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NOVEL TRITERPENES FROM WESTERN WHITE PINE (Pinus monticola Dougl.) BARK

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After a preliminary investigation of the chemistry of western white pine bark (1), a more detailed study of the benzene extract was undertaken. A total of 90 terpenoids were isolated, including 34 triterpenes (2). These include 24-methylenecycloartanol, 10 known and 10 new serratanes (3) and 11 new triterpenes that appear to have a common skeleton. The two major components of this last group are a methoxydiol (I) and a triol (IV) which comprise 0.7 and 0.2% of the benzene extract, respectively. This communication describes the proof of structure of these two novel and biogenetically interesting triterpenes.

The unsaponifiable portion from the benzene extract was freed of wax alcohols by formation of the urea canal inclusion complex and of sterols by precipitation of the digitonides. The petroleum ether-insoluble fraction was chromatographed on silica gel to yield the novel triterpenes.

The methoxydiol, $C_{31}H_{54}O_3$, (m/e 474.409 (4)), m.p. 193-194°, $[\alpha]_D^{22}$ + 77° exhibited in the NMR spectrum, tertiary methyl groups at δ0.66, 0.74, 0.80, 0.97, 1.05, 1.09 and 1.25; a secondary methyl at 0.90 (d, J=6 Hz), an equatorial secondary methoxyl (3.36, s, $OC\underline{H}_3$ and 2.65, m, $C\underline{H}OCH_3$) a multiplet at 3.62 for C<u>H</u>OH and a single olefinic proton at 5.25 (m). It readily formed a monoacetate (II)

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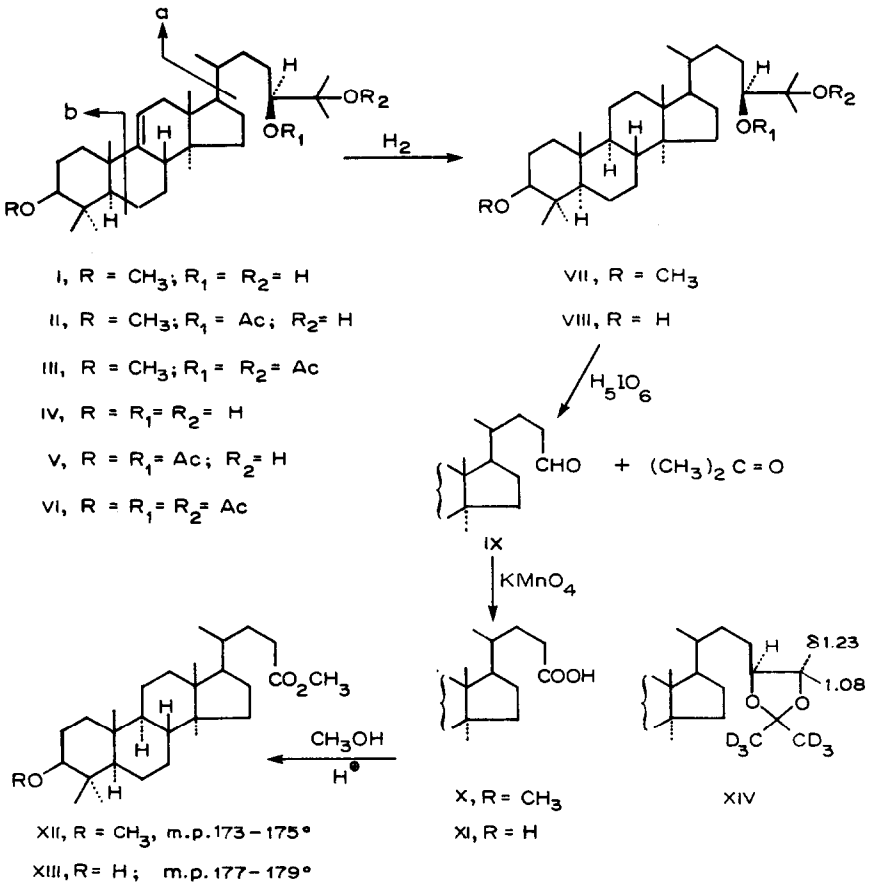
m.p. 229-230°, and with difficulty a diacetate (III) m.p. 169.5-170.5°. The olefinic linkage could be hydrogenated and a crystalline dihydro derivative m.p. 213.5-214.5°, was obtained.

Mass spectrometry showed III ($C_{35}H_{58}O_5$, M^+ 558) undergoes loss of HOAc (m/e 498) and the latter now loses $C_{10}H_{19}O_2$ to give a significant fragment ion at m/e 327. This fragmentation was reminiscent of the pathway followed in the tetracyclic lanostene-type triterpenes studied previously (5,6) and suggested loss of the side chain containing both acetate functions (fragmentation "a" in I). The ion at m/e 327 in the methoxydiol alters to m/e 313 when the ether function is changed to hydroxyl (IV) and to m/e 355 when the latter is acetylated (V), but it remains unaltered in converting the methoxydiol to either its mono-(II) or diacetate (III) derivatives. This data indicates that the two hydroxyl groups in the natural product must be situated in the side chain while the methoxyl function is attached to the tetracyclic ring system, most probably at C-3. Evidence as to the type of skeleton and the position of the olefinic linkage in the methoxydiol was clear from fragmentation pathway "b". A fragment ion at m/e 285 showing the loss of ring A and characteristic of 3-oxygenated-9,11-unsaturated lanostene-type triterpenes such as grandisolide and dihydroparkeyl acetate (5), was evident in the spectra of the various compounds studied. Two different losses of ketene in the fragmentation of III were observed. It is known that such fragmentations occur if two acetoxy groups exhibit a 1,2- or 1,3-relationship (7,8). On the basis of the above it was postulated that the methoxydiol was best represented as a 3β-methoxylanost-9(II)-ene derivative with a vicinal diol in the side chain.

