Stereochemistry of a Macrocyclic Spermidine Alkaloid from *Caesalpinia digyna* Rottl. *X*-Ray Determination of the Structure of Caesalpinine C (Celallocinnine)

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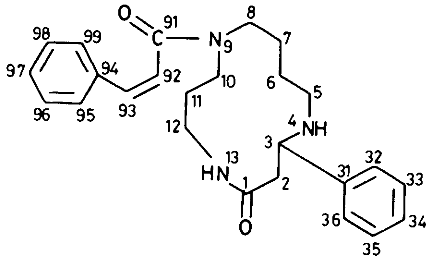
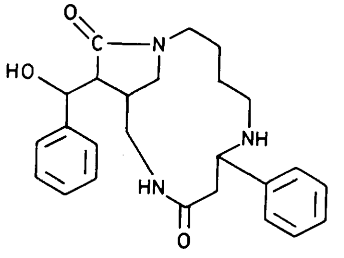
The molecular geometry of caesalpinine C (**1**) (celallocinnine), a macrocyclic spermidine alkaloid isolated from *Caesalpinia digyna* Rottl., has been determined by means of single-crystal *X*-ray analysis. The ^1H and ^{13}C n.m.r. spectra could satisfactorily be interpreted on the basis of the *X*-ray structure. The compound, $C_{25}H_{31}N_3O_2$, is orthorhombic with space group $P2_12_12_1$ and lattice constants $a = 9.963(2)$, $b = 8.026(2)$, $c = 28.627(5)$ Å, cell volume $V = 2\,289.1$ Å^3, and $Z = 4$. Diffractometer intensity measurements were made with Cu-K_α radiation and least-squares adjustment of the atomic parameters converged to a final R value of 0.05.

The structure and stereochemistry of caesalpinine A (**2**), a new skeleton macrocyclic spermidine alkaloid from *Caesalpinia digyna* Rottl. (Leguminosae) along with the isolation of a mixture of caesalpinine B and C have been reported.[1] Further separation and purification of the mixture by preparative t.l.c. followed by crystallization led to the isolation of pure caesalpinine C. Its physical and spectral (u.v., i.r., ^1H n.m.r., and mass) properties revealed its identity with celallocinnine, a minor alkaloid isolated from *Maytenus serrate*[2] (Hochst., ex A. Rich) R. Wilczek (Celastraceae). Although the planar structure of the alkaloid was suggested by chemical and spectral studies, its complete stereochemistry was yet to be established. This paper reports the single-crystal *X*-ray determination of the complete structure and stereochemistry of the alkaloid. The availability of the compound enabled its ^{13}C n.m.r. spectra to be elucidated.



(**1**)



(**2**)

Experimental

The u.v., i.r., n.m.r., c.d., and mass spectral measurements were performed as described previously.[1]

Isolation of Caesalpinine C (*Celallocinnine*) (**1**).—The isolation of the mixture of caesalpinine B and C from the leaves of *Caesalpinia digyna* Rottl. has already been reported.[1] The mixture (102 mg) appeared to be composed of silicate salts of the two alkaloids. This was subjected to repeated preparative t.l.c. on silica gel G and caesalpinine C could be isolated as its silicate salt (55 mg). Purification of caesalpinine B is in progress. The silicate salt of caesalpinine C was taken in 5% HCl (2 × 5 ml). The combined acid extract was cooled, basified with 35% ammonia, the precipitate was taken up in chloroform (3 × 5 ml), and the solvent evaporated to yield a residue (46 mg). This was rechromatographed on a column of neutral alumina (500 mg). Light petroleum–benzene (1 : 1) eluted a homogeneous solid which on crystallization from ethyl acetate yielded prismatic crystals of caesalpinine C, m.p. 170—171 °C; $[\alpha]_D$ $-27°$ (*c*, 0.52 in $CHCl_3$). U.v., i.r., c.d., mass, and ^1H n.m.r. spectral data were found to be similar to those reported for celallocinnine,[2] δ_C ($CDCl_3$; 25.15 MHz) 170.0 (s, C-1), 168.3 (s, C-91), 143.1† (s, C-94), 143.0† (s, C-31), 132.9 (d, C-93), 128.6‡ (d, C-33 + C-35), 128.5‡ (d, C-95 + C-99), 128.3‡ (d, C-34), 127.1‡ (d, C-97), 126.0‡ (d, C-32 + C-36 + C-96 + C-98), 123.2 (d, C-92), 60.6 (d, C-3), 47.0, 44.6, 41.6, 36.7, 28.5, 27.3, 24.3, and 22.8 p.p.m. (all t, C-2, C-5, C-6, C-7, C-8, C-10, C-11, C-12). Assignments of the ^{13}C signals are made on the basis of chemical shifts and off-resonance studies.[3]

