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THE CONSTITUTION AND STEREOCHEMISTRY OF ε-CAESALPIN

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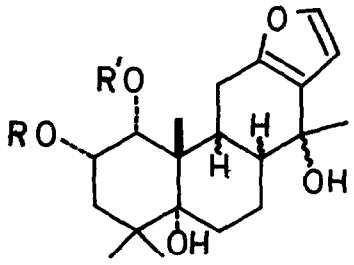
The isolation[1,2] and structural elucidation[2] of α-, β-, γ- and δ-caesalpins from the seeds of Caesalpinia bonducella have been reported. We have isolated, from the same source, a new crystalline compound, ε-caesalpin, which is assigned structure (I) (or enantiomer) on chemical and spectroscopic evidence. This is confirmed by an X-ray analysis of the p-bromobenzoate (II) which, in addition, establishes the stereochemistry at the remaining asymmetric centres and the absolute configuration as in (III).

ε-Caesalpin $C_{24}H_{34}O_7$, m.p. 191-194°, $[\alpha]_D$ +2°, shows in its n.m.r. spectrum a 2,3 disubstituted furan ring [H-16, τ 2·77; H-15, τ 3·61; both doublets, J = 2 c./sec.], two secondary acetates [τ 8·10, 7·94 ($2C\underline{H}_3COO-$); 4·76, doublet and 4·7, multiplet ($2>C\underline{H}OAc$)] and four tertiary C-methyl groups [τ 8·73, 8·83, 8·85 and 8·94]. The i.r. spectrum has acetate and hydroxyl absorption [$\nu_{max.}^{CCl_4}$ 1758, 1745, 3596 cm.$^{-1}$]. There is no $>C\underline{H}OH$ resonance in the n.m.r. spectrum of ε-caesalpin but two sharp $-\overset{|}{C}-O\underline{H}$ signals at τ 7·07 and 8·36 disappear on exchange with deuterium oxide. Thus ε-caesalpin has two tertiary hydroxyl groups in addition to two secondary acetates and a furan ring and is therefore tricarbocyclic. The presence of a 2,3 disubstituted furan and four tertiary C-methyl groups is suggestive of a normal or rearranged vouacapane[3] skeleton with a tertiary hydroxyl group at C-14.

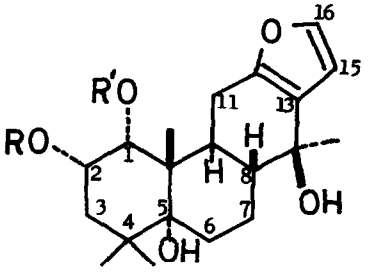
Treatment of ε-caesalpin with lithium aluminium hydride in ether yielded the crystalline tetrol (IV) m.p. 194-196° and the corresponding anhydro-derivative, characterised as the monoacetate (V) m.p. 203-205° [τ 4·89, 5·09, diffuse singlets ($C\underline{H}_2=C<$); disappearance of one C-methyl signal; $\lambda_{max.}$ 232 mμ (ε 8,600)]. The



I. R=R'=Ac

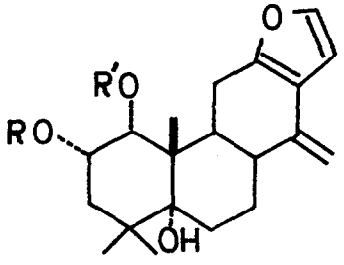
IV. R=R'=H

VI. R=Ac, R'=H

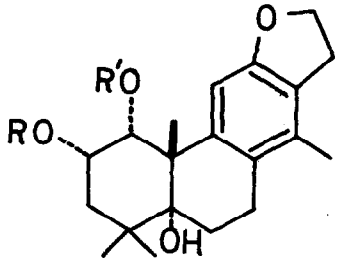


II. R=p-Br.C_6H_4.CO-, R'=H

III. R=R'=Ac

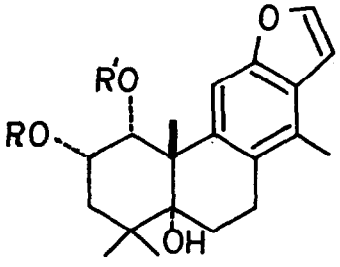


V. R=Ac, R'=H

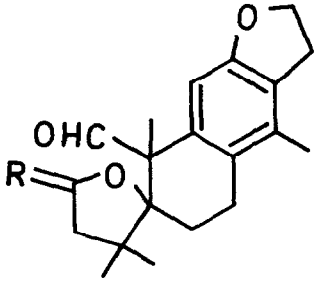


VII. R=R'=Ac

IX. R=R'=H

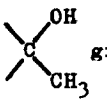
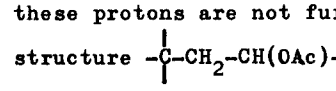


