

SESSION II: SPEAKER ABSTRACTS

Synthesis of Sesquiterpene-Tropolones

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The sesquiterpene-tropolones are fungal metabolites that have been recognized for their compelling biological activities against multiple cancer cell lines and pathogens. Natural products in this class are comprised of a hydroxylated α -humulene-derived core fused to one or two tropolone units by dihydropyran rings. While precise mechanisms of action remain unknown, structural comparisons suggest that the *bis* tropolone structure is required for enhanced biological activities. A general synthesis of sesquiterpene-tropolones has not yet been achieved despite the necessity for a thorough evaluation of their promising therapeutic potential through derivatization.

We have completed the total synthesis of *mono* tropolone epolone B featuring a biomimetic hetero Diels–Alder reaction between the oxygenated α -humulene core and tropolone o-quinone methide fragments. The core is synthesized in racemic form *via* four macrocyclization approaches and in enantiopure form *via* hydrogen atom transfer isomerization of a (–)-caryophyllene oxide derivative. The tropolone o-quinone methide precursor is prepared through either a Lewis acid mediated or photochemical de Mayo-type fragmentation. A challenging second hetero Diels–Alder reaction has granted entry into the *bis* tropolone framework of the natural products pycnidione and deoxypycnidione. Cytotoxicity assays reveal promising preliminary data that encourage further investigation into the biological activity of the sesquiterpene-tropolones and *bis* tropolone derivatives.

