TABLE II

OPTICAL ROTATORY DISPERSION CURVES OF 1-SUBSTITUTED ANDROSTENEDIONES

No substituent	1α - OAc	1α - SAc	1β - OAc	1β - SAc
$\lambda[\phi]$	$\lambda[\phi]$	$\lambda[\phi]$	$\lambda[\phi]$	$\lambda[\phi]$
385 (1560)	400 (1240)	381 (1530)	...	...
367.5 (1170)	369 (480)	359 (1250)	...	...
320 (10,450)	317 (13,300)	310 (14,000)	315 (5750)	317.5 (3580)
Dioxane	Dioxane	Methanol	Methanol	Methanol

Experimental[8]

7α- and 7β-Acetylthio-4-androstene-3,17-dione.—4,6-Androstadiene-3,17-dione, 3.2 g., was mixed with 4 ml. of ethanethiolic acid and warmed on the steam bath for 0.5 hr. Then part of the excess acid was removed under vacuum and the residue was dissolved in benzene and chromatographed on 400 g. of silica gel. From the early fractions eluted with 10% ethyl acetate-benzene there was obtained 0.9 g. of 7α-acetylthio-4-androstene-3,17-dione by crystallization from ether, m.p. 158.5–160.5°, [α]D +31 ± 1°, Δ*M*D −455°, $\lambda_{max}^{CH_3OH}$ 237.5 mμ, ε 19,500.

Anal. Calcd. for $C_{21}H_{28}O_3S$: C, 69.96; H, 7.83. Found: C, 69.94; H, 7.83.

From another run a yield of 43% was obtained by direct crystallization.

From the later 10% fractions two types of crystals formed, prisms (the 7α-isomer) and needles. The needles were separated by hand and recrystallized several times from ether to yield 0.20 g. of 7β-acetylthio-4-androstene-3,17-dione, m.p. 129–132° dec., [α]D +166°, ΔMD +31°, $\lambda_{max}^{CH_3OH}$ 237 mμ, ε 17,400.

Anal. Found: C, 70,35; H, 7.86.

The remaining material was apparently a mixture of the two isomers, but further recovery of pure material was not attempted.

1α- and 1β-Acetylthio-4-androstene-3,17-dione.—1,4-Androstadiene-3,17-dione, 10.0 g., was mixed with 10 ml. of ethanethiolic acid and heated on the steam bath for 15 min. During this time, the solid dissolved and a new solid formed. Fractional crystallization of the material from methylene chloride–ether gave 10.6 g. (83%) of 1α-acetylthio-4-androstene-3,17-dione, same m.p. and infrared spectrum as previously reported material,[1] and 1.15 g. (9%) of 1β-acetylthio-4-androstene-3,17-dione, m.p. 177.5–179° dec., [α]D 1 ± 1°, ΔMD −564°, $\lambda_{max}^{CH_3OH}$ 240.5 mμ, ε 14,900.

Anal. Found: C, 69.76; H, 7.94.

1α-Acetylthiotestosterone.—17β-Hydroxy-1,4-androstadien-3-one, 2.2 g., was heated with 2 ml. of ethanethiolic acid for 20 min. on the steam bath. Ether was added and after 2 days crystals formed. They were recrystallized three times from acetone–ether–petroleum ether to yield 1.65 g. of 1α-acetylthiotestosterone, m.p. 138.5–139° dec., $\lambda_{max}^{CH_3OH}$ 241 mμ, ε 15,400, [α]D +128.5°, ΔMD +126°.

Anal. Calcd. for $C_{21}H_{30}O_3S$: C, 69.57; H, 8.34. Found: C, 69.90; H, 8.40.

Another 0.25 g. of material, m.p. 136.5–138° dec. was obtained from the mother liquors. Chromatography of the residue gave 0.15 g. of impure solid as well as noncrystalline material which may have included the β isomer.

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(8) Rotations taken in chloroform at 24 ± 2°.