VIII. R=R'=Ac



X. R=H, OH

XI. R=O

latter confirms the  grouping at C-14. Under normal acetylation conditions the tetrol (IV) was transformed into the monoacetate (VI) m.p. 195-197° [τ 4·74, double quartet, J = 12, 5, 2 c./sec. ($\geq$C<u>H</u>OAc); 6·3, doublet, J = 2 c./sec. ($\geq$C<u>H</u>OH); $\nu_{max.}^{CHCl_3}$ 1737 (acetate), 3590, 3478 (hydroxyl) cm.$^{-1}$]. The acetate and hydroxyl groups are vicinal since irradiation at τ 6·3 leaves the $\geq$C<u>H</u>OAc resonance as a clean quartet (J = 12, 5 c./sec.). On the other hand irradiation at τ 4·74 causes the $\geq$C<u>H</u>OH signal to collapse to a sharp singlet. The multiplicity of the $\geq$C<u>H</u>OAc proton requires the presence of an adjacent methylene group. Double irradiation experiments show that the axial methylene proton resonates as a partially obscured triplet (J = 13, 12 c./sec) at τ 7·98 and the equatorial proton as a clean quartet (J = 13, 5 c./sec.) at τ 8·63. Since these protons are not further coupled, the above evidence leads to the part-structure  , a sequence which can be accommodated only in ring A of a vouacapane skeleton.

The location of the part-structure in ring A and its position relative to the remaining tertiary hydroxyl group were established in the following manner. Acid treatment of ε-caesalpin afforded the dihydrobenzofuran (VII) m.p. 210-211° [τ 3·61, singlet (aromatic proton); 7·93, singlet (aromatic $-CH_3$); 5·49, 6·87, both triplets (dihydrofuran methylenes)] which still retained an intramolecularly bonded tertiary hydroxyl group [$\nu_{max.}^{CCl_4}$ 3591 cm.$^{-1}$]. Shorter reaction times or inclusion of 2,3-dichloro-5,6-dicyano-p-benzoquinone in the medium resulted in the isolation of the benzofuran (VIII) m.p. 191-192° [$\lambda_{max.}$ 251 mμ (ε 7,500); 282 mμ (ε 2,700); 292 mμ (ε 2,800)] which presumably arises by dehydrogenation of a dihydrobenzene intermediate. Under similar acidic conditions α-caesalpin and 1,6,7-triacetoxy-δ-caesalpin were smoothly transformed to benzofurans with loss of the C-7 oxygen substituent. In the dihydrobenzofuran (VII) the $\geq$C<u>H</u>OAc proton which appears as a doublet (J = 2 c./sec.) is deshielded by 0·64 τ (relative to ε-caesalpin) due to the introduction of the aromatic ring. This strongly suggests that it is attached to C-1 (models) and therefore disfavours the otherwise possible 2,3-glycol system in ε-caesalpin.

Cleavage of the triol (IX) m.p. 263-265° with sodium metaperiodate yielded the hemiacetal aldehyde (X) m.p. 197-199° [τ -0·03, singlet (-CHO); 4·49, triplet (hemiacetal proton)] which was oxidised with Jones reagent to the corresponding γ-lactone (XI) m.p. 289-292° [$\nu_{max.}^{CCl_4}$ 1778 cm.$^{-1}$]. Thus the remaining tertiary hydroxyl group is attached to C-5. The evidence taken *in toto* with the assumption of a *trans* A, B ring junction leads to the structure (I) (or enantiomer) for ε-caesalpin.

The p-bromobenzoate (II) derived from ε-caesalpin crystallises in the monoclinic space group $P2_1$ with two molecules of $C_{27}H_{33}O_6Br$ in the unit cell of dimensions a = 6·563, b = 12·999, c = 14·809 Å; β = 94·50°. From equi-inclination Weissenberg photographs taken along the a and b crystallographic axes with Cu Kα radiation some 3000 reflections were obtained. The structure was solved by the heavy-atom method and refined by block-diagonal least-squares methods to an R-factor of 12·3%. Anomalous dispersion calculations allowed the absolute configuration shown in (II) and (III) to be determined from observed differences in intensities of 17 Bijvoet pairs[4] of reflections in an (h k l) precession photograph taken with Mo Kα radiation.

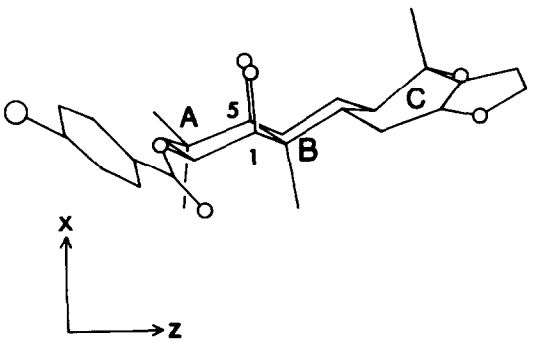


Fig. I.

Figure I gives a view of the molecule down the b-axis and shows the molecular geometry. Rings A, B and C are fused in a trans-anti-trans manner, with A and B in chair and C in half-chair conformations. The hydrogen of the C-5 axial hydroxyl group is involved in an intramolecular hydrogen bond (2·65 Å) with the axial hydroxyl group attached to C-1.

REFERENCES

1. M.Q. Khuda and M.E. Ali, Pakistan J. Sci. Ind. Research, 6, 65 (1963).
2. L. Canonica, G. Jommi, P. Manitto, U.M. Pagnoni and F. Pelizzoni, Gazz. Chim. Ital., 96, 662, 687, 698 (1966).
3. F.E. King, D.H. Godson and T.J. King, J. Chem. Soc., 1117 (1955).
4. J.M. Bijvoet, Endeavour, 14, 71 (1955).