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COMMON METHODS TO SYNTHESIZE 2-(3-HETARYL-1H-1,2,4-TRIAZOLE-5-YL)-PHENYLAMINES FOR EVALUATION AS POTENTIAL CHEMOTHERAPEUTIC AGENTS

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Introduction. Over the past few decades, scientists have been dedicating significant focus to the development of 1,2,4-triazole derivatives [1] that exhibit a wide range of impactful biological properties: antifungal, antitubercular, antioxidant, anticancer, anti-inflammatory, analgesic, antidiabetic, anticonvulsant, and anxiolytic, etc. [2]. The list of new drugs based on this heterocyclic core is constantly updated, namely itraconazole, posaconazole, voriconazole (antifungal), ribavirin (antiviral), rizatriptan (antimigraine), alprazolam (anxiolytic), trazodone (antidepressant), letrozole and anastrozole (antitumor). This is why 1,2,4-triazole consistently garners interest for research.

Aim. Development of effective methods of novel 2-(3-hetaryl-1*H*-1,2,4-triazol-5-yl)phenylamines' synthesis; preliminary study of their antibacterial and antifungal properties.

Materials and methods. The individuality and structure of the synthesized substances were confirmed by physico-chemical methods: elemental analysis, LC-MS, IR and ^{1}H NMR spectrometry. The antimicrobial activity screening was carried out by the serial dilution method against *E. coli*, *S. aureus*, *K. aerogenes*, *P. aeruginosa*, and *C. albicans*.

Results. The synthesis of hydrazides **3** was carried out by acylation of 4-hydrazino-quinazoline **1** with imidazolides of the corresponding acids in dioxane, or by interaction of 4-chloroquinazoline **2** with proper hydrazides (Figure). 2-Hetaryl-[1,2,4]triazolo[1,5-*c*]quinazolines (**4**) were obtained by dehydration of **3** in glacial acetic acid. The latter were converted to 2-(3-hetaryl-1*H*-1,2,4-triazol-5-yl)phenylamines (**5**) in reactions with nucleophilic reagents. Namely, compounds **4** are more completely and with quantitative yields subject to cleavage of the heterocyclic quinazoline system in hydrochloric acid solutions [3].

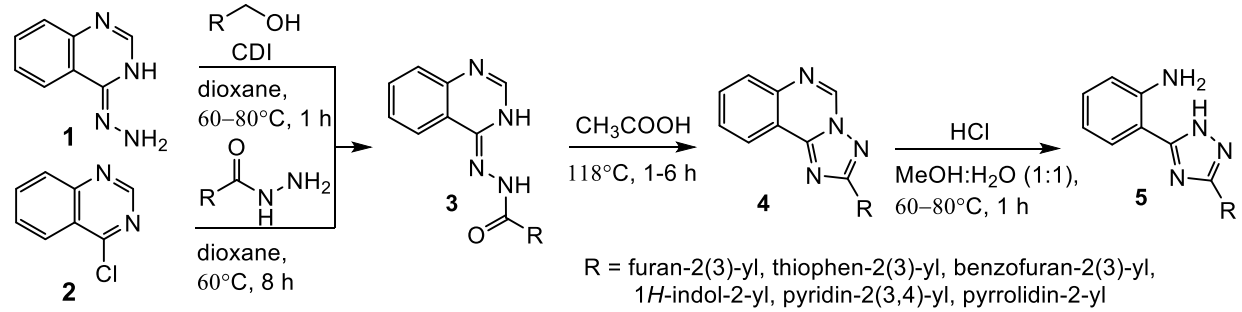

Figure. Synthesis of 2-(3-hetaryl-1*H*-1,2,4-triazol-5-yl)phenylamines.

Most of the synthesized compounds showed absence to moderate antimicrobial activity, but within series 5, those, containing furan-3-yl or thiophen-3-yl, exhibited the most potent antibacterial and antifungal properties, comparable with references nitrofural, trimethoprim and ketoconazole.

Conclusions. The preparative methods to obtain 2-(3-hetaryl-1*H*-1,2,4-triazol-5-yl)phenylamines have been worked out. The investigation of antimicrobial properties revealed the "structure-activity" correlation and pinpointed the additional pharmacophoric fragments responsible for potent antimicrobial activity, specifically furan-3-yl and thiophen-3-yl.

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