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Nitrogen bridgehead compounds, facile synthesis of bioactive cyanopyrimido[1,2-*a*]pyrimidinones

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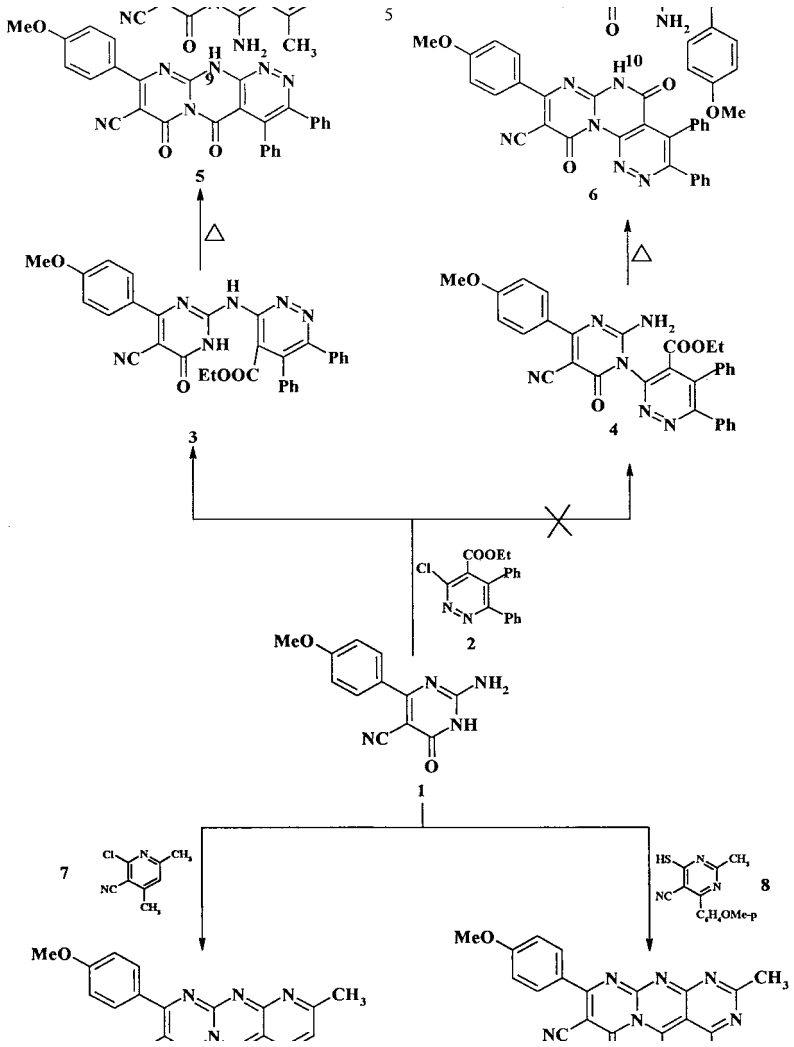
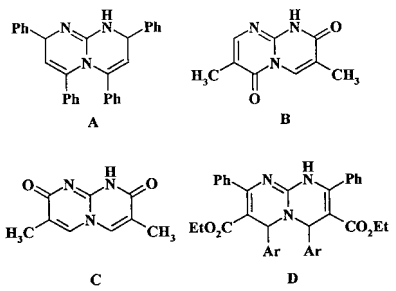
Synthesis of some new cyanopyrimido[1,2-*a*]pyrimidinones **5**–**22** have been achieved via interaction of 2-amino-6-anisyl-5-cyano-4(3*H*)-pyrimidinone (**1**) with some heterocycles having a vicinal chloroester, chlorocyano or mercaptocyano group, dimethyl acetylenedicarboxylate, active methylene compounds, ethyl 2-acetyl-3-anisylpropenoate, ethyl 3-aryl-3-cyanopropenoates, ethyl 2-cyano-3-ethoxyacrylate and some enones or enals. Some of the isolated products were subjected to biological screening tests.

1. Introduction

Various biological activities have been established for pyrimido-pyrimidines [1, 2]. It has been observed that these compounds reduce specification of crystalline lens in diabetic rats [3] and protect from brain injury in a combined model of permanent focal ischemia and global ischemia reperfusion [4]. They are used for inhibition of ferrous-induced lipid-peroxidation in Human liver membranes [5].

Scheme 1





A B C D

We have previously described the chemistry and biological activity of pyrimidines [6, 7] and pyrimidopyrimidinethiones [8, 9]. The present investigation aims to synthesize some new cyanopyrimido[1,2-*a*]pyrimidinones and to evaluate their cellobiase activity.

