SYNTHESIS OF PYRAZOLO[3,4-*d*]PYRIMIDINONES

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Annotation.2-Methyl-6,7,8,9-tetrahydropyrazolo[3,4-*d*]pyrido[1,2-a]pyrimidin-4(2*H*)-one was synthesized as a result of the cyclization reaction of methyl 3-amino-1-methyl-1*H*-pyrazole-4-carboxylate with piperidin-2-one.

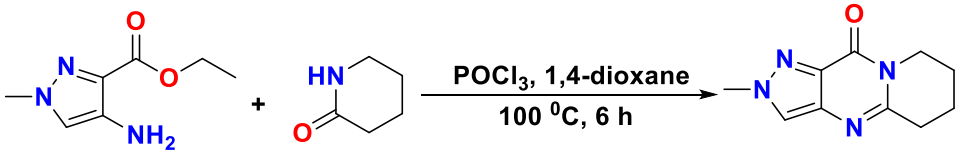
Keywords: 2-Methyl-6,7,8,9-tetrahydropyrazolo[3,4-*d*]pyrido[1,2-a]pyrimidin-4(2*H*)-one, methyl 3-amino-1-methyl-1*H*-pyrazole-4-carboxylate, piperidin-2-one, **phosphoryl chloride.**

Compounds containing a pyrazolopyridopyrimidine core represent an important class of pharmacologically active substances in modern medicine and pharmaceutical chemistry. Because this condensed heterocyclic system simultaneously incorporates pyrazole, pyridine, and pyrimidine fragments, it can engage effectively with biological targets. The pyrazolo[3,4-*d*]pyrimidine core has been reported in numerous studies to exhibit biological activity that inhibits the growth of cancer cells. For example, some synthesized compounds were found to reduce growth in more than 60 human cancer cell lines, and some of them showed very low IC_{50} values, indicating high anticancer activity [1]. In studies, certain pyrazolopyridopyrimidine derivatives have demonstrated

efficacy as VEGFR-2 kinase inhibitors, exhibiting antitumor effects by arresting the cell cycle at the G2/M phase and inducing apoptosis [2]. In broader studies, pyrazolopyrimidine systems have been investigated as potential therapeutic agents for various disease conditions, including the central nervous system, cardiovascular system, inflammation, and cancer, due to their structural similarity to purine analogs [3]. Compounds based on the pyrazolo[3,4-*d*]pyrimidine core exhibit antitumor activity, demonstrating antiproliferative effects in human cancer cell lines and showing VEGFR-2 kinase inhibitory properties, making them promising substrates for the design of antineoplastic agents [4].

RESULTS AND DISCUSSION

2-Methyl-6,7,8,9-tetrahydropyrazolo[3,4-*d*]pyrido[1,2-a]pyrimidin-4(2*H*)-one was synthesized by cyclizing of methyl 3-amino-1-methyl-1*H*-pyrazole-4-carboxylate with piperidin-2-one in the presence of phosphoryl chloride as a catalyst. The reaction was carried out in 1,4-dioxane at 100 °C for 6 h, and the progress of the reaction was monitored by thin-layer chromatography (TLC).



The chemical structure of the newly obtained arylidene **pyrazolopyridopyrimidinones** was confirmed using spectroscopic methods. The chemical and physicochemical properties of the new compounds, including proton and carbon nuclear magnetic resonance **(^{1}H and ^{13}C NMR)** spectra, melting points, and molecular masses, were determined and verified using high-precision analytical techniques.

CONCLUSION

In this study, the chemical properties of newly synthesized arylidene **pyrazolopyridopyrimidinone** derivatives were investigated. The results showed that the chemical composition and structure of the synthesized compounds were fully confirmed using spectroscopic methods. In particular, **^{1}H and ^{13}C NMR** spectra were recorded, and molecular masses and melting points were measured using high-precision instruments. The newly synthesized arylidene pyrazolopyridopyrimidinone derivatives exhibited high reactivity, demonstrating the ability to undergo various chemical transformations with both electrophilic and nucleophilic reagents. The results of this study indicate that the newly synthesized **pyrazolopyridopyrimidinone** derivatives may serve as potential biologically active compounds in the future. This research provides an important foundation for the chemical modification of pyrazolopyridopyrimidinone derivatives and for identifying new areas of their application.

REFERENCES

1. Ahmed M. Abdelhamed, Rasha A. Hassan, *Novel pyrazolo[3,4-d]pyrimidine derivatives: design, synthesis, anticancer evaluation, VEGFR-2 inhibition, and antiangiogenic activity*, RSC Medicinal Chemistry. https://doi.org/10.1039/D3MD00476G
2. Monika Chauhan, Raj Kumar, *Medicinal attributes of pyrazolo[3,4-d]pyrimidines: a review*, Bioorganic & Medicinal Chemistry, 2013, https://doi.org/10.1016/j.bmc.2013.07.0274
3. Zukela Ruzi, Khurshed Bozorov, Lifei Nie, Jiangyu Zhao, Haji Akber Aisa, *Novel pyrazolo[3,4-d]pyrimidines as potential anticancer agents:*

Synthesis, VEGFR-2 inhibition, and mechanisms of action, Biomedicine & Pharmacotherapy, 2022. https://doi.org/10.1016/j.biopha.2022.1139485

4. Zukela Ruzi, et al., *Discovery of novel (E)-1-methyl-9-(3-methylbenzylidene)-6,7,8,9-tetrahydropyrazolo[3,4-d]pyrido[1,2-a]pyrimidin-4(1H)-one as DDR2 kinase inhibitor: Synthesis, molecular docking, and anticancer properties*, Bioorganic Chemistry, 2023, 135: 106506