J. Braz. Chem. Soc., Vol. 20, No. 7, 1275-1286, 2009.
Printed in Brazil - ©2009 Sociedade Brasileira de Química
0103 - 5053 $6.00+0.00

Article

Synthesis, Chemical Reactivity and Fungicidal Activity of Pyrido[1,2-b][1,2,4]triazine Derivatives

Magdy A. Ibrahim,* Reda M. Abdel-Rahman, Ali M. Abdel-Halim, Salah S. Ibrahim and Hassan A. Allimony

Department of Chemistry, Faculty of Education, Ain Shams University, Roxy, 11711, Cairo-Egypt

A síntese de alguns novos derivados de pirido[1,2-b][1,2,4]triazinas (**2**-**12**) foi obtida através da ciclocondensação de 4-aril-1,6-diamino-2-oxo-1,2-diidropiridina-3,5-dicarbonitrilas (**1a**,**b**) com compostos α,β-bifuncionais. Foram também preparadas pirido[1,2:2´,3´]triazino[5´,6´-f] triazinas (**13**-**14**). O comportamento de **1a**,**b** frente às interações com indol-2,3-diona e seu análogo *N*-acetil foi estudado em diferentes condições de reação. As estruturas dos novos produtos foram deduzidas a partir de análise elementar e de dados espectroscópicos (UV, IR, ^{1}H RMN, ^{13}C RMN e espectrometria de massas). Os novos compostos sintetizados foram testados quanto à atividade antifungos.

The synthesis of some new pyrido[1,2-b][1,2,4]triazines (**2**-**12**) was achieved by cyclocondensation of 4-aryl-1,6-diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles (**1a**,**b**) with α,β-bifunctional compounds. Pyrido[1,2:2´,3´]triazino[5´,6´-f]triazines (**13**-**14**) were also prepared. The behavior of **1a**,**b** toward interactions with indole-2,3-dione and its *N*-acetyl analogue have been studied under different reaction conditions. The structures of the new products have been deduced from elemental analysis and spectral data (UV, IR, ^{1}H NMR, ^{13}C NMR and mass spectra). The new synthesized compounds were screened for their antifungal activities.

Keywords: synthesis, *o*-diamines, pyridotriazines, fungicidal activity

Introduction

Polyfunctional pyridines are highly reactive intermediates that have been extensively used in heterocyclic synthesis.[1] *o*-Diamines are very active substrates for building of various heterocyclic systems[2] and are largely used in formation of complexes.[3] In symmetrical diamines, the product will be the same irrespective of which amine participates first in the reaction. In the case of unsymmetrical diamines, the substituents influence the initial participation of a particular amino group in the reaction, resulting in chemoselective products. The electron withdrawing/donating nature of substituents in diamine influences the nucleophilicity of the amino group. On the other hand, 1,2,4-triazine derivatives exhibit marked biological and pharmacological effects and are use for the building fused, condensed and isolated heterobicyclic systems.[4] On the basis of these observations, the objective of this work is the study of the chemical reactivity of 4-aryl-1,6-diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles (**1a**,**b**) and their use for preparation of nitrogen bridgehead pyrido[1,2-b] [1,2,4]triazines in view of their antifungal activity.

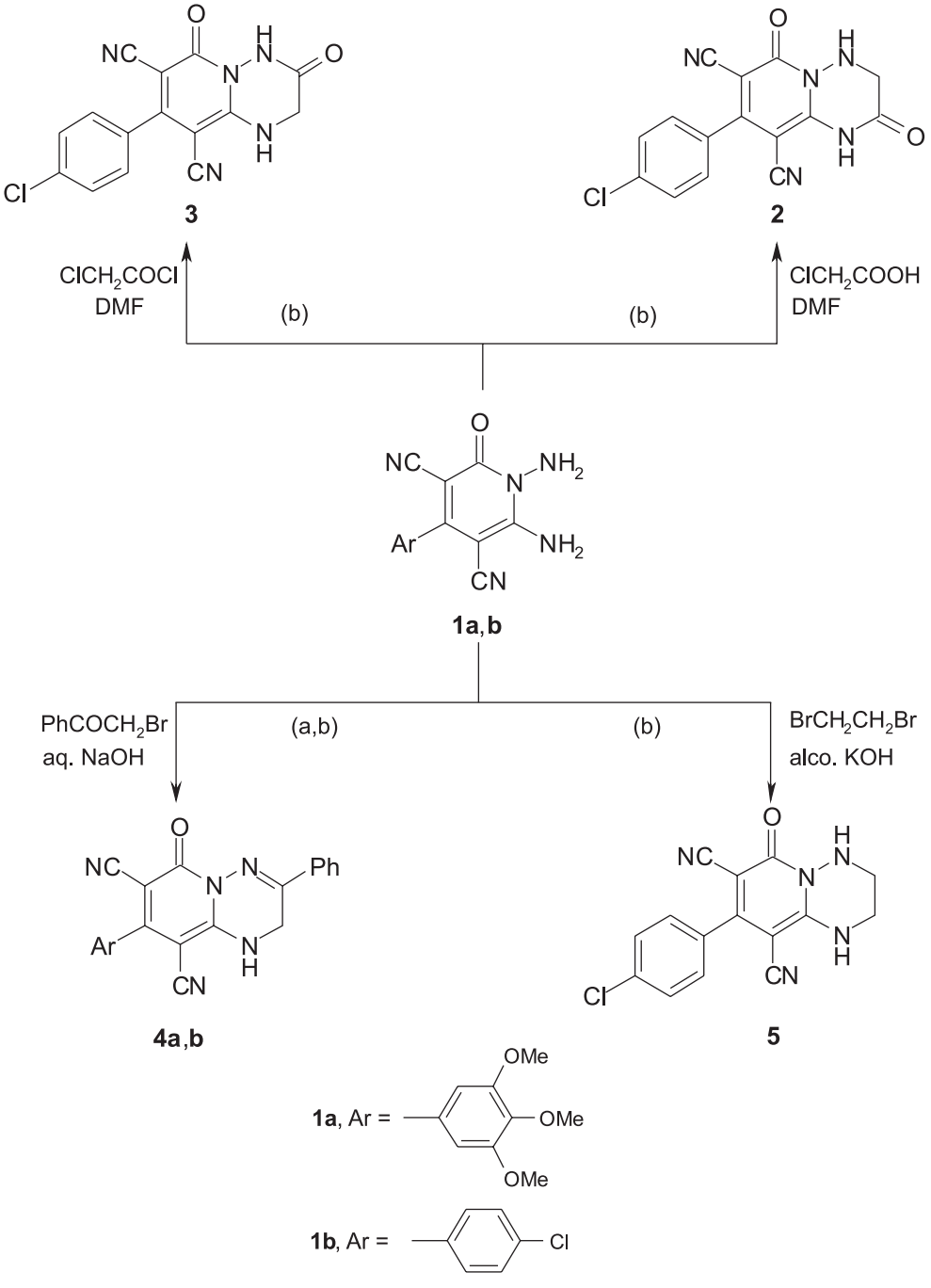
*e-mail: magdy_ahmed1977@yahoo.com

Results and Discussion

1,6-Diamino-4-(4-chlorophenyl or 3,4,5-trimethoxyphenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles (**1a**,**b**) have been obtained from refluxing alcoholic solution of 2-cyanoacetohydrazide and arylmethylidinemalononitriles in the presence of few drops of piperidine as a catalyst.[5] ^{1}H NMR spectra for compounds **1a**,**b** showed two signals for each compound at 5.6 and 8.4 ppm characteristic for the (N-NH_2) and (C-NH_2) protons, respectively. These results indicate the difference in nucleophilicity between the two amino groups. Thus, It is expected the hydrazide β-nitrogen (N-NH_2) more nucleophilic and would react more rapidly with the electron deficient carbon than the amino group at carbon atom (C-NH_2). Mass spectra for compounds **1a** and **1b** showed the molecular ion peaks at m/z 341 and 285, respectively (the base peaks), indicating the high stability the pyridine moiety. Heterocyclic systems

containing 1,2-diamine centers[6] are used for building fused heterocyclic systems *via* a nitrogen bridge. Thus, the regio-isomeric 8-aryl-2,6-dioxo-1,3,4,6-tetrahydro-2H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**2**) and 3,6-dioxo-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**3**) have been obtained from alkylation and acylation of compound **1b** with monochloroacetic acid and chloroacetyl chloride, respectively (Scheme 1). ^{1}H NMR spectra of compounds **2** and **3** showed signals for each CH_2 protons at 2.91 and 3.23 ppm, respectively, while their ^{13}C NMR spectra exhibited signals for each CH_2 carbons at 36.66 and 40.05 ppm, respectively.