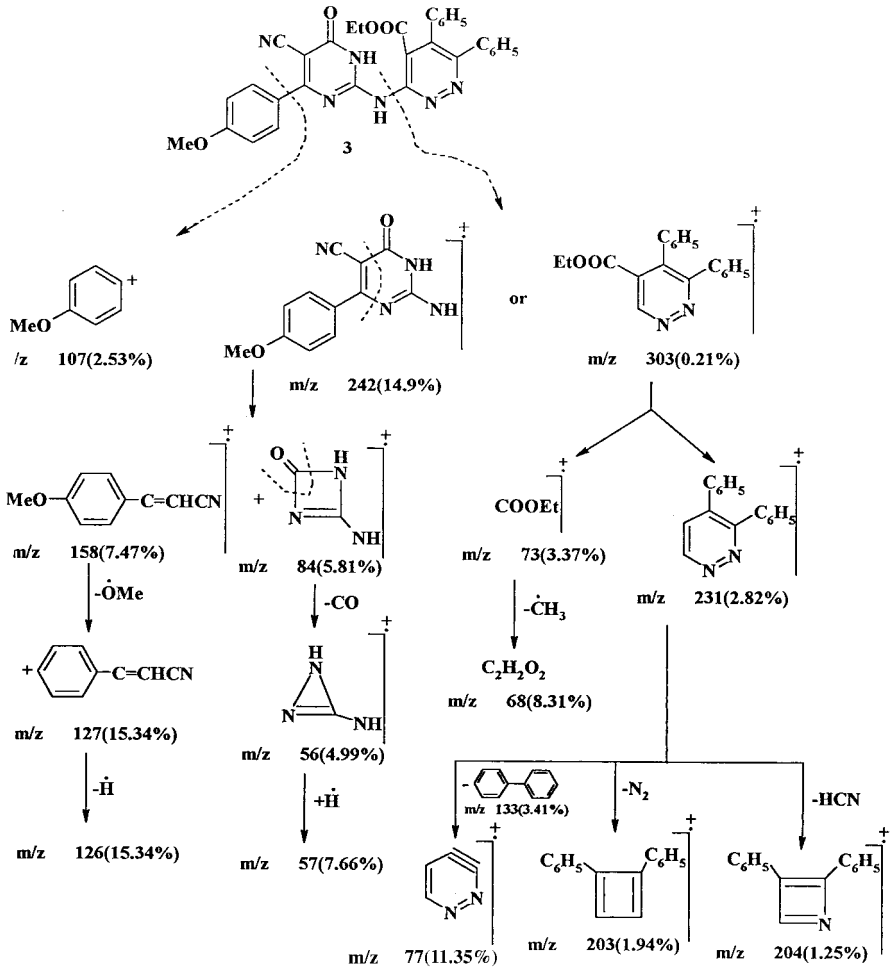
2. Investigations, results and discussion

2.1. Synthesis of the compounds

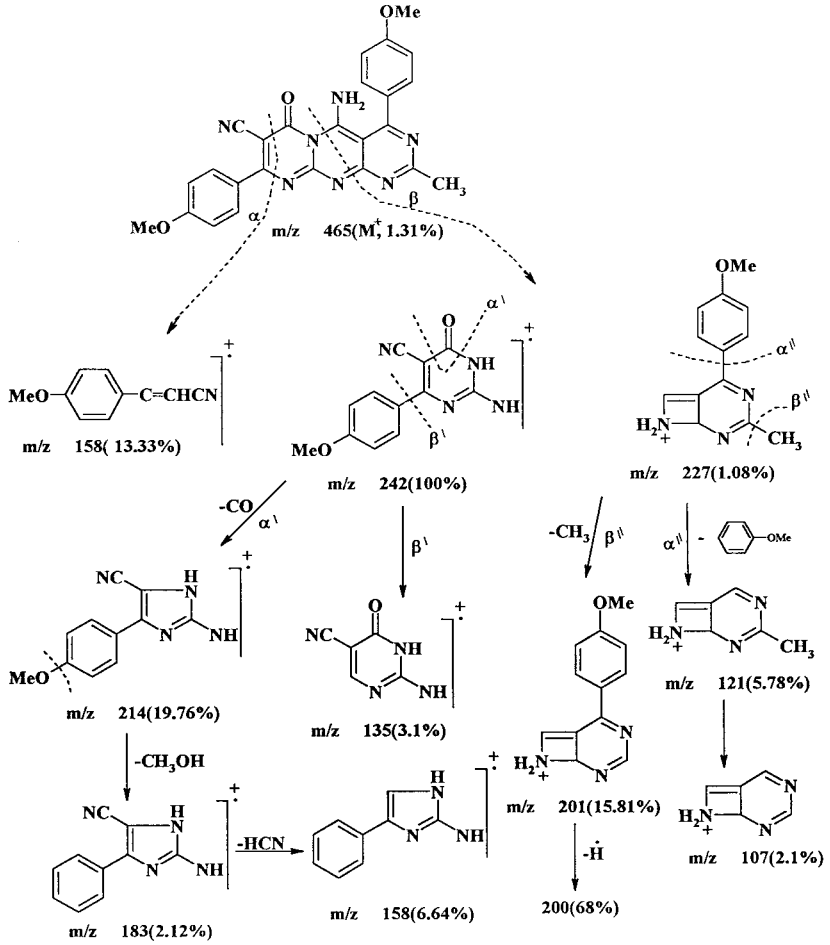
No examples for cyanopyrimido[1,2-*a*]pyrimidinones are reported in the literature. However, some structurally closely related compounds are known. 2,8-Dihydro-2,4,6,8-tetraphenyl-1 H-pyrimido[1,2-*a*]pyrimidine (**A**) was the result of the reaction of 1,3-diphenyl-2-propen-1-one with guanidine [10]. As by-product of a guanidine based thymine synthesis, 3,7-dimethyl-1*H*-pyrimido[1,2-*a*]pyrimidin-2,6-dione (**B**) or the corresponding 2,8-dione **C** were isolated [11]. Also, 3,7-diethoxycarbonyl-4,6-dihydro-2,4,6,8-tetraaryl-1*H*-pyrimido[1,2-*a*]pyrimidine (**D**) was obtained from the reaction of ethyl 3-aryl-2-benzoylpropenoate with guanidine [12].

