The Austrian Journal of Technical and Natural Sciences, No 1–2
ISSN 2310-5607

PREMIER Publishing
ppublishing.org

DOI:10.29013/AJT-25-1.2-39-44

SINTHESIS OF BENZOPYRIMIDIN-4-ONE AND 3-H SUBSTITUTED DERIVATIVES BASED ON THEM

Zulpanov Fazliddin Abduxakimovich [1]***, Elmuradov Burkhon Juraevich*** [1]***,***
Zakhidova Aziza Bakhromovna [2]***, Arzanov Ravshan Xurramovich*** [3]

[1] Akad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of the Republic of Uzbekistan, Tashkent, Uzbekistan

[2] Branch of Russian Mendeleev University of Chemical Technology
in Tashkent Faculty of Chemical Technology

[3] School № 3, Samarkand District, Uzbekistan

Cite: *Zulpanov F.A., Elmuradov B.J., Zakhidova A.B., Arzanov Ravshan X. (2025). Sinthesis of Benzopyrimidin-4-one and 3-H Substituted Derivatives Based on them. Austrian Journal of Technical and Natural Sciences 2025, No. 1–2.* https://doi.org/10.29013/AJT-25-1.2-39-44

Abstract

As a result of studying the synthesis and biological activity of condensed heterocyclic compounds, new drugs have been developed, including derivatives of 3-alkylquinazolin-4-one, and their bioactive derivatives have been identified. The development of new drugs based on them is relevant.

Keywords: *o-aminobenzoic acid, formamide, cyclization, alkyl halides, alkylation, quinazolin 4-one, 3-alkylquinazolin-4-one, IR, 1H and 13C NMR*

