

## The Structure of Abieslactone, a Methoxy-tetracyclic Triterpene Lactone

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ON the basis of selenium dehydrogenation we have suggested previously that abieslactone,\* a triterpenoid isolated from the bark and leaves of *Abies mariesii*, Masters. (Pinaceae) must contain the

skeleton of trimethylsteroids.<sup>1</sup> Further investigations led to structure (I) for this compound based on the following evidence.

The molecular formula, C<sub>31</sub>H<sub>48</sub>O<sub>3</sub>, was confirmed

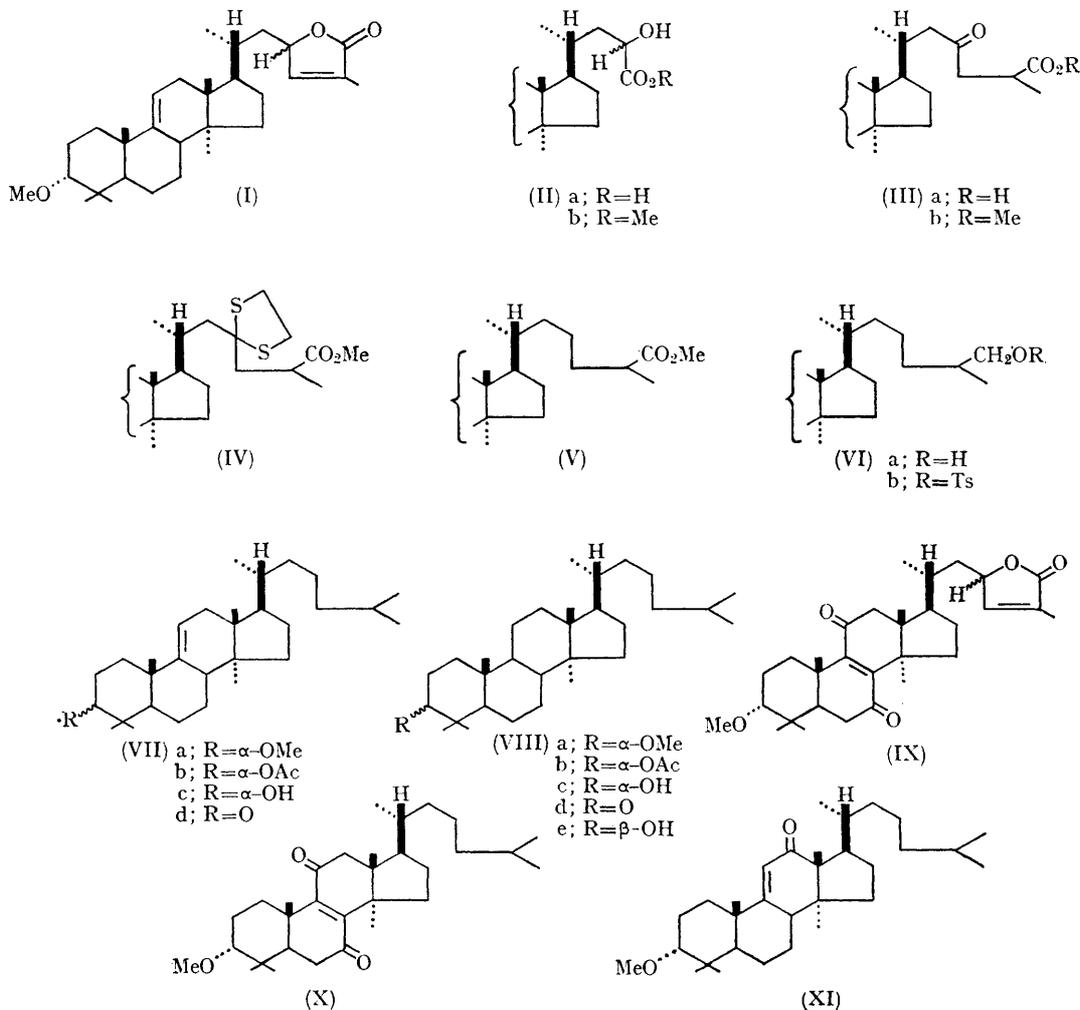
\* Dr. J. W. Rowe, Forest Products Laboratory, Forest Service, U.S. Department of Agriculture, Madison, Wisconsin, has kindly informed us recently that Dr. Herbert L. Hergert, Olympic Research Division, Rayonier Inc., Shelton, Washington, isolated from the bark of *Abies amabilis* (Dougl.) Forbes and also from *A. procera* Rehd, a triterpene which was named methoxyabiesadienolide. This naturally occurring methoxy-triterpene was presented for investigation to Dr. Rowe, who has since been working on this compound and independently came to the same conclusion as we report here, especially concerning the structure of the side chain. Very recently identity of methoxyabiesadienolide with abieslactone has been proved by direct comparison and the details of the chemical investigations carried out in both countries on this triterpene will be published jointly in a forthcoming paper.

