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НОВЫЕ C^1 И N^5 ПРОИЗВОДНЫЕ СЕРПЕЖИНА. СИНТЕЗ И ИССЛЕДОВАНИЕ АНТИБАКТЕРИАЛЬНОЙ АКТИВНОСТИ

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В данной статье рассматриваются биоактивные свойства синтетических соединений, содержащих γ-лактоновые и 2-пиридоновые кольца, которые проявляют широкий спектр фармакологической активности. Эти соединения являются структурными аналогами алкалоида серпежина, выделенного из растения Ceropegia juncea, известного в традиционной индийской медицине. Серпежин обладает успокаивающим, противовоспалительным, анальгезирующим и противоязвенным действием, что делает его синтетические производные перспективными объектами для разработки новых лекарственных препаратов. Особое внимание в работе уделено производным серпежина, таким как C^1 и N^5, которые усиливают клеточный ответ на интерфероны и избирательно ингибируют активность 20S протеасомы млекопитающих. Эти свойства делают указанные соединения потенциально полезными при лечении иммунных и воспалительных заболеваний, а также при создании новых противоопухолевых средств с минимальными побочными эффектами. В рамках исследования была проведена оценка антибактериальной активности 37 новых производных серпежина с использованием метода диффузии в агар при бактериальной нагрузке 20 млн микробных тел/мл. Эксперименты проводились в асептических условиях с применением эталонных штаммов как грамположительных, так и грамотрицательных бактерий. Полученные результаты показали, что соединения первой группы обладают выраженной антибактериальной активностью, особенно в отношении Shigella flexneri, при этом ряд соединений проявил умеренную эффективность. Полученные данные подтверждают необходимость дальнейших исследований антибактериальных свойств производных серпежина, особенно по отношению к более широкой группе грамотрицательных патогенов. Это может способствовать созданию новых эффективных антибактериальных препаратов с улучшенным профилем безопасности и селективности.

Ключевые слова: γ-лактоны, 2-пиридоны, производные серпежина, синтез, грамположительные бактерии, грамотрицательные бактерии, антибактериальная активность

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NEW C^1 AND N^5 DERIVATIVES OF CERPEGINE. SYNTHESIS AND ANTIBACTERIAL ACTIVITY STUDY

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This study explores the bioactive properties of synthetic compounds containing γ-lactone and 2-pyridone ring systems, which exhibit a broad spectrum of pharmacological activities. These compounds are structural analogues of the alkaloid serpegin, originally isolated from Ceropegia juncea, a plant known in traditional Indian medicine for its therapeutic effects. Serpegin has been reported to possess sedative, anti-inflammatory, analgesic, and anti-ulcer properties, making its synthetic analogues attractive candidates for the development of novel therapeutic agents. Among the synthetic derivatives discussed in this work are compounds C1 and N5, which have demonstrated the ability to enhance cellular responses to interferons and selectively inhibit the activity of the mammalian 20S proteasome. These biological effects suggest that such derivatives may have potential applications in the treatment of immune-related and proliferative disorders, with the added benefit of potentially reduced side effects compared to existing drugs. The antibacterial activity of 37 newly synthesized serpegin derivatives was evaluated using the agar diffusion method under aseptic conditions, with a bacterial load of 20 million microbial cells per milliliter. Both Gram-positive and Gram-negative reference bacterial strains were tested. The results revealed that compounds from the first group exhibited noticeable antibacterial effects, especially against Shigella flexneri, with several compounds showing moderate activity. These findings underscore the significance of further research into the antibacterial properties of serpegin-based compounds, particularly against a wider spectrum of Gram-negative bacteria. This could ultimately contribute to the development of new and effective antibacterial agents with improved selectivity and safety profiles.

Keywords: γ-lactones, 2-pyridones, Cerpegine derivatives, synthesis, gram-positive bacterias, gram-negative bacterias, antibacterial activity

INTRODUCTION

Cerpegine alkaloid, a fascinating naturally occurring bioactive compound, has garnered significant attention in medicinal and synthetic chemistry due to its diverse pharmacological activities. Since the beginning of 1990, with the isolation of *Cerpegine* from the plant *Ceropegia juncea*, the development of synthesis routes and studies of the biological activity of the synthesized derivatives began and still continues [1-7]. The plant is used in traditional Indian medicine due to its tranquillizing, anti-inflammatory, analgesic and antiulcer properties [6].

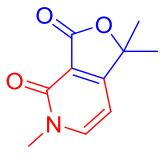


Fig. 1. Cerpegine
Рис. 1. Серпежин

It is known that *Cerpegine* molecule contains γ-lactone and pyridone rings (Fig. 1). Both occurs in many bioactive compounds and officially approved drugs' molecules [8-20]. Thus, pyridone ring containing compound Huperazine A (Fig. 2a) is used in China against Alzheimer's disease, in USA as a nutraceutical,

Fredericamycin A (Fig. 2b) is for human cancer chemotherapy, Camptothecin (Fig. 2c) has anticancer activity, Ripretinib (Fig. 2d), Tazemetostat (Fig. 2e), Doravirine (Fig. 2f), Duvelisib (Fig. 2g) and Palbociclib (Fig. 2h) are kinase inhibitors, so they are officially approved anticancer drugs. Study of the 1999-2022 2-pyridones' literature showed that 31% of works are about anticancer, 31% antibacterial, 24% antifungal, 7% anti-inflamatory, 4% α-glucoside inhibiton and 3% cardiotonic activities [13]. γ-lactone ring containing compounds Xanthatin (Fig. 3a) is antibiotic, Isodeoxypodophyllotoxin (Fig 3b) is tubulin polymerization inhibitor, Encelin (Fig 3c) is fungal growth inhibitor and Arglabin (Fig 3d) is farnesyl transferase inhibitor [20].

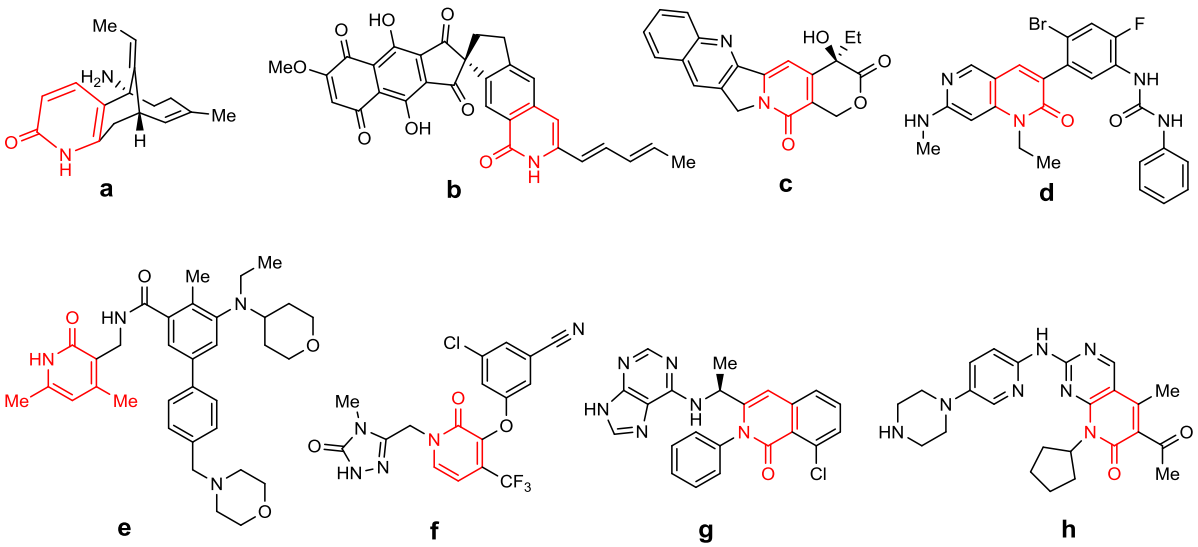


Fig. 2. Pyridone ring containing compounds
Рис. 2. Соединения, содержащие пиридоновое кольцо