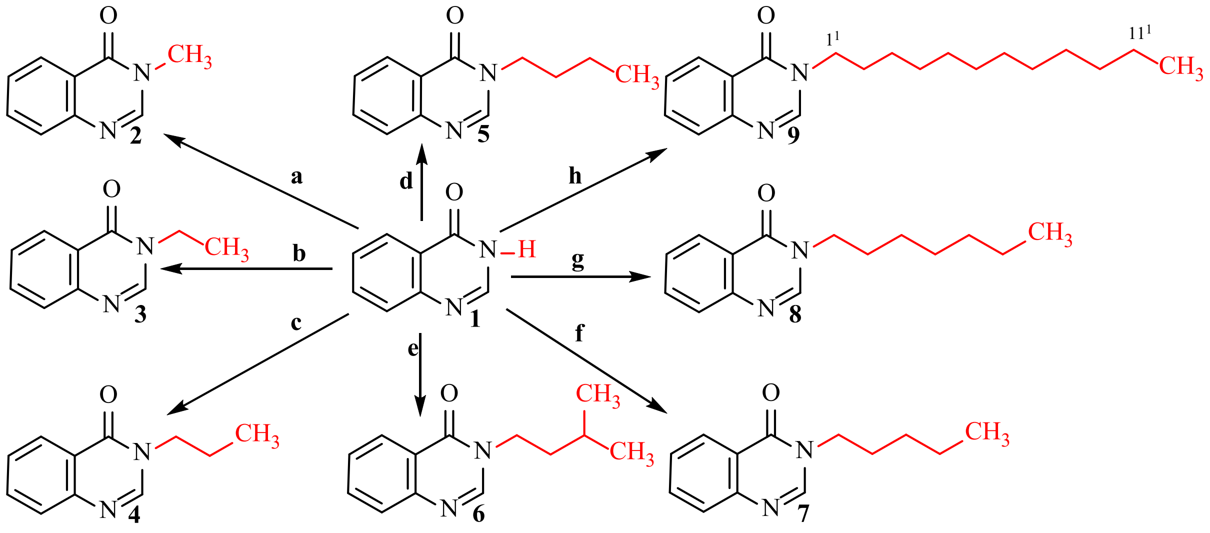
Introduction

Compounds containing a benzopyrimidin ring are considered to have very high medicinal activity. In recent years, various peripa-rations based on many representatives of derivatives formed on the basis of heterocyclic compounds containing benzopyrimidin have been introduced into agricultural and medical practice. Compounds based on benzopyrimidin are widely used against viruses, microbes, fungi, colds and cancer (Xiaoqing Wu, Mingdong Li, Wenhua Tang, Youguang Zheng, Jiqin Lian, Liang Xu, Min Ji., 2011), and as stimulants for plants (Kalpana Singh, P. P. Sharma, A. Kumar, Anurag Chaudhary and R. K. Roy. 2013). In recent years, the incidence of socially significant diseases: cardiovascular diseases (Giovanni Marzaro 2007–2010), diabetes (Expert Opinion on Therapeutic Patents), cancer (Mikra, C., Bairaktari, M., Petridi, M.-T., Detsi, A., Fylaktakidou, K.C., 2022) and viral diseases (Shi-Ben Wang, Xian-Qing Deng, Yan Zheng, Yan-Ping Yuan, Zhe-Shan Quan, Li-Ping Guan. 2012) has been increasing. An example of this is that benzopyrimidin is included in such drugs as imatinib (Raffaella Sordella, Daphne W. Bell, Daniel A. Haber, Jeffrey Settleman. 2004), erlotinib (Martin H. Cohen, John R. Johnson, Yeh-Fong Chen, Rajeshwari Sridhara, Richard Pazdur. 2005), afatinib (Pawan K., Premnath D., Muhammad T., Mazlee S., Yaman M., Nurul S., Muhammad S. et al., 2019), gefitinib (Martin H. Cohen, John R. Johnson, Yeh-Fong Chen, Rajeshwari Sridhara, Richard Pazdur. 2005; Xiaoqing Wu, Mingdong Li, Yang Qu, Wenhua Tang, Youguang Zheng, Jiqin Lian, Min Ji, Liang Xu. 2010; Martin H. Cohen, Grant A. Williams, Rajeshwari Sridhara; Gang Chen, W. David McGuinn, Jr., David Morse Sophia Abraham, Atiqur Rahman, Chenyi Liang, Richard Lostritto, Amy Baird, Richard Pazdur. 2004), which are used against tuberculosis and cancer. In lung cancer, it increased overall survival by 19% and improved progression-free survival (PFS) by 29% compared to chemotherapy (Elmuradov B.Zh., Yakubov U. M., Zhurayev B. B., Tadjimukhamedov K. S., Zakhidov K. A., 2017). These data were approved by the United States Food and Drug Administration (FDA) (Elmuradov B.Zh., Yakubov U. M., Zhurayev B. B., Tadjimukhamedov K. S., Zakhidov K. A., 2017). Anticancer drugs prepared from compounds of the benzopyrimidin family have shown a very low level of toxicity. In this regard, especially the N-3 state electrophilic substitution reactions, i.e. synthesis of new types of derivatives with various halogen compounds of alkyl halides, and with the change of their functional group, it is possible to find new types of fundamental systematic laws and among them, bioactive compounds.

Methods and results

Results and discussion. Bicyclic benzopyrimidin-4-ones are of great practical and theoretical interest. Among the derivatives of benzopyrimidin-4-ones, biologically active compounds have been identified, which are used in medicine and agriculture against various harmful microorganisms. Therefore, it is very important to create efficient synthesis methods of new potentially biologically active derivatives of this class of compounds. For this purpose, in our research, we have identified convenient and effective methods of heterocyclization reaction involving o-aminobenzoic acid and formamide. For this purpose, we considered it appropriate to synthesize new alkyl derivatives as a result of carrying out electrophilic exchange reactions in the 3-position of benzopyrimidin-4-one **(1)**, to determine the regularities in the homologous series of introduced alkyl compounds.

