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# SYNTHESIS AND THE ANTIMICROBIAL ACTIVITY OF 1-ALKYL-5-METHYL-3-PHENYL-6-(5-PHENYL-1,3,4-OXADIAZOL-2-YL) THIENO[2,3-*d*]PYRIMIDINE-2,4(1*H*,3*H*)-DIONES

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*Key words: thiophene; pyrimidine; alkylation*

*An effective approach for synthesis of 5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-d]pyrimidine-2,4(1H,3H)-dione by 1,1'-carbonyldiimidazole promoted interaction of 5-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidine-6-carboxylic acid with benzohydrazide has been developed. The procedure also includes cyclization of N'-benzoyl-5-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidine-6-carbohydrazide obtained by boiling in phosphorous oxychloride and further hydrolysis of the chlorine atom at position 2 of the thieno[2,3-d]pyrimidine system. Alkylation of the assembly of two heterocyclic units obtained with benzyl chlorides, chloroacetamides, and 5-(chloromethyl)-3-aryl-1,2,4-oxadiazoles has allowed obtaining of 1-alkyl-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-d]pyrimidine-2,4(1H,3H)-diones. The structures of the compounds obtained have been confirmed by the $^1$H NMR, chromato-mass spectral and elemental microanalysis data. The results of the screening performed by the agar diffusion method ("well method") have shown the absence of the antimicrobial activity for 1-benzyl-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl) thieno[2,3-d]pyrimidine-2,4(1H,3H)-diones and 2-[5-methyl-2,4-dioxo-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)-3,4-dihydrothieno[2,3-d]pyrimidin-1(2H)-yl]-N-arylacetamides; but the activity for 1-{[3-aryl-1,2,4-oxadiazol-5-yl] methyl}-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-d]pyrimidine-2,4(1H,3H)-diones has been found. The compounds of this range appeared to be active against the strains of Staphylococcus aureus, Escherichia coli and Bacillus subtilis; the diameters of their growth inhibition zones were similar to those for the reference drugs Metronidazole and Streptomycin.*

***СИНТЕЗ ТА АНТИМІКРОБНА АКТИВНІСТЬ 1-АЛКІЛ-5-МЕТИЛ-3-ФЕНІЛ-6-(5-ФЕНІЛ-1,3,4-ОКСАДІАЗОЛ-2-ІЛ)ТІЄНО[2,3-d]ПІРИМІДИН-2,4(1H,3H)-ДІОНІВ***
***С.В.Власов, Т.П.Осолодченко, С.М.Коваленко, В.П.Черних***
***Ключові слова:*** *тіофен; піримідин; алкілювання*
*Розроблено ефективний підхід до синтезу 5-метил-3-феніл-6-(5-феніл-1,3,4-оксадіазол-2-іл)тієно[2,3-d] піримідин-2,4(1H,3H)-діону шляхом промотованої 1,1'-карбонілдіімідазолом взаємодії 5-метил-2,4-діоксо-3-феніл-1,2,3,4-тетрагідротієно[2,3-d]піримідин-6-карбонової кислоти з бензогідразидом. Процедура також включає наступну циклізацію отриманого N'-бензоїл-5-метил-2,4-діоксо-3-феніл-1,2,3,4-тетрагідротієно[2,3-d]піримідин-6-карбогідразиду кип'ятінням у хлорокисі фосфору та подальший гідроліз атома хлору у положенні 2 тієно[2,3-d]піримідинової системи. Алкілювання отриманого дволанкового ансамблю гетероциклів бензилхлоридами, хлороацетамідами та 5-(хлорометил)-3-арил-1,2,4-оксадіазолами дозволило отримати 1-алкіл-5-метил-3-феніл-6-(5-феніл-1,3,4-оксадіазол-2-іл)тієно[2,3-d]піримідин-2,4(1H,3H)-діони. Структури отриманих сполук були підтверджені на основі даних $^1$H ЯМР, хромато-мас спектрів та елементного аналізу. За результатами скринінгу методом дифузії в агар («метод колодязів») встановлено відсутність антимікробної активності у 1-бензил-5-метил-3-феніл-6-(5-феніл-1,3,4-оксадіазол-2-іл)тієно[2,3-d]піримідин-2,4(1H,3H)-діонів та 2-[5-метил-2,4-діоксо-3-феніл-6-(5-феніл-1,3,4-оксадіазол-2-іл)-3,4-дигідротієно[2,3-d]піримідин-1(2H)-іл]-N-арилацетамідів, а також наявність антимікробної активності для 1-{[3-арил-1,2,4-оксадіазол-5-іл]метил}-5-метил-3-феніл-6-(5-феніл-1,3,4-оксадіазол-2-іл)тієно[2,3-d]піримідин-2,4(1H,3H)-діонів. Дані речовини виявили антимікробну активність до штамів Staphylococcus aureus, Escherichia coli та Bacillus subtilis із значеннями зон затримки росту, близькими до препаратів порівняння метронідазолу та стрептоміцину.*

