Abstract

This thesis illustrate strides taken toward the construction of the pyrrolo[1,2-*a*]azepine **4** nucleus *via* enaminone chemistry developed in this University for creating pyrrolizidine **1**, indolizidine **2** and quinolizidine **3** alkaloids. The pyrrolo[1,2-*a*]azepine **4** core is a fused pyrrolidine and azepine system found in lehmizidine, *Stemona*, *Cephalotaxus* alkaloids and other alkaloids. A concise background is given on the nature of enaminones, how they are accessed with strong emphasis on the Eschenmoser sulphide contraction reaction and their versatile reactivity, followed by literature review of this University background on synthesis of alkaloids containing **1**, **2** and **3** nuclei. The aims and strategies presented are preceded by literature review of lehmizidine, *Stemona*, *Cephalotaxus* alkaloids and some reported synthesis.

A range of attempts and successes are reported in chapter 2 for making four-carbon chain length enaminones (*via N*-alkylation, condensation, thionation, Eschenmoser sulphide contraction and tandem acylation/Michael addition reactions) crucial in creating azepane onto pyrrolidine in an acylation or alkylation ring closing steps yielding lehmizidine like compounds (*E*)-ethyl 8-oxo-2,3,5,6,7,8-hexahydro-1*H*-pyrrolo[1,2-*a*]azepine-9-carboxylate **144** and (*E*)-ethyl 2,3,5,6,7,8-hexahydro-1*H*-pyrrolo[1,2-*a*]azepine-9-carboxylate **147**. Vice versa, the synthesis of two carbon chain length N-alkyl vinylogous amides is demonstrated leading to the formation of pyrroles, ethyl 2-phenyl-6,7,8,9-tetrahydro-5*H*-pyrrolo[1,2-*a*]azepine-3-carboxylate **222**, ethyl 2-(4-nitrophenyl)-6,7,8,9-tetrahydro-5*H*-pyrrolo[1,2-*a*]azepine-3-carboxylate **223** and ethyl 2-(4-methoxyphenyl)-6,7,8,9-tetrahydro-5*H*-pyrrolo[1,2-*a*]azepine-3-carboxylate **224** in Knoevenagel condensation reactions similar to those described by Garreth Morgans and Stefania Scalzullo in their PhD theses. The synthesis of 1-benzoyl-6,7,8,9-tetrahydro-5*H*-pyrrolo[1,2-*a*]azepine-2,3-dione **233** and 1-(4-methoxybenzoyl)-6,7,8,9-tetrahydro-5*H*-pyrrolo[1,2-*a*]azepine-2,3-dione **235** in a double acylation reaction between N*H* vinylogous amides and oxalyl chloride is also demonstrated.

In chapter 3, the synthesis of vinylogous urethanes for making the *Cephalotaxus* core *via N*-alkylation, condensation, thionation, Eschenmoser sulphide contraction and tandem acylation/Michael addition reactions are described. A variety of attempts of the arylation reaction on vinylogous urethanes are demonstrated leading to a comparison study to ascertain carbon chain length dependency of the step.

The synthesis of pyrido[1,2-*a*]azonine nucleus of Sessilifoliamide alkaloids, which are a subset of the *Stemona* alkaloids demonstrated in chapter 4 is in line with our fascination with bigger ringed alkaloids. The synthetic route is presented leading the formation of compounds 1-benzoyl-3-methyl-2,3,7,8,9,10,11,12-octahydropyrido[1,2-*a*]azonin-4(6*H*)-one **337**, 3-methyl-1-(4-nitrobenzoyl)-2,3,7,8,9,10,11,12-octahydropyrido[1,2-*a*]azonin-4(6*H*)-one **338** and 1-(4-methoxybenzoyl)-3-methyl-2,3,7,8,9,10,11,12-octahydropyrido[1,2-*a*]azonin-4(6*H*)-one **339**.