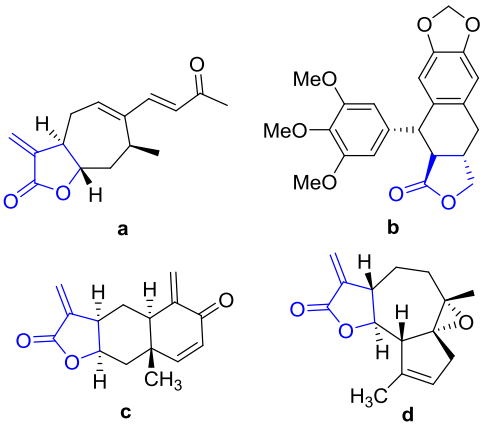


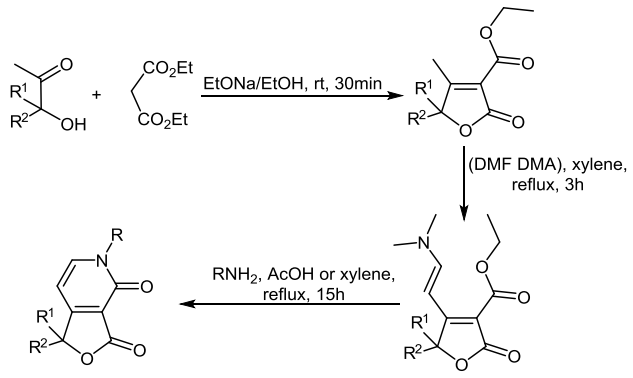
Fig. 3. γ-lactone ring containing compounds
Рис. 3. Соединения, содержащие γ-лактоновое кольцо

Finally, both γ-lactone and pyridone rings containing C^1 and N^5 derivatives of Cerpegine enhance cellular response to interferons by pyrimidine biosynthesis inhibition and also demonstrate selective inhibition of the post-acid activity of mammalian 20S proteasomes [2, 7, 22].

In summary, we can say that synthesis and biological activity study of γ-lactone and pyridone rings containing compounds are important enough for further drug discovery. Thus, the aim of our research is to synthesize the series of Cerpegine C^1 and N^5 derivatives and conduct an antibacterial activity study.

DESCRIPTION

There are several good methods of Cerpegine C^1 and N^5 derivatives' preparation [2, 3, 7]. Dozens of them were successfully synthesized with good yields by three-step synthetic route (Scheme). We also synthesized new 37 Cerpegine derivatives with good yields (52-92%) by the described scheme and conducted the study of antibacterial activity.



Scheme
Схема

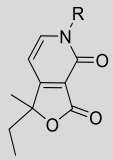
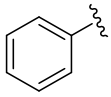
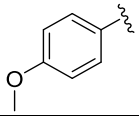
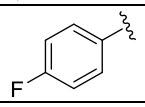
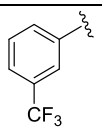
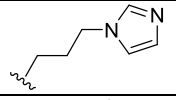
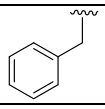
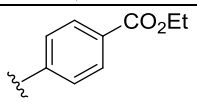
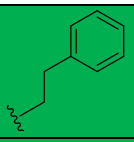
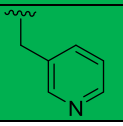
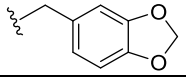
The antibacterial activity of the synthesized *Cerpegine* C^1 and N^5 derivatives' (Table 1) were studied using the "agar diffusion" method [23] at a bacterial load of 20 million microbial bodies/ml of medium. Gram-positive (*Staphylococcus aureus* 209P, *Bacillus subtilis* ATCC 6633) and gram-negative rods (*Shigella flexneri* ATCC 6858, *Escherichia coli* O-55) were used as model bacteria to assess antibacterial activity. The drug Furadonin was used as a positive control. Solutions of the compounds and the control preparation were prepared in DMSO with a concentration of 50 mg/ml. The test substances were applied to Petri dishes with microorganism strains inoculated with them, 0.1 ml each. The results were recorded based on the diameter (d, mm) of the zones of inhibition at the site of applied substances after a day of growing the test cultures in a thermostat at 37 °C.

The study of the antibacterial activity of the compounds showed that the substances of the first group exhibit antibacterial activity against gram-negative microorganisms, especially against S. *Flexneri* 6858. Among them, substances **8**, **9, 12, 13** and **15** exhibit moderate activity against all microorganisms used in the experiment. Compounds of the second and third subgroups demonstrate moderate activity (d15-20 mm) against both gram-negative and gram-positive microorganisms. Among them, the most active are the compounds: **16, 17, 25, 35** and **37**. The antibacterial activity data are presented in the Table.

Table

Antibacterial activity of synthesized compounds

***Таблица.* Антибактериальная активность синтезированных соединений**

Compound			Diameter (d, mm) of the zones of inhibition			
Group	N	R	*S. aureus 209 p*	*B. subtilis 6633*	*S. flexneri 6858*	*E. coli 0-55*
I 			0	0	17	12
			0	13	20	13
			0	17	22	13
			0	17	22	15
			11	17	20	17
			11	16	22	17
			11	0	20	17
			15	16	22	17
			13	15	22	16
			0	15	19	14

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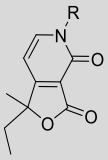
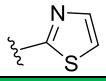
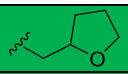
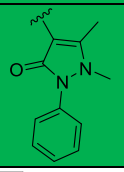
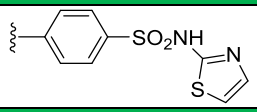
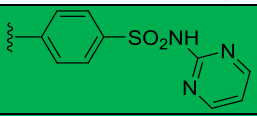
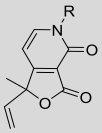
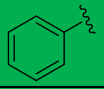
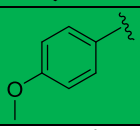
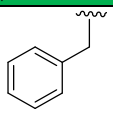
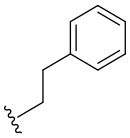
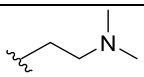
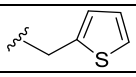
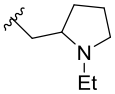
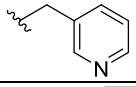
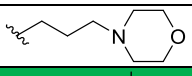
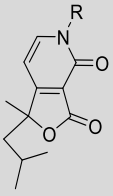
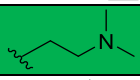
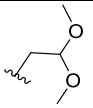
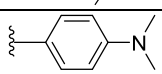
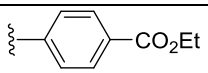
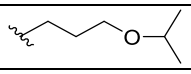
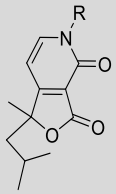
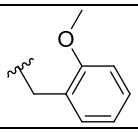
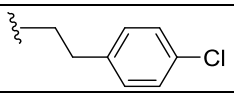
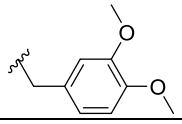
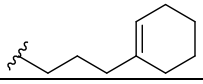
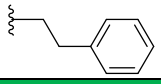
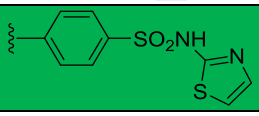
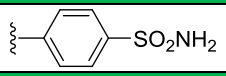
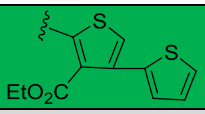
I 			12	16	18	16
			13	16	20	18
			13	16	20	15
			0	15	20	13
			12	18	22	17
II 			14	18	19	14
			14	15	18	15
			14	13	17	18
			18	18	18	18
			0	13	15	17
			11	14	18	15
			13	17	18	12
			10	17	17	12
			11	19	18	15
III 			17	20	20	18
			12	17	17	12
			14	17	17	12
			0	14	13	0
			11	16	14	12

