239. *The Chemistry of Extractives from Hardwoods. Part XII.** *The Cyclitols and Steroids of Opepe* (Sarcocephalus diderrichii).

By F. E. King and L. Jurd.

*meso*Inositol, and an optically active *O*-methyl*meso*inositol (yield 3·5%) possibly identical with bornesitol from Borneo rubber, are present in aqueous and alcoholic extractives of opepe, the wood of *Sarcocephalus diderrichii*. Among the constituents isolable with light petroleum are " β "-sitosterol and the previously unknown " β "-sitosteryl palmitate.

THE West African tree *Sarcocephalus diderrichii* de Wild (family *Rubiaceae*) produces a hard, golden-yellow wood, opepe, which is a valuable commercial timber, and is reported to be highly resistant to wood-rotting fungi and to certain marine parasites. There is no record of a chemical examination of the wood; toxic reactions attributed to it by Harvey-Gibson (*Biochem. J.*, 1906, **1**, 39) were subsequently shown to be due to the somewhat similar " Knysna boxwood " from *Gonioma kamassi*, family *Apocynaceae* (*idem, ibid.*, 1912, **6**, 127).

The oil isolated from the powdered wood with boiling light petroleum gave when fractionally precipitated from organic solvents a crystalline product, $C_{45}H_{80}O_2$ (0·01% of the wood), and a solid, m. p. 77—78°, the latter, however, in amounts too small for identification. From the more soluble residue were obtained a phytosterol, m. p. 135°, and a second alcohol, m. p. 184°, apparently a triterpene derivative. The alcohol, m. p. 184°, gave an acetate, benzoate, and *p*-nitrobenzoate, but the amount available was

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* Part XI, *J.*, 1953, 1055.

insufficient for more extensive investigation; it is tentatively called sarcocephalol and may have the formula $C_{30}H_{48}O$, although it is then necessary to postulate that the compound and its acetate and benzoate were obtained as hemihydrates. The properties of the phytosterol and of four of its esters, and of three derivatives of the dihydrophytosterol, closely resemble those of "β"-sitosterol recorded by Wallis and Chakravarty (*J. Org. Chem.*, 1938, **2**, 335), Simpson and Williams (*J.*, 1937, 733), and Heilbron, Jones, Roberts, and Wilkinson (*J.*, 1941, 344).

From different samples of the wood two specimens of the compound, $C_{45}H_{80}O_2$, were obtained, their m. p.s of 83·5° and 85·5° remaining unchanged by repeated crystallisation and chromatography. When hydrolysed by alkali, each gave a neutral product which apart from its low optical rotation was in other respects indistinguishable from "β"-sitosterol, and the acidic hydrolysate, $C_{16}H_{32}O_2$, had m. p. 59° undepressed by pure palmitic acid. This compound is therefore regarded as "β"-sitosteryl palmitate, but the presence of other similar substances in the natural product is evident from the higher m. p. (88—88·5°) and from the optical rotation of the ester synthesised from authentic components.

The syrupy aqueous extract of the wood was fractionated with boiling methanol into the sparingly soluble *meso*inositol (0·37% of the wood), and a more easily dissolved crystalline product (3½%), $C_7H_{14}O_6$, from which were prepared a penta-acetate and -propionate. Zeisel analysis showed the presence of a methoxyl group, the action of boiling hydriodic acid yielding *meso*inositol. The m. p. (201—202°) and specific rotation (+31·4°) of the opepe cyclitol agree with the values (m. p. 199—203°, $[\alpha]_D$ +31·16°) found by Flint and Tollens (*Annalen*, 1892, **272**, 288) for bornesitol isolated from Borneo rubber by Girard (*Z. Chem.*, 1871, **7**, 335) who recorded m. p. 175°, $[\alpha]_D$ +32°, and it is probable that the two compounds are identical.