Heterocyclization of diaminopyridones **1a**,**b** with phenacyl bromide[7] in refluxing aqueous NaOH yielded 8-aryl-1,2,5,6-tetrahydro-6-oxo-3-phenyl-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles (**4a**,**b**), while the perhydropyridotriazine **5** was obtained from treatment of compound **1b** with 1,2-dibromoethane in alcoholic



Scheme 1

KOH (Scheme 1). The IR spectra of **4a** and **4b** showed absorption bands at 3445 and 3320 cm^{-1} assigned to NH groups, respectively, while the IR spectrum of **5** showed two absorption bands at 3327 and 3243 cm^{-1} for two NH groups.

Some new 8-aryl-2,6-dioxo-1,2-dihydropyrido[1,2-b] [1,2,4]triazine-7,9-dicarbonitriles (**6a**-**g**) have been synthesized by cyclocondensation of compounds **1a**,**b** with α–oxocarboxylic acids, namely pyruvic, α-oxobutyric, 4-chlorostyrylglyoxalic and phenoxypyruvic acids in refluxing glacial acetic acid (Scheme 2). It should be noted that this reaction occurred preferentially between the N^1-amino group (N-NH_2) and the α-keto function of the electrophile to form a hydrazone intermediate, which underwent a cyclodehydration reaction between the other amino group at C^6 (C-NH_2) and the hydroxyl group of the acid function affording the target pyridotriazine derivatives **6a**-**g**. ^{13}C NMR spectra gave good evidence for the formation of compounds **6a**-**g**. For examples, the ^{13}C NMR spectrum of compound **6a** showed a new signal at 18.60 ppm characteristic for a methyl group in position 3. In the case of compound **6f** the vinyl carbons were observed in the spectrum in their expected positions at 122.75 and 135.70 ppm for C_α and C_β, respectively.

Cyclic 1,2-bioxygen compounds were also used for building various fused heterocyclic systems.[8] Thus, compounds **7a**,**b** were prepared from refluxing compound **1a**,**b** with diethyl oxalate in dry dioxane and/or with oxalyl chloride in warm DMF (Scheme 2).

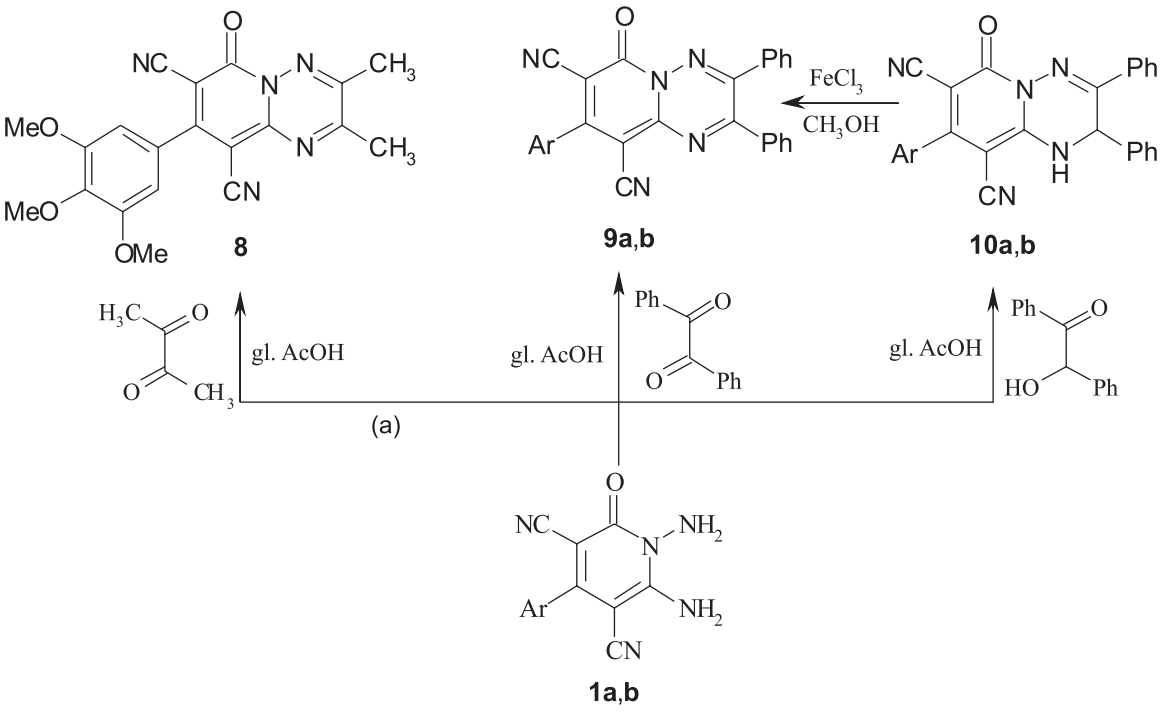
Some new pyridotriazines were obtained from cyclocondensation of 1,6-diaminopyridones **1a**,**b** with α-dicarbonyl compounds. Thus, treatment of **1a** with butane-2,3-dione in glacial acetic acid afforded 2,3-dimethylpyrido[1,2-b][1,2,4]triazine (**8**), while the corresponding 2,3-diphenylpyridotriazine derivatives **9a**,**b** were obtained from refluxing **1a**,**b** with benzil in glacial acetic acid. Dihydro analogues **10a**,**b** were obtained by refluxing compounds **1a**,**b** with benzoin under the same reaction conditions. Oxidation of compounds **10a**,**b** in methanolic ferric chloride[9] produced compounds **9a**,**b** (the same mp and mixed mp) (Scheme 2). ^1H NMR of compound **10b** showed a signal at 5.62 ppm assigned to CH proton in position 2, while its ^{13}C NMR spectrum showed a signal at 77.83 ppm characteristic for the corresponding carbon atom.

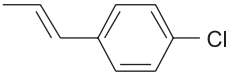
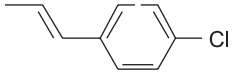
Chlorination of compound **7a** using phosphorus oxychloride afforded 2,3-dichloro-6-oxo-8- (3,4,5-trimethoxy)-6H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**11**) (Scheme 3).

Compounds **7a**,**b** were used as starting materials for the synthesis of fused heteropolycyclic systems. Thus, hydroxymethylation of **7a**,**b** by refluxing with methanol-formaldehyde solution produced 8-aryl-2,3,6-trioxo-1,4-dihydroxymethyl-1,2,3,4,5,6-hexa- hydropyrido[1,2-b] [1,2,4]triazine-7,9-dicarbonitriles (**12a**,**b**), which upon heterocyclization by refluxing with thiosemicarbazide in acetic acid led to 7-oxo-2-thioxo-2,3,5,6,7,11-hexahydropyrido[1,2:2´,3´][1,2,4]triazino[5´,6´-f]triazine-8,10-dicarbonitriles(**13a**,**b**). Hydrazinolysis of **13b** in boiling ethanol furnished the hydrazinotriazine **14** (Scheme 3).

