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TARGETED MODIFICATIONS OF 5,6-DISUBSTITUTED-4-CHLOROTHIENO[2,3-d]PYRIMIDINES WITH BENZYLAMINE

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Abstract

Formed from two different components and covalently linked, hybrid blocks make it possible to achieve more effective results due to the fact that each molecule has specific properties that differ from those expected. This concept has been successfully used in the creation and production of hybrid drugs. The combination of chemically distinct pharmacophores in the form of a single molecule results in at least two or multiple manifestations of the hybrid molecule potential. Therefore, this article highlights the processes of joining two fragments with high biological activity – thienopyrimidine and benzylamine – as well as the synthesis of new hybrid molecules and the study of their structure using modern methods of physical and chemical analysis. The structures of the obtained compounds were elucidated using IR, ¹H and ¹³C NMR spectroscopy. X-ray crystal structure analyses of the synthesized compounds were performed. **Keywords:** 4-chlorothieno[2,3-d]pyrimidines; nucleophilic substitution products; thienopyrimidine derivatives; benzylamine; targeted syntheses

1. Introduction

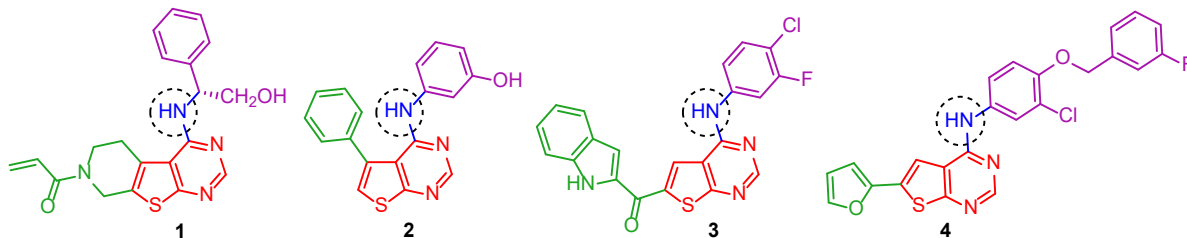
Thieno[2,3-d]pyrimidines most of them are potential biologically active compounds that exhibit activity against microbes (Bozorov Kh., Zhao J. Yu., Elmuradov B., Pataer A., Aisa H. A. 2015; Elmahdy K. M., Elkazak A. M., Megid A. M., Seada M., Mohamed O. F., 2013), viruses (Rashad A. E. Ali M. A., 2006), inflammation (El-Gazzar A. B., Hussein H. A., Hafez H. N., 2007), and diabetes (Deng J. F.,

Peng L., Zhang G. C., Lan X. B., Li C. F., Chen F. X., Zhou Y. Y., Lin Z. X., Chen L., Dai R. K., Xu H. J., Yang L., Zhang X. Q., Hu W. H. Eur. J., 2011). Several TP derivatives are antidepressants, antihypertensive agents (Nagaraju K., Harikrishna N., Vasu K., Rao C. V., 2015), and antioxidants (Guo Y., Li J., Ma J., Yu L. Z., Wang H., Zhu W., Liao X., Zhao Y., 2015). Those with an NH bridge in the 4-position have therapeutic activity against malig-

nant tumors (Bozorov Kh., Zhao J. Yu., Elmuradov B., Pataer A., Aisa H. A., 2015; Zhu W., Chen C., Sun C., Xu S., Wu C., Lei F., Xia H., Tu Q., Zheng P., 2015); Kim Y., Kim M., Park M., Tae J., Baek D., Park K. D., Choo H., 2015) and are especially interesting for synthesizing hybrid nucleophile–thienopyrimidine molecules. In most of the data presented in the literature, as a result of chemical changes in the 4th position of the thieno[2,3-d]pyrimidine ring, in particular, aromatic or heterocyclic fragments connected to the 4th position through -NH-, -NR- bridges and containing various substituents are used in increases the synthetic and biological potential for molecules (Berdiev A. U., Ortikov I. S., Turgunov K. K., Elmuradov B. Zh., Abdullaev N. D., Tashkhodzhaev B., 2024). Especially, compounds with this structure show high activity against cancer cells. It is noteworthy that currently used drugs with high cytotoxic activity (*erlotinib*, *gefitinib*, *lapatinib*, *afatinib*, *canertinib*, etc.) and the active substances of the drugs are also formed by means of such

