Synthesis of 2-Imino-7-methyl-2,3-dihydroimidazo[1,2-*a*]-pyrimidin-5(1*H*)-ones and their Reactions with Nucleophiles

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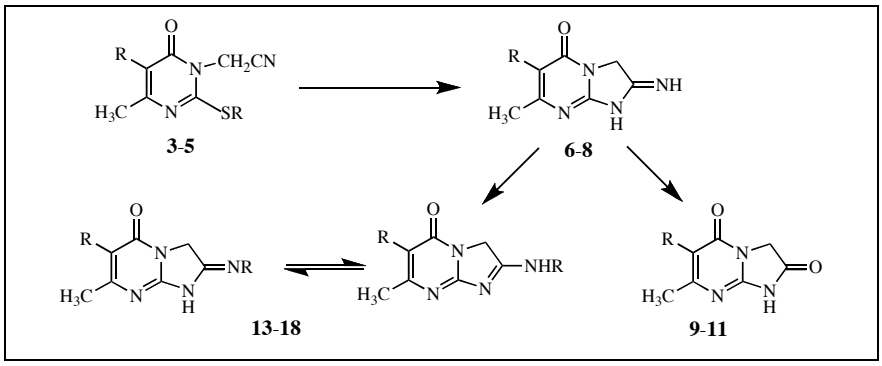

[2-Alkylthio-6-methyl-4-oxopyrimidin-3(4*H*)-yl]acetonitriles (**3**-**5**) treated with sodium methoxide in methanol followed by ammonium chloride were cyclized to 2-imino-7-methyl-2,3-dihydroimidazo[1,2-*a*]-pyrimidin-5(1*H*)-ones (**6**-**8**). Under acid or base-catalyzed hydrolysis they were converted to 7-methyl-imidazo[1,2-*a*]pyrimidine-2,5-[1*H*,3*H*]-diones (**9**-**11**), whereas in the reaction with butyl- or benzylamine the corresponding 7-methyl-2-(substitutedamino)imidazo[1,2-*a*]pyrimidin-5(3*H*)-ones (**13**-**18**) were produced. The latter were found to exist in two tautomeric forms in $CDCl_3$ solution.

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INTRODUCTION

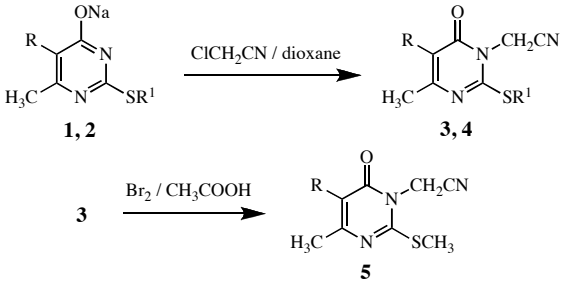
2-Imino-2,3-dihydroimidazo[1,2-*a*]pyrimidin-5(1*H*)-ones are interesting for their chemistry and various biological properties. Such type of compounds possessing the amidine moiety in their structure is able to react either with electrophiles or nucleophiles to give different heterocyclic compounds [1]. On the other hand, the N(3)-substituted pyrimidin-4(3*H*)-ones as well as semicyclic amidine moiety are frequently found in biologically active molecules. There, 3-substituted pyrimidin-4(3*H*)-ones exhibit cardiotonic [2] and anti-inflammatory activity [3]. Semicyclic amidines are known for their hypoglycaemic effects [4]. Cyclic amidines from five to nine-membered rings are reported as potent and selective inhibitors of human inducible nitric oxide synthase (NOS) [5-8].

RESULTS AND DISCUSSION

Imidazo[1,2-*a*]pyrimidinones **6**-**8** were synthesized starting with nitriles **3**-**5**. Nitriles **3**, **4** were prepared by the reaction of corresponding sodium salt **1** or **2** with chloroacetonitrile in dioxane [9]. Nitrile **5** was obtained by bromination of **3** with bromine in glacial acetic acid. The synthesis of nitriles **3**-**5** is outlined in Scheme 1.

