The Chemistry of Carpesterol, a Novel Sterol from *Solanum xanthocarpum*

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The structure of carpesterol (1) has recently been shown to be (22*R*)-22-hydroxy-6-oxo-4α-methyl-5α-stigmast-7-en-3β-yl benzoate. The present work describes some chemical transformations of the sterol as well as its degradation to 4α-methyl-5α-stigmast-8(14)-en-3β-ol (10) from which the 24*R* configuration of the stigmasterol ethyl group was confirmed. The possible implications of 1 to the biogenesis of steroidal alkaloids and sapogenins are presented. The ORD spectra of 1 and some of its derivatives are contrasted with the spectra of the ecdysterols.

Solanum xanthocarpum (Schrad. and Wendl.) has held a place of some importance in the Hindu *materia medica* primarily as an expectorant and antipyretic.[1,2] In 1936 Saiyed and Kanga[3] isolated the substance carpesterol along with a steroidal alkaloid glycoside and alkamine later identified as solasonine and solasodine,[4] respectively. Subsequent investigations of extracts from *S. xanthocarpum* showed the presence of diosgenin[5,6] and β-sitosterol.[6]

As part of our continuing interest in the chemistry and biogenetic relationship of the *Solanum* genus, we undertook the structural and chemical investigation of carpesterol.

Structure of Carpesterol.—In a recent communication[7] we reported the structure of carpesterol as determined by a combination of chemical, spectroscopic, and X-ray diffraction methods. For the application of the latter technique the nicely crystalline *p*-iodobenzenesulfonate derivative (pipsylate) of carpesterol was utilized. Figure 1 is a perspective drawing of carpesterol pipsylate as interpreted by ORTEP[8] showing all the nonhydrogen atoms in the unit cell as thermal ellipsoids and the extended conformation of the side chain and the benzoyl group as it exists in the crystalline state. By assuming that the configurations at C-10 and C-13 are identical with those of cholesterol, the absolute configurations of the side-chain asymmetric centers were determined by internal comparison to be 20*S*, 22*R*, and 24*R*.

Thus, carpesterol is (22*R*)-22-hydroxy-6-oxo-4α-methyl-5α-stigmast-7-en-3β-yl benzoate which can be considered an oxidized elaboration of the (24*R*)-24-ethyllophenol skeleton. As such, carpesterol logically fits into the phytosterol biogenetic scheme suggested by Goad[9] wherein citrostadienol (24-ethylidene lophenol) is placed as a precursor to 24-ethyllophenol. Work has been completed in this laboratory on the identification of sterol components of *S. xanthocarpum* other than carpesterol and will be reported separately.[10]

Bearing in mind that solasodine, the major steroidal alkaloid of *S. xanthocarpum*,[3] contains a spiroaminoketal grouping at C-22 and in a similar way the sapogenin, diosgenin, also found in the same plant,[5,6] has a spiroketal function at C-22, it was gratifying when the structure determination of carpesterol revealed a 22-hydroxyl group. According to biogenetic schemes presented by two authors,[11,12] an intermediate common to both steroidal alkaloids and sapogenins was postulated as a 16-hydroxycholesterol derivative having unsaturations at the side-chain positions, 22 and 25. Oxidation of the double bonds by plant metabolism could then lead to 16-dihydrokryptogenin, which in turn, when cyclized, would afford alkaloids or sapogenins. It is tempting to speculate that carpesterol arises in *S. xanthocarpum* as a result of a branching in the biogenetic pathway that leads to solasodine and diosgenin. If solasodine, diosgenin, and carpesterol are formed from the common intermediate indicated in Scheme I,[13] the sequence of events that produces carpesterol is characterized by incomplete 4-demethylation and by the utilization of the terminal double bond to promote alkylation rather than hydroxylation. Whether demethylation at C-4 is incomplete because of adverse steric influence by the 3β-benzoyloxy substituent is open to further speculation.

Relevant to the present discussion is the isolation of sarsasapogenin as a saponin[14] along with (22*S*)-22-hydroxycholesterol[15] from *Narthecium ossifragum*. Thus, there are now two reported instances of steroidal materials spiroketalized at C-22 that have been found in plants accompanied by 22-hydroxysterols.