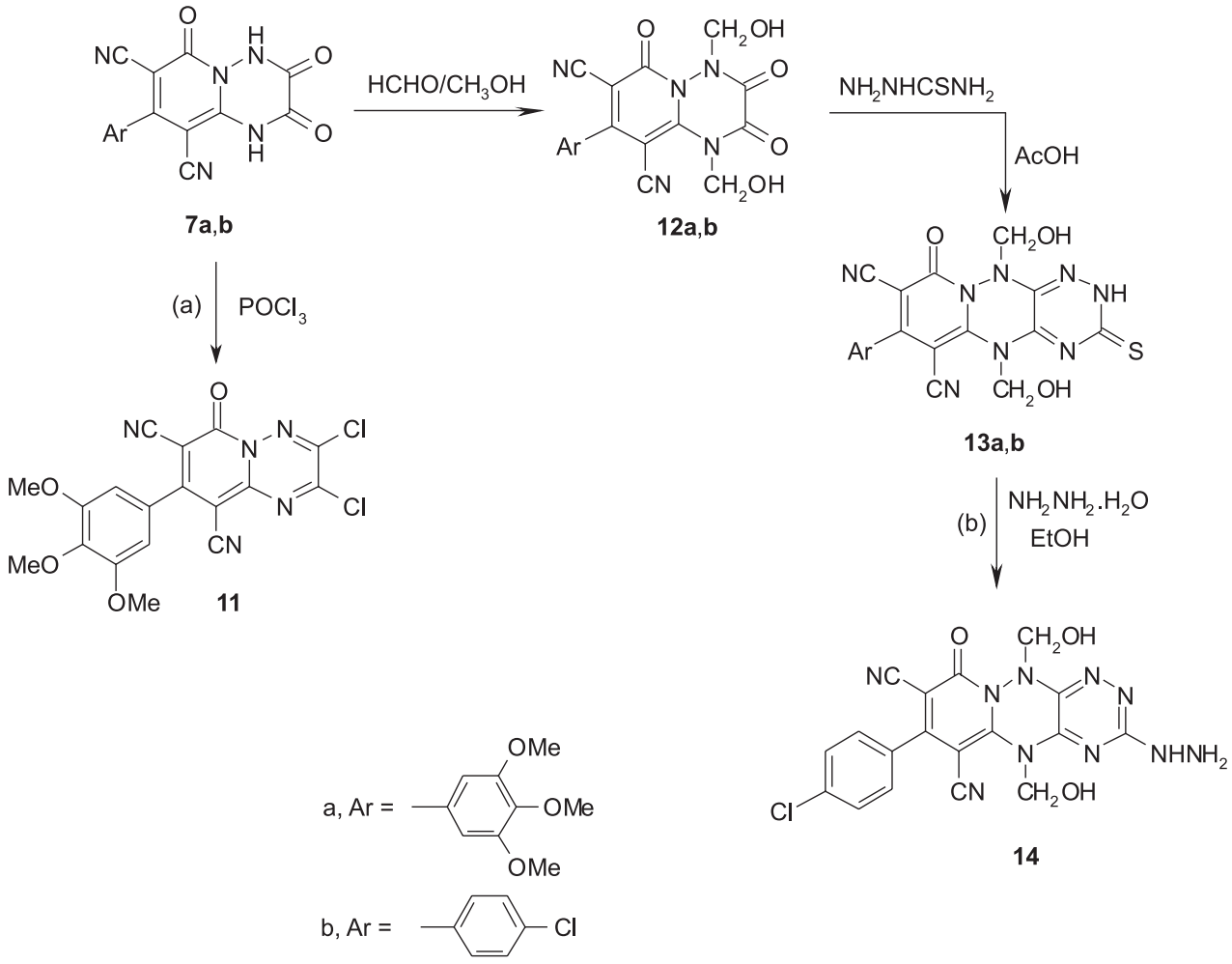
The course of the reactions of cyclic 1,2-bi-oxygen heterocyclic compounds with aromatic heterocyclic *o*-diamines was shown to depend on the reaction conditions, type of solvent and also the substituents in the diamino compounds.[10] Thus, reaction of compounds **1a**,**b** with indole-2,3-dione (isatine) in different media can yield different products. Treating **1a** with indole-2,3-dione in absolute ethanol and few drops of piperidine produced the Schiff base condensate, 6-amino-4-(3,4,5-trimethoxyphenyl)-2-oxo-1-[2-oxo-1,2-dihydro-3-indolo-3-ylidine)amino]-1,2-dihydropyridine-3,5-dicarbonitrile (**15**). Alternatively, warming indole-2,3-dione with alcoholic NaOH solution yielded a 2-aminophenylglyoxalic acid that adds to 1,6-diaminopyridinone **1b** to give the condensation product **16**. Indolotriazinopyridines **17a**,**b** were produced from ring closure reaction of compounds **15** and/or **16** in boiling glacial acetic acid in the presence of freshly fused sodium acetate. Acetylation of compound **17a** by refluxing with acetic anhydride afforded the *N*-acetyl derivative **18** (Scheme 4). IR spectrum of **18** indicated that NH group disappeared and a new characteristic band at 1734 cm^{-1} appeared for the C=O of the acetyl group. The mass spectrum revealed the parent peak at m/z 494 which is coincident with the formula weight in agreement with the postulated structure.

N-acetylisatine showed a different behavior.[11] Reaction of **1a** with *N*-acetylisatine in absolute ethanol in the presence of few drops of piperidine led to 8-(3,4,5-trimethoxyphenyl)-2-(2-acetanilido)-3,6-dioxo-3,6-dihydro-4H-pyrido[1,2-b] [1,2,4]triazine-7,9-dicarbonitrile (**20**) and not to the isomeric product **21** (Scheme 4). This reaction can be explained by an increase in the positive charge on the α-carbon atom in comparison to isatine itself due to the electron withdrawing acetyl group which facilitates the nucleophilic attack of more nucleophilic amino group (N-NH_2) at this position with concomitant opening of five membered ring. Apparently, the reaction can be claimed to proceed *via* intermediate **19**, as also observed by previous workers in reaction with other diamines.[12] However, this type of intermediate was reported to be unstable and not isolated.



6	R	Ar
a	CH_3	a
b	CH_3	b
c	CH_2CH_3	a
d	CH_2CH_3	b
e		a
f		b
g	CH_2OPh	b

Scheme 2



Scheme 3

Fungicidal activity

Several new synthesized compounds were screened for their antifungal activities against two species of fungi, namely *Alternaria alternata* and *Aspergillus niger* using the disc diffusion method.[13] The tested compounds were dissolved in DMF (which has no inhibitory activity) to get concentrations of 1 mg mL^{-1} solution. The antibiotic fluconazole was used as standard antifungal reference. The inhibition zones of microbial growth surrounding the filter paper disc (2.5 mm) were measured in millimeters at the end of an incubation period at 30 C for 3 days. Inhibition of the organisms was evidenced by a clear zone surrounding each disk (Table 1).

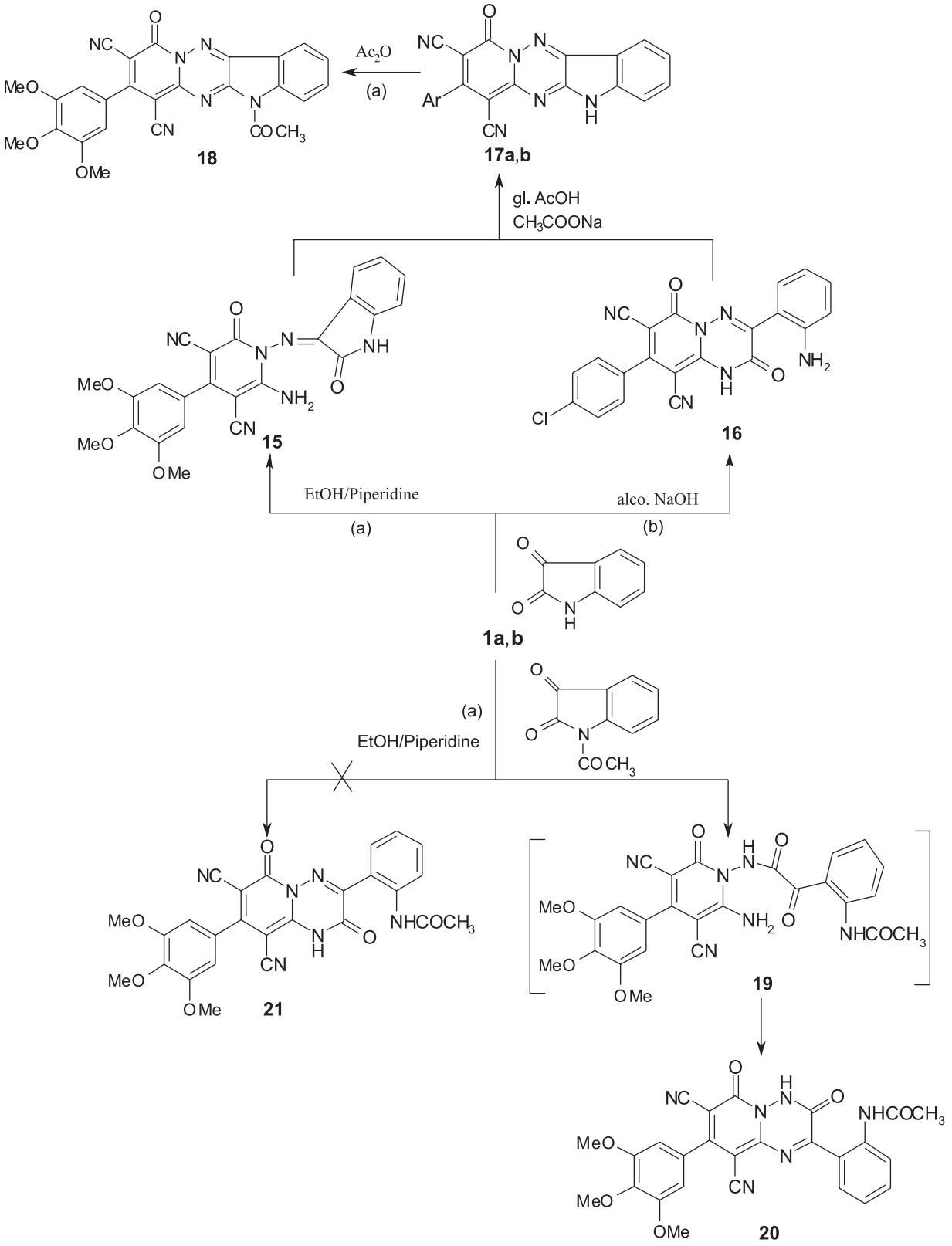
All the tested compounds showed variable activities toward the two species of fungi, some of them comparable to standard fluconazole. The most active triazines were **2d**, **3**, **9b** and **10**.