imino bridges (Berdiev A. U., Mirsodikov M. M., Ortikov I. S., Elmuradov B. Zh., 2023). This is the reason for the synthesis of new types of active thienopyrimidine analogues of these compounds (Berdiev A. U., Ortikov I. S., Elmuradov B. Zh., 2022). Thieno[2,3-d]pyrimidines are one of the most widely used and studied important sections of synthetic organic chemistry, demonstrating activity against various types of cancer tumors by inhibiting protein kinases (Berdiev A. U., Ortikov I. S., Elmuradov B. Zh., 2022). Biological studies of these compounds have shown that the property of inhibiting protein kinases occurs due to the introduction and replacement of various functional groups in the structure of the thienopyrimidine fragment (Berdiev A. U., Mirsodikov M. M., Ortikov I. S., Elmuradov B. Zh., 2022). This leads to the emergence of anticancer activity. Below is the structure of various protein kinase inhibitors, which are obtained on the basis of studies and contain the thieno[2,3-d]pyrimidine base with high inhibition property.

Figure 1. Structure of protein kinase inhibitors with some strong effects



Based on this, among the interesting chemical changes of 4-chlorothieno[2,3-d]pyrimidines, we performed their nucleophilic exchange reactions with benzylamine.

2. Materials and Methods

IR spectra were taken from KBr pellets on a System 2000 FTIR spectrometer (PerkinElmer, USA). ¹H and ¹³C NMR spectra were recorded in CDCl₃, DMSO-d₆, and Py-D₅ solutions with TMS internal standard (0 ppm) on a JNM-ECZ400R instrument (JEOL, Japan) at 400 MHz for ¹H and 100 MHz for ¹³C. TLC used TLC Silicagel 60 F254 L/W 20cm × 20cm (Merck, Germany) and Whatman® UV-254 plates (Sigma-Aldrich, Germany) with elution by C₆H₆ –

– MeOH (5:1, **I**) and hexane – ethyl acetate (5:1, **II**). Melting points of synthesized compounds were determined on Biobase BMP-M70 (China) and Mel-Temp apparatuses (USA).

2-Amino-5,6-disubstituted thio-*phene-3-ethylcarboxylates* (5-9) were prepared by the literature method (Berdiev A.U., Ortikov I.S., Elmuradov B.Zh. (2022)). Cyclopentanone (3.55 mL, 3.36 g, ρ = 0.95 g/mL, 0.04 mol), cyanoacetic ester (4.52 g, ρ = 1.06 g/mL, 0.04 mol), S₈ (1.408 g, 0.044 mol), anhydrous EtOH (12 mL), and morpholine (4.0 mL, 4.05 g, 0.046 mol) gave **5** (7.10 g, 85%), mp 88-90°C (cyclohexane), R_f 0.70 (system II).

5,6-Disubstituted thieno[2,3-d]pyrimidin-4-ones (10-14) were prepared by the literature method (Berdiev A.U., Ortikov I.S., Elmuradov B.Zh. (2022)). *2-Amino-4,5,6-trihydrocyclopenta [b] thiophene-3-ethylcarboxylate (5)*, 4.22 g, 0.002 mol) and formamide (10 mL, 11.3 g, $\rho = 1.13$ g/mL, 0.24 mol) gave **10** (3.27 g, 85%, mp 216-218°C (EtOH), Rf 0.36 (system I)).

