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BULLATANTRIOL, A SESQUITERPENE FROM *ANNONA BULLATA*

LEO KUTSCHABSKY, DAISY SANDOVAL* and HELMUT RIPPERGER†

Central Institute of Molecular Biology, Academy of Sciences of the GDR, Berlin-Buch, German Democratic Republic; *Institute of Botany, Academy of Sciences of Cuba, Havana, Cuba; †Institute of Plant Biochemistry, Academy of Sciences of the GDR, Halle (Saale), German Democratic Republic

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Key Word Index—*Annona bullata*; Annonaceae; sesquiterpene; bullatantriol.

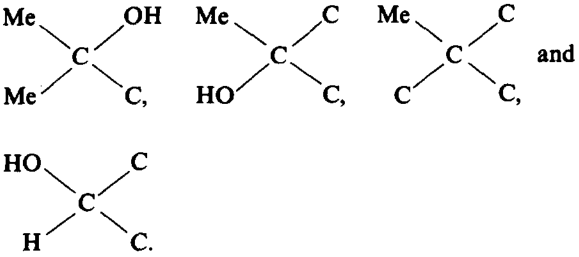
Abstract—Bullatantriol has been isolated from *Annona bullata*. Its constitution and relative configuration have been established by X-ray analysis. Its absolute configuration has been assigned by chiroptical investigation of the corresponding 7-ketone.

INTRODUCTION

Leaves of the bush *Annona bullata* Rich. were collected near Havana, Cuba. Besides the isoquinoline alkaloids (*R*)-anonaine and liriodenine [1], a new compound, bullatantriol, was isolated from the 'alkaloid fraction' of the methanolic extract.

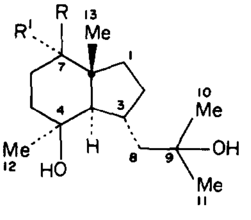
RESULTS AND DISCUSSION

^1H NMR and mass spectroscopy (see Experimental) indicated that bullatantriol has a sesquiterpenoid structure containing the following groups:

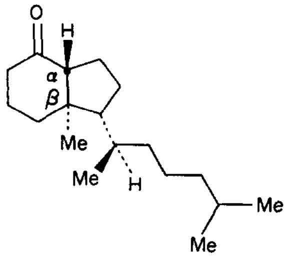


The constitution and relative configuration of the molecule ($C_{15}H_{28}O_3$) were determined by X-ray analysis. A perspective drawing of the final X-ray model is shown in Fig. 1.

To elucidate the absolute configuration, bullatantriol (**1**) was oxidized to its 7-ketone (**2**) which showed a negative Cotton effect at 294 nm in MeOH ($a = -29.5°$, corresponding to $\Delta\varepsilon = -0.73$). The negative sign was in agreement with the stereochemical structure **2** for the ketone as outlined below and hence with structure **1** for bullatantriol. The sign of the Cotton effect of ketone **2** cannot be predicted by a qualitative application of the octant rule because of positive (α-methyl) and negative contributions (5-membered ring, side chain in an opposing rear octant). Therefore the Cotton effect (in MeOH) was estimated in two ways: (1) From 5α-androstan-12-one ($\Delta\varepsilon = +1.46$) eliminating by calculation the contributions of ring B ($\delta\Delta\varepsilon = +1.4$), ring A ($\delta\Delta\varepsilon = \pm 0.0$), and the methyl group C-19 ($\delta\Delta\varepsilon = -0.2$) and considering the effect of C-8, C-9 and C-11 (−0.7, −0.25, −0.3), for which a zig-zag conformation was assumed. Such a conformation can be recognized in the crystal structure of **1** (Fig. 1). In this way a value of $\Delta\varepsilon = -0.99$ was estimated for **2** [2].



1 R = OH, R' = H
2 R + R' = O



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(2) From *trans*-1-(2-isooctyl)-8-methylhydrindan-4-one (**3**) ($a = -155.4°$, corresponding to $\Delta\varepsilon = -3.86$) eliminating by calculation the contribution of the β-methyl group ($\delta\Delta\varepsilon = -0.6$) and considering the effect of

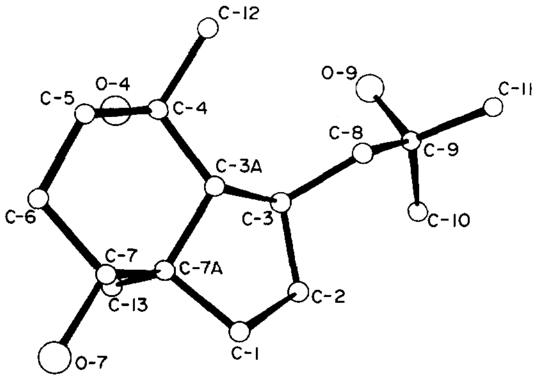

Fig. 1. Molecular structure of bullatantriol (**1**) (numbered by analogy to oppositol [4]).

an α-methyl group ($\delta\Delta\varepsilon = +1.7$). Thus a value of $\Delta\varepsilon = -1.56$ was estimated for **2** [2, 3]. This value was too large because of the longer side chain in ketone **3** relative to **2**.

