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SYNTHESIS OF NEW CONDENSED DERIVATIVES OF THIENO[3,2-*d*]PYRIMIDINES BASED ON 7,7-DIMETHYL-2-MERCAPTO-4-(2-FURYL)-3-CYANO-7,8-DIHYDRO-5*H*-PYRANO[4,3-*b*]PYRIDINE

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Methods for the synthesis of new condensed thieno[3,2-*e*]pyridines and thieno[3,2-*d*]pyrimidines have been developed. The reaction of 7,7-dimethyl-2-mercapto-4-(2-furyl)-3-cyano-7,8-dihydro-5*H*-pyrano[4,3-*b*]pyridine with chloroacetic acid amides has been established depending on temperature. It has been shown that at high temperatures alkylation and intramolecular cyclization (*one pot* reaction) occur with the formation of pyrano[4,3-*b*]thieno[3,2-*e*]pyridines. New derivatives of condensed tetracyclic thieno[3,2-*d*]pyrimidines were synthesized by condensation of pyrano[4,3-b]thieno[3,2-*e*]pyridine carboxamides with orthoformic acid triethyl ester.

Keywords: alkylation, one pot reaction, thieno[3,2-e]pyridine, thieno[3,2-d]pyrimidine
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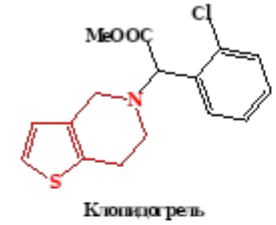
INTRODUCTION

In the arsenal of widely used drugs, a special place is occupied by compounds containing a pyridine or pyrimidine ring [1]. Condensed pyridine- or pyrimidine-containing systems have proven to be the most interesting in terms of their biological activity compared to monocyclic compounds. A special place among them is occupied by derivatives of thienopyridines and thienopyrimidines, and the most studied are the chemical and biological properties of thieno[2,3-*b*Oxidative stress is involved in the pathogenesis of many diseases (metabolic, oncological, neurodegenerative, mental, inflammatory). Oxidative stress leads to dysbiosis, changes in the composition of the microbiota, especially the intestinal microbiota [2]. Commensal bacteria of the intestinal microbiota, predominantly lactobacilli, have antioxidant (AO) defense systems, including mechanisms for ROS inactivation and repair of damaged molecules [3]. Lactobacilli are able to reduce the manifestations of oxidative stress in the macroorganism and *d* are used as pharmabiotics in the treatment of diseases caused by it [4-6]. However, the mechanisms that determine the response of lactobacilli cells to oxidative stress remain poorly understood. Such data are necessary for understanding the interaction of lactobacilli with the macroorganism and characterizing their probiotic properties. In addition, they are important for organizing the optimal production process of probiotic strains.
d]pyrimidines. The interest in these heterosystems is due to their great practical significance, since many of their derivatives exhibit a wide range of biological activity, including antioxidant, anti-inflammatory [2, 3], antibacterial, antitumor [4–6], etc. Moreover, thienopyridine-based compounds play an important role as antiplatelet drugs, for example, the drug clopidogrel is used to prevent blood clots in patients suffering from acute coronary syndrome or at risk of stroke [7]. The drug relegolix (TAK-385) is a derivative of thieno[2,3-d]pyrimidine and the possibility of its use in the treatment of endometriosis and prostate carcinoma as a gonadotropin-releasing hormone (GnRHR) receptor antagonist is currently being studied [8]. In addition, pictilisib (GDC-0941), a derivative of thieno[3,2-d]pyrimidine, inhibits phosphatidylinositol-3-kinase (PI3K) and is used to treat advanced

forms of tumors [9]. Thieno[3,2-*d*]pyrimidine (the drug olmutinib) inhibits the epidermal growth factor receptor (EGFR) and is used in the treatment of lung cancer [10].



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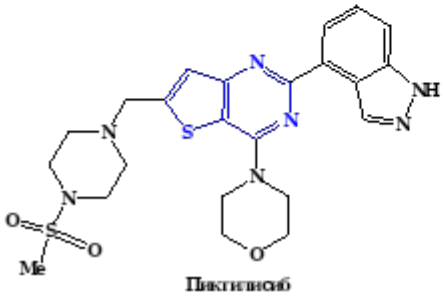

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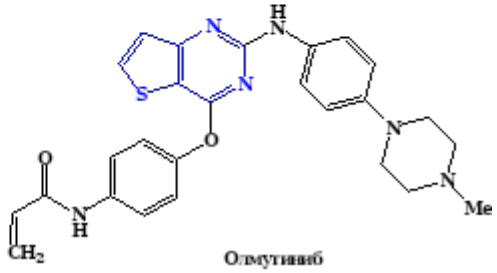


