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SYNTHESIS OF NEW AMINO DERIVATIVES OF 9-(METHYLTHIO)THIENO[3,2-*d*]PYRIMIDINE AND AZIDE-TETRAZOLE EQUILIBRIUM

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Starting from the 7-chloro derivative of thieno[3,2-d]pyrimidine **1** a series of new amino derivatives of cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine **2** were synthesized. By treatment of compound **3** with nitrous acid fused thieno[2,3-e]tetrazolo[1,5-c]pyrimidine **4** was synthesized. The azide/tetrazole equilibrium in this system **4A/4T** was observed and investigated.

References 15.

Fused thieno[3,2-*d*]pyrimidines are one of the ‘privileged medicinal scaffolds’, which are used for the development of pharmaceutical agents, showing a wide range of pharmacological activities [1]. In particular, the amino derivatives of pyrido[3',2':4,5]- thieno[3,2-*d*]pyrimidine have been shown to interact with a number of molecular targets including phosphodiesterase IV with potential use in the treatment of asthma and chronic obstructive pulmonary disease [2] and release control of tumor necrosis factor-α (TNFα) [3]. They also showed beta2 adrenoreceptor agonist activity [4] and distinguished by the pronounced antimicrobial activity [5].

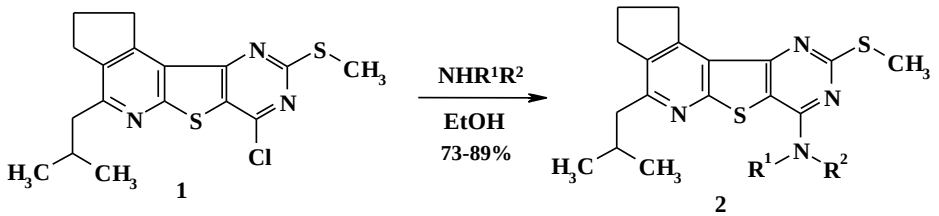
On the other hand, the study of an azide-tetrazole equilibrium has attracted large attention and new condensed systems containing the tetrazole ring have always been investigated by both physico-chemical and computational methods [6–8].

In view of the above observations, the aim of this work is the synthesis and study of the properties of compounds containing amino groups in the pyrimidine ring, as well as compounds with a condensed tetrazolo[1,5-*c*]pyrimidine moiety.

The starting compound was 7-chloro-4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (**1**) [9], which contains an ‘activated’ chlorine atom that could easily be displaced by nucleophiles. Thus, 7-

chlorothieno[3,2-*d*]- pyrimidine **1** was reacted with various amines to give a series of 7-amino-4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]thieno[3,2-*d*]pyrimidines **2a**–**w** in high yields (Scheme 1).

Scheme 1



1 **2**

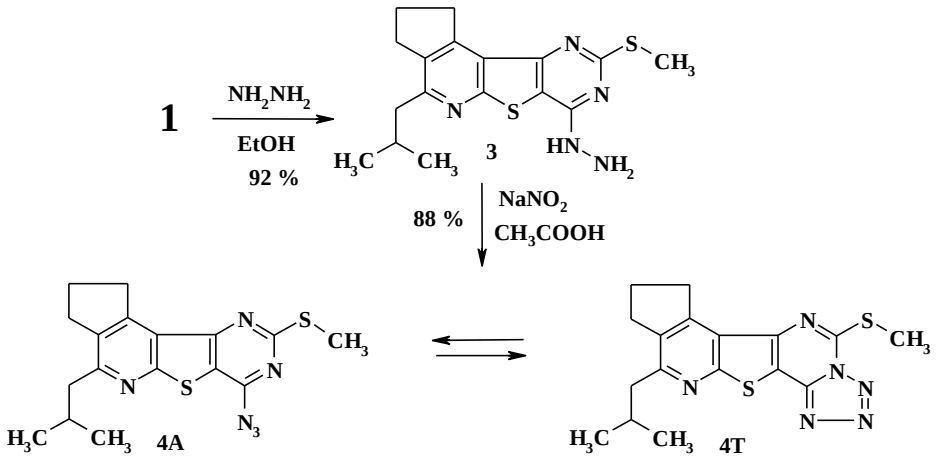
R^1 + R^2 = -$(CH_2)_5$- (**a**); R^1 + R^2 = -$(CH_2)_2O(CH_2)_2$- (**b**); R^1+ R^2 = -$(CH_2)_2NMe(CH_2)_2$- (**c**); R^1+ R^2 = -$(CH_2)_2NEt(CH_2)_2$- (**d**); R^1 + R^2 = -$(CH_2)_2N(CH_2)_2OH(CH_2)_2$- (**e**); R^1 = H, R^2 = CH_2CH_2OH (**f**); R^1 = H, R^2 = CH_2CH_2OMe (**g**); R^1 = H, R^2 = $CH_2CH(OMe)_2$ (**h**); R^1 = H, R^2 = $CH_2CH(Me)OH$ (**i**); R^1 = H, R^2 = $CH_2CH_2N(Me)_2$ (**j**); R^1 = H, R^2 = $CH_2CH_2N(Et)_2$ (**k**); R^1 = H, R^2 = 2-morpholinoethyl (**l**); R^1 = H, R^2 = $(CH_2)_3N(Me)_2$ (**m**); R^1 = H, R^2 = $(CH_2)_3OH$ (**n**); R^1 = H, R^2 = $(CH_2)_3OCH_3$ (**o**); R^1 = H, R^2 = 2-furylmethyl (**p**); R^1 = H, R^2 = Bn (**q**); R^1 = H, R^2 = 2-pyridylmethyl (**r**); R^1 = H, R^2 = 3-pyridylmethyl (**s**); R^1 = H, R^2 = CH_2CH_2Ph (**t**); R^1 = R^2 = C_2H_5 (**u**); R^1 = CH_3, R^2 = CH_2CH_2OH(**v**); R^1 = C_2H_5, R^2 = CH_2CH_2OH (**w**).

