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A Facile Three-Steps, One-Pot Synthesis of Novel 2-Alkylamino and 2-Dialkylamino-4H-Pyrido [1, 2-A][1,3,5] Triazin-4-Ones from 2-Aminopyridine and 2-Aminopicolines

Said Dagdag[1, 2], Mounir Belbahloul[3, 4], Mohamed Anouar[5], Maria Kopp[2], Abdellah Anouar[3], Mohamed Hmyene[6]

[1] University Hassan first. Settat, Morocco. Laboratory of Environmental and Development Sciences. Ecological chemistry team, Faculty of Science and Technology.

[2] Normandy Center for Studies and Research on Medicines, Faculty of Pharmaceutical Sciences, University of Caen. 5, rue Vaubénard, 14032 Caen Cedex, France.

[3] University Hassan first. Settat, Morocco. Applied Chemistry and Environment Laboratory, Faculty of Science and Technology.

[4] University Hassan first.. Settat, Morocco. Health Sciences and Technology Laboratory, higher institute of health sciences.

[5] University Hassan first. Settat, Morocco. physico-chemistry of processes and materials Laboratory, Faculty of Science and Technology.

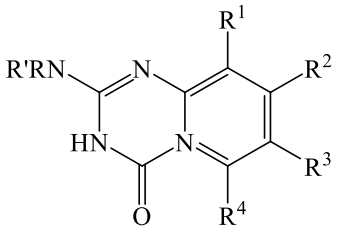
[6] University Hassan first. Settat, Morocco. Matter and Instrumentation Radiation Laboratory, Faculty of Science and Technology.

ABSTRACT: A straightforward approach to novel 2-dialkylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones synthesis is presented. The construction of these compounds was achieved by one-pot synthesis involving condensation of 2-aminopyridine or 2-aminopicolines with ethoxycarbonylisothio cianate, followed by amination of the thioureas, and finally thermal ring closure of resulting guanidines. This allowed access to the unreported title heterocycles. We described an efficient, facile, one-pot synthesis of a novel 2-dialkylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones in order to obtain a library of pyridotriazines which will be used as building blocks in medicinal chemistry.

KEYWORDS: Heterocycles, Infrared and Masse Spectroscopy, NMR spectroscopy, pyridotriazines, Synthesis.

1. INTRODUCTION

The dialkylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones skeleton is common in the structure of many natural and synthetic products associated with a broad spectrum of biological activities and pharmaceutical properties[1, 2]. In contrast with 2-dialkylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones,which have extensively been used as building blocks in medicinal chemistry, few studies have addressed their analogues. To our knowledge, no reports have appeared concerning the synthesis of pyrido[1,2-a][1,3,5] triazin -4-onesskeleton $4_{a\text{-}e}$ (Figure1).



a. $R^1=R^3=R^4=H$
b. $R^1=CH_3$, $R^2=R^3=R^4=H$
c. $R^2=CH_3$, $R^1=R^3=R^4=H$
d. $R^3=CH_3$, $R^1=R^2=R^4=H$
e. $R^4=CH_3$, $R^2=R^2=R^3=H$

Figure 1: Target molecules $4_{a\text{-}e}$ 2-dialkylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones

It is interesting to find a facile and efficient methodology to synthesize this hitherto unknown annulated pyridine ring system. The relevance of pyrido[1,2-a][1,3,5]triazin-4-onessystemarises from its wide biological activity, which stems from its antagonistic effect upon 5-HT_2 and 5-HT_{2a} serotonin receptors. Such effect can result in: mediating coronary blood flow[1], decreasing mean arterial blood pressure [3] and the antithrombotic effect in mammals [4]. Pyrido[1,2-a][1,3,5]triazine derivatives properties can be

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used for prophylactic effect [2] or therapeutic treatment of other disorders such as: airway constriction in human or animals: asthma, emphysema, chronic bronchitis, chronic obstructive pulmonary disease [5], as well as various psychotic conditions including schizophrenia, depression, anorectic or bulimic eating disorders, and anxiety in humans [5]. Thymidine phosphorylase (TP) has been implicated inpath physiological angiogenesis, anti-apoptosis and tumor growth [6,7].The pyrido[1,2-a][1,3,5]triazines analogues, as potential TP inhibitors.

Oda *et al*. [7], described the syntheses of oligomers containing the new artificial C-deoxyribo nucleosides bearing pyrido[1,2-a][1,3,5]triazin-4-onederivatives. Some of C-deoxyribo nucleosides were able to convert to phosphoramidite reagents, which can be used for DNA synthesizers. In addition, the co-planarity and linearity [8,9] of this heterocyclic system could favor DNA intercalation and potentially provide anticancer compounds.

Demeunynck *et al.*[10] published a synthetic route to the 2-alkylaminoquinolino[2,3-f] quinazolin-1-one skeleton from 3-aminoacridine. The authors followed Manimala and Anslyn's methodology [11] by condensing the aminoacridines with ethoxycarbonylisothiocyanate followed by coupling with aliphatic amines anddeprotection of the N-protected guanidine intermediates 5. That was ideally positioned to react by intramolecular Friedel-Crafts type substitution to form, in one step the fused pyrimidinone ring 6 (Figure 2).

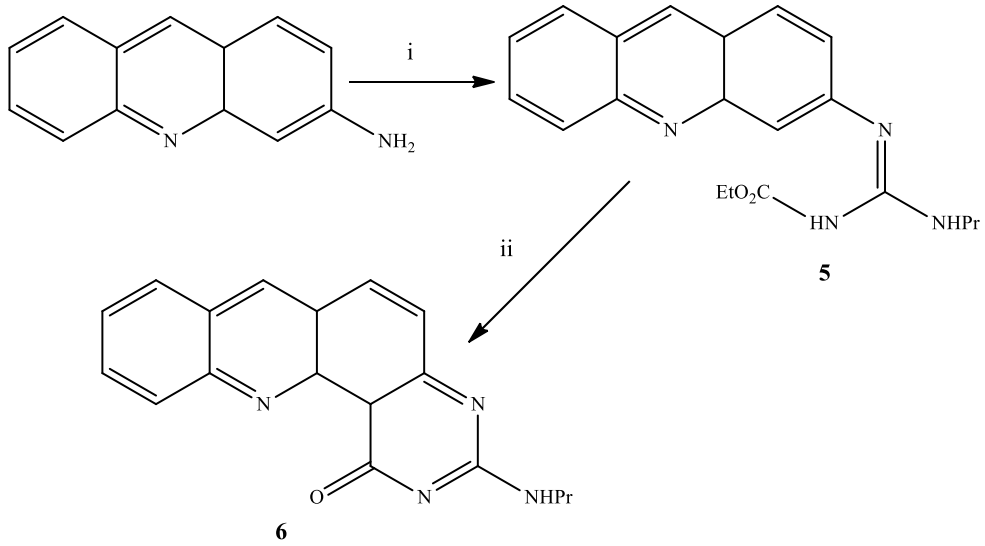

Figure 2: Formation of quinazolino[2,3-*f*]quinazolin-1-*2H*-one skeleton 6 from 3-aminoacridine

Reagents and conditions:
i) EtOOCNCS, DMF, rt. **ii)** Et_3N, RNH_2, EDCI(1-ethyl-3-(3-dimethylaminopropyl)carbodiimide), DMF, rt.