continuation of the table

Group	N	R	*S. aureus 209 p*	*B. subtilis 6633*	*S. flexneri 6858*	*E. coli 0-55*
III 			12	19	17	14
			10	15	14	17
			0	14	20	13
			11	13	18	13
			13	18	20	14
			10	18	22	15
			10	16	20	15
			10	16	23	14
		Furadonine	23	23	23	23

CONCLUSIONS

The conducted study confirms the potential of synthetic Serpegin derivatives as multifunctional bioactive compounds with a broad spectrum of therapeutic activity. It was established that molecules containing γ-lactone and 2-pyridone fragments possess not only anti-inflammatory and analgesic potential, but also exhibit selective inhibitory activity against the 20S proteasome, making them promising candidates for the development of novel anticancer and immunomodulatory agents.

The evaluation of the antibacterial activity of 37 newly synthesized serpegin derivatives demonstrated that several compounds exhibit significant activity against Shigella flexneri, along with moderate activity against other tested bacterial strains. These findings underscore the relevance of further investigation into this class of compounds for the development of effective antibacterial agents, particularly in light of the growing resistance of microorganisms to existing antibiotics.

In conclusion, synthetic Serpegin analogues represent a promising direction for ongoing pharmacological research aimed at creating new multipurpose therapeutics with enhanced efficacy and improved safety profiles.

EXPERIMENTAL

General Information

IR spectra were obtained on a Specord 75 IR spectrometer in KBr pellets. 1H and 13C NMR (300 and 75 MHz, respectively) spectra were recorded on a Varian Mercury VX 300 spectrometer in DMSO-*d*6–CCl4, 1:3, at 30 °C (unless otherwise mentioned), using TMS as internal standard. High-resolution mass spectra were recorded on a Waters Xevo G3 QToF instrument using ES source in a positive mode. All starting compounds were obtained from commercial sources and were used without additional purification. All target compounds were synthesized and purified by well-known procedures [2, 3, 7].

General methodology synthesis of 1-37 compounds:

0.001 mol of primary amine and 3 ml of xylene were added to 0.001 mol of the starting lactone-diaminovinyl, and the mixture was refluxed for 15 h. Then

3 ml of hexane were added, and the resulting crystals were filtered. The crystals were recrystallized from ethanol. Substances with the corresponding yields were obtained.

1-ethyl-1-methyl-5-phenylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (1): Yield 65%, mp 196-198 °C, white solid, IR spectrum, ν, cm^{-1}: 1600.21, 1650, 1721, 1730.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.87t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.61s (3H, CH_3), 1.88-2.08m (2H, $CH_3\underline{CH_2}$), 6.56d (1H, *J* = 6.8), 7.39-7.57m (5H), 7.97d, (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 7.28, 23.80, 30.65, 83.84, 98.45, 112.32, 126.37, 128.14, 128.64, 139.50, 145.89, 155.70, 165.31, 170.87, HRMS (ESI, m/z) calcd. for $C_{16}H_{16}NO_3^+$ $[M+H]^+$: 270.1130, found: 270.1141.

1-ethyl-5-(4-methoxyphenyl)-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (2): Yield 69%, mp 227-229 °C, white solid, IR spectrum, ν, cm^{-1}: 1102.06, 1137.8, 1508.4, 1720.1, 1735.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.60s (3H, CH_3), 1.86-2.07m (2H, $CH_3\underline{CH_2}$), 3.86s (3H, OCH_3), 6.52d (1H, *J* = 6.8), 7.00-7.05m (2H), 7.28-7.33m (2H), 7.93d, (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 7.27, 23.83, 30.67, 54.9, 83.78, 98.23, 112.16, 113.82, 127.36, 132.17, 146.18, 155.90, 158.97, 165.39, 170.68, HRMS (ESI, m/z) calcd. for $C_{17}H_{18}NO_4^+$ $[M+H]^+$: 301.1236, found: 301.1247.

1-ethyl-5-(4-fluorophenyl)-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (3): Yield 59%, mp 241-243 °C, white solid, IR spectrum, ν, cm^{-1}: 1600.51, 1650.3, 1725.2, 1735.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.60s (3H, CH_3), 1.87-2.08m (2H, $CH_3\underline{CH_2}$), 6.56d (1H, *J* = 6.8), 7.23-7.31m (2H), 7.43-7.49m (2H), 7.97d (1H, *J* = 6.81), ^{13}C NMR spectrum, δ, ppm: 7.27, 23.79, 30.64, 83.90, 98.54, 112.30, 115.54, 128.52, 135.47, 145.98, 155.78, 161.54, 165.30, 170.97, HRMS (ESI, m/z) calcd. for $C_{16}H_{15}FNO_3^+$ $[M+H]^+$: 288.1036, found: 288.1042.

1-ethyl-1-methyl-5-(4-(trifluoromethyl)phenyl)furo[3,4-c]pyridine-3,4(1H,5H)-dione (4): Yield 52%, mp 182-184 °C, white solid, IR spectrum, ν, cm^{-1}: 1506.38, 1548.25, 1599.63, 1720.1, 1740, 3104.47, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.61s (3H, CH_3), 1.89-2.09m (2H, $CH_3\underline{CH_2}$), 6.62d (1H, *J* = 6.8), 7.71-7.81m (4H), 8.06d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 7.24, 23.81, 30.60, 84.02, 98.93, 112.44, 123.11, 123.62, 124.89, 129.72, 130.34, 130.43, 139.89, 145.76, 155.68, 165.22, 171.22, HRMS (ESI, m/z) calcd. for $C_{17}H_{15}F_3NO_3^+$ $[M+H]^+$: 338.1004, found: 338.1015.

5-(3-(1H-imidazol-1-yl)propyl)-1-ethyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (5):

Yield 85%, mp 171-173 °C, white solid, IR spectrum, ν, cm^{-1}: 1530.1, 1529.6, 1580.9, 1720.4, 1735.6, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.79t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.54s (3H, CH_3), 1.80-2.01m (2H, $CH_3\underline{CH_2}$), 2.15-2.24m (2H, $CH_2\underline{CH_2}CH_2$), 3.93-4.10m (4H, $\underline{CH_2}CH_2\underline{CH_2}$), 6.40d (1H, *J* = 6.8), 6.82t (1H, *J* = 1.2), 7.06t (1H, *J* = 1.2) 7.52t (1H, *J* = 1.2), 8.04d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 7.21, 23.87, 30.04, 30.68, 43.37, 46.13, 83.71, 98.15, 111.50, 118.30, 128.35, 136.57, 146.09, 156.10, 165.54, 170.04, HRMS (ESI, m/z) calcd. for $C_{16}H_{20}N_3O_3^+$ $[M+H]^+$: 302.1505, found: 302.1513.

