Tetrahedron Letters No.33, pp. 3181-3185, 1967. Pergamon Press Ltd. Printed in Great Britain.

ISOLATION AND STRUCTURE DETERMINATION OF PACHYSANDIOL-A AND A NOTE ON THE STEREOCHEMISTRY OF CERIN

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(Received 15 May 1967)

Alkaloidal constituents of Pachysandra terminalis SIEB. et ZUCC., a Buxaceae plant, have recently been examined by Tomita, Kikuchi, Uyeo and coworkers[1)] and by Knaack and Geissman[2)], but no other constituent of this plant has hitherto been reported in literature. We examined the unsaponified components of the neutral fraction of this plant and isolated two new triterpenediols, named pachysandiol-A and -B, along with friedelin, epifriedelanol, β-sitosterol and stigmasterol.

Pachysandiol-A, m.p. 278-280°*, $[\alpha]_D$ +14°*, and pachysandiol-B, m.p. 262-265°, $[\alpha]_D$ +23°, have the same molecular formula $C_{30}H_{52}O_2$*, which is in agreement with the molecular ion peak at m/e 444 in the mass spectra*.

In this communication, the structure determination of pachysandiol-A (Ia) is described.

Pachysandiol-A (Ia) shows a strong hydroxyl absorption band at 3400 cm^{-1} in the IR spectrum (KBr)* and positive Liebermann-Burchard color reaction.

Upon periodate oxidation, it gave an aldehyde, IR ν_{max} 1720 cm^{-1}, indicatin the presence of α-glycol system in the molecule.

Heating of pachysandiol-A (Ia) with acetic anhydride and pyridine gave a diacetate (Ib), $C_{34}H_{56}O_4$, m.p. 235-236°, $[\alpha]_D$ -18°, MS m/e: 528 (M^+), 513 (M-15), 468 (M-60), 453 (M-75), which shows strong infrared bands at 1735 and 1250 cm^{-1} ($OCOCH_3$) and NMR signals* at 5.15 (2H, m., $W^{1/2}$ about 7 cps.; 2 × $C\underline{H}$-OAc), 7.91, 7.93 (6H, 2 × $COCH_3$), 9.18 (3H, d., J=7 cps.; sec. CH_3) and 8.81~9.15 τ (7 × tert. CH_3).

On the other hand, treatment of pachysandiol-A with acetic anhydride in pyridine at room temperature yielded a monoacetate (III), $C_{32}H_{54}O_3$, m.p. 245-247°, $[\alpha]_D$ -4°, accompanied by a small amount of an isomeric monoacetate (IV), $C_{32}H_{54}O_3 \cdot 1/2H_2O$, m.p. 264-265°, $[\alpha]_D$ -10°. In contrast, the latter (IV) was obtained as the principal product by reduction of the diacetate (Ib) with lithium aluminum hydride for 40 minutes in boiling ether-chloroform.

Upon oxidation with chromium trioxide in acetic acid, III and IV gave rise to the acetoxy-ketone (V), $C_{32}H_{52}O_3$, m.p. 260-262°, $[\alpha]_D$ -31°, and the isomeric acetoxy-ketone (VII), $C_{32}H_{52}O_3 \cdot H_2O$, m.p. 255-257°, $[\alpha]_D$ +44°, respectively.