7-Chlorothieno[3,2-*d*]pyrimidine **1** was reacted with an excess of hydrazine hydrate in ethanol at reflux affording the 7-hydrazino-4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (**3**) [9] (Scheme 2). Next, the 7-hydrazino derivative **3** was treated with sodium nitrite in acetic acid at 0−5°C, giving the targeted 7-azidothieno[3,2-*d*]pyrimidine/thieno[2,3-*e*]tetrazolo[1,5-*c*]pyrimidine **4A/T** in excellent yield (Scheme 2).

It was observed that the azide/tetrazole equilibrium was present in newly synthesized compound **4**. In fact, its ^{1}H NMR spectrum in DMSO-d_6/CCl_4 1/3 showed the expected double set of signals. The ratio of the tautomers **4A**:**4T** in the solution of DMSO-d_6/CCl_4 1/3 was found to be 3:2. In the solution of $CDCl_3$ the **4A**:**4T** ratio was not essentially changed, while in the solution of DMSO-d_6 the **4A**:**4T** ratio was 1:4.56. Moreover, all of the chemical shifts of the tetrazolo form, as a rule, appeared in a weaker field than the corresponding ones of the azido form [6–8, 10, 11].

The IR spectrum of compound **4** in the solution of $CHCl_3$ showed the characteristic bonds of azido group at ν 2155 and 2138 cm^{-1}. Thus, based on spectroscopic results it can be concluded that compound **4** in the solid state is present exclusively in the tetrazolo tautomeric form, while in the solution it exists as a mixture of two isomeric forms.

Scheme 2

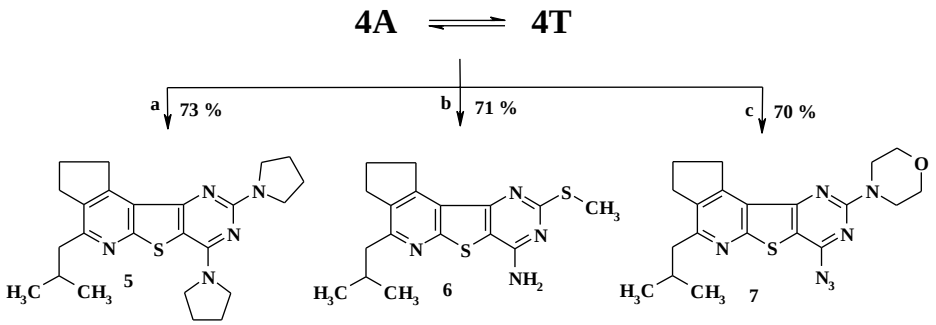


It was also interesting to examine nucleophilic reactivity in compound **4**. For this purpose compound **4** was reacted with some amines (2-aminoethanol, morpholine and pyrrolidine) under harsher experimental conditions: i.e., by refluxing (5 h) in the absence of any solvent and using an excess of amine (substrate:amine ratio = 1:5). Under these experimental conditions, the substitution of an azide group took place only in the case of pyrrolidine. Moreover, the nucleophilic substitution not only of an azide group, but also of the SCH_3 group occurred with formation of the relevant 4-isobutyl-7,9-dipyrrolidin-1-yl-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (**5**) (Scheme 3). The ^{1}H NMR spectra of compound **5** did not show the singlet signal of the SCH_3 group at 2.65/2.94 ppm characteristic of initial compound **4**, but showed the protons of the pyrrolidino group twice. The structure of compound **5** was also supported by the IR and ^{13}C NMR data.

In the case of 2-aminoethanol and morpholine under such experimental conditions the decomposition of the azido group [12–15] with formation of 4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-amine (**6**) [9] took place (Scheme 3).

Further, with the aim to avoid decomposition of azido group and by lengthening the reaction time (15 h) compound **4** was reacted with morpholine in ethanol. As a result the desired 7-azido-4-isobutyl-9-morpholin-4-yl-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5] -thieno[3,2-*d*]pyrimidine (**7**) was obtained (Scheme 3). Interestingly, the azide-tetrazole equilibrium in this compound **7** was not observed. Thus, in the ^{1}H NMR spectra of compound **7** in the solution of DMSO-d_6/CCl_4 1/3 the expected double set of signals was absent. Moreover, the signal of the SCH_3 group at 2.65/2.94 ppm was also absent, while the presence of the morpholino fragment was observed. The IR spectra of compound **7** in the cyristalline state showed the characteristic bond of azido group at ν 2131 cm^{-1}.

Scheme 3



(a) pyrrolidine, reflux 5 h; (b) morpholine or 2-aminoethanol, reflux 5 h; (c) morpholine, EtOH, reflux 15 h

In summary, the synthesis of new amino derivatives of cyclopenta[4',5']pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine **2** as well as of 7-azidothieno[3,2-*d*]pyrimidine/thieno[2,3-*e*] -tetrazolo[1,5-*c*]pyrimidine **4A/T** has been described starting from the corresponding 7-chlorothieno[3,2-*d*]pyrimidine **1**. The studies of azide/tetrazole equilibrium revealed that the insertion of the SCH_3 group in the pyrimidine ring in compound **4** shifted the azide-tetrazole equilibrium to the azido side [8]. In addition, the replacement of SCH_3 as well as azido groups with amines was carried out. It was interesting that the insertion of the amino fragment in the pyrimidine ring (compound **7**) significantly affected the azide/tetrazole equilibrium and completely shifted the azide-tetrazole equilibrium to the azido form.

