

NAMANGAN DAVLAT
UNIVERSITETI
ILMIY AXBOROTNOMASI, [2026-9]
ISSN:2181-1458
ISSN:2181-0427



02.00.00-KIMYO FANLARI
journal.namdu.uz
CHEMICAL SCIENCES

UO' K 547.735'854.218.07:542.976

SYNTHESIS OF NOVEL (E)-2-BROMO-11-(4-ARYLIDENE)-8,9,10,11-TETRAHYDRO-6H-BENZO[4,5]THIENO[3,2-d]PYRIDO[1,2-a]PYRIMIDIN-6-ONES

Buronov Anvarjon Yusuf o' g' li

Institute of Biochemistry, Samarkand State University named after Sharof Rashidov, Samarkand, Uzbekistan
0000-0003-1887-6804

E-mail: anvarjon4488@gmail.com

Bozorov Khurshed Abdulloyevich

Institute of Biochemistry, Samarkand State University named after Sharof Rashidov, Samarkand, Uzbekistan
0000-0001-7449-0936

E-mail: khurshedbek@gmail.com

Abstract: A series of novel fused thieno[3,2-d]pyrimidinone derivatives, namely (E)-2-bromo-11-(4-arylidene)-8,9,10,11-tetrahydro-6H-benzo[4,5]thieno[3,2-d]pyrido[1,2-a]pyrimidin-6-ones, was synthesized through a multistep synthetic sequence. The synthetic route involved an initial cyclocondensation followed by α -methylene condensation to introduce the arylidene fragment. The structures of the synthesized compounds were characterized and confirmed by ^1H and ^{13}C NMR spectroscopy and high-resolution mass spectrometry (HRMS). The obtained results demonstrate that this synthetic strategy provides a convenient approach to structurally diverse fused thieno[3,2-d]pyrimidinone derivatives.

Keywords: aromatic aldehyde, cyclocondensation, α -methylene condensation, caprolactam, fused thieno[3,2-d]pyrimidinone.

YANGI (E)-2-BROM-11-(4-ARILIDEN)-8,9,10,11-TETRAGIDRO-6H-BENZO[4,5]TIENO[3,2-d]PIRIDO[1,2-a]PIRIMIDIN-6-ONLAR SINTEZI

Annotatsiya: Yangi kondensirlangan tiyeno[3,2-d]pirimidinon hosilalari, ya'ni (E)-2-brom-11-(4-ariliden)-8,9,10,11-tetragidro-6H-benzo[4,5]tieno[3,2-d]pirido[1,2-a]pirimidin-6-onlar, ko' p bosqichli sintetik ketma-ketlik orqali sintez qilindi. Sintetik yo' l dastlabki siklokondensatsiya va undan keyin ariliden fragmentini kiritish uchun α -metilen kondensatsiyasini o' z ichiga oldi. Sintez qilingan birikmalarining tuzilishi ^1H va ^{13}C YaMR spektroskopiyasi hamda yuqori aniqlikdagi mass-spektrometriya (HRMS) yordamida tavsiflandi va tasdiqlandi. Olingan natijalar ushbu sintetik strategiya strukturaviy jihatdan xilma-xil kondensirlangan tiyeno[3,2-d]pirimidinon hosilalarini olish uchun qulay yondashuv ekanligini ko' rsatdi.

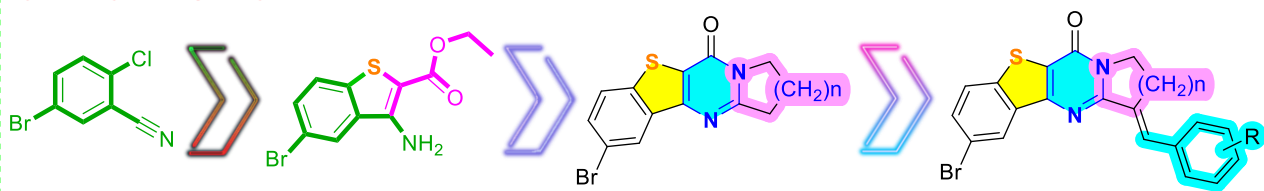
Kalit so' zlar: aromatik aldegid, siklokondensatsiya, α -metilen kondensatsiyasi, kaprolaktam, kondensirlangan tieno[3,2-d]pirimidinon.