From the results obtained, it is clear that increasing the percentage of nitrogen in the tested compounds led to

Table 1. Fungicidal activity of some of the new compounds **1**-**20**

Compound	Nitrogen content N / %	Diameter of inhibition zone	
		Alternaria alternata	Aspergillus niger
1a	20.5	+	++
2d	16.5	++	+++
3	21.6	+++	+++
4	21.6	++	++
5b	18.5	++	++
6b	20.5	++	++
8b	17.5	++	++
9b	24.6	++	+++
10	30.9	+++	+++
14	22.4	++	++
17a	18.5	+	+
(fluconazole)		+++	+++

Lower active = + (inhibition zone 1-10 mm), moderately active = (inhibition zone 11-25 mm) and highly active = +++ (inhibition zone > 25 mm).



Scheme 4

higher effects toward the tested fungi. The antifungal effects decrease in the order of: **10** > **9b** > **3** > **2d** for higher activity and **14** > **6b** > **4** > **8b** > **5b** >**1a** for moderate activity. The lower activity was observed by compound **17a** (Table 1).

Conclusion

Cyclocondensation of 4-aryl-1,6-diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles with α,β-bifunctional compounds takes place regioselectively through condensation of ($N\text{-}NH_2$) group with the more electrophilic carbon center followed by cyclization to produce several new pyrido[1,2-b][1,2,4]triazine derivatives.

Experimental

Melting points are uncorrected and were recorded in open capillary tubes on a Stuart SMP3 melting point apparatus. Infrared spectra were recorded on FT-IR Bruker Vector 22 spectrophotometer using KBr wafer technique. UV absorption spectra (DMF) were recorded on a Jasco model (V-550) UV spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were measured on Gemini (200 MHz) spectrometer and Bruker (250 MHz) AC spectrometer using DMSO-d_6 as solvent and TMS (chemical shift in ppm) as an internal standard. Mass spectra were obtained using a Shimadzu GCMS qp 1000 ex instrument mass spectrometer (70 eV).

*4-Aryl-1,6-diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles (**1a**,**b**)*

Compounds **1a** and **1b** have been prepared according to the reported method.[5]

*Compound **1a***

Crystallized from DMF as white crystals, yield 80%, mp 255-256 ºC. UV λ_{max}/nm (log ε): 344 (3.39), 276 (3.58). IR (KBr) ν_{max}/cm^{-1}: 3334, 3194 (2 NH_2), 2998, 2941, 2839 (CH_3 groups), 2215 (2 C≡N), 1669 (C=O), 1633 (def. NH_2), 1591 (C=N), 1513 (C=C), 1466, 1416 (def. CH_3). ^{1}H NMR (δ, DMSO): 3.78 (s, 3H, CH_3O), 3.81 (s, 6H, $2CH_3O$), 5.60 (s, 2H, $N\text{-}NH_2$), 6.82 (s, 2H, Ar-H), 8.40 ppm (s, 2H, $C\text{-}NH_2$). ^{13}C NMR (δ, DMSO): 56.47 (2 CH_3O), 60.47 (CH_3O), 74.63 (C_5-CN), 86.67 (C_3-CN), 116.01 (C≡N), 116.88 (C≡N), 106.32 (C2` and C6`), 129.94 (C1`), 139.03 (C4`), 153.00 (C3` and C5`), 156.98 (C_4), 159.62 (C_6), 162.65 ppm (C_2 as C=O). M/z (Int.%) 342 (20.1), 341 (100), 326 (49.18), 298 (20.77), 283 (8.89), 268 (10.06), 236 (2.82), 168 (2.88). Anal. Calc. for $C_{16}H_{15}N_5O_4$ (341.3): C, 59.96; H, 2.39; N, 15.21. Found: C, 59.34; H, 2.62; N, 15.34.

*Compound **1b***

Crystallized from dioxane as white crystals, yield 90%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 3455, 3400, 3350, 3310 (2 NH_2), 2222 (2 C≡N), 1665 (C=O), 1624 (def. NH_2), 1590 (C=N), 1562 (C=C). ^{1}H NMR (δ, DMSO): 5.60 (s, 2H, $N\text{-}NH_2$), 7.63 (d, 2H, Ar-H), 7.84 (d, 2H, Ar-H), 8.40 ppm (s, 2H, $C\text{-}NH_2$). Anal. Calc. for $C_{13}H_8ClN_5O$ (285.69): C, 54.60; H, 2.80; N, 24.51. Found: C, 54.59; H, 2.86; N, 24.53.

*8-(4-Chlorophenyl)-2,6-dioxo-1,3,4,6-tetraahydro-2H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**2**)*

A mixture of **1b** (10 mmol) and monochloroacetic acid (10 mmol) in DMF (50 mL) was refluxed for 4 h, after cooling the reaction mixture was poured onto ice. The solid obtained was filtered and crystallized from methanol to give **2** as yellow crystals, yield 66%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 3397 (OH), 3265 (NH), 2218 (2 C≡N), 1640 (C=O), 1522 (C=C), 1491, 1465 (def. CH_2). ^{1}H NMR (δ, DMSO): 2.91 (s, 2H, CH_2), 5.75 (s, 1H, NH), 7.52 (d, 2H, Ar-H), 7.73 (d, 2H, Ar-H), 8.51 ppm (s, 1H, OH of 1,2,4-triazin-5-ol). ^{13}C NMR (δ, DMSO): 36.66 (CH_2), 75.19 (C_9-CN), 87.29 (C_7-CN), 116.22 (C≡N), 117.09 (C≡N), 129.65, 130.89, 134.31 and 135.95 (6C of aryl carbons), 157.48 (C_8), 159.27 (C_{9a}), 159.99 (C_2 as C=O), 161 ppm (C_6 as C=O). Anal. Calc. for $C_{15}H_8ClN_5O_2$ (325.72): C, 55.13; H, 2.48; N, 21.50. Found: C, 55.00; H, 2.72; N, 21.81.

*8-(4-Chlorophenyl)-3,6-dioxo-1,3,4,6-hexahydro-2H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**3**)*

Compound **1b** (10 mmol) was dissolved in DMF (50 mL), chloroacetyl chloride (10 mmol) was added dropwise within 15 min, then refluxed for 4 h. After cooling the reaction mixture was poured onto ice. The solid obtained was filtered and crystallized from ethanol to give **3** as yellow crystals, yield 52%, mp 235-236 ºC. IR (KBr) ν_{max}/cm^{-1}: 3450 (br, OH $\rightleftharpoons$ NH), 2967 (CH_2), 2214 (2 C≡N), 1650 (C=O), 1560 (C=C), 1492, 1423 (def. CH_2). ^{1}H NMR (δ, DMSO): 3.23 (s, 2H, CH_2), 5.30, 5.40 (each s, 2H, 2NH), 8.23 (d, 2H, Ar-H), 8.42 ppm (d, 2H, Ar-H). ^{13}C NMR (δ, DMSO): 40.05 (CH_2), 83.01 (C_9-CN), 89.19 (C_7-CN), 122.13 (C≡N), 123.46 (C≡N), 134.20, 135.63, 136.11 and 140.05 (6C of aryl carbons), 140.20 (C_8), 159.87 (C_{9a}), 161.50 (C_3 as C=O), 162.39 ppm (C_6 as C=O). Anal. Calc. for $C_{15}H_8ClN_5O_2$ (325.72): C, 55.13; H, 2.48; N, 21.50. Found: C, 54.99; H, 2.72; N, 21.81.