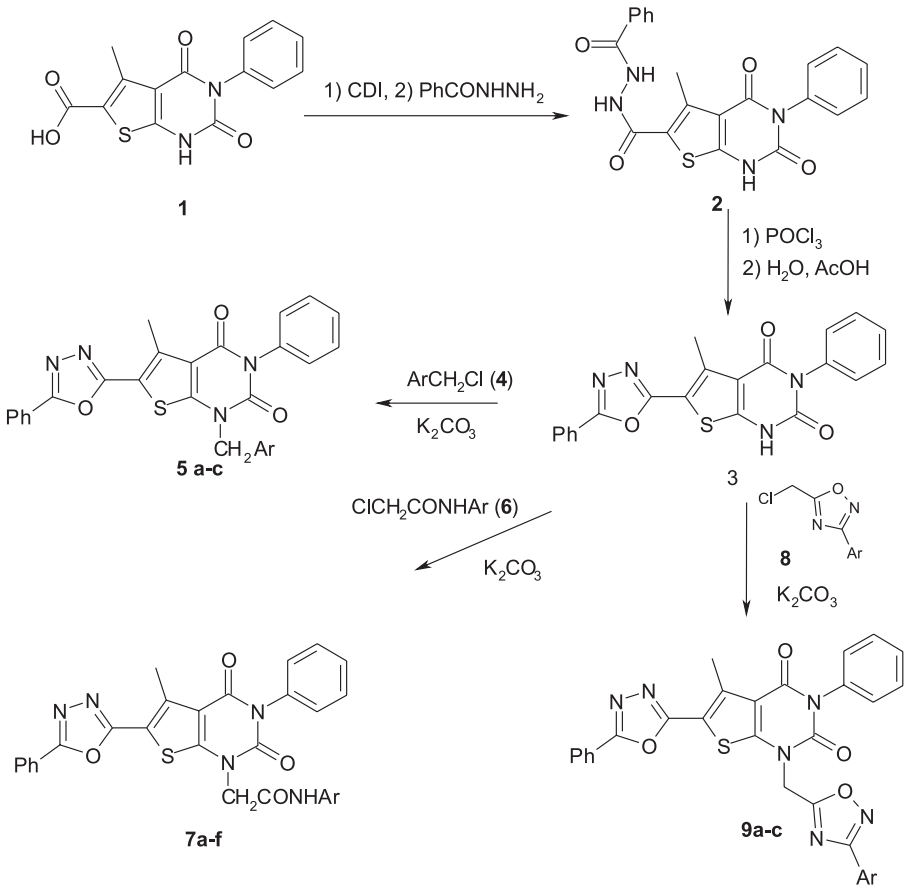
***СИНТЕЗ И ПРОТИВОМИКРОБНАЯ АКТИВНОСТЬ 1-АЛКИЛ-5-МЕТИЛ-3-ФЕНИЛ-6-(5-ФЕНИЛ-1,3,4-ОКСАДИАЗОЛ-2-ИЛ)ТИЕНО[2,3-d]ПИРИМИДИН-2,4(1H,3H)-ДИОНОВ***
***С.В.Власов, Т.П.Осолодченко, С.Н.Коваленко, В.П.Черных***
***Ключевые слова:*** *тиофен; пиримидин; алкилирование*
*Разработан эффективный подход к синтезу 5-метил-3-фенил-6-(5-фенил-1,3,4-оксадиазол-2-ил)тиено [2,3-d]пиримидин-2,4(1H,3H)-диона путем промотированного 1,1'-карбонилдиимидазолом взаимодействия 5-метил-2,4-диоксо-3-фенил-1,2,3,4-тетрагидротиено[2,3-d]пиримидин-6-карбоновой кислоты с бензогидразидом. Процедура также включает циклизацию полученного N'-бензоил-5-метил-2,4-диоксо-3-фенил-1,2,3,4-тетрагидротиено[2,3-d]пиримидин-6-карбогидразида кипячением в хлорокиси фосфора и дальнейший гидролиз атома хлора в положении 2 тиено[2,3-d]пиримидиновой системы. Алкилирование полученного двухзвенного ансамбля гетероциклов бензилхлоридами, хлорацетамидами и 5-(хлорметил)-3-арил-1,2,4-оксадиазолами позволило получить 1-алкил-5-метил-3-фенил-6-(5-фенил-1,3,4-оксадиазол-2-ил)тиено[2,3-d]пиримидин-2,4(1H,3H)-дионы. Структуры полученных соединений были подтверждены на основе данных $^1$H ЯМР, хромато-мас спектров и элементного анализа. По резуль-*