СИНТЕЗ НОВЫХ (Е)-2-БРОМ-11-(4-АРИЛИДЕН)-8,9,10,11-ТЕТРАГИДРО-6Н-БЕНЗО[4,5]ТИЕНО[3,2-d]ПИРИДО[1,2-a]ПИРИМИДИН-6-ОНОВ

Аннотация: Синтезирована серия новых конденсированных производных тиено[3,2-d]пиримидинона, а именно (Е)-2-бром-11-(4-арилиден)-8,9,10,11-тетрагидро-6Н-бензо[4,5]тиено[3,2-d]пиридо[1,2-a]пиримидин-6-онов, в рамках многостадийной синтетической последовательности. Синтетический маршрут включал первоначальную циклоконденсацию с последующей α -метиленовой конденсацией для введения арилиденового фрагмента. Структуры синтезированных соединений были охарактеризованы и подтверждены методами ^1H и ^{13}C ЯМР-спектроскопии и масс-спектрометрии высокого разрешения (HRMS). Полученные результаты показывают, что данная синтетическая стратегия обеспечивает удобный подход к получению структурно разнообразных конденсированных производных тиено[3,2-d]пиримидинона.

Ключевые слова: ароматический альдегид, циклоконденсация, α -метиленовая конденсация, капролактam, конденсированный тиено[3,2-d]пиримидинон.

GRAPHICAL ABSTRACT



Introduction

Heterocyclic compounds, particularly fused systems containing nitrogen and sulfur, occupy an important position in organic and pharmaceutical chemistry. Among them, thienopyrimidine derivatives are regarded as structural motifs of biologically active compounds and promising synthetic platforms for the development of new drug candidates. Fusion of thiophene and pyrimidine rings provides the molecule with a stable, rigid framework and enables its electronic and biological properties to be modulated through functional groups [1].

Thieno[3,2-*d*]pyrimidine derivatives represent a promising class within this family, and their structural diversity can be increased by varying substituents at different positions. In the synthesis of such compounds, 3-aminothiophene-2-carboxylate esters are useful starting materials. Their amino and ester groups provide the reactive centers required for subsequent condensation and intramolecular cyclization processes [2].

The Gewald reaction is one of the practically effective methods for the preparation of aminothiophene derivatives. This method enables the synthesis of aminothiophenes bearing various substituents from carbonyl compounds, cyanoacetate esters, and sulfur sources. In the subsequent stage, cyclocondensation of aminothiophene esters with lactams can generate an additional ring and form a fused thieno[3,2-*d*]pyrimidine framework. The size of the resulting ring can be controlled by varying the carbon chain length of the lactam [3].

Introduction of halogen atoms such as bromine into the thienopyrimidine system also provides useful opportunities for subsequent palladium-catalyzed cross-coupling and other functionalization reactions. Therefore, the efficient and selective synthesis of thieno[3,2-*d*]pyrimidine derivatives is relevant to the investigation of structure–property relationships and the construction of libraries of new biologically active compounds.

The present study was aimed at the synthesis of new fused thieno[3,2-*d*]pyrimidine derivatives from aminothiophene carboxylate esters, their cyclocondensation with lactams, and the evaluation of the structural features of the resulting compounds.