For developing synthetic routes for the preparation of pyrimido[1,2-*a*]pyrimidinone we prepared 2-amino-6-anisyl-5-cyano-4(3*H*)-pyrimidinone (**1**) as starting material [8]. When compound **1** was allowed to react with some heterocycles having two vicinal groups, such as a chloro, ester, cyano or mercapto group, some new nitrogen bridgehead systems containing a cyanopyrimido[1,2-*a*]pyrimidinone moiety often condensed with different heterocyclic systems were produced. Thus, treatment of **1** with 3-chloro-4-ethoxycarbonyl-5,6-diphenylpyridazine (**2**) yielded a product via HCl elimination. This product has one of two possible isomeric structures **3** and **4** (Scheme 1). Structure **3** was preferred over the possible isomer **4** based on the ^{1}H NMR spectrum, which revealed a signal at $\delta = 11.3$ ppm for the endocyclic NH proton of the pyrimidine ring. If this product were the isomer **4**, the amino signals at $\delta = 3.89$ ppm should have been observed with the absence of a signal characteristic for the endocyclic NH proton of the pyrimidine ring. Also, the EI-MS fully support the structure assignments for isomer **3** (Scheme 2), which on heating above its m.p. afforded 9-anisyl-8-cyano-3,4-diphenyl-11*H*-pyridazino[3,4-*d*]pyrimido[1,2-*a*]pyrimidine-5,7-dione (**5**) and not 6-anisyl-5-cyano-10,11-diphenyl-8*H*-pyridazino[3,4-*d*]pyrimido[1,2-*a*]pyrimidine-4,9-dione (**6**) (Scheme 1). In reaction of **1** with 2-chloro-3-cyano-4,6-dimethylpyridine (**7**) or 5-cyano-2-methyl-6-anisyl-4(3*H*)-pyrimidinethione (**8**), one-pot ring closure took place giving rise to 6-amino-2-anisyl-3-cyano-7,9-dimethylpyrido[2,3-

Scheme 2



Scheme 3



d]pyrimido[1,2-*a*]pyrimidine-4-one (**9**) and the cyano dipyrimido-pyrimidinone **10**, respectively (Scheme 1). The EI-MS of compound **10** showed the expected molecular ion peak and other characteristic peaks shown in Scheme 3.

The heterocyclic amidine **1** was readily converted into 7-cyanoxpyrimido[1,2-*a*]pyrimidine-2,6-dione (**11**) when reacted with dimethyl acetylenedicarboxylate in the presence of catalytic amounts of pyridine [13]. Treatment of compound **1** with ethyl acetoacetate in boiling DMF yielded 8-anisyl-7-cyano-4-methyl-1*H*-pyrimido[1,2-*a*]pyrimidin-2,6-dione (**12**). The structure of compound **12** was confirmed by its elemental analysis and spectroscopic data. Refluxing compound **1** with ethyl 3-aryl-2-cyanopropenoate in pyridine for a few hours provided the dicyanopyrimido[1,2-*a*]pyrimidindiones **13a**, **b,** while the reaction of **1** with ethyl 2-acetyl-3-anisylpropenoate in DMF/NaOEt afforded 4,8-dianisyl-7-cyano-3-ethoxycarbonyl-2-methyl-1,4-dihydropyrimido[1,2-*a*]pyrimidin-6-one (**14**) [12]. When compound **1** was allowed to react with ethyl ethoxymethylenecyanoacetate in ethanol containing catalytic amounts of triethylamine, 4-amino-8-anisyl-3-ethoxycarbonyl-7-cyanopyrimido[1,2-a]pyrimidin-6-one (**15**) was produced (Scheme 4).