5-benzyl-1-ethyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (6): Yield 83%, mp 161-163 °C, white solid, IR spectrum, ν, cm^{-1}: 1529.2, 1530.4, 1577.1, 1710.5, 1728.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.79t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.54s (3H, CH_3), 1.80-2.02m (2H, $CH_3\underline{CH_2}$), 5.14d (1H, *J* = 14.0), 5.22d (1H, *J* = 14.0), 6.43d (1H, *J* = 6.8), 7.24-7.39m (5H, Ph), 8.19d, (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 7.22, 23.81, 30.70, 50.80, 83.70, 98.19, 111.74, 127.28, 127.82, 128.09, 136.18, 146.05, 156.00, 165.45, 170.12, HRMS (ESI, m/z) calcd. for $C_{17}H_{18}NO_3^+$ $[M+H]^+$: 284.1287, found: 284.1295.

Ethyl 4-(1-ethyl-1-methyl-3,4-dioxo-1,4-dihydrofuro[3,4-c]pyridin-5(3H)-yl)benzoate (7): Yield 67%, mp 257-259 °C, white solid, IR spectrum, ν, cm^{-1}: 1101.06, 1138.4, 1508.44, 1547.28, 1593.67, 1717.0, 1735.34, 3067.20, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86t (3H, *J* = 7.4, $\underline{CH_3}CH_2C$), 1.41t (3H, *J* = 7.1, $\underline{CH_3}CH_2O$), 1.61s (3H, CH_3), 1.88-2.09m (2H, $CH_3\underline{CH_2}C$), 4.38q (2H, *J* = 14.0, $CH_3\underline{CH_2}O$), 6.61d (1H, *J* = 6.8), 7.54-7.58m (2H), 8.02d (1H, *J* = 6.8), 8.12-8.16m (2H), ^{13}C NMR spectrum, δ, ppm: 7.27, 13.89, 23.78, 30.61, 60.36, 83.98, 98.88, 112.45, 126.59, 129.78, 129.95, 143.08, 145.56, 155.53, 164.22, 165.22, 171.11, HRMS (ESI, m/z) calcd. for $C_{19}H_{20}NO_5^+$ $[M+H]^+$: 342.1342, found: 342.1348.

1-ethyl-1-methyl-5-phenethylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (8): Yield 86%, mp 142-144 °C, white solid, IR spectrum, ν, cm^{-1}:1530.2, 1532.8, 1577.1, 1720.6, 1731.1, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.77t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.53s (3H, CH_3), 1.61s (3H, CH_3), 1.78-2.01m (2H, $CH_3\underline{CH_2}$), 2.97-3.03m (2H, $NCH_2\underline{CH_2}$), 4.12-4.26m (2H, $N\underline{CH_2}CH_2$), 6.27d (1H, *J* = 6.8), 7.15-7.28m (5H, Ph), 7.83d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 7.12, 24.01, 30.68, 34.31, 50.19, 83.59, 97.45, 111.48, 126.03,

127.93, 128.46, 137.28, 146.10, 155.87, 165.50, 169.92, HRMS (ESI, m/z) calcd. for $C_{18}H_{20}NO_3^+$ $[M+H]^+$: 298.1443, found: 298.1454.

1-ethyl-1-methyl-5-(pyridin-3-ylmethyl)furo[3,4-c]pyridine-3,4(1H,5H)-dione (9): Yield 86%, mp 212-214 °C, white solid, IR spectrum, ν, cm^{-1}: 1548.4, 1551.3, 1528.2, 1725.6, 1730.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.79t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.54s (3H, CH_3), 1.80-2.01m (2H, $CH_3\underline{CH_2}$), 5.17d (1H, $N\underline{CH_2}$), 5.25d (1H, $N\underline{CH_2}$), 6.46d (1H, *J* = 6.8), 7.29ddd (1H, *J* = 0.8, 4.8, 7.9), 7.79dt (1H, *J* = 2.0, 7.9), 8.33d (1H, *J* = 6.8, 7.9), 8.46dd (1H, *J* = 1.7, 6.8), 8.64dd (1H, *J* = 0.8, 2.0), ^{13}C NMR spectrum, δ, ppm: 7.23, 23.76, 30.68, 48.80, 83.80, 98.49, 111.82, 122.95, 131.74, 135.65, 146.10, 148.53, 149.31, 156.06, 165.38, 170.31, HRMS (ESI, m/z) calcd. for $C_{16}H_{17}N_2O_3^+$ $[M+H]^+$: 285.1239, found: 285.1245.

5-(benzo[d][1,3]dioxol-5-ylmethyl)-1-ethyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (10): Yield 90%, mp 186-188 °C, pale-yellow solid, IR spectrum, ν, cm^{-1}: 1121.4, 1542.8, 1550.3, 1722.8, 1735.1, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.78t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.53s (3H, CH_3), 1.79-2.01m (2H, $CH_3\underline{CH_2}$), 5.01d (1H, *J* = 14.0), 5.11d (1H, *J* = 14.0), 5.95s (2H), 6.40d (1H, *J* = 6.8), 6.75d (1H, *J* = 7.9), 6.92dd (1H, *J* = 1.7, 7.9), 6.96d (1H, *J* = 1.7), 8.18d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm:7.23, 23.81, 30.69, 50.56, 83.67, 98.16, 100.53, 107.68, 108.75, 111.69, 129.80, 145.83, 146.85, 147.26, 156.00, 165.46, 170.03, HRMS (ESI, m/z) calcd. for $C_{18}H_{18}NO_5^+$ $[M+H]^+$: 328.1185, found: 328.1191.

1-ethyl-1-methyl-5-(thiazol-2-yl)furo[3,4-c]pyridine-3,4(1H,5H)-dione (11): Yield 61%, mp 230-232 °C, white solid, IR spectrum, ν, cm^{-1}: 1540.8, 1589.34, 1650.8, 1759.2, 3021, 3444.8, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.83t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.63s (3H, CH_3), 1.92-2.11m (2H, $CH_3\underline{CH_2}$), 6.89d (1H, *J* = 7.3), 7.54d (1H, *J* = 3.5), 7.70d (1H, *J* = 3.5), 9.21d (1H, *J* = 7.3), ^{13}C NMR spectrum, δ, ppm: 7.19, 23.59, 30.42, 84.54, 100.81, 113.27, 119.51, 137.22, 138.91, 154.18, 154.34, 164.34, 164.53, 170.69, HRMS (ESI, m/z) calcd. for $C_{13}H_{13}N_2O_3S^+$ $[M+H]^+$: 277.0647, found: 277.0657.