Literature review

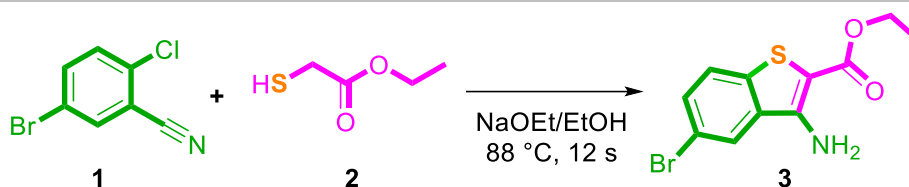
The synthesis of thieno[3,2-*d*]pyrimidine derivatives is a promising area of modern bioorganic and pharmaceutical chemistry owing to the stability of these heterocyclic systems and their ability to exhibit diverse biological activities. The synthesis of compounds in this class generally involves condensation of aminothiophene derivatives with carbonyl-containing compounds, nitriles, or lactams, followed by cyclization. These synthetic approaches not only establish the principal heterocyclic core but also enable the controlled introduction of functional groups at different positions [4].

3-Aminothiophene-2-carboxylic acids and their esters are important synthetic precursors for constructing bicyclic and highly fused thienopyrimidinone systems. The potential interactions among the functional groups within these molecules provide favorable conditions for the formation of various intermediates and their subsequent participation in intramolecular cyclization. In particular, combined synthetic strategies based on the Gewald, Knoevenagel–Cope, Thorpe–Ziegler, and Niementowski reactions can be used to construct complex, including tetracyclic, frameworks [5]. The resulting heterocyclic systems can subsequently undergo halogenation, acylation, and nucleophilic substitution reactions, providing structurally diverse derivatives. In this context, the thieno[3,2-*d*]pyrimidine core represents a promising molecular platform for the development of new biologically active compounds [6].

Research methodology

Synthesis of ethyl benzo-aminothiophene carboxylate derivatives. The synthesis of aminothiophene carboxylate esters generally involves several consecutive steps. To ensure high selectivity, the molar ratios of the reagents, solvent nature, temperature, and reaction time must be appropriately controlled. One effective approach is based on the Gewald reaction, in which an appropriate carbonyl compound is condensed with ethyl cyanoacetate. In the subsequent stage, formation of the thiophene ring is achieved in the presence of elemental sulfur or an appropriate sulfur-containing reagent.

The use of an EtONa/EtOH system as the reaction medium provides the basic conditions required for the process. Precise control of reagent ratios and temperature improves the selectivity of target-product formation. This approach has been used to obtain ethyl aminothiophene carboxylates bearing various substituents, including derivatives fused with other heterocyclic systems.



On this basis, refluxing 5-bromo-2-chlorobenzonitrile (1) with ethyl 2-mercaptoacetate (2) in EtOH in the presence of NaOEt afforded ethyl 3-amino-5-bromobenzo[b]thiophene-2-carboxylate (3). The presence of two different halogen atoms in the starting molecule provides additional opportunities for subsequent functionalization. At the same time, dihalogenated aromatic systems of this type may undergo nucleophilic substitution along more than one pathway, potentially leading to side reactions and a decrease in the yield of the desired product.

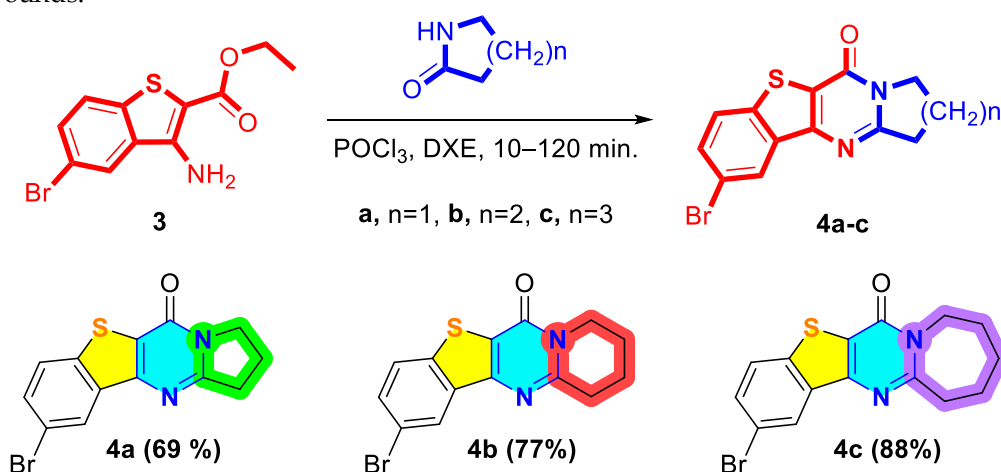
Synthesis of polycyclic thieno[3,2-*d*]pyrimidines. The formation of polycyclic thieno[3,2-*d*]pyrimidine derivatives can be effectively achieved through the reaction of ethyl 3-amino-4- or 5-substituted thiophene-2-carboxylates with lactams. This process involves several consecutive transformations, and its outcome is significantly influenced by the nature of the lactam, catalyst, solvent, and temperature [7].