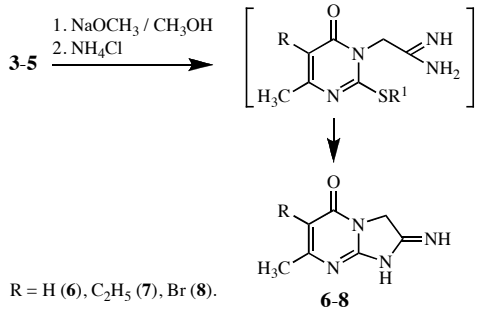
Compounds **3**-**5** reacted with sodium methoxide in methanol followed with ammonium chloride to form amidine intermediates which cyclized *in situ* to corresponding 2-imino-7-methyl-2,3-dihydroimidazo[1,2-*a*]pyrimidin-5(1*H*)-ones **6**-**8** (Scheme 2).

Scheme 1



R = H, R^1 = CH_3 (**1**, **3**), R = R^1 = C_2H_5 (**2**, **4**), R = Br (**5**).

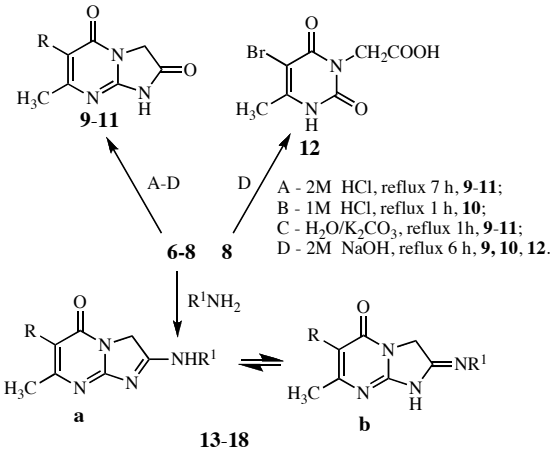
Scheme 2



R = H (**6**), C_2H_5 (**7**), Br (**8**).

It should be pointed out, that compound **6** is already reported. Previously [10] we have used catalytic amount of sodium methoxide for the synthesis of **6**. Herein, the synthesis of **6**-**8** was accomplished with stoichiometric amount of sodium methoxide. In addition, to accelerate formation of compounds **6**-**8** gentle heating to 30 °C is expedient. As it was mentioned above, compounds **6**-**8** bearing in their structure amidine moiety are able to react both with electrophiles and nucleophiles. We studied two types of reactions with nucleophiles – hydrolysis and transamination (Scheme 3).

Scheme 3



R = H (**9**), C_2H_5 (**10**), Br (**11**);
R = H, $R^1 = C_4H_9$ (**13**); R = H, $R_1 = CH_2C_6H_5$ (**14**);
R = C_2H_5, $R^1 = C_4H_9$ (**15**); R = C_2H_5, $R^1 = CH_2C_6H_5$ (**16**);
R = Br, $R^1 = C_4H_9$ (**17**); R = Br, $R^1 = CH_2C_6H_5$ (**18**).

Compounds **6**-**8** were hydrolyzed either by acid-, or by base-catalyzed conditions. Upon refluxing of **6** and **8** for 7 hours in 2 *M* HCl solution, the imine group was converted into the oxo group to give **9** and **11** *(Method A)*. Hydrolysis of compound **7** under the same conditions gave a mixture of compound **10** and unidentified one in a ratio 1:3, respectively (according to the ^{1}H nmr spectrum). The desired compound **10** was, however, obtained selectively performing hydrolysis of **7** under milder conditions – under reflux in 1 *M* HCl solution for an hour *(Method B)*, Scheme 3.

Base-catalyzed hydrolysis of **6**-**8** was accomplished, using either potassium carbonate, or 2 *M* sodium hydroxide solution. Compounds **6**-**8** were treated with potassium carbonate solution to give the corresponding imidazo[1,2-*a*]pyrimidin-2,5-[1*H*,3*H*]-diones **9**-**11** *(Method C)*. Hydrolysis with 2 *M* sodium hydroxide was ambiguous. Compound **9** was isolated in 30% yield *(Method D)*, while compound **10** was formed in a mixture with unidentified side product. Hydrolysis of **8** under analogous conditions produced the acid **12** in 25% yield *(Method D)*. In conclusion, acid- or base-catalysed hydrolysis (using potassium carbonate) of 2-imino-2,3-dihydroimidazo[1,2-*a*]pyrimidin-5(1*H*)-ones **6**-**8** could be successfully used for the synthesis of corresponding imidazo[1,2-*a*]pyrimidin-2,5[1*H*,3*H*]-diones **9**-**11**. It is worthy of noting, that compounds **9** and **11** were synthesized by the reaction of 2-aminopyrimidines with α-haloacids as reported earlier [11] (Scheme 3).