The same paper [10] also described a two-step methodology for substituted 2-propylamino quinazolin-4(*3H*)-ones from simple aromatic or heteroaromatic amines (Figure 3). The preparation of ethoxycarbonylguanidines was performed in one pot by careful control of the stoichiometry of the reagents successively added to the chosen aromatic amine dissolved in CH_2Cl_2. In most cases, the resulting protected guanidines were easily isolated with excellent levels of purity by simple precipitation from water.

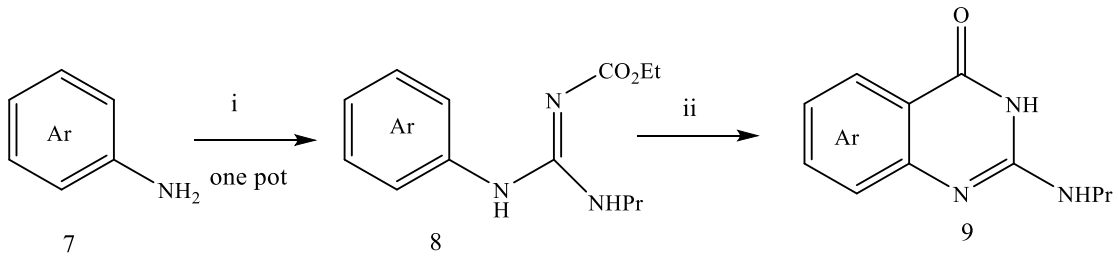

Figure 3: Preparation of 2-propylaminoquinazolin-4(3H)-one 9

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Reagents and conditions:
i) EtOOCNCS 1,2 equiv, CH_2Cl_2, rt, 90min, then Et_3N 3 equiv, $PrNH_2$ 2 equiv and EDCI 1,2 equiv, 6h, rt.
ii) $ClSiMe_3$5 or10 equiv, DMF, 80°C.

On the other hand, we ourselves published [14] in 2002 a quasi-one-pot synthesis of 2-amino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones from 2-aminopyridine (Figure 4). The isolation of the intermediates was not necessary and this sequence became applicable to parallel chemistry techniques.

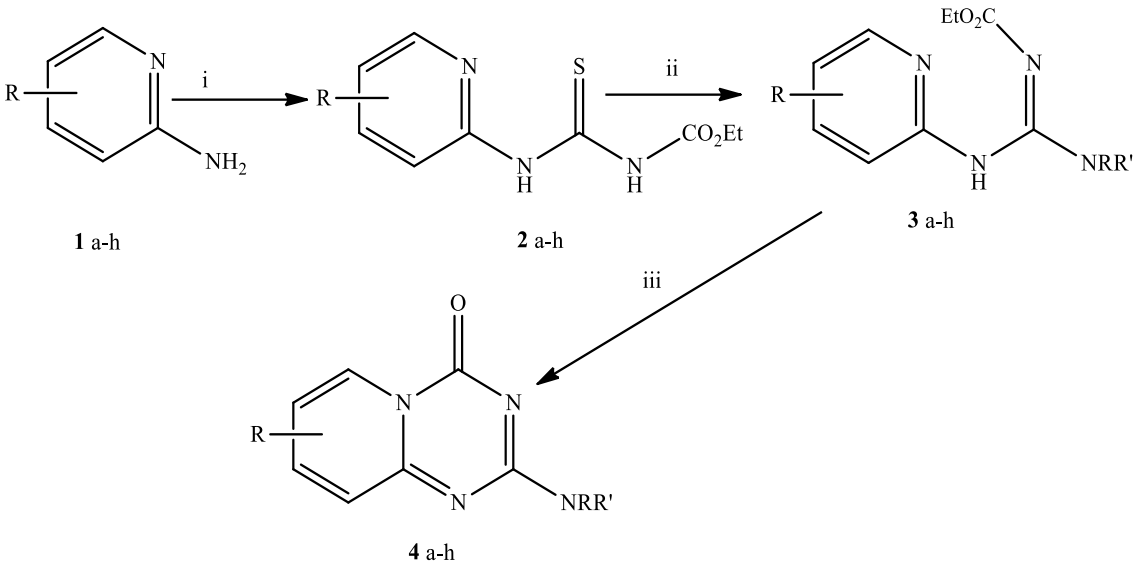

Figure 4: Synthesis of 2-dialkylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones ($4_{a\text{-}e}$) from 2-aminopyridines ($1_{a\text{-}e}$).

i) SCN-CO_2Et, DMF, rt, 2h **ii)** HNRR', $HgCl_2$, DMF, 0 - 5°C then rt, 4h **iii)** quasi one-pot: HCl, dioxane**. iii)** one-pot: DMF, 80°C, 2h

Primas *et al.* [12] have recently studied one pot syntheses of pyrimidocarbazole starting from 3-aminocarbazoles. In another paper, the same authors [13] described a three-steps methodology, one pot synthesis of novel 2-alkyl(aryl)amino and 2-dialkylamino-*7H*-[1,3,5]triazino[3,4-*b*] pyridoilndol-4-one andderivatives starting 3-amino-β-carbolines in similar conditions to our work [14]. Finally, this project aims at synthesizing series of pyrido[1, 2-*a*][1,3,5]triazines analogues [14], *via* ring annulations, as potential TP inhibitors. In the following, we will report a new simple and efficient one-pot synthesis of hitherto unknown title compounds.

2. EXPERIMENTAL SECTION

Commercial reagents were purchased from Aldrich. Acros Organics and used as received without additional purification. Melting points were determined on a Kofler melting point apparatus and are uncorrected. Elemental analyses were performed at the "Institut de Recherche en Chimie Organique Fine" (Rouen, France) and they were found to be within ± 0.4% of theoretical values. IR spectra were taken with a Genisis Series FTIR spectrometer. Mass spectra were taken on JEOL. JMS GCM ate spectrometer at the ionizing potential of 70 eV (EI) or were performed using a LC-MS Waters Alliance 2695 (ESI+) spectrometer. ^{1}HNMR (400 MHz) and ^{13}CMR (100 MHz) spectra were recorded on a JEOL Lambada 400 spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. The organic extract was dried over $MgSO_4$ and evaporated under reduced pressure. Thin layer chromatography (TLC) was performed on silica gel 60F-264 (Merck). The filtration was carried out using celite 545 (Prolabo). 2-amino-5-iodo was prepared as reported in the literature [15].

General procedure for synthesis of 2-dialkylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones using $HgCl_2$ ($1_{a\text{-}e}$)

A mixture of 2-aminopyridine $1_{a\text{-}e}$ (0.02 mol) and ethoxycarbonylisothiocyanate (0.02 mol) in anhydrous DMF (100 ml) was stirred at rt. for 2 hours to form the N-ethoxycarbonyl-N'-(pyridine-2-yl) thiourea intermediate $2_{a\text{-}e}$. The reaction mixture was then

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cooled (0 ± 5°C) before saturation with the appropriate secondary amine (0.05 mol if the amine is not a gas) and the addition of mercuric chloride $HgCl_2$ (0.02 mol) was added successively under stirring. The temperature was allowed to reach rt. and stirring was continued at this temperature overnight. The reaction mixture was then heated under reflux for 2 hours; the black color which appeared was due to the formation of mercuric sulfide HgS, filtered through a celite pad. The filtrate was concentrated under reduced pressure and the solid precipitate was triturated with recrystallized solvent, filtered, dried, and then recrystallized from a large volume of solvent.