Synthesis of (+)-9-Methyl-*trans*-1,4,9,10-tetrahydronaphthalene

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Received February 26, 1962

As part of a research program on the optical rotatory dispersion of nonplanar conjugated dienes,[1] a substance was required on which theoretical predictions of the sign and intensity of the Cotton effect could be tested. The substance had to satisfy the following requirements: Its absolute configuration had to be known, and it had to contain a nonplanar, conformationally fixed cisoid dienic system; furthermore, its structure had to be sufficiently simple for theoretical calculations to be manageable, and the compound had to be available in high optical purity.

These conditions are satisfied by (+)-9-methyl-*trans*-1,4,9,10-tetrahydronaphthalene (I). Dreiding models show that the conformationally rigid diene system of I deviates from planarity by an angle of about 17.5°, the skewness[2] corresponding to that of a right-handed helix. The structural element II present in compound I is quite unusual; we are aware of only one other compound embodying this feature, *viz.*, the 1,3-cholestadiene of Tamm and Albrecht.[3] In particular, the $\Delta^{1,3}$-arrangement does not seem to be represented among the numerous natural sesqui-, di-, and triterpenes. This fact suggested that structure II might be markedly unstable, and that compounds containing it might be quite difficult to prepare. The desired substance

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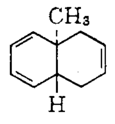
(1) A. Moscowitz, E. Charney, U. Weiss, and H. Ziffer, *J. Am. Chem. Soc.*, **83**, 4661 (1961).

(2) Theory (1) predicts that the skewness (*i.e.*, sense of helicity) governs the sign of the Cotton effect, as its contribution to the rotation far outweighs that of asymmetric substituents; a right-handed helicity produces a positive Cotton effect.

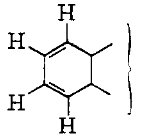
(3) Ch. Tamm and R. Albrecht, *Helv. Chim. Acta*, **42**, 2177 (1959).

was obtained, however, by a pyrolysis reaction without undue difficulty.

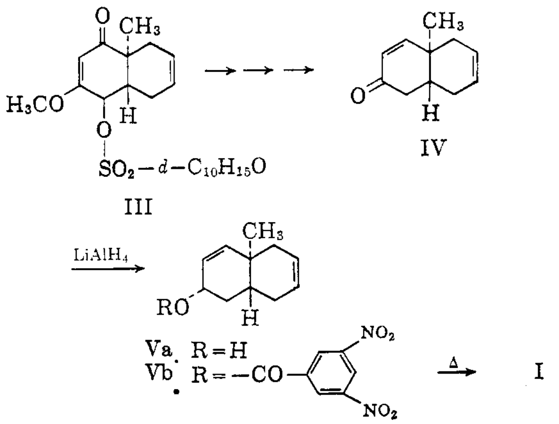
Compound I was prepared from the optically pure *d*-camphor-10-sulfonate of (+)-*trans*-1-hydroxy-4-keto-2-methoxy-10α-methyl-$\Delta^{2,6}$-hexahydronaphthalene (III); a generous sample of this material, which is antipodal to the natural steroids, was obtained from Dr. Q. E. Thompson (Monsanto Chemical Company, St. Louis, Missouri). The conversion of III to (+)-*trans*-2-keto-10-methyl-$\Delta^{3,6}$-hexahydronaphthalene (IV) has been described for the racemate by Woodward *et al.*,[4] for the resolved material by Thompson *et al.*[5]



I



II



Reduction of IV with lithium aluminum hydride in ether gave an oily alcohol (Va) which was characterized as the crystalline 3,5-dinitrobenzoate (Vb). The hydroxyl in Va is assumed to be α, since Tamm and Albrecht[3] found that the hydride reduction of Δ^1-cholestene-3-one proceeds stereospecifically to give Δ^1-cholestene-3β-ol. The desired diene I was prepared from the ester (Vb) by pyrolysis at 150–160° *in vacuo*. The dinitrobenzoate has the advantage that the 3,5-dinitrobenzoic acid formed is not sufficiently volatile under our conditions to contaminate the diene. Compound I, a colorless oil even at −60°, is volatile and readily autoxidized. For these reasons a satisfactory elementary analysis was not obtained; the compound was characterized as the crystalline *adduct* (m.p. 109–111°) with tetracyanoethylene.