*meso*Inositol and the *O*-methyl*meso*inositol are likewise obtained from opepe by alcohol-extraction, a method which has also led to the isolation of an unidentified acid (0·004%). By treatment with hot aqueous hydrochloric acid traces of a yellow alkaloid have been extracted from the wood.

EXPERIMENTAL

The investigation covered three specimens of the wood, each identified at the D.S.I.R. Forest Products Laboratory as *Sarcocephalus diderrichii*, which were obtained through the kindness of Mr. W. O. Woodward, The Nottingham Mills Co. Similar extractives were derived from two of the specimens (A) but the third (B) differed appreciably in both the nature and the quantity of its soluble constituents.

Light Petroleum Extraction.—Specimen (A). The thick yellow oil (180 g.) extracted (Soxhlet; 20 hours) from the powdered heartwood (A) (18 kg.) by boiling light petroleum (b. p. 60—80°) was dissolved in ether (150 c.c.) and added to boiling acetone (1200 c.c.). The solution was decanted from sticky precipitate, concentrated to 800 c.c., and kept at room temperature for 15 hours, thereby giving a partly crystalline deposit (1). Further evaporation, to 300 c.c., and chilling (0°; 12 hours) yielded an unidentified pale yellow compound (0·2 g.) (2), m. p. (after 2 crystallisations from acetone) 75—76°, forming from light petroleum cream-coloured needles, m. p. 77—78° (Found: C, 77·7; H, 12·8%). The light petroleum filtrate, decolorised by passage through alumina, was evaporated and the residue obtained as needles (3), m. p. 79—80°, by crystallisation from acetone. This product and the ethyl acetate-soluble portion of (1) were combined and recrystallised from acetone, further purification in light petroleum solution by chromatography (alumina; light petroleum) giving "β"-*sitosteryl palmitate* in needles, m. p. 83·5°, $[\alpha]_D$ −7·3° (in $CHCl_3$) (Found: C, 82·7; H, 11·9. $C_{45}H_{80}O_2$ requires C, 82·75; H, 12·35%).

The oil (4) from which these compounds were separated was dissolved in ethanol (400 c.c.) containing potassium hydroxide (20 g.) and heated under reflux for 2½ hours. The alkali-insoluble part extracted by ether was purified from light petroleum solution by chromatography on alumina. Elution with benzene gave an oil which dissolved in light petroleum, yielding crystals of sarcocephalol (0·3 g.). Further elution with ether afforded "β"-sitosterol (1 g.), glistening plates, m. p. 136·5°, also obtained in a similar manner from the oil (4) before it had been subjected to hydrolysis.

Specimen (B). The oil (*ca.* 35 g.) obtained from specimen (B) (3·5 kg.) by exhaustion with light petroleum was dissolved in ether (30 c.c.) and added to boiling acetone (250 c.c.). The solution, separated from gummy precipitate and concentrated to 200 c.c., gave clusters of needles which when purified by chromatography and crystallised from acetone gave " β "-sitosteryl palmitate (1 g.), m. p. 85·5°, $[\alpha]_D$ −7·8° (Found : C, 82·7, 82·5; H, 11·9, 12·1%).

" β "-*Sitosteryl Palmitate*.—(a) *Hydrolysis*. The ester (0·8 g.) from (B) was heated under reflux for 2 hours with potassium hydroxide (5 g.) in alcohol (160 c.c.), the neutral product, which was extracted by ether after the addition of water, crystallising from methanol in plates (0·45 g.), m. p. 135°. The ester from (A) gave a similar neutral product, m. p. 129—130°, which after 6 crystallisations from methanol had m. p. 135°, alone or mixed with that from sample (B) and with authentic " β "-sitosterol.

The aqueous alkaline solution yielded on acidification a solid crystallising from methanol in needles, m. p. 59°, and 59—59·5° when mixed with pure palmitic acid, m. p. 62·4° (Found : C, 75·3; H, 12·5. Calc. for $C_{16}H_{32}O_2$: C, 74·95; H, 12·6%).