*татам скрининга методом диффузии в агар («метод колодцев») установлено отсутствие противомикробной активности у 1-бензил-5-метил-3-фенил-6-(5-фенил-1,3,4-оксадиазол-2-ил)тиено[2,3-d]пиримидин-2,4(1H,3H)-дионов и 2-[5-метил-2,4-диоксо-3-фенил-6-(5-фенил-1,3,4-оксадиазол-2-ил)-3,4-дигидротиено[2,3-d]пиримидин-1(2H)-ил]-N-арилацетамидов, а также наличие противомикробной активности для 1-{[3-арил-1,2,4-оксадиазол-5-ил]метил}-5-метил-3-фенил-6-(5-фенил-1,3,4-оксадиазол-2-ил) тиено[2,3-d]пиримидин-2,4(1H,3H)-дионов. Данные вещества проявили противомикробную активность к штаммам Staphylococcus aureus, Escherichia coli и Bacillus subtilis со значениями зон задержки роста, близкими к препаратам сравнения метронидазолу и стрептомицину.*

In the last years the modification of position 6 of the thieno[2,3-*d*]pyrimidine system with 1,3,4-oxadiazole substituents has become popular as the way for obtaining of the novel biologically active compounds. The first attempt of such synthesis was cyclization of thieno[2,3-*d*]pyrimidin-6-carboxylic acids hydrazides with orthoesters [1], or by cyclization using treatment with phosphorous oxychloride of the products of similar hydrazides acylation with acyl halides [2]. The authors of the article [3] also proposed application of the *one-pot* method where the corresponding hydrazide reacts with thieno[2,3-*d*]pyrimidin-6-carboxylic acid right in the $POCl_3$ media. Recently we have reported the approach using generated *in situ* imidazolide of thieno[2,3-*d*]pyrimidin-6-carboxylic acid for the reaction with benzohydrazide suitable for preparation of the product, which after cyclization in phosphorous oxychloride allows forming the 1,3,4-oxadiazole cycle in position 6 of thieno[2,3-*d*]pyrimidine [4]. Our previous data also reported about some derivatives of thieno[2,3-*d*]pyrimidine ranges modified at position 6 with azole heterocyles as the compounds with the promising antimicrobial activity [2, 4, 5, 6].

In view of such biological activity potential of 5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl) thieno[2,3-*d]*pyrimidine-2,4(1*H*,3*H*)-diones and in order to investigate the scope of the method previously proposed for modification of thieno[2,3-*d*]pyrimidine position 6 with 1,3,4-oxadiazole we have performed the interaction of 5-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidine-6-carboxylic acid [6, 7] imidazolide with benzohydrazide.

As the result of our experiment *N*'-benzoyl-5-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydrothieno [2,3-*d*]pyrimidine-6-carbohydrazide **2** was isolated; its further cyclization was performed by heating in phosphorous oxychloride (Scheme). The 2-chlorointermediate obtained was hydrolyzed to 5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno [2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione **3** by heating in the water-acetic acid medium after the continuous heating.




