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THE DITERPENOIDS OF ERYTHROXYLON MONOGYNUM - V
ATISIRENE, ISOATISIRENE AND DEVADARENE

A.H. Kapadi, R.R. Sobti and Sukh Dev
National Chemical Laboratory, Poona (India)

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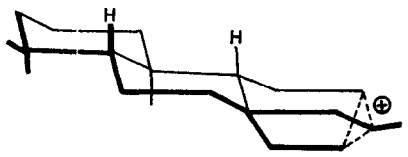
In continuation of our previous work[1,2], we now report on the total composition of the diterpene hydrocarbons from Erythroxylon monogynum, the approximate composition being: (+)-hibaene[1] (74%), (-)-pimaradiene (6%) and three new naturally occurring diterpenes, now designated as (-)-atisirene (5%; II), (-)-isoatisirene (8%; III) and (+)-devadarene (7%; IV).

Atisirene and isoatisirene

Atisirene, $C_{20}H_{32}$, m.p. 57-58°, $[\alpha]_D$ -40.46°($CHCl_3$), has the following structural features: three methyl groups, all quaternary (PMR[3]: 3H signals at 50, 51.5 and 58 cps), two of these being in a gem-position (IR: 1375, 1390 cm^{-1}); a vinylidene group (IR: 3080, 1650, 878 and 890 cm^{-1}; PMR: two 1H signals centred at 269 and 278 cps, the former appears as a doublet with J = 2 cps, while the 278 cps signal occurs as a broad singlet). From its low end-absorption in the UV, and the above data, it is clear that atisirene possesses only one ethylenic linkage and consequently, being $C_{20}H_{32}$, must be tetracyclic. Since

atisirene is different from either kaurene or phyllocladene - the only two known tetracyclic diterpenes with the above structural characteristics - a new structural type was indicated for atisirene. A consideration of the currently accepted biogenetic route[4] to tetracarbocyclic diterpenes revealed the distinct possibility that the new hydrocarbon might have arisen *via* the pathway to diterpene alkaloids of atisine type, a route[5,6] open to the ion I (or its biological equivalent), the immediate precursor of (+)-hibaene, a type common in *Erythroxylon monogynum*. Based on the above, the new hydrocarbon was suspected to be II (the absolute stereochemistry being derived from that of (+)-hibaene). This has indeed been found to be so. Zalkow and Girotra[7] have recently prepared the enantiomer (m.p.



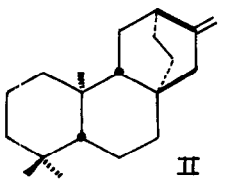
I

(+)-Hibaene

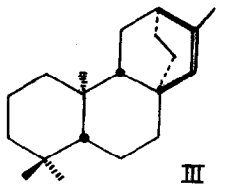
(−)-Kaurene

Atisine and

Trachylobane types.



II



III

60-61°, $[\alpha]_D$ +40.08[8]) of II from maleopimaric acid, and a

direct comparison of their IR and PMR spectra confirmed the structure II for atisirene.

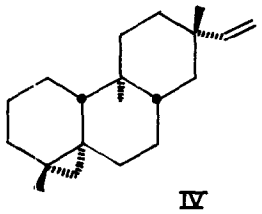
The new tetracarbocyclic hydrocarbon, $C_{20}H_{32}$, m.p. 84-85°, $[\alpha]_D$ -73.99° ($CHCl_3$), described earlier[1], was, from its spectral characteristics[1], clearly related to atisirene. On equilibration with $KOBu^t$ in t-BuOH (12 hr reflux) a small amount of atisirene was formed, as revealed by TLC on $AgNO_3$-SiO_2 gel[9]. Structure III for this compound was confirmed by its direct comparison (IR) with an authentic sample of (±)-III (m.p. 51-52.5°), recently synthesised by Bell and Ireland[10].

Though the carbon-skeleton depicted in II, III is well-recognised in diterpene alkaloids of the atisine group[11], the isolation of nitrogen-free diterpenoids of this type, from a natural source, is being reported for the first time. In order to emphasise that atisine and hydrocarbon II, have the same carbon frame-work, the word atisirene has been coined for II, and in analogy with kaurene-isokaurene nomenclature, III has been designated isoatisirene.

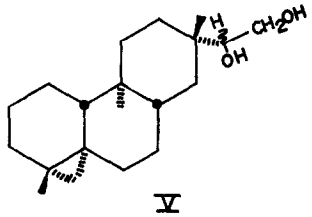
Devadarene

The PMR spectrum of devadarene, $C_{20}H_{32}$, b.p. 140-48° (bath)/2 mm, $[\alpha]_D$ +19.33° ($CHCl_3$), showed, in addition to three quaternary methyls (46, 63, 63 cps), a 2H AB quartet centred at 19 cps [J_{AB} = 4 cps; $J_{AB}/(\delta_B - \delta_A)$ = 0.24], a feature characteristic of the cyclopropane methylene in devadarool[2] (V), a diterpenoid from Erythroxylon monogynum;

furthermore it showed the presence of three vinyl protons,



IV



V

coupled in a typical ABC fashion (a 10 line pattern, located between 281-362 cps). These data suggested structure IV for the new hydrocarbon. This was confirmed by a partial synthesis from devadarool (V), which on $NaIO_4$ oxidation yielded the nor-aldehyde and this on interaction with triphenylmethyl phosphonium bromide in presence of $KOBu^t$, gave a hydrocarbon (yield 75%) identical in all respects with the naturally occurring material. This compound, being the parent of devadarool, has been named devadarene.