Oppositol, a sesquiterpene alcohol with the same carbon skeleton, but enantiomeric stereochemistry, has been isolated from the marine alga *Laurencia subopposita* [4].

EXPERIMENTAL

Plant material. Annona bullata was collected in September in Minas, Campo Florido, Havana, Cuba, and identified by Lic. Pedro Herrera. A voucher specimen is deposited in the Herbarium of the Institute of Botany, Academy of Sciences of Cuba, Havana.

Bullatantriol (**1**). Dried (50°) and ground leaves of *A. bullata* (5.25 kg) were extracted with MeOH at room temp. The extract was concd *in vacuo* and partitioned between 0.5 M HCl and C_6H_6–Et_2O (1:1). After addition of $NaHCO_3$ to the aq. layer, the latter was extracted with $CHCl_3$–EtOH (2:1). The material extracted by the organic solvents was chromatographed over silica gel with Et_2O–MeOH (19:1). Crystallization (MeOH–Et_2O) gave **1** (yield 0.01%), mp 179.5–181.5°, $[\alpha]_D^{20}$ +45.3° (MeOH; *c* 0.61). ^{1}H NMR [200 MHz, $CDCl_3$–CD_3OD (1:1), TMS]: δ1.02 (3H, *s*, H-13), 1.24 (6H, *s*, H-10, H-11), 1.31 (3H, *s*, H-4), 3.30 (1H, *m*, H-7); EIMS 70 eV, *m/z* (rel. int.): 241.1806 $[M - Me]^+$, calc. for $C_{14}H_{25}O_3$: 241.1804 (6), 238.1931 $[M - H_2O]^+$, calc. for $C_{15}H_{26}O_2$: 238.1933 (2), 223 $[M - Me - H_2O]^+$ (30), 220 $[M - 2H_2O]^+$ (3), 205 $[M - Me - 2H_2O]^+$ (9), 202 $[M - 3H_2O]^+$ (2), 197 $[M - Me_2C(OH)]^+$ (10), 187 $[M - Me - 3H_2O]^+$ (4), 179 $[M - Me_2C(OH) - H_2O]^+$ (82), 123 (100), 59 $[Me_2C(OH)]^+$ (33). (Found: C, 70.8; H, 11.8. $C_{15}H_{28}O_3$ requires: C, 70.3; H, 11.0%.)

7-Ketone (**2**). A soln of 95 mg **1** in 2 ml C_5H_5N was added to 126 mg CrO_3 in 4 ml C_5H_5N. After 40 hr at room temp, H_2O was added and the mixture was extracted with $CHCl_3$. The extract was washed with 2 M HCl and $NaHSO_3$ soln, dried over Na_2SO_4 and evaporated *in vacuo*. Crystallization (Et_2O–*n*-hexane) gave **2**; yield 60 mg (64%); mp 119–122°, $[\alpha]_D^{20}$ +59.2° (MeOH, *c* 0.61). IR ν_{max}^{KBr} cm^{-1}: 1710 (ketone); UV λ_{max}^{MeOH} nm (log ε): 289 (1.62); ORD (MeOH): $[\phi]_{313}$ −440° (trough), $[\phi]_{274}$ +2510° (peak); EIMS 10–16 eV *m/z* (rel. int.): 254 M^+ (6), 239 $[M - Me]^+$ (14), 236 $[M - H_2O]^+$ (55), 221 $[M - Me - H_2O]^+$ (57), 179 (78), 123 (100).

Crystal data. $C_{15}H_{28}O_3$, M = 256.4, orthorhombic, space group $C222_1$ with $a = 13.423$ (5), $b = 9.631$ (4), and $c = 23.005$ (8) Å, and $Z = 8$, $D_c = 1.14$ gcm^{-3}, MoK_α radiation. The structure was solved by direct methods using a multisolution weighted tangent formula approach with the Enraf-Nonius structure determination package. Isotropic and later anisotropic least-squares refinement led to $R = 0.134$. A subsequent difference Fourier map revealed the positions of most of the hydrogen atoms. But some were poorly defined and therefore they were generated geometrically except those of the hydroxyl groups. The least-squares refinement of positional and anisotropic thermal parameters for non-hydrogen atoms with fixed positions for hydrogen atoms led to the final value of $R = 0.105$ for 1304 independent reflections [$I > 2\sigma(I)$, $\theta < 27.5°$]. The relatively high *R*-value is explained by the poor quality of the crystals. A final difference Fourier map was everywhere < 0.25 eÅ^{-3}.

The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this paper.

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