Compounds **6**-**8** were allowed to react with butyl- and benzylamine to give transamination products **13**-**18**. Upon heating of **6**-**8** with an excess of butylamine at 70 °C for 3 hours compounds **13**, **15**, **17** were obtained in good yields (60-75%). Benzylation of **6**-**8** was accomplished using excess benzylamine at 120 °C for 0.5 hour to yield 78-81% of **14**, **16**, **18** (Scheme 3).

Compounds **13**-**18** can exist in solutions in two tautomeric forms **a** and **b** (Scheme 3). NH group protons of compounds **13**-**18** in DMSO-d_6 solutions are observed as triplets at δ 8.75-9.48 ppm and the adjacent methylene group protons - as triplets of doublets for **13**, **15** and **17** at δ 3.34-3.37 ppm or doublets for **14**, **16** and **18** at δ 4.59-4.61 ppm. These data are in favour of tautomer **a**. Additionally, such kind of multiplicity confirms, that transamination occurs at the exocyclic imino group and not at the endocyclic amino group.

In ^{1}H nmr spectra of **13**, **15**, **17** in $CDCl_3$ solutions most protons display two sets of signals. The same as in DMSO-d_6, NH group protons appear as high intensity triplets at δ 7.83-8.26 ppm along with smaller intensity singlets at δ 7.96-7.98 ppm. The butyl substituent protons of methylene group adjacent to nitrogen (N-CH_2) appear as triplets of doublets at δ 3.56-3.62 ppm together with less intense triplets at δ 3.3-3.35 ppm. From these data it could be considered that compounds **13**, **15**, **17** exist in tautomeric equilibrium in $CDCl_3$ solutions. The approximate ratio of tautomers **a** and **b** is equal 5:1 (estimated from the ratio of intensity of proton signals in ^{1}H NMR).

Two sets of signals almost for each group of protons were also observed in the ^{1}H NMR spectra of **14** and **16** in $CDCl_3$ solutions (compound **18** is insoluble in $CDCl_3$). Chemical shift of NH proton appeared as a triplet at δ 8.55 and 7.87 ppm for **14** and **16,** respectively. Methylene group protons of benzyl moiety showed doublets at δ 4.74 and 4.71 ppm together with less intense singlets at δ 4.51 and 4.50 ppm for **14** and **16,** respectively. The results discussed let us to maintain, that compounds **14** and **16** in $CDCl_3$ solutions exist as the mixtures of tautomeric forms **a** and **b**. The ratio of tautomers **a**:**b** = 10:1 was estimated by intensity of signals in ^{1}H NMR spectra.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. Nuclear magnetic resonance (nmr) spectra were recorded on a Unity Varian INOVA spectrometer at 300 MHz

for ^{1}H and 75 MHz for ^{13}C. Chemical shifts (δ) are reported in ppm relative to TMS. The ir spectra were recorded on a Spectrum BX FT-IR (Perkin-Elmer, Sweden) as potassium bromide pellets. The reactions and purity of compounds was controlled by tlc on ALUGRAM SIL G/UV$_{254}$ plates (MACHEREY-NAGEL, Germany). Elemental analyses were performed at the Microanalyses Laboratory of the Department of Organic Chemistry of Vilnius University.

6-Methyl-2-(methylthio)pyrimidin-4(3*H*)-one and 5-ethyl-2-ethylthio-6-methylpyrimidin-4(3*H*)-one were synthesized as reported in references [12,13].

The Na-salts **1** and **2** were synthesized according [14].

[2-Alkylthio-6-methyl-4-oxopyrimidin-3(4*H*)-yl]acetonitriles 3, 4. To a suspension of 0.01 mol of sodium salt **1** or **2** in dioxane (10 mL) at reflux chloroacetonitrile was added dropwise (0.76 mL, 0.91 g, 0.012 mol). The reaction mixture was heated at reflux for 3 hours, the solvent was removed in vacuum and the residue was cooled and diluted with water (50 mL). The solid formed was collected by filtration, dried at room temperature and recrystallized from hexane.