<sup>1</sup> S. Uyeyo, J. Okada, and S. Matsunaga, *J. Pharm. Soc. Japan*, 1964, **84**, 453.

by the parent peak at  $m/e$  468 in the mass spectrum of abieslactone. The n.m.r. spectrum of abieslactone exhibited signals corresponding to six C-methyls (18-H,  $\tau$  8.98, 9.00, 9.06, and 9.08), a vinylic methyl (3-H,  $\tau$  8.10, triplet), a secondary O-methyl (3-H,  $\tau$  6.73, singlet, and 1-H,  $\tau$  7.20,

infrared bands at 1745 and 1660  $\text{cm}^{-1}$  (KBr disc) and the ultraviolet absorption maximum at 207.5  $m\mu$  ( $\log \epsilon$  4.30 in EtOH).

Oxidation of abieslactone (I) with potassium permanganate in acetic acid gave an  $\alpha$ -hydroxy-acid (IIa), as a result of cleavage of the unsaturated



narrow diffused triplet) and two trisubstituted ethylenic linkages (1-H,  $\tau$  4.48, multiplet, and 1-H,  $\tau$  3.00, quintet). Spin decoupling showed the vinylic methyl to be coupled to both the vinylic proton at  $\tau$  3.00 and to another proton (1-H,  $\tau$  5.05, multiplet) geminal to the lactone oxygen. The presence of an  $\alpha\beta$ -unsaturated  $\gamma$ -lactone in abieslactone was indicated by the

lactone ring and loss of three carbon atoms from the parent molecule. The methyl ester of this acid (IIb) showed signals of six C-methyls in the region  $\tau$  8.93—9.30 in the n.m.r. spectrum. These results indicated clearly that the lactone ring of abieslactone is on the side chain. Saponification of abieslactone with ethanolic potassium hydroxide gave a  $\gamma$ -keto-acid (IIIa), a hydrolysis product

characteristic of  $\alpha\beta$ -unsaturated  $\gamma$ -lactones, which reverted to the original lactone on boiling in acetic anhydride.

The keto-acid (IIIa) was converted into its methyl ester (IIIb), and subsequently into the thioketal (IV), which was desulphurised by heating with Raney nickel in ethanol. The resulting deoxo-ester (V) was reduced with lithium aluminium hydride, giving an alcohol (VIa), which was converted into the tosylate (VIb). Reduction of (VIb) with lithium aluminium hydride gave the compound (VIIa), in which the oxygen functions on the side chain of abieslactone were completely reduced to a saturated hydrocarbon residue. The n.m.r. spectrum of (VIIa) showed seven peaks at  $\tau$  8.93, 9.07, 9.09, 9.13, 9.18, 9.26, and 9.35 corresponding to eight C-methyls and a signal at  $\tau$  4.75 (1-H, multiplet) arising from a vinylic proton. In addition, two signals due to a secondary O-methyl group appeared at  $\tau$  6.70 (3-H, singlet) and  $\tau$  7.18 (1-H, narrow diffused triplet). The latter was assigned to an equatorial hydrogen geminal to the O-methyl group. Thus the O-methyl group was shown to have an axial orientation.

Hydrogenation of (VIIa) over Adams' catalyst in acetic acid at elevated temperature and atmospheric pressure gave the dihydro-derivative (VIIIa), which exhibited no signals of olefinic protons in the n.m.r. spectrum. The O-methyl group of (VIIIa) was hydrolysed with hydrogen bromide in a boiling mixture of acetic anhydride and acetic acid and the resulting acetate (VIIIb) saponified. The alcohol (VIIIc) thus obtained was oxidised with chromic acid-pyridine complex to the ketone (VIIIId),  $C_{30}H_{52}O$ , m.p. 133–134°,  $[\alpha]_D^{21} + 28.4^\circ$ , which was identical in all respects with authentic lanostan-3-one.<sup>2</sup> Reduction of this ketone (VIIIId) with sodium borohydride gave lanostan-3 $\beta$ -ol (VIIIe), which was not identical with (VIIIc) and exhibited a quartet centred at  $\tau$  6.80 (1-H,  $J_{AX} = 9.0$  c./sec.,  $J_{BX} = 5.5$  c./sec.), in the n.m.r. spectrum confirming the axial nature of the proton geminal to the secondary hydroxyl group.

