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31-NORCYCLOARTANOL AND CYCLOARTANOL FROM POLYPODIUM VULGARE°

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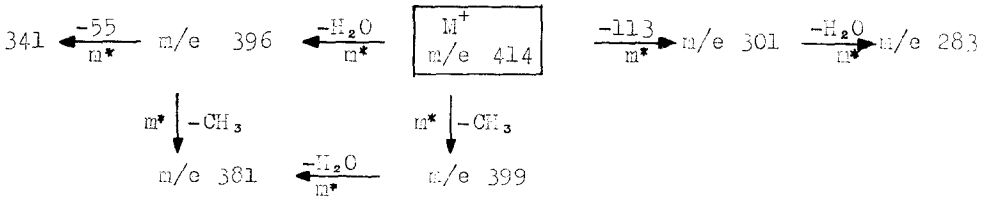
The rhizome of the fern Polypodium vulgare is particularly rich in triterpenoids.[1,2] During the work that led to the isolation of the two main constituents of the triterpene alcohol mixture of this fern, 31-norcyclolaudenol (I) and cyclolaudenol (II),[1] we observed that, while it was relatively easy to separate I from II by chromatography on alumina, the products thus obtained often had poor melting points, and were very difficult to isolate in a completely pure state. GLC of their trimethylsilyl ethers showed that such impure products each contained a second constituent, with lower retention time (Compounds A and B). When the benzoates of these mixtures were subjected to ozonolysis, while the derivatives of I and II were transformed into the corresponding 26-nor-25-ketones, the benzoates of A and B were recovered unchanged, and easily separated from the nor-ketones by chromatography on alumina. Therefore, as A and B do not contain double bonds, a more simple method for their separation from I and II was found in the chromatography of the benzoates over $AgNO_3$-impregnated silica,[3] from which the esters of A and B were eluted by 2% benzene in petroleum ether much earlier than the derivatives

° Dedicated to Prof. Remo de Fazi on his 75th birthday.

of I and II.

The mass spectrum of A, which contained more than 90 significant peaks and over 30 metastable peaks, showed a molecular weight of 414, which confirmed the formula $C_{29}H_{50}O$, deduced from elemental analysis. The origin of a part of the metastable transitions could be determined unequivocally with the aid of the computer program,[4] and the following partial fragmentation scheme could be written:



The m/e 301 ion must contain an oxygen atom, since it loses a molecule of water, leading to the m/e 283 ion. Since the molecular ion contains only one oxygen atom, the m/e 113 radical, lost when the m/e 301 is formed, does not contain the heteroatom, and can therefore be only C_8H_{17}. This points strongly to a cholesterol type of side-chain. Compound B gave M^+ 428 ($C_{30}H_{52}O$) and a rather similar fragmentation pattern.

The IR spectra of A and B were almost superimposable on those of I and II, respectively, except for the absence of the $=CH_2$ bands at 6.10 and 11.22 μ. High-field AB quartets (J = 4 c/s) in the NMR spectra of the benzoates of A and B were attributed to CH_2 protons on cyclopropane rings; the doublets were respectively at 9.80 and 9.55 τ for A, and at 9.63 and 9.40 τ for B, a fact that indicated that probably A had one and B two methyl groups on C-4.[1] It was concluded that A and B corresponded respectively to structures III (31-norcycloartanol) and IV (cycloartanol). In a recent paper, Audier, Beugelmans and Das[5] discuss the mass spectra of several 9,19-cyclolanostane derivatives, including that of cycloartanol,

and indicate four types of characteristic fragmentation peaks. Our data are in agreement with their findings: a peak at m/e 288, which corresponds to the loss of ring A and C-6 or C-19, is present in both III and IV; the same applies to the characteristic m/e 341 peak, which apparently arises from the loss of H_2O and C_4H_7 from ring A. The peak at (M-18)-43, which is present in the spectrum of IV and in that of several other 4,4--dimethyl derivatives,[5] is of extremely low intensity in the mass spectrum of III ($\%\Sigma_{40} \sim 0.05$).

The data in Table I show a rather good concordance between the m.ps. and specific rotations of compound B and those given in the literature for IV. The identification was completed by a direct comparison with an authentic sample of cycloartanol, obtained by catalytic reduction of cycloartenol.[6] Cycloartanol has been previously found in nature only as a minor constituent of rice-bran oil.[7]

Compound III, which had never before been isolated from a natural source, has been obtained as an intermediate in the structure determination of cycloeucalenol.[8] The fit between the data for our compound A and those in the literature for III (see Table II) was not too good, particularly in the specific rotations of the alcohol and the benzoate; this induced us to repeat the degradation of cycloeucalenol to III. The products that were obtained in this way, turned out to be perfectly identical with those prepared from P.vulgare. The difference in the literature data may have been due to the difficulty in the purification of the intermediate nor-ketone VI, which is obtained by ozonolysis in rather low yield: also for this compound we found a very different specific rotation (Table II), and in order to verify its purity we also prepared it, in much better yield, by lead tetraacetate cleavage of the mixture of 24-epimeric triols (VII), m.p.176-180°,

$[\alpha]_D$ + 42°, obtained from cycloeucalenol acetate (V) with OsO_4. The keto alcohol VIII, m.p. 110-113°, $[\alpha]_D$ + 47°, thus obtained, was acetylated to VI, which was identical in m.p. and specific rotation with our ozonolysis product.

