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SYNTHESIS OF 3-(PYRIMIDINYL)PYRROLE DERIVATIVES

Igor Yu. Nestorak,[a,b] Anton V. Tverdokhlebov,*[a,b] Andrey A. Tolmachev,[a,b] and Yulian M. Volovenko[b]

[a] Enamine Ltd., Alexandra Matrosova str. 23, 01103, Kiev, Ukraine; e-mail: atver@univ.kiev.ua

[b] Kiev National Taras Shevchenko University, Volodimirska str. 62, 01033, Kiev, Ukraine

Abstract – Alkylation of 4,6-dimethyl-2-pyrimidineacetonitrile and 2,6-dimethyl-4-pyrimidineacetonitrile with chloroacetic acid anilides was shown to give 5-amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-1-arylpyrrol-2-ones and 5-amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-1-arylpyrrol-2-ones, respectively. Corresponding isomeric compounds, 5-amino-4-pyrimidinyl-2,3-dihydropyrrol-3-ones were obtained by Claisen condensation of the mentioned pyrimidineacetonitriles with *N-Boc* α-aminoacids imidazolides followed by removal of the protecting group accompanied with simultaneous ring closure.

INTRODUCTION

Over the last 5 years among 3-(2- and 4-pyrimidinyl)pyrrole derivatives the substances with promising pharmacological properties were found.[1-3] Thus, CDK inhibitors,[1] HIV integrase inhibitors,[2] and selective GSK-3β inhibitors[3] all reaching nanomolar activity level were discovered. Of course, it caused increasing interest in these scaffolds. However, to date there are at about 10 papers only devoted to the preparation of various pyrimidinylpyrroles.[1-5] The different approaches were used, namely pyrimidine ring formation from the suitably substituted pyrroles,[1,4] pyrrole ring construction on the basis of properly substituted pyrimidines,[2] and finally, cross-coupling reactions between pyrrole and pyrimidine derivatives.[3,5] Nevertheless, all the methods had some shortcomings. The first one provided quite limited products diversity thus being disadvantageous for medicinal chemistry, whereas the latter two required hardly available pyrimidine derivatives so making the whole synthesis very laborious.

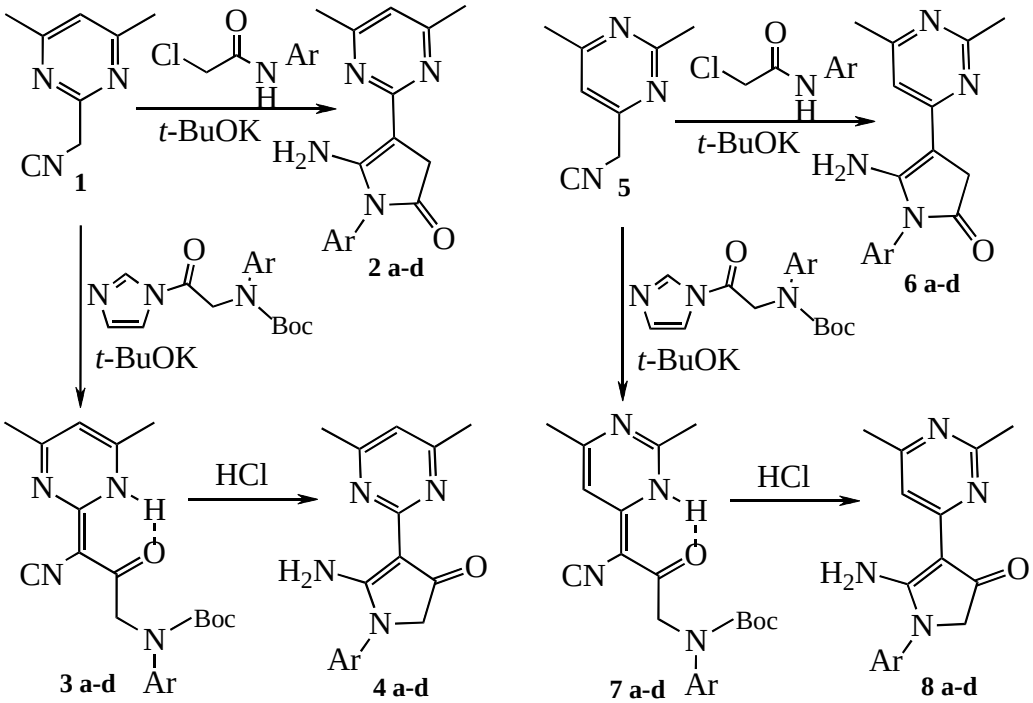
Applications of different hetarylacetonitriles for preparation of various heterocycles including pyrroles were widely studied in our laboratory.[6,7] Continuing these researches we have turned our attention to the

isomeric pyrimidineacetonitriles **1** and **5** (Scheme 1). They were obtained in good yields from the corresponding 2- and 4-chloro dimethylpyrimidines using slightly modified protocol developed by Atwal with co-workers.[8] The sequence included hetarylation of *tert*-butyl cyanoacetate followed by removal of the ester group by acidic hydrolysis with simultaneous decarboxylation. So, utility of the nitriles **1**, **5** for the synthesis of pyrimidinylpyrrole derivatives has been examined and the results obtained are reported herein.

RESULTS AND DISCUSSION

Alkylation of malononitrile and ethyl cyanoacetate with chloroacetic acid anilides was known to give 5-aminopyrrol-2-one derivatives.[9] Usually K_2CO_3 or triethylamine were used in this reaction as the bases. However application of this procedure to the nitriles **1**, **5** afforded unsatisfactory results. Nevertheless in the presence of the stronger base, potassium *tert*-butoxide desired pyrroles **2a-d** and **6a-d** were obtained in 50-60 % yields. Apparently the reaction occurred through initial alkylation of the methylene group followed by the intramolecular addition of the secondary amide to the nitrile.

