SECTION IV

PROBABLE BIOGENESIS OF THE SEVEN NEW DITERPENE LACTONES

The leaves of *Gelonium multiflorum* afforded seven new diterpene lactones. It is therefore quite relevant to outline briefly the present-day views regarding the biogenesis of the diterpene lactones.

Formal $\text{SN}_1'$ and $\text{SN}_2'$ reactions are proposed to account for the biosynthesis of impressive number of natural products including diterpenes. In the plant cell, in presence of specific enzymes, geranyl-geranyl pyrophosphate is assumed to undergo the electrophilic cyclisation to form a bicyclic intermediate copalyl pyrophosphate, which is enantiomeric to the corresponding labdane intermediate of resinolactone biosynthesis. The further cyclisation results in the generation of the ring C in which the steric course of the allylic displacement is important since it leaves the stereochemical information on the angular vinyl and the methyl groups. An intimate details of the entire enzymatic process are already known in the literature$^{74,75}$. Allylic displacement of the pyrophosphate generates a carbocation at C-8 which collapses into an olefin through the loss of an appropriate C$_{14}$-H to form sandarocopimaradiene with $\alpha$-methyl and $\beta$-vinyl at C-13. The stereochemistry of the angular vinyl group indicates that the allylic

$^{74}$ David E. Cane (Tetrahedron Report No.82), *Tetrahedron* 36, 1109-1159 (1980)

displacement, which generates the ring C, has taken place on the 'Si'-face of 13,14-double bond of copalyl pyrophosphate.

A number of biological events takes place on sandarocopimaradine, the chronology of which is unpredictable. However, one of the possible sequences is shown in the scheme 9.

Regiospecific epoxidation at C-15/C-16, followed by the opening of the epoxide through the migration of C\textsubscript{13}-Me, as shown in the Scheme 9, leaves a carbocation at C-13, which in turn collapses into an olefin through the loss of adjacent H-15. The next two steps may be looked upon as an oxidation of the CH\textsubscript{2}OH group to COOH and allylic \(\beta\)-hydroxylation at C-12 and lactonisation involving these two stereochemically suitably disposed groups to have H-12\(\alpha\) and axial. The epoxidation then takes place across C-8/C-14 double bond from more exposed less hindered \(\beta\)-face to form the diterpene lactones.

Further hydroxylation/oxidation/acetylation etc. takes place to attain gelomulide A or gelomulide C-G (21 or 23-27) structure. Enzymatic dehydrogenation at C-11 and C-12 followed by epoxidation at the \(\alpha\)-face (keeping the lactone ring at the less strained \(\beta\)-face and the ring C in the more or less planar form) would give rise to the diepoxylactone gelomulide B (22) or jolkinolide B (10).

In absence of any biosynthetic experimental support with tracer, the chronology of the biological events like epoxidation, \(\beta\)-hydroxylation at C-12, oxidation of CH\textsubscript{2}OH to COOH which takes place on sandarocopimaradiene is unpredictable.
However, one of the possible sequences is shown in the scheme.9

Scheme 9: Probable biogenesis of seven novel gelomulides