Initially, the aminothiophene ester undergoes condensation with the carbonyl group of the lactam. The electrophilicity of the carbonyl carbon is an important factor determining the efficiency of the reaction. Appropriate selection of the solvent and temperature promotes formation of the intermediate and facilitates the subsequent cyclization step. In practice, polar aprotic solvents such as DCE, 1,4-dioxane, and related media may provide suitable reaction conditions.

Following condensation, the resulting intermediate undergoes intramolecular cyclization to form a fused heterocyclic core based on the thieno[3,2-*d*]pyrimidine system. At this stage, the acidity of the reaction medium, temperature, and nature of the catalyst are important parameters influencing the reaction pathway. The use of lactam-type electrophilic components such as γ -butyrolactam, δ -valerolactam, and ϵ -caprolactam provides an opportunity to control the size of the newly formed fused ring.

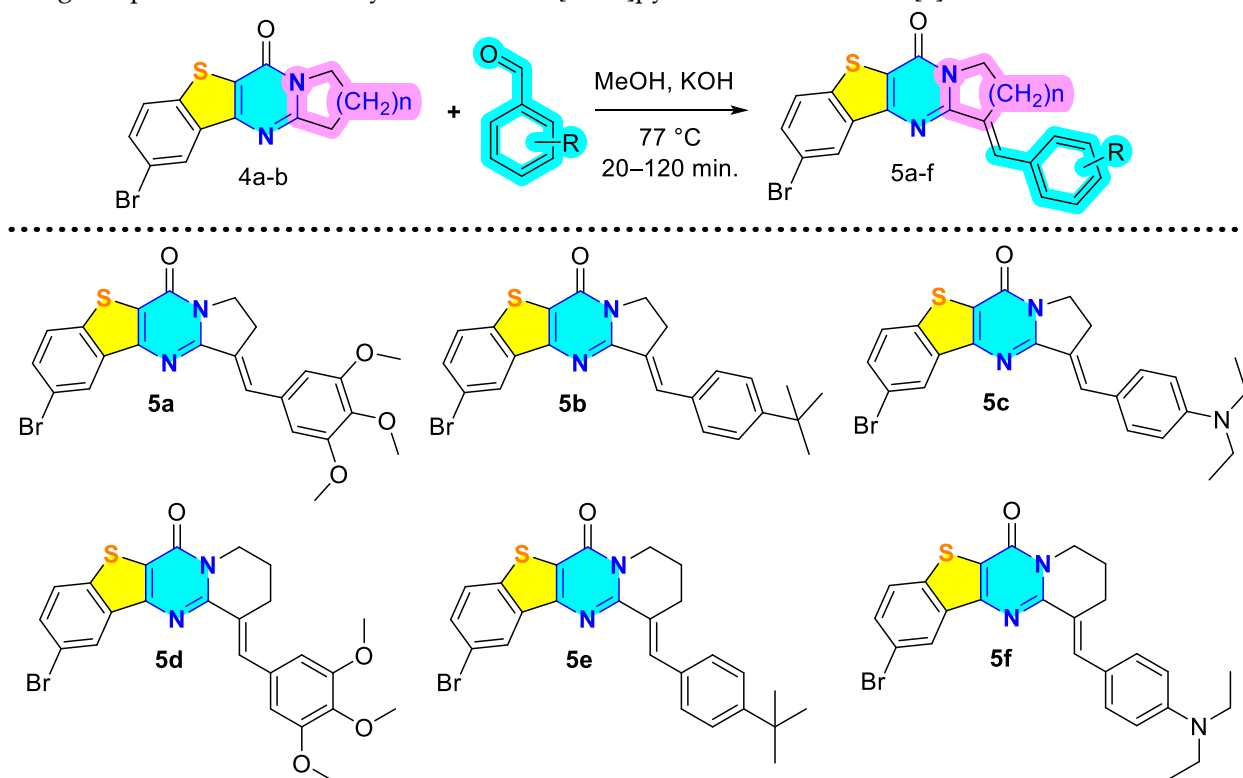
The synthesis of polycyclic thieno[3,2-*d*]pyrimidines is particularly important for increasing the structural diversity of fused heterocyclic systems. Such compounds can be obtained through cyclization reactions of benzo- or pyridoaminothiophene carboxylic acid derivatives with various electrophilic reagents. Cyclization is often performed in the presence of POCl₃ or polyphosphoric acid (PPA). The use of 1,2-dichloroethane (DCE), 1,4-dioxane, and other relatively inert solvents can stabilize the reaction medium and facilitate cyclization of the intermediates.