Experimental Section

^1H and ^{13}C NMR spectra were recorded in DMSO-d_6, DMSO/CCl_4, 1/3 and $CDCl_3$ solutions (300 *MHz* for ^1H and 75 *MHz* for ^{13}C, respectively) on a Varian "Mercury 300VX" spectrometer. Chemical shifts were reported as δ (parts per million) relative to TMS as an internal standard. IR spectra were recorded on "Nicolet Avatar 330 FT-IR" spectrophotometer and the reported wave numbers were given in cm^{-1}. The elemental analyses were obtained by the Korshun–Klimova (C, H) and Dumas–Pregl methods (N). The melting points were determined with a Boetius micro hot stage. Compounds **1**, **6** and **3** [9] were already described.

General procedure for the synthesis of compounds 2a–w. A mixture of compound **1** (1.82 *g*, 5 *mmol*) and of corresponding amine (11 *mmol*) in absolute ethanol (50 *mL*) was refluxed for 5 *h*. The ethanol was distilled off to dryness, water (25 *mL*) was added to the residue. The separated crystals were filtered off, washed with water, dried, and recrystallized from ethanol.

4-Isobutyl-9-(methylthio)-7-piperidin-1-yl-2,3-dihydro-1*H*-cyclopenta[4',5'] pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine (2a). Yield 85%; mp 122-124°C. Anal. Calcd for $C_{22}H_{28}N_4S_2$: C 64.04; H 6.84; N 13.58 %. Found: C 64.34; H 7.02; N 13.82 %. ^1H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, $CH(C\underline{H}_3)_2$); 1.67–1.82 (m, 6H, $(CH_2)_3$, $C_5H_{10}N$); 2.15-2.33 (m, 3H, $C\underline{H}(CH_3)_2$, 2-CH_2); 2.55 (s, 3H, SCH_3); 2.71 (d,

2H, *J* = 7.2 *Hz*, CHC$\underline{H}_2$); 2.99 (t, 2H, *J* = 7.5, 3-CH_2); 3.56 (t, 2H, *J* = 7.6, 1-CH_2); 3.87-3.99 (m, 4H, N(CH_2)$_2$).

4-Isobutyl-9-(methylthio)-7-morpholin-4-yl-2,3-dihydro-1*H*-cyclopenta [4',5']pyri-do[3',2':4,5]thieno[3,2-*d*]pyrimidine (2b). Yield 89%; mp 159-161^{o}C. Anal. Calcd for $C_{21}H_{26}N_4OS_2$: C 60.84; H 6.32; N 13.51 %. Found: C 61.17; H 6.54; N 13.76%. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 2.15-2.33 (m, 3H, C$\underline{H}$(CH_3)$_2$, 2-CH_2); 2.56 (s, 3H, SCH_3); 2.72 (d, 2H, *J* = 7.2, CHC$\underline{H}_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.58 (t, 2H, *J* = 7.6, 1-CH_2); 3.76-3.85 (m, 4H, N(CH_2)$_2$); 3.90–3.98 (m, 4H, O(CH_2)$_2$).

4-Isobutyl-7-(4-methylpiperazin-1-yl)-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta-[4',5']-pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (2c). Yield 74%; mp 132-134^{o}C. Anal. Calcd for $C_{22}H_{29}N_5S_2$: C 61.79; H 6.84; N 16.38%. Found: C 62.14; H 7.04; N 16.63 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 2.15-2.33 (m, 3H, C$\underline{H}$(CH_3)$_2$, 2-CH_2); 2.29 (s, 3H, NCH_3); 2.48-2.53 (m, 4H, CH_3N(C$\underline{H}_2$)$_2$); 2.54 (s, 3H, SCH_3); 2.70 (d, 2H, *J* = 7.2 *Hz*, CHC$\underline{H}_2$), 2.98 (t, 2H, *J* = 7.5, 3-CH_2); 3.54 (t, 2H, *J* = 7.6, 1-CH_2); 3.86–3.99 (m, 4H, N(CH_2)$_2$).

7-(4-Ethylpiperazin-1-yl)-4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta-[4',5']-pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (2d). Yield 77%; mp 157-159^{o}C. Anal. Calcd for $C_{23}H_{31}N_5S_2$: C 62.55; H 7.07; N 15.86%. Found: C 62.87; H 7.25; N 16.10 %.^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 1.15 (t, *J* = 7.2 *Hz*, 3H, $NCH_2C\underline{H}_3$), 2.16-2.33 (m, 3H, C$\underline{H}$(CH_3)$_2$, 2-CH_2); 2.45 (q, *J* = 7.2 *Hz*, 2H, $NC\underline{H}_2CH_3$); 2.54–2.60 (m, 4H, C_2H_5N(C$\underline{H}_2$)$_2$); 2.55 (s, 3H, SCH_3); 2.70 (d, 2H, *J* = 7.2 *Hz*, CHC$\underline{H}_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.58 (t, 2H, *J* = 7.6, 1-CH_2); 3.96–4.07 (m, 4H, N(CH_2)$_2$).