Next, for the purpose of determining the position of the trisubstituted ethylenic linkage in the ring system of abieslactone, it was oxidised with chromic acid in the acetic acid to give (IX) which exhibited  $\nu_{max}$  1678  $cm^{-1}$  ( $CHCl_3$ ), and  $\lambda_{max}$ (EtOH) 274  $m\mu$  ( $\log \epsilon$  3.84). The ultraviolet absorption band of (IX) was characteristic of those of steroids of

$\Delta^8$ -7,11-dione type.<sup>2</sup> One of the olefinic protons which were present in abieslactone disappeared, as revealed by the n.m.r. spectrum of (IX), suggesting that the double bond in the skeleton of abieslactone shifted to C-8:9 in the course of oxidation. It was inferred from this finding that the original double bond was either at C-7:8 or more probably at C-9:11, since only the latter can be readily hydrogenated.

Oxidation of 3 $\alpha$ -methoxylanostene (VIIa), obtained above, under the similar conditions as used for the oxidation of abieslactone gave two compounds. One of them is an enedione (X),  $\lambda_{max}$ (EtOH) 275  $m\mu$  ( $\log \epsilon$  3.89), and  $\nu_{max}$  1600 and 1678  $cm^{-1}$  ( $CHCl_3$ ), and the other is an  $\alpha\beta$ -unsaturated ketone (XI) which had  $\lambda_{max}$ (EtOH) 245  $m\mu$  ( $\log \epsilon$  4.10), and  $\nu_{max}$  1600 and 1673  $cm^{-1}$  ( $CHCl_3$ ). The ultraviolet spectrum of the former showed close resemblance to that of the dioxo-abieslactone (IX) and that of the latter to those of 3 $\beta$ -acetoxy- $\Delta^9(11)$ -lanosten-12-one ( $\lambda_{max}$  242  $m\mu$ ) and 3 $\alpha$ -acetoxy- $\Delta^9(11)$ -12-one ( $\lambda_{max}$  243  $m\mu$ ).<sup>4</sup> The n.m.r. spectrum of (XI) showed a doublet at  $\tau$  4.40 ( $J = 2.0$  c./sec.) corresponding to an olefinic proton at C-11, due to a long-range coupling with an axial allylic proton at C-8.<sup>3</sup> The o.r.d. curve of the compound (XI) showed a negative multiple Cotton effect and resembled that of 3 $\alpha$ -acetoxy- $\Delta^9(11)$ -arbornen-12-one<sup>3</sup> or 3 $\beta$ -acetoxy- $\Delta^9(11)$ -18 $\alpha$ -oleanen-12-one.<sup>4</sup>

The above evidence supported the view that the position of the double bond in the 3 $\alpha$ -methoxylanostene (VIIa) derived from abieslactone is at C-9:11. This inference is in good agreement with the facts that the double bond of (VIIa) did not shift by the action of mineral acid, and that the mass spectrum of (VIIa) showed a cracking pattern quite similar to those of  $\Delta^9(11)$ -triterpenes.<sup>5</sup>

Conclusive evidence has now been provided by demethylation of 3 $\alpha$ -methoxylanostene (VIIa) with hydrogen bromide. The resulting acetate (VIIb) was saponified to an alcohol (VIIc), which on oxidation with chromic acid-pyridine complex afforded the ketone (VIId),  $C_{30}H_{50}O$ , m.p. 121–122°,  $[\alpha]_D^{18} + 46.6^\circ$ , and  $\nu_{max}$  1712  $cm^{-1}$  (KBr disc), identical in every respect with authentic  $\Delta^9(11)$ -lanosten-3-one (dihydroparkeone).<sup>6</sup>

The above experimental results established firmly the structure of abieslactone as 3 $\alpha$ -methoxy- $\Delta^9(11)$ ,<sup>24</sup>-lanostadien-27:23-olide, as shown in formula (I).

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<sup>2</sup> W. Voser, M. Montavon, Hs. H. Günthard, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1950, **33**, 1893.

<sup>3</sup> H. Vorbrüggen, S. Chandra, S. C. Pakrashi, and C. Djerassi, *Annalen*, 1963, **668**, 57.

<sup>4</sup> C. Djerassi, J. Osiecki, and W. Closson, *J. Amer. Chem. Soc.*, 1959, **81**, 4587.

<sup>5</sup> H. Budzikiewicz, J. M. Wilson, and C. Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 3688.

<sup>6</sup> D. H. R. Barton, F. McCapra, P. J. May, and F. Thudiam, *J. Chem. Soc.*, 1960, 1297.