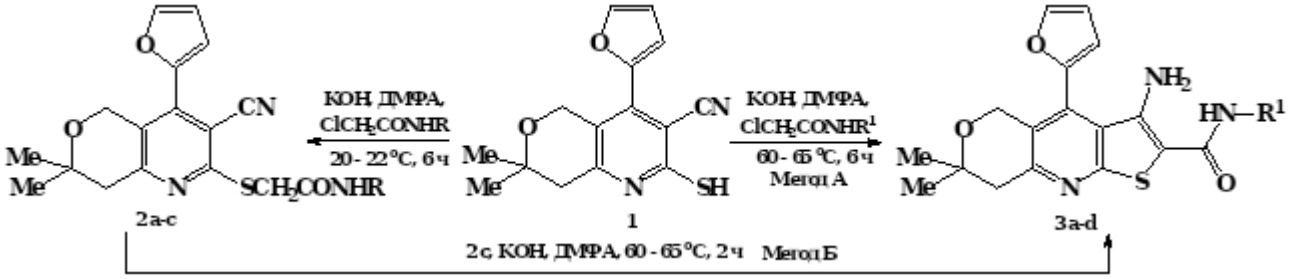
Олмутиниб

Based on the above, the work carried out on the synthesis of thienopyridines and thienopyrimidines is modern and interesting from the point of view of both chemistry and biology. Therefore, the purpose of this work was the synthesis of new derivatives of thienopyridines and thienopyrimidines, the development of optimal conditions for their production, as well as the study of the structure and purity of the final products obtained as a result of the reaction, using physicochemical methods.

RESULTS AND DISCUSSION

Taking into account the exceptional biological importance of thieno[2,3b *b* pyridines and thieno[3,2d *d* pyrimidines, their further study was carried out based on 7,7-dimethyl-2-mercapto-4-(2-furyl)-3-cyano-7,8-dihydro-5 *H* -pyrano[4,3b *b* pyridine (**1**) [11]. The study of the interaction of **1** with chloroacetic acid amides showed that, depending on the reaction conditions, various products can be obtained (Scheme 1). For example, stirring compound **1** with chloroacetic acid amides in DMF in the presence of potassium hydroxide at room temperature leads to alkylation with the formation of thioacetamides **2a–c** .

Scheme 1



2a–c : R = C_6H_4-4-Cl (**2a**); R = $CH(C_6H_5)_2$ (**2b**); R = C_6H_4-4-Me (**2c**); **3a–d:** R^1 = $CH_2C_6H_5$ (**3a**); R^1 = C_6H_4-3-Me (**3b**); R^1 = C_6H_4-3-Cl (**3c**); R^1 = C_6H_4-4-Me (**3d**).

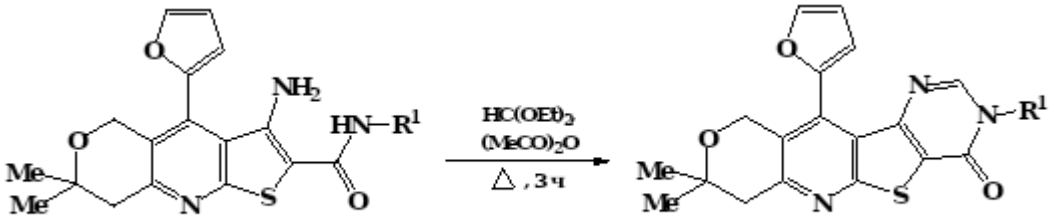
In the IR spectra of the latter, absorption bands of the CN group were present at 2216–2222 cm^{-1} . In the NMR ^1H spectrum, the signals of SCH_2 group protons were observed at 3.99–4.08 ppm, and in the NMR ^{13}C spectrum, the signals of the CN group were at 114.7 ppm. A different pattern was observed when the same reagents were heated at 60–65 °C for 6 h. The reaction was accompanied by alkylation of compound **1** and intramolecular cyclization (method A) with the formation of corresponding thieno[2,3-b *b*]pyridine derivatives **3a–d** . The proof that the synthesis

of cyclic products **3a–d** proceeds through the intermediate formation of corresponding alkylated products was the synthesis of cyclic product **3d** from the alkylated derivative **2c** when heated in a mixture with DMF and KOH for 2 h (method B) (scheme 1).

In the IR spectra of compounds **3a–d** , absorption bands of NH_2 groups were present at 3311–3479 cm^{-1} and absorption bands characteristic of CN groups were absent. In the NMR ^1H spectra of compounds **3a–d** , broadened signals of NH_2 group protons were observed at 5.97–6.15 ppm.

The thienopyridines **3a–d** obtained in this way were introduced into a condensation reaction with triethyl orthoformate in the presence of acetic anhydride to form thieno[3,2-d *d*]pyrimidines **4a–d** (scheme 2).

Scheme 2



3a-d 4a-d

3a–d , **4a–d** : $R^1 = CH_2C_6H_5$ (**3a** , **4a**); $R^1 = C_6H_4$-3-Me (**3b** , **4b**); $R^1 = C_6H_4$-3-Cl (**3c** , **4c**); $R^1 = C_6H_4$-4-Me (**3d** , **4d**).

In the NMR ^1H spectra of compounds **4a–d** , signals of CH groups of pyrimidine cycles were present at 8.12–8.43 ppm, and signals of NH_2 group protons were absent.