[6-Methyl-2-methylthio-4-oxopyrimidin-3(4*H*)-yl]acetonitrile (3). This compound was obtained in 1.31 g (67%) yield, mp 120-122 °C; (mp 120-122 °C, Ref. [9]).

[5-Ethyl-2-ethylthio-6-methyl-4-oxopyrimidin-3(4*H*)-yl]-acetonitrile (4). This compound was obtained in 1.47 g (62%) yield, mp 78-79 °C; ir: 1665 (C=O) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 1.02 (t, J = 7.5 Hz, 3H, CH$_3$), 1.35 (t, J = 7.3 Hz, 3H, CH$_3$), 2.27 (s, 3H, CH$_3$), 2.43 (q, J = 7.5 Hz, 2H, CH$_2$), 3.24 (q, J = 7.3 Hz, 2H, SCH$_2$), 5.05 (s, 2H, NCH$_2$) ppm; ^{13}C nmr (DMSO-d$_6$): δ 13.2, 14.6, 19.5, 21.8, 27.0, 32.4, 115.7, 120.7, 157.0, 158.4, 161.1 ppm. *Anal*. Calcd. for $C_{11}H_{15}N_3OS$ (237.32): C 55.67; H 6.37; N 17.71. Found: C 55.96; H 6.30; N 18.01.

[5-Bromo-6-methyl-2-methylthio-4-oxopyrimidin-3(4*H*)-yl]-acetonitrile (5). To a solution of acetonitrile **3** (1.95 g, 0.01 mol) in glacial acetic acid (70 mL) bromine (0.77 mL, 2.49 g, 0.015 mol) was added dropwise at room temperature. The reaction mixture was stirred at room temperature for 1 hour, the precipitate was collected by filtration, washed with water and crystallized from methanol to yield **5**, 1.81 g (66 %), mp 170-171°C; ir: 1679 (C=O), 2360 (C≡N) cm^{-1}; ^{1}H nmr (CDCl$_3$): δ 2.51 (s, 3H, CH$_3$), 2.70 (s, 3H, SCH$_3$), 5.04 (s, 2H, NCH$_2$) ppm; ^{13}C nmr (CDCl$_3$): δ 15.7, 25.1, 32.0, 107.3, 113.0, 157.7, 158.9, 162.0 ppm. *Anal*. Calcd. for $C_8H_8BrN_3OS$ (274.14): C 35.05; H 2.94; N 15.33. Found: C 35.38; H 2.65; N 15.62.

General Procedure for the Synthesis of 2-imino-7-methyl-2,3-dihydroimidazo[1,2-*a*]pyrimidin-5(1*H*)-ones 6-8. A mixture of 0.01 mol of acetonitrile **3**, **4** or **5** and sodium methoxide, prepared of sodium (0.23 g, 0.01 mol) and methanol (15 mL), was stirred at room temperature for 1 hour. Ammonium chloride (0.59 g, 0.011 mol) was then added to the mixture and stirring at 30 °C was continued for 1 hour. The reaction mixture was allowed to cool to room temperature, the solid was collected by filtration, washed with ether and crystallized from water.

2-Imino-7-methyl-2,3-dihydroimidazo[1,2-*a*]pyrimidin-5(1*H*)-one (6). This compound was obtained in 1.25 g (76%) yield, mp > 300 °C (decomp.); (mp 308-310 °C, Ref. [10]).

6-Ethyl-2-imino-7-methyl-2,3-dihydroimidazo[1,2-*a*]-pyrimidin-5(1*H*)-one (7). This compound was obtained in 1.17 g (61%) yield, mp > 270 °C (decomp.); ir: 1650 (C=O), 3248, 3376 (NH) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 0.98 (t, J = 7.4 Hz, 3H, CH$_3$), 2.17 (s, 3H, CH$_3$), 2.39 (q, J = 7.4 Hz, 2H, CH$_2$), 4.62 (s, 2H, NCH$_2$), 8.22 (s, 1H, NH), 8,45 (s, 1H, NH) ppm; ^{13}C nmr (DMSO-d$_6$): δ 14.0, 19.1, 22.0, 50.5, 117.1, 160.4, 160.5, 164.2, 175.8 ppm. *Anal*. Calcd. for $C_9H_{12}N_4O$ (192.22): C 56.24; H 6.29; N 29.15. Found: C 56.28; H 6.52; N 29.05.