2-{4-[4-Isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]-thieno[3,2-*d*]pyrimidin-7-yl]piperazin-1-yl}ethanol (2e). Yield 81%; mp 166-168^{o}C. Anal. Calcd for $C_{23}H_{31}N_5OS_2$: C 60.36; H 6.83; N 15.30%. Found: C 60.67; H 7.04; N 15.52 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 2.16-2.33 (m, 3H, C$\underline{H}$(CH_3)$_2$, 2-CH_2), 2.56 (s, 3H, SCH_3); 2.48–2.54 (m, 2H, OHC$\underline{H}_2$); 2.71 (d, 2H, *J* = 7.2 *Hz*, CHC$\underline{H}_2$); 2.62-2.73 (m, 4H, CH_2N(C$\underline{H}_2$)$_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.57 (t, 2H, *J* = 7.6, 1-CH_2); 3.53–3.61 (m, 2H, OHCH_2C$\underline{H}_2$); 3.82–3.96 (br, 1H, O$\underline{H}$CH_2CH_2); 3.92–4.02 (m, 4H, N(CH_2)$_2$).

2-{[4-Isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]-thieno-[3,2-*d*]pyrimidin-7-yl]amino}ethanol (2f). Yield 87%; mp 134-136^{o}C. Anal. Calcd for $C_{19}H_{24}N_4OS_2$: C 62.14; H 6.78; N 14.49 %. Found: C 62.50; H 6.97; N 14.73%. ^{1}H NMR δ, ppm, *Hz*: 0.99 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 2.15–2.33 (m, 3H, C$\underline{H}$(CH_3)$_2$, 2-CH_2); 2.55 (s, 3H, SCH_3); 2.71 (d, 2H, *J* = 7.2 *Hz*, CHC$\underline{H}_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.57 (t, 2H, *J* = 7.6, 1-CH_2); 3.61–3.72 (m, 4H, NHC$\underline{H}_2$C$\underline{H}_2$OH); 3.66 (br, 1H, OH); 7.32 (br. t, 1H, *J* = 4.8, NH).

4-Isobutyl-N-(2-methoxyethyl)-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyri-do[3',2':4,5]-thieno[3,2-*d*]pyrimidin-7-amine (2g). Yield 77%; mp 148-150^{o}C. Anal. Calcd for $C_{20}H_{26}N_4OS_2$: C 59.67; H 6.51; N 13.92%. Found: C 60.02; H 6.71; N 14.18 %.^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7,

CH(C<u>H</u>$_3$)$_2$); 2.15–2.33 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.55 (s, 3H, SCH$_3$); 2.70 (d, 2H, *J* = 7.2 *Hz*, CHC<u>H</u>$_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.35 (s, 3H, OCH$_3$); 3.56 (t, 2H, *J* = 7.6, 1-CH$_2$); 3.51–3.62 (m, 2H, NHCH$_2$C<u>H</u>$_2$OCH$_3$); 3.66–3.76 (m, 2H, HNC<u>H</u>$_2$CH$_2$); 7.51 (br. t, 1H, *J* = 5.5, NH).

***N*-(2,2-Dimethoxyethyl)-4-isobytyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta-[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-amine (2h).** Yield 84%; mp 138-140°C. Anal. Calcd for $C_{21}H_{28}N_4O_2S_2$: C 58.30; H 6.52; N 12.95%. Found: C 58.64; H 6.73; N 13.18%.^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 2.15–2.33 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.56 (s, 3H, SCH$_3$); 2.70 (d, 2H, *J* = 7.2 *Hz*, CHC<u>H</u>$_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.36 (s, 6H, CH(OC<u>H</u>$_3$)$_2$); 3.56 (t, 2H, *J* = 7.6, 1-CH$_2$); 3.58–3.65 (m, 2H, HNC<u>H</u>$_2$); 4.64 (t, *J* = 5.7 *Hz*, 1H, HNCH$_2$C<u>H</u>); 7.57 (br. t, 1H, *J* = 5.7, NH).

1-{[4-Isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]-thieno[3,2-*d*]pyrimidin-7-yl]amino}propan-2-ol (2i). Yield 82%; mp 153-155°C. Anal. Calcd for $C_{20}H_{26}N_4OS_2$: C 59.67; H 6.51; N 13.92%. Found: C 59.97; H 6.69; N 14.17%. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.17 (d, *J* = 6.3 *Hz*, 3H, CHC<u>H</u>$_3$); 2.15–2.33 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.56 (s, 3H, SCH$_3$); 2.70 (d, 2H, *J* = 7.2, CHC<u>H</u>$_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.35 (ddd, 1H, *J* = 13.4, 7.4, 5.0, NHC<u>H</u>$_2$); 3.55 (t, 2H, *J* = 7.6, 1-CH$_2$); 3.60 (br, 1H, OH); 3.63 (ddd, 1H, *J* = 13.4, 6.4, 4.4, NHC<u>H</u>$_2$); 3.88–3.99 (m, 1H, C<u>H</u>CH$_3$); 7.21 (t, 1H, *J* = 5.7, NH).

***N'*-[4-Isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]-thieno[3,2-*d*]pyrimidin-7-yl]-*N*,*N*-dimethylethane-1,2-diamine (2j).** Yield 89%; mp 112-114°C. Anal. Calcd for $C_{21}H_{29}N_5S_2$: C 60.69; H 7.03; N 16.85 %. Found: C 61.01; H 7.25; N 17.09 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 2.15–2.31 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.33 (s, 6H, N(CH$_3$)$_2$), 2-CH$_2$); 2.56 (s, 3H, SCH$_3$); 2.63 (t, *J* = 6.7, 2H, C<u>H</u>$_2$N(CH$_3$)$_2$); 2.70 (d, 2H, *J* = 7.2, CHC<u>H</u>$_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.57 (t, 2H, *J* = 7.6, 1-CH$_2$); 3.67 (td, 2H, *J* = 6.5, 5.9, NHC<u>H</u>$_2$); 7.20 (t, 1H, *J* = 5.5, NH).

