ethanol as orange crystals; yield 43%; m.p. 185°C; IR (KBr) $\nu$ $cm^{-1}$ 3363–3193 (NH);[1] H NMR (DMSO-$d_6$) $\delta = 1.90$ (s, 3H, $CH_3$); 2.08 (s, 6H, $NMe_2$); 7.41–7.70 (m, 5H, Ar-H ); 8.15 (s, 1H, pyridine-CH); 10.95 (s, 1H, N = CH); 12.95 (s, 1H, NH); Calcd. for $C_{16}H_{17}N_5$ (279.35): C, 68.80; H, 6.13; N, 25.07. Found C, 68.92; H, 6.26; N, 25.18.



## General Preparation of Compounds (34a,b)

### *Method (A)*

To a solution of **37** (2.79 g, 10.0 mmol) in DMF (30 ml), phenacyl cyanide or *p*-methylphenacyl cyanide (10.0 mmole) were added. The reaction mixture was refluxed for 3 h, and the solvent was removed under vacuo the solid product so formed was recrystallized from the proper solvent.

### *Method (B)*

To a solution of **32** (2.0 g, 10.0 mmol) in absolute ethanol (20 ml) in presence a few drops of piperidine, the aminopyrazolopyridine **12** (2.12 g, 10.0 mmol) was added. The reaction mixture was refluxed for 3 hand then left to cool. After cooling the solid product so formed was collected by filtration and recrystallized from the proper solvent.

### *2-Methyl-3,8-diphenyl-1,5,8a,9-tetraaz-flourene-7-carbonitrile (34a)*

It was obtained from DMF/ethanol (1:3) as yellow crystals; yield 55%; m.p. 305°C; IR (KBr) $\nu$ $cm^{-1}$ 2229 (CN); $^1$H NMR (DMSO-$d_6$) $\delta = 2.60$

(s, 3H, $CH_3$); 7.44–7.90 (m, 5H, Ar-H); 8.47 (s, 1H, pyridine-CH); 9.22 (s, 1H, pyrimdine- CH); Calcd. for $C_{23}H_{15}N_5$ (361.41): C, 76.44; H, 4.18; N, 19.38. Found C, 76.56; H, 4.21; N, 19.45.

### *2-Methyl-3-phenyl-8-p-tolyl-1,5,8a,9 tetraaza-fluorene-7-carbonitrile (34b)*

It was obtained as brown crystals from DMF/ethanol; yield 73%; m.p. 213°C; IR (KBr) $\nu$ $cm^{-1}$ 2129 (CN); Calcd. for $C_{24}H_{17}N_5$ (375.44): C, 76.78; H, 4.56; N, 18.65. Found: C, 76.83; H, 4.67; N, 18.76.

## 2,8-Dimethyl-3,7-diphenyl-1,5,8a,9-tetraaza-fluorene (38)

### *Method (A)*

A mixture of enaminone **3** (1.91 g, 10.0 mmol) and aminopyrazole **12** (2.12 g, 10.0 mmol) in absolute ethanol (30 ml), was treated with a few drops of piperidine and refluxed for 3 h. After cooling, the solid product formed was collected by filtration and recrystallized from DMF/ethanol (1:3) as green crystals; yield 43%; m.p. 185–187°C; IR (KBr) $\nu$ $cm^{-1}$ 2995 (CH-aliphatic). $^1$H NMR (DMSO-$d_6$) $\delta = 2.32$ (s, 3H, $CH_3$); 2.37 (s, 3H, $CH_3$); 7.05–7.68 (m, 5H, Ar-H ); 7.73 (s, 1H, Pyridine-CH); 7.90 (s, 1H, pyrimidine-CH); Calcd. for $C_{23}H_{18}N_4$ (350.43): C, 78.83; H, 5.18; N, 15.99. Found: C, 78.92; H, 5.24; N, 16.06.

### *Method (B)*

A mixture of phenylacetone **1** (1.34 g, 10.0 mmol) and compound **12** (2.12 g, 10.0 mmol) in absolute ethanol (30 ml), was treated with a few drops of piperidine and refluxed for 3 h. After cooling, the solid product formed was collected by filtration and recrystallized from DMF/ethanol (1:3).