EXPERIMENTAL PART

The work used commercial reagents from "Fluka" (Germany), "Aldrich", "Sigma" (USA). IR spectra were recorded on a NicoletAvatar 330 FT-IR spectrometer (USA) in mineral oil. NMR spectra ^1H and ^{13}C (δ, ppm; coupling constant *J* , Hz) were recorded on a Mercury 300 Vx instrument (USA) with a frequency of 300 and 75.462 MHz, respectively, internal standard - TMS. The DEPT method was used for signal assignment in NMR spectra ^1H and ^{13}C. Mass spectra were recorded on a QTof XEVO G3 spectrometer (Milford, Massachusetts). Elemental analysis was performed on an Elemental Analyzer Euro EA 3000 (Germany). Melting points were determined on a Boetius microheating table (Germany).

Acetamides 2a–c. *General procedure.* A mixture of 2.9 g (0.01 mol) of compound **1,** KOH solution, prepared by dissolving 0.56 g (0.01 mol) of KOH in 5 ml of water, and 20 ml of absolute DMF was stirred at room temperature for 15 min. Then 0.01 mol of the corresponding halide was added and stirring was continued for 6 h at room temperature. The precipitated crystals were filtered, washed with water, ether, and recrystallized from ethanol.

IR spectrum of compounds **2a–c** , ν, cm^{-1} : 1648–1653 (C=O), 2216–2222 (CN), 3235–3250 (NH).

***N* -(4-Chlorophenyl)-2-{[3-cyano-4-(2-furyl)-7,7-dimethyl-7,8-dihydro-5 *H* -pyrano[4,3b *b* pyridin-2-yl]thio}acetamide (2a)** . Taken 2.0 g (0.01 mol) of 2-chloroN *N* -(4-chlorophenyl)acetamide. Yield 3.3 g (72%), cream crystals, m.p. 208–209 °C. NMR spectrum ^1H (DMSOd *d* $_6$-CCl_4, 1:3), δ, ppm: 1.26 s (6H, $C(CH_3)_2$), 2.81 br.s (2H, 8-CH_2), 4.08 s (2H, SCH_2), 4.76 br.s (2H, 5-CH_2), 6.70 d.d (1H, CH_{furyl}, *J* 3.6, 1.8 Hz), 7.18 d.d (1H, CH_{furyl}, *J* 3.6, 0.6 Hz), 7.19–7.25 m (2H, $2CH_{Ar}$), 7.56–7.62 m (2H, $2CH_{Ar}$), 7.83 d.d (1H, CH_{furyl}, *J* 1.8, 0.6 Hz), 10.10 br.s (1H, NH). NMR spectrum ^{13}C (DMSOd *d* $_6$-CCl_4, 1:3), δ_c, ppm: 25.9 ($C(CH_3)_2$), 34.5 (SCH_2), 43.0 (8-CH_2), 60.2 (5-CH_2), 70.0 (C^7), 100.4 (C^3), 111.8 (CH_{furyl}), 114.7 (CN), 115.2 (CH_{furyl}), 120.2 ($2CH_{Ar}$), 122.2 (C), 127.0 (C), 127.9 ($2CH_{Ar}$), 136.8 (C), 137.5 (C), 144.8 (CH

furyl), 145.8 (C), 157.1 (C), 160.0 (C), 165.2 (CO). Found, %: C 60.91; H 4.50; N 9.28; S 7.02. C 23 H 20 ClN 3 O 3 S. Calculated, %: C 60.85; H 4.44; N 9.26; S 7.06.

2-{[3-Cyano-4-(2-furyl)-7,7-dimethyl-7,8-dihydro-5 *H* -pyrano[4,3b *b* pyridin-2-yl]thio}N *N* -(diphenylmethyl)acetamide (2b). Taken 2.6 g (0.01 mol) of 2-chloroN -(diphenylmethyl)acetamide. Yield 3.7 g (73%), yellow crystals, m.p. 164–165 °C. NMR spectrum 1 H (DMSOd - 6 -CCl 4, 1:3), δ, ppm: 1.22 s (6H, C(CH 3) 2), 2.61 br.s (2H, 8-CH 2), 3.99 s (2H, SCH 2), 4.74 br.s (2H, 5-CH 2), 6.13 d (1H, NH *CH* , *J* 8.5 Hz), 6.70 dd (1H, CH furyl , *J* 3.6, 1.8 Hz), 7.17 dd (1H, CH furyl , *J* 3.6, 0.6 Hz), 7.19–7.31 m (10H, 10CH Ar), 7.83 dd (1H, CH furyl , *J* 1.8, 0.6 Hz), 8.73 br.d (1H, *NH* CH, *J* 8.5, 0.6 Hz). NMR spectrum 13 C (DMSOd - 6 -CCl 4, 1:3), δ C , ppm: 25.9 (C(*C* H 3) 2), 33.5 (SCH 2), 42.8 (8-CH 2), 55.0 (NHCH), 60.1 (5-CH 2), 69.9 (C 7), 100.5 (C 3), 111.1 (CH furyl), 114.7 (CN), 115.2 (CH furyl), 122.1 (C), 126.4 (2CH Ar), 127.1 (4CH Ar), 127.7 (4CH Ar), 136.7 (C), 141.8 (2C), 144.7 (CH furyl), 145.8 (C), 157.2 (C), 160.2 (C), 165.6 (CO). Found, %: C 70.65; H 5.38; N 8.27; S 6.27. C 30 H 27 N 3 O 3 S. Calculated, %: C 70.70; H 5.34; N 8.25; S 6.29.