TABLE I

Physical constants of cycloartanol (IV) and derivatives

Compound	Literature		From P.vulgare (Compound B)	
	m.p.	$[\alpha]_D$	m.p.	$[\alpha]_D$
3 -OH[a]	99°	+50°	101-2°	+51°
3 -acetate[a]	130-2°	+59°	130-2°	+61°
3 -benzoate[b]	137-8°(149°)	+66°	136-8°(149°)	+69°
3-ketone[a]	110°	+24°	110°	+23°

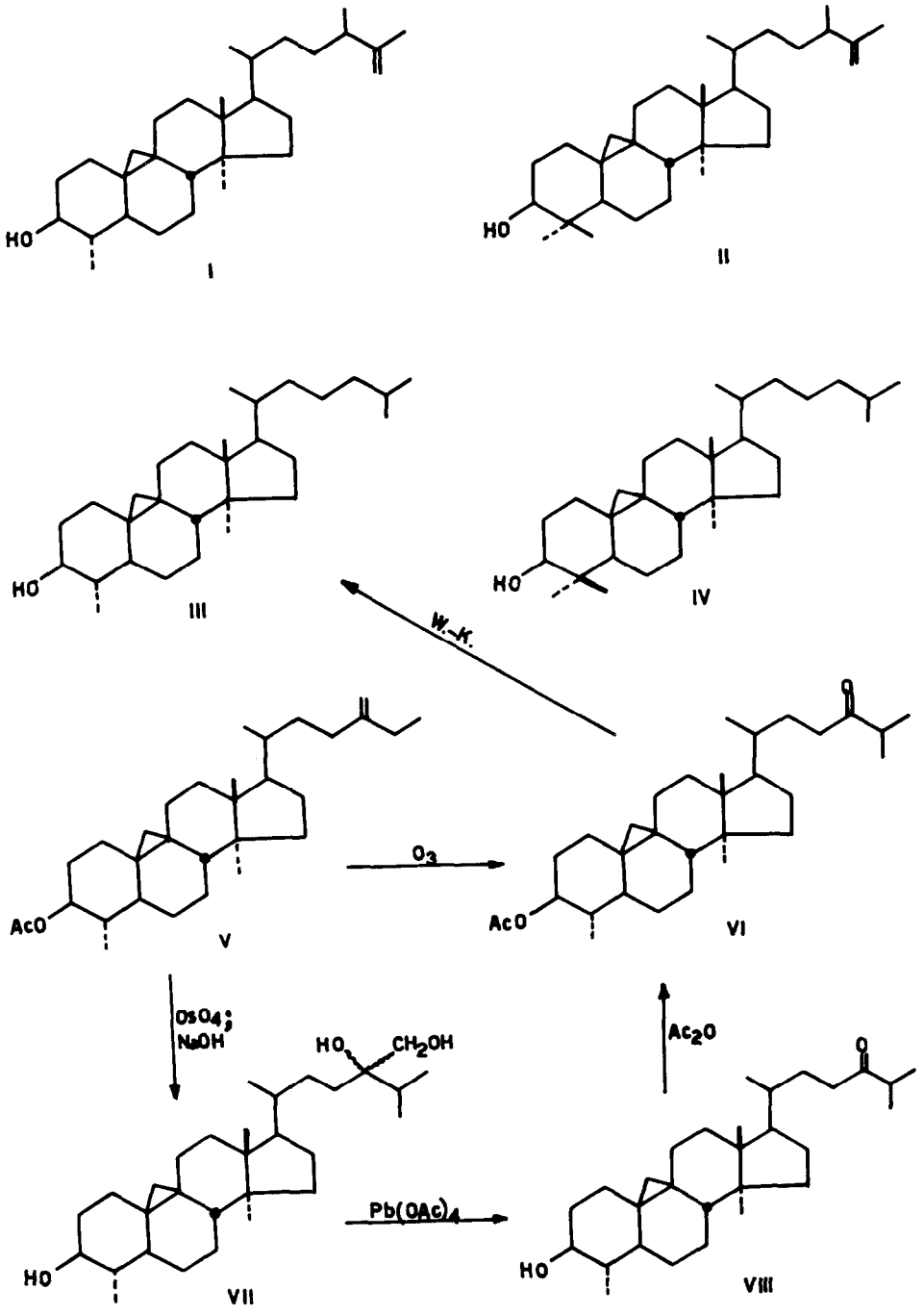
All specific rotation in $CHCl_3$.
a) H.R.Bentley, J.A.Henry, D.S.Irvine and F.S.Spring, J.Chem.Soc., 1953,3673; b) See ref.6.

TABLE II

Physical constants of 31-norcycloartanol (III) and derivatives

Compound	From cycloeucalenol				From P.vulgare (Compound A)	
	Literature		Present work			
	m.p.	$[\alpha]_D$	m.p.	$[\alpha]_D$	m.p.	$[\alpha]_D$
3 -OH[a]	126-7°	+33°	128-32°	+48°	128-32°	+49°
3 -acetate[a]	98-100°	+57°	-	-	97-9°	+64°
3 -benzoate[b]	121-2°	+91°	121-4°	+72°	122-4°	+71°
3-ketone[b]	109°	+55°	-	-	104-6°	+57°
24-oxo-3 -acetate[a]	97-8°	+35°	95-7°	+64°	-	-

All specific rotation in $CHCl_3$.
a) See ref.8; b) J.S.G.Cox, T.E.King and T.J.King, J.Chem.Soc., 1959,514.


HO
I
HO
II
HO
III
HO
IV
W.-K.
AcO
V
O3
AcO
VI
OsO4;
NaOH
HO
CH2OH
VII
Pb(OAc)4
Ac2O
HO
VIII
O

The isolation from the same plant of I, II, III and IV is of interest, as they could constitute metabolic intermediates of two different pathways for the transformation of a common precursor, probably cycloartenol,[9] into steroid compounds. Work is under way for the identification of several other minor alcoholic constituents, which have been detected by GLC in the same extract, with the hope of identifying other possible intermediates of these pathways.

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