*8-Aryl-1,2,5,6-tetrahydro-6-oxo-3-phenyl-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles (**4a,b**)*

A mixture of **1a** or **1b** (5 mmol) and phenacyl bromide (5 mmol) was refluxed in aqueous NaOH (5%, 50 mL) for

4 h, after cooling the reaction mixture was neutralized with conc. HCl. The solid obtained was filtered, washed several times with water and crystallized to give **4a**,**b**.

*Compound **4a***

Crystallized from ethanol as white crystals, yield 74%, mp 195-196 ºC. IR (KBr) ν_{max}/cm^{-1}: 3445 (NH), 2940, 2838 (CH_3 and CH_2), 2211 (2 C≡N), 1653 (C=O), 1588 (C=N), 1508 (C=C), 1459, 1417 (def. CH_2). ^{1}H NMR (δ, DMSO): 3.31 (s, 2H, CH_2), 4.43 (s, 3H, CH_3O), 4.52 (s, 3H, CH_3O), 4.64 (s, 3H, CH_3O), 6.22 (s, 1H, NH exchangeable with D_2O), 7.59 (s, 2H, Ar-H), 8.36 ppm (s, 5H, Ar-H). Anal. Calc. for $C_{24}H_{19}N_5O_4$ (441.45): C, 65.30; H, 4.34; N, 15.86. Found: C, 65.13; H, 4.25; N, 15.69.

*Compound **4b***

Crystallized from ethanol as white crystals, yield 71%, mp 143-144 ºC. IR (KBr) ν_{max}/cm^{-1}: 3320 (NH), 2980 (CH_2), 2208 (C≡N), 1636 (C=O), 1591 (C=N), 1516 (C=C), 1495, 1443 (def. CH_2). Anal. Calc. for $C_{21}H_{12}ClN_5O$ (385.81): C, 65.32; H, 3.11; N, 18.14. Found: C, 64.89; H, 3.07; N, 18.12.

*8-(4-Chlorophenyl)-6-oxo-1,3,4,6-tetrahydro-2H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**5**)*

A mixture of **1b** (5 mmol) and 1,2-dibromoethane (5 mmol) in alcoholic KOH (5%, 50 mL) was refluxed for 4 h, cooled and neutralized with conc. HCl. The solid so formed was filtered, washed with water and crystallized from methanol to give **5** as white crystals, yield 67%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 3327 and 3243 (2NH), 2900 (CH_2), 2210 (2 C≡N), 1649 (C=O), 1581 (C=N). ^{1}H NMR (δ, DMSO): 3.31 (m, 4H, 2 CH_2), 4.98-5.06 (bs, 2H, 2NH exchangeable with D_2O), 8.22 (d, 2H, Ar-H), 8.40 ppm (d, 2H, Ar-H). Anal. Calc. for $C_{15}H_{10}ClN_5O$ (311.73): C, 57.80; H, 3.23; N, 22.47. Found: C, 57.68; H, 3.17; N, 22.32.

*8-Aryl-2,6-dioxo-3-substituted-1,2,5,6-tetrahydropyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles (**6a-g**)*

A mixture of **1a** or **1b** (10 mmol) and acyclic 1,2-bioxo compounds such as pyruvic acid, α-oxo-butyric acid, *p*-chlorostyryl glyoxalic acid and phenoxy pyruvic acids (10 mmol) in glacial acetic acid (30 mL) was refluxed for 4 h. The solid obtained after cooling was filtered, washed with water and crystallized from a proper solvents to give **6a**-**g**. IR (KBr) ν_{max}/cm^{-1} of **6a-g:** 3463 (OH $\rightleftharpoons$ NH), 2211-2219 (2 C≡N), 1695-1633 (2 C=O).

*Compound **6a***

Crystallized from ethanol as white crystals, yield 90%, mp > 300 ºC. ^{1}H NMR (δ, DMSO): 1.60 (s, 3H, CH_3), 2.31 (s, 1H, NH of triazinone), 3.76 (s, 3H, CH_3O), 3.82 (s, 6H, 2 CH_3O), 6.81 ppm (s, 2H, Ar-H). ^{13}C NMR (δ, DMSO): 18.60 (CH_3), 56.99 (2 CH_3O), 60.99 (CH_3O), 82.00 (C_9-CN), 86.10 (C_7-CN), 107.04 (C2` and C6`), 118.12 (2 C≡N), 132.24 (C1`), 137.00 (C4`), 153.41 (C3`and C5`), 154.09 (C3), 155.02 (C_8), 157.16 (C_{9a}), 159.00 (C_2 as C=O), 161.05 ppm (C_6 as C=O). Anal. Calc. for $C_{19}H_{15}N_5O_5$ (393.36): C, 58.02; H, 3.84; N, 17.80. Found: C, 57.98; H, 3.77; N, 17.74.

*Compound **6b***

Crystallized from ethanol as white crystals, yield 88%, mp > 300 ºC. ^{1}H NMR (δ, DMSO): 1.91 (s, 3H, CH_3), 3.43 (bs, 1H, NH of triazinone), 7.53 (d, 2H, Ar-H), 7.68 ppm (d, 2H, Ar-H).

*Compound **6c***

Crystallized from methanol as white crystals, yield 91%, mp 130-131 ºC. Anal. Calc. for $C_{20}H_{17}N_5O_3$ (407.39): C, 58.97; H, 4.21; N, 17.19. Found: C, 59.72; H, 4.13; N, 17.04.

*Compound **6d***

Crystallized from methanol as white crystals, yield 84%, mp 120-122 ºC. M/z (Int.%): 351 (0.5), 257 (36.36), 201 (45.0), 180 (100), 152 (87.88), 139 (33.33), 124 (39.39), 96 (54.55).

*Compound **6e***

Crystallized from methanol as white crystals, yield 87%, mp 248-249 ºC. ^{1}H NMR (δ, DMSO): 3.77 (s, 3H, CH_3O), 3.84 (s, 6H, 2 CH_3O), 6.85 (s, 2H, Ar-H of trimethoxy ring), 7.34 and 8.16 (each d, 2H of CH=CH), 7.49-7.78 ppm (m, 4H, Ar-H), 8.42 (bs, 1H, NH of triazinone)**.** Anal. Calc. for $C_{26}H_{18}ClN_5O_5$ (515.92): C, 60.53; H, 3.52; N, 13.57. Found: C, 60.42; H, 3.41; N, 13.44.

*Compound **6f***

Crystallized from ethanol as white crystals, yield 85%, mp > 300 ºC. ^{1}H NMR (δ, DMSO): 7.25 and 8.25 (each d, 2H of CH=CH), 7.35-7.82 ppm (m, 8H, Ar-H), 8.50 (bs, 1H, NH of triazinone). ^{13}C NMR (δ, DMSO) 75.19 (C_9-CN), 87.28 (C_7-CN), 116.21 (C≡N), 117.09 (C≡N), 122.75 (C_α of C=C), 129.50-138.56 (12C of aryl groups and C_β of C=C), 148.46 (C_8), 157.48 (C_{9a}), 157.77 (C_3), 159.26 (C_2 as C=O) and 159.99 ppm (C_6 as C=O). Anal. Calc. for $C_{23}H_{11}Cl_2N_5O_2$ (460.28): C, 60.02; H, 2.41; N, 15.22. Found: C, 60.00; H, 2.34; N, 15.10.

*Compound **6g***

Crystallized from methanol as white crystals, yield 65%, mp > 300 ºC. M/z (Int.%): 429 (0.19), 285 (100), 256 (25.84), 173 (10.76), 146 (1.17) and 111 (26.39).

*8-Aryl-2,3,6-trioxo-1,2,3,4,5,6-hexahydropyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles (**7a**,**b**)*

Method 1

A mixture of **1a** or **1b** (0.01 mol) and diethyl oxalate (0.01 mol) in dry dioxane (50 mL) was refluxed for 4 h, after cooling the reaction mixture was concentrated. The solid obtained was filtered and crystallized to give **7a**,**b**.

Method 2

Compound **1a** or **1b** (10 mmol) was dissolved in DMF (50 mL), oxalyl chloride (10 mmol) was added dropwise within 15 min. The reaction mixture was refluxed for 4 h, after cooling the reaction mixture was poured into ice. The solid obtained was filtered and crystallized to give **7a**,**b**.