β-Dicarbonyl reagents such as diethyl malonate, acetylacetone [13] and benzoylacetanilide [14] reacted with compound **1** to give the corresponding cyanopyrimido[1,2-*a*]pyrimidindiones **16**–**18**. Active methylene compounds such as a ω-cyanoacetophenone derivative gave 2-amino-8-anisyl-4-(*p*-bromophenyl)-7-cyanopyrimido[1,2-*a*]pyrimidin-6-one (**19**) when reacted with heterocyclic amidine **1** in acetic acid containing fused sodium acetate (Scheme 4).

On the other hand, the 7-cyano-2,4,8-triarylpyrimido[1,2-*a*]pyrimidin-6-ones **20a**–**c** were obtained upon refluxing compound **1** with the appropriate enones in acetic acid-fused sodium acetate mixture. The structures of these compounds were consistent with their elemental analysis and spectral data, e.g. the EI-MS of **20c** showed some expected peaks as shown in Scheme 5.

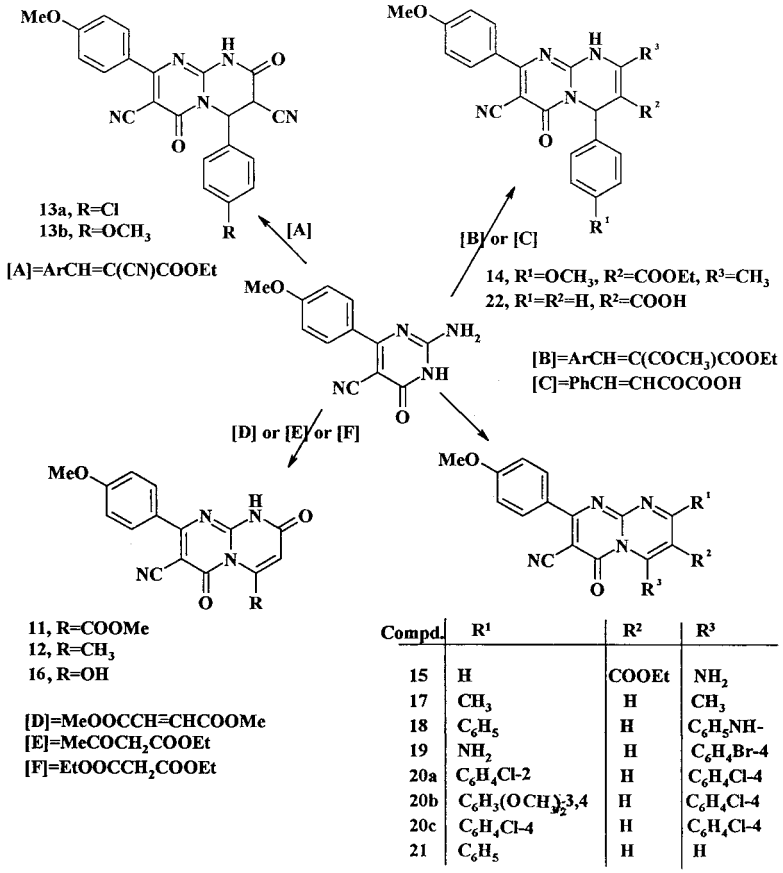
Similar reaction occurred on treatment of **1** with cinnamaldehyde which led directly to the formation of 7-cyano-2,8-diarylpyrimido[1,2-*a*]pyrimidin-6-one (**21**). Also, α,β-unsaturated ketoacid (obtained from condensation [15] of pyruvic acid with benzaldehyde) reacted with the cyclic amidine **1** to furnish 7-cyanopyrimido[1,2-*a*]pyrimidin-6-one **22**. The structure of **22** was deduced from acidity test, elemental analysis and spectral data (Scheme 4).

2.2. Biological activity

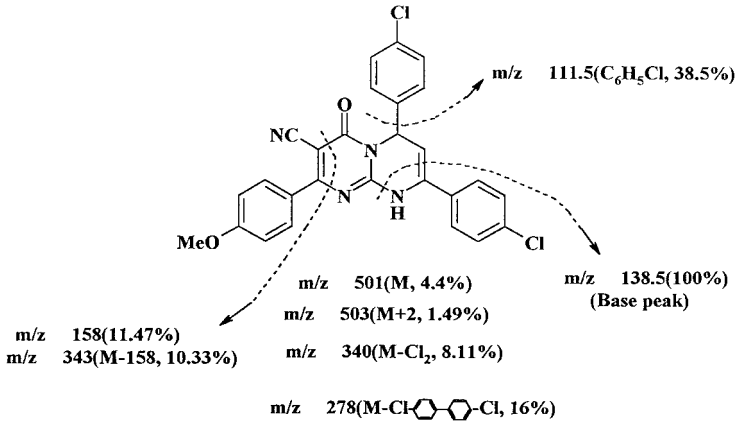
As a part of a research program directed to the selection of some new synthesized cyanopyrimidine derivatives [9, 19, 20], we investigated their potential activity towards the enzyme cellobiase produced by thermophilic fungi. Such an activity has great industrial importance especially in production of glucose syrups from inexpensive cellulosic by-products. In the present work, the effect of some novel cyanopyrimidopyrimidinones on the activity of the enzyme cellobiase produced by the thermotolerant fungus *Absidia corymbifera* was studied.