1-ethyl-1-methyl-5-((tetrahydrofuran-2-yl)methyl)furo[3,4-c]pyridine-3,4(1H,5H)-dione (12): Yield 74%, mp 119-121 °C, white solid, IR spectrum, ν, cm^{-1}: 1542.1, 1572.31, 1655.3, 1748.3, 3526.9, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.78t (0.5H, *J* = 7.4, $\underline{CH_3}CH_2$), 0.81t (0.5H, *J* = 7.4), 1.55s (0.5H, CH_3), 1.56s (0.5H, CH_3), 1.56-1.68m (1H, $CH_3\underline{CH_2}$), 1.81-2.11m (5H, $CH_3\underline{CH_2}$), 3.65-3.87m (3H), 4.07-4.15m (1H), 4.22-4.32m (1H), 6.37d (1H, *J* = 6.8), 7.96d (0.5H, *J* = 6.8), 7.97d (0.5H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 7.26, 23.90, 24.99, 28.19, 30.72, 51.26, 51.42, 67.01, 75.72, 83.62, 97.32, 111.18, 147.02, 156.06, 165.52, 170.09, HRMS (ESI, m/z) calcd. for $C_{15}H_{20}NO_4^+$ $[M+H]^+$: 278.1392, found: 278.1403.

5-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-1-ethyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (13): Yield 60%, mp 217-219 °C, white solid, IR spectrum, ν, cm^{-1}: 1545.8, 1589.34, 1652.9, 1759.7, 3071.2, 3415.80, 3526.9, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.82d (3H, *J* = 6.6), 0.86t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.61s (3H, CH_3), 1.86-2.07m (2H, $CH_3\underline{CH_2}$), 2.25s (3H), 3.29s (3H), 6.56d (1H, *J* = 6.8), 7.32-7.37m (2H), 7.39-7.43m (2H), 7.48-7.53m (2H), 7.87d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 7.34, 11.39, 23.63, 30.70, 35.06, 83.98, 98.52, 108.03, 112.03, 124.02, 126.40, 128.60, 134.29, 147.35, 151.92, 155.01, 159.67, 165.38, 170.82, HRMS (ESI, m/z) calcd. for $C_{21}H_{22}N_3O_4^+$ $[M+H]^+$: 380.1610, found: 380.1618.

4-(1-ethyl-1-methyl-3,4-dioxo-1,4-dihydrofuro[3,4-c]pyridin-5(3H)-yl)-N-(thiazol-2-yl) benzenesulfonamide (14): Yield 60%, mp 304-306 °C, pale-yellow solid, IR spectrum, ν, cm^{-1}: 1543.6, 1572.26, 1678.4, 1755.84, 3095.5, 3147.1, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.85t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.60s (3H, CH_3), 1.87-2.08m (2H, $CH_3\underline{CH_2}$), 6.61d (1H, *J* = 6.8), 6.72d (1H, *J* = 4.7), 7.11d (1H, *J* = 4.7), 7.55-7.59m (2H), 8.07d (1H, *J* = 6.8), 7.96-8.00m (2H), 8.08d (2H, *J* = 6.8), 12.50-12.90bs (1H, NH), ^{13}C NMR spectrum, δ, ppm: 7.31, 23.74, 30.60, 84.13, 98.98, 107.67, 112.28, 123.74, 126.49, 127.01, 141.93, 142.72, 145.91, 155.70, 165.38, 168.61, 171.27, HRMS (ESI, m/z) calcd. for $C_{19}H_{18}N_3O_5S_2^+$ $[M+H]^+$: 432.0688, found: 432.0685.

4-(1-ethyl-1-methyl-3,4-dioxo-1,4-dihydrofuro[3,4-c]pyridin-5(3H)-yl)-N-(pyrimidin-2-yl)benzenesulfonamide (15): Yield 59%, mp 327-329 °C, pale-yellow solid, IR spectrum, ν, cm^{-1}: 1545.3, 1579.3, 1682.0, 1752.7, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.84t (3H, *J* = 7.4, $\underline{CH_3}CH_2$), 1.60s (3H, CH_3), 1.87-2.07m (2H, $CH_3\underline{CH_2}$), 6.63d (1H, *J* = 6.8), 7.02t (1H, *J* = 4.9), 7.61-7.65m (2H), 8.07d (1H, *J* = 6.8), 8.17-8.21m (2H), 8.50d (2H, *J* = 4.9), 11.60-11.90bs (1H, NH), ^{13}C NMR spectrum, δ, ppm: 7.30, 23.73, 30.56, 84.20, 99.12, 112.30, 126.88, 128.49, 140.61, 142.61, 145.83, 155.65, 156.69, 157.72, 165.40, 171.36, HRMS (ESI, m/z) calcd. for $C_{20}H_{19}N_4O_5S^+$ $[M+H]^+$: 427.1076, found: 427.1081.

1-methyl-5-phenyl-1-vinylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (16): Yield 66%, mp 234-236 °C, white solid, IR spectrum, ν, cm^{-1}: 1548.1, 1580.2, 1658.1, 1730.7, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.73s (3H, CH_3), 5.29dd (1H, *J* = 0.6, 10.7), 5.49dd (1H, *J* = 17.1, 0.6), 6.09dd (1H, *J* = 10.7, 17.1), 6.59d (1H, *J* = 6.8), 7.38-7.42m (2H), 7.44-7.50m (1H), 7.51-7.56m (2H), 7.99d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.54, 82.77, 98.81, 110.96, 115.60, 126.34, 128.18, 128.67, 136.16, 139.44, 146.20, 155.75, 165.06, 169.89, HRMS (ESI, m/z) calcd. for $C_{16}H_{14}NO_3^+$ $[M+H]^+$: 268.0974, found: 268.0984.

5-(4-methoxyphenyl)-1-methyl-1-vinylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (17): Yield 70%, mp 232-234 °C, white solid, IR spectrum, ν, cm^{-1}: 1125.4, 1544.1, 1570.3, 1650.4, 1730.8, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.72s (3H, CH_3), 3.86s (3H, OCH_3), 5.28dd (1H, *J* = 0.6, 10.7), 5.48dd (1H, *J* = 0.6, 17.1), 6.08dd (1H, *J* = 10.7, 17.1), 6.55d (1H, *J* = 6.8), 7.00-7.05m (2H), 7.27-7.32m (2H), 7.95d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.56, 54.91, 82.69, 98.57, 110.80, 113.85, 115.53, 127.34, 132.10, 136.21, 146.45, 155.95, 159.00, 165.11, 169.68, HRMS (ESI, m/z) calcd. for $C_{17}H_{16}NO_4^+$ $[M+H]^+$: 298.1079, found: 298.1087.

5-benzyl-1-methyl-1-vinylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (18): Yield 81%, mp 182-184 °C, white solid, IR spectrum, ν, cm^{-1}: 1548.2, 1570.8, 1650.5, 1732.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.66s (3H, CH_3), 5.15d (1H, *J* = 14.0), 5.19d (1H, *J* = 14.0), 5.22dd (1H, *J* = 0.6, 10.7), 5.22dd (1H, *J* = 0.6, 17.1), 6.02dd (1H, *J* = 10.7, 17.1), 6.45d (1H, *J* = 6.8), 7.23-7.39m (5H), 8.21d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.54, 50.85, 82.61, 98.52, 110.40, 115.36, 127.31, 127.89, 128.09, 136.10, 136.30, 156.03, 165.15, 169.16, HRMS (ESI, m/z) calcd. for $C_{17}H_{17}NO_3^+$ $[M+H]^+$: 282.1130, found: 282.1141.