In reactions of aminothiophene derivatives with lactams or amides, an addition–condensation process initially occurs at the carbonyl center. Subsequent intramolecular cyclization of the resulting intermediate forms an additional ring, leading to polycyclic systems, including tetracyclic thieno[3,2-*d*]pyrimidine frameworks. The efficiency of this transformation depends not only on the nature of the reagents but also on the solvent, temperature, and catalytic system. Therefore, identification of suitable reaction conditions is an important prerequisite for the targeted synthesis of new fused heterocyclic compounds.



Cyclocondensation reactions of ethyl 3-amino-5-bromobenzo[b]thiophene-2-carboxylate (3) with various lactams were performed. The reactions were generally carried out in DCE in the presence of POCl₃ under heating. As a result, thieno[3,2-*d*]pyrimidine derivatives containing additional rings of different sizes were obtained according to the length of the methylene chain in the lactam. Specifically, pyrrolidin-2-one afforded 4a with a trimethylene bridge, piperidin-2-one afforded 4b containing a tetramethylene fragment, and azepan-2-one afforded 4c containing a pentamethylene fragment. The reactions proceeded through an initial condensation step followed by intramolecular cyclization, ultimately furnishing

polycyclic heterocyclic systems. Variation of the methylene-chain length in the lactam thus enabled control over the size of the fused ring and provided structurally diverse thieno[3,2-d]pyrimidine derivatives [8].



New arylidene derivatives (5a–f) of the thieno[3,2-d]pyrimidine series were obtained through condensation with the corresponding carbonyl compounds. During investigation of the reaction conditions, the highest product yield, 55%, was obtained at 77 °C. The yield decreased under other conditions. This may be associated with the steric bulk of the tert-butyl group and the resulting steric hindrance. Thus, the nature and spatial characteristics of the base, together with the reaction temperature, significantly affect the product yield.

Structural Characterization. The structures of the synthesized intermediates and target compounds were established primarily by nuclear magnetic resonance spectroscopy. Both ^1H and ^{13}C NMR spectra were recorded using a VARIAN 400 MHz spectrometer. The observed chemical shifts, signal multiplicities, and coupling constants were analyzed and assigned according to the proposed molecular structures. Particular attention was paid to spin–spin coupling patterns, which provided additional evidence for the connectivity of the structural fragments and, where applicable, the regioselectivity of the transformations. Comparison of the experimental spectral features with the expected structural characteristics also served to assess the completeness of the corresponding synthetic steps.