The tested compound (10 mg) was dissolved in DMF (1 ml) and added to the assay mixture which consisted of 0.5 ml enzymatic solution and 4.5 ml citrate phosphate

Scheme 4



Scheme 5



buffer (pH = 5.0) containing cellobiase (1%). The assay mixture was incubated at 40 °C for 30 min and the amount of glucose released was estimated colorimetrically (Speakol-K) at λ = 505 nm as indicated for cellobiase activity using the glucose oxidase method [21, 22].

A control assay mixture was prepared containing 1 ml DMF without the tested compound and a blank mixture, 1 ml of distilled water.

The results are recorded in the Table. The amount of produced glucose in the case of compounds **20a** and compound **20c** is due to the presence of a bicyclic guanidine moiety with several chlorine atoms, while compounds **10**, **11**, **12** and **14** have no effect on the cellobiase activity.

Regarding the structure-activity relationship it is clear that only one compound, **20a**, had a considerable effect in comparison with the other tested compounds, which con-

Table: Effect of synthesized compounds on cellobiase activity

Compound	Amount of glucose produced (μg/ml)
3	1.74
10	0.00
11	0.00
12	0.00
13a	0.72
14	0.00
15	0.14
16	0.26
17	0.20
18	0.46
20a	3.43
20c	2.42

Blank: 0.592 μg/ml; control 1.8 μg/ml

firms that this type of compounds can be used as co-enzymatic factor in acceleration of cellobiase activity.

3. Experimental

M.p's reported are not corrected. IR spectra were obtained (KBr) on a Perkin-Elmer 598 spectrophotomer (ν cm^{-1}), ^1H NMR were measured on Bruker 200 M Hz 152 MM spectrometer using DMSO-d_6 as a solvent and TMS as internal standard (chemical shifts in δ, ppm) and MS were recorded using a MS 5988 spectrometer (70 eV). All the results of elemental analyses were in an acceptable range.

3.1. 2-Amino-6-anisyl-5-cyano-4(3H)-pyrimidinone (**1**)

A mixture of guanidine hydrochloride (0.012 mol) and ethyl 3-anisyl-2-cyanopropenoate (0.015 mol) in sodium ethoxide (0.23 g Na in 30 ml absolute ethanol) was refluxed for 6 h, cooled, poured into crushed ice and neutralized with acetic acid. The solid obtained was filtered off and recrystallized from DMF/H_2O to give **1** as colourless crystals, m.p. 260–261 °C, yield 96%; IR (cm^{-1}): ν 3400–3200 (NH, NH_2), 2200 (C≡N), 1700 (CO); ^1H NMR (DMSO-d_6): δ 3.6 (s, 3 H, OCH_3), 3.8 (s, 2 H, NH_2) 7.2–7.6 (m, 4 H, aromatic protons), 11.3 (s, 1 H, endocyclic NH proton, disappeared on D_2O exchange). m/z 242 (M^+).
$C_{12}H_{10}N_4O_2$

3.2. 3-Chloro-4-ethoxycarbonyl-5,6-diphenylpyridazine (**2**)

This compound was prepared as described in the literature [16].

3.3. 6-Anisyl-5-cyano-2-[5,6-diphenyl-4-ethoxycarbonylpyridazin-3-yl amino]pyrimidin-4(3 H)-one (3)

A mixture of **1** (0.01 mol) and **2** (0.011 mol) in DMF (30 ml) was refluxed for 4 h and poured into cold H_2O. The solid produced was filtered off and recrystallized from EtOH to give **3** as pale yellow crystals, m.p 110 °C. Yield 86%, IR (cm^{-1}): ν 3320 (NH), 2900 (aliphatic CH), 2220 (C≡N). 1720 and 1680 (C=O); ^1H NMR (DMSO-d_6) δ 0.8 (t, 3 H, ethyl ester), 3.2 (s, 1 H exocyclic NH), 3.6 (s, 3 H, OCH_3), 3.8 (q, 2 H, $COCH_2$–), 7.1 (m, 14 H, Ar–H), 11.3 (s, 1 H, endocyclic NH proton, disappeared on D_2O exchange). m/z 544 (M^+) (Scheme 2).
$C_{31}H_{24}N_6O_5$

