Synthesis of 4-(Trihalomethyl)dipyrimidin-2-ylamines from β-Alkoxy-α,β-unsaturated Trihalomethyl Ketones

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The synthesis of a novel series of twelve 4-(trihalomethyl)dipyrimidin-2-ylamines, from the cyclocondensation reaction of 4-(trichloromethyl)-2-guanidinopyrimidine, with β-alkoxyvinyl trihalomethyl ketones, of general formula: X_3C-C(O)-C(R^2)=C(R^1)-OR, where: X = F, Cl; R = Me, Et, -$(CH_2)_2$-, -$(CH_2)_3$-; R^1 = H, Me; R^2 = H, Me, -$(CH_2)_2$-, -$(CH_2)_3$-, is reported. The reactions were carried out in acetonitrile under reflux for 16 hours, leading to the dipyrimidin-2-ylamines in 65-90% yield. Depending on the substituents of the vinyl ketone, tetrahydropyrimidines or aromatic pyrimidine rings were obtained from the cyclization reaction. When X = Cl, elimination of the trichloromethyl group was observed during the cyclization step. The structure of 4-(trihalomethyl)dipyrimidin-2-ylamines was studied in detail by ^{1}H-, ^{13}C- and 2D-nmr spectroscopy.

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Dipyrimidin-2-ylamines have been the subject of few publications. In a search from the literature only two methods were found for the synthesis of dipyrimidin-2-ylamines. The first method was reported in 1969 and relies on the condensation of 2-guanidinopyrimidine sulfate with diethyl malonate to obtain a series of hydroxydipyrimidin-2-ylamines [1]. Several other alkoxy- and amino-dipyrimidin-2-ylamine derivatives were reported in the same paper and they were obtained by derivatization of hydroxydipyrimidin-2-ylamines. The second method to obtain dipyrimidin-2-ylamines, reported by Akhemerov *et al.*, consists on the interamination of amnooxypyrimidines with its hydrochloride or another aminooxypyrimidine hydrchloride [2].

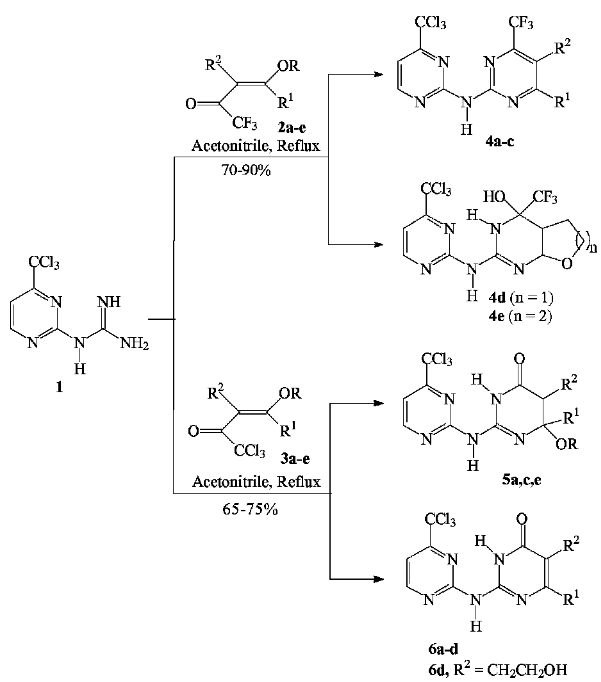
The applications and biological activities of dipyrimidin-2-ylamines are largely unknown, although several reports have described 2-guanidinopyrimidines and bipyrimidines as metal-cage complexes[3,4] and potential potassium-sparing diuretics [5].