(b) *Synthesis*. The acid chloride prepared by refluxing palmitic acid (0·2 g.), m. p. 62·4°, with thionyl chloride (2 c.c.) for 30 minutes was dissolved in benzene (2 c.c.) and mixed with β-sitosterol (0·2 g.), m. p. 137°, and pyridine (1 c.c.) and heated on a steam-bath for 30 minutes, Addition of water, extraction with ether, washing, etc., gave " β "-*sitosteryl palmitate*, forming after several crystallisations from acetone, clusters of needles, m. p. 88—88·5°, $[\alpha]_D$ −18·6° (Found : C, 82·7; H, 12·3%), and m. p. 86—87° when mixed with the ester, m. p. 85·5°, from (B).

" β "-*Sitosterol*.—(*a*) The sitosterol, m. p. 136·5°, isolated from the light petroleum extract had $[\alpha]_D$ −33° (recorded for " β "-sitosterol, −37°, and m. p.s from 135° to 137°). The low carbon analysis for " β "-sitosterol, attributed to solvation (Heilbron *et al.*, *J.*, 1941, 344), was obtained also in this work (Found : C, 82·5; H, 12·0. Calc. for $C_{29}H_{50}O$: C, 84·0; H, 12·1%). The acetate had m. p. 120—121° (Found : C, 81·2; H, 11·4. Calc. for $C_{31}H_{52}O_2$: C, 81·5; H, 11·5%) (" β "-sitosteryl acetate has m. p.s from 123·5° to 127°); the benzoate had m. p. 141° (Found : C, 83·4; H, 9·7. Calc. for $C_{36}H_{54}O_2$: C, 83·3; H, 10·5) (" β "-sitosteryl benzoate had m. p. 145—147°); the *p*-nitrobenzoate had m. p. 187° (Found : C, 76·3; H, 9·2; N, 2·6. Calc. for $C_{36}H_{53}O_4N$: C, 76·7; H, 9·5; N, 2·5%) (" β "-sitosteryl *p*-nitrobenzoate has m. p. 183—184°); and the 3 : 5-dinitrobenzoate had m. p. 207° (Found : C, 70·8; H, 8·4. Calc. for $C_{36}H_{52}O_6N_2$: C, 71·0; H, 8·6%) (" β "-sitosteryl 3 : 5-dinitrobenzoate has m. p. 202—203° or 207—209°). Reduction of the sterol in acetic acid over palladised charcoal at N.T.P. gave the stigmastanol (dihydrositosterol), m. p. 132°, characterised by the acetate, m. p. 129° (Found : C, 81·2; H, 12·0. Calc. for $C_{31}H_{54}O_2$: C, 81·5; H, 11·5%) (stigmastanyl acetate has m. p. from 128° to 130·5°), the benzoate, m. p. 135° (Found : C, 83·3; H, 11·1. Calc. for $C_{36}H_{56}O_2$: C, 83·0; H, 10·8%) (stigmastanyl benzoate has m. p. 137°), and the p-*nitrobenzoate*, m. p. 209° (Found : C, 76·7; H, 9·4. $C_{36}H_{55}O_4N$ requires C, 76·7; H, 9·5%).

(*b*) The neutral hydrolysate, m. p. 135°, of the palmitate from (A) had $[\alpha]_D$ −17·6° (Found : C, 82·6; H, 12·2%), and that from (B) had m. p. 135°, $[\alpha]_D$ −16·8° (Found : C, 82·5; H, 11·7%) but the sterols otherwise closely resembled " β "-sitosterol in the m. p. and anlyses of their acetates, benzoates, *p*-nitrobenzoates and 3 : 5-dinitrobenzoates (L. Jurd, Thesis, Nottingham, 1952).