The triol, $C_{30}H_{52}O_3$ (m/e 460.393), m.p. 214-215°, $[\alpha]_D^{22}$ + 56°, revealed in the NMR spectrum, tertiary methyls at δ0.64, 0.73, 0.80, 0.97, 1.03 and 1.23; a secondary methyl at 0.90 (d, J=6 Hz), two multiplets at 3.22 and 3.60 (CHOH) and a single vinylic proton at 5.25 (multiplet). The triol formed a diacetate, m.p. 210-211° and with difficulty a triacetate, m.p. 208-210°. A dihydro derivative, m.p. 211-212°, could be obtained by catalytic reduction of the triol. Mass spectral fragmentation patterns revealed that there was a close structural comparison between the two natural products and it was postulated that the triol was simply the 3β-hydroxy analogue of the methoxydiol.

Conclusive chemical evidence to support the above postulates was obtained by the sequence of reactions outlined in Scheme 1. The side chain hydroxyl groups of I were cleaved by periodate to yield the crystalline aldehyde (IX) and acetone, isolated as its 2,4-dinitrophenylhydrazone derivative. Oxidation of IX and esterification of the resultant acid (X) provided the ester XII.



Scheme I

A parallel series of experiments was performed with the triol except that the crystalline acid (XI) was obtained directly from the triol with $NaIO_4$-$KMnO_4$. Esterification of the acid provided the known methyl 3β-hydroxy-25,26,27-tris-nor-5α-lanostan-24-oate (XIII) identical with an authentic sample (9) (m. m.p.; tlc; superimposable IR, NMR and mass spectra). Methylation (K, CH_3I) of the latter provided a product identical with that obtained from the methoxydiol series thereby relating the two natural products.

Finally the stereochemistry at C-24 was elucidated by means of two spectroscopic methods recently developed by Nakanishi. The CD of the methoxydiol, $\Delta\varepsilon$ = +0.92, 314 nm, CCl_4 employing $Pr(DPM)_3$ as the complexing agent, reveals a 24-S configuration (10, 11) as shown in I. Further support for this assignment is available from an NMR study of the deuterioacetonide derivatives (XIV). of both natural products. Irradiation at the frequency of the methyl groups (δ1.23) cis to the

C-24 H in the triol provides a nuclear Overhauser effect (intensity increase of C-24 signal 26%) in accord with expectation (12). A similar experiment with the methoxydiol provides an NOE of 19%. The above data completely define the structures of the novel triterpenes as shown in I and IV.

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REFERENCES

1. W.C. Nickles and J.W. Rowe, Forest Prod. J., 12, 274 (1962).

2. B.A. Nagasampagi, J.K. Toda, A.H. Conner and J.W. Rowe, Abstracts 161st ACS meeting, Los Angeles, April 1971, and 11th Phytochemical Soc. N. Amer. meeting, Monterrey, Mexico, Oct. 1971. J.W. Rowe, R.C. Ronald and B.A. Nagasampagi, Phytochemistry, 11, 365 (1972, footnotes 5 and 14. D.F. Zinkel, J.K. Toda and J.W. Rowe, ibid., 10, 1161 (1971). J.W. Rowe, B.A. Nagasampagi, A.W. Burgstahler and J.W. Fitzsimmons, ibid., 10, 1647 (1971).

3. J.W. Rowe and C.L. Bower, Tetrahedron Letters, 2745 (1965); J.W. Rowe, ibid., 2347 (1964).

4. High resolution mass measurements and elemental analyses were obtained on all compounds reported. Mass spectra were obtained on AEI MS902 or Atlas CH4B instruments. Fragmentation patterns are confirmed by metastable peaks. NMR data, reported in δ values, was obtained in $CDCl_3$ on a Varian XL 100 spectrometer.

5. J.P. Kutney, D.S. Grierson, G.D. Knowles, N.D. Westcott and I.H. Rogers, Tetrahedron, 29, 13 (1973).

6. J.P. Kutney, N.D. Westcott, F.H. Allen, N.W. Issacs, O. Kennard and W.D.S. Motherwell, Tetrahedron Letters, 3463 (1971).

7. H. Budzikiewicz, C. Djerassi and D.H. Williams, Structure Elucidation of Natural Products by Mass Spectrometry, Holden-Day, San Francisco, 1964, Vol.2, p.206.

8. K. Biemann, D.C. DeJongh and H.K. Schnoes, J. Amer. Chem. Soc., 85, 1763 (1963).

9. C.S. Barnes, Aust. J. Chem., 9, 228 (1956).

10. K. Nakanishi, D.A. Schooley, M. Koreeda and J. Dillon, J. Chem. Soc., (D), 1235 (1971).

11. K. Nakanishi and J. Dillon, J. Amer. Chem. Soc., 93, 4058 (1971). We are grateful to Professor Nakanishi for performing this determination for us.

12. K. Nakanishi, D.A. Schooley, M. Kareeda and I. Miura, ibid., 94, 2865 (1972).