In this work, we wish to report the synthesis of a new series of 4-(trihalomethyl)dipirimidin-2-ylamines obtained from the cyclo-condensation reaction of 4-(trichloromethyl)-2-guanidinopyrimidine with a series of β-alkoxyvinyl trihalomethyl ketones. The importance of β-alkoxyvinyl trihalomethyl ketones as potential building blocks for the synthesis of many heterocyclic systems such as isoxazoles [6-12], pyrazoles [13-18], pyrimidines [19-23], diazepines [24,25], and aliphatic compounds [26,27] has been demonstrated in previous publications of our group and by other groups [28].

The 4-(trichloromethyl)-2-guanidinopyrimidine (**1**) was prepared from 4-(trichloromethyl)pyrimidin-2(1*H*)-one by treatment with phosphorus oxychloride followed by nucleophilic substitution of the 2-chloropyrimidine derivative by guanidine hydrochloride in the presence of potassium *tert*-butoxide in *tert*-butyl alcohol, according to reference [29].

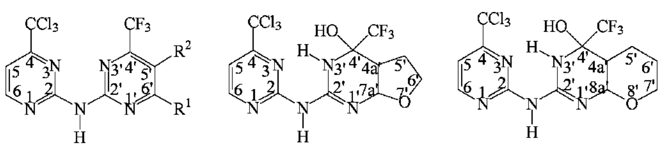
The synthesis of dipyrimidin-2-ylamines **4a-e**, **5a**,**c**,**e**, and **6a-d**, were carried out by refluxing the 4-(trichloromethyl)-2-guanidinopyrimidine (**1**) with β-alkoxyvinyl trihalomethyl ketones **2a-e** and **3a-e** in methanol or acetonitrile as solvents. The most satisfactory yields were obtained when the reactions were refluxed for 16 hours in acetonitrile, as shown in Scheme 1.

Scheme 1



2 - 6	R^1	R^2	R
a	H	H	Et
b	Me	H	Me
c	H	Me	Et
d	H	¾$(CH_2)_2$¾	
e	H	¾$(CH_2)_3$¾	

The cyclization of the 2-guanidinopyrimidine **1** with β-alkoxyvinyl trifluoromethyl ketones **2a-c** afforded the expected dipyrimidin-2-ylamines **4a-c** in which both pyrimidine rings are aromatic. However, the reaction of ketones **2d** and **2e** with the pyrimidine **1** lead to the formation of 2-{[4-(trichloromethyl)pyrimidin-2-yl]amino}-4-(trifluoromethyl)tetrahydropyrimidin-4-ol derivatives **4d** and **4e**, respectively (Scheme 1). The cyclization of **1** with the ketones **2d** and **2e** occurred with the formation of three asymmetric carbon atoms but only a single set of nmr signals was observed for both compounds **4d** and **4e**, which indicates that the reactions are highly stereoselective. The observation of a strong cross-peak between H-4a' and H-7a' in the NOESY experiment and a coupling constant of 5.6 Hz, indicates that the hexahydrofuropyrimidine ring closure of **4d** occurred with *cis* configuration. On the other hand, a weak cross-peak observed in the NOESY spectrum between H-4a' and H-8a' of compound **4e** suggests a *trans-diaxial* relationship between these two hydrogens. The coupling constant between H-4a' and H-8a' of 9.2 Hz further reinforce the *trans-diaxial* relationship of these two hydrogens which confirms that the hexahydropyranopyrimidine ring closure of **4e** was accomplished with *trans* configuration. Selected physical and spectral data of compounds **4a-e**, **5a,c,e**, and **6a-d** are reported in the experimental part. A sequence of 2D nmr experiments such as COSY HH, HMQC, and HMBC were performed in order to achieve unambiguous assignment of all hydrogen and carbon atoms of compounds **4a-e**, **5a,c,e**, and **6a-d.** Figure 1 shows the atom numbering used for the nmr assignment of representative dipyrimidin-2-ylamines obtained in this work.



4a-c **4d** **4e**

Figure 1. Atom numbering used for the nmr assignment of dipyrimidin-2-ylamines.

The reaction of the pyrimidine **1** with β-alkoxyvinyl trichloromethyl ketones **3a-e** occurred with elimination of the trichloromethyl group. The reaction of the ketone **3a** with the pyrimidine **1** furnished a mixture of 6-ethoxy-2-{[4-(trichloromethyl)pyrimidin-2-yl]amino}-5,6-dihydropyrimidin-4(3*H*)-one (**5a**) and 2-{[4-(trichloromethyl)-pyrimidin-2-yl]amino}pyrimidin-4(3*H*)-one (**6a**) in a ratio of 3:1 respectively. The cyclization of **1** with the ketone **3c** showed a similar trend as described for the cyclization of **1** with the ketone **3a**. The mixtures of **5a**/**6a** and of **5c**/**6c** were not possible to separate by means of recrystallization or column chromatography, therefore the mixtures were treated with concentrated sulfuric acid and stirred for 4 hours to give pure **6a** and **6c**, respectively. The nmr data of compounds **5a** and **5c** were taken from the spectra of the mixture of **5a/6a** and **5c/6c**.

The reaction of the pyrimidine **1** with the ketone **3d** gave compound **6d** where the pyrimidine ring closure occurred with opening of the furanyl ring. The reaction of **1** with the ketone **3e** furnished the 2-{[4-(trichloromethyl)pyrimidin-2-yl]amino}-3,4a,5,6,7,8a-hexahydro-4*H*-pyrano[2,3-*d*]-pyrimidin-4-one (**5e**) in 70 % yield. A coupling constant between H-4a' and H-8a' of 3.2 Hz indicates that these two hydrogens bear an *axial-equatorial* relationship and this suggests that the pyranopyrimidine ring closure occurred with *cis* configuration.

In conclusion, this work reported a convenient synthesis of a series of 4-(trihalomethyl)dipyrimidin-2-ylamines, in good yields, from the reaction of 4-(trichloromethyl)-2-guanidinopyrimidine, with β-alkoxyvinyl trihalomethyl ketones. In addition, we have obtained dipyrimidin-2-ylamines with a dihydro- and tetrahydro-pyrimidine moiety, which have not been reported previously.

EXPERIMENTAL

β-Alkoxyvinyl trifluoro[chloro]methyl ketones (**2a-e**, **3a-e**) were prepared according to reference [30]. The 4-(trichloromethyl)-2-guanidinopyrimidine (**1**) was prepared according to reference [29]. All melting points were determined on a Reichert Thermovar apparatus and are uncorrected. The microanalysis were performed using a Vario EL Elementar Analysensysteme. IR spectra were recorded on a Bruker IFS 28 FT-IR spectrometer as KBr pellets. ^{1}H- and ^{13}C-nmr spectra were acquired on a Bruker DPX 200 spectrometer (^{1}H at 200.13 MHz and ^{13}C at 50.62 MHz) or on a Bruker DPX 400 spectrometer (^{1}H at 400.13 MHz and ^{13}C at 100.62 MHz) in $CDCl_3$ or DMSO-d_6 and TMS as the internal reference.

Homonuclear correlated spectroscopy (COSY H-H) spectra were acquired as 1024 x 256 hypercomplex files, spectral widths in F_2 and F_1 were approximately 0.5 – 12.0 ppm in both dimensions, relaxation delay of 1 s, one scan per experiment using z field gradient to suppress the phase cycling. The Fourier Transform was performed with a zero filling on the second dimension.

Phase sensitive nuclear Overhauser spectroscopy (NOESY) spectra were acquired as 1024 x 256 hypercomplex files, spectral widths in F_2 and F_1 were approximately 0.5 – 9.0 ppm in both dimensions, relaxation delay of 1 s, mixing time of 400 ms, eight scan per experiment. The Fourier Transform was performed with a zero filling on the second dimension.

Heteronuclear multiple quantum coherence (HMQC) spectra were acquired as 4096 x 256 hypercomplex files, spectral widths in F_2 and F_1 were approximately 0.5 – 9.0 ppm for ^{1}H and 5 – 190 ppm for ^{13}C, respectively. The mixing time was optimized to 3.45 ms (145 Hz), and a total of 16 scans were acquired for each experiment with relaxation delay of 1 s. Z field gradient was used to suppress the phase cycling.

Heteronuclear multiple bond coherence (HMBC) spectra were acquired as 4096 x 256 hypercomplex files, spectral widths in F_2 and F_1 were approximately 0.5 – 9.0 ppm for proton and 5 – 190 ppm for ^{13}C, respectively. The long-range delay was optimized for 7 Hz (70 msec). A total of 32 scans were accumulated with a 2 s inter-pulse delay.

General Procedure for the Reaction of Enones **2a-e**, **3a-e** with 2-Guanidinopyrimidine (**1**).

A solution of **1a** (0.51 g, 2.0 mmoles) and β-alkoxyvinyl trihalomethyl ketone **2a-e**, **3a-e** (2.0 mmoles) in acetonitrile (20 ml) was refluxed for 16 hours. The solvent was partially evaporated and the residue was poured in cold water. The precipitate was collected by filtration and the solid was dried and recrystallized from chloroform or from a mixture of chloroform/methanol.

4-(Trichlorometyl)-*N*-[4-(trifluoromethyl)pyrimidin-2-yl]pyrimidin-2-amine (**4a**).

This compound was obtained as colorless prisms (chloroform), in 87% yield, mp 178-179 °C; ir (KBr pellet, cm^{-1}): ν 3242, 3174, 1609, 1568, 1533; ^{1}H nmr ($CDCl_3$/TMS): δ 7.29 (d, 1H, *J* = 4.0 Hz, H-5), 7.60 (d, 1H, *J* = 4.0 Hz, H-5'), 8.98 (d, 1H, *J* = 4.0 Hz, H-6), 9,03 (d, 1H, *J* = 4.0 Hz, H-6'), 10.28 (s, 1H, NH); ^{13}C nmr ($CDCl_3$/TMS): δ 95.46 (CCl_3), 109.68 (C-5'), 110.51 (C-5), 120.24 ($^1J_{CF}$ = 275 Hz, CF_3), 156.68 (C-4), 157.83 (C-2'), 158.65 (C-2), 160.78 (C-6'), 160.96 (C-6), 167.26 ($^2J_{CF}$ = 36 Hz, C-4').

Anal. Calcd. for $C_{10}H_5Cl_3F_3N_5$ (358.53): C, 33.50; H, 1.41; N, 19.53. Found: C, 33.65; H, 1.58; N 19.06.

4-Methyl-*N*-[4-(trichloromethyl)pyrimidin-2-yl]-6-(trifluoromethyl)pyrimidin-2-amine (**4b**).

This compound was obtained as colorless needles (chloroform) in 90% yield, mp 60-62 °C; ir (KBr pellet, cm^{-1}): ν 3241, 3176, 1612, 1585, 1536; ^{1}H nmr ($CDCl_3$/TMS): δ 2.63 (s, 3H, CH_3), 7.15 (s, 1H, H-5'), 7.57 (d, 1H, *J* = 5.2 Hz, H-5), 8.96 (d, 1H, *J* = 5.2 Hz, H-6), 9.71 (bs, 1H, NH); ^{13}C nmr ($CDCl_3$/TMS), δ 24.65 (CH_3), 95.67 (CCl_3), 109.54 (C-5). 110.40 (C-5'), 123.23 ($^1J_{CF}$ = 281 Hz, CF_3), 156.31 (C-4), 157.93 (C-2'), 158.46 (C-2), 160.80 (C-6), 167.24 ($^2J_{CF}$ = 36 Hz, C-4'), 171.63 (C-6').

Anal. Calcd. for $C_{11}H_7Cl_3F_3N_5$ (372.56): C, 35.46; H, 1.89; N, 18.80. Found: C, 35.72; H, 1.93; N 19.11.

5-Methyl-*N*-[4-(trichloromethyl)pyrimidin-2-yl]-4-(trifluoromethyl)pyrimidin-2-amine (**4c**).

This compound was obtained as white needles (chloroform) in 70% yield, mp 146-147°C; ir (KBr pellet, cm^{-1}): ν 3237, 3152, 1645, 1576; ^{1}H nmr ($CDCl_3$/TMS): δ 2.42 (s, 3H, CH_3), 7.54 (d, 1H, J_{CF} = 4.0 Hz, H-5), 8.81 (s, 1H, H-6'), 8.93 (d, 1H, *J* = 4.0 Hz, H-6), 10.02 (bs, 1H, NH); ^{13}C nmr ($CDCl_3$/TMS): δ 14.18 (CH_3), 95.55 (CCl_3), 109.08 (C-5), 121.04 ($^1J_{CF}$ = 277 Hz, CF_3), 121.62 (C-5'), 153.95 (C-4), 156.45 (C-2'), 158.13 (C-2), 160.74 (C-6), 162.11 (C-6'), 167.11 ($^2J_{CF}$ = 35 Hz, C-4').

Anal. Calcd. for $C_{11}H_7Cl_3F_3N_5$ (372.56): C, 35.46; H, 1.89; N, 18.80. Found: C, 35.72; H, 2.05; N 18.37.

2-{[4-(Trichloromethyl)pyrimidin-2-yl]amino}-4-(trifluoromethyl)-3,4,4a,5,6,7a-hexahydrofuro[2,3-*d*]pyrimidin-4-ol (**4d**).

This compound was obtained as white powder (chloroform) in 76% yield, mp 166-168 °C; ir (KBr pellet, cm^{-1}): ν 3250, 3154, 1639, 1575; ^{1}H nmr ($CDCl_3$/TMS): δ 2.36 (m, 2H, H-5'), 2.96 (m, 1H, H-4a'), 4.02 (m, 2H, H-6'), 5.46 (d, 1H, *J* = 5.6 Hz, H-7a'), 7.31 (d, 1H, *J* = 5.3 Hz, H-5), 8.53 (d, 1H, *J* = 5.3 Hz, H-6), 10,20 (bs, 1H, OH) 10.74 (bs, 2H, NH); ^{13}C nmr ($CDCl_3$/TMS): δ 24.82 (C-5'), 40.92 (C-4a'), 66.12 (C-6'), 81.04 ($^2J_{CF}$ = 31 Hz, C-4'), 82.05 (C-7a'), 95.64 (CCl_3), 106.52 (C-5), 124.62 ($^1J_{CF}$ = 290 Hz, CF_3), 154.71 (C-2'), 158.92 (C-6), 163.47 (C-2), 165.25 (C-4).

Anal. Calcd. for $C_{12}H_{11}Cl_3F_3N_5O_2$ (420.60): C, 34.27; H, 2.64; N, 16.65. Found: C, 34.27; H, 2.92; N 16.24.

2-{[4-(Trichloromethyl)pyrimidin-2-yl]amino}-4-(trifluoromethyl)-3,4a,5,6,7,8a-hexahydro-4*H*-pyrano[2,3-*d*]pyrimidin-4-ol (**4e**).

This compound was obtained as white powder (chloroform) in 78% yield, mp 176-178 °C; ir (KBr pellet, cm^{-1}): ν 3265, 3160, 1639, 1575; ^{1}H nmr ($CDCl_3$/TMS): δ 1.73 - 1.91 (m, 3H, 2H-6', H-5'), 2.02 – 2.14 (m, 2H, H-5', H-4a'), 3.64, 4.08 (m. 2H, H-7'), 4.83 (d, 1H, $J_{H8a'-H4a'}$ = 9.1 Hz, H-8a'), 7.25 (d, 1H, *J* = 5.2 Hz, H-5), 8.53 (d, 1H, *J* = 5.6 Hz, H-6), 9.00 (bs, 1H, OH), 10.60 (bs, 1H, NH), 11.60 (bs, 1H, NH); ^{13}C nmr ($CDCl_3$/TMS): δ 21.05 (C-6'), 24.96 (C-5'), 40.18 (C-4a'), 67.02 (C-7'), 80.62 ($^2J_{CF}$ = 32 Hz, C-4'), 80.94 (C-8a'), 95.75 (CCl_3), 106.36 (C-5), 124.21 ($^1J_{CF}$ = 289 Hz, CF_3), 154.93 (C-2'), 159.42 (C-6), 163.27 (C-2), 165.20 (C-4).

Anal. Calcd. for $C_{13}H_{13}Cl_3F_3N_5O_2$ (434.63): C, 35.92; H, 3.01; N, 16.11. Found: C, 35.86; H, 3.17; N 15.82.

6-Ethoxy-2-{[4-(trichloromethyl)pyrimidin-2-yl]amino}-5,6-dihydropyridin-4(3*H*)-one (**5a**).

This compound was obtained as a mixture of **5a**/**6a** as white powder (chloroform/methanol), in a ratio of 3:1, respectively. The mixture of **5a**/**6a** was not possible to separate by means of recrystallization or column chromatography. The nmr data of **5a** was taken from the mixture of compounds **5a**/**6a**. ^{1}H nmr (DMSO-d_6/TMS): δ 1.17 (t, 3H, *J* = 7.0 Hz, CH_3), 2.87 (dd, 1H, $^2J_{H5'a-H5'b}$ = 16.4 Hz, $^3J_{H5'a-H6'}$ = 1.9 Hz, H-5'b), 3.01 (dd, 1H, $^2J_{H5'b-H5'a}$ = 16.4 Hz, $^3J_{H5'b-H6'}$ = 4.6 Hz, H-5'b), 3.53 – 3.80 (m, 2H, -OCH_2-), 5.12 (dd, 1H, $^3J_{H6'-H5'b}$ = 4.6 Hz, $^3J_{H6'-H5'a}$ = 1.9 Hz, H-6'), 7.61 (d, 1H, *J* = 5.2 Hz, H-5), 8.90 (d, 1H, *J* = 5.2 Hz, H-6), 11.00, 12,4 (bs, 2H, NH); ^{13}C nmr (DMSO-d_6/TMS): δ 14.92 (CH_3), 58.40 (C-5'), 63.11 (-OCH_2-), 78.15 (C-6'), 95.75 (CCl_3), 108.45 (C-5), 152.07 (C-2), 153.36 (C-2'), 161.65 (C-6), 165.81 (C-4), 167.06 (C-4').

6-Ethoxy-5-methyl-2-{[4-(trichloromethyl)pyrimidin-2-yl]-amino}-5,6-dihydropyrimidin-4(3*H*)-one (**5c**).

This compound was obtained as a mixture of **5c**/**6c** as white powder (chloroform), in a ratio of 3:1, respectively. The mixture of **5c**/**6c** was not possible to separate by means of recrystallization or column chromatography. The nmr data of **5c** was taken from the mixture of compounds **5c**/**6c**. ^{1}H nmr ($CDCl_3$/TMS): δ 1.17 (t, 3H, *J* = 7.0 Hz, -$OCCH_3$), 1.36 (d, 3H, *J* = 7.5 Hz, CH_3), 2.88 (dq, 1H, $^3J_{H5'-CH3}$ = 7.5 Hz, $^3J_{H5'-H6'}$ = 2.2 Hz, H-5'), 3.47-3.55, 3.68 – 3.76 (m, 2H, -OCH_2-), 4.80 (bs, 1H, H-6'), 7.47 (d, 1H, *J* = 5.2 Hz, H-5), 8.81 (d, 1H, *J* = 5.2 Hz, H-6), 10.80, 12,00 (bs, 2H, NH); ^{13}C nmr ($CDCl_3$/TMS): δ 14.40 (CH_3), 14.82 (-$OCCH_3$), 41.87 (C-5'), 63.25 (-OCH_2-), 83.79 (C-6'), 95.70 (CCl_3), 108.58 (C-5), 153.13 (C-2'), 160.38 (C-6), 162.28 (C-2), 163.22 (C-4), 171.40 (C-4').

2-{[4-(Trichloromethyl)pyrimidin-2-yl]amino}-3,4a,5,6,7,8a-hexahydro-4*H*-pyrano[2,3-*d*]pyrimidin-4-one (**5e**).

This compound was obtained as white powder (chloroform/methanol) in 65% yield, mp 174-177 °C; ir (KBr pellet, cm^{-1}): ν 3273, 3158, 1638, 1532; ^{1}H nmr (DMSO-d_6/TMS): δ 1.68 (m, 2H, H-6'), 2.36 (m, 2H, H-5'), 3.00 (m, 1H, H-4a') 3.50, 3.84 (m, 2H, H-7'), 7.57 (d, 1H, *J* = 5.2 Hz, H-5)), 8.86 (d, 1H, *J* = 5.2 Hz, H-6) 10.39, 11.40 (bs, 2H, NH); ^{13}C nmr (DMSO-d_6/TMS): δ 21.41 (C-6'), 21.46 (C-5'), 39.36 (C-4a'), 66.30 (C-7'), 78.50 (C-8a'), 95.93 (CCl_3), 107.86 (C-5), 152.77 (C-2'), 160.84 (C-6), 164.46 (C-2), 165.41 (C-4), 169.73 (C-4').

Anal. Calcd. for $C_{12}H_{12}Cl_3N_5O_2$ (363.01): C, 39.53; H, 3.32; N, 19.21. Found: C, 39.55; H, 3.01; N 19.55.

General Procedure for the Preparation of Dipyrimidin-2-ylamines **6a** and **6c**.

A mixture of **5a/6a** or **5c/6c** (0.3 g), chloroform (2 ml), and concentrated sulfuric acid (0.3 ml) was stirred for 4 hours at room temperature. The mixture was poured in cold water and the solid was collected by filtration, washed with distilled water and dried in dessicator under silica gel and vacuum. With this procedure only **6a** and **6c** were obtained, which were recrystallized from chloroform or mixture of chloroform and methanol.

2-{[4-(Trichloromethyl)pyrimidin-2-yl]amino}pyrimidin-4(3*H*)-one (**6a**).

This compound was obtained as white powder (chloroform/methanol) in 75% yield, mp 295-299 °C (temperature of decomposition); ir (KBr pellet, cm^{-1}): ν 3275, 3112, 1685, 1625, 1576; ^{1}H nmr (DMSO-d_6/TMS): δ 5.90 (d, 1H, *J* = 6.0 Hz, H-5'), 7.64 (d, 1H, *J* = 5.2 Hz, H-5), 7.75 (d, 1H, *J* = 6.0 Hz, H-6'), 8.90 (d, 1H, *J* = 5.2 Hz, H-6), 12.00 (bs, 2H, NH); ^{13}C nmr (DMSO-d_6/TMS): δ 95.75 (CCl_3), 108.09 (C-5'), 109.63 (C-5), 152.07 (C-2), 153.36 (C-2'), 160.54 (C-6'), 161.65 (C-6), 164.29 (C-4), 167.06 (C-4').

Anal. Calcd. for $C_9H_6Cl_3N_5O$ (306.54): C, 35.26; H, 1.97; N, 22.85. Found: C, 35.22; H, 2.01; N 22.88.

6-Methyl-2-{[4-(trichloromethyl)pyrimidin-2-yl]amino}pyrimidin-4(3*H*)-one (**6b**).

This compound was obtained as white powder (chloroform) in 75% yield, mp 248-252 °C; ir (KBr pellet, cm^{-1}): ν 3271, 3125, 1710, 1624, 1572; ^{1}H nmr ($CDCl_3$/TMS): δ 2.23 (s, 3H, CH_3), 5.82 (s, 1H, H-5'), 7.62 (d, 1H, *J* = 5.0 Hz, H-5), 8.89 (d, 1H, *J* = 5.0 Hz, H-6), 11.88 (bs, 2H, NH); ^{13}C nmr (DMSO-d_6/TMS): δ 22.58 (CH_3), 94.58 (CCl_3), 104.54 (C-5), 109.14 (C-5'), 150.78 (C-2), 154.50 (C-2'), 161.23 (C-6), 162.29 (C-6'), 164.88 (C-4), 164.88 (C-4').

Anal. Calcd. for $C_{10}H_8Cl_3N_5O$ (320.56): C, 37.47; H, 2.52; N, 21.85. Found: C, 37.18; H, 2.67; N 20.81.

5-Methyl-2-{[4-(trichloromethyl)pyrimidin-2-yl]amino}pyrimidin-4(3*H*)-one (**6c**).

This compound was obtained as white powder (chloroform), mp 252-260 °C (temperature of decomposition); ir (KBr pellet, cm^{-1}): ν 3138, 1679, 1638, 1598; ^{1}H nmr ($CDCl_3$/TMS): δ 2.06 (s, 3H, CH_3), 7.56 (d, 1H, *J* = 5.4 Hz, H-5), 8.06 (s, 1H, H-6'), 8.84 (d, 1H, *J* = 5.4 Hz, H-6), 11.80 (bs, 2H, NH); ^{13}C nmr ($CDCl_3$/TMS): δ 18.38 (CH_3), 95.06 (CCl_3), 109.11 (C-5), 117.16 (C-5'), 149.77 (C-6'), 150.64 (C-2'), 158.54 (C-2), 160.57 (C-6), 162.28 (C-4), 167.22 (C-4').

Anal. Calcd. for $C_{10}H_8Cl_3N_5O$ (320.56): C, 37.47; H, 2.52; N, 21.85. Found: C, 37.00; H, 2.34; N 22.24.

5-(2-Hydroxyethyl)-2-{[4-(trichloromethyl)pyrimidin-2-yl]amino}pyrimidin-4(3*H*)-one (**6d**).

This compound was obtained as white powder (chloroform/methanol) in 65% yield, mp (did not melt until 330 °C); ir (KBr pellet, cm^{-1}): ν 3334, 1696, 1619, 1546; ^{1}H nmr (DMSO-d_6/TMS): δ 2.47 (t, 2H, *J* = 7.0 Hz, $-CH_2-$), 3.32 (bs, 1H, OH), 3.54 (t, 2H, *J* = 7.0 Hz, $-CH_2OH$), 7.70 (s, 1H, H-6'), 7.71 (d, 1H, *J* = 5.2 Hz, H-5), 8.97 (d, 1H, *J* = 5.2 Hz, H-6), 12.17 (bs, 2H, NH); ^{13}C nmr (DMSO-d_6/TMS): δ 30.39 ($-CH_2-$), 59.32 ($-CH_2OH$), 95.09 (CCl_3), 108.78 (C-5), 116.89 (C-5'), 149.87 (C-6') 158.37 (C-2'), 161.34 (C-2), 162.01 (C-6), 163.99 (C-4'), 164.89 (C-4).

Anal. Calcd. for $C_{11}H_{10}Cl_3N_5O$ (350.59): C, 37.69; H, 2.87; N, 19.98. Found: C, 37.80; H, 3.18; N 19.87.

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