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THE ABSOLUTE CONFIGURATION OF DICHAPETALIN A*

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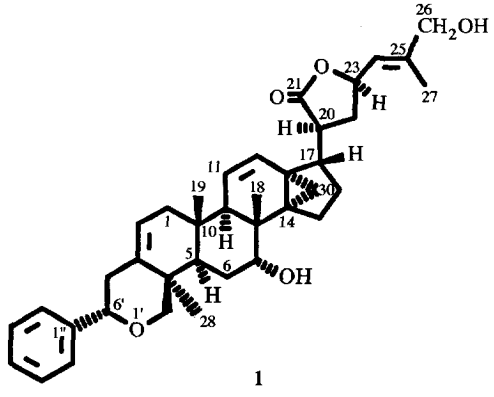
Key Word Index—*Dichapetalum madagascariense*; Dichapetalaceae; dichapetalin A; 13,30-cyclo-29-nordammarano[4,3-c]pyran; absolute configuration; X-ray crystal structure.

Abstract—The absolute configuration of dichapetalin A, [(4α,6′α,7α,17α,20*S*,23*R*,24*E*)-2′,3′,5′,6′-tetrahydro-7,23,26-trihydroxy-6′-phenyl-13,30-cyclo-29-nordammara-2,11,24-tri-eno[4,3-c]pyran-21-oic acid γ-lactone], the major cytotoxic constituent from *Dichapetalum madagascariense* has been established to be 4*R*,5*R*,7*R*,8*R*,9*R*,10*S*,13*R*,14*S*,17*S*,20*S*,23*R*,6′*S*.

INTRODUCTION

In the course of a phytochemical examination of the West African plant *Dichapetalum madagascariense* we isolated as a major component the novel 13,30-cyclo-29-nordammarano[4,3-c]pyran, dichapetalin A (**1**) [2], which exhibits significant cytotoxic activity. Among the other relatively minor plant constituents we found further dichapetalins, whose structures vary in: (i) the presence or otherwise of the 11,12-double bond; (ii) the structure of the side chain at C-17 [1].

The basic structures and relative configurations of the isolated compounds were determined spectroscopically [1, 2]. We now report on an X-ray crystallographic determination of the absolute configuration of **1**, which also enabled us to establish the absolute configurations of the ring systems of other dichapetalins.



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*Part 75 in the series 'Constituents of Tropical Medicinal Plants'. For Part 74 see ref. [1].

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RESULTS AND DISCUSSION

Dichapetalin A (**1**), $C_{38}H_{48}O_5$, $[\alpha]_D^{21}$ +35°, was isolated from an extract of *D. madagascariense* [2]. Crystals suitable for X-ray measurements were grown from ethanol. The structure and the absolute configuration resulting from the crystallographic measurements are as shown by the projection of the molecule with displacement ellipsoids in Fig. 1.

EXPERIMENTAL

$C_{38}H_{48}O_5 \cdot H_2O$, $M_r = 602.81$, crystals of size $0.4 \times 0.3 \times 0.3$ mm^3, orthorhombic, space group $P2_12_12_1$ (No. 19 of IT [4]). Lattice parameters are $a = 7.758(4)$ Å, $b = 10.783(5)$ Å, $c = 39.42(2)$ Å and $V = 3297.66$ Å^3 (determined from 50 reflections, $14° < \vartheta < 25°$), $Z = 4$, $d_{calc} = 1.214$ g cm^{-3} and μ_x (CuK_α radiation, $\lambda = 1.5405$ Å) $= 6.051$ cm^{-1}. Reflections were recorded with an automatic four circle diffractometer using CuK_α radiation and a graphite monochromator and $\omega - 2\vartheta$ scans. Data collection was performed in the range $-2 \leq h \leq 8$, $-2 \leq k \leq 11$ and $-43 \leq l \leq 43$ with $(\sin \vartheta/\lambda)_{max} = 0.56$. Four standard reflections were monitored every 4 hr. A decay of 12% was observed over the whole data collection. Intensities were scaled relative to the standard reflections. Total number of measured reflections was 7933 from which 4104 were unique ($R_{merge} = 2.8\%$). 3377 reflections had $I(h) > 3\sigma(I(h))$ and were retained for further analysis. Intensities were corrected for absorption using experimental data from ψ-scans. The structure was solved by direct methods [5]. All non-H atoms were refined anisotropically using full matrix least-squares [6] based on $|F|$ with weights $1/\sigma(|F|)^2$. The coordinates of H-1 to H-13 were refined where the angles between the