6-Bromo-2-imino-7-methyl-2,3-dihydroimidazo[1,2-*a*]-pyrimidin-5(1*H*)-one (8). This compound was obtained in 1.6 g (66%) yield, mp > 270 °C (decomp.); ir: 1655 (C=O), 3259, 3378 (NH) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 2.34 (s, 3H, CH$_3$), 4.72 (s, 2H, NCH$_2$), 8.48 (s, 1H, NH), 8,75 (s, 1H, NH) ppm; ^{13}C nmr (DMSO-d$_6$): δ 25.7, 51.3, 102.3, 156.5, 163.7, 165.6, 176.8 ppm. *Anal*. Calcd. for $C_7H_7BrN_4O$ (243.06): C 34.59; H 2.90; N 23.05. Found: C 34.85; H 2.81; N 23.05.

Hydrolysis of 2-imino-7-methyl-2,3-dihydroimidazo[1,2-*a*]-pyrimidin-5(1*H*)-ones 6-8.

Method A. A mixture of 0.005 mol of compound **6**, **7** or **8** in 2M HCl (3.5 mL) was heated at reflux for 7 hours. The reaction mixture was allowed to cool to room temperature. The precipitate formed was collected by filtration and crystallized from water.

7-Methylimidazo[1,2-*a*]pyrimidine-2,5[1*H*,3*H*]-dione (9). This compound was obtained in 0.42 g (51%) yield, mp > 300 °C (decomp.); (mp 281-283 °C (decomp.), Ref. [11]); ir: 1701, 1755, 1776 (C=O), 3175, 3428 (NH) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 2.16 (s, 3H, CH$_3$), 4.39 (s, 2H, NCH$_2$), 5.92 (s, 1H, CH), 12.02 (br s, 1H, NH) ppm; ^{13}C nmr (DMSO-d$_6$): δ 24.1, 48.6, 106.1, 155.8, 159.3, 164.7, 171.4 ppm. *Anal*. Calcd. for $C_7H_7N_3O_2$ (165.15): C 50.91; H 4.27; N 25.44. Found: C 51.27; H 4.33; N 25.14.

6-Bromo-7-methylimidazo[1,2-*a*]pyrimidine-2,5[1*H*,3*H*]-dione (11). This compound was obtained in 0.82 g (67%) yield, mp 266-268 °C (decomp.); (mp 242-244 °C (decomp.), Ref. [11]); ir: 1685, 1758, 1783 (C=O), 3115 (NH) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 2.37 (s, 3H, CH$_3$), 4.47 (s, 2H, NCH$_2$), 12.22 (s, 1H, NH) ppm; ^{13}C nmr (DMSO-d$_6$): δ 25.4, 49.7, 104.0, 154.2, 155.6, 162.8, 170.8 ppm. *Anal*. Calcd. for $C_7H_6BrN_3O_2$ (244.05): C 34.45; H 2.48; N 17.22. Found: C 34.73; H 2.53; N 16.99.

Method B. A mixture of compound **7** (0.96 g, 0.005 mol) and 1M HCl (7 mL) was refluxed for 1 hour and left to cooled to room temperature. The solid formed was collected by filtration and crystallized from water.

6-Ethyl-7-methylimidazo[1,2-*a*]pyrimidine-2,5[1*H*,3*H*]-dione (10). This compound was obtained in 0.5 g (52%) yield, mp 274-276 °C (decomp.); ir: 1691, 1749, 1769 (C=O), 3436 (NH) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ ppm; δ 0.99 (t, J = 7.5 Hz, 3H, CH$_3$), 2.20 (s, 3H, CH$_3$), 2.41 (q, J = 7.5 Hz, 2H, CH$_2$), 4.40 (s, 2H, NCH$_2$), 11.91 (s, 1H, NH) ppm; ^{13}C nmr (DMSO-d$_6$): δ 13.2, 19.0, 21.4, 48.9, 118.9, 153.0, 158.4, 159.4, 171.4 ppm. *Anal*. Calcd. for $C_9H_{11}N_3O_2$ (193.20): C 55.95; H 5.74; N 21.75. Found: C 56.22; H 5.93; N 22.02.