2-Amino-*4H*-pyrido[1, 2-*a*][1,3,5]triazin-4-one (4a$_1$)

Recrystallization of the crude product from acetonitrile gave 4a$_1$a white powder (1.55 g, 48 %), mp > 260°C; IR(KBr): υ 3287, 3119, 1713, 1630 cm $^{-1}$; ^{1}HNMR (DMSO-d$_6$): 8.60 (d, J = 6.84 Hz, 1H), 7.86 (dd, J = 8.92 Hz, J = 6.68 Hz,1H), 7.24 (s, 2H), 7.12 (d, J = 8.92 Hz, 1H), 7.00 (dd,J = 6.84 Hz, J = 6.68 Hz,1H), ^{13}CN, 78.7. Anal. Calcd for $C_7H_6N_4O$ [M$^+$] 162, found: [MH$^+$] 162. Anal.Calcd. for$C_7H_6N_4O$: C: 51.85, H: 3.73, N: 34.55, Found: C: 51.56, H: 3.55, N: 34.62.

2-Dimethylamino-4H-pyrido[1,2-a][1,3,5]triazin-4-one (4a2)

Recrystallization of the crude product from ether gave 4a$_2$a yellow powder (1.94 g, 51 %), mp 135°C; IR (KBr): υ 3085, 1715, 1637 cm^{-1}; ^{1}HNMR (DMSO-d$_6$): 8.59 - 8.58 (d, J = 6.84 Hz, 1H), 7.87-7.83 (t, J = 8.16 Hz, J = 7.44 Hz,1H),7.10 (d, J = 8.88Hz,1H), 6.94 (m,1H),3.09 (s,3H), 3.03 (s,3H); ^{13}CNMR(DMSO-d$_6$): 161.6, 154.8, 149.9, 141.5, 129.3,122.8, 113.9, 36.5, 36.3; MS, m/z = 190 (M$^+$), 175, 161, 146, 119, 78, 67. Anal. Calcd. for $C_9H_{10}N_4O$: C: 56.83; H: 5.83, N: 29.46, Found: C: 56.78, H: 5.34, N: 29.61.

2-Diethylamino-*4H*-pyrido[1,2-a][1,3,5]triazin-4-one (4a$_3$)

Recrystallization of the crude product from acetonitrile gave 4a$_3$ a white powder (1.66 g, 38 %), mp 176 °C; IR (KBr): υ 2974, 1683, 1633 cm^{-1}; ^{1}HNMR (DMSO-d$_6$):8.59 (d, J = 6.84Hz,1H), 6.99 (m,1H), 3.60 (q, J = 6.96 Hz, 2H), 3.53 (q, J = 6.84 Hz, 2H), 1,12 (t, J = 6.96 Hz, 3H), 1.11(t, J = 6.84 Hz, 3H), ^{13}CNMR (DMSO-d$_6$): 160.6, 155.0, 149.9, 141.3, 129.3,122.8, 113.7, 41.2, 41.0, 13.4, 12.9; MS, m/z = 218 (M$^+$), 203, 189, 146, 120,78.7. Anal. Calcd. for $C_{11}H_{14}N_4O$: C: 60.53, H: 6.47, N: 25.67, Found: C: 60.68, H: 6.32, N: 25.56.

2-Dipropylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4a$_4$)

Recrystallization of the crude product from petroleum ether gave 4a$_4$ a yellow powder (1.92 g, 39 %), mp 90 °C; IR (KBr): υ 2962, 1710, 1631 cm $^{-1}$; ^{1}HNMR (DMSO-d$_6$): 8.58 (d, J = 6.96 Hz, 1H), 7.83 (dd, J = 8.88 Hz, J = 6.76 Hz,1H), 7.14 (d, J = 8.88 Hz,1H), 6.98 (m,1H), 3.50 (m, 2H), 3.44 (m, 2H), 1.56 (m, 4H), 0.84 (t, J = 7.00 Hz, 6H); ^{13}CNMR (DMSO-d$_6$): 161.2, 154.8, 149.8, 141.3, 129.2, 122.8, 113.7, 48.5, 48.3, 20.9, 20.4,11.2, 10.9; MS, m/z = 246 (M$^+$), 231.1, 175.1, 146.1, 120.1, 78.5. Anal. Calcd. for $C_{13}H_{18}N_4O$: C: 63.39; H: 7.37, N: 22.75, Found: C: 63.16, H: 7.41, N: 22.65.

2-Isopropylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4a$_5$) Recrystallization of the crude product from ether gave 4a$_5$ a white powder (0.60 g, 15 %), mp 139 °C; IR (KBr): υ 3212, 1720, 1595 cm $^{-1}$; ^{1}HNMR (DMSO-d$_6$): 8.55 (d, J = 6.72 Hz, 1H), 7.83 (dd, J = 8.80 Hz, J = 6.76 Hz,1H), 7.66 (d, J = 7.20 Hz,1H), 7.20 (d, J = 8.80 Hz, 1H), 6.93 (m,1H), 4.12(m, 1H), 1.13 (d, J = 5.72 Hz,6H); ^{13}CNMR (DMSO-d$_6$): 160.8, 155.0, 149.8, 141.4, 129.2, 122.7, 113.8, 44.3, 22.5; MS, m/z = 204.2 (M$^+$), 189.2, 146, 119.4, 78.4, 45.8. Anal. Calcd. for $C_{10}H_{12}N_4O$: C: 58.81, H: 5.92, N: 27.43, Found: C: 58.92, H: 5.86, N: 27.34.

2-Cyclohexylamino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4a$_6$)

Recrystallization of the crude product from acetonitrile gave 4a$_6$ a grey powder (1.05 g, 21 %), mp 180 °C; IR (KBr): υ 3211, 2925, 1717, 1595; ^{1}HNMR(DMSO-d$_6$): 8.55 (d, J = 6.84 Hz, 1H), 7.80 (dd, J = 8.28 Hz, J = 6.84 Hz,1H), 7.03 (d, J = 8.28 Hz,1H), 6.93 (m, 1H), 3.73 (m, 1H), 3.35 (br, 1H), 1.80 (m, 2H), 1.68 (m, 2H), 1.56 (m, 1H), 1.24 (m, 4H), 1.08 (m, 1H); ^{13}CNMR (DMSO-d$_6$): 161.8, 155.6, 150.3, 141.6, 129.5,122.8, 113.8, 49.0, 32.4, 24.7; MS, m/z = 244,2 (M$^+$), 216.2, 187.1, 162.1, 120.1, 99.1, 94.1, 78.7. Anal. Calcd. for $C_{13}H_{16}N_4O$: C: 63.90,H: 6.60, N: 22.94, Found: C: 64.03, H: 6.42, N: 22.66.

2-amino-9-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4b$_1$)

Recrystallization of the crude product from acetonitrile gave 4b$_1$ a white powder (1.40 g, 40 %), mp > 260 °C; IR (KBr): υ 3377, 3155, 1690, 1647 cm^{-1}; ^{1}HNMR(DMSO-d$_6$): 2.27 (s,3H), 6.91 (dd, J = 6.76 Hz, J =6.56 Hz, 1H), 7.27 (s,2H), 7.74 (d, J = 6.76 Hz,1H), 8.50 (d, J = 6.56 Hz,1H); ^{13}CNMR (DMSO-d$_6$): 164.2, 155.4, 150.5, 139.0, 130.7, 126.9, 112.5, 16.4; MS, m/z =176.0 (M $^+$) ;161.0; 150.0; 134.0; 108.0; 92 ;81.6.

