SYNTHESIS OF NOVEL ISOXAZOLIDINE ISOQUINOLINONE FUSED HYBRIDS AS POTENTIAL PARP INHIBITORS

Konstantinos A. Ouzounthanasis, Alexandros E. Koumbis

Laboratory of Organic Chemistry, Department of Chemistry
Aristotle University of Thessaloniki, Thessaloniki 54124

Poly-ADP ribose polymerases (PARP) hold a crucial role in repairing DNA single strand breaks. Inhibition of PARP can be used unassisted or in combination with other methods against cancer cells. Compounds bearing the benzamide moiety tend to exhibit PARP inhibition (**Figure 1**), thus synthetic protocols for the preparation of such derivatives in a simple and versatile manner are highly desirable.

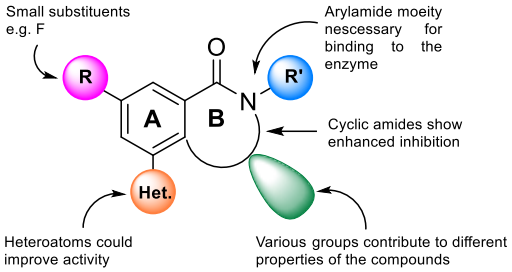
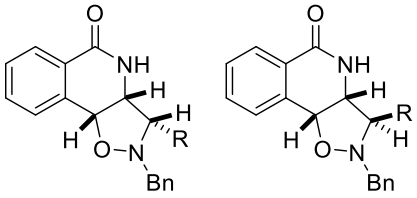


Figure 1: General proposed pharmacophore for PARP inhibitors

In this context, we describe the synthesis of novel benzamide derivatives (isoquinolinones) fused with an isoxazolidine heterocycle. Our synthetic approach utilizes a key 1,3-dipolar cycloaddition reaction employing *N*-benzyl nitrones of various benzaldehydes for the construction of the isoxazolidine ring. The benzamide moiety is formed via a Schmidt reaction on the obtained cycloadducts (**Figure 2**). With the structural features of the benzamide and the heterocyclic ring in place we expect the newly prepared compounds to show increased potential as PARP inhibitors.



26 new compounds

Figure 2: Prepared isoxazolidine isoquinolinone fused hybrids

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