Further we attempted to prepare pyrrol-3-one derivatives **4**, **8**, the isomers of compounds **2**, **6**. It should be noted that Claisen type acylation of malononitrile and alkyl cyanoacetates with aminoacids esters is well documented.[10] Moreover, in case of malononitrile direct carbonyldiimidazole assisted acylation was reported.[11] We have collated the both approaches and carried out Claisen type acylation with acid imidazolides. Thus, treatment of the *Boc*-protected anilinoacetic acids imidazolides generated *in situ* as

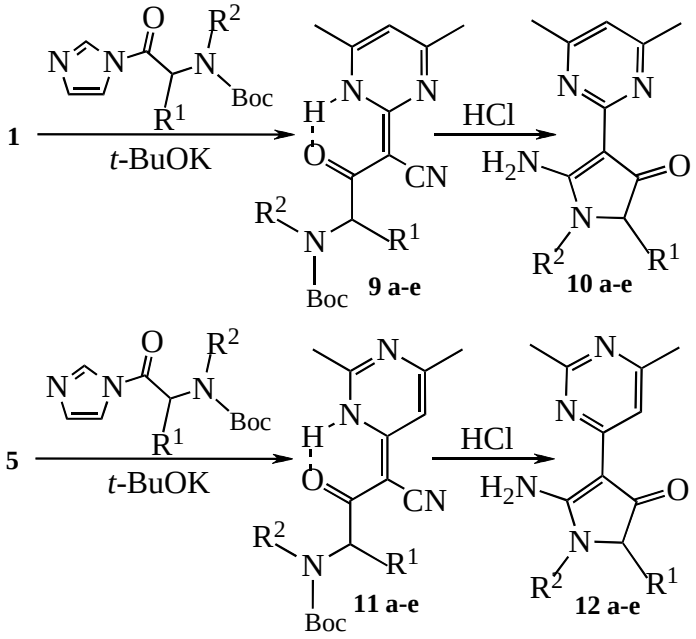


Scheme 1. Ar = **a**: Ph; **b**: 4-ClC_6H_4; **c**: 4-$MeOC_6H_4$; **d**: 4-MeC_6H_4.

usual with the nitriles **1**, **5** in the presence of potassium *tert*-butoxide furnished crude derivatives **3a-d** and **7a-d** (80-90% purity) in 75-90% yields. Compounds **3a** and **7a** were purified by chromatography and completely characterized as the representative examples. However, the purification procedure appeared not to be obligatory, since the crude compounds **3**, **7** were converted successfully into the target pyrroles **4a-d**, **8a-d** by means of deprotection with hydrochloric acid and simultaneous cyclization at the expense of intramolecular addition of the liberated amine to the nitrile. Also it should be mentioned that the similar Claisen condensation of *N*-protected proline imidazolides with certain methylene compounds of non-nitrile nature was reported previously.[12]

Moreover, the method was successfully extended to the synthesis of pyrroles **10** and **12** (Scheme 2) starting from the common aminoacids set. Thus, acylation of the nitriles **1**, **5** with *N-Boc* aminoacids imidazolides in the presence of potassium *tert*-butoxide yielded crude compounds **9a-e**, **11a-e**. Again, derivatives **9a**, **11a** were purified by chromatography and characterized as representative samples. Nevertheless, similarly to the previous case the purification was not needed, and treatment of crude compounds **9**, **11** with hydrochloric acid led to the pyrroles **10a-e**, **12a-e** in 50-65% overall yields based on the nitriles **1**, **5**.

The structures of the prepared pyrimidinylpyrroles **2**, **4**, **6**, **8**, **10**, **12** were confirmed by ^{1}H and ^{13}C NMR data. According to the spectral data all pyrroles **2-12** in DMSO-d_6 solutions exist entirely in the amino-oxo form. Neither keto-enol nor amine-imine tautomerisms were observed. Noteworthy, there was significant difference in the amino group signal shape of 2-oxo and 3-oxo isomers **2**, **6** and **4**, **8**, **10**, **12**, respectively.



	R^1	R^2
a	H	H
b	H	Me
c	Me	H
d	-$(CH_2)_3$-	
e	$PhCH_2$	H

Scheme 2.

Thus, in the spectra of pyrrol-2-ones **2**, **6** the habitual two-proton singlet of the amino group was present at 7.0-7.5 ppm. At the same time in the spectra of pyrrol-3-ones **4**, **8**, **10**, **12** the amino group signals appeared as two separate one-proton singlets at 7.7-8.0 and 9.5-9.8 ppm. This magnetical non-equivalence of the amino group protons is caused by the strong vinylogous amide-like conjugation between amino and carbonyl moieties in the compounds **4**, **8**, **10**, **12**, which evidently is absent in the isomeric derivatives **2**, **6**. The same effect was observed previously by us[7] and other researchers[10] for close related cyclic enaminones.

To resume, pyrimidineacetonitriles **1**, **5** have been shown to be suitable precursors for various pyrimidinylpyrrole derivatives, the substances of potential pharmacological interest. The several approaches elaborated provide high diversity of the available products favorable for medicinal chemistry. Moreover, Claisen condensation with acid imidazolides has been worked out. It seems to be helpful alternative for the typical reaction with esters.

EXPERIMENTAL

Chloroacetic acid anilides were prepared according to the described procedure.[13] *N-Boc* aminoacids were either commercially available or obtained as reported.[14] Other reagents were commercially available and were used without extra purification. All melting points were determined in open capillary tubes in a Thiele apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity plus 400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) in DMSO-d_6, $CDCl_3$ or CF_3COOD solutions. Chemical shifts (δ) are given in ppm downfield from internal Me_4Si. *J* values are in Hz. The purity of all compounds obtained was checked by ^{1}H NMR and LC/MS on an Agilent 1100 instrument.

Pyrimidineacetonitriles 1, 5. General Procedure: *Step A*. Powdered K_2CO_3 (3.00 g, 22 mmol) was added to a solution of the corresponding chlorodimethylpyrimidine (1.43 g, 10 mmol) and *tert*-butyl cyanoacetate (1.55 g, 11 mmol) in anhydrous DMF (25 mL) and the mixture was stirred at 120 °C for 6 h. The solvent was evaporated in vacuo, the residue was dissolved in water (30 mL) and acidified with 20% hydrochloric acid (4 mL). The solid precipitated was filtered and recrystallized from aqueous EtOH to give α-cyano-4,6-dimethyl-2-pyrimidineacetic acid *tert*-butyl ester (1.78 g, 72%, mp 198 °C) or α-cyano-2,6-dimethyl-4-pyrimidineacetic acid *tert*-butyl ester (1.90 g, 77%, mp 184 °C).

Step B. Conc. hydrochloric acid (9 mL) was added to a solution of compounds prepared on previous step (2.47 g, 10 mmol) in EtOH (40 mL) and the mixture obtained was refluxed for 40 min. The solvent was removed in vacuo, and the residue was dissolved in water (30 mL). K_2CO_3 (1.50 g, 11 mmol) was added to this solution and then the water was evaporated to dryness in vacuo. The residue was treated with Et_2O (30 mL), the inorganic materials were filtered off and washed with Et_2O (3 x 20 mL). Combined ethereal

filtrate and washings were evaporated in vacuo yielding pure nitriles **1**, **5** as oily materials, which solidified quickly.