Initially, when benzopyrimidin-4-one is heated in the presence of o-aminobenzoic acid and formamide, two mole of water are separated. As a result of the reaction, we managed to obtain substance **1** in a quantitative yield (98%). Various new types of alkyl compounds were synthesized by interacting benzopyrimidin-4-one with alkyl halides in the 3rd state. This work was carried out in an oil bath at 70–80 °C with the participation of various homologues of alkyl halides **(2–9)**:



a) methyl iodide; b) etyl bromide; c) propyl bromide; d) butyl bromide; e) *izo*-butyl bromide; f) amyl chloride;g) heptyl chloride; h) dodecyl bromide.

Table 1. *IR-spectra (n, cm^{-1}) of 3-alkylbenzopyrimidin-4-ones (1–9)*

№	C-N	C-H	CH_2	C=O	C=N
1	3129	2980	–	2996	1603
2	3067	2989	2971	1649	1612
3	3067	2964	2990	1653	1598
4	3044	2968	2947	1699	1606
5	3067	2877	2936	1666	1607
6	3043	2971	2948	1698	1609
7	3054	2965	2950	1655	1608
8	3054	2966	2926	1655	1509
9	3052	2931	2921	1656	1508

Experimental Part

Synthesis of benzopyrimidin-4-one (1). 1.37 g (0.01 mole) of o-aminobenzoic acid and 6.37 ml (0.04 mole, 7.2 g p = = 1.13 g/sm^3) of formamide were added to a 100-ml round bottom flask and heated for 2–2.5 hours in an oil bath connected with a reflux condenser at 150–155 °C, The substance is recrystallized from water (H_2O) and as a yield 1.43 g (98%) of substance **1**. Melting point 218–120 °C, Rf=0.63 (system: chloroform: methanol – 10:1) is obtained.^{1}H NMR (400 MHz, DMSO-d_6, ppm, δ, J/Hz) δ 12.10 (1H, s, NH), 8.12 (1H, dd, *J* = 8.0, 1.6 Hz, H-5), 7.95 (1H, s, H-2), 7.72 (1H, br t, *J* = 7.5 Hz, H-7), 7.61 (1H, br d, *J* = 7.5 Hz, H-8), 7.44 (1H, br t, *J* = 8.0 Hz, H-6).^{13}C NMR (101 MHz, DMSO-D_6) δ 161.19 (C-4), 149.37 (C-4a), 145.29 (C-2), 134.00 (C-7), 127.59 (C-5), 126.56 (C-6), 126.34(C-8), 123.43 (C-8a).

Synthesis of 3-metylbenzopyrimidin-4-one (2). Put 1.46 g (0.01 mole) of quinazolin-4-one, 30 ml of ethyl alcohol (C_2H_5OH)and 0.616 g (0.011 mole) of KOH into a 100 ml round-bottomed flask and boil and mix slightly. The reaction mixture is cooled and 3.74 ml (0.03 mole) (4.26 g, d=2.28 g/ml) methyl iodide (CH_3I) is added and heated at 75–80 °C for 8 hours. The resulting reaction mixture was cooled and mixed by adding 40 ml of an aqueous solution of 5% NaOH, and then 80 ml of chloroform was poured over it and stirred for 5–10 minutes, and the chloroform layer was separated using a separatory funnel. Chloroform was removed, and the resulting substance was filtered by adding activated carbon in ethyl alcohol (C_2H_5OH) and the liquid part was evaporated and recrystallized. As a yield, 1.12 g (70%) of product **2** was obtained, melting point 102–104 °C, Rf=0.62 (system: chloroform: methanol – 10:1).^{1}H NMR (400 MHz, CD_3OD, ppm. δ, J/Hz): 8.00 (1H, ddd, J=8.1, 1.6, 0.6, H-5), 7.67 (1H, ddd, J=8.5, 7.1, 1.5, H-7), 7.44 (1H, ddd, J=8.2, 1.2, 0.6, H-8), 7.37 (1H, ddd, J=8.2, 7.1, 1.2, H-6), 3.50 (3H, s, 1`), 2.52 (3H, s, H-9).$^{13}$C NMR (100 MHz, $CD_3OD$, δ, ppm.): 157.51 (C-2), 163.62 (C-4), 120.82 (C-4a), 127.61 (C-5), 126.85 (C-6), 135.56 (C-7), 127.41 (C-8), 148.01 (C-8a), 31.50 (C-1`).