Chemistry.—In order to characterize the 6-oxo-7-ene chromophore in the uv, it was necessary to remove the interfering benzoyl group. Simple hydrolysis with ethanolic HCl or NaOH was not effective. Although benzoic acid was isolated from the hydrolysates, the neutral product was a complex (tlc) mixture. Inspection of the ir carbonyl region of the crude neutral fraction suggested that the Δ^7 double bond had been, in part, isomerized out of conjugation with the 6-keto group. Reduction of carpesterol (1) with $LiAlH_4$ followed by regeneration of the 6-keto function with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), pro-

(1) K. T. Kirtikar and B. D. Basu, "Indian Medicinal Plants," Part II, The Indian Press, 1918, p 896.

(2) R. N. Chopra, S. L. Nayar, and I. C. Chopra, "Glossary of Indian Medicinal Plants," C. S. I. R., New Delhi, 1956, p 230.

(3) I. Z. Saiyed and D. D. Kanga, *Proc. Indian Acad. Sci.*, **4A**, 255 (1936).

(4) L. H. Briggs, *J. Amer. Chem. Soc.*, **59**, 1404, 2467 (1937).

(5) Y. Sato and H. G. Latham, *ibid.*, **75**, 6067 (1953).

(6) M. R. Heble, S. Narayanaswami, and M. S. Chadha, *Science*, **161**, 1145 (1968).

(7) Y.-H. Tsay, J. V. Silverton, J. A. Beisler, and Y. Sato, *J. Amer. Chem. Soc.*, **92**, 7005 (1970).

(8) C. K. Johnson, ORTEP (ORNL-3794), Oak Ridge National Laboratory, Oak Ridge, Tenn.

(9) L. J. Goad in "Terpenoids in Plants," J. B. Pridham, Ed., Academic Press, London, 1967, pp 182, 183.

(10) G. Kusano, Y. Sato, and J. A. Beisler, manuscript in preparation.

(11) K. Schreiber in "The Alkaloids," Vol. X, R. H. F. Manske, Ed., Academic Press, New York, N. Y., 1968, pp 122, 123.

(12) H. R. Schütte in "Biosynthese der Alkaloide," K. Mothes and H. R. Schütte, Ed., Deutscher Verlag der Wissenschaften, VEB, Berlin, 1969, p 628.

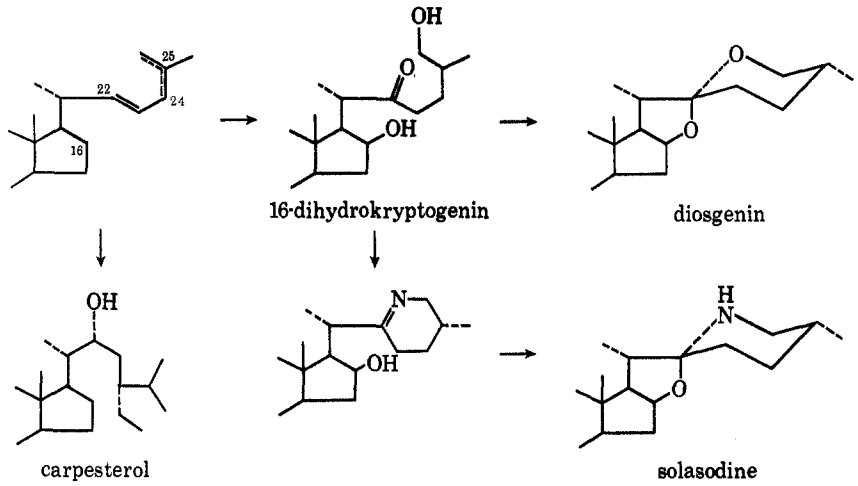
(13) Scheme I is an abbreviated and slightly modified form of the more comprehensive biogenetic schemes published elsewhere.[11,12]

(14) A. Stabursvik, *Acta Chem. Scand.*, **8**, 1304 (1954).