3.4. 9-Anisyl-8-cyano-3,4-diphenyl-11H-pyridazino[3,4-d]pyrimido[1,2-a]-pyrimidin-5,7-dione (**5**)

Compound **3** (1.0 g) was heated above its m.p. for 30 min, then treated with cold H_2O. The solid obtained was filtered off and recrystallized from DMF-H_2O to give **5** as yellow crystals m.p. 250–251 °C (yield 68%); IR (cm^{-1}): ν 3340 (NH), 2200 (C≡N), 1700, 1680 (C=O), ^1H NMR (DMSO-d_6) δ 3.6 (s, 3 H, OCH_3), 7.2–7.6 (m, 15 H, Ar–H and NH).
$C_{29}H_{18}N_6O_3$

3.5. 2-Chloro-3-cyano-4,6-dimethylpyridine (**7**)

Compound **7** was prepared as described in the literature [17].

3.6. 5-Cyano-4-mercapto-2-methyl-6-phenylpyrimidine (**8**)

Compound **8** was prepared as described previously [18].

3.7. 6-Amino-2-anisyl-3-cyano-7,9-dimethylpyrido[2,3-d]pyrimido[1,2-a]-pyrimidine-4-one (**9**)

A mixture of **1** (0.01 mol) and **7** (0.01 mol) in DMF (30 ml) containing fused sodium acetate (1 g) was refluxed for 8 h, cooled and poured into cold H_2O. The solid obtained was filtered off and recrystallized from DMF to produced **9** as pale yellow crystals, m.p. >290 °C (Yield 75%), IR (cm^{-1}), ν 3420–3130 (NH_2), 2210 (C≡N). 1690 (C=O); ^1H NMR (DMSO-d_6): δ 1.1 (s, 3 H, C_7–CH_3), δ 1.3 (s, 3 H, C_9–CH_3), 3.2 (s, 2 H, NH_2), 3.6 (s, 3 H, OCH_3), 7.6 (m, 5 H aromatic protons and C_9–H).
$C_{20}H_{16}N_6O_2$

3.8. 5-Amino-4,9-dianisyl-8-cyano-2-methylpyrimido[4,5-d]pyrimido-[1,2-a]pyrimidin-7-one (**10**)

A mixture of **1** (0.01 mol) and **8** (0.01 mol) in abs. EtOH (50 ml) containing triethylamine (1 ml) was heated under reflux for 6 h, cooled and the solid obtained collected and recrystallized from abs. EtOH to give **10** as pale yellow crystals, m.p. >280 °C (yield 75%), IR (cm^{-1}): ν 3410–3220 (NH_2), 2200 (C≡N). 1710 (C=O); ^{1}HNMR (DMSO-d_6): δ 1.6 (s, 3 H, CH_3), 3.2 (s, 2 H, NH_2), 3.5 (s, 3 H, OCH_3), 3.6 (s, 3 H, OCH_3), 7.2–4.6 (m, 8 H, Ar–H).
$C_{25}H_{19}N_7O_3$

3.9. 8-Anisyl-7-cyano-4-methoxycarbonyl-1H-pyrimido[1,2-a]pyrimidin-2,6-dione (**11**)

Equimolecular amounts of **1** and dimethyl acetylenedicarboxylate were treated with catalytic amounts of pyridine (1 ml) and stirred at RT for 3 h, then triturated with EtOH. The solid obtained was collected and recrystallized from acetic acid to produce **11** as yellow crystals; m.p. 240 °C (yield 65%), IR (cm^{-1}): ν 3400 (NH), 2200 (C≡N). 1690, 1660 (C=O); ^1H NMR (DMSO-d_6): δ 3.6 (s, 3 H, OCH_3), 4.2 (s, 3 H, methyl ester), 7.6 to 6.8 (m, 5 H, Ar–H), 11.1 (s, 1 H, NH). M/z 352 (M^+).
$C_{17}H_{12}N_4O_5$

3.10. 8-Anisyl-7-cyano-4-methyl-1H-pyrimido[1,2-a]pyrimidin-2,6-dione (**12**)

A mixture of **1** (0.01 mol) and ethyl acetoacetate (0.012 mol) in absolute ethanol (30 ml) was refluxed for 3 h, cooled and poured into crushed ice. The solid obtained was filtered off and recrystallized from butanol to produce **12** as pale yellow crystals, m.p. 255 °C (yield 54%), IR (cm^{-1}): ν 3340 (NH), 2200 (C≡N). 1710–1690 (C=O); ^1H NMR (DMSO-d_6): δ 1.8 (s, 3 H, CH_3), 3.5 (s, 3 H, OCH_2), 7.6–7.2 (m, 5 H, Ar–H), 11.0 (s, 1 H, NH).
$C_{16}H_{12}N_4O_3$