*Compound **7a***

Crystallized from benzene as white crystals, yield 82%, mp 146-147 ºC. UV λ_{max}/nm (log ε): 349 (0.131), 273 (2.857). IR (KBr) ν_{max}/cm^{-1}: 3269, 3195 (2 NH), 2989, 2969, 2935, 2904, 2841 (CH_3 groups), 2255 (2 C≡N), 1741 (weak band for C=O), 1462, 1424 (def. CH_3). ^{1}H NMR (δ, DMSO) 3.65 (s, 3H, CH_3O), and 3.80 (s, 6H, 2 CH_3O), 5.10 (s, 2H, 2OH of 1,2,4-triazinediol), 6.72 (s, 2H, Ar-H). ^{13}C NMR (δ, DMSO): 56.73 (2 CH_3O), 60.84 (CH_3O), 107.57 (C_7–CN and C_9–CN), 115.01 (2 C≡N), 131.12 (aromatic carbons), 137.93 (C_8), 153.70 ppm (3 C=O and C_{9a}). Anal. Calc. for $C_{18}H_{13}N_5O_6$ (395.33): C, 54.69; H, 3.31; N, 17.71. Found: C, 54.67; H, 3.30; N, 17.73.

*Compound **7b***

Crystallized from DMF as yellow crystals, yield 80%, mp > 300 ºC. ^{1}H NMR (δ, DMSO): 7.54 (d, 2H, Ar-H), 7.63 (d, 2H, Ar-H), 8.39 ppm (s, 2H, 2OH of 1,2,4-triazinediol). ^{13}C NMR (δ, DMSO): 74.31 (C_9-CN), 86.54 (C_7-CN), 115.18 (C≡N), 115.98 (C≡N), 128.69, 129.90, 133.39 and 135.07 (6C of aryl carbons), 156.49 (C_8), 158.27 (C_{9a}), 158.90 (C_2 and C_3 as 2 C=O), 171.77 ppm (C_6 as C=O). M/z (Int.%): 339 (33.33), 187 (100), 175 (23.81), 142 (54.76), 124 (60.61) and 86 (42.42). Anal. Calc. for $C_{15}H_6ClN_5O_3$ (339.69): C, 53.04; H, 1.78; N, 20.62. Found: C, 52.91; H, 1.75; N, 20.58.

*2,3-Dimethyl-6-oxo-8-(3,4,5-trimethoxy)-6H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**8**)*

A mixture of **1a** (5 mmol) and butane-2,3-dione (5 mmol) in glacial acetic acid (20 mL) was refluxed for 2 h, after cooling the reaction mixture was concentrated. The solid obtained was filtered, washed with cold ethanol and crystallized from acetic acid to give **8** as yellow crystals, yield 70%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 2926, 2849 (CH_3 groups), 2213 (2 C≡N), 1696 (C=O), 1635 (C=N), 1585 (C=C), 1466, 1412 (*def.* CH_3). ^{1}H NMR (δ, DMSO): 3.20 (s, 3H, CH_3), 3.62 (s, 3H, CH_3), 3.75 (s, 3H, CH_3O), 4.01 (s, 6H, 2 CH_3O), 6.65 ppm (s, 2H, Ar-H). M/z (Int.%): 391 (2.99), 365 (4.25), 337 (6.77), 224 (5.20), 197 (8.50), 171 (21.42), 167 (15.91), 137 (21.57), 109 (38.92), 82 (37.46), 55 (100). Anal. Calc. for $C_{20}H_{17}N_5O_4$ (391.39): C, 61.23; H, 2.55; N, 17.88. Found: C, 60.94; H, 2.10; N, 17.50.

*8-Aryl-2,3-diphenyl-6-oxo-5,6-dihydropyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles (**9a**,**b**)*

A mixture of **1a** or **1b** (5 mmol) and benzil (5 mmol) in glacial acetic acid (50 mL) and anhydrous sodium acetate (1 g) was refluxed for 8 h, after cooling the reaction mixture was poured onto ice. The solid obtained was filtered and crystallized to give **9a**,**b**. For compound **9a**; Crystallized from DMF/H_2O as yellow crystals, yield 60%, mp 265 ºC. UV λ_{max}/nm (log ε): 347 (4.33), 282 (4.084). IR (KBr) ν_{max}/cm^{-1}: 2935, 2861 (CH_3 groups), 2215 (2 C≡N), 1674 (C=O), 1611 (C=N), 1593 (C=C), 1466, 1418 (def. CH_3). ^{1}H NMR (δ, DMSO): 3.78 (s, 3H, CH_3O), 3.80 (s, 2H, 2 CH_3O), 6.97 (s, 2H, Ar-H of trimethoxy ring), 7.14-7.52 ppm (m, 10H, Ar-H). M/z (Int.%): 515 (45.83), 426 (41.67), 328 (100), 232 (41.67), 221 (45.83) and 147 (45.83). Anal. Calc. for $C_{30}H_{21}N_5O_4$ (515.53): C, 69.83; H, 4.07; N, 13.58. Found: C, 70.06; H, 3.97; N 13.54.

*Compound **9b***

Crystallized from DMF/H_2O as yellow crystals, yield 54%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 2219 (2 C≡N), 1669 (C=O), 1608 (C=N), 1585 (C=C). ^{1}H NMR (δ, DMSO): 7.19-7.55 ppm (m, 10H, Ar-H), 7.72 (d, 2H, Ar-H), 7.83 (d, 2H, Ar-H). Anal. Calc. for $C_{27}H_{14}ClN_5O$ (459.89): C, 70.52; H, 3.07; N, 15.23. Found: C, 70.36; H, 3.02; N, 15.20.

*8-Aryl-2,3-diphenyl-6-oxo-1,2,5,6-tetrahydropyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles (**10a**,**b**)*

Method 1

A mixture of **1a** or **1b** (5 mmol) and benzoin (5 mmol) in glacial acetic acid (50 mL) and anhydrous sodium acetate (1 g) was refluxed for 8 h, after cooling the reaction mixture was poured onto ice. The solid obtained was filtered, washed several times with water and crystallized to give **10a**,**b**.

Method 2

Compounds **10a** or **10b** (5 mmol) was dissolved in methanol (50 mL), ferric chloride (10%, 20 mL) in methanol (30 mL) was added and refluxed for 3 h, after cooling the reaction mixture was concentrated. The solid obtained was filtered and crystallized to give **9a**,**b**. Melting point and mixed melting point showed no depression with **9a**,**b** obtained from the above experiment.

*Compound **10a***

Crystallized from DMF/H_2O as yellow crystals, yield 49%, mp 278-279 ºC. IR (KBr) ν_{max}/cm^{-1}: 3449 (NH), 2977, 2944, 2846 (CH_3), 2212 (2 C≡N), 1650 (C=O), 1591 (C=N), 1562 (C=C), 1458, 1416 (def. CH_3). Anal. Calc. for $C_{30}H_{23}N_5O_4$ (517.55): C, 69.62; H, 4.48; N, 13.53. Found: C, 69.50; H, 4.35; N 13.38.

*Compound **10b***

Crystallized from DMF/H_2O as white crystals, yield 44%, mp 290-291 ºC. ^{1}H NMR (δ, DMSO): 5.62 (s, 1H, CH of 1,2,4-triazin-5-yl), 7.21-8.05 (m, 14H, Ar-H), 8.53 ppm (s, 1H, NH). ^{13}C NMR (δ, DMSO): 75.19 (C_9-CN), 77.83 (C_2), 87 (C_7-CN), 117.09 (2 C≡N), 129.51-135.95 (18C of aryl carbons), 157.49 (C_8), 159.27 (C_{9a}), 170.78 (C_3), 194.49 ppm (C_6 as C=O). Anal. Calc. for $C_{27}H_{16}ClN_5O$ (461.91): C, 70.21; H, 3.49; N, 15.16. Found: C, 70.09; H, 3.42; N, 15.08.

*2,3-Dichloro-6-oxo-8-(3,4,5-trimethoxy)-6H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**11**)*

A mixture of **7a** (5 mmol) and phosphorus oxychloride (10 mL) was refluxed for 2 h, after cooling the reaction mixture was poured onto ice with stirring. The solid obtained was filtered, washed several times with water and crystallized from benzene to give **11** as white crystals, yield 55%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 2964, 2936, 2842 (CH_3 groups), 2240 (2 C≡N), 1680 (C=O), 1605 (C=N), 1582 (C=C), 1473, 1414 (def. CH_3). ^{1}H NMR (δ, DMSO): 3.79 (s, 3H, CH_3O), 3.83 (s, 6H, 2CH_3O) and 6.81 (s, 2H, Ar-H). Anal. Calc. for $C_{18}H_{11}Cl_2N_5O_4$ (432.22): C, 50.20; H, 2.57; N, 16.20. Found: C, 50.31; H, 2.46; N, 16.24.

