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THE STEREOSTRUCTURES OF PULCHELLIDINE AND PULCHELLIN.

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In the foregoing communication(1), we have described that the degradation product of pulchellidine(I), epipulchellin, must be differentiated from pulchellin (2) on the basis of slight, but distinct differences of the spectral data of two compounds, the latter of which now is not found to be in high purity. However, the former has been shown to be identical with the pure pulchellin(II) separated from the pulchellin mixture by Florida group*2 through the direct comparison of certain derivatives of both materials. We now wish to report the spacial structure determination of I and II, the latter of which has been separated from the other constituents in the cultivated species of Gaillardia pulchella Foug(Tenningiku)*3.

The triclene extract from the air-dried whole plant yielded a crystalline mixture on elution mainly with $CHCl_3$ of neutral alumina chromatography after benzene-chloroform elution(0.01%)*4. The powdery crystals remained after a mechanical separation of large prisms*5, were converted to the acetates mixture(II/IIa= 6/1, estimated by GLC*6 and NMR*7). By combination of recrystallizations and silica gel chromatographies, the derivatives of II(0.004%) and a new lactone isomer, neopulchellin(IIa)*8(3) (0.003%), were isolated gas chromatographically pure.

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*2 The private communication from Prof. W. Herz. The report for purification of pulchellin and its stereostructure determination is submitted to the Journal of Organic Chemistry by the American group.

*3 Presented in the 13th Symposium on Chemistry of Natural Products of Japan held in Sapporo, Sep. 25-27, 1969; paper abstracts p.257-264.

*4 A new sesquiterpene named "Compound L": $C_{17}H_{22}O_5$ (M^+ 306); mp 165-167°(d.); $(\alpha)_D$ +4.22°(c,0.474; EtOH; 21°) was isolated from this fraction.

*5 A new basic constituent refered to "Compound I": $C_{10}H_{19}O_{11}N_3$; mp 147-148.5°; $(\alpha)_D$ +3.4°(c,1.03; EtOH; 27°) was isolated from this division.

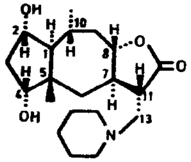
*6 Silicon OV-17 1.5% on 80/100" Chromosorb-AW; temp. 225°(column) and 300° (sample).

*7 Elementary analyses, rotations($CHCl_3$), TLC and absorption spectra were run and recorded in the usual manner as described in the preceeding paper(1).

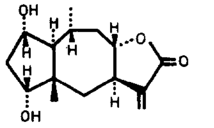
*8 $C_{15}H_{22}O_4$; mp 166.5-167.5°; $(\alpha)_D$ +43.5°(c,1.01; 25°): Acetate, mp 151.5-152.5°; $(\alpha)_D$ +26°(c,1.73; 20°). See the following paper(7).

Pulchellin (II)[$C_{15}H_{22}O_4$ *6; mp 162-164°; $(\alpha)_D^{25°}$ -43.3°(c,0.65) *6: Cf. mp 165-168°; $(\alpha)_D^{26°}$ -36.21°(c,2.43)(2)] and diacetylpulchellin[mp 128.5-129.5°; $(\alpha)_D^{20°}$ -58.7°(c,0.46); GLC 23 min: Cf. mp 123-125°; $(\alpha)_D^{26°}$ -28.9°(c,1.83)(2)] were identical in all respects with the authentic samples(1). II was readily converted to I(1) by addition of piperidine under the drastic conditions(100°, N_2, 1 day) rather than the mild(r.t., N_2, 2 days)(1).

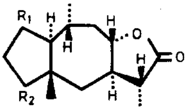
The similar contribution of asymmetric centers at C_2 and C_4 shown by negative ΔM_D of II[-90.3 cf. -5.2(2)] with its acetate suggests that cis-cyclopentane-2,4-diol[cyclic sulfite and cyclopentenone formation(2)] in II should have α configuration. On the other hand, NMR signals of C_4-H, appeared as doublet (J= 5-6 Hz) centered at 3.62(II), 3.73(I), and at 4.78, 4.64 in the corresponding acetates as well as at 3.92 in the ketol(IV) v.i., suggest that the C_4-βH should be cis to C_5-CH_3 group being probably β on biogenetic grounds in half-chair conformation of A-ring, while, if C_4-H is α(i.e. trans), it would probably exhibit quartet signal.



I



II



	R_1	R_2
III :	..OH	..OH
IV,IVa :	=O	..OH
V :	VI($\Delta^{3,4}$)	
VI :	=O	H
VII :	III(11βBr,13Br)	

Catalytic hydrogenation(5%-pd/C, 30 lbs, r.t.)[cf.(2)] or $NaBH_4$ reduction of II afforded single dihydro derivative(III). Dihydropulchellin(III): mp 146-148°, cf. mp 136-138°(2); $(\alpha)_D^{23.5°}$ -3.3°(c,2.8); $(\alpha)_D^{20°}$ +5.82°(c,1.03; 50%-MeOH) and +15.05°(c,0.99; 50%-MeOH) for the hydroxy acid salt(ΔM_D-33.4°); ν 3472, 3346, 1763, 1751^{sh}; δ 4.18 c (H_2 and H_8), 3.63 d,5 (H_4), 0.85 s ($3\times H_{15}$), 1.22 d,5 ($3\times H_{14}$), 1.22 d,5 (1.19 in pyridine)($3\times H_{13}$). Diacetate: mp 156.5-157.5°; $(\alpha)_D^{25.5°}$ +5.0°(c,1.0); δ 0.98 s ($3\times H_{15}$), 1.03 d,6 ($3\times H_{14}$), 1.20 d,6 (1.21 in py)($3\times H_{13}$).