2-Propylamino-9-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4b$_2$)

Recrystallization of the crude product from acetonitrile gave 4b$_2$ a white powder (2.22g, 51 %), mp 146 °C; IR (KBr): υ3530, 3045, 1726, 1652 cm^{-1}; ^{1}HNMR (DMSO-d$_6$), temperature at 100 °C: 0.90(t, J = 7.27 Hz, 3H), 1.57 (m,2H), 2.29(s, 3H), 3.29 (m,2H)6.86

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IJCSRR @ 2022
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(m, 1H), 7.41 (m, 1H), 7.67(m, 1H), 8.48(m, 1H); ^{13}CNMR (DMSO-d_6): 162.5, 154.6, 150.8, 145.1, 127.2, 124.8, 122.6, 42.6, 17.7, 12.1; MS, m/z = 218 (M^+), 203, 189, 175.99, 159.98, 134, 92, 84.

2-Isopropylamino-9-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4b$_3$)

Recrystallization of the crude product from acetonitrile gave 4b$_3$ a white powder (2.22g, 51 %), mp 196 °C; IR (KBr): υ 3225, 3086, 1716, 1645 cm^{-1}; ^{1}HNMR (DMSO-d_6), temperature at 100°C: 1.18 (d, J = 6.67 Hz, 6H), 2.29 (s, 3H), 4.16 (m,1H), 6.86 (m, 1H), 7.25 (m, 1H), 8.49 (m, 1H); ^{13}CNMR (DMSO-d_6): 161.75, 153.84, 150.12, 142.96, 122.62, 121.68, 121.75, 41.80, 23.10, 17.12; MS, m/z = 218 (M^+), 203, 176, 160, 134, 108, 92, 84.

2-Cyclohexylamino-9-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4b$_4$)

Recrystallization of the crude product from acetonitrile gave 4b$_4$ a white powder (3.01g, 70 %), mp 176 °C; IR (KBr): υ 3232, 3086, 1720, 1642 cm^{-1}; ^{1}HNMR (DMSO-d_6): 1.08 (m, 1H, H_c), 1.25 (m, 3H, 3 H_c), 1.50 at 1.80 (m, 6H, 2.24 (s, 3H,4H_b ,2H_d), 2.24 (s, 3H), 3.76 (m, 1H), 6.85 (s, 1H), 7.67 (m, 1H, H_a), 7.67 (m,1H), 7.71 (m, 1H), 8.45 (m, 1H).; ^{13}CNMR (DMSO-d_6): 161.84, 155.12, 152.92, 137.04, 115.20, 112.35, 106.95, 49.06, 32.10, 25.12, 22.95; MS, m/z = 258 (M^+), 200, 176, 132, 98, 84.

2-Diethylamino-9-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4b$_5$)

Recrystallization of the crude product from acetonitrile gave 4b$_5$ a white powder (1.84g, 40 %), mp124 °C; IR (KBr): υ 3180, 3070, 1670, 1610 cm^{-1}; ^{1}HNMR (DMSO-d_6): 1.10 (m, 6H), 2.20(s, 3H), 3.52 (m, 2H), 3.57 (m, 2H), 6.84 (dd, J = 5.87 Hz, J = 6.95 Hz, 1H), 7.66 (d, J = 5.87 Hz,1H), 8.43 (d, J = 6.95Hz, 1H); ^{13}CNMR (DMSO-d_6): 160.07, 154.25, 150.18, 138.87, 130.73, 126.81, 112.65, 41.62, 41.06, 16.46, 13.00, 12.91; MS, m/z = 232 (M^+) ,217, 203, 160, 134, 92.0.

2-Dipropylamino-9-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4b$_6$)

Recrystallization of the crude product from acetonitrile gave 4b$_6$ a white powder (1.66g, 32 %) , mp112 °C; IR (KBr): υ 2970, 2930, 1720, 1650 cm^{-1}; ^{1}HNMR (DMSO-d_6): 0.84(m, 6H), 1.55(m, 4H), 2.21(s, 3H), 3.42(t, ^{3}J = 15.30 Hz, 2H), 3.49(t, ^{3}J = 15.30 Hz, 2H), 6.85(dd, J = 6.75 Hz, J = 6.87 Hz, 1H), 7.67(d, J = 6.75 Hz,1H), 8.43(d, J = 6.87Hz, 1H) ; ^{13}CNMR (DMSO-d_6): 160.66, 154.20, 150.23, 138.96, 130.78, 126.86, 112.74, 48.98,48.42, 20.82, 20.50, 16.45, 11.35, 11.15; MS, m/z = 260 (M^+) ,231, 188.9, 159.9, 133.9, 92, 86, 72.9.

2-Diisopropylamino-9-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4b$_7$)

Recrystallization of the crude product from acetonitrile gave 4b$_7$ a white powder (1.61 g, 31 %) , mp 112 °C; IR (KBr): υ 2974, 2925, 1705, 1645 cm^{-1}; ^{1}HNMR (DMSO-d_6): 1.18 (d, ^{3}J = 6.31 Hz, 6H), 1.37 (d, ^{3}J = 6.19 Hz, 6H), 2.26 (s, 3H), 4.08 (m, 1H), 4.79 (t, 1H), 6.84 (dd, J = 6.95 Hz, J = 6.83 Hz, 1H), 7.68 (d, J = 6.95 Hz,1H), 8.43 (d, J = 6.83Hz, 1H) ; ^{13}CNMR (DMSO-d_6): 160.21, 153.82, 149.96, 138.83, 130.79, 126.79, 112.62, 45.65,45.41, 20.47, 19.74, 16.94; MS, m/z = 260 (M^+) ,217, 134, 92, 84.3.

2-amino-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4c$_1$)

Recrystallization of the crude product from acetonitrile gave 4c$_1$ a pink powder (2.21g, 63 %), mp> 260 °C; IR (KBr): υ 3378 - 3300, 3150,1680, 1642 cm^{-1}; ^{1}H NMR (DMSO-d_6): 2.37 (s,3H), 6.78(m,2H), 6.86 (d, J = 7.20 Hz, 1H), 6.92 (s,1H), 8.51 (d, J = 7.20Hz,1H); ^{13}C NMR (DMSO-d_6): 164.3, 155.0, 152.6, 149.6, 128.0, 119.7, 115.5, 20.4; MS, m/z = 176.0(M^+), 161.0, 150.0, 134.0, 108.0, 92.

2-Propylamino-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4c$_2$)

Recrystallization of the crude product from acetonitrile gave 4c$_2$ a white powder (1.31g, 30 %), mp 138 °C; IR (KBr): υ 3520, 3035, 1730, 1650 cm^{-1}; ^{1}HNMR (DMSO-d_6), temperature at 100 °C: 0.90 (t, J = 14.47 Hz, 3H), 1.56 (m,2H), 2.36 (s, 3H), 2.28 (m,2H), 6.82 (m, 1H), 6.91(s, 1H),7.16 (m, 1H) 8.49 (m, 1H); ^{13}CNMR (DMSO-d_6): 163.1, 155.2, 150.5, 144.7, 127.0, 125.2, 123.1, 42.2, 23.1, 17.5, 12.1; MS, m/z =218 (M^+), 203, 189, 176, 160, 134, 108, 92, 84.3.