*8-Aryl-2,3,6-trioxo-1,4-dihydroxymethyl-1,2,3,4,5,6-hexahydropyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles (**12a**,**b**)*

A mixture of **7a** or **7b** (5 mmol) and formaldehyde solution (10 mmol) in methanol (50 mL) was refluxed for 6 h. The solid obtained after cooling was filtered, washed several times with water and crystallized to give **12a**,**b**.

*Compound **12a***

Crystallized from methanol as yellow crystals, yield 73%, mp 214-215 ºC. UV λ_{max}/nm (log ε): 348 (1.89), 337 (1.54), 269 (2.55). IR (KBr) ν_{max}/cm^{-1}: 3399, 3280 (2 OH), 2940, 2940, 2839 (CH_3), 2215 (2 C≡N), 1660 (C=O), 1595 (C=C), 1467, 1414 (def. CH_3). ^{1}H NMR (δ, DMSO): 3.25 (s, 4H, 2-CH_2-), 3.75 (s, 3H, CH_3O), 3.81 (s, 6H, 2 CH_3O), 5.68 (s, 1H, OH), 6.84 (s, 1H, Ar-H), 6.86 (s, 1H, Ar-H), 8.41 ppm (s, 1H, OH). Anal. Calc. for $C_{20}H_{17}N_5O_8$ (455.39): C, 52.70; H, 3.37; N, 15.37. Found: C, 52.52; H, 3.15; N, 15.25.

*Compound **12b***

Crystallized from methanol as yellow crystals, yield 69%, mp 219-220 ºC. IR (KBr) ν_{max}/cm^{-1}: 3293, 3212 (2 OH), 2990, 2932 (CH_2), 2217 (2 C≡N), 1667 (C=O), 1618 (def. OH), 1497, 1450 (def. CH_2). M/z (Int.%) 399 (26.19), 239 (35.17), 187 (100), 142 (26.19), 124 (28.57), 112 (30.95) and 88 (26.19).

*9-Aryl-5,11-dihydroxymethyl-7-oxo-2-thioxo-2,3,5,6,7,11-hexahydropyrido[1,2:2´,3´]triazino[5´,6´-f]triazine-8,10-dicarbonitriles (**13a,b**)*

A mixture of **12a** or **12b** (2 mmol) and thiosemicarbazide (2 mmol dissolved in hot water) in acetic acid (40 mL) was refluxed for 4 h. The solid obtained after cooling was filtered and crystallized to give **13a**,**b**.

*Compound **13a***

Crystallized from acetic acid as yellow crystals, yield 77%, mp > 300 ºC. UV λ_{max}/nm (log ε): 379 (3.9), 345 (4.4). IR (KBr) ν_{max}/cm^{-1}: 3412, 3281 (2-OH), 3214 (NH), 2973, 2941, 2840 (CH_3), 2213 (2 C≡N), 1670 (C=O), 1609 (C=N), 1513 (C=C), 1468, 1413 (def. CH_3), 1184 (C=S). ^{1}H NMR (δ, DMSO): 3.04 (s, 4H, 2 CH_2O-), 3.77 (s, 3H, CH_3O), 3.80 (s, 6H, 2 CH_3O), 5.95 (s, 1H, OH), 6.84 (s, 1H, Ar-H), 6.89 (s, 1H, Ar-H), 8.63 (s, 1H, OH), 10.25 ppm (s, 1H, NH). Anal. Calc. for $C_{21}H_{18}N_8O_6S$ (510.49): C, 49.41; H, 3.55; N, 21.94. Found: C, 49.94; H, 4.10; N, 22.10.

*Compound **13b***

Crystallized from acetic acid as yellow crystals, yield 65%, mp > 300 ºC. λ_{max} /nm(ε): 346 (3.4), 273 (2.98). IR (KBr) ν_{max}/cm^{-1}: 3416 (OH), 3344 (OH), 3307 (NH), 2217 (C≡N), 1668 (C=O), 1613 (C=N), 1549 (C=C). ^{1}H NMR (δ, DMSO): 2.87 (s, 4H, 2 CH_2), 5.43 (s, 2H, 2 OH), 7.54 (d, 2H, Ar-H), 7.65 (d, 2H, Ar-H), 9.89 ppm (s, 1H, 1NH).

*9-(4-Chlorophenyl)-5,11-dihydroxymethyl-7-oxo-2-hydrazino-2,3,5,6,7,11-hexahydropyrido[1,2:2´,3´]triazino[5´,6´-f]triazine-8,10-dicarbonitrile (**14**)*

A mixture of **13b** (10 mmol) and hydrazine hydrate (100 mmol) in absolute ethanol (100 mL) was refluxed for 12 h. The solid obtained after cooling was filtered and crystallized from DMF to give **14** as yellow crystals, yield 54%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 3470 (OH), 3304, 3187 (NH, NH_2), 2926 (CH_2), 2214 (2 C≡N), 1636 (C=O), 1579 (C=N), 1489 (def. CH_2). ^{1}H NMR (δ, DMSO): 2.73 (s, 2H, CH_2), 2.89 (s, 2H, CH_2), 5.09 (bs, 2H, NH_2), 5.75 (s, 2H, 2OH), 7.54 (d, 2H, Ar-H), 7.65 (d, 2H, Ar-H), 7.94 ppm (s, 1H, 1NH). Anal. Calc. for $C_{18}H_{13}ClN_{10}O_3$ (452.82): C, 47.70; H, 2.87; N, 30.92. Found: C, 47.84; H, 2.53; N, 30.89.

*6-Amino-4-(3,4,5-trimethoxyphenyl)-2-oxo-1-[2-oxo-1,2-dihydro-3-indolo-3-ylidine)amino]-1,2-dihydropyridine-3,5-dicarbonitrile (**15**)*

A mixture of **1a** (5 mmol) and isatine (5 mmol) in ethanol (75 mL) and piperidine (2 drops) was refluxed for 4 h. The solid obtained was filtered and crystallized from ethanol to give **15** as yellow crystals, yield 51%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 3310, 3172 (NH_2, NH), 2921, 2851 (CH_3), 2207 (2 C≡N), 1646 (C=O), 1518 (C=N), 1496, 1442 (def. CH_3). ^{1}H NMR (δ, DMSO): 3.03 (s, 1H, NH), 3.79 (s, 3H, CH_3O), 3.83 (s, 3H, CH_3O), 3.85 (s, 3H, CH_3O), 6.97 (s, 2H, Ar-H of trimethoxy phenyl), 7.39-7.99 (m, 4H, Ar-H of indole), 8.28 ppm (s, 2H, NH_2). Anal. Calc. for $C_{24}H_{18}N_6O_5$ (470.45): C, 61.28; H, 3.86; N, 17.86. Found: C, 61.19; H, 3.84; N, 17.81.

*3-(2-Aminophenyl)-8-(4-chlorophenyl)-2,6-dioxo-1,6-dihydro-2H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**16**)*

A mixture of **1a** (5 mmol) and isatine (5 mmol) in alcoholic NaOH (5%, 50 mL) was refluxed for 4 h, cooled and neutralized with conc. HCl. The solid so formed was filtered, washed several times with water and crystallized from DMF/H_2O to give **16** as yellow crystals, yield 46%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 3500-3336 (b, OH, NH_2), 2200 (2 C≡N), 1621 (C=O), 1548 (C=N). ^{1}H NMR (δ, DMSO): 4.87 (bs, 2H, NH_2), 7.23-8.10 (m, 8H, Ar-H), 11.62 ppm (bs, 1H, NH). Anal. Calc. for $C_{21}H_{11}ClN_6O_2$ (414.81): C, 60.81; H, 2.67; N, 20.26. Found: C, 61.04; H, 2.61; N, 20.14.

*8-Aryl-10-oxo-11-hydroindolo[2,3-e]pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles (**17a,b**)*

Compound **15** or **16** (2 mmol), glacial acetic acid (50 mL) and anhydrous sodium acetate (1 g) was refluxed for 12 h, after cooling the reaction mixture was concentrated. The solid so formed was filtered and crystallized to give **17a**,**b** (Table 2).

*Compound **17a***

Crystallized from acetic acid as orange crystals, yield 73%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 3491 (NH), 2996, 2943, 2834 (CH_3), 2218 (2 C≡N), 1667 (C=O), 1640 (C=N), 1587 (C=C), 1474, 1428 (def. CH_3). M/z (Int.%): 452 (3.27), 377 (4.24), 337 (6.63), 339 (12.68), 309 (6.34), 172 (23.44), 145 (40.44), 117 (65.03), 108 (36.31), 90 (19.88). Anal. Calc. for $C_{24}H_{16}N_6O_4$ (452.43): C, 63.71; H, 3.56; N, 18.58. Found: C, 63.59; H, 3.49; N, 18.45.