The little differences of the solvent shifts($\delta^{CHCl_3-C_5H_5N}$)(4) for III(+0.02), III-acetate(-0.01) and VI(+0.07) v.i. demonstrated C_{11}-CH_3 configurations, showing the stereospecific hydrogenation at $\Delta^{11,13}$ of II, can be assigned thermodynamically more stable α position. Moreover, the absolute configuration of C_{11}-α-CH_2Br of 11,13-dibromopulchellin(VII) has been fonfirmed through X-ray studies, determining the complete structures of I and II as described in the following paper(5).

The negative shifts of molecular rotation of III with that of the corresponding hydroxy acid salt(ΔM_D -33.4°) as well as that of I with the corresponding tetraol(1)(ΔM_D -44.9°) suggest the configurations of C_8-βH on application of the Hudson-lactone rule. Cautious RD and CD determinations of III in MeOH solutions display negative signs of the lactone Cotton effects (C.E.), at 233mμ([φ] -3100) and 200mμ(θ -4678) in the range of $n \rightarrow \pi^*$ transition, respectively*9, being in accordance with the prediction from the lactone sector rule(6). Hence the stereochemistry of γ-lactone junction with cycloheptane ring in II and III should be C_8-βH/C_7-αH(trans).

The high field shifts of C_{10}-methyl signals in II and I(0.19 and 0.22 Hz) were observed on structural changes from II to its acetate, and from I to the acetate of III, respectively. Similarly, those signals of III and I cause by 0.18 and 0.20 upward shifts from the ketols, IV and IV(C_{13}-NC_5H_{10}) described below, respectively. C_{10}-methyl configurations in I, II and III should be then estimated α providing that both possess trans-bicyclo(5.3.0)decane ring fusion, which are in fashion among most pseudoguaianolides.

Dihydrocyclopentane(III) was oxidized with CrO_3/Py to the hydroxyketone(IV), which in turn gave the cyclopentanone(VI) via cyclopentenone(V)(2,1). It can be considered that trans-fused hydroxyketone has suffered epimerization at C_1 adjacent to the carbonyl group during dehydration to cis-fused cyclopentenone, whose stereochemistry at the ring junctions proves as follows. trans-Dehydrodihydropulchellin(IV)(2): mp 186-190°(prisms); δ 3.92 d,4.5 (H_4), 4.15 c (H_8), 0.98 s (3×H_{15}) 1.40 d,6 (3×H_{14}), 1.24 d,6 (3×H_{13}). Acetate: $C_{17}H_{24}O_5$; mp 138-141° (prisms): Cf. mp 182-185°(pillars)(2).

The RD curve of the ketol(IV) displays pronounced positive C.E. at 315-275mμ in MeOH solution(a +149.8*10) like that(a +119) of the nitrogen containing analogue(IV, C_{13}-NC_5H_{10})(1), suggesting that those bicyclo(5.3.0)decane ring fusion

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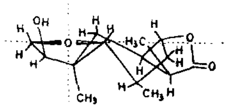
*9 Each sign of II in both RD and CD C.E.s at about 250-260mμ for the α-methylene-γ-lactone $n \rightarrow \pi^*$ transition show positive [a +119.8 and (φ)258+486.6] is opposite with the case for the dihydro derivative(III)[cf. T. G. Waddell, W. Stocklin and T. A. Geissman, Tetrahedron Letters, 1313 (1969)].

*10 The signs and amplitudes of the corresponding derivatives from pulchellin(2) communicated from Dr. W. Herz are almost identical with the present data.



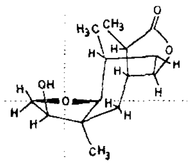


Fig. 3. The octant sector diagram of trans-pseudoguaian-2-one-8,12-olides.
Fig. 4. The octant sector diagram of cis-pseudoguaian-2-one-8,12-olides.

must be trans(C_5-βH/C_1-αH) being obeyed the Octant rule(Fig. 3). In addition, another ketol(IVa) was obtained as plates on recrystallization of IV from Me_2CO-HCl, and found to exhibit a comparable negative C.E.(a -202.3) with that(a -200.8[*10]) of the afore-mentioned VI as well as of 5α,14β-androstan-15-one(7) indicating cis-fused ring system(Fig. 4). cis-Dehydrodihydropulchellin(IVa): $C_{15}H_{24}O_4$; mp 182-184°; $(\alpha)_D^{31°}$ -51.4°(c,0.97); ν 3484, 1763, 1728; δ 4.06 d,8.2 & d,10.5 (H_4), 3.79 c (H_8), 1.22 s (3×H_{15}), 1.33 d,5.3 (3×H_{14}), 1.18 d,6.0 (3×H_{13}). Acetate:$C_{17}H_{24}O_5$; mp 159-160°(needles). The equillibration ratio(IV/IVa≈ 3/7), deduced from the periodical change of the C.E.s of both compounds in HOAc solution, impregnates that trans-bicyclo(5.3.0)decane ring fusion is less stable than the corresponding cis-fused counterpart in all cyclopentanone and pentenone system v.s.

Now it should be so decisive that the starting dihydroxycyclopentanes, I and II, must be in trans ring fusion. The full stereochemistry of pulchellin and pulchellidine have been thus established as represented in II and I on the basis of the preceeding chemical studies.

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