2-{[3-Cyano-4-(2-furyl)-7,7-dimethyl-7,8-dihydro-5 *H* -pyrano[4,3b *b*]pyridin-2-yl]thio}N *N* -(4-methyl)acetamide (2c) . Taken 1.8 g (0.01 mol) of 2-chloroN *N* -(4-methylphenyl)acetamide. Yield 3.1 g (71%), cream crystals, m.p. 192–193 °C. NMR spectrum 1 H (DMSOd *d* 6 –CCl 4, 1:3), δ, ppm: 1.27 s (6H, C(CH 3) 2), 2.30 s (3H, CH 3), 2.83 br.s (2H, 8-CH 2), 4.07 s (2H, SCH 2), 4.76 br.s (2H, 5-CH 2), 6.69 d.d (1H, CH furyl , *J* 3.5, 1.8 Hz), 7.00–7.05 m (2H, 2CH Ar), 7.18 br.d (1H, CH furyl , *J* 3.5 Hz), 7.40–7.45 m (2H, 2CH Ar), 7.83 br.s (1H, CH furyl), 9.83 br.s (1H, NH). NMR spectrum 13 C (DMSOd *d* 6 –CCl 4, 1:3), δ c , ppm: 20.3 (CH 3), 25.9 (C(*C* H 3) 2), 34.4 (SCH 2), 43.0 (8-CH 2), 60.2 (5-CH 2), 70.0 (C 7), 95.5 (C 3), 111.8 (CH furyl), 114.7 (CN), 115.2 (CH furyl), 118.9 (2CH Ar), 122.2 (C), 128.4 (2CH Ar), 131.6 (C), 136.2 (C), 136.8 (C), 144.7 (CH furyl), 145.8 (C), 157.1 (C), 160.1 (C), 160.9 (C), 164.8 (CO). Mass spectrum (TOF MS ES+[MH] +): *m/z* 434.1538 calculated for C 24 H 23 N 3 O 3 S 434.1538. Found, %: C 66.52; H 5.39; N 9.61; S 7.42. C 24 H 23 N 3 O 3 S. Calculated, %: C 66.49; H 5.35; N 9.69; S 7.40

Thieno[3,2e *e*]pyridines 3a–d. *General procedure* (method A). The mixture of 2.9 g (0.01 mol) of compound **1,** KOH solution obtained by dissolving 0.56 g (0.01 mol) of KOH in 5 ml of water and 30 ml of absolute DMF was stirred at room temperature for 10 min. Then 0.01 mol of the corresponding halide was added and stirring was continued for 6 h at 60–65°C. The precipitated crystals were filtered off, washed with water, and recrystallized from ethanol.

IR spectrum of compounds **3a–d** , ν, cm $^{-1}$: 1629–1649 (C=O), 3311–3479 (NH, NH 2).

3-AminoN *N* -benzyl-4-(2-furyl)-7,7-dimethyl-7,8-dihydro-5 *H* -pyrano[4,3-b *b*]thieno[3,2-e *e*]pyridine-2-carboxamide (3a) . Taken 1.8 g (0.01 mol) *N-benzyl-2-chloroacetamide.* Yield 3.0 g (69%), cream crystals, m.p. 204–205°C. NMR spectrum 1 H (DMSO-d *d* 6 -CCl 4, 1:3), δ, ppm: 1.31 s (6H, C(CH 3) 2), 2.94 br.s (2H, 8-CH 2), 4.44 d (2H, NH *CH* 2 , *J* 6.0 Hz), 4.59 br.s (2H, 5-CH 2), 5.97 br.s (2H, NH 2), 6.67–6.72 m (2H, CH furyl), 7.15–7.34 m (5H, 5CH Ar), 7.81 d.d (1H, CH furyl , *J* 1.8, 0.7 Hz), 8.00 br.t (1H, NH, *J* 6.0 Hz). NMR spectrum 13 C (DMSO-d *d* 6 -CCl 4, 1:3), δ c , ppm: 26.1 (C(*C* H 3) 2), 42.2 (8-CH 2), 42.8 (NHCH 2), 60.0 (5-CH 2), 70.4 (C 7), 99.1 (C), 111.0 (CH furyl), 111.9 (CH furyl), 121.4 (C), 125.0 (C), 126.0 (CH Ar), 127.1 (2CH Ar), 127.5 (2CH Ar), 129.8 (C), 139.6 (C), 143.7 (CH furyl), 144.7 (C), 144.8 (C), 153.7 (C), 157.5 (C), 164.5 (C). Mass spectrum (TOF MS ES + +[MH] +): *m/z* 434.1545 calculated for C 24 H 23 N 3 O 3 S 434.1538. Found, %: C 66.53; H 5.40; N 9.62; S 7.43. C 24 H 23 N 3 O 3 S. Calculated, %: C 66.49; H 5.35; N 9.69; S 7.40.