3.11. 4,8-Diaryl-3,7-dicyano-1,3,4-trihydropyrimido[1,2-a]pyrimidin-2,6-diones (**13a, b**)

An equimolar amount of **1** and ethyl 3-anisyl- or 3-(p-chloro-phenyl)-2-cyanopropenoate in pyridine (30 ml) were refluxed for 3 h, cooled and poured into crushed ice and neutralized with dil. HCl. The solid produced was filtered off and recrystallized from the proper solvent to give **13a**, **13b** respectively.
13a: m.p. 245 °C (yield 55%), IR (cm^{-1}): ν 3400 (NH), 2220 and 2200 (C≡N), 1710 (C=O) $C_{22}H_{14}N_5Cl$
13b: m.p. 240 °C (yield 65%), IR (cm^{-1}): ν 3300 (NH), 2220 and 2200 (C≡N), 1710 (CO); ^1H NMR (DMSO-d_6): δ 3.5 (s, 3 H, OCH_3), 3.7 (s, 3 H, OCH_3), 6.7–7.8 (m, 8 H, Ar–H), 11.3 (s, 1 H, NH). $C_{23}H_{17}N_5O_4$

3.12. 4,8-Dianisyl-7-cyano-3-ethoxycarbonyl-2-methyl-1,4-dihydropyrimido[1,2-a]pyrimidin-6-one (**14**)

A mixture of **1** (0.01 mol) and ethyl 2-acetyl-3-anisylpropenoate (0.01 mol) in DMF (30 ml)/NaOEt (0.29 g Na in 20 ml abs. EtOH) mixture was refluxed for 4 h, cooled and pour into crushed ice containing conc. HCl (1 ml). The solid obtained was recrystallized from DMF-H_2O to afford **14** as pale yellow crystals, m.p. 275 °C (yield 86%), IR (cm^{-1}): ν 3400 (NH), 2220 (C≡N). 1720–1680 (C=O); ^1H NMR (DMSO-d_6): δ 0.8 (t, 3 H, CH_3 ester), 1.8 (s, 3 H, CH_3), 3.5 (s. 3 H, OCH_3), 3.6 (s, 3 H, OCH_3), 3.8 (q, 2 H, CH_2, ester), 6.7–7.9 (m, 8 H, Ar–H), 11.7 (s, 1 H, NH).
$C_{26}H_{23}N_4O_5$

3.13. 4-Amino-8-anisyl-3-ethoxycarbonyl-7-cyanopyrimido[1,2-a]-pyrimidin-6-one (**15**)

A mixture of **1** (0.01 mol) and ethyl ethoxymethylene cyanoacetate (0.012 mol) in ethanol (30 ml) containing triethylamine (1 ml) was refluxed for 1 h, then the solvent was evaporated. The solid obtained was collected and recrystallized from absolute ethanol to give **15** as pale yellow crystals, m.p. 290 °C (yield 78%), IR (cm^{-1}): ν 3410, 3370 (NH_2), 2190 (C≡N), 1690 (C=O); ^1H NMR (DMSO-d_6): δ 1.3 (t, 3 H, CH_3), 3.6 (s, 3 H, OCH_3), 4.2 (q, 2 H, CH_2), 7.6–8.1 (m, 5 H, Ar–H), 9.0 (br. s, 2 H, NH_2).
$C_{18}H_{15}N_5O_4$

3.14. 8-Anisyl-7-cyano-1,3-dihydropyrimido[1,2-a]pyrimidin-2,4,6-trione (**16**)

A mixture of **1** (0.01 mol) and diethyl malonate (0.012 mol) in dry toluene (20 mol) containing *p*-toluenesulphonic acid (1 ml) was refluxed for 6 h, then the solvent was evaporated. The solid obtained was collected and recrystallized from DMF to yield **15** as yellow crystals, m.p. >280 °C (yield 62%), IR (cm^{-1}): 3450, 3360 (NH, OH), 2200 (C≡N), 1690 (C=O).
$C_{15}H_{10}N_4O_4$

3.15. 8-Anisyl-7-cyano-2,4-dimethylpyrimido[1,2-a]pyrimidin-6-one (17)

A mixture of **1** (0.01 mol) and acetylacetone (0.012 mol) in dry toluene (10 mol) was refluxed for 3 h, cooled and diluted with MeOH (15 ml). The resulting solid was washed with cold MeOH, filtered and crystallized from MeOH to give **17** as pale yellow crystals, m.p. 280 °C (yield 66%), IR (cm^{-1}): ν 2220 (C≡N), 1690 (C=O).
$C_{17}H_{14}N_4O_2$

3.16. 8-Anisyl-4-anilino-2-phenylpyrimido[1,2-a]pyrimidin-6-one (**18**)