Synthesis of 3-Etylbenzopyrimidin-4-one (3). We put 1.46 g (0.01 mole) of benzopyrimidin-4-one, 30 ml of ethyl alcohol (C_2H_5OH) and 0.616 g (0.011 mole) of KOH into a 100 ml round-bottom flask and mix it slightly. After cooling the reaction mixture, 1.94 ml (2.85 g, d=1.47 g/ml) (0.015 mole) ethyl bromide (C_2H_5Br) was added and heated at 75–80 °C for 7 hours. The resulting reaction mixture is cooled and mixed with 30 ml of 5% NaOH aqueous solution, and 60 ml of chloroform is added and extracted. After chloroform extraction, the substance was recrystallized from ethyl alcohol. As a yield, 1.305 g (75%) of substance **3** was obtained, melting point 99–101 °C, R_f=0.62 (system: chloroform: methanol – 10:1).^{1}H NMR (400 MHz, CD_3OD, ppm. δ, J/Hz): 8.08 (1H, ddd, J=8.1, 1.5, 0.6, H-5), 7.67 (1H, ddd, J=8.4, 7.1, 1.5, H-7), 7.51 (1H, ddd, J=8.4, 1.1, 0.6, H-8), 7.42 (1H, ddd, J=8.1, 7.1, 1.1, H-6), 4.13 (2H, k, J=7.1, H-1`), 1.30 (2H, t, J=7.2, H-2`).^{13}C NMR (100 MHz, CD_3OD, δ, ppm.): 156.87 (C-2), 163.32 (C-4), 121.30 (C-4a), 127.76 (C-5), 126.98 (C-6), 135.67 (C-7), 127.42 (C-8), 148.17 (C-8a), 40.92 (C-1`), 13.78 (C-2`).

Synthesis of 3-propylbenzopyrimidin-4-one (4). 1.46 g (0.01 mole) of benzopyrimidin-4-one, 30 ml of ethyl alcohol (C_2H_5OH) and 0.672 g (0.012 mole) of KOH were added to a 100 ml round-bottomed flask and mixed with a little heat. After cooling the reaction mixture, 1.94 ml (1.83 g, d=0.89 g/ml) (0.02 mole) of propyl chloride (C_3H_7Cl) was added and heated at 75–80 °C for 7 hours. The resulting reaction mixture was cooled, mixed with 30 ml of an aqueous solution of 5% NaOH and extracted with 60 ml of chloroform. As a yield, 1.448 g (77%) of substance **4** was obtained, melting point 95–97 °C Rf=0.63 (system: chloroform: methanol – 10:1).^{1}H NMR (400 MHz, CD_3OD+CCl_4, ppm. δ, J/Hz): 8.1 (1H, dd, J=8.13, 1.5, 0.6, H-5), 7.7 (1H, ddd, J=8.4, 7.1, 1.5, H-7), 7.5 (1H, dd, J=8.4, 1.1, 0.6, H-8), 7.4 (1H, ddd, J=8.1, 7.1, 1.1, H-6), 4.14 (2H, k, J=7.1, H-1`), 2.42 (2H, t, J=6.9, H-3`). 1.31 (3H, t, J=7.1, H-2`).$^{13}$C NMR (100 MHz, $CD_3OD$, δ, ppm.): 156.87 (C-2), 164.33 (C-4), 120.31 (C-4a), 126.75 (C-5), 126.98 (C-6), 134.66 (C-7), 127.42 (C-8), 147.17 (C-8a), 39.76 (C-1`), 38.83 (C-2`), 13.72 (C-3`).