Crystal Data.—$C_{25}H_{31}N_3O_2$, $a = 9.963(2)$, $b = 8.026(2)$, $c = 28.627(5)$ Å, cell volume $V = 2\,289.1$ Å^3, $Z = 4$, space group orthorhombic, $P2_12_12_1$, $D_x = 1.169$ g cm^{-3}, linear absorption coefficient (Cu-K_α) $\mu = 6.03$ cm^{-1}, total number of reflections ($\theta < 64.5°$) 2 234, unobserved [$I < 2\sigma(I)$] 865.

Crystallographic Measurements.—Colourless prismatic crystals of caesalpinine C were obtained from ethyl acetate. A specimen with dimensions 0.12 × 0.25 × 0.40 mm was selected for the *X*-ray measurements. From preliminary rotation and Weissenberg photographs the space group was determined to be orthorhombic, $P2_12_12_1$. Precise lattice constants and the intensity data of an octant (*h*, *k*, *l*, all $\geqslant 0$) were measured on a DEC PDP 15/40 controlled four-circle diffractometer with Ni-filtered Cu-K_α radiation ($\lambda = 1.5418$ Å). The lattice constants were refined from 15 high-order reflections. The reflection intensities were recorded by using the θ–2θ scan technique. A variable scan range $\Delta\theta$ was used with $\Delta\theta = 0.70 +$

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†,‡ May be interchanged.

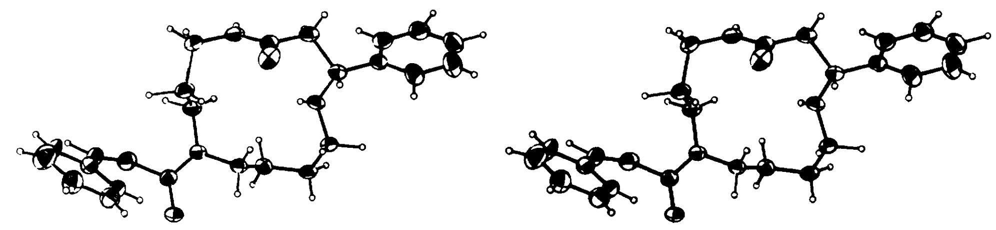

Figure 1. ORTEP[6] stereoview of (**1**). The thermal ellipsoids are plotted at a 20% probability level (absolute configuration not determined)

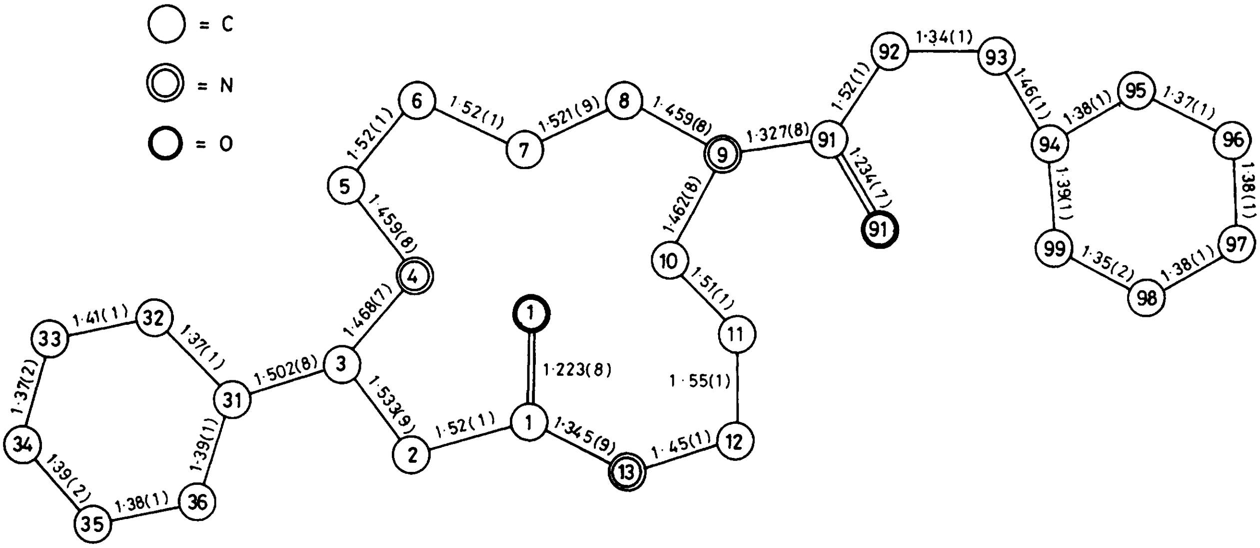

Figure 2. Atom numbering scheme and bond lengths (Å, e.s.d.s in parentheses) for (**1**)

0.46 tanθ. Maximum and minimum scan speeds were 0.05 and 0.025 degree s^{-1}. In each background, counting rates were measured stationarily for half the time needed for the reflection scan.

