SYNTHETIC STUDIES USING THE OPTICALLY ACTIVE γ-LACTONE DERIVATIVE AS A CHIRAL SYNTHON.
—ASYMMETRIC TOTAL SYNTHESIS OF ANTILEUKEMIC LIGNAN STEGANACIN—

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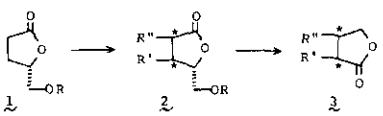
A new methodology for the asymmetric synthesis of natural products was developed by applying the optically active γ-hydroxymethyl-γ-butyrolactone (1), easily available from L-glutamic acid, as a chiral synthon. This procedure is constituted from the two key steps, the first is the creation of new chiral centers (2) on 1 under the influence of its asymmetric center, and the second is the removal of the original chiral center of (2) to give 3.

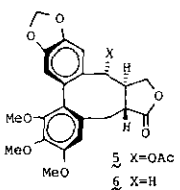
Applying this new methodology to the asymmetric synthesis of pharmacologically active lignans, the key intermediate (S)-β-piperonyl-γ-butyrolactone (4), as well as (R)-4 were successfully synthesized by 1,3-asymmetric induction technique. Employing 1,2-asymmetric induction technique the chiral butenolide, easily available from 1, was also shown to be highly useful for the completely stereocontrolled synthesis.

In addition to the development of the above fundamental methodology, the total synthesis of natural lignans involving antileukemic burseran, isodeoxypodophyllotoxin have been achieved.

As a goal of our studies directed toward asymmetric total synthesis of antileukemic lignans, the regio- and stereo-controlled total synthesis of steganacin (5) in optically pure form was achieved this time. The key steps of the present synthesis are selective isomerization of isostegane into stegane (6), and also regio- and stereoselective oxidation of 6 to steganacin (5). As a result of the present asymmetric synthesis, the absolute configuration of natural steganacin was revised.



1 2 3



5 X=OAc
6 X=H

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