The molecular compositions of the obtained compounds were further examined by high-resolution mass spectrometry. HRMS measurements were carried out on a SCIEX QTRAP 6500+ instrument equipped for electrospray ionization (ESI). The experimentally observed mass-to-charge values were compared with the theoretical values calculated for the proposed molecular formulas. The isotope distribution patterns were additionally considered when assigning the molecular ions, particularly for compounds containing halogen atoms. The combined NMR and HRMS data provided complementary evidence for the identity and structural integrity of the synthesized products.

Analysis results

Commercially available starting materials were used without further purification. Ethanol, petroleum ether, toluene, ethyl acetate, and DCE were used as anhydrous solvents. Reaction progress was monitored by TLC on HSGF₂₅₄ silica plates (2.5 × 5 cm), with visualization under UV light (254 and 365 nm) or by iodine staining.

^1H and ^{13}C NMR spectra were recorded at room temperature on a VARIAN 400 MHz spectrometer using TMS as the internal reference. Chemical shifts, multiplicities, and coupling constants were analyzed for structural assignment. HRMS data were obtained on a QTRAP® 6500+ LC–MS system equipped with an ESI source. Molecular formulas were verified by comparison of calculated and experimental m/z values, with isotope patterns considered for halogen-containing compounds.

Synthesis of ethyl 3-amino-5-bromobenzo[b]thiophene-2-carboxylate (3)

In the initial stage of the synthesis, 20 mL of ethanol was placed in a 35 mL high-pressure vessel, and the solution was cooled to 0 °C. Sodium ethoxide (820 mg, 12 mmol) was added at this temperature. Ethyl 2-mercaptoacetate (2, 1440 mg, 12 mmol) and 5-bromo-2-chlorobenzonitrile (1, 2165 mg, 10 mmol) were then added sequentially to the reaction

mixture. The resulting suspension was heated at 90 °C in a glycerol bath and stirred for 12 h. Reaction progress was monitored periodically by thin-layer chromatography (TLC).

After completion of the reaction, ethyl 3-amino-5-bromobenzo[b]thiophene-2-carboxylate (3), formed by cyclization of compounds 1 and 2, was isolated by column chromatography. A 5:1 mixture of petroleum ether and ethyl acetate was used as the eluent. The isolated product had an *R_f* value of 0.70.

Ethyl 3-amino-5-bromobenzo[b]thiophene-2-carboxylate (3). ¹H NMR (400 MHz, CDCl₃): δ 7.77 (d, *J* = 1.8 Hz, 1H), 7.60–7.56 (m, 1H), 7.53 (ddd, *J* = 8.6, 1.8, 0.5 Hz, 1H), 5.80 (s, 2H), 4.36 (qd, *J* = 7.1, 0.5 Hz, 2H), 1.39 (td, *J* = 7.1, 0.5 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 165.37, 147.29, 138.64, 133.23, 131.29, 124.97, 124.28, 117.91, 101.27, 60.87, 14.70.

HRMS (ESI): *m/z* calcd for C₁₁H₁₀BrNO₂S [M+H]⁺ 299.9688 and 301.9668; found 299.9688 (5.82%) and 301.9667 (6.12%).

Synthesis of fused thieno[3,2-*d*]pyrimidine derivatives (4a–c)

In the next stage, reactions for the formation of fused thieno[3,2-*d*]pyrimidine derivatives were carried out using precursor 3. For this purpose, 3 (300 mg, 1 mmol) was placed in each 15 mL high-pressure vessel and dissolved in 3 mL of DCE. Lactams (1.2 mmol each) were then added. Phosphorus oxychloride (POCl₃; 0.15 mL) was added dropwise to each reaction mixture over 10 min.

