Photochemical Preparation of Novel Tetracyclic Indenoquinolines from Benzotropolone Derivatives

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INTRODUCTION

Heteroatom-bearing tetracyclic backbones are important scaffolds for a number of biological targets. These compounds have been widely used as antimicrobial and anticancer agents, and include tetracycline antibiotics and topoisomerase inhibitors.[1,2] We have shown that a novel class of tetracyclic tetraindenoquinolines could be obtained through photoisomerization of benzotropolone derivatives.[3] In this presentation we detail the preparation of a series of these compounds as well as the corresponding indenoquinolines (Figure 1), and discuss their biological evaluation.

RESULTS AND DISCUSSION

As we recently reported, Diels-Alder adducts formed between benzotropolones and nitrosobenzene can be photoisomerized in fair yields to novel tetraindenoquinolines.[3] Based on these results, and on previous work carried out by our groups,[4] we were able to increase the diversity of the compounds in the series. Starting form trimethylpurporogallin, a series of aliphatic and aromatic ethers were prepared using standard Williamson conditions. These were subsequently treated with nitrosobenzene to afford a series of Diels-Alder adducts bearing endocyclic -N-O- bonds. As shown in **Figure 1**, phoisomerization of these oxazines leads to the novel tetrahydoindenoquinoline frameworks. Planar aromatic tetracyclic systems can then be readily obtained by oxidation. In addition, a the preparation of a number of amide derivatives based on one of these compounds is also described. Preliminary biological data indicated that some of these compounds have µM activity against cervical (HeLa), ovarian (A2780), endometrial (Ishikawa), and lung (SW1573) cancers.

CONCLUSION

The preparation of novel tetracyclic indenoquinolines through photoisomerization of readily available benzotropolone derivatives is described. Their biological activity and potential mode of action is also briefly discussed.

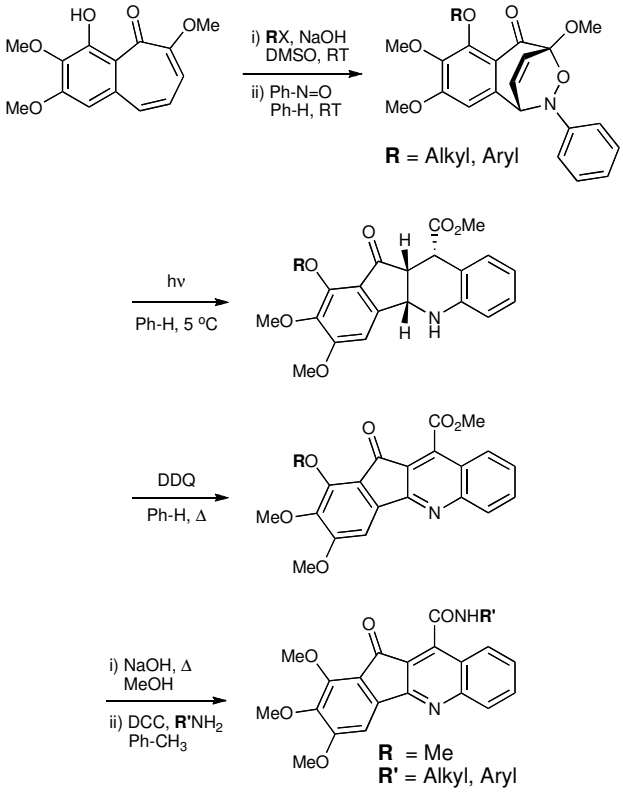

Figure 1. Synthetic route to tetracyclic indenoquinoline and and tetrahydroindenoquinoline libraries.

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