Sarcocephalol.—After 4 crystallisations from methanol, *sarcocephalol* formed plates, m. p. 184°, $[\alpha]_D$ +40·7° [Found, after drying *in vacuo* at 140—150° : C, 83·2, 83·7; H, 11·5, 11·6; loss, 3·2%; *M* (Rast), 441, 462. $C_{30}H_{48}O,\frac{1}{2}H_2O$ requires C, 83·1; H, 11·4%; *M*, 434]. Its solution in chloroform–acetic anhydride developed with sulphuric acid a permanent pink colour. The *acetate*, from sodium acetate–acetic anhydride, crystallised from methanol in plates, m. p. 220° (Found, after drying at 100° *in vacuo* : C, 80·8; H, 11·0. $C_{32}H_{50}O_2,\frac{1}{2}H_2O$ requires C, 80·8; H, 10·8%). The *benzoate*, from pyridine–benzoyl chloride, purified in benzene by chromatography, formed shining needles, m. p. 244°, from acetone–methanol (Found, after drying at 100° *in vacuo* : C, 82·9; H, 9·8. $C_{37}H_{52}O_2,\frac{1}{2}H_2O$ requires C, 82·6; H, 9·9%). *Sarcocephalyl* p-*nitrobenzoate*, flattened rods (from acetone–methanol), had m. p. 268°, $[\alpha]_D$ +5·8° (Found, after drying at 100° *in vacuo* : C, 77·4; H, 9·2. $C_{37}H_{51}O_4N$ requires C, 77·4; H, 9·0%).

Aqueous Extraction.—Fine shavings of (A) (400 g.) were covered with water which was boiled for 30 minutes. The extraction was repeated and the united solutions were evaporated *in vacuo* to a thick syrup which was heated under reflux with methanol (400 c.c.) for 1 hour. The solid residue was further treated with boiling methanol (400 c.c.), and the two solutions were combined and kept at 0°, thus yielding a crystalline product (14·4 g.) (*X*). Extraction of (*X*) with boiling methanol (2 × 300 c.c.) left *meso*inositol (1·5 g.) which separated from aqueous ethanol in rectangular prisms, m. p. 221°. When concentrated to 250 c.c. and set aside for several days, the methanol solution deposited the cyclitol (11·5 g.), m. p. 199—200°, and a further amount (2·6 g.), m. p. 198°, was similarly obtained by reducing the original methanol solution (800 c.c.) to 80 c.c. Recrystallisation from aqueous methanol gave pure bornesitol, $[\alpha]_D^{20}$ +31·4° (*c*, 4·213 in H_2O), m. p. 201—202°.

No crystalline compounds were obtained when an evaporated aqueous extract of the wood specimen (B) was treated with methanol. However, acetylation of the crude substance, and recrystallisation from ethanol of the ether-soluble portion of the product, gave penta-acetylbornesitol, m. p. 137—138° (see below).

meso*Inositol*.—(*a*) The recrystallised compound had m. p. 221° alone or with an authentic specimen, and gave hexa-acetyl*meso*inositol, needles (from benzene–light petroleum), m. p. 215° (Found : C, 49·9; H, 5·5; OAc, 57·9. Calc. for $C_{18}H_{24}O_{12}$: C, 50·0; H, 5·6; 6OAc, 59·2%).

(*b*) Bornesitol (0·2 g.) was heated under reflux with hydriodic acid (3 c.c.; *d* 1·7) for 1 hour. Evaporation *in vacuo* yielded *meso*inositol, m. p. and mixed m. p. 221°; hexa-acetate, m. p. and mixed m. p. 215°.

Bornesitol.—The pure cyclitol, m. p. 201—202°, crystallises in rectangular prisms (Found : C, 43·5; H, 7·0; OMe, 19·3. Calc. for $C_7H_{14}O_6$: C, 43·3; H, 7·3; 1OMe, 16·0%), very soluble in water, and moderately soluble in hot acetic acid. The *penta-acetate*, prepared with acetic anhydride–sodium acetate, is obtained in good yield (80%) only if excess of anhydride is evaporated *in vacuo* before treatment with water. Crystallisation from light petroleum gave needles, m. p. 138—139°, and either 138—139° or 157° from alcohol or benzene–light petroleum. When seeded, alcoholic solutions of the low-melting form gave the variety m. p. 157°, $[\alpha]_D^{20}$ +11·8° (*c*, 0·76 in $COMe_2$) [Found : C, 50·2; H, 6·0; OMe, 7·9; OAc, 53·7%; *M* (Rast), 425. $C_{17}H_{24}O_{11}$ requires C, 50·5; H, 6·0; 1OMe, 7·7; 5OAc, 53·2%; *M*, 404].

