



**Title:** Novel Furan Cycloadditions for Preparation of Medicinally Important Compounds

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**Summary:**

This research involves the development of new furan and pyrrole-based cycloaddition reactions that result in the formation of complex ring systems from simple and readily available components. The cycloaddition mode depends upon the synthetic route and the substitution pattern for the furan/pyrrole core.

The [8+2]-cycloaddition mode occurs when alkynes couple with dienylfurans. This reaction assembles the core ring system (furan-bridged ten-membered ring) of the marine-derived experimental anticancer agent eleutherobin. The full synthetic potential of this reaction will be developed, including delineation of the scope, limit, and stereochemistry of the [8+2]-cycloaddition followed by a study of the reactivity profile for densely functionalized [8+2]-cycloadducts. These chemical processes will be employed in the design of new anticancer agents that structurally resemble eleutherobin. The ability of these compounds to promote microtubule polymerization will be tested, and active candidates will be further tested as anticancer agents.

The coupling of chromium carbene complexes with ortho-alkynylbenzoyl derivatives leads to activated furan/pyrrole rings, which undergo efficient cycloaddition with a variety of alkenes and alkynes. A variant of this process will be developed where highly unsaturated chromium carbene complexes afford phenanthroid ring systems in a formal [5+5]-cycloaddition reaction. These reactions are the cornerstone for versatile and efficient synthetic approaches to tanshinones, useful for the treatment of hypertension, and to apomorphine, a dopamine receptor useful for the treatment of Parkinson's disease.

This research provides structurally complex and medicinally important compounds from simple and readily available components. The reaction process can conveniently provide compounds (or more importantly structural analogs) that have shown potent anticancer activity, antihypertension activity, and activity against neurologic disorders such as Parkinson's disease. These are all very common ailments that negatively impact the quality of life a large portion of the US population.