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ZAMONAVIY INNOVATSION TADQIQOTLARNING DOLZARB MUAMMOLARI VA RIVOJLANISH TENDENSIYALARI: YECHIMLAR VA ISTIQBOLLAR

mavzusidagi Respublika ilmiy-texnik anjuman materiallari to‘plami

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“Zamonaviy innovatsion tadqiqotlarning dolzarb muammolari va rivojlanish tendensiyalari: yechimlar va istiqbollar” mavzusidagi Respublika ilmiy-texnik anjuman materiallari to‘plami – Jizzax: O‘zMU Jizzax filiali, 2024-yil 17-18-may. 410-bet.

Respublika miqyosidagi ilmiy-texnik anjuman materiallarida zamonaviy innovatsion tadqiqotlarning dolzarb muammolari va rivojlanish tendensiyalari sohasidagi innovatsion tadqiqotlar aks etgan.

Globallashuv sharoitida davlatimizni yanada barqaror va jadal sur’atlar bilan rivojlantirish bo‘yicha amalga oshirilayotgan islohotlar samarasini yaxshilash sohasidagi ilmiy-tadqiqot ishlariga alohida e’tibor qaratilgan. Zero iqtisodiyotning, ijtimoiy sohalarni qamrab olgan modernizatsiya jarayonlari, hayotning barcha sohalarini liberallashtirishni talab qilmoqda.

Ushbu ilmiy ma’ruza tezislari to‘plamida mamlakatimiz va xorijlik turli yo‘nalishlarda faoliyat olib borayotgan mutaxassislar, olimlar, professor-o‘qituvchilar, ilmiy tadqiqot institutlari va markazlarining ilmiy xodimlari, tadqiqotchilari, magistr va talabalarning ilmiy-tadqiqot ishlari natijalari mujassamlashgan.

Mas’ul muharrirlar: DSc.prof. Turakulov O.X., PhD. O‘ralov A.I.

Tahrir hay’ati a’zolari: p.f.d.(DSc), prof. Turakulov O.X., b.f.f.d. (PhD) O‘ralov A.I., t.f.f.d.(PhD), dotsent Abdumalikov A.A., t.f.n., dots. Baboyev A.M., t.f.f.d.(PhD), dots. Abduraxmanov R.A., p.f.f.d.(PhD) Eshankulov B.S., p.f.n., dots. Alimov N.N., p.f.f.d.(PhD), dotsent Alibayev S.X., p.f.f.d. (PhD) Halimov O‘.H., p.f.f.d.(PhD), dotsent Karshiyev A.A., f.f.f.d.(PhD), dotsent Sindorov L.K., t.f.f.d.(PhD), dotsent Nasirov B.U., b.f.f.d. (PhD), dotsent Mustafaqulov M.A., f.f.f.d. (PhD) Alibekov D.A.., f-m.f.f.d. (PhD) Sharipov X.F., ps.f.f.d.(PhD) Norbekova B.Sh., i.f.n., dots. Tsoy M.P., Qayumov O.A., Jo‘rayev M.M.

Mazkur to‘plamga kiritilgan ma’ruza tezislarining mazmuni, undagi statistik ma’lumotlar va me’yoriy hujjatlarning to‘g‘riligi hamda tanqidiy fikr-mulohazalar, keltirilgan takliflarga mualliflarning o‘zlari mas’uldirlar.

$XY = \sqrt{MY \cdot NY}$. Откладывая отрезок XY на прямой l, строим точку X. Зная положение трёх точек окружности M, N, X легко построить всю окружность.

*Построение:*1. точка $Y = MN \cap l$;

2. отрезок $m = \sqrt{MY \cdot NY}$;

3. точка X на прямой l, для которой $YX = m$;

4. окружность через три точки M, N, X.

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SYNTHESIS OF TRICYCLIC PYRAZOLO[4,5-D]PYRIMIDINONES BY REACTION OF PYRROLIDONE-2 AND ETHYL ESTERS OF 5-AMINO-1-*N*-ARYL-1H-1,2,3-TRIAZOLES

Murtazaeva Z., Buronov A., Bozorov Kh.
Samarkand State University named after Sh.Rashidov
zarifamurtazayeva92@gmail.com

Abstract. The condensation reaction of 5-Amino-1-*N*-aryl-1H-1,2,3-triazole ethyl ethers with piperidine-2-one was carried out in 3 steps. Phenyl azide derivatives were obtained in the first step, 5-amino-1-N-aryl-1H-1,2,3-triazole ethyl ethers in the second step, and new tricyclic triazolo[4,5-d]pyrimidinone derivatives were obtained in the third step, and their structures were determined by ^{1}H, ^{13}C NMR and HRMS analysis.