Scheme

**Table 1**

Physico-chemical properties of 1-alkyl-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **5**, **7** and **9**

| Compd No. | Ar | Mol. formula M.w. | Yield %, in the alkylation step | M.p., °C | N% calc./found |
|---|---|---|---|---|---|
| 5a | $C_6H_5$ | $C_{28}H_{20}N_4O_3S$ 492.56 | 87 | 295-297 | 11.37/11.56 |
| 5b | $C_6H_4$-4-$CH_3$ | $C_{29}H_{22}N_4O_3S$ 506.59 | 85 | 290-291 | 11.06/11.13 |
| 5c | $C_6H_3$-3,4-diF | $C_{28}H_{18}F_2N_4O_3S$ 528.54 | 83 | 266-267 | 10.60/10.79 |
| 7a | $C_6H_5$ | $C_{29}H_{21}N_5O_4S$ 535.59 | 76 | >300 | 13.08/13.20 |
| 7b | $C_6H_4$-4-$CH_3$ | $C_{30}H_{23}N_5O_4S$ 549.61 | 83 | >300 | 12.74/12.79 |
| 7c | $C_6H_4$-4-i-Pr | $C_{32}H_{27}N_5O_4S$ 577.67 | 79 | >300 | 12.12/12.34 |
| 7d | $C_6H_3$-3,4-diOMe | $C_{31}H_{25}N_5O_6S$ 595.64 | 68 | >300 | 11.76/11.81 |
| 7e | $C_6H_4$-4-OEt | $C_{31}H_{25}N_5O_5S$ 579.64 | 85 | >300 | 12.08/12.25 |
| 7f | $C_6H_3$-4-Me-2-Cl | $C_{30}H_{22}ClN_5O_4S$ 584.06 | 92 | 297-298 | 11.99/12.03 |
| 9a | $C_6H_4$-4-$CH_3$ | $C_{31}H_{22}N_6O_4S$ 574.62 | 63 | 272-273 | 14.63/14.79 |
| 9b | $C_6H_4$-2-Cl | $C_{30}H_{19}ClN_6O_4S$ 595.04 | 68 | 215-217 | 14.12/14.37 |
| 9c | $C_6H_4$-4-Cl | $C_{30}H_{19}ClN_6O_4S$ 595.04 | 59 | 281-283 | 14.12/14.30 |

The further modification of product **3** was performed by its alkylation with benzyl chlorides **4**, chloroacetamides **6** and 5-(chloromethyl)-3-aryl-1,2,4-oxadiazoles **8**; using this versatile synthetic procedure 1-alkyl-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **5,7,9** were obtained. All of the final products were isolated as crystalline substances with high melting points (Tab. 1).

The structures of all of the compounds obtained were confirmed by the data of $^1$H NMR spectroscopy and elemental analysis. In all spectra of 1-alkyl-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl) thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **5,7,9** obtained (Tab. 2) the signals of the methyl group protons at the thiophene ring are observed in the range of 2.82-2.87 ppm. The signals of the methylene group protons are located for compounds **5** at 5.21-5.26 ppm, while for the derivatives of acetamides **7** at 4.85-4.96 ppm; such location of these signals well correlate with the previously reported data [6, 8, 9] confirming the alkylation of the nitrogen atom at position 1, but not the oxygen attached at position 2. For compounds **9** of the (3-phenyl-1,2,4-oxadiazol-5-yl)methylene range the signal of the methylene group is observed at 5.68-5.74 ppm. All of the spectra of compounds **7** contain the signal of the NH fragment in the range from 10.05 to 10.47 ppm.

The antimicrobial activity of the compounds obtained was evaluated by the agar diffusion screening method ("well method") [10, 11]. The results showed that compounds **5** and **7** tested did not reveal any antimicrobial activity, however, compounds **9** showed the antimicrobial effect against the strains of *Staphylococcus aureus*, *Escherichia coli* and *Bacillus subtilis*; the diameters of their growth inhibition zones were similar to those for the reference drugs Metronidazole and Streptomycin (Tab. 3).

## Experimental Part

### Chemical Part

The melting points (°C) were measured with a Koeffler melting point apparatus and were not corrected. $^1$H NMR spectra were recorded on Varian Mercury (200 MHz) spectrometers in DMSO-$d_6$ using TMS as an internal standard (chemical shifts are in ppm). LC/MS was recorded with PE SCIEX API 150EX chromatograph equipped with the mass-spectrometer using the column C18 (100×4 мм), the cycle of analysis was 25 min.