4-Chloro-5,6-disubstituted thieno[2,3-d]pyrimidines (15-19) (General Method). A mixture of *3,5,6,7-tetrahydro-4H-cyclopenta (El-Gazzar A.B., Hussein H.A., Hafez H.N. (2007); Deng J.F., Peng L., Zhang G.C., Lan X.B., Li C.F., Chen F.X., Zhou Y.Y., Lin Z.X., Chen L., Dai R.K., Xu H.J., Yang L., Zhang X.Q., Hu W.H. Eur. J. (2011)) thieno[2,3-d]pyrimidin-4-one (10)*, 0.96 g, 0.005 mol), POCl₃ (2.0 mL), CCl₄ (5.0 mL), and Et₃N (1.0 mL) was refluxed at 77°C for 4 h and cooled to room temperature. The mixture was diluted with CHCl₃ (15 mL), neutralized with NaHCO₃ solution (15%, 50 mL), and washed several times with distilled H₂O. The CHCl₃ part was dried over anhydrous Na₂SO₄ (4 h). The Na₂SO₄ was filtered off. The CHCl₃ was distilled in a rotary evaporator. The solid was recrystallized from EtOH to afford **15** (1.0 g, 96%) as a white crystalline product, mp 103-104°C, Rf 0.89 (system II). ¹H NMR (400 MHz, CDCl₃, δ , ppm): 2.53 (2H, m, H-6), 3.06 (2H, m, H-5), 3.16 (2H, m, H-7), 8.70 (1H, s, H-2).

Synthesis of N-benzyl-5,6-disubstituted thieno[2,3-d]pyrimidin-4-amines (20-24) (General Method)

In a 50 ml round-bottomed flask were poured 0.002 mol of *4-Chloro-5,6-disubstituted thieno[2,3-d]pyrimidines (15-19)*, 0.50 ml (0.490 g, $\rho = 0.981$ g/ml, 0.004 mol) of benzylamine, 0.55 ml (0.40 g, $\rho = 0.726$ g/ml, 0.004 mol) of triethylamine, 15.0 ml of ethanol, a reflux condenser was connected and the mixture was boiled in a water bath for 6 hours. The mixture was left overnight at room temperature and the resulting precipitate was filtered off. The precipitate was washed with 5% NaOH solution, then several times with water, dried at room temperature and the product was obtained. The resulting technical mass was purified by recrystallization from ethanol. As a result, white crystalline products (**20-24**) were obtained.

N-Benzyl-6,7-dihydro-5H-cyclopenta thieno[2,3-d]pyrimidin-4-amine (20) was prepared analogously to the method above from **15** (0.421 g) to afford **20** (0.522 g, 93%) mp 152-154°C (ethanol), Rf 0.73 (system I). Table 2 presents the ¹H NMR spectral data. ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 28.07, 29.33, 29.61, 44.76, 113.38, 127.65, 127.70, 128.94, 134.38, 138.67, 138.94, 153.25, 156.73, 171.00.

N-Benzyl-5,6,7,8-tetrahydrobenzo thieno[2,3-d]pyrimidin-4-amine (21) was prepared by the above method from **16** (0.449 g) to afford **21** (0.578 g, 98%) mp 112-114°C (ethanol), Rf 0.78 (system I). Table 2 presents the ¹H NMR spectral data. ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 22.57, 22.62, 25.54, 26.52, 44.99, 116.16, 125.45, 127.69, 127.73, 128.96, 133.50, 138.72, 153.19, 157.31, 165.58.

N-Benzyl-6,7,8,9-tetrahydro-5H-cyclohepta thieno[2,3-d] pyrimidine-4-amine (22) was prepared analogously to the method above from **17** (0.477 g) to afford **22** (0.587 g, 95%) mp 95–97 °C (ethanol), Rf 0.77 (system I). Table 2 presents the ¹H NMR spectral data. ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 26.35, 27.12, 28.97, 30.40, 30.42, 45.15, 117.28, 127.67, 127.76, 128.94, 130.26, 137.27, 138.78, 152.74, 157.23, 164.43.

N-Benzyl-5,6-dimethylthieno [2,3-d] pyrimidin-4-amine (23) was prepared by the above method from **18** (0.397 g) to afford **23** (0.505 g, 94%) mp 164–166 °C (ethanol), Rf 0.69 (system I). Table 2 presents the ¹H NMR spectral data. ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 13.48, 14.56, 45.02, 117.06, 123.05, 127.69, 128.94, 130.09, 138.68, 153.10, 157.26, 164.84.