## General Procedure of Triazine (42a–b)

To a stirred cold solution of diazonium chloride **40** (10.0 mmol, prepared by treating of aminopyrazole **12** (2.12 g, 10.0 mmol) with sodium nitrite (10.0 mmol) in HCl in ethanol (30 ml) and catalytic of sodium acetate, the active methylene reagents was added dropwise after the complete addition. The stirring was continuous for two hrs.. The sold product so formed was filtered of, washed with water several times, dried and recrystallized from the proper solvent.

### *8-Amino-2-methyl-3-phenyl-1,5,6,8a,9-pentaaza-fluorene-7-carbonitrile (42a)*

It was obtained as brown crystals from DMF/dioxan; yield 73%; m.p.177°C; IR (KBr) $\nu$ $cm^{-1}$ 2133 (CN); $^1$H NMR (DMSO-$d_6$) $\delta = 2.48$

(s, 3H, $CH_3$); 3.86 (s, 2H, $NH_2$); 7.17–7.61 (m, 5H, Ar-H); 8.34 (s, 1H,pyridine-CH); Calcd. for $C_{16}H_{11}N_7$ (301.31): C, 63.78; H, 3.68; N, 32.54. Found: C, 63.83; H, 3.75; N, 32.67.

### *1-(2,8-Dimethyl-3-phenyl-1,5,6,8a,9,-pentaaza-fluoren-7-yl)-ethanone (42b)*

It was obtained as red crystals from DMF/dioxan; yield 73 %; m.p. 166°C; IR (KBr) $\nu$ $cm^{-1}$ 1674 (CO); Calcd. for $C_{18}H_{15}N_5O$ (317.35): C, 68.13; H, 4.76; N, 22.07. Found: C, 68.21; H, 4.87; N, 22.10.

## 2-Methyl-3,6,8-triphenyl-1,5,8a,9-tetraaza-fluorene (44)

To a solution of compound **12** (2.12 g, 10.0 mmol) in acetic acid (20 ml) containing 2 g of ammonium acetate, 2-benezyle; deneacetophenone (2.08 g, 10.0 mmol) was added. The reaction mixture was refluxed for 3 h, then poured into ice-cold water. The solid product formed was filtered off and recrystallized from acetic acid as yellow crystals; yield 65%; m.p. 211°C; IR (KBr) $\nu$ $cm^{-1}$ 2995 (CH-aliphatic); $^1$H NMR (DMSO-$d_6$) $\delta = 2.48$ (s, 3H, $CH_3$); 7.04–7.71 (m, 15H, Ar-H); 8.36 (s.1H, pyridine-CH); 9.36 (s,1H, pyrimidine-CH); 14.15 (br, 1H, OH); Calcd. for $C_{28}H_{20}N_4$ (412.50): C, 81.53; H, 4.89; N, 13.58. Found C, 81.61; H, 4.93; N, 13.64.



## General Preparation of Compounds (46a,b)

A mixture of compound **12** (2.12 g, 10.0mmol) and acteylaceton or ethyl acetoacetate (10.0 mmol) in DMF (30 ml), a few drops of piperidine was added. The reaction mixture was refluxed the 3 h. After cooling, the solid product formed was collected by filtration and recrystallized from DMF/EtOH (1:3).

### *2,6,8-Trimethyl-3-phenyl-1,5,8a,9-tetraaza-fluorene (46a)*

It was obtained as red crystals; yield 73%; m.p. 176°C; IR (KBr) $\nu$ $cm^{-1}$ 2905 (CH-aliphatic); $^1$H NMR (DMSO-$d_6$) $\delta = 2.23$ (s, 3H, $CH_3$); 2.25 (s, 3H, $CH_3$); 2.38 (s, 3H, $CH_3$); 7.45–7.50 (m, 5H, Ar-H); 8.14 (s, 1H, pyridine-CH); 8.16 (s, 1H, pyrimidine-CH); Calcd. for $C_{18}H_{16}N_4$ (288.36): C, 74.98; H, 5.59; N, 19.43. Found: C, 75.03; H, 5.62; N, 19.51.