3-Amino-4-(2-furyl)-7,7-dimethyl-N *N* -(3-methylphenyl)-7,8-dihydro-5 *H* -pyrano[4,3-b *b*]thieno[3,2-e *e*]pyridine-2-carboxamide (3b). Taken 1.8 g (0.01 mol) of *N* -(3-methylphenyl)glycyl chloride. Yield 2.9 g (68%), light yellow crystals, m.p. 215–216 °C. NMR spectrum 1 H (DMSOd *d* 6 –CCl 4, 1:3), δ, ppm: 1.32 s (6H, C(CH 3) 2), 2.35 s (3H, CH 3), 2.96 br.s (2H, 8-CH 2), 4.60 br.s (2H, 5-CH 2), 6.08 br.s (2H NH 2), 6.70 d.d (1H, CH furyl, *J* 3.3, 1.8 Hz),

6.75 br.d (1H, CH $_{furyl,}$ *J* 3.3 Hz), 6.82 br.d (1H, CH $_{Ar,}$ *J* 7.5 Hz), 7.12 d.d (1H, CH $_{Ar,}$ *J* 8.0, 7.5 Hz), 7.47 br.d (1H, CH $_{Ar,}$ *J* 8.0 Hz), 7.52 br.s (1H, CH $_{Ar}$), 7.83 br.d (1H, CH $_{furyl,}$ *J* 1.8 Hz), 9.05 br.s (1H, NH). NMR spectrum ^{13}C (DMSOd *d* $_6$–CCl $_4$, 1:3), δ $_c$, ppm: 21.0 (CH $_3$), 26.1 (C(*C* H $_3$) $_2$), 42.9 (8-CH $_2$), 60.0 (5-CH $_2$), 70.5 (C ^{7}), 98.9 (C), 111.1 (CH $_{furyl}$), 112.0 (CH $_{furyl}$), 117.9 (CH $_{Ar}$), 121.2 (C), 121.4 (CH $_{Ar}$), 123.5 (CH $_{Ar}$), 125.2 (C), 127.5 (CH $_{Ar}$), 130.0 (C), 136.8 (C), 138.5 (C), 143.9 (CH $_{furyl}$), 144.7 (C), 145.7 (C), 154.2 (C), 157.8 (C), 163.3 (C). Mass spectrum (TOF MS ES $^+$ [MH] $^+$): *m/z* 434.1545 calculated for C $_{24}$H $_{23}$N $_3$O $_3$S 434.1538. Found, %: C 66.52; H 5.39; N 9.73; S 7.44. C $_{24}$H $_{23}$N $_3$O $_3$S. Calculated, %: C 66.49; H 5.35; N 9.69; S 7.40.

3-Amino -*N* -(3-chlorophenyl)-4-(2-furyl)-7,7-dimethyl-7,8-dihydro-5 *H* -pyrano[4,3b *b*]thieno[3,2e *e*]pyridine-2-carboxamide (3c). Taken 2.0 g (0.01 mol) *N* -(3-chlorophenyl)chloride. Yield 3.2 g (70%), cream crystals, m.p. 220-221 °C. NMR spectrum ^{1}H (DMSOd *d* $_6$-CCl $_4$, 1:3), δ, ppm: 1.32 s (6H, C(CH $_3$) $_2$), 2.96 br.s (2H, 8-CH $_2$), 4.60 br.s (2H, 5-CH $_2$), 6.15 br.s (2H, NH $_2$), 6.71 d.d (1H, CH $_{furyl,}$ *J* 3.3, 1.9 Hz), 6.75 d.d (1H, CH $_{furyl,}$ *J* 3.3, 0.8 Hz), 6.99 d.d.d (1H, CH $_{Ar,}$ *J* 8.0, 2.1, 0.9 Hz), 7.22 d.d (1H, CH $_{Ar,}$ *J* 8.3, 8.0 Hz), 7.67 d.d.d (1H, CH $_{Ar,}$ *J* 8.3, 2.0, 0.9 Hz), 7.84 d.d (1H, CH $_{furyl,}$ *J* 1.9, 0.8 Hz), 7.87 t (1H, CH $_{Ar,}$ *J* 2.0 Hz), 9.37 br.s (1H, NH). NMR spectrum ^{13}C (DMSOd *d* $_6$-CCl $_4$, 1:3), δ $_c$, ppm: 26.1 (C(*C* H $_3$) $_2$), 42.9 (8-CH $_2$), 60.0 (5-CH $_2$), 70.5 (C ^{7}), 98.2 (C), 111.1 (CH $_{furyl}$), 112.1 (CH $_{furyl}$), 118.6 (CH $_{Ar}$), 120.3 (CH $_{Ar}$), 121.0 (C), 122.3 (CH $_{Ar}$), 125.3 (C), 128.8 (CH $_{Ar}$), 130.1 (C), 132.8 (C), 140.2 (C), 143.9 (CH $_{furyl}$), 144.6 (C), 146.3 (C), 154.5 (C), 157.9 (C), 163.6 (C). Found, %: C 60.90; H 4.47; N 9.33; S 7.12. C $_{23}$H $_{20}$ClN $_3$O $_3$S. Calculated, %: C 60.85; H 4.44; N 9.26; S 7.06.