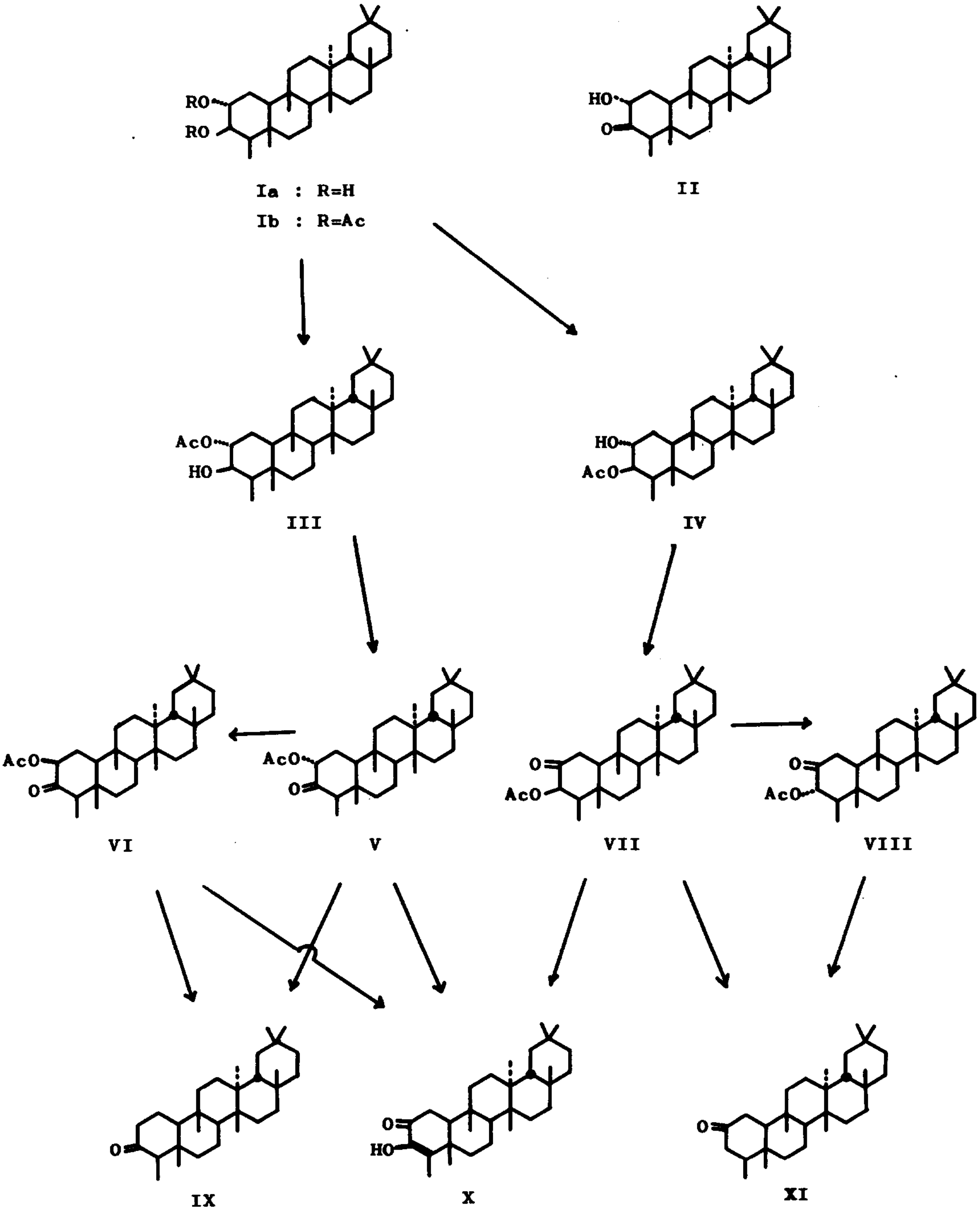
When the acetoxy-ketone (V) was treated with zinc in boiling acetic acid, there was obtained a ketone, m.p. 259-260°, $[\alpha]_D$ -20°, IR ν_{max} 1700 cm^{-1}, which was identified with authentic friedelin (IX). Furthermore, mild alkaline hydrolysis of V followed by oxidation with bismuth trioxide$^{3)}$ in acetic acid afforded 3-hydroxy-Δ_3-friedelen-2-one (X), m.p. 270-273°, $[\alpha]_D$ +29°, IR ν_{max} 3460, 1640, 1668 cm^{-1}; UV $\lambda_{max}^{Dioxane}$ 275 mμ (ε 9,650), NMR τ: 8.18 (3H, s., C_4-CH_3). Identity was established by direct comparison with an authentic sample, m.p. 273-275°$^{4),\ 5)}$.

The acetoxy-ketone (VII) also yielded X upon treatment with KOH in boiling methanol$^{6)}$. On the other hand, reduction of VII with zinc in acetic acid gave a ketone (XI), m.p. 287-288°, $[\alpha]_D$ -7°, IR ν_{max} 1700 cm^{-1}, UV $\lambda_{max}^{Dioxane}$ 277 mμ, whose properties are in good agreement with those of friedelan-2-one (XI)$^{4)}$.

Accordingly, pachysandiol-A must be 2,3-dihydroxyfriedelane.

Table 1.

Compound	NMR (CH-OAc)	UV (λ_{max}) (in dioxane)	ORD (Cotton effect in dioxane)		
			Sign	Peak	Trough
V	5.05τ triplet J=2.5 cps.	295 mμ	-	$[\Phi]_{279}$ +1300	$[\Phi]_{324}$ -3100
VI	4.81τ quartet J=6, 11 cps.	287 mμ	-	$[\Phi]_{269}$ +5040	$[\Phi]_{307}$ -6100
VII	5.00τ doublet J=4 cps.	295 mμ	+	$[\Phi]_{324}$ +2900	$[\Phi]_{280}$ -1650
VIII	5.05τ doublet J=12 cps.	277 mμ	-	$[\Phi]_{265}$ +2710	$[\Phi]_{307}$ -3390