The reaction mixtures were placed in a glycerol bath at 90 °C and heated with stirring for 6 h (Scheme 2). The reactions were monitored by TLC. After completion, the products were isolated by column chromatography. Compounds **4a**, **4b**, and **4c** were obtained as white solids and purified by column chromatography using a 1:1 petroleum ether–ethyl acetate system.

*9-Bromo-2,3-dihydrobenzo[4,5]thieno[3,2-*d*]pyrrolo[1,2-*a*]pyrimidin-5(1H)-one (4a).* ¹H NMR (400 MHz, CDCl₃): δ 8.38 (d, *J* = 1.9 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 1H), 7.63 (dd, *J* = 8.6, 2.0 Hz, 1H), 4.28 (t, *J* = 7.34 Hz, 2H), 3.27 (t, *J* = 8.0 Hz, 2H), 2.38 (qd, *J* = 7.9, 6.2 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 162.30, 157.60, 152.93, 140.24, 135.98, 131.89, 126.52, 124.92, 122.42, 119.33, 47.10, 32.47, 20.11.

HRMS (ESI): calcd for C₁₃H₉BrN₂OS [M+H]⁺ 320.9692 (100%) and 322.9672 (97.3%), found 320.9689 (98.56%) and 322.9666 (100%).

*2-Bromo-8,9,10,11-tetrahydro-6H-benzo[4,5]thieno[3,2-*d*]pyrido[1,2-*a*]pyrimidin-6-one (4b).* ¹H NMR (400 MHz, pyridine-*d*₅): δ 8.62 (d, *J* = 1.9 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.70 (dd, *J* = 8.6, 2.1 Hz, 1H), 4.00 (t, *J* = 6.0 Hz, 2H), 3.01 (t, *J* = 6.4 Hz, 2H), 1.77–1.63 (m, 4H). ¹³C NMR (100 MHz, pyridine-*d*₅): δ 158.99, 158.45, 151.58, 140.69, 137.26, 132.33, 127.12, 126.10, 122.42, 119.83, 43.30, 32.30, 22.40, 19.73.

HRMS (ESI): *m/z* calcd for C₁₄H₁₁BrN₂OS [M+H]⁺ 334.9849 and 336.9828; found 334.9847 (93.54%) and 336.9819 (100%).

*2-Bromo-9,10,11,12-tetrahydrobenzo[4',5']thieno[3',2':4,5]pyrimido[1,2-*a*]azepin-6(8H)-one (4c).* ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.29 (d, *J* = 2.0 Hz, 1H), 8.12 (d, *J* = 8.6 Hz, 1H), 7.80 (dd, *J* = 8.6, 2.1 Hz, 1H), 4.41 (t, *J* = 4.6 Hz, 2H), 3.17 (t, *J* = 4.8 Hz, 2H), 1.84–1.69 (m, 6H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 163.60, 158.18, 150.54, 139.94, 136.31, 132.07, 126.53, 125.78, 121.82, 119.16, 42.80, 37.01, 29.25, 27.30, 24.87.

HRMS (ESI): *m/z* calcd for C₁₅H₁₃BrN₂OS [M+H]⁺ 349.0005 and 350.9985; found 349.0006 (91.25%) and 350.9979 (100%).

α-Methylene Condensation of Tetracyclic Thieno[3,2-*d*]pyrimidines (5a–f). Two reaction vessels were each charged with KOH (56 mg, 1 mmol) in 3 mL of anhydrous methanol, followed by addition of 4a (97 mg, 0.5 mmol) and 4b (104 mg, 0.5 mmol), respectively. The mixtures were stirred using magnetic stirring, after which an aldehyde (0.7 mmol) was added. The reaction mixtures were heated to 88 °C and stirred under reflux for 2 h. Reaction progress was monitored by TLC, and the products were purified by column chromatography.