2-Isopropylamino-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4c$_3$))

Recrystallization of the crude product from acetonitrile gave 4c$_3$ a white powder (1.18g, 27 %), mp 212 °C; IR (KBr): υ 3230, 3090, 1712, 1644 cm^{-1}; ^{1}HNMR (DMSO-d_6), temperature at 100 °C: 1.17 (m, 6H), 2.36 (s, 3H), 4.14 (m,1H), 6.81 (m, 1H),6.90 (s, 1H) 7.00 (m, 1H), 8.49 (m, 1H); ^{13}CNMR (DMSO-d_6): 162.20, 154.10, 150.30, 143.75, 127.30, 122.72, 121.82, 42.10, 22.30, 17.20; MS, m/z = 218 (M^+), 203,189, 176, 160, 134, 108, 92.

2-Diethylamino-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4c$_5$)

Recrystallization of the crude product from acetonitrile gave 4c$_5$ a white powder (2.09g, 45 %), mp 124 °C; IR (KBr): υ 3180, 3069, 1667, 1603 cm^{-1}; ^{1}HNMR (DMSO-d_6): 1.15 (m, 6H), 2.33 (s, 3H), 3.53 (m, 4H), 6.85 (s, 1H), 7.02 (s,1H), 8.48 (s, 1H); ^{13}CNMR

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(DMSO-d_6): 161.60, 155.00, 150.20, 128.30, 121.10, 113.00, 41.70, 41.10, 16.50, 13.05, 12.95; MS, m/z = 232 (M^+) ,217, 203,189, 160, 134,108.9, 92, 81.6.

2-Dipropylamino-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4c$_6$)

Recrystallization of the crude product from acetonitrile gave 4c$_6$ a white powder (2.25g, 43 %), mp 112 °C; IR (KBr): υ 2961, 2932, 1713, 1648 cm^{-1}; ^{1}HNMR (DMSO-d_6): 0.85(t, ^{3}J = 7.00 Hz, 6H), 1.56 (m, 4H), 2.33(s, 3H), 3.42 (t, ^{3}J = 7.00 Hz, 2H), 3.50 (t, ^{3}J = 7.00 Hz, 2H), 6.85(d, J = 6.68 Hz, 1H), 7.00 (s,1H), 8.48 (d, J = 6.68Hz, 1H); ^{13}CNMR (DMSO-d_6): 161.4, 154.50, 149.90, 128.50, 120.70, 116.00, 48.50,48.30, 20.90, 20.50, 11.20; MS, m/z = 260 (M^+), 231, 217, 189, 160,134,108, 92.

2-Diisopropylamino-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4c$_7$)

Recrystallization of the crude product from acetonitrile gave 4c$_7$ a white powder (2.08g, 40 %), mp 112 °C; IR (KBr): υ 2963, 2930, 1707, 1652 cm^{-1}; ^{1}H NMR (DMSO-d_6): 1.27 (m, 12H), 2.34 (s, 3H), 4.47 (m, 2H), 6.84 (d, J = 7.07 Hz, 1H), 6.99 (s, 1H), 8.47 (d, J = 7.07Hz, 1H); ^{13}C NMR (DMSO-d_6): 160.89, 153.81, 152.49, 149.07, 128.00, 120.40, 115.00, 45.40,45.23, 20.47, 20.07; MS, m/z = 260 (M^+) ,217, 133, 99,92, 84.

2-amino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4d$_1$)

Recrystallization of the crude product from acetonitrile gave 4d$_1$ a white powder (2.29g, 65 %), mp> 260 °C; IR (KBr): υ 3266 ,3092 ,1719 ,1671, 1644 cm^{-1}; ^{1}HNMR (DMSO-d_6):2.28(s,3H), 6.81 (m, 2H), 7.07(d, J = 8.7 Hz, 1H), 7.74 (d, J = 8.7 Hz, 1H), 8.45 (s,1H); ^{13}CNMR (DMSO-d_6): 164.0, 154.2, 150.5, 149.8, 143.4, 126.2, 112.7,121.6 16.8; MS, m/z = 176.0(M^+), 134.0, 92.

2-Propylamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4d$_2$)

Recrystallization of the crude product from acetonitrile gave 4d$_2$ a white powder (2.40g, 65 %), mp 140 °C; IR (KBr): υ 3525 ,3044-2963 ,1728 ,1649 cm^{-1}; ^{1}HNMR (DMSO-d_6), temperature at 100 °C: 0.89 (m, 3H), 1.54 (m,2H), 2.26 (s, 3H), 3.26 (m,2H), 7.04 (m, 1H), 7.27(m, 1H),7.70 (m, 1H), 8.42 (s, 1H); ^{13}C NMR (DMSO-d_6): 162.7, 154.5, 150.6, 144.6, 126.8, 124.4, 122.4, 42.4, 22.6, 17.6, 11.7; MS, m/z = 218 (M^+), 189, 160, 134, 108, 92.

2-Isopropylamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4d$_3$)

Recrystallization of the crude product from acetonitrile gave 4d$_3$ a white powder (2.40g, 55 %), mp 206°C; IR (KBr): υ 3222, 3094 - 2968, 1714, 1649 cm^{-1}; ^{1}HNMR (DMSO-d_6), temperature at 100°C: 1.10 (d, J = 6.5 Hz, 6H), 2.26 (s, 3H), 4.15 (m,1H), 7.05 (m, 1H),7.12(m, 1H), 7.70 (m, 1H), 8.41(s, 1H); ^{13}CNMR (DMSO-d_6): 161.50, 153.93, 149.58, 143.46, 126.27, 122.51, 121.67, 41.75, 22.19, 17.15; MS, m/z = 218 (M^+), 203, 176, 160, 134, 108, 92.

2-Cyclohexylamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4d$_4$)

Recrystallization of the crude product from acetonitrile gave 4d$_4$ a beige sheet powder (1.81g, 35 %), mp = 260 °C; IR (KBr): υ 3224, 3094-2924, 1715, 1649 cm^{-1}; ^{1}HNMR (DMSO-d_6): 1.30 (m, 5H), 1.60 at 1.86 (m, 6H), 2.26 (s, 3H), 3.18 (m, 1H), 7.15 (m, 1H), 7.71 (m,1H), 8.41 (s, 1H); ^{13}CNMR (DMSO-d_6): 161.92, 155.15, 153.75., 136.52, 114.87, 112.18, 107.15, 48.85, 31.95, 25.04, 23.75; MS, m/z = 258 (M^+), 224,201, 176, 143, 133, 99.

2-Diethylamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4d$_5$)

Recrystallization of the crude product from diethyl ether gave 4d$_5$ a white powder (3.06g, 66 %), mp 90°C; IR (KBr): υ 2969, 2932, 1712, 1644 cm^{-1}; ^{1}HNMR (DMSO-d_6): 1.09 (d, J = 4.47 Hz, 6H), 2.22 (s, 3H), 3.5 (q,^{3} J = 13.70 Hz, 2H), 3.56 (q, ^{3} J = 13.70 Hz, 2H), 7.05 (d, J = 8.95 Hz, 1H), 7.68 (d, J = 8.95 Hz 1H), 8.38 (s, 1H); ^{13}CNMR (DMSO-d_6): 160.00, 153.75, 149.76, 143.63, 126.33, 123.07, 122.28, 41.09, 40.89, 13.33, 12.90; MS: m/z = 232 (M^+), 203,189, 160, 134,108, 92.