Table 1. Geometric parameters (Å, °) for dichapetalin A

O1′-C6′	1.445 (5)	C10-C9	1.552 (4)
O1′-C2′	1.438 (4)	C5-C6	1.536 (5)
O2-C7	1.429 (4)	C9-C8	1.551 (4)
O3-C21	1.212 (4)	C9-C11	1.505 (4)
O4-C21	1.355 (4)	C8-C7	1.539 (5)
O4-C23	1.497 (4)	C8-C18	1.555 (4)
O5-C26	1.414 (5)	C8-C14	1.520 (4)
C1″-C2″	1.357 (5)	C7-C6	1.511 (5)
C1″-C6″	1.396 (5)	C11-C12	1.343 (4)
C1″-C6′	1.509 (5)	C12-C13	1.475 (4)
C2″-C3″	1.394 (5)	C13-C14	1.524 (4)
C3″-C4″	1.376 (6)	C13-C30	1.519 (5)
C4″-C5″	1.382 (6)	C13-C17	1.519 (4)
C5″-C6″	1.385 (5)	C14-C30	1.499 (5)
C6′-C5′	1.531 (5)	C14-C15	1.524 (5)
C5′-C3	1.509 (5)	C17-C16	1.535 (5)
C3-C4	1.521 (4)	C17-C20	1.526 (5)
C3-C2	1.312 (4)	C16-C15	1.550 (5)
C4-C2′	1.548 (4)	C20-C21	1.511 (5)
C4-C28	1.556 (5)	C20-C22	1.522 (5)
C4-C5	1.551 (4)	C23-C22	1.520 (5)
C2-C1	1.497 (4)	C23-C24	1.498 (5)
C1-C10	1.538 (4)	C24-C25	1.316 (4)
C10-C5	1.550 (4)	C25-C26	1.506 (5)
C10-C19	1.550 (5)	C25-C27	1.500 (5)
C2′-O1′-C6′	111.1 (3)	C4-C3-C5′	113.9 (3)
C23-O4-C21	108.9 (3)	C2-C3-C5′	122.2 (3)
C6″-C1″-C2″	119.1 (4)	C2-C3-C4	123.8 (3)
C6′-C1″-C2″	121.1 (4)	C2′-C4-C3	105.9 (3)
C6′-C1″-C6″	119.8 (4)	C28-C4-C3	111.8 (3)
C3″-C2″-C1″	121.5 (4)	C28-C4-C2′	106.7 (3)
C4″-C3″-C2″	119.1 (4)	C5-C4-C3	110.7 (3)
C5″-C4″-C3″	120.5 (4)	C5-C4-C2′	114.6 (3)
C6″-C5″-C4″	119.5 (4)	C5-C4-C28	107.3 (3)
C5″-C6″-C1″	120.3 (4)	C4-C2′-O1′	111.0 (3)
C1″-C6′-O1′	107.6 (3)	C1-C2-C3	124.6 (3)
C5′-C6′-O1′	110.7 (3)	C10-C1-C2	112.8 (3)
C5′-C6′-C1″	112.0 (3)	C5-C10-C1	106.4 (3)
C3-C5′-C6′	110.3 (3)	C19-C10-C1	105.8 (3)
C19-C10-C5	114.1 (3)	C13-C14-C8	116.8 (3)
C9-C10-C1	108.0 (3)	C30-C14-C8	123.3 (3)
C9-C10-C5	107.7 (3)	C30-C14-C13	60.3 (2)
C9-C10-C19	114.3 (3)	C15-C14-C8	120.9 (3)
C10-C5-C4	116.8 (3)	C15-C14-C13	107.2 (3)
C6-C5-C4	114.1 (3)	C15-C14-C30	111.8 (3)
C6-C5-C10	112.5 (3)	C14-C30-C13	60.7 (2)
C8-C9-C10	117.2 (3)	C16-C17-C13	105.0 (3)
C11-C9-C10	114.2 (3)	C20-C17-C13	114.3 (3)
C11-C9-C8	110.6 (3)	C20-C17-C16	116.1 (3)
C7-C8-C9	109.5 (3)	C15-C16-C17	105.0 (3)
C18-C8-C9	111.1 (3)	C16-C15-C14	105.7 (3)
C18-C8-C7	108.5 (3)	C21-C20-C17	112.8 (3)
C14-C8-C9	109.3 (3)	C22-C20-C17	119.0 (3)
C14-C8-C7	111.2 (3)	C22-C20-C21	101.6 (3)
C14-C8-C18	107.2 (3)	O4-C21-O3	119.4 (3)
C8-C7-O2	111.7 (3)	C20-C21-O3	129.7 (3)
C6-C7-O2	108.5 (3)	C20-C21-O4	111.0 (3)
C6-C7-C8	112.7 (3)	C22-C23-O4	102.7 (3)
C7-C6-C5	111.5 (3)	C24-C23-O4	109.0 (3)
C12-C11-C9	121.6 (3)	C24-C23-C22	116.7 (3)
C13-C12-C11	121.4 (3)	C23-C22-C20	103.0 (3)
C14-C13-C12	116.9 (3)	C25-C24-C23	123.9 (4)
C30-C13-C12	117.2 (3)	C26-C25-C24	121.1 (4)
C30-C13-C14	59.0 (2)	C27-C25-C24	125.3 (4)
C17-C13-C12	122.2 (3)	C27-C25-C26	113.5 (4)
C17-C13-C14	108.0 (3)	C25-C26-O5	115.6 (3)
C17-C13-C30	116.3 (3)		