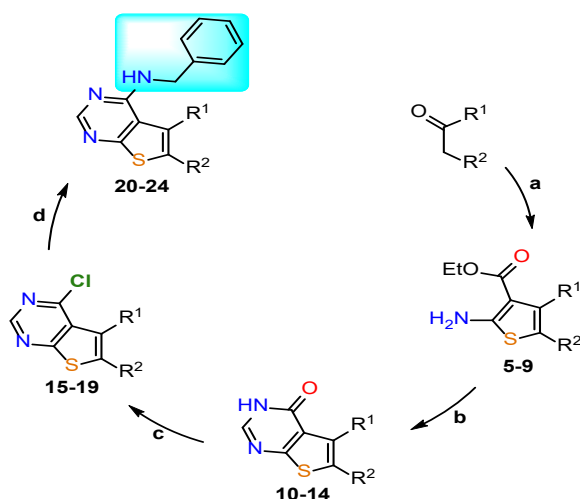
N-Benzyl-5-methyl-6-ethoxycarbonylthieno[2,3-d]pyrimidin-4-amine (24) was prepared analogously to the method above from **19** (0.513 g) to afford **24** (0.621 g, 95%) mp 129-131 °C (ethanol), Rf 0.81 (system I). Table 2 presents the ¹H NMR spectral data. ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 14.41, 15.95, 45.26, 61.55, 117.17, 122.94, 127.81, 127.96, 129.09, 137.89, 138.04, 156.04, 159.00, 163.00, 167.35.

3. Results and Discussion

For this, substituted thieno[2,3-d]pyrimidine-4-ones (**10–14**) were synthesized in two steps via formation of 2-aminothiophene esters (**5–9**) according to the published method (Berdiev A.U., Ortikov I.S., Elmuradov B.Zh. (2022)). Compounds **10–14** reacted with POCl_3 in CCl_4 solution to form 4-chlorothieno[2,3-d]pyrimidines (**15–19**) with a 4-Cl atom in high yields. These compounds were intermediates for the synthesis of antitumor agents and played important roles as necessary synthons in targeted organic syntheses. The imidoyl Cl atom on the pyrimidine ring was highly reactive although the molecules (**15–19**) were stable, so they could be used in reactions with various nucleophilic reagents.

Reactions were carried out by boiling a 1:2 equiv mixture of substrate and reagent in ethanol medium (80 °C) in the presence of TEA (2 equiv) for 6 h. As a result, corresponding substances **20–24** were synthesized with high yields (93–98%).

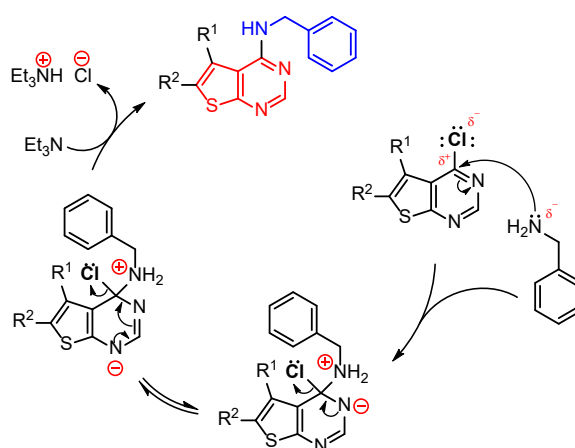
Figure 2. Reagents and reaction conditions: (a) Ethyl cyanoacetate, S_8 , morpholine, anhydr. EtOH, 40–45 °C, 24 h; (b) formamide, 150 °C, 8 h; (c) POCl_3 , CCl_4 , TEA, 77 °C, 4 h; (d) benzylamine, TEA, anhydr. EtOH, 80 °C, 6 h



Accordingly, the electron density of the carbon bound to chlorine and nitrogen atoms in the pyrimidine ring is reduced due to the effect of atoms with high electronegativity, so the nucleophilic attack of ben-

zylamine nitrogen takes place. At the next stage, the energetic instability of the sp^3 hybridized C atom in the 4th state decreases as a result of redistribution of electrons in the pyrimidine ring, hydrogen and chlorine ions are released, and a new C-N bond is formed. TEA participating in the reaction, in turn, acts as an acceptor for the formed HCl. Below is an approximate mechanism of the process:

Figure 3. The structure of all obtained compounds was fully proved based on the results of modern physicochemical methods, including IR, ^1H , ^{13}C NMR spectroscopy and X-ray structure analysis (XRD) of some of them



In the IR spectra of the compounds, there are absorption lines belonging to the NH group bridging thienopyrimidine-benzyl fragments, and this absorption appears at 3367 cm^{-1} in compound **20**, **21** at 3370 cm^{-1} , **22** at 3351 cm^{-1} , **23** at 3430 cm^{-1} and for compound **24** is 3446 cm^{-1} . Also, the absorption frequencies of the C-H aryl bond in the aromatic ring are at $3028\text{--}3032\text{ cm}^{-1}$, at $2919\text{--}2945\text{ cm}^{-1}$ for the C-H bonds of the aliphatic groups in the molecule, at $2840\text{--}2860\text{ cm}^{-1}$ at the aliphatic C-H bonds of the benzyl fragment, $2\text{C}=\text{N}$ and Intense absorption max. characteristic of $^4\text{C}=\text{N}$ bond at $1551\text{--}1573\text{ cm}^{-1}$ and valence vibrations of imino group nitrogen at $1493\text{--}1510\text{ cm}^{-1}$ characteristic of both C-N-C bonds were determined.

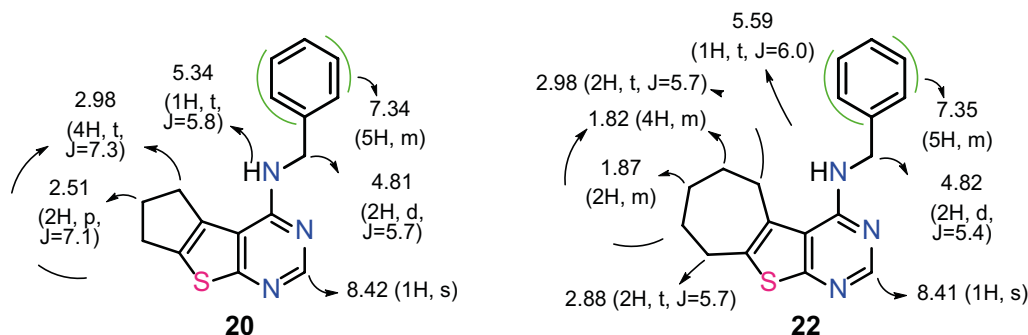
Table 1. Some physicochemical data of the obtained compounds 20–24

Compounds	R ¹	R ²	Brutto formula	Time, h	Yields, %
20	-(CH ₂) ₃ -		C ₁₆ H ₁₅ N ₃ S		93
21	-(CH ₂) ₄ -		C ₁₇ H ₁₇ N ₃ S		98
22	-(CH ₂) ₅ -		C ₁₈ H ₁₉ N ₃ S	6	95
23	-CH ₃	-CH ₃	C ₁₅ H ₁₅ N ₃ S		94
24	-CH ₃	-CO ₂ Et	C ₁₇ H ₁₇ N ₃ O ₂ S		95

In their NMR spectra (**20–24**) CDCl₃ ¹H, the most characteristic chemical shifts are the presence of the aromatic proton (H-2) at position 2 of the pyrimidine ring as a one-proton singlet in the range of 8.41–8.53 ppm, which is slightly stronger than that of the starting products (**15–19**), showing that it has shifted upfield. In addition, we can see that the signal corresponding to the ⁴C-NH hydrogen is in the form of a single proton triplet present in the 5.34–5.98 ppm regions.

Also, chemical shifts in the form of a two-proton doublet in the 4.81–4.85 ppm area belonging to the hydrogens of the benzyl group of methylene (CH₂) and in the form of a five-proton multiplet characteristic of hydrogens of the aromatic phenyl group in the area of 7.34–7.37 ppm (C₆H₅) characterize the structure of all compounds in general.

