STUDIES TOWARDS THE TOTAL SYNTHESIS OF THE TAXOİD DİTERPENE FRAMEWORK

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The goal of the present investigation is to assemble the 20-carbon unit of the taxoid diterpene skeleton in a step efficient way and with a high level of stereocontrol. This was achieved by a three-reaction sequence developed in the laboratory starting from two achiral aldol partners 1 and 2, derived from methylcyclopentenone and benzoic acid respectively.

The aldol - annulation approach constitutes an efficient construction of the fragmentation precursor 4, by installing five stereogenic centers in two C-C bonding steps (only one out of 16 enantiomeric pairs of diastereoisomers is obtained). C2-C10 cleavage leads then to the key synthetic intermediate 5.

To further elaborate the A-secottaxoid framework thus obtained, starting from the BC-subunit 5, we divided the strategy into two distinct paths to reach advanced intermediates 6 and 8. Following a series of functional group interconversion, 6 ultimately provides the bridged / fused ABC ring system 7 with a total of 23 linear steps from 1 and 2.

The successful synthesis of ABC ring system 7 demonstrates the viability of our aldol-annulation-fragmentation approach for the synthesis of taxoid analogs. The application of this methodology to 9 is currently under investigation.