1-methyl-5-phenethyl-1-vinylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (19): Yield 84%, mp 162-164 °C, white solid, IR spectrum, ν, cm^{-1}: 1547.5, 1577.8, 1650.5, 1770.5, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65s (3H, CH_3), 2.96-3.02m (2H), 4.16-4.22m (2H), 5.23dd (1H, *J* = 0.6, 10.7), 5.41dd (1H, *J* = 0.6, 17.1), 6.01dd (1H, *J* = 10.7, 17.1), 6.32d (1H, *J* = 6.8), 7.16-7.79m (5H), 7.91d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.62, 34.42, 50.14, 82.50, 97.89, 110.13, 115.33, 126.03, 127.93, 128.44, 136.35, 137.27, 146.31, 155.90, 165.17, 169.05, HRMS (ESI, m/z) calcd. for $C_{18}H_{18}NO_3^+$ $[M+H]^+$: 296.1287, found: 296.1297.

5-(2-(dimethylamino)ethyl)-1-methyl-1-vinylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (20): Yield 72%, mp 164-166 °C, white solid, IR spectrum, ν, cm^{-1}: 1543.6, 1655.4, 1735.4, 1740.8, 3012.8, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.66s (3H, CH_3), 2.24s (6H, $N(CH_3)_2$), 2.55t (2H, *J* = 6.2), 4.04t (2H, *J* = 6.2), 5.23dd (1H, *J* = 0.6, 10.7), 5.43dd (1H, *J* = 0.6, 17.1), 6.02dd (1H, *J* = 10.7, 17.1), 6.39d (1H, *J* = 6.8), 8.00d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.64, 44.99, 45.81, 57.18, 82.50, 97.65, 109.82, 115.26, 136.41, 146.90, 155.97, 165.26, 168.92, HRMS (ESI, m/z) calcd. for $C_{14}H_{19}N_2O_3^+$ $[M+H]^+$: 263.1396, found: 263.1407.

1-methyl-5-(thiophen-2-ylmethyl)-1-vinylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (21): Yield 76%, mp 204-206 °C, white solid, IR spectrum, ν, cm^{-1}:1538.6, 1644.8, 1655.4, 1730.8, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65s (3H, CH_3), 5.22dd (1H, *J* = 0.6, 17.1), 5.31d (1H, *J* = 14.4), 5.36d (1H, *J* = 14.4), 5.42dd (1H, *J* = 0.6, 17.1), 6.01d (1H, *J* = 17.1, 10.7), 6.45d (1H, *J* = 6.8), 6.94dd (1H, *J* = 3.5, 5.1), 7.20dd (1H, *J* = 1.1, 3.5), 7.31dd (1H, *J* = 1.1, 5.1), 8.25d (1H, *J* = 6.8) ^{13}C NMR spectrum, δ, ppm:23.52, 45.55, 82.66, 98.65, 110.33, 115.38, 126.11, 126.15, 127.63, 136.26, 137.59, 145.85, 155.73, 165.07, 169.29, HRMS (ESI, m/z) calcd. for $C_{15}H_{13}NO_3S^+$ $[M+H]^+$: 288.0694, found: 288.0704.

5-((2-ethylpyrrolidin-1-yl)methyl)-1-methyl-1-vinylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (22): Yield 78%, mp 138-140 °C, orange solid, IR spectrum, ν, cm^{-1}: 1548.4, 1638.9, 1652.3, 1740.8, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99t (0.5H, *J* = 7.1), 1.00t (0.5H, *J* = 7.1), 1.65s (0.5H, CH_3), 1.66s (0.5H, CH_3), 1.52-1.88m (4H), 2.19-2.37m (2H), 2.58-2.70m (1H), 2.84-2.92m (1H), 3.05-3.11 (1H), 3.80-3.98m (1H), 5.22dd (0.5H, *J* = 0.6, 17.1), 5.23dd (0.5H, *J* = 0.6, 10.7), 5.40dd (0.5H, *J* = 0.6, 17.1), 5.43dd (0.5H, *J* = 0.6, 17.1), 6.02dd (0.5H, *J* = 0.6, 17.1), 6.02dd (1H, *J* = 0.6, 17.1), 6.36d (1H, *J* = 6.8), 8.00d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 13.47, 22.94, 23.71, 27.69, 48.66, 51.77, 52.92, 60.91, 82.45, 97.21, 109.55, 115.24, 136.47, 147.34, 156.25, 165.19, 169.05, HRMS (ESI, m/z) calcd. for $C_{17}H_{23}N_2O_3^+$ $[M+H]^+$: 303.1709, found: 303.1719.

1-methyl-5-(pyridin-3-ylmethyl)-1-vinylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (23): Yield 83%, mp 226-228 °C, pale-yellow solid, IR spectrum, ν, cm^{-1}: 1547.8, 1640.7, 1650.4, 1730.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65s (3H, CH_3), 5.18d (1H, *J* = 14.4), 5.22d (1H, *J* = 14.4), 5.23dd (1H, *J* = 0.6, 10.7), 5.41dd

(1H, *J* = 0.6, 17.1), 6.03dd (1H, *J* = 10.7, 17.1), 6.53d (1H, *J* = 6.8), 7.31ddd (1H, *J* = 0.8, 4.8, 7.9), 7.78dt (1H, *J* = 1.6, 7.9), 8.37d (1H, *J* = 6.8), 8.46dd (1H, *J* = 1.6, 4.8), 8.64dd (1H, *J* = 0.8, 1.6), ^{13}C NMR spectrum, δ, ppm: 23.48, 48.92, 82.91, 99.02, 110.37, 115.53, 123.09, 131.75, 135.71, 136.29, 146.54, 148.2, 149.35, 156.16, 165.33, 169.52, HRMS (ESI, m/z) calcd. for $C_{16}H_{15}N_2O_3^+$ $[M+H]^+$: 283.1083, found: 283.1094.

1-isobutyl-1-methyl-5-(3-morpholinopropyl)furo[3,4-c]pyridine-3,4(1H,5H)-dione (24): Yield 82%, mp 154-156 °C, pale-yellow solid, IR spectrum, ν, cm^{-1}:1546.7, 1645.1, 1655.3, 1728.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.66s (3H, CH_3), 1.87q (2H, *J* = 7.0), 2.32-2.38 (6H), 3.53-3.58m (4H), 4.02t (2H, *J* = 7.0), 5.23dd (1H, *J* = 0.6, 10.7), 5.42dd (1H, *J* = 0.6, 17.1), 6.02dd (1H, *J* = 10.7, 17.1), 6.41d (1H, *J* = 6.8), 8.09d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.56, 24.65, 47.19, 52.81, 54.70, 65.90, 82.49, 97.87, 109.97, 115.25, 136.38, 146.74, 156.05, 165.24, 168.96, HRMS (ESI, m/z) calcd. for $C_{19}H_{29}N_2O_4^+$ $[M+H]^+$: 319.1658, found: 319.1666.

5-(2-(dimethylamino)ethyl)-1-isobutyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (25): Yield 84%, mp 134-136 °C, orange solid, IR spectrum, ν, cm^{-1}: 1543.1, 1633.8, 1651.4, 1750.1, 3124.8, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.84d (3H, *J* = 6.6), 0.92d (3H, *J* = 6.6), 1.53s (3H, CH_3), 1.51-1.63m (1H), 1.68dd (1H, *J* = 6.6, 14.6), 1.90dd (1H, *J* = 5.8, 14.6), 2.56t (2H, *J* = 6.2), 3.98-4.10m (2H), 6.38d (1H, *J* = 6.8), 7.98d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm:23.33, 23.56, 23.79, 24.86, 44.98, 45.83, 46.00, 57.18, 83.53, 97.48, 110.91, 146.52, 155.94, 165.51, 170.61, HRMS (ESI, m/z) calcd. for $C_{16}H_{25}N_2O_3^+$ $[M+H]^+$: 293.1865, found: 293.1875.