Synthesis of 3-Butylbenzopyrimidin-4-one (5). We put 1.46 g (0.01 mole) of benzopyrimidin-4-one, 30 ml of ethyl alcohol (C_2H_5OH) and 0.672 g (0.012 mole) of KOH into a 100 ml round-bottom flask and mix it slightly. After cooling the reaction mixture, add 2.16 ml (2.74 g, d=1.27 g/ml) (0.02 mole) of butyl bromide (C_4H_9Br) and heat it at 75–80 °C for 8 hours. The resulting reaction mixture was cooled, mixed with 30 ml of 5% NaOH aqueous solution, and extracted with 60 ml of chloroform, the chloroform layer was separated, and the resulting substance was recrystallized from ethyl alcohol. As a result, 1.64 g (81%) of substance **5** was obtained, melting point 91–93 °C, Rf=0.64 (system: chloroform: methanol – 10:1).^{1}H NMR spectrum (400 MHz, CD_3OD, δ, ppm, *J*/Hz): 8.32 (1H, s, H-2), 8.23 (1H, ddd, *J*=8.0, 1.6, 0.6, H-5), 7.82 (1H, ddd, *J*=8.5, 7.2, 1.6, H-7), 7.68 (1H, ddd, *J*=8.2, 1.2, 0.6, H-8), 7.55 (1H, ddd, *J*=8.2, 7.1, 1.2, H-6), 4.06 (2H, m, H-1`), 1.77 (2H, m, H-2`), 1.41 (2H, m, H-3`), 0.99 (3H, t, *J*=7.4, H-4`).^{13}C NMR spectrum (100 MHz, CD_3OD, δ, ppm): 149.18 (C-2), 162.61 (C-4), 122.98 (C-4a), 127.39 (C-5), 127.87 (C-6), 135.65 (C-7), 128.53 (C-8), 149.10 (C-8a), 47.86 (C-1`), 32.37 (C-2`), 20.87 (C-3`), 14.00 (C-4`).

Synthesis of 3-*Izo*-butylbenzopyrimidin-4-one (6). We put 1.6 g (0.01 mole) of benzopyrimidin-4-one, 30 ml of ethyl alcohol (C_2H_5OH) and 0.672 g (0.012 mole) of KOH into a 100 ml round-bottom flask and mix it slightly. After cooling the reaction mixture, add 2.16 ml (2.74 g, d=1.27 g/ml) (0.02 mole) of butyl bromide (C_4H_9Br) and heat it at 75–80 °C for 8 hours. The resulting reaction mixture was cooled, mixed with 30 ml of 5% NaOH aqueous solution, and extracted with 60 ml of chloroform, the chloroform layer was separated, and the resulting substance was recrystallized from ethyl alcohol. As a result, 1.6 g (79%) of substance **6** was obtained, melting point 90–92 °C, Rf=0.66 (system: chloroform: methanol – 10:1).^{1}H NMR spectrum (400 MHz, CD_3OD, δ, ppm, *J*/Hz): 8.22 (1H, s, H-2), 8.13 (1H, ddd, *J*=8.0, 1.7, 0.6, H-5), 7.83 (1H, ddd, *J*=8.6, 7.2, 1.6, H-7), 7.66 (1H, ddd, *J*=8.3, 1.2, 0.6, H-8), 7.57 (1H, ddd, *J*=8.3, 7.2, 1.2, H-6), 4.08 (2H, m, H-1`), 1.76 (2H, m, H-2`), 1.43 (2H, m, H-3`), 0.97 (3H, t, *J*=7.4, H-4`).^{13}C NMR spectrum (100 MHz, CD_3OD, δ, ppm): 149.18 (C-2), 162.61 (C-4), 122.98 (C-4a), 127.39 (C-5), 127.87 (C-6), 135.65 (C-7), 128.53 (C-8), 149.10 (C-8a), 47.86 (C-1`), 32.37 (C-2`), 20.86 (C-3`), 14.03 (C-4`).