A mixture of **1** (0.01 mol) and benzoylacetanilide (obtained by fusion of ethyl benzoylacetate with aniline) (0.012 mol) in DMF (30 mol) containing

fused sodium acetate (1 g) was refluxed for 6 h, cooled and poured into cold H_2O the solid obtained was filtered off and washed with cold MeOH to give **18** as yellow crystals, m.p. 280 °C (yield 88%), IR (cm^{-1}): ν 3330 (NH), 2210 (C≡N), 1690 (C=O).
$C_{27}H_{19}N_5O_2$

3.17. 2-Amino-8-anisyl-4-(4-bromophenyl)-7-cyanopyrimido[1,2-a]-pyrimidin-6-one (**19**)

A mixture of **1** (0.01 mol) and *p*-bromobenzoyl acetonitrile (0.01 mol) in acetic acid (30 ml) containing fused sodium acetate (2 g) was refluxed for 3 h, cooled and poured into cold H_2O. The solid obtained was filtered off and recrystallized from DMF-water to give **19** as yellow crystals, m.p. >280 °C. (yield 68%), IR (cm^{-1}): ν 3430, 3360 (NH_2), 2200 (C≡N), 1710 (C=O); ^{1}H NMR (DMSO-d_6): δ 3.5 (s, 3 H, OCH_3), 7.9–6.9 (m, 9 H, Ar–H), 9.1 (br. s, 2 H, NH_2).
$C_{21}H_{14}N_5O_2Br$

3.18. 7-Cyano-2,4,8-triarylpyrimido[1,2-a]pyrimidin-6-one (**20a–c**)

A mixture of **1** (0.01 mol) and appropriate enones (obtained by condensation of acetophenone derivative with aromatic aldehydes)
(0.01mol) in acetic acid (30 ml) containing fused sodium acetate (2 g) was refluxed for 8 h, cooled and poured into crushed ice. The solid produced was collected and recrystallized from the proper solvent to give **20a–c.**
20a: 8-anisyl-2-(4-chlorophenyl)-4-(2-chlorophenyl)-7-cyano derivative; m.p. 248 °C (yield 82%) IR (cm^{-1}): ν 3320 (NH), 2200 (C≡N), 1710 (C=O)
20b: 8-anisyl-2-(4-chlorophenyl)-4-(3,4-dimethoxyphenyl)-7-cyano derivative; m.p. 230 °C. (yield 84%) IR (cm^{-1}): ν 3340 (NH), 2210 (C≡N), 1700 (C=O)
20c: 8-Anisyl-2,4-(bis-4-chlorophenyl)-7-cyano derivative; m.p. 220 °C. (yield 88%), IR (cm^{-1}): ν 3340 (NH), 2200 (C≡N), 1690 (C=O), ^{1}H NMR (DMSO-d_6): δ 3.6 (s, 3 H, OCH_3), 3.2 (s, 1 H, NH), 6.0–7.6 (m, 14 H, Ar–H), m/z 501 (M^+) (Scheme 5).
$C_{27}H_{16}N_4O_2Cl_2$

3.19. 8-Anisyl-7-cyano-2-phenylpyrimido[1,2-a]pyrimidin-6-one (**21**)

A mixture of **1** (0.01 mol) and cinnamaldehyde (0.012) in acetic acid (30 ml) containing fused sodium acetate (2 g) was refluxed for 8 h, cooled and pour into cold H_2O. The solid is filtered off and recrystallized from butanol to give **21** as yellow crystals, m.p. >300 °C (yield 78%), IR (cm^{-1}): ν 3420 (NH), 2220 (C≡N), 1700 (C=O); ^{1}H NMR (DMSO-d_6): δ 3.2 (s, 2 H, CH_2), 3.6 (s, 3 H, OCH_3), 6.8–7.8 (m, 10 H, Ar–H), m/z 356 (M^+).
$C_{21}H_{14}N_4O_2$

3.20. 8-Anisyl-2-carboxy-4-phenyl-3,4-dihydropyrimido[1,2-a]pyrimidin-6-one (**22**)

A mixture of **1** (0.01 mol) and 2-oxo-4-phenyl-butenoic acid (0.011 mol) in DMF (30 ml) was refluxed for 3 h, cooled. The solid obtained was collected and recrystallized from DMF to yield **22** as brownish crystals, m.p. 280 °C. (yield 82%), IR (cm^{-1}): ν 2890 (OH), 2200 (C≡N), 1720, 1680 (C=O); ^{1}H NMR (DMSO-d_6): δ 3.6 (s, 3 H, OCH_3), 6.9–7.5 (m, 10 H, Ar–H), 9.0 (s, H, NH), 11.2 (s, 1 H, OH).
$C_{22}H_{15}N_4O_4$

Acknowledgement: The author is very grateful to Dr. Usama F. Ali, Biological Department, Faculty of Education, Ain-Shams University, Roxy, Cairo, Egypt, for evaluation of the cellobiase activity.

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Received June 4, 1999

Accepted August 24, 1999

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