***N*,*N*-diethyl-*N'*-[4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5'] pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-yl]ethane-1,2-diamine (2k).** Yield 78%; mp 99-101°C. Anal. Calcd for $C_{23}H_{33}N_5S_2$: C 62.26; H 7.50; N 15.78 %. Found: C 61.95; H 7.71; N 16.00 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.06 (t, 6H, *J* = 7.0, (CH$_2$C<u>H</u>$_3$)$_2$); 2.15–2.31 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$), 2.57 (s, 3H, SCH$_3$); 2.54–2.64 (m, 4H, (CH$_2$C<u>H</u>$_3$)$_2$); 2.60 (t, *J* = 7.0, 2H, C<u>H</u>$_2$N(C$_2$H$_5$)$_2$); 2.70 (d, 2H, *J* = 7.2, CHC<u>H</u>$_2$); 2.98 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.50–3.63 (m, 2H, NHC<u>H</u>$_2$); 3.56 (t, 2H, *J* = 7.6, 1-CH$_2$); 7.12 (br. t, 1H, *J* = 4.8, NH).

4-Isobutyl-9-(methylthio)-*N*-(2-morpholin-4-ylethyl)-2,3-dihydro-1*H*-cyclopenta-[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-amine (2l). Yield 84%; mp 125-127°C. Anal. Calcd for $C_{23}H_{31}N_5OS_2$: C 60.36; H 6.83; N 15.30 %. Found: C 59.99; H 6.63; N 15.06 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 2.15–2.31 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.56 (s, 3H, SCH$_3$); 2.48–2.58 (m, 4H, N(CH$_2$)$_2$); 2.59 (t, *J* = 6.7, 2H, C<u>H</u>$_2$N(CH$_2$)$_2$); 2.71 (d, 2H, *J* = 7.2, CHC<u>H</u>$_2$);

3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.57 (t, 2H, *J* = 7.6, 1-CH_2); 3.56–3.62 (m, 4H, O(CH_2)$_2$); 3.70 (td, 2H, *J* = 6.5, 5.9, NHC$\underline{H}_2$); 7.29 (t, 1H, *J* = 5.6, NH).

***N'*-[4-Isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]-thieno[3,2-*d*]pyrimidin-7-yl]-*N*,*N*-dimethylpropane-1,3-diamine (2m).** Yield 84%; mp 129-131°C. Anal. Calcd for $C_{22}H_{31}N_5S_2$: C 61.50; H 7.27; N 16.30 %. Found: C 61.85; H 7.46; N 16.55 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 1.78–1.90 (m, 2H, NHCH$_2$C$\underline{H}_2$); 2.15–2.31 (m, 3H, C$\underline{H}$(CH$_3$)$_2$, 2-CH_2); 2.30 (s, 6H, N(CH_3)$_2$); 2.45 (br, 2H, C$\underline{H}_2$N(CH_3)$_2$); 2.55 (s, 3H, SCH_3); 2.71 (d, 2H, *J* = 7.2, CHC$\underline{H}_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.56 (t, 2H, *J* = 7.6, 1-CH_2); 3.61 (td, 2H, *J* = 6.8, 5.5, NHC$\underline{H}_2$); 7.73 (t, 1H, *J* = 5.5, NH).

3-{[4-Isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]-thieno[3,2-*d*]pyrimidin-7-yl]amino}propan-1-ol (2n). Yield 89%; mp 177-179°C. Anal. Calcd for $C_{20}H_{26}N_4OS_2$: C 59.67; H 6.51; N 13.92 %. Found: C 59.98.; H 6.68; N 14.15 %.^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 1.77–1.87 (m, 2H, NHCH$_2$C$\underline{H}_2$); 2.15–2.31 (m, 3H, C$\underline{H}$(CH$_3$)$_2$, 2-CH_2); 2.56 (s, 3H, SCH_3); 2.70 (d, 2H, *J* = 7.2 *Hz*, CHC$\underline{H}_2$); 2.99 (t, 2H, *J* = 7.5, 3-CH_2); 3.55 (t, 2H, *J* = 7.6, 1-CH_2); 3.57–3.68 (m, 4H, OHC$\underline{H}_2$, NHC$\underline{H}_2$); 4.17 (br, 1H, OH); 7.42 (br t, 1H, *J* = 5.5, NH).

4-Isobutyl-*N*-(3-methoxypropyl)-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta [4',5']-pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-amine (2o). Yield 83%; mp 142-144°C. Anal. Calcd for $C_{21}H_{28}N_4OS_2$: C 60.54; H 6.77; N 13.45 %. Found: C 60.88; H 6.98; N 13.70 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 1.85–1.97 (m, 2H, NHCH$_2$C$\underline{H}_2$); 2.15–2.33 (m, 3H, C$\underline{H}$(CH$_3$)$_2$, 2-CH_2); 2.55 (s, 3H, SCH_3); 2.71 (d, 2H, *J* = 7.2, CHC$\underline{H}_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.31 (c, 3H, OCH_3); 3.45 (t, 2H, *J* = 7.6, 1-CH_2); 3.51–3.64 (m, 4H, NHC$\underline{H}_2$C$\underline{H}_2$); 7.44 (br t, 1H, *J* = 5.5, NH).