4,6-Dimethyl-2-pyrimidineacetonitrile (1): (1.29 g, 88%). Mp 79 °C, lit.,[15] mp 71 °C. The spectra were in complete agreement with the published data.[15]

2,6-Dimethyl-4-pyrimidineacetonitrile (5): (1.15 g, 78%). Mp 60 °C. ^{1}H NMR (DMSO-d_6) δ = 2.42 (s, 3H, CH_3), 2.55 (s, 3H, CH_3) 4.17 (s, 2H, CH_2), 7.20 (s, 1H, 5-H). ^{13}C NMR (DMSO-d_6) δ = 23.5 (CH_3), 25.1 (CH_3), 25.3 (CH_2), 116.1 (5-C), 117.2 (CN), 159.6 (4-C), 167.1 (6-C), 167.7 (2-C). Anal. Calcd for $C_8H_9N_3$: C, 65.29; H, 6.16; N, 28.55. Found: C, 65.25; H, 6.20; N, 28.50.

5-Amino-2,3-dihydropyrrol-2-ones 2a-d, 6a-d. General Procedure: Potassium *tert*-butoxide (0.59 g, 5.3 mmol) was added to a stirred solution of nitrile **1, 5** (0.90 g, 6.1 mmol) and appropriate chloroacetic acid amide (5.0 mmol) in anhydrous THF (10 mL) and the mixture was stirred at reflux for 10 min. The solvent was evaporated in vacuo, the residue was triturated with water (70 mL), filtered and washed with water. Recrystallization from dioxane – *i*-propanol (1:1, v/v) mixture afforded derivatives **2a-d**, **6a-d**.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-1-phenylpyrrol-2-one (2a): (0.87 g, 62%). Mp 197 °C. ^{1}H NMR (DMSO-d_6) δ = 2.28 (s, 6H, $2CH_3$), 3.41 (s, 2H, CH_2), 6.56 (s, 1H, 5-H_{Pyrim}), 7.11 (br s, 2H, NH_2), 7.34 (d, J = 7.0, 2H, 2,6-H_{Ar}), 7.47 (t, J = 7.0, 1H, 4-H_{Ar}), 7.54 (t, J = 7.0, 2H, 3,5-H_{Ar}). ^{13}C NMR (DMSO-d_6) δ = 24.3 ($2CH_3$), 35.7 (CH_2), 81.0 (4-C), 111.6 (5-C_{Pyrim}), 128.4 (3,5-C_{Ar}), 128.9 (4-C_{Ar}), 129.9 (2,6-C_{Ar}), 133.1 (1-C_{Ar}), 152.1 (4,6-C_{Pyrim}), 164.0 (2-C_{Pyrim}), 165.4 (5-C), 174.8 (2-C=O). Anal. Calcd for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.69; H, 5.94; N, 19.82.

5-Amino-1-(4-chlorophenyl)-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydropyrrol-2-one (2b): (0.99 g, 63%). Mp 175 °C. ^{1}H NMR (DMSO-d_6) δ = 2.29 (s, 6H, $2CH_3$), 3.41 (s, 2H, CH_2), 6.56 (s, 1H, 5-H_{Pyrim}), 7.16 (br s, 2H, NH_2), 7.38 (d, J = 7.4, 2H, $2H_{Ar}$), 7.60 (d, J = 7.4, 2H, $2H_{Ar}$). ^{13}C NMR (DMSO-d_6) δ = 24.3 ($2CH_3$), 35.7 (CH_2), 81.2 (4-C), 111.7 (5-C_{Pyrim}), 129.9 (2,6-C_{Ar}), 130.3 (3,5-C_{Ar}), 132.1 (4-C_{Ar}), 133.4 (1-C_{Ar}), 151.9 (4,6-C_{Pyrim}), 164.0 (2-C_{Pyrim}), 165.0 (5-C), 174.7 (2-C=O). Anal. Calcd for $C_{16}H_{15}ClN_4O$: C, 61.05; H, 4.80; N, 17.80; Cl, 11.26. Found: C, 61.21; H, 4.73; N, 17.62; Cl, 11.30.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-1-(4-methoxyphenyl)pyrrol-2-one (2c): (0.81 g, 52%). Mp 176 °C. ^{1}H NMR (DMSO-d_6) δ = 2.27 (s, 6H, $2CH_3$), 3.38 (s, 2H, CH_2), 3.80 (s, 3H, OCH_3), 6.53 (s, 1H, 5-H_{Pyrim}), 7.07 (m, 4H, $2H_{Ar}$, NH_2), 7.24 (d, J = 8.6, 2H, $2H_{Ar}$). ^{13}C NMR (DMSO-d_6) δ = 24.3 ($2CH_3$), 35.6 (CH_2), 55.9 (OCH_3), 80.7 (4-C), 111.2 (5-C_{Pyrim}), 111.4 (3,5-C_{Ar}), 125.6 (1-C_{Ar}), 129.9 (2,6-C_{Ar}), 152.6 (4,6-C_{Pyrim}), 159.6 (4-C_{Ar}), 164.1 (2-C_{Pyrim}), 165.1 (5-C), 175.0 (2-C=O). Anal. Calcd for $C_{17}H_{18}N_4O_2$: C, 65.79; H, 5.85; N, 18.05. Found: C, 65.70; H, 5.85; N, 17.86.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-1-(4-methylphenyl)pyrrol-2-one (2d): (0.90 g, 61%). Mp 167 °C. ^{1}H NMR (DMSO-d_6) δ = 2.27 (s, 6H, $2CH_3$), 2.36 (s, 3H, CH_3), 3.39 (s, 2H, CH_2),