2-Dipropylamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4d$_6$)

Recrystallization of the crude product from acetonitrile gave 4d$_6$ a white powder (2.70g, 52 %), mp120°C; IR (KBr): υ 3023, 2961, 1720, 1649 cm^{-1}; ^{1}HNMR (DMSO-d_6): 0.85 (t, ^{3}J = 13.27 Hz, 6H), 1.57 (m, 4H), 2.24(s, 3H), 3.43 (t, ^{3}J = 14.26 Hz, 2H), 3.50 (t, ^{3}J = 13.90 Hz, 2H), 7.10 (d, J = 8.95 Hz, 1H), 7.73 (d,, j = 8.95 Hz1H), 8.42(s, 1H) ; ^{13}CNMR (DMSO-d_6): 161.06, 153.70, 149.82, 143.76, 126.37, 123.17,122.40, 48.48,48.27, 20.44, 18.92, 17.18, 11.15, 10.96; MS, m/z = 260 (M^+), 217, 203, 160,134 92.

2-Diisopropylamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4d$_7$)

Recrystallization of the crude product from acetonitrile gave 4d$_7$ a white powder (2.60g, 50 %), mp210°C; IR (KBr): υ2970, 2930, 1710, 1650 cm^{-1}; ^{1}HNMR (DMSO-d_6): 1.30 (d, J = 3.75 Hz, 12H), 2.25 (s, 3H), 4.45 (m, 2H), 7.10 (d, J = 8.59 Hz, 1H), 6.99 (s, 1H), 7.72 (d, J = 8.59Hz, 1H), 8.41 (s, 1H); ^{13}CNMR (DMSO-d_6): 160.68, 153.22, 149.45, 143.58, 126.24, 123.00, 122.41, 45.53,45.40, 20.59, 20.02,17.19; MS, m/z = 260 (M^+), 231,217, 189,160, 134, 92, 72.

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2-Morpholino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4d$_8$)

Recrystallization of the crude product from acetonitrile gave 4d$_8$ a white powder (2.42g, 49 %), mp 208°C; IR (KBr): υ 3093 - 2945, 1702, 1646 cm^{-1}; ^{1}HNMR (DMSO-d$_6$): 2.26 (s, 3H), 3.61 (m, 4H), 3.77 (m, 4H), 7.15 (d, J = 8.51 Hz, 1H), 7.79 (d, J = 8.51Hz, 1H), 8.45 (s, 1H); ^{13}CNMR (DMSO-d$_6$): 160.69, 153.99, 149.00, 144.22, 126.64, 123.83, 122.33, 65.95, 43.76, 17.21; MS, m/z = 246 (M$^+$), 231.

2-amino-6-methyl-4H-pyrido[1,2-a][1,3,5]triazin-4-one (4e$_1$)

Recrystallization of the crude product from acetonitrile gave 4e$_1$ a white powder (2.29g, 65 %), mp > 260 °C; IR (KBr): υ 3266 ,3092 ,1719 ,1671, 1644 cm^{-1}; ^{1}HNMR (DMSO-d$_6$):2.29(s, 3H), 6.87 (dd, J = 6.65, J = 6.67 1H), 7.27 (s, 2H), 7.74 (d, J = 6.65 Hz, 1H), 8.50 (d, J = 6.67 Hz, 1H); ^{13}CNMR (DMSO-d$_6$): 164.2, 154.2, 150.5, 139.00, 130.75, 126.2, 112.50, 16.40; MS: m/z = 176.0(M$^+$); 161, 150, 134, 108, 92.

2-Diethylamino-6-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4e$_2$)

Recrystallization of the crude product from diethylether gave 4e$_2$a white powder (1.84g, 40 %), mp 122°C; IR (KBr): υ 3110 - 3070, 1690, 1640 cm^{-1}; ^{1}HNMR (DMSO-d$_6$): 1.11 (m, 6H), 2.26 (s, 3H), 3.53 (m, 2H), 3.58 (m, 2H), 6.43 (d, J = 8.15 Hz, 1H), 6.48 (d, J = 7.50 Hz 1H), 7.32(m, 1H); ^{13}CNMR (DMSO-d$_6$): 160.13, 154.12, 150.23, 138.92, 130.70, 126.63,112.59, 41.72, 41.32, 16.48, 13.03, 12.93; MS: m/z = 232 (M$^+$), 217, 203, 160, 134, 92.

2-Dipropylamino-6-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4e$_3$)

Recrystallization of the crude product from acetonitrile gave 4e$_3$ a white powder (2.15g, 41 %) , mp 120°C; IR (KBr): υ 2961, 2930, 1699, 1614 cm^{-1}; ^{1}HNMR (DMSO-d$_6$): 0.84 (t,^{3}J = 13.27 Hz, 6H), 1.57 (m, 4H), 2.24 (s, 3H), 3.43 (t, ^{3}J = 14.26 Hz, 2H), 3.50 (t, ^{3}J = 13.90 Hz, 2H), 7.10 (d, J = 8.95 Hz, 1H), 7.73 (d,, j = 8.95 Hz1H), 8.42 (s, 1H) ; ^{13}CNMR (DMSO-d$_6$): 161.06, 153.70, 149.82, 143.76, 126.37, 123.17,122.40, 48.48,48.27, 20.44, 18.92, 17.18, 11.15, 10.96; MS: m/z = 260 (M$^+$), 217, 203, 160,134 92.

2-Diisopropylamino-6-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (4e$_4$)

Recrystallization of the crude product from acetonitrile gave 4e$_4$ a white powder (2.16g, 42 %), mp 128°C; IR (KBr): υ 2960, 2930, 1700, 1614 cm^{-1}; ^{1}HNMR (DMSO-d$_6$): 1.19 (d, J = 6.54 Hz, 6H), 1.36 (d, J = 6.24 Hz, 6H), 2.27 (s, 3H), 4.07 (m, 1H), 4.80 (m, 1H), 6.41 (d, J = 8.10 Hz, 1H), 6.45 (d, J = 7.32Hz, 1H), 7.30 (m, 1H); ^{13}CNMR (DMSO-d$_6$): 160.22, 153.84, 150.07, 138.90,130.95,126.80, 112.65, 45.75,45.43, 20.55, 19.95,16.95; MS: m/z =260 (M$^+$), 217, 160, 134, 92.

Synthesis of 2-Pyrollo-(7or 8)-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one 7$_{a-b}$:

2-amino-(7 or 8)-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (0.01mol) is dissolved in acetic acid (50ml), and 2,5-dimethoxytetrahydrofuranne (0.01mol) were added and then heated under reflux for 3 hours, the mixture was concentrated under reduced pressure and the solid precipitate was triturated with recrystallized solvent, filtered, dried and then recrystallized from a large volume of solvent.

Synthesis of 2-Alkoxy(7 or 8)-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one 8$_{a-h}$:

2-amino-(7 or 8)-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (0.01 mol) is dissolved in acetic acid (50ml), and alkyl anhydride (0.01mol) were added and then heated under reflux for 2 hours, the mixture was concentrated under reduced pressure and the solid precipitate was triturated with recrystallized solvent filtered, dried and then recrystallized from a large volume of solvent.