RO
RO
Ia : R=H
Ib : R=Ac
HO
O
II
AcO
HO
III
HO
AcO
IV
AcO
O
VI
AcO
O
V
O
AcO
VII
O
AcO
VIII
O
IX
O
HO
X
O
XI

Our attention was then turned to the configuration at 2- and 3-positions. When the acetoxy-ketone (V) was adsorbed on alumina overnight and then eluted with benzene-chloroform, there was obtained an epimer (VI)7), $C_{32}H_{52}O_3$, m.p. 226-228°, $[\alpha]_D$ -55°. The latter could be transformed to IX and to X in the same manner as run with V. These observations led to the assignment of 2α(axial)-configuration to the less stable acetoxy-ketone (V) and 2β(equatorial)-orientation to the more stable epimer (VI). The ORD curves8) and UV8) and NMR9) spectra of compounds V and VI (see Table 1.) also support the above assignments.

On the other hand, the acetoxy-ketone (VII) was easily epimerized by alumina chromatography to VIII, m.p. 270-272°, $[\alpha]_D$ -55°. The latter compound (VIII) can be formulated in term of 3-epimer of VII, since both VII and VIII gave rise to the same ketone XI, m.p. 286-288°, upon reduction with zinc in boiling acetic acid. As shown in Table 1., its spectroscopic behavior indicates evidently the α(equtorial)-configuration of the 3-acetoxyl group in VIII. Hence the 3-acetoxyl group in the compound VII must have the β-orientation.

Of interest is the observation that the ORD curve of VII shows a positive Cotton effect with the peak at 324 mμ in contrary to the anticipation. This can be consistently explained if we assume a twist form for the ring-A in VII which may become preferred because of the large 1,3-interaction between the 3β-acetoxyl group and 5β-methyl group in the alternative chair conformation.

On the basis of foregoing evidences, the structure of pachysandiol-A is now represented by the formula Ia.

It should be mentioned in this connection that the structure of cerin has been proposed to be 2β-hydroxyfriedelin by Corey et al.4) and by Ourisson et al.10) and hence cerin acetate to be VI. However, the acetoxy-ketone (V) was found to be identical with the acetate, m.p. 259-262°, derived from authentic cerin which was kindly provided by Professor Ourisson. Therefore, the structure of cerin should be revised to II.

ACKNOWLEDGEMENT: The authors express their deep gratitude to Prof. M. Tomita, Dean of Kyoto College of Pharmacy, for his guidance and hearty encouragements.

REFERENCES

* All the melting points were determined on a Kofler type microscopic hot stage and are uncorrected. Optical rotations were taken at 15-25°C in $CHCl_3$ unless otherwise specified. All compounds given by formula in this communication gave satisfactory elemental analyses. All NMR spectra were measured on a Varian A-60 spectrometer (60 Mc) in $CDCl_3$ with $SiMe_4$ as the internal standard and mass spectra on a Hitachi RMU-6D mass spectrometer equipped with a direct inlet system. Unless otherwise stated, IR spectra were taken in $CHCl_3$ solutions.

1) M. Tomita, S. Uyeo, Jr. and T. Kikuchi, Tetrahedron Letters, 1053 (1964). For the latest paper on this subject, see T. Kikuchi, S. Uyeo, Jr. and T. Nishinaga, Chem. Pharm. Bull. (Tokyo), **15**, 577 (1967).

2) W. F. Knaack, Jr. and T. A. Geissman, Tetrahedron Letters, 1381 (1964).

3) W. Rigby, J. Chem. Soc., 793 (1951).

4) E. J. Corey and J. J. Ursprung, J. Am. Chem. Soc., **78**, 5041 (1956).

5) V. V. Kane and R. Stevenson, J. Org. Chem., **25**, 1394 (1960). We wish to thank Prof. R. Stevenson of Brandeis University for the authentic sample of 3-hydroxy-Δ_3-friedelen-2-one.

6) The formation of X may be due to air-oxidation of a initially produced keto-alcohol during the hydrolysis.

7) This compound (VI) is probably identical with the acetate of the $LiAlH_4$-reduction product of 3-hydroxy-Δ_3-friedelen-2-one (X), which was reported by Kane and Stevenson (see reference 5)), although direct comparison has not been done.

8) C. Djerassi, "Optical Rotatory Dispersion", McGraw-Hill, New York, pp.111 (1960).

9) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Org. Chem.", Holden-Day, Inc., San Francisco, pp.49 (1964).

10) T. Takahashi and G. Ourisson, Bull. soc. chim. France, 353 (1956). In Ourisson's later paper, the structure of cerin was depicted as II, but no comment on this alteration appeared in hitherto published literature (see P. Witz, H. Herrmann, J. M. Lehn and G. Ourisson, Bull. soc. chim. France, 1101 (1963) .