3-Amino *4-(2-furyl)-7,7-dimethyl-* 4-(2-furyl)-7,7-dimethyl-*N* -(4-methylphenyl)-7,8-dihydro-5 *H* -pyrano[4,3b *b*]thieno[3,2e *e*]pyridine-2-carboxamide (3d) (method A) **.** Taken 1.8 g (0.01 mol) of 2-chloroN *N* (4-methylphenyl)acetamide. Yield 3.0 g (70%), cream crystals, m.p. 162-163°C. NMR spectrum ^{1}H (DMSOd *d* $_6$-CCl $_4$, 1:3), δ, ppm: 1.32 s (6H, C(CH $_3$) $_2$), 2.32 s (3H, CH $_3$), 2.96 br.s (2H, 8-CH $_2$), 4.60 br.s (2H, 5-CH $_2$), 6.08 br.s (2H, NH $_2$), 6.70 d.d (1H, CH $_{furyl,}$ *J* 3.3, 1.9 Hz), 6.74 br.d (1H, CH $_{furyl,}$ *J* 3.3 Hz), 7.02-7.07 m (2H, CH $_{Ar}$), 7.53-7.58 m (2H, CH $_{Ar}$), 7.83 br.d (1H, CH $_{furyl,}$ *J* 1.9 Hz), 9.07 br.s (1H, NH). NMR spectrum ^{13}C (DMSOd *d* $_6$-CCl $_4$, 1:3), δ $_C$, ppm: 20.3 (CH $_3$), 26.1 (C(*C* H $_3$) $_2$), 42.9 (8-CH $_2$), 60.0 (5-CH $_2$), 70.5 (C ^{7}), 98.9 (C), 111.1 (CH $_{furyl}$), 112.0 (CH $_{furyl}$), 120.8 (2CH $_{Ar}$), 121.2 (C), 125.2 (C), 128.1 (2CH $_{Ar}$), 129.9 (C), 131.7 (C), 136.0 (C), 143.8 (CH $_{furyl}$), 144.7 (C), 145.6 (C), 154.1 (C), 157.7 (C), 163.3 (C). Found, %: C 66.42; H 5.32; N 9.73; S 7.43. C $_{24}$H $_{23}$N $_3$O $_3$S. Calculated, %: C 66.49; H 5.35; N 9.69; S 7.40.

Synthesis of compound 3d by method B. A mixture of 4.3 g (0.01 mol) of compound **2c** , KOH solution, obtained by dissolving 0.28 g (0.005 mol) of KOH in 3.0 ml of water, in 20 ml of absolute DMF was stirred at 60-65°C for 2 h. The precipitated crystals were filtered, washed with water, recrystallized from ethanol. Yield 3.2 g (75%), the physicochemical characteristics coincide with those of compound **3d** , obtained by method A.

Thieno[3,2-d *d*]pyrimidine derivatives 4a-d . *General procedure.* A mixture of 0.01 mol of compound **3a–d** , 15 ml of triethyl orthoformate and 15 ml of acetic anhydride was refluxed for 3 h. The excess of solvents was distilled off, 10 ml of water was added to the residue, the precipitated crystals were filtered, washed with water, ether, and recrystallized from ethanol.

IR spectrum of compounds **4a–d** , ν, cm $^{-1}$: 1672–1684 (C=O), 1587–1594 (C=C $_{Ar}$).

3-Benzyl-11-(2-furyl)-8,8-dimethyl-7,10-dihydro-8 *H* -pyrano[3",4":5',6']pyrido [3',2':4,5]thieno[3,2d *d*]pyrimidin-4(3 *H*)-one (4a). Taken 1.8 g (0.01 mol) of compound **3a** . Yield 3.2 g (75%), cream crystals, m.p. 182–183°C. NMR spectrum ^{1}H (DMSOd *d* $_6$–CCl $_4$, 1:3), δ, ppm: 1.32 s (6H, C(CH $_3$) $_2$), 3.01 s (2H, 7-CH $_2$), 4.72 s (2H, 10-CH $_2$), 5.23 s (2H, NCH $_2$), 6.60 d.d (1H, CH $_{furyl,}$ *J* 3.3, 1.8 Hz), 6.72 d.d (1H, CH $_{furyl,}$ *J* 3.3, 0.8 Hz), 7.21–7.33 m (3H, 3CH $_{Ar}$), 7.38–7.43 m (2H, CH $_{Ar}$), 7.68 d.d (1H, CH $_{furyl,}$ *J* 1.8, 0.8 Hz), 8.43 s (1H, 2-CH). Found, %: C 67.69; H 4.78; N 9.42; S 7.33. C $_{25}$H $_{21}$N $_3$O $_3$S. Calculated, %: C 67.70; H 4.77; N 9.47; S 7.23.