Structure Determination.—Phase determination was carried out successfully with direct methods (MULTAN).[4] The refinement with least-squares methods was executed with the corresponding programs of the *X*-Ray 76[5] program system. Scattering factors were taken from the corresponding standard routine of the *X*-Ray 76 system.[6,7] Absorption corrections were not applied. All hydrogen atoms were located from difference syntheses. During the refinement, which was made with anisotropic temperature factors for the non-hydrogen atoms and isotropic thermal parameters for the hydrogens, a third-order weighting function was used ($W^{-1} = 1.344 - 0.111\,F + 0.005\,F^2 - 0.496 \times 10^{-4}\,F^3$). Unobserved reflections were included in the refinement only if $|F_c| > |F_o|$. After convergence of all parameters a final R value of 5.0% $\{R_w = [\Sigma\omega(|F_o| - |F_c|)^2/\Sigma\omega F_o^{\,2}]^{\frac{1}{2}} = 4.9\%\}$ was obtained. The maximum and average shift/error ratio at the end of the refinement were 2.2 and 0.23. A final electron density map showed all residual density below 0.2 e Å^{-3}. The absolute configuration of caesalpinine C has not been determined.

Results and Discussion

Chemical and spectroscopic investigations revealed that among the 30 non-hydrogen atoms of one molecule of caesalpinine C, three nitrogens and two oxygens are present. All these five positions could be assigned with certainty. The molecular skeleton, the peak height, the refinement results for the isotropic temperature factors, and the distribution of the hydrogen atoms gave unambiguous results for the positions of the heteroatoms. Thus the chemical structure of caesalpinine C is (**1**). The molecular conformation is displayed in the stereoplot of Figure 1. The atom numbering scheme and bond lengths are shown in Figure 2. The final atomic co-ordinates are given in Table 1. Bond angles and selected torsion angles are listed in Tables 2 and 3. Complete atomic parameters are listed in Supplementary Publication No. 56100 (4 pp.).*

As seen from Figure 1 the cinnamoyl double bond has the *cis* configuration. The macrocyclic 13-membered ring of caesalpinine C has a different conformation compared with that of caesalpinine A due to the absence of the bridged five-membered ring in the former. For 13-membered cycloalkane rings Dale[8] has calculated some low-energy conformations with a [12433] conformation as the lowest and a [13333] conformation the next lowest, which is 1.1 kcal mol^{-1} less stable. In the present structure the 13-membered macrocycle is very similar to the [13333] conformation, C(2)–C(3) being the isolated gauche bond.

In caesalpinine A two intramolecular hydrogen bonds were observed while caesalpinine C totally lacks this type of interaction. However, two intermolecular hydrogen bonds are present in the caesalpinine C (Table 4). Bond distances and valence angles are in the expected ranges and require no special comment.

The structures of the significant mass spectral fragments of (**1**) may reasonably be assigned as shown in the Scheme, based on the high-resolution mass spectral values (Table 5).

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*For details of Supplementary Publications see Instructions for Authors in *J. Chem. Soc., Perkin Trans. 2*, 1985, Issue 1.

Table 1. Final atomic parameters and standard deviations (in parentheses) for non-hydrogen atoms in caesalpinine C