6.54 (s, 1H, 5-H_{Pyrim}), 7.07 (br s, 2H, NH_2), 7.19 (d, J = 7.0, 2H, 2H_{Ar}), 7.33 (d, J = 7.0, 2H, 2H_{Ar}). ^{13}C NMR (DMSO-d_6) δ = 21.2 (CH_3), 24.3 (2CH_3), 35.6 (CH_2), 80.8 (4-C), 111.5 (5-C_{Pyrim}), 128.2 (3,5-C_{Ar}), 130.4 (2,6-C_{Ar}), 130.5 (4-C_{Ar}), 138.4 (1-C_{Ar}), 152.3 (4,6-C_{Pyrim}), 164.0 (2-C_{Pyrim}), 165.3 (5-C), 174.8 (2-C=O). Anal. Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.03. Found: C, 69.31; H, 6.34; N, 19.25.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-1-phenylpyrrol-2-one (6a): (0.80 g, 57%). Mp 212 °C. ^{1}H NMR (DMSO-d_6) δ = 2.24 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 3.38 (s, 2H, CH_2), 6.39 (s, 1H, 5-H_{Pyrim}), 7.35 (d, J = 7.5, 2H, 2,6-H_{Ar}), 7.49 (m, 3H, 4-H_{Ar}, NH_2), 7.56 (t, J = 7.5, 2H, 3,5-H_{Ar}). ^{13}C NMR (DMSO-d_6) δ = 24.1 (CH_3), 26.4 (CH_3), 34.4 (CH_2), 79.0 (4-C), 108.5 (5-C_{Pyrim}), 128.4 (3,5-C_{Ar}), 129.1 (4-C_{Ar}), 130.0 (2,6-C_{Ar}), 132.8 (1-C_{Ar}), 152.8 (4-C_{Pyrim}), 161.8 (6-C_{Pyrim}), 164.1 (2-C_{Pyrim}), 165.2 (5-C), 174.4 (2-C=O). Anal. Calcd for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.42; H, 5.70; N, 19.89.

5-Amino-1-(4-chlorophenyl)-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydropyrrol-2-one (6b): (0.77 g, 49%). Mp 217 °C. ^{1}H NMR (DMSO-d_6) δ = 2.24 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.37 (s, 2H, CH_2), 6.40 (s, 1H, 5-H_{Pyrim}), 7.37 (d, J = 8.5, 2H, 2H_{Ar}), 7.53 (br s, 2H, NH_2), 7.60 (d, J = 8.5, 2H, 2H_{Ar}). ^{13}C NMR (DMSO-d_6) δ = 24.1 (CH_3), 26.4 (CH_3), 34.4 (CH_2), 79.2 (4-C), 108.5 (5-C_{Pyrim}), 130.0 (2,6-C_{Ar}), 130.4 (3,5-C_{Ar}), 131.7 (4-C_{Ar}), 133.6 (1-C_{Ar}), 152.5 (4-C_{Pyrim}), 161.8 (6-C_{Pyrim}), 164.2 (5-C), 165. (2-C_{Pyrim}), 174.3 (2-C=O). Anal. Calcd for $C_{16}H_{15}ClN_4O$: C, 61.05; H, 4.80; N, 17.80; Cl, 11.26. Found: C, 61.14; H, 4.81; N, 17.67; Cl, 11.46.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-1-(4-methoxyphenyl)pyrrol-2-one (6c): (0.76 g, 49%). Mp 180 °C. ^{1}H NMR (DMSO-d_6) δ = 2.23 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 3.34 (s, 2H, CH_2), 3.80 (s, 3H, OCH_3), 6.37 (s, 1H, 5-H_{Pyrim}), 7.07 (d, J = 8.0, 2H, 2H_{Ar}), 7.23 (d, J = 8.0, 2H, 2H_{Ar}), 7.41 (br s, 2H, NH_2). ^{13}C NMR (DMSO-d_6) δ = 24.1 (CH_3), 26.3 (CH_3), 34.3 (CH_2), 55.9 (OCH_3), 78.8 (4-C), 108.3 (5-C_{Pyrim}), 115.2 (3,5-C_{Ar}), 125.2 (1-C_{Ar}), 129.9 (2,6-C_{Ar}), 153.3 (4-C_{Pyrim}), 159.8 (4-C_{Ar}), 161.8 (6-C_{Pyrim}), 163.9 (5-C), 165.1 (2-C_{Pyrim}), 174.7 (2-C=O). Anal. Calcd for $C_{17}H_{18}N_4O_2$: C, 65.79; H, 5.85; N, 18.05. Found: C, 65.73; H, 5.64; N, 18.10.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-1-(4-methylphenyl)pyrrol-2-one (6d): (0.82 g, 56%). Mp 188 °C. ^{1}H NMR (DMSO-d_6) δ = 2.24 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 3.35 (s, 2H, CH_2), 6.37 (s, 1H, 5-H_{Pyrim}), 7.20 (d, J = 7.0, 2H, 2H_{Ar}), 7.33 (d, J = 7.0, 2H, 2H_{Ar}), 7.43 (br s, 2H, NH_2). ^{13}C NMR (DMSO-d_6) δ = 21.3 (CH_3), 24.1 (CH_3), 26.4 (CH_3), 34.3 (CH_2), 78.9 (4-C), 108.4 (5-C_{Pyrim}), 128.3 (3,5-C_{Ar}), 130.1 (4-C_{Ar}), 130.5 (2,6-C_{Ar}), 138.6 (1-C_{Ar}), 153.0 (4-C_{Pyrim}), 161.8 (6-C_{Pyrim}), 164.1 (5-C), 165.2 (2-C_{Pyrim}), 174.5 (2-C=O). Anal. Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.03. Found: C, 69.40; H, 6.14; N, 19.22.

***tert*-Butyl (3-cyano-3-pyrimidinyl-2-oxopropyl)carbamates 3a-d, 7a-d, 9a-e, 11a-e. General**

Procedure: Carbonyldiimidazole (1.62 g, 10 mmol) was added to a stirred solution of appropriate *N-Boc* aminoacid (10 mmol) in anhydrous MeCN (20 mL) and the stirring was continued until CO_2 evolution had ceased (at about 40 min). Then the corresponding nitrile **1**, **5** (1.47 g, 10 mmol) and potassium *tert*-butoxide (2.24 g, 20 mmol) were added sequentially and the mixture was stirred at reflux for 1 h. Upon cooling the solvent was evaporated in vacuo, the residue was dissolved in water (30 mL) and acidified with acetic acid (2.00 g, 33 mmol) causing separation of a brownish oil, which slowly solidified being left overnight. It was filtered and dried yielding crude derivatives **3a-d, 7a-d, 9a-e, 11a-e** employed in further step. The representative compounds **3a**, **7a**, **9a,** and **11a** were purified by column chromatography on silica gel using 4:1 v/v hexane – EtOAc mixture as eluent.