*Compound **17b***

Crystallized from DMF as orange-yellow crystals, yield 84%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 3381 (NH), 2202 (2 C≡N), 1622 (C=O). ^{1}H NMR (δ, DMSO): 6.80-7.82 (m, 8H, Ar-H), 12.30 ppm (s, 1H, NH). ^{13}C NMR (δ, DMSO): 75.19 (C_7-CN), 87.29 (C_9-CN), 116.22 (C≡N), 117.09 (C≡N), 129.65-135.95 (18C of aryl carbons), 157.48 (C_8 and C_{12a}), 159.26 (C_{5a}), 160 (C_{6a}), 163.17 ppm (C_{10} as C=O). M/z (Int.%): 396 (3.39), 368 (9.05), 319 (15.49), 285 (12.14), 254 (41.10), 209 (6.03), 117 (13.50), 111 (64.20), 57 (100). Anal. Calc. for $C_{21}H_9ClN_6O$ (396.80): C, 63.57; H, 2.29; N, 21.18. Found: C, 63.42; H, 2.25; N, 20.98.

*8-(3,4,5-Trimethoxy)-5-acetyl-10-oxo-11-hydroindolo[2,3-e]pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitrile (**18**)*

A mixture of **17a** (5 mmol) and acetic anhydride (10 mL) was refluxed for 2 h. The solid obtained after cooling was filtered, washed with cold ethanol and crystallized from acetic acid to give **18** as yellow crystals, yield 80%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 2999, 2947, 2840 (CH_3), 2216 (2 C≡N), 1695 (C=O), 1604 (C=N), 1583 (C=C), 1477, 1416 (def. CH_3). M/z (Int.%): 494 (5.57), 452 (3.27), 337 (4.62), 327 (5.89), 311 (7.01), 299 (6.69), 211 (8.76), 185 (5.57), 133 (8.28), 116 (10.35), 93 (10.67) and 55 (100). Anal. Calc. for $C_{26}H_{20}N_6O_5$ (494.47): C, 63.16; H, 3.67; N, 17.00. Found: C, 63.10; H, 3.54; N, 16.84.

*8-(3,4,5-Trimethoxyphenyl)-2-(2-acetylaminophenyl)-3,6-dioxo-3,6-dihydro-4H-pyrido[1,2-b] triazine-7,9-dicarbonitrile (**20**)*

A mixture of **1a** (5 mmol) and *N*-acetylisatine (5 mmol) in absolute ethanol (100 mL) and few drops of piperidine was refluxed for 4 h, after cooling the reaction mixture was concentrated. The solid obtained was filtered, washed with cold ethanol and crystallized from DMF to give **20** as orange crystals, yield 65%, mp > 300 ºC. IR (KBr) ν_{max}/cm^{-1}: 3452, 3283 (2NH), 2939, 2838 (CH_3), 2213 (2 C≡N), 1673, 1680 (3C=O), 1618 (C=N), 1589 (C=C), 1490, 1415 (def. CH_3). ^{1}H NMR (δ, DMSO): 2.02 (s, 3H, $COCH_3$), 3.79 (s, 3H, CH_3O), 3.83 (s, 6H, $2CH_3O$), 5.69 (s, 1H, NH), 6.85 (s, 1H, Ar-H of trimethoxy phenyl), 6.96 (s, 1H, Ar-H trimethoxy phenyl), 7.27 (s, 1H, Ar-H), 7.57 (s, 1H, Ar-H), 7.94 ppm (s, 2H, Ar-H), 10.8 (s, 1H, NH). Anal. Calc. for $C_{26}H_{20}N_6O_6$ (512.48): C, 60.94; H, 3.93; N, 16.40. Found: C, 60.91; H, 3.88; N, 16.35.

References

1. Abdel-Monem, W. R.; *Chem. Pap*. **2004**, *58*, 276; Attaby, F. A.; Eldin, S. M.; Abdel- Razik, M.; *Phosphorus, Sulfur Silicon Relat. Elem.* **1995**, *21*, 106; Elnagdi, M. H.; Ghozlan, S. A.; Abdel-Razik, F. M.; Maghraby, A. S.; *Chem. Synop*. **1991**, *5*, 116.
2. Fronabarger, J. W.; Chapman, R. D.; Gilardi, R. D.; *Tetrahedron Lett*. **2006**, *47*, 7707; Bhosale, R. S.; Sarda, S. R.; Ardhapure, S. S.; Jadhav, W. N.; Bhusare, S. R.; Pawar, R. P.; *Tetrahedron Lett.* **2005**, *46*, 7183; Harb, A. A.; *Chem. Pap*. **2004**, *58*, 260; Kuethe, J. T.; Wong, A.; Davies, I. W.; *J. Org. Chem*. **2004**, *69*, 7752.
3. Ganjali, M. R.; Norouzi, P.; Faridbod, F.; Ghorbani, M.; Adib, M.; *Anal. Chim. Acta* **2006**, *569*, 35; Gustaffon, B.; Hakansson, M.; Hutton, A. T.; Moss, J. R.; Jagner, S.; *Inorg. Chim. Acta* **2005**, *358*, 1327; Na, H.; Lee, D. C.; Lim, J. W.; Choi J. H.; Byun, J. C.; Park, Y. C.; *Polyhedron* **2002**, *21*, 917; Boghaei, D. M.; Mohebi, S.; *Tetrahedron* **2002**, *58*, 5357; Jeewoth, T.; Bhowon, M. G.; Wah, H. L. K.; *Transition Met. Chem*. **1999**, *24*, 445.
4. Abdel-Rahman, R. M.; *Trends Heterocycl. Chem. (India)* **2002**, *8*, 187; Abdel- Rahman, R. M.; *Pharmazie* **2001**, *56*, 275; Abdel-Rahman, R. M.; *Pharmazie* **2001**, *56*, 195.
5. Al-Najjar, A. A. A.; Amer, S. A.; Riad, M.; Elghamy, I.; Elnagdi, M. H.; *J. Chem. Res.* **1996**, 296.
6. Gindets, V. P.; Kherson, I.; Povstyanoi, M. V.; Kapov, P. B.; Grandberg, I. I.; *Ukr. Khim. Zh.* **1988**, *54*, 531. *(CA 110:75450v)*; Kang-Chien, L. S.; Jane-Bi; Tao-Tung, M.; *Zhonghua Yaoxue Zazhi* **1993**, *45*, 89. *(CA 119:203378c)*; Yamada, Y.; Kurokawa, S.; Yasuda, H.; *Utsunomiya Daigaku Kyoikugakubkiyo* **1993**, *43*, 35. (*CA 120:19162z*).
7. El-Gendy, Z.; Morsy, J. M.; Allimony, H. A.; Abdel-Monem, W. R.; Abdel-Rahman, R. M.; *Phosphorus, sulfur silicon Relat. Elem*. **2003**, *178*, 2055.
8. Abdel-Rahman, R. M.; Morsy, J. M.; Allimony, H. A.; Abdel-Monem, W. R.; *Boll. Chin. Farmaceutico* **1999**, *138*, 176.
9. Seada, M.; Abdel-Rahman, R. M.; Hanafy, F.; *Indian J. Chem. Soc*. **1992**, *69*, 882.
10. Juhasz-Riedel, Z.; Hajious, G.; Kollenz, R.; Massmer, A.; *Chem. Ber*. **1989**, *122*, 1935. (*CA 112:7454r*); Riedel, Z.; Hajious, G.; Kollenz, R.; Massmer, A.; *Monatsh Chem*. **1992**, 123, 1181. (*CA 118:254860u*).
11. Wiedermannova, I.; Jirovsky, D.; Hlavac, J.; Slouka, J.; *Chemica* **2000**, *39*, 69; Wiedermannova, I.; Slouka, J.; Hlavac, J.; *Chemica* **1999**, *38*, 83.
12. Dandi, A.; Sanno, S.; Bhagat, S.; Arya, K.; *Six International Electronic Conference on Synthetic Organic Chemistry*, *ecsoc-6*, 2002; http://www. mdpi.net/ecsoc-6.
13. Gould, J. C.; Bowie, J. M.; *Edinb. Med. J.* **1952**, *59*, 198; Singh, A.; Latita, R.; Dhakarey, R.; Saxena, G.; *J. Indian Chem. Soc*. **1996**, *73*, 339.

Received: September 16, 2008
Web Release Date: June 4, 2009