Synthesis of 3-amylbenzopyrimidin-4-one (7). Put 1.46 g (0.01 mole) of benzopyrimidin-4-one 25 ml of ethyl alcohol (C_2H_5OH) and 0.72 g (0.013 mole) of KOH into a 100 ml round-bottom flask and heat it a little. After cooling the reaction mixture, add 1.45 ml (1.28 g, d=0.88 g/ml) (0.012 mole) of amyl chloride ($C_5H_{11}Cl$) and heat it at 75–80 °C for 9 hours. The resulting reaction mixture is cooled, mixed with 40 ml of 5% NaOH aqueous solution and extracted with 50 ml of chloroform, the chloroform layer is separated, the substance formed by driving off chloroform is recrystallized from ethyl alcohol (C_2H_5OH). As a result, 1.79 g (83%) of substance **7** is obtained, melting point 88–90 °C, R_f=0.63 (system: chloroform: methanol – 10:1).^{1}H NMR spectrum (400 MHz, CD_3OD, δ, ppm, *J*/Hz): 8.25 (1H, s, H-2), 8.16 (1H, dd, *J*=8.0, 1.6, H-5), 7.76 (1H, ddd, *J*=8.3, 7.2, 1.6, H-7), 7.62 (1H, dd, *J*=8.2, 1.1, H-8), 7.49 (1H, ddd, *J*=8.2, 7.1, 1.2, H-6), 3.98 (2H, m, H-1`), 1.72 (2H, m, H-2`), 1.31 (2H, m, H-3`), 1.31 (2H, m, H-4`), 0.86 (3H, t, *J*=7.0, H-5`).$^{13}C$ NMR spectrum (100 MHz, $CD_3OD$, δ, ppm): 149.13 (C-2), 162.59 (C-4), 122.90 (C-4a), 128.55 (C-5), 127.37 (C-6), 135.67 (C-7), 127.83 (C-8), 149.01 (C-8a), 48.10 (C-1`), 29.81 (C-2`), 29.93 (C-3`), 23.30 (C-4`), 14.27 (C-5`).

Synthesis of 3-geptylbenzopyrimidin-4-one (8). We put 1.46 g (0.01 mole) of benzopyrimidin-4-one, 30 ml of ethyl alcohol (C_2H_5OH) and 0.73 g (0.013 mole) of KOH into a 100 ml round-bottom flask and mix it slightly. After cooling the reaction mixture, 1.857 ml (1.615 g, d=0.87 g/ml) (0.012 mole) of heptyl chloride ($C_7H_{15}Cl$) was added and boiled at 75–80 °C for 9 hours. The resulting reaction mixture was cooled, mixed with 30 ml of an aqueous solution of 5% NaOH and extracted with 60 ml of chloroform. As a result, 2.07 g (85%) of substance **8** was obtained, melting point 87–89 °C, R_f 0.64 (system: chloroform: methanol – 10:1).^{1}H NMR spectrum (400 MHz, CD_3OD, δ, ppm, *J*/Hz): 8.26 (1H, s, H-2), 8.17 (1H, dd, *J*=8.1, 1.7, H-5), 7.76 (1H, m, H-7), 7.63 (1H, m, H-8), 7.50 (1H, m, H-6), 3.99 (2H, m, H-1`), 1.72 (2H, m, H-2`), 1.30 (2H, m, H-3`), 1.30 (2H, m, H-4`), 1.23 (2H, m, H-5`), 1.23 (2H, m, H-6`), 0.82 (3H, t, *J*=6.7, H-7`).$^{13}C$ NMR spectrum (100 MHz, $CD_3OD$, δ, ppm): 149.16 (C-2), 162.63 (C-4), 122.92 (C-4a), 128.58 (C-5), 127.39 (C-6), 135.70 (C-7), 127.85 (C-8), 149.03 (C-8a), 48.14 (C-1`), 29.96 (C-2`), 27.62 (C-3`), 30.23 (C-4`), 32.82 (C-5`), 23.59 (C-6`), 14.39 (C-7`).