Atom	x	y	z	$10^2 U_{eq}$†/Å^2
C(1)	1.021 0(7)	0.235 4(8)	0.982 1(2)	7.9(2)
O(1)	1.127 4(4)	0.310 3(7)	0.978 9(2)	10.0(2)
C(2)	0.969 9(8)	0.171 9(8)	1.028 8(3)	7.8(3)
C(3)	0.967 2(6)	0.311 0(7)	1.065 4(2)	6.8(2)
N(4)	0.868 0(5)	0.433 7(5)	1.049 5(2)	6.8(2)
C(5)	0.885 0(7)	0.599 6(7)	1.069 5(2)	7.1(2)
C(6)	0.772 5(8)	0.716 2(8)	1.055 3(3)	8.3(3)
C(7)	0.731 2(7)	0.711 4(9)	1.004 2(2)	7.5(2)
C(8)	0.847 1(6)	0.729 6(8)	0.969 9(2)	6.6(2)
N(9)	0.807 0(5)	0.688 4(5)	0.922 3(2)	6.9(2)
C(10)	0.813 3(8)	0.512 1(8)	0.090 7(3)	8.0(3)
C(11)	0.952 6(8)	0.458 0(8)	0.895 4(3)	8.7(3)
C(12)	0.968 6(9)	0.266 8(9)	0.898 4(3)	8.9(3)
N(13)	0.942 3(7)	0.205 3(7)	0.944 9(2)	8.3(2)
C(31)	0.943 6(6)	0.245 0(7)	1.113 9(2)	7.2(2)
C(32)	1.025 2(8)	0.289(1)	1.150 5(3)	10.1(3)
C(33)	1.002(1)	0.226(2)	1.195 8(3)	13.3(5)
C(34)	0.899(1)	0.117(1)	1.203 2(4)	12.2(4)
C(35)	0.814(1)	0.070(1)	1.167 0(3)	11.8(4)
C(36)	0.837 7(8)	0.136(1)	1.123 1(3)	9.7(3)
C(91)	0.764 9(6)	0.806 4(8)	0.893 3(2)	7.4(2)
O(91)	0.756 1(4)	0.954 4(5)	0.904 7(1)	8.4(2)
C(92)	0.725 2(8)	0.755(1)	0.844 0(3)	9.4(3)
C(93)	0.802 4(9)	0.755(1)	0.805 6(3)	9.9(3)
C(94)	0.943 1(8)	0.799 7(9)	0.799 4(2)	8.6(3)
C(95)	1.020 5(8)	0.882 9(9)	0.832 1(2)	8.5(3)
C(96)	1.151 6(9)	0.924(1)	0.823 3(3)	9.4(3)
C(97)	1.213(1)	0.880(1)	0.781 8(3)	11.5(4)
C(98)	1.135(1)	0.797(2)	0.749 7(4)	14.3(5)
C(99)	1.006(1)	0.758(1)	0.757 5(3)	11.8(4)

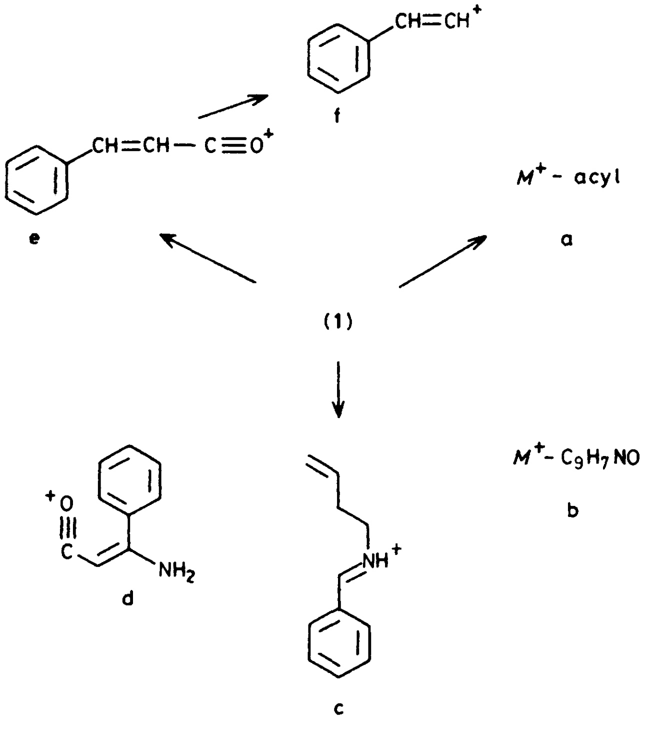
† U_{eq} Values are calculated from W. C. Hamilton, *Acta Crystallogr.*, 1959, **12**, 609.

Table 2. Valence angles in degrees (e.s.d.s in parentheses)