Method C. A mixture of 0.005 mol of compound **6**, **7** or **8**, K_2CO_3 (2.07 g, 0.015 mol) and water (7.5 mL) was stirred at reflux for 1 hour. The solution was cooled, acidified to pH 4 by dropwise addition of conc. HCl. The precipitate was collected by filtration and crystallized from water to yield a white solid of **9**, 0.5 g (61%), **10**, 0.7 g (57%) or **11**, 0.8 g (66%).

Method D. A mixture of 0.005 mol of compound **6**, **7** or **8** and 2 *M* NaOH (6 mL) was stirred ar reflux for 6 hours. The solution was cooled, acidified to pH 4 by dropwise addition of conc. HCl. The precipitate was collected by filtration and crystallized from water. Compound **9** was obtained in 0.25 g (30 %) yield.

[5-Bromo-6-methyl-2,4-dioxo-3,4-dihydropyrimidin-3(4*H*)-yl]acetic acid (12). This compound was obtained in 0.33 g (25%) yield, mp 235-236 °C; ir: 1643, 1718, 1736 (C=O), 3200, 3253 (NH, OH) cm^{-1}; ^1H nmr (DMSO-d_6): δ 2.28 (s, 3H, CH_3), 4.47 (s, 2H, NCH_2), 11.78 (s, 1H, NH), 13.04 (s, 1H, OH), ppm; ^{13}C nmr (DMSO-d_6): δ 20.2, 42.8, 95.0, 150.6, 151.3, 159.5, 169.7 ppm. *Anal*. Calcd. for $C_7H_7BrN_2O_4$ (263.05): C 31.96; H 2.68; N 10.65. Found: C 32.22; H 2.86; N 11.01.

General Procedure for the Synthesis of 7-methyl-2-(substitutedamino)imidazo[1,2-a]pyrimidin-5(3*H*)-ones 13-18. A mixture of 0.005 mol of compound **6**, **7** or **8** and 0.025 mol of butyl- or benzylamine under Ar was stirred in an oil bath at 70 or 120 °C temperature for 3 or 0.5 hour, respectively. The cold reaction mixture was worked up with ether to give a solid, which was crystallized from dioxane.

2-Butylamino-7-methylimidazo[1,2-*a*]pyrimidin-5(3*H*)-one (13). This compound was obtained in 0.83 g (75%) yield, mp 198-200 °C; ir: 1669 (C=O), 3176 (NH) cm^{-1}; ^1H nmr (DMSO-d_6): δ 0.92 (t, J = 7.3 Hz, 3H, CH_3), 1.31-1.43 (m, 2H, CH_2), 1.51-1.61 (m, 2H, CH_2), 2.13 (s, 3H, CH_3), 3.36 (dt, J = 5.2, 6.8 Hz, 2H, CH_2), 4.64 (s, 2H, NCH_2), 5.75 (s, 1H, CH), 8.88 (t, J = 5.2 Hz, 1H, NH) ppm; ^1H nmr ($CDCl_3$): δ 0.94-1.03 (m, 3H, CH_3), 1.37-1.50 (m, 2H, CH_2), 1.64-1.75 (m, 2H, CH_2), 2.29 (**b**) and 2.31 (**a**) (2s, 3H, CH_3), 3.32 (**b**) and 3.59 (**a**) [(t, J = 7.1 Hz (**b**) and dt, J = 5.4, 7.1 Hz (**a**), 2H, CH_2], 4.75 (**b**) and 4.76 (**a**) (2s, 2H, NCH_2), 5.88 (**a**) and 5.94 (**b**) (2s, 1H, CH), 7.97 (**b**) and 8.26 (**a**) [s (**b**) and t, J = 5.4 Hz (**a**), 1H, NH] ppm; ^{13}C nmr (DMSO-d_6): δ 14.3, 20.2, 24.5, 31.0, 42.5, 50.0, 104.4, 160.6, 166.1, 166.7, 174.1 ppm. *Anal*. Calcd. for $C_{11}H_{16}N_4O$ (220.27): C 59.98; H 7.32; N 25.44. Found: C 59.84; H 7.26; N 25.31.

