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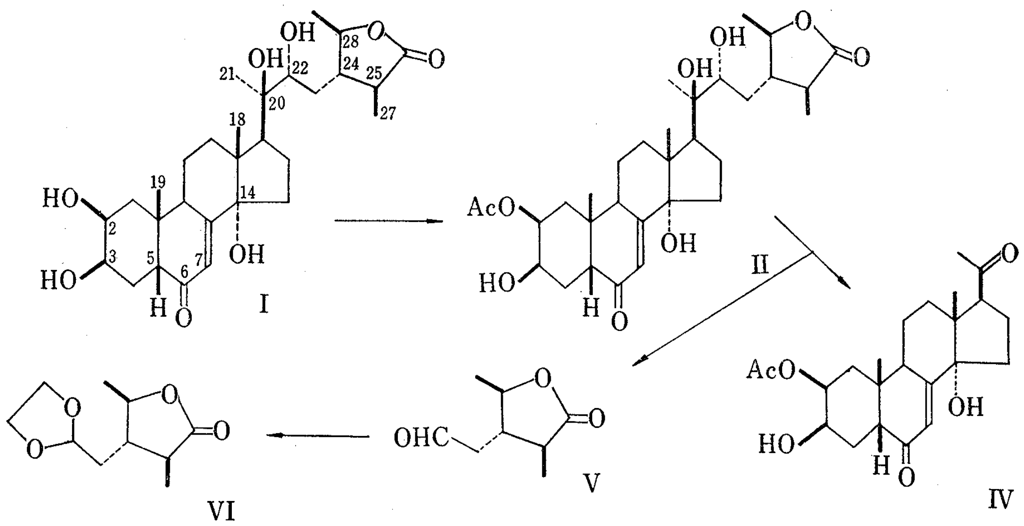
Absolute Configuration of Cyasterone, An Insect-Moulting Substance from *Cyathula capitata*

Cyasterone is the first ecdysterol possessing the C_{29} stigmastane skeleton isolated from a plant source, *Cyathula capitata* Moquin-Tandon (Amaranthaceae).[1] It has been shown that cyasterone exhibits high moulting hormone activity in insects,[1,2] and the highest anabolic activity in mouse.[3]

We have previously deduced the structure along with part of the stereochemistry of cyasterone as 2β,3β,14α,20,22-pentahydroxy-6-oxo-5β-stigmast-7-eno-26,28-lactone,[1] but a conclusive proof for the complete stereostructure would be required. The present communication describes evidence leading to stereoformula I for cyasterone.



Selective acetylation of cyasterone with acetic anhydride and pyridine in chloroform gave the 2-acetate (II) together with the 2,3,22-triacetate (III). On periodate oxidation, the 2-acetate (II) afforded the known methyl ketone (IV)[4] and the aldehyde (V). Hence, the stereochemistry of the nucleus has been established.

Cyasterone, as with ecdysterone and ponasterone A, rapidly consumes two molecules of periodate and readily gives the 20,22-acetonide. The chemical shifts of the C-18 and C-21 methyl proton signals in the nuclear magnetic resonance (NMR) spectra of cyasterone and its triacetate (III) and the chemical shift and shape of the C-22 carbinyl proton signal in that of the triacetate (III) are very similar to the corresponding data of ecdysterone and ponasterone A and their 2,3,22-triacetates, showing that these hydrogens of cyasterone reside in the like

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environment as those of ecdysterone an ponasterone A having the 20(*R*),22(*R*)-moiety.[5] Further, we have recently isolated from the same plant source another ecdysterol, precyasterone,[6] which has been converted into cyasterone by alkaline hydrolysis followed by acidification, all the asymmetric centers in both substances having the same absolute configurations. Application of the Hudson–Klyne lactone rule to precyasterone indicates the C-22 configuration to be (*R*). The combined evidence has deduced that the C-20 and C-22 configurations are both (*R*).

Table I. Proton Signals[a]

	C-18	C-21	C-22
Ecdysterone[b]	1.19s	1.55s	3.83dd
Ponasterone A[b]	1.16s	1.51s	3.74dd
Cyasterone[b]	1.19s	1.51s	3.90[c]
Ecdysterone 2,3,22-triacetate[d]	0.85s	1.24s	4.82dd
Ponasterone A 2,3,22-triacetate[d]	0.85s	1.24s	4.79dd
Cyasterone 2,3,22-triacetate[d]	0.85s	1.24s	4.98[c]

a) abbreviations: s=singlet, dd=doublet of doublets
b) in C_5D_5N
c) Although the coupling constants are unclear due to overlapping of signals, the signal shape quite resembles those of the other congeners.
d) in $CDCl_3$

In the NMR spectrum of the lactone–aldehyde (V), the large values (8 and 11 Hz) for the coupling constants between the C-24 and C-28 hydrogens and between the C-24 and C-25 hydrogens, respectively, are consistent with diquasiaxial couplings.[7] The quasiequatorial orientation of the C-25 methyl group was confirmed by the solvent effect of the C-27 methyl proton signal ($\delta(CDCl_3)-\delta(C_6H_6)=+0.21$ ppm and $\delta(CDCl_3)-\delta(C_5H_5N)=-0.03$ ppm)[8] in the NMR spectra of the acetal (VI) derived from the aldehyde (V). Application of the Hudson–Klyne lactone rule to the lactone (VI) shows the C-28 configuration to be (*R*) and consequently the C-24 and C-25 configurations to be both (*S*). This was corroborated by the CD curve of the lactone (VI) exhibiting a positive Cotton effect at 218 nm.[9]

The accumulated data have led to the conclusion that cyasterone possesses the stereostructure I which supports the most probable assumption that β-sitosterol[10] serves as a precuror of cyasterone in the plant.

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