Also, as an example of the specific signals of some of these compounds, the hydrogen atoms belonging to the methylene groups at positions C-5 and C-7 of substance **20** represent a four-proton (4H, t, J = 7.3) triplet in the region of 2.98 ppm; the methylene group at position 6 at 2.51 ppm can give signals of hydrogens in the form of a two-proton pentet (2H, p, J = 7.1). Moreover, in the 2.98 and 2.88 ppm fields corresponding to the hydrogens of the C-5 and C-9 methylene groups of substance **22**, they appear as triplets with two protons (2H, t, J=5.7) each. The chemical shift values of the hydrogens of the -CH₂- group in position C-7 in the two-proton (2H, m) multiplet at 1.87 ppm and the four-proton (4H, m) multiplet in the region of 1.82 ppm methylene hydrogens in positions C-6 and C-8 indicate the structure of the compounds.

Figure 4. ¹H NMR spectrum analysis of compounds **20** and **22**

It should be noted that the results of the ¹³C NMR (CDCl₃) spectrum prove that all carbon atoms in the synthesized compounds (**20–24**) are compatible (in the experimental part) and, in turn, confirm their molecular structures.

The synthesized compounds include N-benzyl-6,7-dihydro-5H-cyclopenta (El-Gazzar A.B., Hussein H.A., Hafez H.N. (2007); Deng J.F., Peng L., Zhang G.C., Lan X.B., Li C.F., Chen F.X., Zhou Y.Y., Lin Z.X., Chen L., Dai R.K., Xu H.J., Yang L., Zhang X.Q., Hu W.H. Eur. J. (2011)) thieno

(Elmahdy K. M., Elkazak A. M., Megid A. M., Seada M., Mohamed O. F. (2013); Rashad A. E. Ali M. A. (2006)) pyrimidin-4-amine (**20**) and N-benzyl-6,7,8,9-tetrahydro-5H-cyclohepta thieno (Elmahdy K. M.,

Elkazak A. M., Megid A. M., Seada M., Mohamed O. F. (2013); Rashad A. E. Ali M. A. (2006)) pyrimidin-4-amines (**22**) which were also fully confirmed by X-ray diffraction (XRD) analysis.

Table 2. Multiplets of the corresponding protons in the ^1H NMR spectra of the obtained compounds (20–24) (δ , ppm, J, Hz)

No	N=CH	C ₆ H ₅	NH	C ₆ H ₅ CH ₂	Protons of substituents in positions 5 and 6
20	8.42 (1H, s)	7.34 (5H, m)	5.34 (1H, t, J=5.8)	4.81 (2H, d, J=5.7)	C-5 and C-7, $-(\text{CH}_2)_2-$, 2.98 (4H, t, J=7.3), C-6, $-\text{CH}_2-$, 2.51 (2H, p, J=7.1)
21	8.42 (1H, s)	7.35 (5H, m)	5.55 (1H, t, J=5.6)	4.81 (2H, d, J=5.4)	C-5, $-\text{CH}_2-$, 2.87 (2H, t, J=5.1), C-8, $-\text{CH}_2-$, 2.81 (2H, t, J=4.7), C-6 and C-7, $-(\text{CH}_2)_2-$, 1.89 (4H, m)
22	8.41 (1H, s)	7.35 (5H, m)	5.59 (1H, t, J=6.0)	4.82 (2H, d, J=5.4)	C-5, $-\text{CH}_2-$, 2.98 (2H, t, J=5.7), C-9, $-\text{CH}_2-$, 2.88 (2H, t, J=5.7), C-7, $-\text{CH}_2-$, 1.87 (2H, m), C-6 and C-8, $-(\text{CH}_2)_2-$, 1.82 (4H, m)
23	8.42 (1H, s)	7.35 (5H, m)	5.71 (1H, t, J=5.5)	4.82 (2H, d, J=5.4)	C-5, $-\text{CH}_3$, 2.41 (3H, s), C-6, $-\text{CH}_3$, 2.42 (3H, s),
24	8.53 (1H, s)	7.37 (5H, m)	5.98 (1H, t, J=5.6)	4.85 (2H, d, J=5.4)	C-5, $-\text{CH}_3$, 2.94 (3H, s), C-6, $-\text{CO}_2\text{CH}_2\text{CH}_3$, 1.40 (3H, t, J=7.1), C-6, $-\text{CO}_2\text{CH}_2\text{CH}_3$, 4.36 (2H, q, J=7.1)