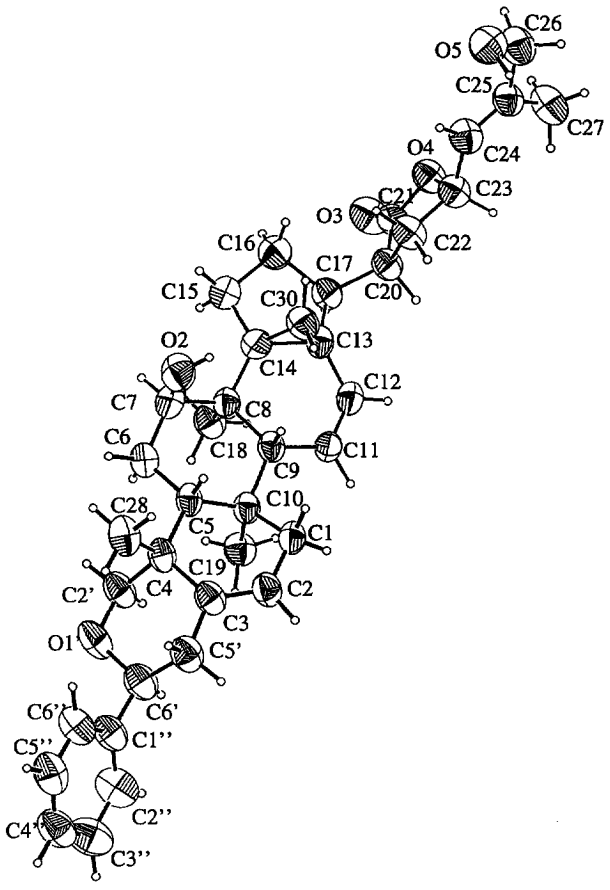

Fig. 1. Projection of the molecule with anisotropic displacement ellipsoids (50% probability) for non-H atoms and arbitrary small displacement factors for H atoms [3].

H-11 to H-13 of methyl group C27 were restrained to 109.7(1.0)°. The isotropic displacement factors of these H atoms were refined independently except for H-1, H-2, H-4 and H-11 to H-13 where they were refined together with one of the binding C or O atoms. The positions of all other H atoms were calculated with a C–H distance of 1.0 Å and a H displacement factor 1.05 times the one of the corresponding C atom. The shifts $(\Delta/\sigma)_{max}$ of the final least square cycle were smaller than 0.01. *R*-values were $R_w = 0.04$ and $R_w = 0.036$ for 444 refined parameters. Goodness of fit was 1.64. Final difference Fourier was featureless ($\Delta\rho_{min} = -0.23$, $\Delta\rho_{max} = 0.19$ e Å^{-3}). The extinction parameter [7] was refined to 19.98. The absolute configuration was determined by refining Flack's parameter [8] $x = -0.1(0.3)$. The same absolute configuration was obtained by comparing the 300 largest Bijvoet differences. Distance and angles for non-H atoms are compiled in Table 1.

The O21 of the water molecule shows several H-bonds to two independent molecules. These are O3 · · · H4-O21 with 2.907 Å, O5-H2 · · · O21 with 2.755 Å and O5 · · · H3-O21 with 2.732 Å.

All crystallographic details are deposited with the Cambridge Crystallographic Data Center.

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