The *pentapropionate*, prepared with propionic anhydride and sodium salt, crystallised from light petroleum (b. p. 40—60°) in rods, m. p. 47—48° (Found : C, 55·5; H, 7·2; OMe, 7·6. $C_{22}H_{34}O_{11}$ requires C, 55·6; H, 7·2; 1OMe, 6·5%). *Pentabenzoylbornesitol*, obtained with benzoyl chloride–pyridine, crystallised from ethanol in needles, m. p. 125—126° (Found : C, 71·2; H, 5·1. $C_{42}H_{34}O_{11}$ requires C, 70·6; H, 4·8%).

Ethyl Alcohol Extraction.—Fine shavings of the wood specimen (B) (10 kg.) were extracted with boiling ethanol (Soxhlet; 20 hours). From the cold solution (9 l.) an amorphous red solid (55 g.) separated and was discarded. Concentration to 1500 c.c. gave a semi-crystalline deposit (6 g.) (1) which was removed; when the filtrate was treated with ether (4½ l.) a yellow granular solid (205 g.) (2) was obtained. Evaporation of the ether–ethanol solution to 400 c.c. gave, after 24 hours at room temperature, a crystalline mass (3). Further concentration (to 150 c.c.) and the addition of light petroleum caused the deposition of sticky material from which the solution was decanted. Evaporation left an oil which was dissolved in a little boiling acetone, thus yielding when cold a crystalline solid (0·4 g.) (4).

By treatment of (2) with hot methanol (500 c.c.) crystalline material (14·7 g.) (5) was obtained, and the extraction of (3) with light petroleum (2 × 100 c.c.) left a residue (5·6 g.) (6). The petroleum-soluble portion was isolated and when crystallised from acetone afforded "β"-sitosteryl palmitate (1·4 g.), m. p. 83°. The combined products (1), (5), and (6) were powdered and extracted with boiling methanol (2 × 500 c.c.). The residue (5·6 g.) consisted of *meso*inositol, m. p. 221° after crystallisation from aqueous alcohol. When the methanol solution was concentrated to 300 c.c., bornesitol (17·8 g.), m. p. 200—201°, was isolated.

The highly crystalline pale yellow solid (4) was washed with warm benzene and recrystallised from a large volume of methanol, thereby forming an *acid*, in glistening cubes, m. p. 286° (Found : C, 73·0, 73·1; H, 9·0, 9·0; OMe, nil; act. H, 0·66%; equiv., 276, 273).

Acid Extraction.—The powdered wood (B) (1600 g.) was covered with 1% hydrochloric acid which was heated at 100° for 2 hours. The treatment was repeated and the combined solutions were extracted with ether. After addition of excess of ammonia to the aqueous liquid, basic material was isolated by means of ether. The yellow product was treated with light petroleum (50 c.c.), and amorphous solid removed by filtration. The filtrates concentrated to 10 c.c. deposited a further amount of amorphous substance, and after further evaporation the solution (3 c.c.) gave clusters of bright yellow prisms (50 mg.) which when recrystallised from light petroleum darkened at 182—183° and had m. p. 200° (Found : C, 74·6; H, 5·7; N, 13·3; OMe, nil%).

The authors thank Professor E. R. H. Jones, Manchester, for generously providing "β"-sitosterol, and Dr. J. C. Smith, Oxford, for pure palmitic acid.

THE UNIVERSITY, NOTTINGHAM. [*Received, December 18th, 1952.*]