Biogenetic considerations

We have described, so far, the isolation and structure determination of ten new diterpenoids, elaborated by Erythroxylon monogynum. Though during the elucidation of these structures, biogenetic considerations played a vital role, the structures ultimately rest on sound chemical evidence. Fig.1 shows how these structures fit eminently in a biogenetic sequence, based on current concepts.

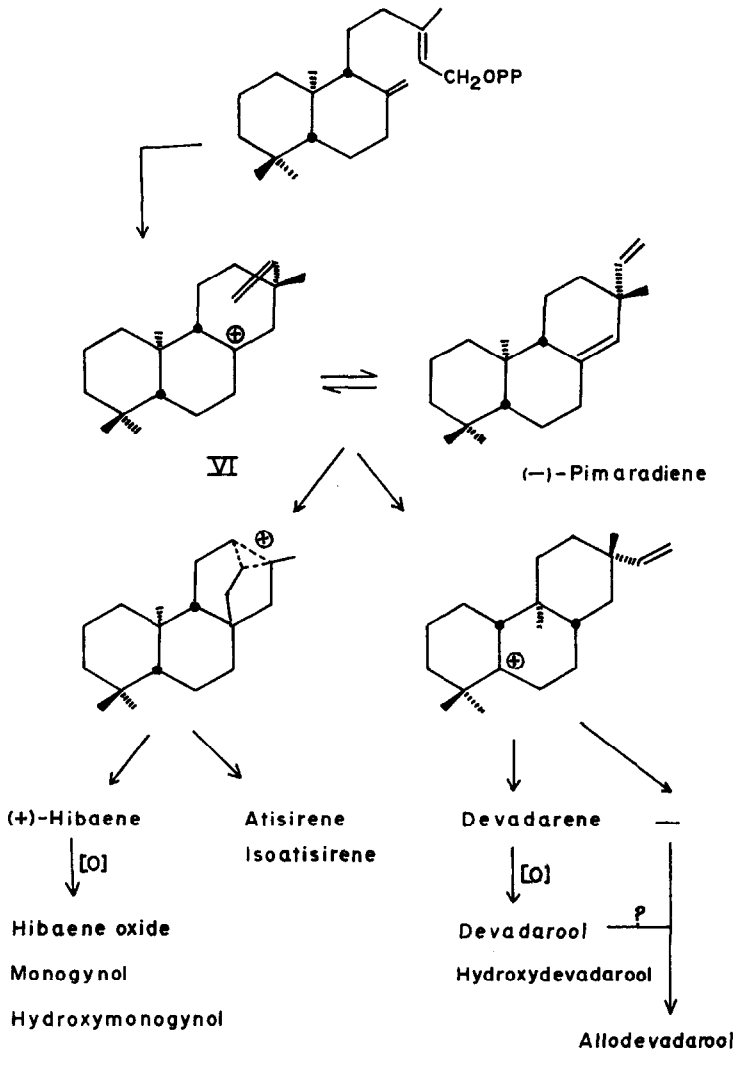

CH2OPP
VI
(−)-Pimaradiene
(+)-Hibaene
Atisirene
Isoatisirene
Devadarene
[O]
Hibaene oxide
Monogynol
Hydroxymonogynol
[O]
Devadarool
Hydroxydevadarool
Allodevadarool

Fig. 1

A detailed analysis of the hydrocarbon portion (constituting $\sim$ 1% of total diterpenoids) of the diterpenes from Erythroxylon monogynum, as described in the present Communication, was undertaken to check a working hypothesis briefly outlined below.

Starting with a (currently accepted) terpene precursor (e.g., geranyl-geraniol pyrophosphate) a terpenoid could, conceivably, be formed from this by a one-step or a multi-step process; the term one-step implying that only the final product leaves the enzyme surface. If a multi-step sequence is operative, then pools of intermediate compounds, acting as substrates in subsequent steps, must exist in the living plant at a given time; the pools represent the balance of feed-in and utilisation processes occurring side by side, though this balance could, conceivably, be vanishingly minute. Since monogynol[1,12], devadarool[2,13] (the major diterpenoids of E. monogynum) must be formed in subsequent oxidation steps, it is gratifying to isolate their hydrocarbon precursors from the same source. Furthermore, since both hibaene and devadarene cannot be formed in a single enzymatic step involving the ion VI, (-)-pimaradiene, which has also been isolated, is presumably involved as a substrate in two distinct pathways.

The above hypothesis besides aiding in the characterisation of various terpene compounds of a given plant also implies that the absolute stereochemistry of the

various constituents must be the same (or derivable therefrom) at a common reference point (e.g. C_{10} in Fig.1) (unless each component is formed by a one-step process, which is considered unlikely). This is fully borne out by the absolute stereo-structures of the diterpenoids isolated from E. monogynum.

A detailed and wider discussion of these ideas will be reported elsewhere.

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