The identity of I was established by the following pieces of evidence: λ_{max} 261 mμ, (ε 3450), calcd. by Woodward's rules 263 mμ[6] (*cf.* 262 mμ for 1,3-cholestadiene[3]); integrated NMR (calcd. ratio for methyl—aliphatic—vinyl protons 3:5:6; found, 3.0: 5.2: 5.8); and mass spectroscopy (mol. wt. calcd., 146; found, 146). These findings prove that the desired compound I has actually been obtained, and that the possible shift of the dienic system to the 2,4-position (calcd., λ_{max} 267mμ) has not taken place during pyrolysis. Furthermore, cleavage in the mass spectrometer into mass numbers 92 and 54 (toluene and butadiene, respectively) is the expected one for structure I.[7] Several samples of I proved homogeneous by gas chromatography (the column, under the conditions used, readily separated *cis*- and *trans*-decalin). A slight contamination, presumably by an autoxidation product, was noted by mass spectroscopy (mass 160) and by two weak absorption bands (at 218 mμ, and 225 mμ in cyclohexane) having variable intensity ratios with respect to the principal absorption band.

The effect of acid on I was studied spectroscopically. The expected transformation into the 2,4-diene seemed to take place only slowly after the addition of a few drops of alcoholic hydrochloric acid to a solution of I in ethanol, as indicated by broadening of the principal absorption band.

Experimental

(+)-*trans*-2α-Hydroxy-10α-methyl-$\Delta^{3,6}$-hexahydronaphthalene (Va).—A solution of 4.3 g. of IV in 25 ml. of dry ether was added to a slurry of 1.5 g. of lithium aluminum hydride in 25 ml. of dry ether. The solution was stirred at room temperature for 3–4 hr., cooled to 0°, and decomposed with 10 ml. of a 10% aqueous solution of ammonium chloride. After several extractions of the aqueous layer with ether, the combined organic layers were dried, and the solvent was removed *in vacuo*, yielding 4.0 g. of an oil (Va) that did not crystallize.

3,5-Dinitrobenzoate (Vb).—The crude oily Va (3.9 g.) was dissolved in a small quantity of pyridine and added to a solution of 7.0 g. (excess) of 3,5-dinitrobenzoyl chloride in 55 ml. of dry pyridine. The solution was heated for two hours on a steam bath, cooled, and poured into 500 ml. of aqueous 5% sodium bicarbonate. The mixture was extracted several times with ether, and the combined ether layers were washed several times with water, dilute acetic acid, and finally with dilute sodium bicarbonate. They were next dried with sodium sulfate and concentrated *in vacuo;* the residue of solid Vb was purified by crystallization from 60 ml. of methanol. Yield, 1.8 g.; m.p. 114–115°. An additional amount of less pure Vb was obtained by further concentration of the mother liquors. For analysis, the compound was recrystallized several more times from methanol, without change in m.p.

Anal. Calcd. for $C_{18}H_{18}N_2O_6$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.13; H, 5.23; N, 7.94.

(+)-9α-Methyl-*trans*-1,4,9,10-tetrahydronaphthalene (I). Four hundred milligrams of Vb was heated in a Pyrex tube connected to a high-vacuum line (pressure 10^{-6} mm.) at 150–155° for approximately 16 hr. The diene (I) formed was collected over a molecular sieve in a cooled trap (−60°) inserted between the pyrolysis tube and the high-vacuum line. Dinitrobenzoic acid and some undecomposed Vb collected on the walls of the pyrolysis tube. The dry I was distilled, at room temperature *in vacuo*, into another receiver.

The NMR spectrum of I was determined in deuterochloroform; 60 kc. Optical rotatory dispersion (in cyclo-

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(4) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. H. McLamore, *J. Am. Chem. Soc.*, **74**, 4223 (1952).

(5) A. J. Speziale, J. A. Stephens, and Q. E. Thompson, *ibid.*, **76**, 5011 (1954).

(6) R. B. Woodward, *ibid.*, **64**, 72 (1942).

(7) K. Biemann, *Angew. Chem.*, **74**, 102 (1962).

hexane) (see also Fig. 1 of ref. 1): $[\alpha]_{589}$ + 268°; $[\alpha]_{284}$ + 13,000°; $[\alpha]_{258}$ ± 0°; $[\alpha]_{234}$ −11,000°; $[\alpha]_{228}$ −6800°.

Tetracyanoethylene Adduct of I.—Approximately 80 mg. of I was treated at room temperature with a solution of 79.2 mg. of tetracyanoethylene in 1.0 ml. of freshly distilled tetrahydrofuran. The mixture turned red immediately; on standing for several days it became yellow. It was concentrated under reduced pressure, and the residue was taken up in 8 ml. of hot hexane. On cooling, the adduct separated in long needles, which were recrystallized from hexane-benzene; m.p. 109–111°.

Anal. Calcd. for $C_{17}H_{14}N_4$: C, 74.45; H, 5.11; N, 20.44. Found: C, 74.56; H, 5.11; N, 20.55.

Acknowledgment.—The authors are much indebted to Professor K. Biemann, M.I.T., for permission to quote the results of his mass-spectrographic investigation of I, and to Dr. E. D. Becker and Mr. R. B. Bradley of this Institute for the NMR data.

Steroids and Related Natural Products. XII. *Fomes applanatus*[1,2]

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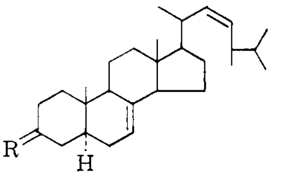
Received February 27, 1962

The Polyporaceae family (Agaricales order) contains tube-bearing basidiomycetous fungi of a fleshy-tough to woody consistency. Members of this family are wood-inhabiting annuals or perennials commonly known as bracket or shelf fungi.[3] Interest in locating new sources of lanostane-type tetracyclic triterpenes has led us to begin a phytochemical survey of the Polyporaceae genus *Fomes*.[4,5]

Although *Fomes* species have been recognized since 1878,[3] preliminary chemical examinations of only six, apparently, have been described.[6] One of these, *Fomes applanatus*, was reported to contain a pigment, mannitol and "ergosterol-like compounds."[6a] Our initial study has been concerned with evaluating *Fomes applanatus* as a source of lanostane derivatives.

Specimens of *Fomes applanatus*[7,8] collected in northeastern Maine, were successively extracted with petroleum ether, diethyl ether, and 95% ethanol. A small quantity of crystalline material which separated from the petroleum ether extract yielded 3-oxo-24S-methyl-5α-cholesta-7,22-diene (Ia)[9] and 3β-hydroxy-24S-methyl-5α-cholesta-7,22-diene (Ib)[10] following chromatographic separation on activated alumina. The remaining hydrocarbon extract was saponified and small amounts of sterols Ia and Ib were again isolated from the neutral components. Tentative identification of these substances was based on elemental analyses, physical constants, and their infrared spectra. The structures were confirmed by comparison with authentic samples prepared from ergosterol.



Ia. R = O

b. R = $\overset{\vdots}{\underset{\text{H}}{}}\!-$OH

c. R = $\overset{\vdots}{\underset{\text{H}}{}}\!-$OCOCH$_3$

Both the disaccharide trehalose[11] and 5α-dihydroergosterol (Ib) were eventually isolated from the 95% ethanol extracts. However, attempts at isolating in a pure form reasonable quantities of other neutral (or acidic) sterols from the petroleum ether, diethyl ether, or ethanol extracts were unsuccessful. For example, separation of the petroleum ether extract based on isolating reactive carbonyl compounds with Girard's reagent T and sterols with digitonin held no particular advantage.

Similar evaluation of other *Fomes* species is now in progress.

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[1] Part XI, G. R. Pettit and D. M. Piatak, *J. Org. Chem.*, **27**, 2127 (1962).

[2] This investigation was supported by PHS Research Grants CY-4074(C2) and CY-4074(C3) from the National Cancer Institute, Public Health Service and in part by National Science Foundation Research Grant G-19500.

[3] North American Polyporaceae, for example, comprise 8 genera and approximately 235 species: L. O. Overholts, "The Polyporaceae of the United States, Alaska and Canada," University of Michigan Press, Ann Arbor, Michigan, 1953.

[4] Isolation of the polyporenic acids from several *Polyporus* species (annuals) suggested that the closely related *Fomes* genera might also produce unusual lanostane derivatives. A summary of the elegant structural studies involving polyporenic acids has been prepared by E. R. H. Jones and T. G. Halsall, "Progress in the Chemistry of Organic Natural Products," Vol. XII, L. Zechmeister, ed., Springer-Verlag, Vienna, 1955, p. 44; *cf.* also, J. J. Beereboom, H. Fazakerley, and T. G. Halsall, *J. Chem. Soc.*, 3437 (1957).

[5] A distinguishing characteristic of this genus is the perennial nature of its species. Certain *Fomes* have been known to survive seventy years.

[6] Refer to: (a, *F. applanatus*), J. Zellner, *Monatsh. Chem.*, **36**, 611 (1915) [*Chem. Abstr.*, **9**, 3083 (1915)]; (b, *F. fomentarius*), H. R. Arthur, T. G. Halsall and R. D. Smith, *J. Chem. Soc.*, 2603 (1958); (c, *F. hartigii*), L. Canonica and A. Fiecchi, *Gazz. chim. ital.*, **89**, 818 (1959) [*Chem. Abstr.*, **54**, 22711 (1960)]; (d, *F. juniperinus*), M. Anchel, A. Hervey, and W. J. Robbins, *Proc. Natl. Acad. Sci.* (U.S.), **38**, 655 (1952) [*Chem. Abstr.*, **47**, 4957 (1953)]; (e, *F. officinalis*), R. M. Gascoigne, J. S. E. Holker, B. J. Ralph, and A. Robertson, *J. Chem. Soc.*, 2346 (1951) and J. Valentin and S. Knutter, *Pharm. Zentralhalle*, **96**, 478 (1957) [*Chem. Abstr.*, **52**, 13187 (1958)]; and (f, *F. pinicola*), T. Shibamoto, K. Minami, and T. Tajima, *J. Japan Forest Soc.*, **35**, 56 (1953) [*Chem. Abstr.*, **48**, 6993 (1954)].

[7] This cosmopolitan species variously known as *Boletus* or *Polyporus applanatus* and as *Ganoderma applanatum*, *Polyporus megaloma*, or *Elfvingia megaloma* is most frequently encountered in hardwood regions. Samples measuring from *ca.* ten to forty cm., at the widest point along their horizontal plane, were used in this study.

[8] We are indebted to Dr. Martin A. Rosinski, Department of Botany and Plant Pathology, University of Maine, for identifying the plant material and for valuable counsel with several botanical problems.

[9] The 24-methyl of 5α-dihydroergosterol (Ib) has been assigned a β_F configuration by K. Tsuda, Y. Kishida, and R. Hayatsu, *J. Am. Chem. Soc.*, **82**, 3396 (1960). Employing the valuable system proposed by R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956), this position may now be designated S. Ketone Ia has also been isolated from a specimen of *Fomes fomentarius* (see footnote 6b).

[10] Recently, sterol Ib was found to be a constituent of *Polyporus pinicola:* T. G. Halsall and G. C. Sayer, *J. Chem. Soc.*, 2031 (1959).

[11] Isolation of trehalose from *Fomes pinicola* has been reported by T. Shibamoto, K. Minami, and T. Tajima, *J. Japan Forest Soc.*, **34**, 390 (1952).