11-(2-Furyl)-8,8-dimethyl-3-(3-methylphenyl)-7,10-dihydro-8 *H* -pyrano[3",4":5',6']pyrido[3',2':4,5]thieno[3,2d *d*]pyrimidin-4(3 *H*)-one (4b). Taken 1.8 g (0.01 mol) of compound **3b** . Yield 3.4 g (78%), light brown crystals, m.p. 175–176 °C. NMR spectrum ^{1}H (DMSOd d_6), δ, ppm: 1.34 s (6H, C(CH$_3$)$_2$), 2.44 s (3H, CH$_3$), 3.02 s (2H, 7-CH$_2$), 4.76 s (2H, 10-CH$_2$), 6.60 d.d (1H, CH$_{furyl,}$ *J* 3.3, 1.8 Hz), 6.76 br.d (1H, CH$_{furyl,}$ *J* 3.3 Hz), 7.23–7.31 m (3H, 3CH$_{Ar}$), 7.38–7.45 m (1H, CH$_{Ar}$), 7.68 br.d (1H, CH$_{furyl,}$ *J* 1.8 Hz), 8.13 s (1H, 2-CH). NMR spectrum ^{13}C (DMSOd d_6), δ$_c$, ppm: 20.7 (CH$_3$), 26.2 (C(*C*H$_3$)$_2$), 43.2 (7-CH$_2$), 60.4 (10-CH$_2$), 70.4 (C^8), 110.7 (CH$_{furyl}$), 113.1 (CH$_{furyl}$), 122.8 (C), 123.3 (C), 123.7 (CH$_{Ar}$), 125.9 (C), 127.2 (CH$_{Ar}$), 128.6 (CH$_{Ar}$), 129.2 (CH$_{Ar}$), 132.1 (C), 136.3 (C), 138.5 (C), 142.9 (CH$_{furyl}$), 144.8 (C), 147.0 (2-CH), 149.7 (C), 155.7 (C), 155.9 (C), 160.8 (CO). Mass spectrum (TOF MS ES$^+$[MH]$^+$): *m/z* 444.1386 calculated for C$_{25}$H$_{21}$N$_3$O$_3$S 444.1382. Found, %: C 67.75; H 4.71; N 9.44; S 7.30. C$_{25}$H$_{21}$N$_3$O$_3$S. Calculated, %: C 67.70; H 4.77; N 9.47; S 7.23.

3-(3-Chlorophenyl)-11-(2-furyl)-8,8-dimethyl-3-(3-methylphenyl)-7,10-dihydro-8 *H* -pyrano[3",4":5',6']pyrido[3',2':4,5]thieno[3,2d *d*]pyrimidin-4(3 *H*)-one (4c). Taken 2.0 g (0.01 mol) of compound **3c** . Yield 3.7 g (79%), cream crystals, m.p. 223–224 °C. NMR ^{1}H spectrum (DMSOd d_6–CCl$_4$, 1:3), δ, ppm: 1.34 s (6H, C(CH$_3$)$_2$), 3.02 s (2H, 7-CH$_2$), 4.76 s (2H, 10-CH$_2$), 6.61 d.d (1H, CH$_{furyl,}$ *J* 3.3, 1.8 Hz), 6.77 d.d (1H, CH$_{furyl,}$ *J* 3.3, 0.8 Hz), 7.43–7.60 m (4H, 4CH$_{Ar}$), 7.69 br.s (1H, CH$_{furyl}$), 8.18 s (1H, 2-CH). NMR ^{13}C spectrum (DMSOd d_6–CCl$_4$, 1:3), δ$_s$, ppm: 26.2 (C(*C*H$_3$)$_2$), 43.3 (7-CH$_2$), 60.4 (10-CH$_2$), 70.5 (C^8), 110.8 (CH$_{furyl}$), 113.3 (CH$_{furyl}$), 122.7 (C), 123.3 (C), 125.4 (CH$_{Ar}$), 126.0 (C), 127.1 (CH$_{Ar}$), 128.8 (CH$_{Ar}$), 130.2 (CH$_{Ar}$), 132.2 (C), 133.7 (C), 137.5 (C), 143.0 (CH$_{furyl}$), 144.8 (C), 146.8 (2-CH), 149.7 (C), 155.8 (C), 155.9 (C), 160.8 (CO). Mass spectrum (TOF MS ES$^+$[MH]$^+$): *m/z* 464.0843 calculated for C$_{24}$H$_{18}$ClN$_3$O$_3$S 464.0836. Found, %: C 62.09; H 3.95; N 9.11; S 6.95. C$_{24}$H$_{18}$ClN$_3$O$_3$S. Calculated, %: C 62.13; H 3.91; N 9.06; S 6.91.

11-(2-Phenyl)-8,8-dimethyl-3-(4-methylphenyl)-7,10-dihydro-8 *H* -pyrano[3",4":5',6']pyrido[3',2':4,5]thieno[3,2d *d*]pyrimidin-4(3 *H*)-one (4d) . Taken 1.8 g (0.01 mol) of compound **3d** . Yield 3.4 g (77%), cream crystals, m.p. 227–228 °C. NMR spectrum ^{1}H (DMSOd d_6–CCl$_4$, 1:3), δ, ppm: 1.35 s (6H, C(CH$_3$)$_2$), 2.45 s (3H, CH$_3$), 3.02 s (2H, 7-CH$_2$), 4.76 s (2H, 10-CH$_2$), 6.61 d.d (1H, CH$_{furyl,}$ *J* 3.3, 1.8 Hz), 6.77 br.d (1H, CH$_{furyl,}$ *J* 3.3 Hz), 7.34 s (4H, 4CH$_{Ar}$), 7.70 br.d (1H, CH$_{furyl,}$ *J* 1.8 Hz), 8.12 s (1H, 2-CH). NMR spectrum ^{13}C (DMSOd d_6–CCl$_4$, 1:3), δ$_c$, ppm: 20.6 (CH$_3$), 26.2 (C(*C*H$_3$)$_2$), 43.2 (7-CH$_2$), 60.4 (10-CH$_2$), 70.4 (C^8), 110.7 (CH$_{furyl}$), 113.1 (CH$_{furyl}$), 122.9 (C), 123.3 (C), 125.9 (C), 126.4 (2CH$_{Ar}$), 129.3 (2CH$_{Ar}$), 132.1 (C), 133.9 (C), 138.2 (C), 142.9 (CH$_{furyl}$), 144.8 (C), 147.0 (2-CH), 149.7 (C), 155.7 (C), 160.0 (C), 160.8 (CO). Mass spectrum (TOF MS ES$^+$[MH]$^+$): *m/z* 444.1388 calculated for C$_{25}$H$_{21}$N$_3$O$_3$S 444.1382. Found, %: C 67.75; H 4.71; N 9.45; S 7.30. C$_{25}$H$_{21}$N$_3$O$_3$S. Calculated, %: C 67.70; H 4.77; N 9.47; S 7.23.