Synthesis of 3-dodecylbenzopyrimidin-4-one (9). We put 1.46 g (0.01 mole) of benzopyrimidin-4-one, 30 ml of ethyl alcohol (C_2H_5OH) and 0.896 g (0.016 mole) of KOH into a 100 ml round-bottom flask and mix it slightly. The reaction mixture was cooled and 2.64 ml (2.74 g, d=1.04 g/ml) (0.011 mole) of dodecyl bromide ($C_{12}H_{25}Br$) was added to it and heated at 75–80 °C for 9 hours. The resulting reaction mixture was cooled, mixed with 30 ml of 5% NaOH aqueous solution and extracted with 70 ml of chloroform, the chloroform layer was separated, and the resulting substance was recrystallized from ethyl alcohol. As a result, 2.7 g (86%) of substance **9** was obtained, melting point 86–88 °C, Rf=0.62 (system: chloroform: methanol – 10:1).^{1}H NMR spectrum (600 MHz, $CDCl_3$, δ, ppm, *J*/Hz): 8.03 (1H, s, H-2), 8.32 (1H, dd, *J*=8.1, 1.4, H-5), 7.76 (1H, ddd, *J*=8.3, 6.9, 1.5, H-7), 7.71 (1H, dd, *J*=8.2, 1.4, H-8), 7.51 (1H, ddd, *J*=8.2, 6.8, 1.4, H-6), 4.00 (2H, m, H-1`), 1.78 (2H, m, H-2`), 1.37 (2H, m, H-3`), 1.34 (2H, m, H-5`), 1.28 (2H, m, H-6`), 1.28 (2H, m, H-11`), 1.27 (2H, m, H-9`), 1.26 (2H, m, H-7`), 1.26 (2H, m, H-8`), 1.25 (2H, m, H-4`), 1.25 (2H, m, H-10`), 0.87 (3H, t, *J*=7.0, H-12`).^{13}C NMR spectrum (150 MHz, $CDCl_3$, δ, ppm): 146.74 (C-2), 161.19 (C-4), 122.32 (C-4a), 126.83 (C-5), 127.33 (C-6), 134.25 (C-7), 127.53 (C-8), 148.26 (C-8a), 47.24 (C-1`), 29.52 (C-2`), 26.80 (C-3`), 29.66 (C-4`), 29.31 (C-5`), 29.45 (C-6`), 29.72 (C-7`), 29.72 (C-8`), 29.57 (C-9`), 32.02 (C-10`), 22.80 (C-11`), 14.25 (C-12`).

Conclusion

An improved method of quantitative yield synthesis of benzopyrimidin-4-onewas developed by carrying out the heterocyclization reaction in the presence of formamide and o-aminobenzoic acid. Synthesis of 3-alkylbenzopyrimidin-4-ones as a result of alkylation reactions of the obtained substance in the presence of alkylating agents of different structures was systematically studied. The obtained substances can be used as important synthons for further modifications. The structure of the obtained substances was analyzed and confirmed using modern physical research methods.

References

Xiaoqing Wu, Mingdong Li, Wenhua Tang, Youguang Zheng, Jiqin Lian, Liang Xu, Min Ji. Design synthesis and in vitro antitumor activity evaluation of novel 4-pyrrylamino quinazoline derivatives. *Chemical biology & drug design*. 2011; 78(6): 932–940 p. URL: https://doi.org/10.1111/j.1747–0285.2011.01234.x

Kalpana Singh, P. P. Sharma, A. Kumar, Anurag Chaudhary and R. K. Roy. 4-Aminoquinazoline Analogs: A Novel Class of Anticancer Agents. Mini-Reviews in Medicinal Chemistry. olume 13, – Issue 8, 2013. – P. 1177–1194. DOI: 10.2174/1389557511313080006

Giovanni Marzaro. (PhD), Adriano Guiotto, Adriana Chilin. Quinazoline derivatives as potential anticancer agents: a patent review (2007–2010).