**Table 2**

$^1$H NMR spectral data of 1-alkyl-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **5**, **7** and **9**

| Compd No. | Chemical shift, δ, ppm. | | | |
|---|---|---|---|---|
| | NH | Thiophene $CH_3$ (3H, s.) | Aliphatic protons | Aromatic protons |
| 5a | – | 2.82 | 5.26 (2H, s, $CH_2$) | 7.20-7.65 (13H, m, Ar-H); 8.01 (2H, m, Ar-H) |
| 5b | – | 2.82 | 2.27 (3H, s, $CH_3$); 5.21 (2H, s, $CH_2$) | 7.11-7.67 (12H, m, Ar-H); 8.00 (2H, m, Ar-H) |
| 5c | – | 2.83 | 5.25 (2H, s, $CH_2$) | 7.24-7.70 (11H, m, Ar-H); 8.02 (2H, m, Ar-H) |
| 7a | 10.47 | 2.85 | 4.89 (2H, s, $CH_2$) | 7.08 (1H, m, Ar-H); 7.21-7.70 (12H, m, Ar-H); 8.05 (2H, m, Ar-H) |
| 7b | 10.39 | 2.85 | 2.23 (3H, s, $CH_3$); 4.87 (2H, s, $CH_2$) | 7.11 (1H, d, Ar-H); 7.22-7.73 (11H, m, Ar-H); 8.02 (2H, m, Ar-H) |
| 7c | 10.41 | – | 1.13 (3H, s, $CH_3$); 1.17 (3H, s, $CH_3$); 2.84 (4H, m, $CH_3$+CH); 4.87 (2H, s, $CH_2$) | 7.05-7.70 (12H, m, Ar-H); 8.03 (2H, m, Ar-H) |
| 7d | 10.45 | 2.86 | 3.69 (6H, s, 2 $OCH_3$); 4.87 (2H, s, $CH_2$) | 6.24 (1H, m, Ar-H); 6.82 (2H, d, Ar-H); 7.26-7.69 (8H, m, Ar-H); 8.05 (2H, m, Ar-H) |
| 7e | 10.32 | 2.85 | 1.28 (3H, t, $CH_3$); 3.95 (2H, q, $CH_2$); 4.85 (2H, s, $CH_2$) | 6.86 (2H, d, Ar-H); 7.29 (2H, d, Ar-H); 7.35-7.70 (8H, d, Ar-H); 8.04 (2H, m, Ar-H) |
| 7f | 10.05 | 2.85 | 2.24 (3H, s, $CH_3$); 4.96 (2H, s, $CH_2$) | 7.13 (1H, d, Ar-H); 7.24-7.69 (8H, d, Ar-H); 8.05 (2H, m, Ar-H) |
| 9a | – | 2.85 | 2.35 (3H, s, $CH_3$); 5.68 (2H, s, $CH_2$) | 7.22-7.68 (10H, d, Ar-H); 7.86 (2H, d, Ar-H) 8.05 (2H, m, Ar-H) |
| 9b | – | 2.85 | 5.74 (2H, s, $CH_2$) | 7.25-7.73 (11H, d, Ar-H); 7.88 (1H, d, Ar-H) 8.04 (2H, m, Ar-H) |
| 9c | – | 2.86 | 5.70 (2H, s, $CH_2$) | 7.31 (2H, d, Ar-H); 7.47 (3H, m, Ar-H); 7.62 (5H, m, Ar-H); 7.62 (4H, m, Ar-H) |

**Table 3**

The antimicrobial activity of 1-{[3-aryl-1,2,4-oxadiazol-5-yl]methyl}-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **9**

| | Diameter of the growth inhibition zone in mm The number of the repeated experiment n=3 | | | | | |
|---|---|---|---|---|---|---|
| | *Staphylococcus aureus* ATCC 25923 | *Escherichia coli* ATCC 25922 | *Proteus vulgaris* ATCC 4636 | *Pseudomonas aeruginosa* ATCC 27853 | *Bacillus subtilis* ATCC 6633 | *Candida albicans* ATCC 653/885 |
| 9a | 15, 16, 15 | 14, 14, 15 | growth | growth | 17, 16, 18 | growth |
| 9b | 16, 15, 14 | 14, 15, 14 | growth | growth | 17, 17, 17 | growth |
| 9c | 15, 15, 15 | 15, 14, 14 | growth | growth | 17, 17, 17 | growth |
| Metr.** | 14, 15, 14 | 14, 13, 14 | growth | growth | 16, 15, 16 | 14, 14, 14 |
| Strept.** | 15, 16, 15 | 15, 16, 17 | growth | growth | 17, 16, 17 | growth |

**Metr. – Metronidazole, DMSO solution, the concentration of 30 μg/ml; **Strept. – Streptomycin, $H_2O$ solution, the concentration of 30 μg/ml.