O(1)–C(1)–C(2)	121.6(6)	C(3)–C(31)–C(36)	120.9(6)
O(1)–C(1)–N(13)	122.2(6)	C(32)–C(31)–C(36)	117.7(6)
C(2)–C(1)–N(13)	116.2(6)	C(31)–C(32)–C(33)	120.7(8)
C(1)–C(2)–C(3)	111.3(5)	C(32)–C(33)–C(34)	119.7(9)
C(2)–C(3)–N(4)	106.7(5)	C(33)–C(34)–C(35)	121.0(1)
C(2)–C(3)–C(31)	112.2(5)	C(34)–C(35)–C(36)	118.0(1)
N(4)–C(3)–C(31)	114.7(5)	C(31)–C(36)–C(35)	122.8(8)
C(3)–N(4)–C(5)	114.4(5)	N(9)–C(91)–O(91)	123.0(5)
N(4)–C(5)–C(6)	111.9(5)	N(9)–C(91)–C(92)	117.9(6)
C(5)–C(6)–C(7)	116.3(6)	O(91)–C(91)–C(92)	119.2(6)
C(6)–C(7)–C(8)	114.4(6)	C(91)–C(92)–C(93)	127.6(7)
C(7)–C(8)–N(9)	111.9(5)	C(92)–C(93)–C(94)	130.6(7)
C(8)–N(9)–C(10)	116.0(5)	C(93)–C(94)–C(95)	124.9(6)
C(8)–N(9)–C(91)	120.6(5)	C(93)–C(94)–C(99)	118.3(7)
C(10)–N(9)–C(91)	123.3(5)	C(95)–C(94)–C(99)	116.8(8)
N(9)–C(10)–C(11)	112.6(6)	C(94)–C(95)–C(96)	121.4(7)
C(10)–C(11)–C(12)	111.4(6)	C(95)–C(96)–C(97)	121.3(8)
C(11)–C(12)–N(13)	111.8(6)	C(96)–C(97)–C(98)	117.0(1)
C(1)–N(13)–C(12)	124.3(6)	C(97)–C(98)–C(99)	123.0(1)
C(3)–C(31)–C(32)	121.4(6)	C(94)–C(99)–C(98)	120.9(9)

Table 3. Dihedral angles in degrees (e.s.d.s in parentheses) (absolute configuration not determined)

O(1)–C(1)–C(2)–C(3)	52.7(9)
O(1)–C(1)–N(13)–C(12)	−5.0(1)
C(1)–C(2)–C(3)–N(4)	65.0(7)
C(2)–C(3)–N(4)–C(5)	−158.7(5)
C(3)–N(4)–C(5)–C(6)	−174.7(5)
N(4)–C(5)–C(6)–C(7)	−44.2(8)
C(5)–C(6)–C(7)–C(8)	−51.3(8)
C(6)–C(7)–C(8)–N(9)	167.6(5)
C(7)–C(8)–N(9)–C(10)	−85.5(7)
C(8)–N(9)–C(10)–C(11)	−83.0(8)
N(9)–C(10)–C(11)–C(12)	160.8(6)
C(10)–C(11)–C(12)–N(13)	−58.3(9)
C(11)–C(12)–N(13)–C(1)	−68.3(9)
C(12)–N(13)–C(1)–C(2)	175.1(6)
N(13)–C(1)–C(2)–C(3)	−127.0(6)
C(1)–C(2)–C(3)–C(31)	−168.6(5)
C(5)–N(4)–C(3)–C(31)	76.4(6)
C(2)–C(3)–C(31)–C(32)	129.6(7)
N(4)–C(3)–C(31)–C(32)	−108.4(7)
O(91)–C(91)–N(9)–C(8)	−0.6(9)
C(92)–C(91)–N(9)–C(8)	179.8(6)
C(93)–C(92)–C(91)–N(9)	−93.7(9)
C(94)–C(93)–C(92)–C(91)	1.0(1)
C(95)–C(94)–C(93)–C(92)	−13.0(1)
C(7)–C(8)–N(9)–C(91)	93.0(7)
C(11)–C(10)–N(9)–C(91)	98.6(8)



Scheme.

Table 4. Hydrogen bonding for caesalpinine C

X–H···Y	X–H (Å)	X···Y (Å)	H···Y (Å)	Symmetry operation for Y
N(13)–H(13)···O(91)	0.89(7)	2.971(7)	2.36(7)	$x, -1 + y, z$
N(4)–H(4)···O(1)	1.04(9)	3.201(7)	2.39(9)	$-\frac{1}{2} + x, \frac{1}{2} - y, 2 - z$

Table 5. Most characteristic mass spectral ions (experimental high-resolution values) of caesalpinine C

Ion[a]	Accurate mass	Empirical formula	% of base peak
$M^{+\cdot}$	405.2438	$C_{25}H_{31}N_3O_2$	10.5
a	274.1924	$C_{16}H_{24}N_3O$	71.4
b	260.1884	$C_{16}H_{24}N_2O$	13.6
c	160.1120	$C_{11}H_{14}N$	19.0
d	146.0605	C_9H_8NO	20.5
e	131.0497	C_9H_7O	57.9
f	103.0551	C_8H_7	100

[a] See Scheme.

Acknowledgements

We thank Shri S. K. Roy, IICB, Calcutta, for his help in the isolation work.

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Received 6*th March* 1984; *Paper* 4/374