[3-Cyano-3-(4,6-dimethyl-2-pyrimidinyl)-2-oxopropyl]phenylcarbamic acid, *tert*-butyl ester (3a): (2.85 g, 75%). Mp 149 °C. ^{1}H NMR ($CDCl_3$) δ = 1.45 (s, 9H, *t*-Bu), 2.48 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 4.83 (s, 2H, CH_2), 6.63 (s, 1H, 5-C_{Pyrim}), 7.16 (m, 1H, 4-H_{Ar}), 7.27 - 7.30 (m, 4H, 2,3,5,6-H_{Ar}), 12.16 (s, 1H, NH...O). ^{13}C NMR (DMSO-d_6) δ = 22.2 ($2CH_3$), 27.8 ($3CH_3$, *t*-Bu), 55.6 (CH_2), 74.4 ($C_{t\text{-Bu}}$), 79.8 (<u>C</u>-CN), 113.2 (5-C_{Pyrim}), 118.6 (CN), 125.3 (4-C_{Ar}), 125.9 (2,6-C_{Ar}), 128.3 (3,5-C_{Ar}), 143.0 (1-C_{Ar}), 153.6 (4,6-C_{Pyrim}), 159.9 (COO), 172.7 (2-C_{Pyrim}), 190.3 (C=O). Anal. Calcd for $C_{21}H_{24}N_4O_3$: C, 66.30; H, 6.36; N, 14.73. Found: C, 66.45; H, 6.20; N, 14.93.

[3-Cyano-3-(2,6-dimethyl-4-pyrimidinyl)-2-oxopropyl]phenylcarbamic acid, *tert*-butyl ester (7a): (3.19 g, 84%). Mp 134 °C. ^{1}H NMR ($CDCl_3$) δ = 1.46 (s, 9H, *t*-Bu), 2.47 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 4.76 (s, 2H, CH_2), 6.88 (s, 1H, 5-H_{Pyrim}), 7.19 (m, 1H, 4-H_{Ar}), 7.32 (m, 4H, 2,3,5,6-H_{Ar}), 10.17 (s, 1H, NH...O). ^{13}C NMR (DMSO-d_6) δ = 22.0 ($2CH_3$), 27.8 ($3CH_3$, *t*-Bu), 56.9 (CH_2), 78.2 ($C_{t\text{-Bu}}$), 79.5 (<u>C</u>-CN), 108.3 (5-C_{Pyrim}), 116.7 (CN), 125.2 (4-C_{Ar}), 126.0 (2,6-C_{Ar}), 128.2 (3,5-C_{Ar}), 143.1 (1-C_{Ar}), 154.2 (6-C_{Pyrim}), 158.7 (COO), 167.6 (4-C_{Pyrim}), 168.3 (2-C_{Pyrim}), 189.5 (C=O). Anal. Calcd for $C_{21}H_{24}N_4O_3$: C, 66.30; H, 6.36; N, 14.73. Found: C, 66.15; H, 6.56; N, 14.59.

[3-Cyano-3-(4,6-dimethyl-2-pyrimidinyl)-2-oxopropyl]carbamic acid, *tert*-butyl ester (9a): (2.49 g, 82%). Mp 167 °C. ^{1}H NMR ($CDCl_3$) δ = 1.47 (s, 9H, *t*-Bu), 2.49 (s, 3H, CH_3), 2.55 (s, 3H, CH_3), 4.36 (s, 2H, CH_2), 5.21 (s, 1H, NHBoc), 6.64 (s, 1H, 5-H_{Pyrim}), 9.98 (s, 1H, NH...O). ^{13}C NMR (DMSO-d_6) δ = 22.1 ($2CH_3$), 28.2 ($3CH_3$, *t*-Bu), 45.9 (CH_2), 74.3 ($C_{t\text{-Bu}}$), 77.9 (<u>C</u>-CN), 113.1 (5-C_{Pyrim}), 118.7 (CN), 155.7 (4,6-C_{Pyrim}), 159.9 (COO), 178.9 (2-C_{Pyrim}), 191.0 (C=O). Anal. Calcd for $C_{15}H_{20}N_4O_3$: C, 59.20; H, 6.62; N, 18.41. Found: C, 59.07; H, 6.60; N, 18.57.

[3-Cyano-3-(2,6-dimethyl-4-pyrimidinyl)-2-oxopropyl]carbamic acid, *tert*-butyl ester (11a): (2.40 g, 79%). Mp 131 °C. ^{1}H NMR ($CDCl_3$) δ = 1.47 (s, 9H, *t*-Bu), 2.46 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 4.31 (s, 2H, CH_2), 5.19 (s, 1H, NHBoc), 6.87 (s, 1H, 5-H_{Pyrim}), 10.79 (s, 1H, NH...O). ^{13}C NMR (DMSO-d_6) δ = 21.8 ($2CH_3$), 28.2 ($3CH_3$, *t*-Bu), 47.1 (CH_2), 74.2 ($C_{t\text{-Bu}}$), 77.8 (<u>C</u>-CN), 107.7 (5-C_{Pyrim}), 117.3 (CN),

156.3 (6-C_{Pyrim}), 158.3 (COO), 166.6 (4-C_{Pyrim}), 169.2 (2-C_{Pyrim}), 189.7 (C=O). Anal. Calcd for $C_{15}H_{20}N_4O_3$: C, 59.20; H, 6.62; N, 18.41. Found: C, 59.30; H, 6.51; N, 18.50.

5-Amino-2,3-dihydropyrrol-3-ones 4a-d, 8a-d, 10a-e, 12a-e. General Procedure: Conc. hydrochloric acid (3 mL) was added to a solution of the crude compounds **3**, **7**, **9**, **11** (2.5 mmol) in EtOH (30 mL) and the mixture was heated at reflux for 1h. After cooling it was evaporated to dryness in vacuo, the residue was triturated with the mixture of anhydrous dioxane (10 mL) and ether (20 mL), filtered and washed with ether affording compounds **4a-d, 8a-d, 10a-e, 12a-e** as hydrochlorides. These salts were dissolved in water (5 mL) and treated with 10% aqueous K_2CO_3 solution (5 mL). The precipitate formed was filtered, washed with water and dried to give derivatives **4**, **8**, **10**, **12**. The yields of compounds **4, 8**, **10**, **12** given below are calculated on the basis of the nitriles **1**, **5** through the two-step sequence.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-1-phenylpyrrol-3-one (4a): (0.41 g, 59%). Mp 221 °C. ^{1}H NMR (DMSO-d_6) δ = 2.35 (s, 6H, 2CH_3), 4.10 (s, 2H, CH_2), 6.76 (s, 1H, 5-H_{Pyrim}), 7.31 (t, J = 7.0, 1H, 4-H_{Ar}), 7.48 (m, 4H, 2,3,5,6-H_{Ar}), 7.71 (s, 1H, NH), 9.67 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 23.8 (2CH_3), 59.6 (2-CH_2), 91.0 (4-C), 116.4 (5-C_{Pyrim}), 125.6 (2,6-C_{Ar}), 130.5 (4-C_{Ar}), 131.0 (3,5-C_{Ar}), 133.8 (1-C_{Ar}), 154.9 (2-C_{Pyrim}), 162.2 (4,6-C_{Pyrim}), 164.4 (5-C), 193.1 (3-C=O). Anal. Calcd for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.50; H, 5.85; N, 19.93.

