SYNTHESIS OF 3-((4-(*N*-(5-METHYLISOXAZOL-3-YL)SULFAMOYL)PHENYL)AMINO)PROPANOIC ACID DERIVATIVES

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Heterocycles being as a bridge between life and chemical sciences attract considerable attention of researchers. A wide variety of investigations in heterocycle chemistry is currently carried out worldwide. Isoxazoles represent a large group of these compounds, the majority of which display broad-spectrum pharmacological potential [1–11]. Isoxazole derivatives such as *Sufamethoxazole* (**1**), *Sulfisoxazole* (**2**) or *Oxacillin* (**3**) (Figure 1) are frequently applied in clinical and therapeutic practice for the treatment of various infections (middle ear, respiratory, urine, and intestinal infections).

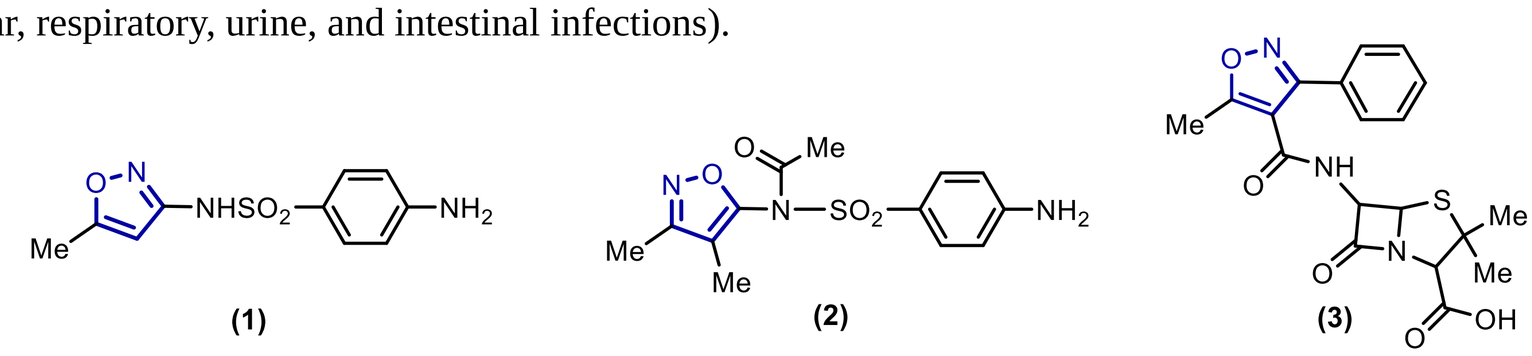
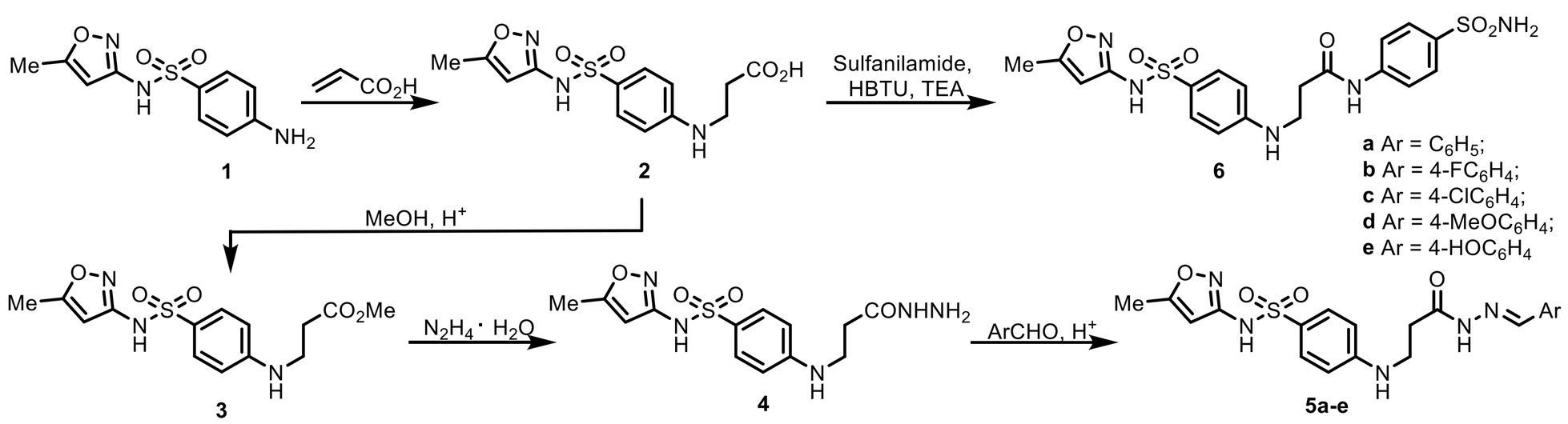


Figure 1. Antibiotics based on isoxazole scaffold.

Taking into account the above-mentioned facts, as a starting material for the study we have selected a 4-amino-*N*-(5-methylisoxazol-3-yl)benzenesulfonamide (**1**), which is known as *Sulfamethoxazole*, an oral antibiotic used to treat bronchitis, urinary track infections, prostatitis as well as is effective for both Gram negative and positive bacteria.

An interaction of sulfonamide **1** with acrylic acid in water at reflux afforded *β*-amino acid **2** (Scheme 1) in 95% yield. The esterification of **2** was performed with methanol, and the formed methyl ester **3** was then reacted with hydrazine monohydrate in propan-2-ol at reflux for 24 hours to give acid hydrazide **4**. A set of hydrazones **5a–e** was developed by condensation of **4** with various aromatic aldehydes. The reactions were carried out in 1,4-dioxane at reflux for 24 hours in the presence of a catalytic amount of hydrochloric acid.



Scheme 1. Synthesis of 4-amino-*N*-(5-methylisoxazol-3-yl)benzenesulfonamide derivatives **2–6**.

To expand the variety of sulfonamide derivatives the amidation reaction of acid **2** was carried out. It was performed in DMSO at room temperature, at stirring for 20 h, in the presence of HBTU as a coupling agent in combination with TEA and gave the amide **6**. The synthesized compounds were confirmed by their spectroscopic and elemental analyses data.

The performed work is the initial part of a large-scale study. The preliminary *in vitro* antimicrobial tests revealed promising results, which encourage further investigation.

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