CONCLUSION

Based on 7,7-dimethyl-2-mercapto-4-(2-furyl)-3-cyano-7,8-dihydro-5 *H* -pyrano[4,3b *b*]pyridine, a method for synthesizing new condensed thieno[3,2d *d*]pyridines and thieno[3,2d *d*]pyrimidines has been developed. It was found that the type of synthesis products depends on the reaction conditions, specifically at room temperature *S* -alkylated pyrano[4,3b *b*]pyridines are formed, while upon heating, pyrano[4,3b *b*]thieno[3,2e *e*]pyridines are formed as a result of intramolecular cyclization. The synthesis of new derivatives of condensed thieno[3,2d *d*]pyrimidines was also carried out by condensation of the corresponding thienopyridines with triethyl orthoformate.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Chiacchio M. A., Iannazzo D., Romeo R., Giofrè S. V., Legnani, L. *Curr. Med. Chem.* , **2019** , *26* (40), 7166 – 7195. doi 10.2174/0929867325666180904125400
2. El-Mekabaty A., Fouda A.E.A.S., Shaaban I.E. *J. Heterocycl. Chem.* , **2020** , *57* (7), 2928 – 2935. doi 10.1002/jhet.4002
3. Zaki R.M., Kamal El-Dean A.M., Radwan S.M., Ammar M.A. *Russ. J. Bioorg. Chem.* , **2022** , *48* (Suppl 1), S121 – S135. doi 10.1134/S1068162023010314
4. Alenazi N.A., Alharbi H., Qarah A.F., Alsoliemy A., Abualnaja M.M., Karkashan A., Abbas B., El-Metwaly N.M. *Arab. J. Chem.* , **2023** , *16* (11), 105226. doi 10.1016/j.arabjc.2023.105226
5. Mohi El-Deen E.M., El-Gwaad A., Amina A., Anwar M.M. *Egypt. J. Chem.* , **2023** , *66* (2), 231 – 242. doi 10.21608/EJCHEM.2022.136967.6042
6. Saber A.F., Kamal El-Dean A.M., Redwan S.M., Zaki R.M. *J. Chinese Chem. Soc.* , **2020** , *67* (7), 1239 – 1246. doi 10.1002/jccs.201900374
7. Binsaleh N.K., Wigley C.A., Whitehead K.A., van Rensburg M., Reynisson J., Pilkington L.I., Barker D., Jones S., Dempsey-Hibbert N.C. *Eur. J. Med. Chem.* , **2018** , *143* , 1997 – 2004. doi 10.1016/j.ejmech.2017.11.014
8. Liu Y.F., Fu S.Q., Yan Y.C., Gong B.B., Xie W.J., Yang X.R., Sun T., Ma M. *Drug Des. Devel. Ther.* **2021** , *15* , 639–649. doi 10.2147/DDDT.S291369
9. Sarker D., Ang J.E., Baird R., Kristeleit R., Shah K., Moreno V., Clarke P.A., Raynaud F.I., Levy G., Ware J.A., Mazina K., Lin R., Wu J., Fredrickson J., Spoerke J.M., Lackner M.R., Yan Y., Friedman L.S., Kaye S.B., Derynck M.K., Workman P., de Bonoet J.S. *Clin. Cancer Res.* **2015** , 21, 77–86. doi 10.1158/1078-0432.CCR-14-0947
10. Kim D.W., Lee D.H., Han J.Y., Lee J., Cho B.C., Kang J.H., Lee K. H., Cho E. K., Kim J.-S., Min Y. J., Cho J.Y., An H.J., Kim H.-G., Lee K.H., Kim B.-S., Jang I.-J., Yoon S., Han O.P., Noh Y.S., Hong K.Y., Park K. *Lung Cancer* . **2019** , *135* , 66–72. doi 10.1016/j.lungcan.2019.07.007
11. Dabaeva V.V., Bagdasaryan M.R., Barkhudaryants I.M., Paronikyan E.G., Panosyan G.A., Dashyan Sh.Sh. *Russ. J. Gen. Chem* ., **2022** , *92* , 1686–1691. doi: 10.1134/S1070363222090109

Graphical abstract: