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TRITERPENES OF PINE BARKS:
NATURALLY OCCURRING DERIVATIVES OF SERRATENEDIOL*

John W. Rowe and Carol L. Bower
Forest Products Laboratory,** Forest Service
U.S. Department of Agriculture

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In a recent paper (2) we reported on the isolation of the triterpene, pinusenediol, and its identity with serratenediol (I) whose structure has been elucidated and confirmed via synthesis by Inubushi (3). Apparently this triterpene, together with several related triterpenes, normally occurs in minute amounts in pine bark. We have previously reported (2) the isolation and preliminary characterization of several of these compounds which appeared to be related to serratenediol. We now wish to report that the investigation of these related triterpenes has been concluded with the proof of structure of the following new triterpenes: 3β-methoxy-21α-hydroxy-Δ^{14}-serratene (II); 3β,21α-dimethoxy-Δ^{14}-serratene (III); 3β-methoxy-21-keto-Δ^{14}-serratene (V); 3α,21β-dihydroxy-Δ^{14}-serratene (VII); 3β-hydroxy-21-keto-Δ^{14}-serratene (IX); and 3β,21β-dihydroxy-Δ^{14}-serratene (X). All of these are new natural products except X, which is identical to the 21-episerratenediol previously isolated by Inubushi (4)

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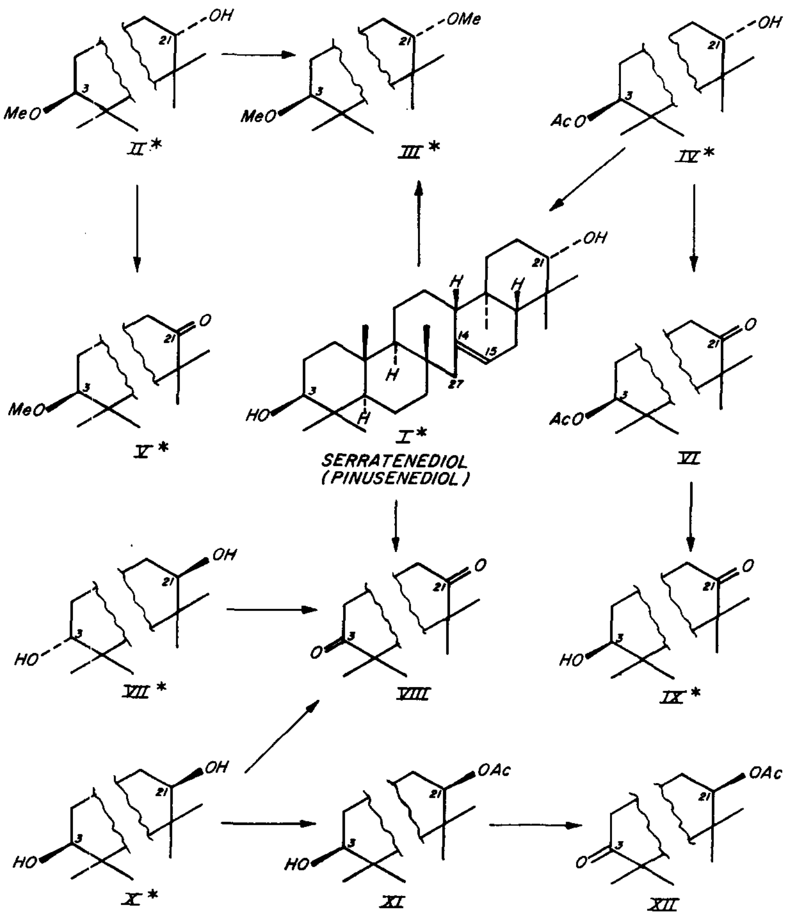
[*] Previous paper in this series: "Structures of Contortadiol (Agathadiol), Contortolal (Agatholal), and Hydroxyepimanool (Epitorulosol)" (1).

[**] Maintained at Madison, Wis., in cooperation with the University of Wisconsin.



STARRED COMPOUNDS ARE NATURAL PRODUCTS

along with serratenediol (I), serratenediol 3-acetate (IV), serratriol, tohogeninol and tohogenol from the club moss, Lycopodium serratum Thunb. var. thunbergii Makino. The occurrence of triterpene methyl ethers in pines is noteworthy. This may be a characteristic of the Pinaceae family since triterpenes from spruces and firs have also been found to contain methoxyl groups (5).

Serratenediol dimethyl ether (III), m.p. 320-1/2--323-1/2,* $[\alpha]_D^{22}$ +21°, was discussed previously (2). The structure originally suggested was shown to be correct by methylating serratenediol with potassium t-butoxide and methyl iodide in ether. The synthetic dimethyl ether was identical with the natural dimethyl ether according to i.r. and n.m.r. spectra, t.l.c., optical rotation, and mixed melting point.

Serratenediol monomethyl ether from sugar pine (II), m.p. 319--322-1/2°, $[\alpha]_D^{22}$ -5°, was also discussed previously (2). It has now been shown to possess the previously suggested structure by methylation as above to serratenediol dimethyl ether, and by oxidation with chromic acid (6) to the methoxyketone (V), m.p. 267-270°, $[\alpha]_D^{23}$ -29°. Inubushi (3) has shown that the o.r.d. curve of VI with a 21-keto group has a single negative Cotton effect curve with a molecular amplitude of -31, while 3-keto-Δ^{14}-serratene has a single positive Cotton effect curve with a molecular amplitude of +30. Therefore the o.r.d. was determined on V. This showed a single negative Cotton effect curve centered at 300 mμ with a molecular amplitude of -27, thus proving that the monomethyl ether (II) has a 21-hydroxy group.

In working up the serratenediol mother liquors from sugar pine, a small amount of a new compound was isolated whose u.v., i.r., and n.m.r. spectra

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* Melting points, determined in evacuated capillaries and corrected, are given only for analyzed samples. Optical rotations are measured in chloroform solution, o.r.d. in dioxane solution, n.m.r. in deuterochloroform at 60 Mc. with tetramethylsilane as an internal standard, and i.r. in KBr.

indicated seven angular methyls, a single vinylic proton (τ 4.62, ν_{max} 794 cm^{-1}), a carbonyl (ν_{max} 1706 cm^{-1}, λ_{max}^{EtOH} 287 mμ (ϵ 48)), and a methoxyl (τ 6.66, ν_{max} 1103 cm^{-1}). These data suggested that it might be identical to V prepared above, and this was confirmed by comparison via o.r.d., i.r., n.m.r., t.l.c., and mixed melting point.

We previously reported the isolation of a monomethyl ether similar to II from the sterols of jack pine bark (2,7). The data given strongly suggested a monomethyl ether of serratenediol. However, the n.m.r. showed that although the hydroxyl was equatorial (triplet at τ 6.8, J = 9 c.p.s., for a proton geminal to an equatorial hydroxyl), the methoxyl was axial (triplet at τ 7.19, J = < 2 c.p.s., for a proton geminal to an axial methoxyl). This suggests that it is rather 3β-hydroxy-21β-methoxy-Δ^{14}-serratene (the 21-monomethyl ether of 21-episerratenediol). Unfortunately, insufficient material was available to confirm this, although this assumption is supported by the fact that episerratenediol is the main triterpene of jack pine bark.

Another new compound isolated in trace amounts from the serratenediol mother liquors from sugar pine appeared to contain a serratene skeleton. It had seven angular methyls in the n.m.r. and a vinylic proton (τ 4.60, ν_{max} 795 cm^{-1}), a carbonyl [ν_{max} 1706 cm^{-1}, λ_{max}^{EtOH} 288 (ϵ 63)], and a secondary equatorial hydroxyl [broad multiplet at τ 6.8 in the n.m.r. for an axial proton geminal to an equatorial hydroxyl; $\nu_{max}^{CCl_4}$ 3627 cm^{-1} for a secondary equatorial hydroxyl (8)]. The o.r.d. curve in chloroform showed a single negative Cotton effect centered at 298 mμ with a molecular amplitude of -36, strongly suggesting that this compound was the hydroxyketone, IX. This was confirmed by synthesis from serratenediol monoacetate (IV), which was oxidized with chromic acid (6) to VI and then saponified to yield IX, m.p. 268--268-1/2°, $[\alpha]_D^{22}$ -40°; this was identical with the natural product by o.r.d., n.m.r., i.r., u.v., and mixed melting point.

Episerratenediol (X) and diepiserratenediol (VII) were discussed previously (2). Both gave authentic serratenedione (VIII) identical to that from serratenediol (I) on oxidation with chromic acid (6). To determine which of the hydroxyls was epimerized in episerratenediol, its diacetate was partially saponified to yield about 70% of 3β-hydroxy-21β-acetoxy-Δ^{14}-serratene (XI), m.p. 238-242°, $[\alpha]_D^{22}$ – 27-1/2°. This was shown to possess an equatorial hydroxyl group by n.m.r. and i.r. [broad multiplet at τ 6.7 for an axial proton geminal to equatorial hydroxyl; $\nu_{max}^{CCl_4}$ 3625 cm^{-1} (8)], and an acetoxy group which is axial (ν_{max} 1724, 1242 cm^{-1}; sharp triplet at τ 5.28 in the n.m.r. for an equatorial proton geminal to an axial acetoxyl at τ 7.91). Oxidation with chromic acid (6) yielded 3-keto-21β-acetoxy-Δ^{14}-serratene (XII), m.p. 204-1/2--207-1/2°, $[\alpha]_D^{22}$ -1°. The o.r.d. curve showed a positive Cotton effect curve centered at 295 mμ with a molecular amplitude of +35, thus proving that the ketone is at C-3, and that X is 21-episerratenediol identical to that already isolated by Inubushi (4). Chromatography and crystallization of XI and XII gave no indications of the presence of any appreciable amounts of compounds derived from 3-episerratenediol which might be expected to cooccur with 21-episerratenediol.

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