2-Pyrollo-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (7$_a$)

Recrystallization of the crude product from acetonitrile gave 7$_a$a white powder (1.40 g, 62 %), mp 208°C; IR (KBr): υ 3097-2963, 1722, 1641 cm^{-1}; ^{1}HNMR (DMSO-d$_6$): 2.40 (s, 3H), 6.33 (s, 2H), 7.58 (d, J = 8.87 Hz, 1H), 7.69 (s, 2H), 8.11 (d, J = 8.87 Hz, 1H), 8.78 (s, 1H); ^{13}CNMR (DMSO-d$_6$): 157.22, 153.98, 150.03, 145.48, 127.69, 127.47, 123.09, 118.90, 112.17, 17.07; MS: m/z = 226 (M$^+$), 160, 92.

2-Pyrollo-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (7$_b$)

Recrystallization of the crude product from acetonitrile gave 7$_b$a white powder (1.35g, 60 %), mp 214°C; IR (KBr): υ 3100 - 2970, 1720, 1640 cm^{-1}; ^{1}HNMR (DMSO-d$_6$): 2.54 (s, 3H), 6.38 (s, 2H), 7.37 (m, 1H), 7.52 (s, 1H),7.73 (s,2H), 8.85 (m, 1H); ^{13}CNMR (DMSO-d$_6$): 156.93, 15.20, 151.10, 145.50, 127.80, 127.50, 122.95, 119.12, 112.16, 17.20; MS: m/z = 226 (M$^+$), 160, 92.

2-Acetoxyamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (8$_a$)

Recrystallization of the crude product from ethanol gave 8$_a$a white powder (1.44g, 66 %), mp 228°C; IR (KBr): υ 3249, 3026, 1712, 1690, 1644 cm^{-1}; ^{1}H NMR (DMSO-d$_6$): 2.26 (s, 3H), 2.37 (s, 3H), 2.24 (s, 3H), 7.42 (d, J = 8.87 Hz, 1H), 8.02 (d, J = 8.87 Hz, 1H),

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8.68 (s, 1H), 10.44 (s, 1H); ^{13}C NMR (DMSO-d_6): 170.05, 154.13, 150.41, 146.70, 127.14, 123.99,122.00, 25.37, 16.76; MS: m/z = 218 (M^+), 203, 175, 160, 133, 108, 92.

2-Propoxyamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (8_b)

Recrystallization of the crude product from ethanol gave 8_ba white powder (1.51g, 65 %), mp186°C; IR (KBr): υ 3288, 3077, 1734, 1701, 1646 cm^{-1}; ^{1}HNMR (DMSO-d_6):1.03 (t,^{3}J = 14.70 Hz, 3H) 2.37 (s, 3H), 2.58 (q, ^{3}J = 14.70 Hz, 2H), 7.40 (d, J = 8.87 Hz, 1H), 8.02 (d, J = 8.87 Hz, 1H), 8.68 (s, 1H), 10.39 (s, 1H); ^{13}CNMR (DMSO-d_6): 173.33, 160.24, 154.17, 150.45, 145.22, 127.20, 127.05, 123.12, 30.24, 17.41, 8.87; MS: m/z = 232 (M^+), 203, 175, 160, 133, 92, 81.

2-Butoxyaamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (8_c)

Recrystallization of the crude product from ethanol gave 8_ca white powder (1.52 g, 62%), mp175°C; IR (KBr): υ 3274, 2954-2872, 1726, 1707, 1646 cm^{-1}; ^{1}HNMR (DMSO-d_6): 0.89 (m, 3H), 1.57 (m, 2H), 2.37 (s, 3H), 2.53 (m, 2H), 7.41 (d, J = 8.11 Hz, 1H), 8.02 (d, J = 8.11 Hz, 1H), 8.68 (s, 1H), 10.40 (s, 1H); ^{13}CNMR (DMSO-d_6): 172.31, 160.22,154.17, 150.46, 145.21, 127.20, 127.06, 123.13, 17.93, 17.41, 13.56; MS: m/z = 246 (M^+), 231, 203, 175, 160, 133, 92.

2-Isobutoxyaamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (8_d)

Recrystallization of the crude product from ethanol gave 8_da white powder (1.48 g, 60 %), mp 167°C; IR (KBr): υ 3317 - 3268, 3060 - 2926, 1715, 1691, 1646 cm^{-1}; ^{1}HNMR (DMSO$_6$): 1.05 (d, J = 6.67 Hz, 6H), 2.37 (s, 3H), 2.9 3(m, 1H), 7.40 (d, J = 9.15 Hz, 1H), 8.03(d, J = 9.15 Hz, 1H), 8.68 (s, 1H), 10.43 (s, 1H); ^{13}CNMR (DMSO-d_6): 173.80, 160.30,156.10, 153.20, 148.30, 128.01, 126.75, 122.53, 51.10, 27.93, 20.55, 19.70; MS: m/z = 246 (M^+), 203, 175, 160, 134, 92, 81.6.

2-Hexyloxyamino-7-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (8_e)

Recrystallization of the crude product from isopropanol gave 8_ea white powder (1.64g, 60%), mp 167°C; IR (KBr): υ 3292 - 3077, 2951 - 2855, 1731, 1705, 1647 cm^{-1}; ^{1}HNMR (DMSO-d_6): 0.85 (m, 3H),1.27 (m, 4H), 1.54 (m, 2H) 2.36 (s, 3H), 2.54 (m, 2H), 7.40 (d, J = 8.87 Hz, 1H), 8.03 (d, J = 8.87 Hz, 1H), 10.42 (s, 1H); ^{13}CNMR (DMSO-d_6): 172.44, 160.20,154.16, 150.45, 145.21, 127.20,127.04 123.12, 38.75, 30.78, 24.18, 21.87, 17.40, 13.83; MS: m/z = 274 (M^+), 231, 203, 175, 160,133, 108, 92.

2-Acetoxyamino-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (8_f)

Recrystallization of the crude product from ethanol gave 8_fa white powder (1.42g, 65%) mp 163°C; IR(KBr): υ 3250-3200, 3028-3010, 1710, 1690, 1640 cm^{-1}; ^{1}HNMR (DMSO-d_6): 2.30 (s, 3H), 2.52(s,3H), 7.25 (d, J = 6.95 Hz, 1H), 7.32 (s, 1H) 8.74 (d, J = 6.67 Hz, 1H), 10.45 (s, 1H); ^{13}CNMR (DMSO-d_6): 170.10, 160.70,155.40, 155.00150.40, 129.00,121.70, 119.20, 25.40, 21.10; MS: m/z = 218 (M^+), 203, 175, 160, 133, 108, 92.

2-Propoxyamino-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (8_g)

Recrystallization of the crude product from ethanol gave 8_ga white powder (1.39g, 60%), mp 172°C; IR (KBr): υ3290, 3080-2990, 1730, 1705, 1642 cm^{-1}; ^{1}HNMR (DMSO-d_6):1.05 (m, 3H), 2.51 (s, 3H), 2.62 (m, 2H), 7.24 (d, J = 5.60 Hz, 1H),7.31 (s, 1H), 8.75 (d, J = 5.60 Hz, 1H), 10.43(s, 1H); ^{13}CNMR (DMSO-d_6): 173.38, 160.70,155.33, 155.06, 150.51, 129.01, 121.71, 119.22, 30.26, 21.13, 8.95; MS: m/z = 232 (M^+), 203, 175, 160, 133, 92, 81.