2-Benzylamino-7-methylimidazo[1,2-*a*]pyrimidin-5(3*H*)-one (14). This compound was obtained in 0.99 g (78%) yield, mp 217-219 °C; ir: 1679 (C=O), 3162, 3231 (NH) cm^{-1}; ^1H nmr (DMSO-d_6): δ 2.13 (s, 3H, CH_3), 4.61 (d, J = 5.9 Hz, 2H, CH_2), 4.73 (s, 2H, NCH_2) 5.78 (s, 1H, CH), 7.29-7.41 (m, 5H, Ar-H), 9.36 (t, J = 5.9 Hz, 1H, NH) ppm; ^1H nmr ($CDCl_3$): δ 2.21 (**a**) and 2.24 (**b**) (2s, 3H, CH_3), 4.51 (**b**) and 4.74 (**a**) [s (**b**) and d, J = 5.4 Hz (**a**), 2H, CH_2], 4.66 (**b**) and 4.69 (**a**) (2s, 2H, NCH_2), 5.48 (**a**) and 5.90 (**b**) (2s, 1H, CH), 7.30-7.41 (m, 5H, Ar-H), 8.55 (**a**) (t, J = 5.4 Hz, 1H, NH] ppm; ^{13}C nmr (DMSO-d_6): δ 24.5, 46.3, 50.2, 104.6, 128.1, 128.4, 129.2, 138.3, 160.5, 166.1, 166.5, 174.4 ppm. *Anal*. Calcd. for $C_{14}H_{14}N_4O$ (254.29): C 66.13; H 5.55; N 22.03. Found: C 65.98; H 5.66; N 22.20.

2-Butylamino-6-ethyl-7-methylimidazo[1,2-*a*]pyrimidin-5(3*H*)-one (15). This compound was obtained in 0.74 g (60%) yield, mp 196-198 °C; ir: 1642 (C=O), 3241 (NH) cm^{-1}; ^1H nmr (DMSO-d_6): δ 0.90-1.01 (m, 6H, $2CH_3$), 1.29-1.42 (m, 2H, CH_2), 1.50-1.60 (m, 2H, CH_2), 2.17 (s, 3H, CH_3), 2.39 (q, J = 7.4 Hz, 2H, CH_2), 3.35 (dt, J = 5.2, 6.6 Hz, 2H, CH_2), 4.64 (s, 2H, NCH_2), 8.75 (t, J = 5.2 Hz, 1H, NH) ppm; ^1H nmr ($CDCl_3$): δ 0.91-1.01 (m, 3H, CH_3), 1.05-1.14 (m, 3H, CH_3), 1.33-1.50 (m, 2H, CH_2), 1.61-1.76 (m, 2H, CH_2), 2.31 (**b**) and 2.33 (**a**) (2s, 3H, CH_3), 2.47-2.59 (m, 2H, CH_2), 3.31 (**b**) and 3.56 (**a**) [(t, J = 7.1 Hz (**b**) and dt, J = 5.4, 7.2 Hz (**a**), 2H, CH_2], 4.73 (**b**) and 4.76 (**a**) (2s, 2H, NCH_2), 7.83 (**a**) and 7.98 (**b**) [t, J = 5.4 Hz (**a**), s (**b**), 1H, NH] ppm; ^{13}C nmr (DMSO-d_6): δ 14.0, 14.3, 19.0, 20.2, 22.0, 31.1, 42.4, 50.3, 117.0, 160.3, 160.5, 163.8, 173.3 ppm. *Anal*. Calcd. for $C_{13}H_{20}N_4O$ (248.33): C 62.88; H 8.12; N 22.56. Found: C 63.06; H 7.87; N 22.25.