5-(2,2-dimethoxyethyl)-1-isobutyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (26): Yield 79%, mp 124-126 °C, white solid, IR spectrum, ν, cm^{-1}: 1125.3, 1135.4, 1546.8, 1641.4, 1738.4, 1745.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.84d (3H, *J* = 6.6), 0.92d (3H, *J* = 6.6), 1.54s (3H, CH_3), 1.52-1.64m (1H), 1.69dd (1H, *J* = 6.4, 14.6), 1.91dd (1H, *J* = 5.8, 14.6), 3.372s (3H), 3.374s (3H), 3.99-4.10m (2H), 4.57t (1H, *J* = 5.3), 6.41d (1H, *J* = 5.3), 7.93d (1H *J* = 6.8) ^{13}C NMR spectrum, δ, ppm: 23.30, 23.56, 23.76, 24.78, 45.93, 49.90, 54.04, 54.13, 83.67, 97.89, 100.88, 111.02, 147.00, 156.13, 165.36, 171.05, HRMS (ESI, m/z) calcd. for $C_{16}H_{24}NO_5^+$ $[M+H]^+$: 310.1654, found: 310.1664.

5-(4-(dimethylamino)phenyl)-1-isobutyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (27): Yield 64%, mp 204-206 °C, pale-yellow solid, IR spectrum, ν, cm^{-1}: 1548.3, 1637.8, 1740.0, 1755.1, 3128.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.91d (3H, *J* = 6.6), 0.96d (3H, *J* = 6.6), 1.58s (3H, CH_3), 1.58-1.70m (1H), 1.75dd (1H, *J* = 6.6, 14.6), 1.94dd (1H, *J* = 6.6, 14.6), 3.04s (6H), 6.52d (1H, *J* = 6.8), 6.80-6.88m (2H), 7.17-7.22m (2H), 7.90d (2H *J* = 6.8) ^{13}C NMR spectrum, δ, ppm: 23.52, 23.64, 24.83, 40.13, 45.87, 83.74, 98.27, 111.76, 112.10, 126.68, 146.17, 149.36, 156.05, 165.46, 171.15, HRMS (ESI, m/z) calcd. for $C_{20}H_{25}N_2O_3^+$ $[M+H]^+$: 341.1865, found: 341.1873.

Ethyl 4-(1-isobutyl-1-methyl-3,4-dioxo-1,4-dihydrofuro[3,4-c]pyridin-5(3H)-yl)benzoate (28): Yield 61%, mp 133-135 °C, white solid, IR spectrum, ν, cm^{-1}: 1125.4, 1134.8, 1547.4, 1710.4, 1730.8, 1735.6, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.91d (3H, *J* = 6.6), 0.96d (3H, *J* = 6.6), 1.42t (6H, *J* = 6.1, $\underline{CH_3}CH_2O$), 1.57s (3H, CH_3), 1.59-1.71m (1H), 1.77dd (1H, *J* = 6.4, 14.6), 1.96dd (1H, *J* = 5.8, 14.6), 3.38q (2H, *J* = 7.1), 6.23d (1H, *J* = 6.8), 7.54-7.58m (2H), 8.01d (1H, *J* = 6.8), 8.13-8.17m (2H) ^{13}C NMR spectrum, δ, ppm: 13.89, 23.54, 23.63, 23.76, 24.74, 45.75, 60.35, 83.98, 90.06, 112.21, 126.65, 129.77, 129.96, 143.05, 145.41, 155.53, 164.21, 165.15, 171.80, HRMS (ESI, m/z) calcd. for $C_{21}H_{24}NO_5^+$ $[M+H]^+$: 370.1654, found: 370.1663.

1-isobutyl-5-(3-isopropoxypropyl)-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (29): Yield 82%, mp 114-116 °C, white solid, IR spectrum, ν, cm^{-1}: 1025.3, 1110.5, 1546.4, 1730.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.84d (3H, *J* = 6.6), 0.92d (3H, *J* = 6.6), 1.11d (6H, *J* = 6.1), 1.53s (3H, CH_3), 1.68dd (1H, *J* = 6.6, 14.6), 1.86-1.97m (2H), 3.35-3.44m (2H), 3.52q (1H, *J* = 6.1), 3.98-4.10m (2H), 6.40d (1H, *J* = 6.8), 7.96d (1H, *J* = 6.8) ^{13}C NMR spectrum, δ, ppm: 21.63, 21.66, 23.38, 23.55, 23.77, 24.93, 28.55, 45.96, 46.56, 63.87, 70.53, 83.54, 97.75, 111.25, 146.11, 155.96, 165.44, 170.63, HRMS (ESI, m/z) calcd. for $C_{18}H_{28}NO_4^+$ $[M+H]^+$: 322.2018, found: 322.2026.

1-isobutyl-5-(2-methoxybenzyl)-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (30): Yield 87%, mp 181-183 °C, white solid, IR spectrum, ν, cm^{-1}: 1103.4, 1125.4, 1548.4, 1740.8, 1750.8, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.85d (3H, *J* = 6.6), 0.93d (3H, *J* = 6.6), 1.53s (3H, CH_3), 1.53-1.65m (1H), 1.68dd (1H, *J* = 6.4, 14.6), 1.90dd (1H, *J* = 5.8, 14.6), 3.89s (3H), 5.07d (1H, *J* = 14.5), 5.13d (1H, *J* = 14.5), 6.40d (1H, *J* = 6.8), 6.90dt (1H, *J* = 0.9, 7.5), 6.96dd (1H,

J = 0.9, 8.3), 7.19dd (1H, *J* = 1.7, 7.5), 7.27dd (1H, *J* = 1.7, 8.3), 7.99d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.33, 23.56, 23.81, 24.74, 45.96, 46.93, 54.91, 83.61, 97.86, 110.20, 111.36, 120.03, 123.29, 128.94, 129.79, 145.94, 156.30, 156.82, 165.43, 170.74, HRMS (ESI, m/z) calcd. for $C_{20}H_{24}NO_4^+$ $[M+H]^+$: 342.1705, found: 342.1714.

5-(4-chlorophenethyl)-1-isobutyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (31): Yield 87%, mp 158-160 °C, white solid, IR spectrum, ν, cm^{-1}: 1553.8, 1549.1, 1730.4, 1745.1, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.82d (3H, *J* = 6.6), 0.92d (3H, *J* = 6.6), 1.51s (3H, CH_3), 1.48-1.58m (1H), 1.68dd (1H, *J* = 6.4, 14.6), 1.89dd (1H, *J* = 5.8, 14.6), 2.94-3.06m (2H), 4.10-4.27m (2H), 6.31d (1H, *J* = 6.8), 7.19-7.26m (4H) ^{13}C NMR spectrum, δ, ppm: 23.41, 23.53, 23.73, 25.09, 33.51, 45.89, 49.91, 83.59, 97.79, 111.27, 127.94, 130.15, 131.47, 136.02, 146.00, 155.89, 165.44, 170.69, HRMS (ESI, m/z) calcd. for $C_{20}H_{23}ClNO_3^+$ $[M+H]^+$: 360.1367, found: 360.1372.

