ORGANIC SEMINAR

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“Title: $TiCl4$-Promoted Reaction of Dihydrofurans with Unactivated Aldehydes: A Modular Strategy toward Tetrahydrofuran-Based Mono- and Tricyclic Frameworks”

Tetrahydrofuran (THF) motifs are present in many FDA-approved drugs, ranging from antiviral to anticancer agents. Consequently, the development of THF-containing frameworks is of high importance in medicinal chemistry and drug discovery. Over the years, the Ghosh laboratory has developed various functionalized tetrahydrofuran-based scaffolds in high yields and with excellent diastereoselectivity via TiCl4-promoted reactions of cyclic enol ethers with activated carbonyl compounds. Owing to the versatility of this chemistry, we sought to expand its scope to include unactivated aldehydes, thereby enabling access to unprecedented THF-based frameworks.

Herein, we report TiCl4-promoted multicomponent and cascade reactions for the synthesis of diverse tetrahydrofuran-based mono- and tricyclic scaffolds. Specifically, a $TiCl_4$-mediated tandem reaction between dihydrofurans, aromatic aldehydes, and aryl-tethered aliphatic aldehydes generates an oxocarbenium intermediate that undergoes intramolecular trapping to afford tricyclic 5/5/6 tetrahydro-benzocyclopentafurans and 5/6/6 hexahydro-benzocyclohexafurans bearing three contiguous stereocenters in good yields and selectivity. Further expansion of this strategy enables intermolecular trapping of the oxocarbenium intermediate with external nucleophiles, providing access to a range of mono- and disubstituted functionalized tetrahydrofurans and tetrahydropyran motifs.

PURDUE UNIVERSITY | James Tarpo Jr. and Margaret Tarpo Department of Chemistry

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