Keywords: cancer, triazole, cyanoacetate, ethyl esters of 5-amino-1-*N*-aryl-1H-1,2,3-triazole, synthesis.

Over the years, heterocyclic compounds, especially five- and six-membered compounds, have attracted increasing attention from the pharmaceutical community due to their therapeutic value [1,2]. Drug evaluation reports of drugs on the market show that 68% of them are heterocycles [3]. Therefore, in recent decades, it is not surprising that compounds with heterocyclic nuclei have attracted much attention in the development of new pharmaceuticals due to their chemotherapeutic value [4]. N-containing heterocycles play an important role not only in biology but also in many other industrial fields related to specialty and fine chemistry. 1,2,3-triazole derivatives are widely used as a key structure with many interesting applications in the humanitarian field [5]. They can form hydrogen bonds, which may be of great importance for their bioavailability and solubility [6]. In addition, 1,2,3-triazoles represent an important category of compounds that have various industrial, agricultural and biological properties such as antimicrobial, anticancer, antidiabetic, anti-inflammatory, antiviral, antituberculosis, antimalarial, antileishmanial and antifungal [7-14].

The skeleton of 1,2,3-triazole, usually formed by a versatile, efficient and selective copper-catalyzed azido-alkyne cycloaddition reaction can not only serve as a pharmacophore but also act as a linker to bind various pharmacophores [15,16]. Mechanistically, 1,2,3-triazoles are able to inhibit cancer cell proliferation, arrest the cell cycle and induce apoptosis. In turn, 1,2,3-triazoles have demonstrated promising in vitro and in vivo activity against both drug-sensitive and drug-resistant cancers, including multidrug-resistant forms [17,18]. In particular, 1,2,3-triazole-containing hybrids can exert dual or multiple anticancer mechanisms of action, representing an important source for the development of novel anticancer candidates.

In this context, our research group presents a novel condensed tricyclic compound containing 1,2,3-triazole ring and their biological properties.

Results and Discussion.

1. Preparation of phenyl azides (2a~2e)

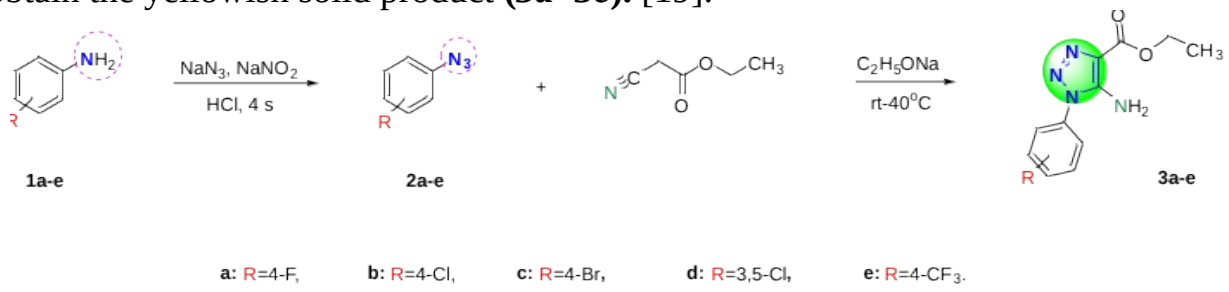
Under the condition of ice bath, substituting aniline (30 mmol), hydrochloric acid (6 mol/L, 50 ml) were added into 250 ml reaction bottle, stirred for 10 min, $NaNO_2$ (2.8 g) aqueous solution of 25 ml was added slowly dropwise, stirred for 30 min, sodium azide (2.6 g) aqueous solution 50 ml was added slowly dropwise. The stirring was continued until the raw materials disappeared, the reaction solution was extracted with ethyl acetate, the organic phases were combined, dried with anhydrous sodium sulfate, and concentrated in a vacuum to obtain the intermediate phenyl azide

(***2a~2e***). The reaction solution was extracted with ethyl acetate, the organic phases were combined, dried with anhydrous sodium sulfate and concentrated in a vacuum to obtain the intermediate phenyl azide (***2a~2e***). The product is used directly without further purification.

2. Preparation of ethyl 1-phenyl-5-amino-4-ethoxycarbonyl-1,2,3-triazole-4-carboxylate (3a~3e):

Take 0.26 g of sodium, shear it in petroleum ether and dry it with filter paper, place it carefully/slowly in 15 ml of anhydrous ethanol and leave it to dissolve all together (to form ethanol sodium solution) and set aside.