4. Conclusion

Thus, nucleophilic exchange reactions of benzylamine with various substituted-4-chlorothieno[2,3-d]pyrimidine series compounds were carried out, and as a result, the corresponding new products were synthesized with high yields. Due to the high nucleophilicity of benzylamine and the high reactivity of compounds of the imidoyl chloride type, it was found that the nature of the substituents in the 5th and 6th positions of 4-chlorothieno (Elmahdy K. M., Elkazak

A. M., Megid A. M., Seada M., Mohamed O. F. (2013); Rashad A. E. Ali M. A. (2006)) pyrimidines (electron-donating or electron-withdrawing), and the size of the polymethylene rings do not significantly affect the yields of the target compounds.

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References

- Bozorov Kh., Zhao J. Yu., Elmuradov B., Pataer A., Aisa H.A. (2015). *Eur. J. Med. Chem.*, – 102. – 552 p.
- Elmahdy K. M., Elkazak A. M., Megid A. M., Seada M., Mohamed O. F. (2013). *Adv. Chem.*, – 5, – 581 p.
- Rashad A. E. Ali M. A. (2006). *Nucleosides, Nucleotides Nucleic Acids*, – 25. – 17 p.
- El-Gazzar A. B., Hussein H. A., Hafez H. N. (2007). *Acta Pharm.*, – 57 (4). – 395 p.

- Deng J.F., Peng L., Zhang G.C., Lan X.B., Li C.F., Chen F.X., Zhou Y.Y., Lin Z.X., Chen L., Dai R.K., Xu H.J., Yang L., Zhang X.Q., Hu W.H. *Eur. J. (2011). Med. Chem.*, – 46 (1). – 71 p.
- Nagaraju K., Harikrishna N., Vasu K., Rao C.V. (2015). *Indo Am. J. Pharm. Res.*, – 5 (4). – 1604 p.
- Guo Y., Li J., Ma J., Yu L.Z., Wang H., Zhu W., Liao X., Zhao Y. (2015). *Chin. Chem. Lett.*, – 26. – 755 p.
- Zhu W., Chen C., Sun C., Xu S., Wu C., Lei F., Xia H., Tu Q., Zheng P. (2015). *Eur. J. Med. Chem.*, – 93. – 64 p.
- Kim Y., Kim M., Park M., Tae J., Baek D., Park K.D., Choo H. (2015). *Molecules*, – 20 (3). – 5074 p.
- Berdiev A. U., Ortikov I. S., Turgunov K. K., Elmuradov B. Zh., Abdullaev N. D., Tashkhodzhaev B. (2024). *Chem. Nat. Compd.*, – 60 (1). – P. 127–132.
- Berdiev A. U., Mirsodikov M. M., Ortikov I. S., Elmuradov B. Zh. (2023). *Uzbek chemical journal*, – 3. – P. 76–84.
- Berdiev A. U., Ortikov I. S., Elmuradov B. Zh. (2022). *Proceedings of the Republican scientific-practical conference, Abstarcts*, – Tashkent, – P. 110–111.
- Berdiev A. U., Ortikov I. S., Elmuradov B. Zh. (2022). *Actual problems of the chemistry of natural compounds, Abstarcts*, – Tashkent, – 22.
- Berdiev A. U., Mirsodikov M. M., Ortikov I. S., Elmuradov B. Zh. (2022). *Proceedings of the 10th Republican Conference of Young Chemists, Part II, Namangan*, – P. 46–48.
- Berdiev A. U., Ortikov I. S., Elmuradov B. Zh. (2022). *Uzbek chemical journal*, – 4. – P. 59-65.

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