### *2,6,-Dimethyl-3-phenyl-1,5,8a,9-tetraaza-fluoren-8-ol (46b)*

It was obtained as brown crystals; yield 71%; m.p. 135°C; IR (KBr) $\nu$ $cm^{-1}$ 2905 (CH-aliphatic); $^1$H NMR (DMSO-$d_6$) $\delta = 2.33$ (s, 3H, $CH_3$); 2.45 (s, 3H, $CH_3$); 7.37–7.51 (m, 5H, Ar-H); 7.74 (s, 1H, pyridine-CH);

8.68 (s, 1H, pyrimdine-CH); Calcd. for $C_{17}H_{14}N_4$ O (290.33): C, 70.33; H, 4.86; N, 19.30. Found: C, 70.46; H, 4.94; N, 19.45.

## REFERENCES


[1] R. Troschutz and A. Karger, *J. Heterocycl. Chem.*, **34,** 1147, (1997).
[2] R. M. Robertson and D. Robertson, *The Pharmacological Basis of Therapeutics, Goodman and Gillman's*, A. G. Gilman, Ed., (Mc-Graw-Hill Health Professions Divisions, New York, 1996), 9th ed., p. 759.
[3] A. E. Farag and A. A. Alousi, *Life Sci.*, **22,** 1139 (1978).
[4] A. A. Alousi, J. M. Canter, M. J. Montenaro, D. J. Fort, and R. A. J. Ferrari, *Cardiovasc. Pharmacol.*, **5,** 792 (1983).
[5] W. Gobel, *Pharmiz*, **29,** 744 (1974).
[6] J. G. Black and D. Howes, *Toxicology Annual*, **3,** 1 (1979).
[7] M. Nakanish, H. Imamura, and Hirsoki. *Chem. Abst.*, **90,** 272 (1970); *Chem. Abst.*, **90,** 54,504 (1970).
[8] K. M. Al-Zyadi, E. A. Hafez, and M. H. Elnagdi, *J. Chem. Res.*, *(S)* 154 (2000); *(M)* 510 (2000).
[9] F. Al-Omran, N. Al-Awadi, A. A. El-Khair, and M. H. Elnagdi, *Pharmazie* **8,** 571 (1999).
[10] A. M. Hussein, F. A. Abu-Shanab, and E. A. Ishak., *Phosphorous, Sulfur, and Silicon*, **159,** 55, (2000).
[11] M. H. Elnagdi and A. W. Erian, *Bull. Chem. Soc. Jpn.*, **63,** 1854 (1990).
[12] J. Figueras, *J. Org. Chem*., **34,** 803, (1960).
[13] J. V. Grenhill, *Comprehensive, J. Heterocyclic Chem.*, **5,** 307 (1985).
[14] K. M. El-Zadi, M. A. Al-Shiekh, and E. A. Hafez, *J. Chem. Resh (S*), 13 (2000); (*M*), 0173 (2000).
[15] J. L. Soto, C. Seoane, P. Zamnorano, and F. Javier, *Synthesis*, 529 (1981).
[16] A. S. Shawali; M. Sami; S. M. Sherif, and T. Parkanyi, *J. Heterocyclic. Chem*., **17,** 877 (1980).
[17] G. E. H. Elgemeie, N. M. Fathy , L. M. Fahah, M. Y. Ebeide, and M. K. El-said, *Arch. Pharm. (Weinheim)*, **324,** 149 (1991).
[18] M. H. El-nagdi, F. A. Abd-Elaal, and G. E. H. Elgemeie, *Heterocycles*, **23,** 3121 (1985).
[19] R. Gompper and W. Toepfl, *Chem. Ber.*, **95,** 2861 (1962).
[20] J. J. Li., D. Anderson., E. G. Burton, J. N. Cogburn, J. T. Collins, D. J. Garland., S. A. G. Gregory., H. C. Huang., P. C. Isakson,, C. M. Koboldt, E. W. Logusch, M. B. Morton, W. E. Perkins,, E. J. Reinhard, , K. Seibert, A. W. Veenhuizem, Y. Zang, D. B. Reitz, J. Seibert, A. W. Veenhuizem, Y. Zang, and D. B. Reitz, *J. Med. Chem.,* **38,** 4570 (1995).