5-Amino-1-(4-chlorophenyl)-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydropyrrol-3-one (4b): (0.49 g, 62%). Mp 247 °C. ^{1}H NMR (DMSO-d_6) δ = 2.32 (s, 6H, 2CH_3), 4.06 (s, 2H, CH_2), 6.74 (s, 1H, 5-H_{Pyrim}), 7.45 (d, J = 7.5, 2H, 2H_{Ar}), 7.52 (d, J = 7.5, 2H, 2H_{Ar}), 7.80 (s, 1H, NH), 9.65 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 24.7 (2CH_3), 59.7 (2-CH_2), 90.9 (4-C), 116.5 (5-C_{Pyrim}), 127.1 (2,6-C_{Ar}), 131.2 (3,5-C_{Ar}), 132.3 (1-C_{Ar}), 137.1 (4-C_{Ar}), 154.8 (2-C_{Pyrim}), 163.2 (4,6-C_{Pyrim}), 167.0 (5-C), 189.3 (3-C=O). Anal. Calcd for $C_{16}H_{15}ClN_4O$: C, 61.05; H, 4.80; N, 17.80; Cl, 11.26. Found: C, 61.00; H, 4.51; N, 17.70; Cl, 10.99.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-1-(4-methoxyphenyl)pyrrol-3-one (4c): (0.48 g, 62%). Mp 213 °C. ^{1}H NMR (DMSO-d_6) δ = 2.34 (s, 6H, 2CH_3), 3.80 (s, 3H, OCH_3), 4.01 (s, 2H, CH_2), 6.74 (s, 1H, 5-H_{Pyrim}), 7.05 (d, J = 8.5, 2H, 2H_{Ar}), 7.37 (d, J = 8.5, 2H, 2H_{Ar}), 7.48 (s, 1H, NH), 9.50 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 22.8 (2CH_3), 55.4 (OCH_3), 59.7 (2-CH_2), 90.7 (4-C), 116.2 (5-C_{Pyrim}), 116.4 (3,5-C_{Ar}), 127.1 (1-C_{Ar}), 127.5 (2,6-C_{Ar}), 154.5 (2-C_{Pyrim}), 154.7 (4-C_{Ar}), 159.8 (4,6-C_{Pyrim}), 164.5 (5-C), 199.9 (3-C=O). Anal. Calcd for $C_{17}H_{18}N_4O_2$: C, 65.79; H, 5.85; N, 18.05. Found: C, 65.70; H, 5.75; N, 17.86.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-1-(4-methylphenyl)pyrrol-3-one (4d): (0.36 g, 49%). Mp 244 °C. ^{1}H NMR (DMSO-d_6) δ = 2.33 (s, 9H, 3CH_3), 4.04 (s, 2H, CH_2), 6.74 (s, 1H, 5-H_{Pyrim}), 7.29 (d, J = 7.5, 2H, 2H_{Ar}), 7.33 (d, J = 7.5, 2H, 2H_{Ar}), 7.61 (s, 1H, NH), 9.60 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 19.32 (CH_3), 22.7 (2CH_3), 59.4 (CH_2), 90.7 (4-C), 116.04 (5-C_{Pyrim}), 125.1 (3,5-C_{Ar}),

130.7 (4-C_{Ar}), 131.2 (2,6-C_{Ar}), 141.5 (1-C_{Ar}), 154.6 (2-C_{Pyrim}), 155.3 (4,6-C_{Pyrim}), 164.1 (5-C), 191.5 (3-C=O). Anal. Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.03. Found: C, 69.30; H, 6.20; N, 19.10.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-1-phenylpyrrol-3-one (8a): (0.44 g, 63%). Mp 251 °C. ^{1}H NMR (DMSO-d_6) δ = 2.33 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 4.21 (s, 2H, CH_2), 7.34 (t, J = 6.8, 1H, 4-H_{Ar}), 7.49 (m, 4H, 2,3,5,6-H_{Ar}), 7.93 (s, 1H, NH), 8.04 (s, 1H, 5-H_{Pyrim}), 9.70 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 18.3 (CH_3), 20.7 (CH_3), 58.5 (2-CH_2), 97.8 (4-C), 115.0 (5-C_{Pyrim}), 125.5 (3,5-C_{Ar}), 130.7 (4-C_{Ar}), 130.9 (2,6-C_{Ar}), 133.0 (1-C_{Ar}), 159.7 (6-C_{Pyrim}), 162.0 (2-C_{Pyrim}), 164.0 (5-C), 164.8 (4-C_{Pyrim}), 188.6 (3-C=O). Anal. Calcd for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.33; H, 5.64; N, 19.90.