Expert Opinion on Therapeutic Patents, – 22(3). – P. 223–252. URL: https://doi.org/10.1517/13543776.2012.665876

Mikra, C., Bairaktari, M., Petridi, M.-T., Detsi, A., Fylaktakidou, K. C. Green Process for the Synthesis of 3-Amino-2-methyl-quinazolin- 4(3H)-one Synthones and Amides Thereof: DNA Photo-Disruptive and Molecular Docking Studies. Processes 2022. – 10. – 384 p. URL: https://doi.org/10.3390/pr10020384

Shi-Ben Wang, Xian-Qing Deng, Yan Zheng, Yan-Ping Yuan, Zhe-Shan Quan, Li-Ping Guan. Synthesis and evaluation of anticonvulsant and antidepressant activities of 5-alkoxytetrazolo[1,5-c]thieno[2,3-e]pyrimidine derivatives. European Journal of Medicinal Chemistry – Vol. 56. – October 2012. – P. 139–144. URL: https://doi.org/10.1016/j.ejmech.2012.08.027

Raffaella Sordella, Daphne W. Bell, Daniel A. Haber, Jeffrey Settleman. Gefitinib-Sensitizing EGFR Mutations in Lung Cancer Activate Anti-Apoptotic Pathways. Europe PMC. 20 Aug. 2004. – Vol 305. – Issue 5687. – P. 1163–1167. DOI: 10.1126/science.1101637

Martin H. Cohen, John R. Johnson, Yeh-Fong Chen, Rajeshwari Sridhara, Richard Pazdur. FDA Drug Approval Summary: Erlotinib (Tarceva®) Tablets. The Oncologist, – Vol. 10. – Issue 7. – August 2005. – P. 461–466. URL: https://doi.org/10.1634/theoncologist.10–7–461

Pawan K., Premnath D., Muhammad T., Mazlee S., Yaman M., Nurul S., Muhammad S. et al. A controlled, efficient and robust process for the synthesis of an epidermal growth factor receptor inhibitor: *Afatinib Dimaleate*. February 4, 2019. – 5. – P. 105–106. DOI:10.25082/CR.2019.01.001

Xiaoqing Wu, Mingdong Li, Yang Qu, Wenhua Tang, Youguang Zheng, Jiqin Lian, Min Ji, Liang Xu. Design and synthesis of novel Gefitinib analogues with improved anti-tumor activity. Bioorg Med Chem. 2010. Apr 21; 18(11): 3812–3822. Doi: 10.1016/j.bmc.2010.04.046

Martin H. Cohen, Grant A. Williams, Rajeshwari Sridhara; Gang Chen, W. David McGuinn, Jr., David Morse Sophia Abraham, Atiqur Rahman, Chenyi Liang, Richard Lostritto, Amy Baird, Richard Pazdur. RFDA drug approval summary: gefitinib (ZD1839) (Iressa) tablets. *Oncologist*; – 8: 2004: 303–306. URL: https://doi.org/10.1158/1078-0432.CCR-03-0564

Elmuradov B. Zh., Yakubov U. M., Zhurayev B. B., Tadjimukhamedov K. S., Zakhidov K. A. Selective Bromination of Tricyclik Quinazolines // World wide journal of multidisciplinary research and development. 2017. – 3(10). – P. 1–5.

submitted 29.01.2025;
accepted for publication 12.02.2025;
published 28.03.2025

Contact: zulpanovf@g.mail.com