Poster #30

Total Synthesis of the Soybean Flavonoids Glyceollin I and II

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The glyceollins are penta-cyclic flavonoid ethers that can interact with human estrogen receptors (HER). Selective agonist activity offers the possibility for estrogen replacement therapy while anti-estrogenic activity offers the potential for development as breast cancer chemotherapeutic agents. There have been four glyceollins reported to date and they were isolated as a mixture and only in a few milligrams quantity. Here we outline our approach to the first total synthesis of the glyceollins I and II.

Chalcone obtained by Claisen-Schmidt condensation was subjected to oxidative rearrangement with thallium (III) nitrate-trihydrate to give an acetal which was efficiently cyclized to an isoflavone that serves as a chemical model for our proposed synthesis. The 1,2 reduction of this isoflavone with sodium borohydride, followed by dehydration provided 3-isoflavene via a one-pot sequence. The most crucial step is the stereospecific introduction of the 6-a hydroxyl group, which can be achieved by osmium tetroxide-mediated asymmetric dihydroxylation using chiral ligands. In the next step, reductive cyclization of 3,4 diol with H_2 over 10% Pd-C will furnish the pterocarpan nucleus. The final step will involve the construction of the upper chromene ring by isoprenylation. Thus, the total synthesis of glyceollins I and II should be achievable in reasonable yield via a stereospecific approach.

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