5-Amino-1-(4-chlorophenyl)-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydropyrrol-3-one (8b): (0.45 g, 57%). Mp 244 °C. ^{1}H NMR (DMSO-d_6) δ = 2.34 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 4.21 (s, 2H, CH_2), 7.49 (d, J = 8.5, 2H, 2H_{Ar}), 7.56 (d, J = 8.5, 2H, 2H_{Ar}), 8.03 (m, 2H, 5-H_{Pyrim}, NH), 9.68 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 18.2 (CH_3), 20.7 (CH_3), 58.6 (2-CH_2), 97.3 (4-C), 114.5 (5-C_{Pyrim}), 127.0 (3,5-C_{Ar}), 131.1 (2,6-C_{Ar}), 131.6 (4-C_{Ar}), 137.3 (1-C_{Ar}), 159.3 (6-C_{Pyrim}), 161.9 (2-C_{Pyrim}), 164.0 (5-C), 165.1 (4-C_{Pyrim}), 189.4 (3-C=O). Anal. Calcd for $C_{16}H_{15}ClN_4O$: C, 61.05; H, 4.80; N, 17.80; Cl, 11.26. Found: C, 60.95; H, 4.83; N, 17.80; Cl, 11.47.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-1-(4-methoxyphenyl)pyrrol-3-one (8c): (0.42 g, 54%). Mp 239 °C. ^{1}H NMR (DMSO-d_6) δ = 2.32 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 4.12 (s, 2H, CH_2), 7.05 (d, J = 9.0, 2H, 2H_{Ar}), 7.39 (d, J = 9.0, 2H, 2H_{Ar}), 7.73 (s, 1H, NH), 8.02 (s, 1H, 5-H_{Pyrim}), 9.51 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 18.3 (CH_3), 20.7 (CH_3), 55.3 (OCH_3), 58.8 (2-CH_2), 97.7 (4-C), 114.9 (5-C_{Pyrim}), 116.4 (3,5-C_{Ar}), 126.4 (1-C_{Ar}), 127.5 (2,6-C_{Ar}), 159.7 (6-C_{Pyrim}), 160.3 (4-C_{Ar}), 162.0 (2-C_{Pyrim}), 164.0 (4-C_{Pyrim}), 165.1 (5-C), 188.7 (3-C=O). Anal. Calcd for $C_{17}H_{18}N_4O_2$: C, 65.79; H, 5.85; N, 18.05. Found: C, 65.72; H, 5.73; N, 18.03.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-1-(4-methylphenyl)pyrrol-3-one (8d): (0.41 g, 56%). Mp 230 °C. ^{1}H NMR (DMSO-d_6) δ = 2.32 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 4.16 (s, 2H, CH_2), 7.30 (d, J = 8.0, 2H, 2H_{Ar}), 7.35 (d, J = 8.0, 2H, 2H_{Ar}), 7.83 (s, 1H, NH), 8.03 (s, 1H, 5-H_{Pyrim}), 9.62 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 18.1 (CH_3), 19.2 (CH_3), 20.5 (CH_3), 58.3 (2-CH_2), 97.7 (4-C), 114.8 (5-C_{Pyrim}), 125.0 (3,5-C_{Ar}), 129.8 (4-C_{Ar}), 131.2 (2,6-C_{Ar}), 141.9 (1-C_{Ar}), 159.5 (6-C_{Pyrim}), 161.8 (2-C_{Pyrim}), 163.7 (5-C), 164.5 (4-C_{Pyrim}), 188.2 (3-C=O). Anal. Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.03. Found: C, 69.40; H, 6.20; N, 18.87.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-1*H*-pyrrol-3-one (10a): (0.30 g, 59%). Mp 283 °C. ^{1}H NMR (DMSO-d_6) δ = 2.31 (s, 6H, 2CH_3), 3.55 (s, 2H, CH_2), 6.68 (s, 1H, 5-H_{Pyrim}), 7.28 (s, 1H, 1-H), 7.64 (s, 1H, NH), 8.95 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 22.9 (2CH_3), 51.6 (2-CH_2), 89.9

(4-C), 115.8 (5-C_{Pyrim}), 154.5 (4,6-C_{Pyrim}), 160.3 (2-C_{Pyrim}), 166.2 (5-C), 194.3 (3-C=O). Anal. Calcd for $C_{10}H_{12}N_4O$: C, 58.81; H, 5.92; N, 27.43. Found: C, 58.74; H, 5.90; N, 27.60.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-1-methylpyrrol-3-one (10b): (0.30 g, 55%). Mp 288 °C. ^{1}H NMR (DMSO-d_6) δ = 2.32 (s, 6H, $2CH_3$), 3.02 (s, 3H, NCH_3), 3.61 (s, 2H, CH_2), 6.66 (s, 1H, 5-H_{Pyrim}), 7.76 (br s, 1H, NH), 9.39 (br s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 20.3 ($2CH_3$), 30.2 (NCH_3), 58.7 (2-CH_2), 91.2 (4-C), 116.4 (5-C_{Pyrim}), 154.8 (4,6-C_{Pyrim}), 154.9 (2-C_{Pyrim}), 164.8 (5-C), 192.8 (3-C=O). Anal. Calcd for $C_{11}H_{14}N_4O$: C, 60.53; H, 6.47; N, 25.67. Found: C, 60.78; H, 6.54; N, 25.59.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-2-methyl-1*H*-pyrrol-3-one (10c): (0.35 g, 64%). Mp 286 °C. ^{1}H NMR (DMSO-d_6) δ = 1.17 (d, J = 7.0, 3H, CH_3), 2.31 (s, 6H, $2CH_3$), 3.53 (q, J = 7.0, 1H, 2-H), 6.67 (s, 1H, 5-H_{Pyrim}), 7.46 (s, 1H, 1-H), 7.59 (s, 1H, NH), 8.96 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 14.8 (CH_3), 21.9 ($2CH_3$), 58.8 (2-C), 88.3 (4-C), 115.5 (5-C_{Pyrim}), 154.6 (4,6-C_{Pyrim}), 160.1 (2-C_{Pyrim}), 164.8 (5-C), 197.6 (3-C=O). Anal. Calcd for $C_{11}H_{14}N_4O$: C, 60.53; H, 6.47; N, 25.67. Found: C, 60.29; H, 6.40; N, 25.58.

3-Amino-2-(4,6-dimethyl-2-pyrimidinyl)-5,6,7,7*a*-tetrahydro-1*H*-pyrrolizin-1-one (10d): (0.32 g, 53%). Mp 284 °C. ^{1}H NMR (DMSO-d_6) δ = 1.38 (m, 1H, 6-H), 2.00 (m, 3H, 6,7,7-H), 2.33 (s, 6H, $2CH_3$), 3.29 (m, 2H, 5-CH_2), 3.71 (m, 1H, 7*a*-H), 6.72 (s, 1H, 5-H_{Pyrim}), 8.15 (s, 1H, NH), 9.24 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 23.7 ($2CH_3$), 25.8 (6-CH_2), 27.6 (7-CH_2), 44.8 (5-CH_2), 70.4 (7*a*-C), 91.0 (2-C), 115.9 (5-C_{Pyrim}), 154.5 (4,6-C_{Pyrim}), 161.1 (2-C_{Pyrim}), 167.5 (3-C), 196.3 (1-C=O). Anal. Calcd for $C_{13}H_{16}N_4O$: C, 63.92; H, 6.60; N, 22.93. Found: C, 64.16; H, 6.42; N, 22.77.