Conclusion

In this study, an effective method for the synthesis of fused thieno[3,2-*d*]pyrimidines from aminothiophene derivatives was developed. Ethyl 3-amino-5-bromobenzo[b]thiophene-2-carboxylate, obtained from 5-bromo-2-chlorobenzonitrile and ethyl 2-mercaptoacetate in the NaOEt/EtOH system, was used as a bifunctional precursor. Its cyclocondensation with various lactams in the presence of POCl₃ afforded fused thieno[3,2-*d*]pyrimidine derivatives bearing rings of different sizes. The structures of the products were confirmed by ¹H and ¹³C NMR spectroscopy and HRMS. In addition, arylidene analogues were synthesized through *α*-methylene condensation, affording yields of up to 55% under the reported optimal conditions. The proposed synthetic strategy provides a promising approach for the preparation and subsequent functionalization of new fused thieno[3,2-*d*]pyrimidine derivatives.

Authors' Contributions, Conflict of Interest, and Funding

Authors' Contributions: All authors contributed equally to the conceptualization of the study, data analysis, and preparation of the manuscript.

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding: This research was conducted without any external financial support.

Foydalanilgan adabiyotlar

1. Murtazaeva, Z.; Nasrullaev, A.; Buronov, A.; Gaybullaev, S.; Nie, L.; Numonov, S.; Khushnazarov, Z.; Turgunov, D.; Kuryazov, R.; Zhao, J.; et al. Imidazole Hybrids: A Privileged Class of Heterocycles in Medicinal Chemistry with New Insights into Anticancer Activity. *Molecules* 2025, 30, 1-34, doi:10.3390/molecules30102245.
2. Astanakulova Gulsanam; Buronov Anvarjon. Rational targeting of protein kinases in pediatric leukemia: mechanisms, pathogenesis and inhibitory potential of thieno[3,2-d]pyrimidine derivatives. *Development of science* 2026, 2, 128-132.
3. Ruzi, Z.; Buronov, A.; Nie, L.; Nasrullaev, A.; Murtazaeva, Z.; Kuryazov, R.; Zhao, J.; Efferth, T.; Aisa, H.A.; Bozorov, K. Scaffold-hopping design and synthesis of thieno[3,2-d]pyrimidines: Anticancer activity, apoptosis induction, and in silico inhibition of CDKs. *International Journal of Molecular Sciences* 2025, 26, 1-29, doi:10.3390/ijms26178528.
4. A.Buronov; A.Nasrullaev; N.Lifei; Kh.Bozorov; H.A.Aisa. Synthesis of novel tetracyclic thieno[3,2-d]pyrimidinones Samarkand state university - scientific journal 2025, 1, 5-11, doi:10.59251/2181-1296.2025.v1.149.2.3206.
5. Rakhimov Khafizjon; Anvarjon., B. Design and evaluation of thieno[3,2-d]pyrimidinone-based cdk inhibitors. *Development of science* 2026, 2, 133-138.
6. Anvarjon Buronov; Azizbek Nasrullaev; Nie Lifei; Khurshed Bozorov; Aisa, H.A. Synthesis of (E)-5-(3,4-dimethoxybenzylidene)-3-methyl-6,7-dihydropyrrolo[1,2-a]thieno[3,2-d]pyrimidin-9(5H)-one. *Scientific bulletin of namangan state university* 2025, 6, 107-111.
7. Anvarjon Buronov; Azizbek Nasrullaev; Nie Lifei; Khurshed Bozorov; Haji Akber Aisa. Synthesis of (E)-5-(3,4-dimethoxybenzylidene)-3-methyl-6,7-dihydropyrrolo[1,2-a]thieno[3,2-d]pyrimidin-9(5H)-one O'zbekiston milliy universiteti xabarlari 2025, 1, 253-256, doi:https://doi.org/10.69617/nuuz.v3i3.1.7512.
8. A.Buronov; A.Nasrullaev; N.Lifei; Kh.Bozorov; H.A.Aisa. New tetracyclic thieno[3,2-d]pyrimidine scaffold derivatives synthesized and aminated Samarkand state university - scientific journal 2025, 1, 12-17, doi:10.59251/2181-1296.2025.v1.149.2.3208.