The starting **5-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidine-6-carboxylic acid 1** was obtained using the previously reported method [6].

**5-Methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (3).**

To the mixture of 5.0 g (0.0165 Mole) of acid **1** add 2.75 g (0.017 Mole) of 1,1'-carbonyldiimidazole and heat in 50 ml of anhydrous DMF for 25 minutes at 80°C. Then to the clear solution formed add 2.25 g (0.0165 Mole) of benzohydrazide, heat the reaction (130°C) and stir for 3-4 hours. After that quench the cool reaction mixture with water (50 ml) and filter the precipitate formed, washed with a plenty of 2-propanol-water mixture (1:1). $^1$H NMR spectrum: 2.66 (3H, s), 7.27 (2H, d), 7.38-7.63 (6H, m), 7.90 (2H, m) 10.14 (1H, br.s), 10.53 (1H, br.s).

Suspend the dried compound **2** (6 g) in 45 ml of $POCl_3$, boil the mixture, stir till dissolution of the precipitate and then stir additionally for 5 hours. After that pour the reaction onto the crashed ice and filter the precipitate of chloroderivative. Suspend the filtered pad of chloroderivative in 70% acetic acid and boil with stirring for 12-15 hours. Next quench the reaction with water to the volume of about 250 ml, filter the precipitate formed and wash with a plenty of cold water.

M.p. >300°C.

Yield – 63%.

$^1$H NMR: 2.79 (3H, s), 7.30 (2H, d), 7.39-7.67 (6H, m), 8.03 (2H, m), 12.64 (1H ,br.s).

LC/MS: m/z ($M^+$) 402.

Found, %: N 14.15. $C_{21}H_{14}N_4O_3S$. Calculated, %: N 13.92. M. 402.43.

**General method for synthesis of 1-alkyl-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl) thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones 5, 7 and 9.**

To 0.15 g (0.372 mmole) 5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione **3** in 3 ml of dimethylformamide add the corresponding alkylating agent (0.372 mmole) and 0.053 g (0.372 Mole) of $K_2CO_3$. Stir the mixture at 70-100°C for 8-10 hours. Then dilute the cool reaction mixture with water, filter the precipitate formed and crystallized from the suitable lower alcohol.

**The study of the antimicrobial activity**

According to the WHO recommendations [10, 11] the following test-strains were used: *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Proteus vulgaris* ATCC 4636, *Bacillus subtilis* ATCC 6633, *Candida albicans* ATCC653/885. The bacterial concentration was $10^7$ CFU/ml (determined by McFarland standard). Overnight cultures kept for 18-24 h at 36°C±1°C were used. The bacterial suspension was inoculated onto the entire surface of a Mueller-Hinton agar (Dagestan Scientific Research Institute of Nutrient Media). The compounds were introduced to the wells in the form of DMSO solution in the concentrations of 100 μg/ml; the open wells were filled with 0.3 ml of the solution.

## Conclusions

An effective approach for synthesis of 5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno [2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione based on the interaction of 1,1'-carbonyldiimidazole promoted the interaction of 5-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidine-6-carboxylic acid with benzohydrazide has been proposed. The procedure also includes cylcization of *N*'-benzoyl-5-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydrothieno [2,3-*d*]pyrimidine-6-carbohydrazide by boiling in phosphorous oxychloride with subsequent hydrolysis of the chlorine atom of the intermediate formed. Alkylation of the heterocyclic system obtained with benzyl chlorides, chloroacetamides, and 5-(chloromethyl)-3-aryl-1,2,4-oxadiazoles resulted in the series of 1-alkyl-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones. The results of the antimicrobial activity screening have shown that 1-{[3-aryl-1,2,4-oxadiazol-5-yl] methyl}-5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones are antimicrobial agents.

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