***N*-(2-Furylmethyl)-4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta [4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-amine (2p).** Yield 80%; mp 80-82 °C. Anal. Calcd for $C_{22}H_{24}N_4OS_2$: C 62.23; H 5.70; N 13.20 %. Found: C 62.59; H 5.89; N 13.43 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 2.15–2.33 (m, 3H, C$\underline{H}$(CH$_3$)$_2$, 2-CH_2), 2.55 (s, 3H, SCH_3); 2.71 (d, 2H, *J* = 7.2, CHC$\underline{H}_2$); 2.98 (t, 2H, *J* = 7.5, 3-CH_2); 3.56 (t, 2H, *J* = 7.6, 1-CH_2); 4.74 (d, 2H, *J* = 5.6, NHC$\underline{H}_2$); 6.25–6.32 (m, 2H, 3,4-CH_{fur}.); 7.37 (dd, 1H, *J* = 1.7, 0.8, 5-CH_{fur}); 7.98 (br t, 1H, *J* = 5.7, NH).

***N*-Benzyl-4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]thieno[3,2-*d*]pyrimidin-7-amine (2q).** Yield 86%; mp 76-78°C. Anal. Calcd for $C_{24}H_{26}N_4S_2$: C 66.32; H 6.03; N 12.89 %. Found: C 66.64; H 6.21; N 13.13 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C$\underline{H}_3$)$_2$); 2.15–2.33 (m, 3H, C$\underline{H}$(CH$_3$)$_2$, 2-CH_2); 2.52 (s, 3H, SCH_3); 2.70 (d, 2H, *J* = 7.2, CHC$\underline{H}_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.56 (t, 2H, *J* = 7.6, 1-CH_2); 4.76 (d, 2H, *J* = 5.9 , NHC$\underline{H}_2$); 7.16–7.41 (m, 5H, Ph); 8.08 (t, 1H, *J* = 5.7, NH).

4-Isobutyl-9-(methylthio)-*N*-(pyridin-2-ylmethyl)-2,3-dihydro-1*H*-cyclopenta-[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-amine (**2r**). Yield

73%; mp 181-183 °C. Anal. Calcd for $C_{23}H_{25}N_5S_2$: C 63.42; H 5.78; N 16.08%. Found: C 63.77; H 5.98; N 16.31 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 2.15–2.33 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.47 (s, 3H, SCH$_3$); 2.72 (d, 2H, *J* = 7.2, CHC<u>H</u>$_2$); 3.01 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.56 (t, 2H, *J* = 7.6, 1-CH$_2$); 4.86 (d, 2H, *J* = 5.8, NHC<u>H</u>$_2$); 7.20 (ddd, 1H, *J* = 7.5, 4.7, 1.0, 5-CH-C$_5$H$_4$N); 7.38 (ddd, 1H, *J* = 7.6, 1.1, 0.9, 3-CH-C$_5$H$_4$N); 7.68 (ddd, 1H, *J* = 7.9, 7.4, 1.8, 4-CH-C$_5$H$_4$N); 8.10 (t, 1H, *J* = 5.8, NH); 8.51 (ddd, 1H, *J* = 4.8, 1.8, 0.9, 6-CH-C$_5$H$_4$N).

4-Isobutyl-9-(methylthio)-*N*-(pyridin-3-ylmethyl)-2,3-dihydro-1*H*-cyclopenta-[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-amine (2s). Yield 77%; mp 109-111°C. Anal. Calcd for $C_{23}H_{25}N_5S_2$: C 63.42; H 5.78; N 16.08%. Found: C 63.72; H 5.97; N 16.33 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 2.15–2.33 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.53 (c, 3H, SCH$_3$); 2.71 (2H, d, *J* = 7.2, CHC<u>H</u>$_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.56 (t, 2H, *J* = 7.6, 1-CH$_2$); 4.75 (d, 2H, *J* = 5.9, NHC<u>H</u>$_2$); 7.23 (dd, 1H, *J* = 7.9, 4.9, 5-CH-C$_5$H$_4$N); 7.76 (dt, 1H, *J* = 7.8, 2.0, 6-CH-C$_5$H$_4$N); 8.15 (t, 1H, *J* = 5.9, NH); 8.40 (dd, 1H, *J* = 4.8, 2.0, 4-CH-C$_5$H$_4$N); 8.60 (t, 1H, *J* = 2.0, 2-CH-C$_5$H$_4$N).).

4-Isobutyl-9-(methylthio)-*N*-(2-phenylethyl)-2,3-dihydro-1*H*-cyclopenta[4',5']-pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-amine (2t). Yield 85%; mp 83-85°C. Anal. Calcd for $C_{25}H_{28}N_4S_2$: C 66.93; H 6.29; N 12.49 %. Found: C 67.29; H 6.51; N 12.73 %. ^{1}H NMR δ, ppm, *Hz*: 0.99 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 2.15–2.33 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.58 (c, 3H, SCH$_3$); 2.70 (d, 2H, *J* = 7.2, CHC<u>H</u>$_2$); 2.99 (t, 2H, *J* = 7.2, C<u>H</u>$_2$Ph); 3.03 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.56 (t, 2H, *J* = 7.6, 1-CH$_2$); 3.69–3.81(m, 2H, NHC<u>H</u>$_2$); 7.10–7.31 (m, 5H, Ph); 7.55 (t, 1H, *J* = 5.7, NH).

***N*,*N*-Diethyl-4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5'] pyrido-[3',2':4,5]-thieno[3,2-*d*]pyrimidin-7-amine (2u).** Yield 81%; mp 121-123°C. Anal. Calcd for $C_{21}H_{28}N_4S_2$: C 62.96; H 7.04; N 13.99 %. Found: C 63.28; H 7.24; N 14.21 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.35 (t, 6H, *J* = 7.0, (CH$_2$C<u>H</u>$_3$)$_2$); 2.15–2.33 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.54 (s, 3H, SCH$_3$); 2.70 (d, 2H, *J* = 7.2, CHC<u>H</u>$_2$); 2.99 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.57 (t, 2H, *J* = 7.6, 1-CH$_2$); 3.80 (q, 4H, *J* = 7.0, N(C<u>H</u>$_2$CH$_3$)$_2$).

2-[[4-Isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]-thieno[3,2-*d*]pyrimidin-7-yl](methyl)amino]ethanol (2v). Yield 88%; mp 144-146°C. Anal. Calcd for $C_{20}H_{26}N_4OS_2$: C 59.67; H 6.51; N 13.92%. Found: C 60.02; H 6.70; N 14.18 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 2.15–2.33 (m, 3H, C<u>H</u>(CH$_3$)$_2$, 2-CH$_2$); 2.55 (s, 3H, SCH$_3$); 2.71 (2H, d, *J* = 7.2, CHC<u>H</u>$_2$); 2.99 (t, 2H, *J* = 7.5, 3-CH$_2$); 3.50 (s, 3H, NCH$_3$); 3.58 (t, 2H, *J* = 7.6, 1-CH$_2$); 3.71–3.78 (m, 2H, NHC<u>H</u>$_2$CH$_2$OH); 3.83–3.90 (m, 2H, NHCH$_2$C<u>H</u>$_2$OH); 4.56 (br, 1H, OH).

2-{Ethyl[4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-yl]amino}ethanol (2w). Yield 79%; mp 137-139°C. Anal. Calcd for $C_{21}H_{28}N_4OS_2$: C 60.54; H 6.77; N 13.45 %. Found: C 60.85; H 6.94; N 13.68 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.30-1.41

(m, 3H, $CH_2C\underline{H}_3$); 2.15–2.33 (m, 3H, $C\underline{H}(CH_3)_2$, 2-CH_2); 2.55 (s, 3H, SCH_3); 2.71 (d, 2H, *J* = 7.2, $CHC\underline{H}_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.58 (t, 2H, *J* = 7.6, 1-CH_2); 3.71-3.86 (m, 4H, $C\underline{H}_2C\underline{H}_2OH$); 3.91 (q, *J* = 7.0, 2H, $C\underline{H}_2CH_3$); 4.51 (br, 1H, OH).

Procedure for the synthesis of compound 4. To an ice-cold solution of compound **1** (2 *mmol*) in glacial acetic acid (35 *mL*), a solution of sodium nitrite (276 *mg*, 4 *mmol*, dissolved in the least amount of water) was added dropwise under stirring in an ice-bath at 5°C. The reaction mixture was maintained at room temperature for 12 *h*, and then water (50 *mL*) was added. The resulting crystals were filtered off, washed with water, dried, and recrystallized from a mixture of ethanol/dichloromethane (1:3).

7-Azido-4-isobutyl-9-(methylthio)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine/10-isobutyl-5-(methylthio)-8,9-dihydro-7*H*-cyclopenta-[4',5']pyrido[3',2':4,5]thieno[2,3-e]tetrazolo[1,5-*c*]pyrimidine (4A/T). Yield 88%; mp 148–149°C; IR ν/cm^{-1} ($CHCl_3$): 2155, 2138 (N_3). Anal. Calcd for $C_{17}H_{18}N_6S_2$: C 55.11; H 4.90; N 22.68 %. Found: C 54.79; H 5.08; N 22.92 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 3.6H, *J* = 6.6, $CH(C\underline{H}_3)_2$);1.02 (d, 2.4H, *J* = 6.6, $CH(C\underline{H}_3)_2$); 2.21–2.38 (m, 3H, 8-CH_2 and $C\underline{H}(CH_3)_2$); 2.65 (s, 1.8H, SCH_3); 2.94 (s, 1.2H, SCH_3); 2.73 (d, 1.2H, *J* = 7.1, $CHC\underline{H}_2$); 2.77 (d, 0.8H, *J* = 7.1, $CHC\underline{H}_2$); 3.03 (t, 1.2H, *J* = 7.5, 9-CH_2); 3.08 (t, 0.8H, *J* = 7.5, 9-CH_2); 3.56 (t, 1.2H, *J* = 7.6, 7-CH_2); 3.64 (t, 0.8H, *J* = 7.6, 7-CH_2).

Procedure for the synthesis of compound 5. A mixture of compound **4** (1 *mmol*) and pyrrolidine (5 *mL*) was refluxed for 5 *h*. The reaction mixture was cooled, water (25 *mL*) was added, and the separated crystals were filtered off, washed with water, dried, and recrystallized from ethanol.

4-Isobutyl-7,9-dipyrrolidin-1-yl-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido [3',2':4,5]-thieno[3,2-*d*]pyrimidine (5). Yield 73%; mp 218–220°C. ^{1}H NMR (δ, ppm, *Hz*: 0.98 (d, 6H, = 6.6, $CH(C\underline{H}_3)_2$); 1.95-2.00 (m, 4H, 2CH_2, C_4H_8N); 2.02-2.07 (m, 4H, 2CH_2, C_4H_8N); 2.14–2.30 (m, 3H, 2-CH_2, $C\underline{H}(CH_3)_2$); 2.68 (d, 2H, *J* = 7.1, $CHC\underline{H}_2$); 2.96 (t, 2H, *J* = 7.5, 3-CH_2); 3.56 (t, 2H, *J* = 7.6, 1-CH_2); 3.56-3.62 (m, 4H, $N(CH_2)_2$); 3.83-3.88 (m, 4H, $N(CH_2)_2$). ^{13}C NMR (75 MHz, DMSO/CCl_4, 1/3) δ: 22.2 (2CH_3); 24.2 (CH_2); 24.7 ($(CH_2)_2$); 25.0 ($(CH_2)_2$); 27.7 (CH); 29.8 (CH_2); 31.8 (CH_2); 44.1 (CH_2); 45.8 ($(NCH_2)_2$); 46.7 ($(NCH_2)_2$); 101.41; 134.2; 150.2; 155.9; 157.0; 158.1.

