SYNTHESIS OF NEW 3-(2-OXOBENZODOXAZOL-3(2H)-YL)PROPANOIC ACID DERIVATIVES

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The novel research and many scientific publications demonstrate the 2-oxobenzo[d]oxazole fragment to be versatile for drug discovery. Nowadays a large number of pharmaceutics are developed for medicinal use but the increasing resistance of pathogens to available pharmaceuticals has created an essential demand for new efficient classes of antimicrobial agents. A unique small-ring heterocycle – oxazole containing nitrogen and oxygen atoms, play an important role in medicinal chemistry and is widely used in the development of bioactive compounds, drugs, as well as industrial products [1, 2]. Pharmaceuticals based on oxazole and its derivatives are used in medical practice for the treatment of hypertension, Alzheimer's disease, diabetes, schizophrenia, allergies and act as anti-cancer, antimicrobial, antifungal agents [3].

In this study, the prepared compound 1 was used as a precursor for the preparation of hydrazide 3 by the hydrozonolysis reaction by combining methyl 3-(2-oxobenzo[d]oxazol-3(2H)-yl)propanoate 2 with the hydrazine monohydrate (Scheme 1). 3-(2-(1H-benzo[d]imidazol-2-yl)ethyl)benzo[d]oxazol-2(3H)-one 4 was synthesized in the Phillips reaction by reacting compound 1 with 1,2-phenylenediamine in a mixture of hydrochloric acid and water (1:2). Acid 1 was esterified with methanol at reflux for 2 hours in the presence of a catalytic amount of sulfuric acid in the reaction mixture. The obtained methyl ester 2 was transformed into hydrazide 3 using hydrazine monohydrate in 2-propanol. Condensation of compound 3 with aromatic or heterocyclic aldehydes in propan-2-ol and using a catalytic amount of glacial acetic acid led to the formation of N'-benzylidene hydrazides 5–9. The structures of the obtained compounds were confirmed by the data of the ^{1}H, ^{13}C NMR and FT-IR spectroscopy and elemental analysis.

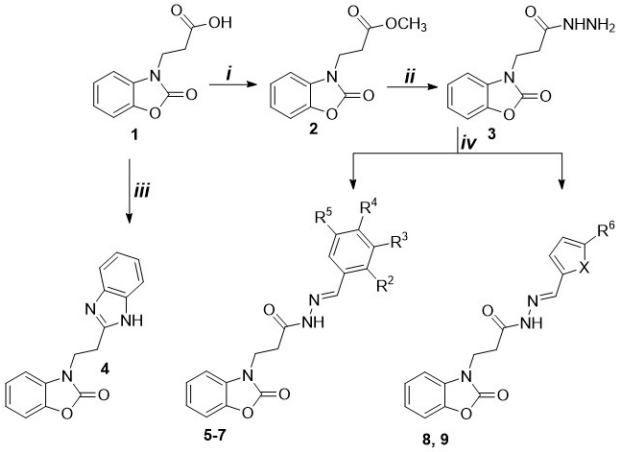

Fig. 1. Synthesis of new 3-(2-oxobenzo[d]oxazol-3(2H)-yl)propanoic acid derivatives **2-9**. **5** R^2,R^3,R^4,R^5=H; **6** R^2,R^3,R^5=H, R^4=F; **7** R^3,R^5=H, R^2,R^4=F; **8** X=S; R^6=H; **9** X=S; R^6=NO_2; Reagents and conditions: *i*) MeOH, H_2SO_4, D, *ii*) i-PrOH, $N_2H_4 \cdot H_2O$, D, *iii*) o-phenylendiamine, HCl:H_2O mixture, reflux, $NH_3 \cdot H_2O$, *iv*) i-PrOH, aromatic or heterocyclic aldehyde, glacial AcOH.

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