5-(3,4-dimethoxybenzyl)-1-isobutyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (32): Yield 92%, mp 129-131 °C, white solid, IR spectrum, ν, cm^{-1}: 1121.4, 1215.6, 1547.6, 1550.4, 1720.4, 1740.8, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.84d (3H, *J* = 6.6), 0.92d (3H, *J* = 6.6), 1.51s (3H, CH_3), 1.51-1.63m (1H), 1.67dd (1H, *J* = 6.4, 14.6), 1.89dd (1H, *J* = 5.8, 14.6), 3.77s (3H), 3.79s (3H), 5.03d (1H, *J* = 14.0), 5.12d (1H, *J* = 14.0), 6.41d (1H, *J* = 6.8), 6.81d (1H, *J* = 8.2), 6.92dd (1H, *J* = 2.0, 8.2), 7.01d (1H, *J* = 2.0), 8.16d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.37, 23.58, 23.76, 24.77, 45.91, 50.56, 55.09, 55.13, 83.63, 98.26, 111.36, 111.49, 112.39, 120.69, 128.54, 145.68, 148.63, 148.79, 156.05, 165.44, 170.72, HRMS (ESI, m/z) calcd. for $C_{21}H_{26}NO_5^+$ $[M+H]^+$: 372.1811, found: 372.1819.

5-(3-(cyclohex-1-en-1-yl)propyl)-1-isobutyl-1-methylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (33): Yield 78%, mp 204-206 °C, white solid, IR spectrum, ν, cm^{-1}: 1547.1, 1550.3, 1730.4, 1740.5, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.81d (3H, *J* = 6.6), 0.91d (3H, *J* = 6.6), 1.52s (3H, CH_3), 1.47-1.73m (6H), 1.86-1.94m (3H), 1.97-2.03m (2H), 2.21-2.35m (2H), 3.93-4.13m (2H), 5.30t (1H, *J* = 3.8), 6.36d (1H, *J* = 6.8), 7.93d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 21.58, 22.20, 23.37, 23.53, 23.74, 24.58, 25.18, 27.49, 36.64, 45.94, 46.97, 83.46, 97.51, 111.11, 123.52, 133.08, 146.00, 155.79, 165.46, 170.45, HRMS (ESI, m/z) calcd. for $C_{21}H_{30}NO_3^+$ $[M+H]^+$: 344.2226, found: 344.2267.

1-isobutyl-1-methyl-5-phenethylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (34): Yield 89%, mp 169-171 °C, white solid, IR spectrum, ν, cm^{-1}: 1538.4, 1542.6, 1730.4, 1850.4, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.82d (3H, *J* = 6.6), 0.92d (3H, *J* = 6.6), 1.51s (3H, CH_3), 1.48-1.60m (1H), 1.68dd (1H, *J* = 6.4, 14.6), 1.89dd (1H, *J* = 5.8, 14.6), 2.96-3.05m (2H), 4.11-4.29m (2H), 6.29d (1H, *J* = 6.8), 7.15-7.27m (5H, Ph), 7.80d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.43, 23.52, 23.74, 25.10, 34.29, 45.91, 50.19, 83.56, 97.68, 111.24, 126.00, 127.91, 128.47, 137.26, 145.96, 155.88, 165.46, 170.65, HRMS (ESI, m/z) calcd. for $C_{20}H_{24}NO_3^+$ $[M+H]^+$: 326.1756, found: 326.1766.

4-(1-isobutyl-1-methyl-3,4-dioxo-1,4-dihydrofuro[3,4-c]pyridin-5(3H)-yl)benzenesulfonamide (35): Yield 62%, mp 274-276 °C, white solid, IR spectrum, ν, cm^{-1}: 1524.2, 1548.73, 1565.2, 1750.6, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.90d (3H, *J* = 6.6), 0.96d (3H, *J* = 6.6), 1.59s (3H, CH_3), 1.59-1.71m (1H), 1.75dd (1H, *J* = 6.4, 14.6), 1.95dd (1H, *J* = 5.8, 14.6), 6.62d (1H, *J* = 6.8), 6.70d (1H, *J* = 4.6), 7.09d (1H, *J* = 4.6), 7.54-7.59m (2H), 7.96-8.01m (2H), 8.07d (1H, *J* = 6.8), 12.73bs (1H), ^{13}C NMR spectrum, δ, ppm: 23.50, 23.63, 23.78, 24.65, 45.75, 84.04, 99.09, 107.55, 112.05, 123.64, 126.48, 126.93, 141.86, 142.75, 145.69, 155.6, 165.22, 168.56, 171.90, HRMS (ESI, m/z) calcd. for $C_{21}H_{22}N_3O_5S_2^+$ $[M+H]^+$: 460.1001, found: 460.1003.

4-(1-isobutyl-1-methyl-3,4-dioxo-1,4-dihydrofuro[3,4-c]pyridin-5(3H)-yl)benzenesulfonamide (36): Yield 66%, mp 237-239 °C, white solid, IR spectrum, ν, cm^{-1}: 1520.8, 1548.6, 1565.2, 1750.6, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.91d (3H, *J* = 6.6), 0.96d (3H, *J* = 6.6), 1.60s (3H, CH_3), 1.59-1.71m (1H), 1.77dd (1H, *J* = 6.4, 14.6), 1.96dd (1H, *J* = 5.8, 14.6), 6.63d (1H, *J* = 6.8), 7.28s (2H, NH_2), 7.56-7.61m (2H), 7.99-8.04m (2H), 8.10d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 23.51, 23.64, 23.78, 24.70, 45.76, 84.05, 99.07, 112.05, 126.59, 126.92, 141.67, 144.28, 145.74, 155.71, 165.23, 171.91, HRMS (ESI, m/z) calcd. for $C_{18}H_{21}N_2O_5S^+$ $[M+H]^+$: 377.1171, found: 377.1177.

Ehyl 5'-(1-isobutyl-1-methyl-3,4-dioxo-1,4-dihydrofuro[3,4-c]pyridin-5(3H)-yl)-[2,3'-bithiophene]-4'-carboxylate (37): Yield 62%, mp 189-191 °C, yellow solid, IR spectrum, ν, cm^{-1}: 1544.04, 1602.6, 1683.8, 1723.5, 1754.3, ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.91d (3H, *J* = 6.6), 0.96d (3H, *J* = 6.6), 1.03t (3H, *J* = 7.1), 1.60s (3H, CH_3), 1.58-1.70m (1H), 1.77dd (1H, *J* = 6.4, 14.6), 1.97dd (1H, *J* = 5.8, 14.8), 4.08q (2H, *J* = 7.1), 6.67d (1H, *J* = 6.8), 7.05dd (1H, *J* = 3.6, 5.1), 7.18dd (1H, *J* = 1.2, 3.6), 7.39dd (1H, *J* = 1.2, 5.1), 7.61s (1H), 8.05d (1H, *J* = 6.8), ^{13}C NMR spectrum, δ, ppm: 13.15, 23.43, 23.65, 23.76, 24.64, 45.62,

60.29, 84.18, 99.11, 112.02, 123.22, 125.28, 126.52, 126.55, 128.55, 133.07, 135.73, 142.96, 146.55, 155.50, 160.68, 164.84, 172.51, HRMS (ESI, m/z) calcd. for $C_{23}H_{24}NO_5S_2^+$ $[M+H]^+$: 458.1096, found: 458.1103.

CONFLICT OF INTERESTS

The authors declare the absence of a conflict of interest warranting disclosure in this article.

Авторы заявляют об отсутствии конфликта интересов, требующего раскрытия в данной статье.

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