2-Benzylamino-6-ethyl-7-methylimidazo[1,2-*a*]pyrimidin-5(3*H*)-one (16). This compound was obtained in 1.1 g (78%) yield, mp 214-216 °C (decomp.); ir: 1641 (C=O), 3248 (NH) cm^{-1}; ^1H nmr (DMSO-d_6): δ 0.98 (t, J = 7.4 Hz, 3H, CH_3), 2.18 (s, 3H, CH_3), 2.40 (q, J = 7.4 Hz, 2H, CH_2), 4.59 (d, J = 5.7 Hz, 2H, CH_2), 4.72 (s, 2H, NCH_2), 7.25-7.43 (m, 5H, Ar-H), 9.22 (t, J = 5.7 Hz, 1H, NH) ppm; ^1H nmr ($CDCl_3$): δ 1.02-1.10 (m, 3H, CH_3), 2.25 (**b**) and 2.29 (**a**) (2s, 3H, CH_3), 2.48 (q, J = 7.4 Hz, 2H, CH_2), 4.50 (**b**) and 4.71 (**a**) 4.51 (**b**) and 4.74 (**a**) [s (**b**) and d, J = 5.6 Hz (**a**), 2H, CH_2], 4.62 (**b**) and 4.65 (**a**) (2s, 2H, NCH_2), 7.24-7.41 (m, 5H, Ar-H), 7.87 (**a**) (t, J = 5.6 Hz, 1H, NH] ppm; ^{13}C nmr (DMSO-d_6): δ 14.0, 19.1, 22.0, 46.2, 50.5, 117.3, 127.9, 128.3, 129.1, 138.5, 160.3, 160.5, 163.6, 173.7 ppm. *Anal*. Calcd. for $C_{16}H_{18}N_4O$ (282.34): C 68.06; H 6.43; N 19.84. Found: C 67.83; H 6.20; N 19.67.

6-Bromo-2-butylamino-7-methylimidazo[1,2-*a*]pyrimidin-5(3*H*)-one (17). This compound was obtained in 1.11 g (74%) yield, mp 210-212 °C (decomp.); ir: 1669 (C=O), 3166, 3223 (NH) cm^{-1}; ^1H nmr (DMSO-d_6): δ 0.92 (t, J = 7.2 Hz, 3H, CH_3), 1.28-1.43 (m, 2H, CH_2), 1.49-1.62 (m, 2H, CH_2), 2.34 (s, 3H, CH_3), 3.37 (dt, J = 5.4, 7.0 Hz, 2H, CH_2), 4.73 (s, 2H, NCH_2), 9.02 (t, J = 5.4 Hz, 1H, NH) ppm; ^1H nmr ($CDCl_3$): δ 0.93-1.03 (m, 3H, CH_3), 1.35-1.49 (m, 2H, CH_2), 1.64-1.77 (m, 2H, CH_2), 2.50 (**b**) and 2.53 (**a**) (2s, 3H, CH_3), 3.35 (**b**) and 3.62 (**a**) [(t, J = 7.2 Hz (**b**) and dt, J = 5.5, 7.3 Hz (**a**), 2H, CH_2], 4.83 (**b**) and 4.85 (**a**) (2s, 2H, NCH_2), 7.83 (**a**) and 7.96 (**b**) [t, J = 5.5 Hz (**a**), s (**b**), 1H, NH] ppm; ^{13}C nmr (DMSO-d_6): δ 14.3, 20.1, 25.7, 31.0, 42.6, 51.1, 102.3, 156.5, 163.7, 165.1, 174.2 ppm. *Anal*. Calcd. for $C_{11}H_{15}BrN_4O$ (229.17): C 44.16; H 5.05; N 18.73. Found: C 44.21; H 5.18; N 18.78.

2-Benzylamino-6-bromo-7-methylimidazo[1,2-*a*]pyrimidin-5(3*H*)-one (18). This compound was obtained in 1.35 g (81%) yield, mp 230-232 °C (decomp.); ir: 1655, 1674 (C=O), 3169, 3236 (NH) cm^{-1}; ^1H nmr (DMSO-d_6): δ 2.34 (s, 3H, CH_3), 4.61 (d, J = 5.4 Hz, 2H, CH_2), 4.81 (s, 2H, NCH_2), 7.29-7.41 (m, 5H, Ar-H), 9.49 (t, J = 5.4 Hz, 1H, NH) ppm; ^{13}C nmr (DMSO-d_6): δ 25.7, 46.4, 51.3, 102.6, 128.1, 128.5, 129.2, 138.1, 156.5, 163.7, 165.0, 174.5 ppm. *Anal*. Calcd. for $C_{14}H_{13}BrN_4O$ (333.18): C 50.47; H 3.93; N 16.82. Found: C 50.62; H 3.92; N 17.11.

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