SYNTHESIS OF PYRAZOLE- AND BENZIMIDAZOLE DERIVATIVES FUSED VIA OXAZACYCLES

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Heterocyclic compounds play a central role in drug discovery due to their versatile structures and potential medicinal applications [1,2]. While pyrazole- or benzimidazole-fused heterocycles [3-5] and various six-, seven-, or eight-membered oxazacycles [6,7] have been reported individually, polycyclic molecules combining pyrazole, benzimidazole, and a variable oxazacycles have not yet been synthesized. Developing methods to access these novel fused scaffolds provides an opportunity to expand the chemical space of biologically relevant heterocycles.

The primary aim of this study is to develop a general and efficient syntheticstrategy for the preparation of novel polycyclic molecules combining pyrazole, benzimidazole, and variable six-, seven-, or eight-membered oxazacycles. This study seeks to expand the chemical space of biologically relevant heterocycles and provide new scaffolds for potential future pharmacological evaluation.

The pyrazole-benzimidazole systems fused via different oxazacycles systems were synthesized using a two-step modular approach. In the first step, a pyrazole carbaldehyde was condensed with a diamine to form a pyrazole-benzimidazole intermediate. In the second step, a dihalogenated alkane-induced annulation, linking the pyrazole hydroxyl group with the benzimidazole NH group, was used to form the four-ring scaffold. Reactions were monitored by TLC, and the structures of intermediates and final products were confirmed by NMR spectroscopy, mass spectrometry, and IR analysis. The modular two-step synthesis successfully yielded a series of pyrazole-benzimidazoles fused via oxazine, oxazepine, and oxazocine rings.

These results demonstrate the feasibility and versatility of the synthetic strategy for accessing previously unreported polycyclic systems. The approach expands the chemical space of biologically relevant heterocycles and provides a foundation for the future exploration of their pharmacological potential.

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