Procedure for the synthesis of compound 6. A mixture of compound **4** (1 *mmol*) and 2-aminoethanol or morpholine (5 *mL*) was refluxed for 5 *h*. The reaction mixture was cooled, water (50 *mL*) was added, and the separated crystals were filtered off, washed with water, dried, and recrystallized from ethanol. Yield 71%.

The physico-chemical data of obtained compound **4** in all aspects were identical with those of the same earlier synthesized compound and described in reference [9].

Procedure for the synthesis of compound 7. A mixture of compound **4** (370.5 *mg*, 1 *mmol*) and morpholine (2.2 *mmol*) in ethanol (10 *mL*) was refluxed for 15 *h*. The reaction mixture was cooled, water (25 *mL*) was added, and the separated crystals were filtered off, washed with water, dried, and recrystallized from ethanol.

7-Azido-4-isobutyl-9-morpholin-4-yl-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (7). Yield 70%; mp 194–196 °C; IR ν/cm^{-1}: 2131 (N_3). Anal. Calcd for $C_{20}H_{23}N_7OS$: C 58.66; H 5.66; N 23.94 %. Found: C 58.39; H 5.81; N 23.73 %. ^{1}H NMR δ, ppm, *Hz*: 0.98 (d, 6H, *J* = 6.6, $CH(C\underline{H}_3)_2$); 2.19–2.33 (m, 3H, 2-CH_2, $C\underline{H}(CH_3)_2$); 2.70 (d, 2H, *J* = 7.1, $CHC\underline{H}_2$); 3.00 (t, 2H, *J* = 7.5, 3-CH_2); 3.51 (t, 2H, *J* = 7.6, 1-CH_2); 3.72-3.77 (m, 4H, $N(CH_2)_2$); 3.81-3.86 (m, 4H, $O(CH_2)_2$). ^{13}C NMR (75 MHz, DMSO/CCl_4, 1/3) δ: 22.2 ($2CH_3$); 24.0 (CH_2); 27.7 (CH); 29.7 (CH_2); 31.7 (CH_2); 40.0 ($N(CH_2)_2$); 44.4 (CH_2); 68.5 ($O(CH_2)_2$); 106.8; 121.4; 135.0; 150.5; 155.5; 159.0; 159.3; 159.4; 160.7.

9-(ՄԵԹԻԼԹԻՈ)ԹԻԵՆՈ[3,2-D]ՊԻՐԻՄԻԴԻՆԻ ՆՈՐ ԱՄԻՆՈԱԾԱՆՑՅԱԼՆԵՐԻ ՍԻՆԹԵԶԸ և ԱԶԻԴ-ՏԵՏՐԱԶՈԼԱՅԻՆ ՀԱՎԱՍԱՐԱԿՇՌՈՒԹՅՈՒՆԸ

Է. Կ. ՀԱԿՈԲՅԱՆ

Աշխատանքում նկարագրված է ցիկլոպենտա[4',5']պիրիդո[3',2':4,5]թիենո[3,2-d]պիրիմիդինի նոր ամինոածանցյալների սինթեզը համապատասխան 7-քլորթիենո[3,2-d]պիրիմիդինի հիման վրա: Ուսումնասիրված է ազիդ-տետրազոլային տաուտոմերիան 10-իզոբուտիլ-5-(մեթիլթիո)-8,9-դիհիդրո-7H-ցիկլոպենտա[4',5']պիրիդո[3',2':4,5] թիենո[2,3-e]տետրազոլո[1,5-c]պիրիմիդինում: Պարզվել է, որ եթե մեթիլթիո խմբի ներմուծումը պիրիմիդինային օղակ հավասարակշռությունը չեղում է դեպի ազիդային ձևը, իսկ ամինային խմբի ներմուծման դեպքում այն ամբողջովին տեղաշարժվում է դեպի ազիդային ձևը:

СИНТЕЗ НОВЫХ АМИНОПРОИЗВОДНЫХ 9-(МЕТИЛТИО)ТИЕНО[3,2-*d*] ПИРИМИДИНА И АЗИДО-ТЕТРАЗОЛЬНОЕ РАВНОВЕСИЕ

Э. К. АКОПЯН

В работе описан синтез новых 7-аминопроизводных циклопента[4',5']пиридо-[3',2':4,5]тиено[3,2-*d*]пиримидина на основе соответствующего 7-хлортиено[3,2-*d*]пиримидина. Исследована азидо-тетразольная таутомерия в 10-изобутил-5-(метилтио)-8,9-дигидро-7*H*-циклопента[4',5']пиридо[3',2':4,5]тиено[2,3-*e*]тетразоло[1,5-*c*]пиримидине. Выявлено, что, если введение метилтиогруппы в пиримидиновый цикл сдвигает равновесие в сторону азидной формы, то при введения аминогруппы равновесие полностью перемещается в сторону азидной формы.

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