Towards the Total Synthesis of the TRAIL-Resistance-Overcoming Cytotoxic Pannokin D for the Development of New Anticancer Pharmaceuticals and a Novel Regioselective Diprenylated Chromone-Derived Flavonoid Synthesis

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The recent characterization of the natural product Pannokin D (a novel benzoxanthone-type diprenylated flavonoid with cytotoxic activity and the rare biochemical capability of overcoming TRAIL resistance) by Toume et al. presents a promising treatment option for gastric cancer. Current treatment options contribute to the 800,000 deaths caused by gastric cancer yearly as they involve chemotherapeutics with high failure rates and ineffective radiotherapy treatments. Herein, the first proposed schematic for the total synthesis of Pannokin D is reported for the development of a benzoxanthone-type prenylated flavonoid synthesis. The synthesis of Pannokin D presents a novel method for preparing the unique diprenylated chromone moiety it possesses which sets the stage for the development of over 25 different classes of highly unexplored medicinally relevant natural products. While synthesizing Pannokin D, the first accomplished halogenation of the 2H-benzopyran core (high purity, 62.73% yield, gram scale) was achieved. While being extensively studied for reaction development, prenyl bromide and n-butyllithium will react with this 2H-chromene for a regioselective prenylation at its halogenated position. A Friedel-Crafts acylation with 4-hexanoyl chloride followed by an enolate alkylation with 1-bromomethyl-2,4,5-trimethoxybenzene will be performed for prenylation and addition of a phloroglucinol. Demethylation with boron tribromide followed by an organometallic palladium on carbon-catalyzed oxidant-free cascade reaction will prepare the chromone ring. The hypothesized regioselective synthesis of the prenylated 2H-chromene moiety will be studied extensively with nuclear magnetic resonance and gas chromatography for reaction development and optimization.

Awards Won:

Drug, Chemical &amp

Associated Technologies Association (DCAT): $1,000 scholarship will will be awarded &#x0D

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