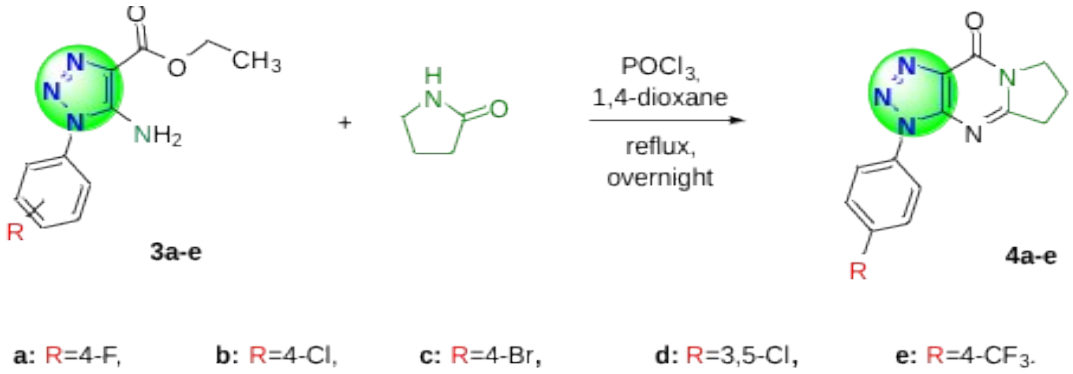
To the reaction flask, ethyl cyanoacetate (1.17 ml, 0.11 mol), substituted phenyl azide (0.1 mol) were added sequentially, and the freshly prepared sodium ethanol solution was added drop by drop with stirring, the reaction gradually precipitated solid, and the reaction was monitored for completeness by TLC. The residual ethanol was removed under reduced pressure, saturated aqueous NH_4Cl solution was added to the reaction solution, extracted with 100 ml of dichloromethane, the organic layer was washed three times with 100 ml of saturated saline, dried with anhydrous sodium sulfate, concentrated under reduced pressure, and recrystallized in 20 mL of ethanol to obtain the yellowish solid product **(*3a~3e*).** [19].



Scheme 1: General scheme for the synthesis of 5-amino-1-N-aryl-1H-1,2,3-triazoles ethyl esters derivatives

2.3 Synthesis of target compounds (4a-4e):

Intermediates ***3a~3e*** (0.4 mmol) were dissolved in 2 ml of anhydrous 1,4-dioxane, anhydrous phosphorous trichloride (0.8 mmol, 73 ml) was added, stirred at room temperature for 10 min, the pyrrolidone-2 (0.44 mmol, 1.1 times the amount of substance) was added, heated to reflux, and the reaction was monitored for completeness by TLC. The system was reduced to room temperature, the solvent was removed under reduced pressure, the product was dissolved in 100 mL of water and extracted with 50 ml of ethyl acetate, the organic layer was washed with 50 mL of saturated saline, dried with anhydrous sodium sulfate, concentrated under reduced pressure, and the crude product was purified by column chromatography [V(petroleum ether): V(ethyl acetate) = 3:1 - 1:1] to afford the target compounds (***4a-4e***). (***Scheme** 2*).



Scheme 2: General scheme for the synthesis of tricyclic triazolo[4,5-d]pyrimidinone derivatives

All the synthesized ethyl esters of 5-amino-1-N-aryl-1H-1,2,3-triazoles and tricyclic triazolo[4,5-d]pyrimidinone derivatives were determined by 1H-, 13C-NMR and HRMS analysis.

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O‘SMIRLIK DAVRINING PSIXIK HOLATLARI (IRODAVIY HOLATLARI)

Adilova Madina Shamsidinovna
O‘zbekiston Milliy universiteti Jizzax filiali
Pardayev Humoyun Farhod o‘g‘li,
Mamarasulova Xolida Xo‘jaaxmad qizi
O‘zbekiston Milliy universiteti Jizzax filiali talabalari

Annotatsiya: Ushbu maqolada o‘smirlarda iroda shakllanishining psixologik xususiyatlari xulq-atvor ko‘rinishlari, ta‘sir etuvchi omillar, fiziologik o‘zgarishlar, o‘zligini anglashi, o‘smir shaxsining irodaviy sifatlarini o‘rganish, ijtimoiy muhutdagi turli holatlarda ham o‘smirning jismoniy,ruhiy,psix jarayonlarda har tamonlama irodasi sog‘lom va mustahkam shakillangan bo‘lishi kerak