5-Amino-4-(4,6-dimethyl-2-pyrimidinyl)-2,3-dihydro-2-benzylpyrrol-3-one (10e): (0.35 g, 48%). Mp 228 °C. ^{1}H NMR (DMSO-d_6) δ = 2.31 (s, 6H, $2CH_3$), 2.62 (dd, J^2 = 13.5, J^3 = 8.5, 1H, α-H_{R1}), 3.08 (dd, J^2 = 13.5, J^3 = 3.0, 1H, α-H_{R1}), 3.82 (dd, J^3 = 8.5, J^3 = 3.0, 1H, 2-H), 6.67 (s, 1H, 5-H_{Pyrim}), 7.20 (t, J = 6.5, 1H, 4-H_{R1}), 7.26 (m, 4H, 2,3,5,6-H_{R1}), 7.34 (m, 2H, 1-H, NH), 8.91 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 20.4 ($2CH_3$), 37.2 (α-C_{R1}), 64.6 (2-C), 89.6 (4-C), 115.9 (5-C_{Pyrim}), 127.6 (4-C_{R1}), 128.7 (3,5-C_{R1}), 128.8 (2,6-C_{R1}), 134.3 (1-C_{R1}), 154.9 (4,6-C_{Pyrim}), 161.0 (2-C_{Pyrim}), 165.4 (5-C), 196.4 (3-C=O). Anal. Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.03. Found: C, 69.42; H, 6.07; N, 19.10.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-1*H*-pyrrol-3-one (12a): (0.29 g, 57%). Mp 145 °C. ^{1}H NMR (DMSO-d_6) δ = 2.28 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.66 (s, 2H, CH_2), 7.49 (s, 1H, 1-H), 7.80 (s, 1H, NH), 7.92 (s, 1H, 5-H_{Pyrim}), 8.98 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 18.9 (CH_3), 21.3 (CH_3), 51.5 (2-CH_2), 98.4 (4-C), 116.1 (5-C_{Pyrim}), 161.2 (4-C_{Pyrim}), 162.8 (6-C_{Pyrim}), 164.6 (2-C_{Pyrim}), 167.3 (5-C), 189.5 (3-C=O). Anal. Calcd for $C_{10}H_{12}N_4O$: C, 58.81; H, 5.92; N, 27.43. Found: C, 58.87; H, 5.84; N, 27.45.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-1-methylpyrrol-3-one (12b): (0.34 g, 62%). Mp

285 °C. ^{1}H NMR (DMSO-d_6) δ = 2.28 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.02 (s, 3H, NCH_3), 3.72 (s, 2H, CH_2), 7.92 (s, 1H, 5-C_{Pyrim}), 7.99 (s, 1H, NH), 9.41 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 18.4 (CH_3), 20.8 (CH_3), 30.2 (NCH_3), 57.1 (2-CH_2), 98.4 (4-C), 115.5 (5-C_{Pyrim}), 160.3 (4-C_{Pyrim}), 162.2 (6-C_{Pyrim}), 163.6 (2-C_{Pyrim}), 164.6 (5-C), 186.6 (3-C=O). Anal. Calcd for $C_{11}H_{14}N_4O$: C, 60.53; H, 6.47; N, 25.67. Found: C, 60.39; H, 6.34; N, 25.53.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-2-methyl-1*H*-pyrrol-3-one (12c): (0.29 g, 54%). Mp 100 °C. ^{1}H NMR (DMSO-d_6) δ = 1.19 (d, J = 7.0, 3H, 2-CH_3), 2.28 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.66 (q, J = 7.0, 1H, 2-H), 7.73 (s, 1H, 1-H), 7.78 (s, 1H, NH), 7.91 (s, 1H, 5-H_{Pyrim}), 8.98 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 15.9 (2-CH_3), 18.5 (CH_3), 20.9 (CH_3), 58.6 (2-C), 96.5 (4-C), 115.2 (5-C_{Pyrim}), 160.1 (4-C_{Pyrim}), 162.3 (6-C_{Pyrim}), 164.4 (2-C_{Pyrim}), 165.7 (5-C), 195.1 (3-C=O). Anal. Calcd for $C_{11}H_{14}N_4O$: C, 60.53; H, 6.47; N, 25.67. Found: C, 60.41; H, 6.67; N, 25.60.

3-Amino-2-(2,6-dimethyl-4-pyrimidinyl)-5,6,7,7*a*-tetrahydro-1*H*-pyrrolizin-1-one (12d): (0.41 g, 67%). Mp 115 °C. ^{1}H NMR (DMSO-d_6) δ = 1.37 (m, 1H, 6-H), 2.04 (m, 3H, 6,7,7-H), 2.29 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 3.29 (m, 2H, 5-CH_2) 3.84 (m, 1H, 7*a*-H), 7.91 (s, 1H, 5-H_{Pyrim}), 8.38 (s, 1H, NH), 9.28 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 18.5 (CH_3), 20.9 (CH_3), 26.9 (6-CH_2), 28.0 (7-CH_2), 45.3 (5-CH_2), 69.8 (7*a*-C), 98.8 (4-C), 115.2 (5-C_{Pyrim}), 160.0 (4-C_{Pyrim}), 162.2 (6-C_{Pyrim}), 163.8 (2-C_{Pyrim}), 164.2 (3-C), 186.4 (1-C=O). Anal. Calcd for $C_{13}H_{16}N_4O$: C, 63.92; H, 6.60; N, 22.93. Found: C, 63.90; H, 6.65; N, 22.90.

5-Amino-4-(2,6-dimethyl-4-pyrimidinyl)-2,3-dihydro-2-benzylpyrrol-3-one (12e): (0.48 g, 65%). Mp 102 °C. ^{1}H NMR (DMSO-d_6) δ = 2.29 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 2.72 (dd, J^2 = 13.5, J^3 = 7.5, 1H, α-H_{R1}), 3.09 (dd, J^2 = 13.5, J^3 = 3.5, 1H, α-H_{R1}), 3.96 (dd, J^3 = 7.5, J^3 = 3.5, 1H, 2-H), 7.19 (t, J = 7.0, 1H, 4-H_{R1}), 7.23 (m, 4H, 2,3,5,6-H_{R1}), 7.47 (s, 1H, 1-H), 7.58 (s, 1H, NH), 7.91 (s, 1H, 5-H_{Pyrim}), 8.88 (s, 1H, NH). ^{13}C NMR (CF_3COOD) δ = 18.1 (CH_3), 20.5 (CH_3), 37.4 (α-C_{R1}), 63.5 (2-C), 96.8 (4-C), 114.3 (5-C_{Pyrim}), 127.8 (4-C_{R1}), 128.6 (3,5-C_{R1}), 128.7 (2,6-C_{R1}), 133.3 (1-C_{R1}), 159.1 (4-C_{Pyrim}), 161.7 (6-C_{Pyrim}), 163.9 (2-C_{Pyrim}), 165.7 (5-C), 192.4 (3-C=O). Anal. Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.03. Found: C, 69.59; H, 6.18; N, 19.18.

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