2-Isobutoxyaamino-8-methyl-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-one (8_h)

Recrystallization of the crude product from ethanol gave 8_ha white powder (1.47g, 60%), mp 169°C; IR (KBr): υ 3320 - 3270, 3060 - 2930, 1710, 1690, 1645 cm^{-1}; ^{1}H NMR (DMSO-d_6): 1.08 (m, 6H), 2.51 (s, 3H), 3.00 (m, 1H), 7.23(m, 1H), 7.30 (s,1H), 8.74 (m,1H) 10.43 (s, 1H); ^{13}C NMR (DMSO-d_6): 175.90, 160.82,155.33, 155.12, 150.62, 128.06, 122.60, 116.72, 50.57, 28.64, 20.52, 19.71; MS: m/z = 246 (M^+), 203, 175, 160, 134, 92.

3. RESULTS AND DISCUSSION

As a first approach towards the synthesis of this heterocyclic system we envisaged a synthetic strategy using 2-aminopyridine or derivatives as starting material. Thus, a solution of the compound in anhydrous DMF was treated at the room temperature with ethoxycarbonyl isothiocianate, and to the resulting thiourea, the appropriate dialkylamine and $HgCl_2$ were added to obtain the ethoxycarbonylguanidines. Heating the DMF solution of the latter compounds under reflux induced a ring closure of the ethoxycarbonyl function into a triazine ring and the products obtained were identified as 2-dialkylamino-*4H*-pyrido [1,2-*a*][1,3,5]triazin-4-ones.

Furthermore, considering that no work has yet taken advantage of these new methods yet to produce cyclic polysubstituted guanidines by direct ring closure of suitable substrates, we studied the total one pot synthesis of 2-dialkylamino-*4H*-pyrido[1,2-

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a][1,3,5]triazin-4-ones starting 2-aminopyridines and 2-aminopicolines 1_{a-h}. We would now like to report a new simple and efficient one-pot synthesis of the hitherto unknown compounds.

In the light of all these works, we first verified a general method for the one pot syntheses 2-dialkylamino-*4*H-pyrido[1,2-*a*][1,3,5]triazin-4-ones starting 2-aminopyridines 1_{a-e} usable in combinatorial approaches.

In order to build blocks, we focused on a general protocol facile three-steps, for the synthesis 2-dialkylamino-*4H*-substituted-pyrido[1,2-*a*][1,3,5]triazin-4-ones skeleton 4_{a-e} starting 2-amino pyridine 1_a; 2-aminopicolines $1_{b-e.}$ With this aim, we particularly studied the synthesis of compounds skeleton 4_{a-e} according to the (Figure 3). We envisaged a synthetic strategy using 2-aminopyridines1_{a-e} as starting material. Thus, a solution of 2-aminopyridine in anhydrous DMF was treated at room temperature with ethoxy carbonylisothiocyanate, and to the resulting N-ethoxycarbonyl-N'-(2-pyridyl)thiourea 2_{a-e} intermediate which was next able to produce by reaction with appropriate dialkylamines in mercuric chloride tobtain the ethoxycarbonylguanidines 3_{a-e}. Heating the DMF solution of the latter compounds under reflux induced a ring closure of the ethoxycarbonyl function into a triazine ring and the products obtained as 2-dialkylamino-*4H*-pyrido[1,2-a][1,3,5]triazin-4-ones 4_{a-e} in good yield through a one-pot protocol staring 2-aminopyridine 1_a and 2-aminopicolines 1_{b-e} (Figure 4). The isolation of the two intermediates 2_{a-e} and 3_{a-e} was an unnecessary sequence that became applicable to parallel chemistry techniques.

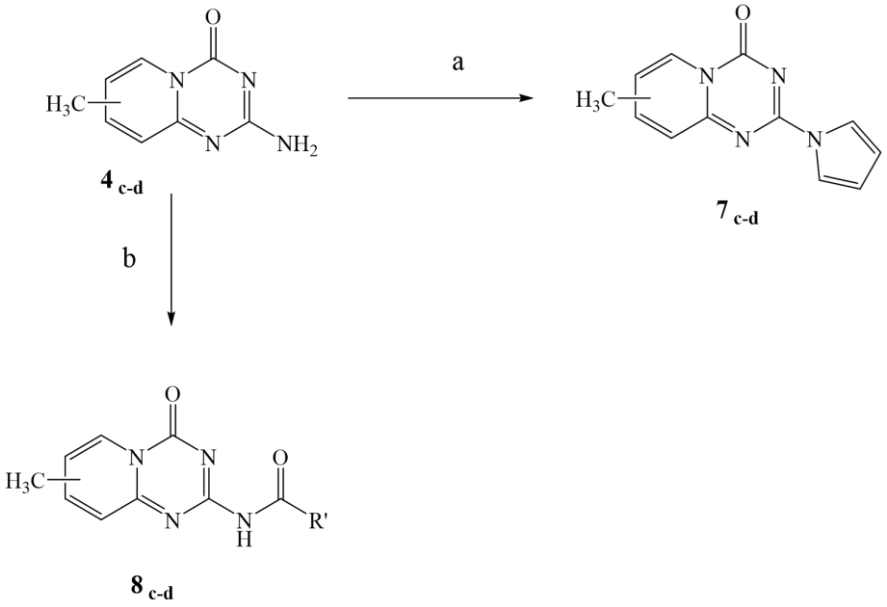

Figure 5: Synthesis of 2-pyrrolo-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones (7_{c-d}) and amides corresponding (8_{a-h}) derivatives from 2-amino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones (4_{c-d}).

Reagents and conditions:
i) 2,5-dimethoxytetrahydrofuranne, acetic acid, 90°C, 3h. **ii)** alkylanhydrid, acetic acid, 90°C, 2h.

We studied the synthesis of 2-pyrrolo-*4H*-Pyrido[1,2-*a*][1,3,5]triazin-4-ones 7_{c-d} following Clausson-Kass's methodology [16] by condensing in acetic acid and heating for 3 hours, the 2-amino-*4H*-pyrido[1,2-*a]*[1,3,5]triazin-4-ones 4_{a-b} with 2,5-dimethoxytetrahydrofuran to gave 8_{a-b} in good yields. 2-amino-*4H*-pyrido[1,2-*a*][1,3,5]triazin-4-ones 4_{c-d} react with many anhydride acids, in acetic acid mild condition, by heating and give the corresponding amides 8_{a-h} (Figure 5). We also attempted to apply the $HgCl_2$ methodology to primary or secondary amines (aliphatic or aromatic), but this was unsuccessful and no cyclized products were being observed [14,16]. This failure prompts us to modify our reaction conditions.

4. CONCLUSION

In conclusion, we have developed facile and efficient three-steps, synthesis system of novel class of hetero-aromatic compounds, namely:

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2-dialkylammino-*4H*-pyrido [1, 2-*a*][1, 3, 5] triazin-4-ones starting 2-aminopyridine1_a or 2-aminopiccolines 1_{b-e}

The success of this protocol as one-pot synthesis of compounds of the title further underscores the ease as well as the efficiency of this protocol. The co-planarity and linearity of this heterocyclic scaffold suggest that the 2-amino derivatives may intercalate between DNA base pairs. Further biological studies are in progress. Additional experiments concerning the synthesis of 2-diethylammino-7-(Het)aryl-*4H*-pyrido [1,2-a][1,3,5]triazin-4-ones skeleton type 4 using palladium catalyzed Suzuki type coupling, are currently under investigation in order to obtain great potentialities in medicinal chemistry of compounds class.

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