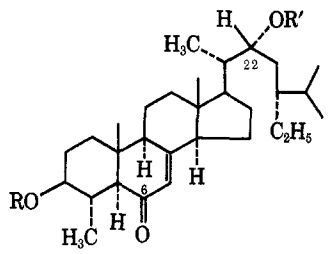
(15) A. Stabursvik, *ibid.*, **7**, 1220 (1953).

SCHEME I

BIOGENETIC RATIONALIZATION OF THE STEROIDAL PRODUCTS FROM *S. xanthocarpum*



vided a route to debenzoylcarpesterol which was isolated as the diacetate (2). Diacetate 2 gave a maxi-



1, R = COPh; R′ = H
2, R = R′ = $COCH_3$
3, R = COPh; 22-oxo
4, R = COPh; R′ = $SO_2C_6H_4CH_3$
5, R = COPh; 22-oxo; 6ξ-H, 6ξ-OH

mum in the uv at 245 mμ (ε 12,500) which agrees well with the calculated value (244 mμ) for a trisubstituted α,β-unsaturated ketone.[16]

Since 2 gives an ORD spectrum similar in appearance and amplitude to the curve obtained for carpesterol (1) (Figure 2), it is reasonable to assume that no stereochemical alterations occurred when converting 1 into 2. Again with reference to Figure 2, the enantiomeric environment of the 12-oxo-9(11)-ene chromophore of 12-oxolanost-9(11)-en-3β-yl acetate[17] with respect to the 6-oxo-7-ene chromophore of 1 is evident in the near mirror-image relationship of their ORD curves. Although the steroidal insect-metamorphosing hormones (ecdysterols), which also have 6-oxo-7-ene chromophores, give ORD curves that are similar in sign and appearance to 1 and 2, the amplitudes are significantly smaller. The difference can be attributed to the ecdysterol 5β configuration where 1 and 2 have a 5α hydrogen at the A–B ring junction.[18] The range of the absolute magnitudes of the amplitudes for the curves shown in Figure 2 (*i.e.*, 450–570) is higher by a factor of *ca.* 6 than the 68–110 range reported[19] for five ecdy-

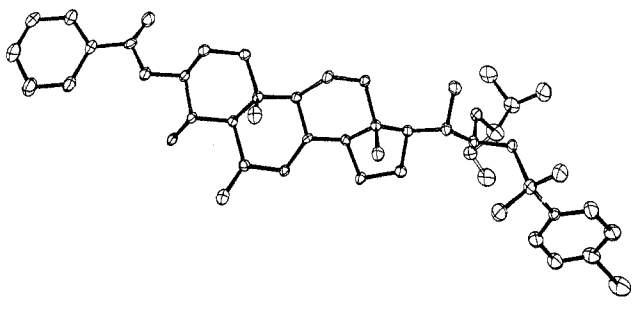


Figure 1.—An ORTEP projection from an input of the positional and anisotropic thermal parameters of carpesterol pipsylate.

sterols. This observation could be used to determine the absolute configuration at C-5 in 6-oxo-7-ene steroids and perhaps at C-13 in the case of 12-oxo-9(11)-ene steroids.

There have been a number of examples recorded in the literature pointing to a diminished reactivity with respect to reduction of the 22-keto group in the side chain of cholesterol derivatives. For example, Mazur, *et al.*,[20] made use of this property in a sapogenin synthesis. We have found indications that C-22 in ketocarpesterol (3) and carpesterol tosylate (4) has a similar reduced reactivity with nucleophilic reagents. When 3, formed by chromic acid oxidation of carpesterol, was reduced with sodium borohydride a single product was isolated in good yield. Structure 5, which indicates a preferential reduction of the 6-keto group, was assigned to the reduction product on the basis of its ir spectrum and combustion analysis. This structure assignment was supported by the regeneration of 3 by allylic oxidation with DDQ. When tosylate 4 is refluxed with $LiAlH_4$ in THF, displacement of the tosylate group does not occur, but instead, the energetically favored reaction, the elimination of the elements of toluenesulfonic acid to form a double bond (Scheme II), occurs.

The action of $LiAlH_4$ on tosylate 4 not only leads to 22 unsaturation, but also reduces the 6-keto function and reductively removes the benzoyl group to provide intermediate 6. This intermediate was particularly useful in the degradation of carpesterol. Successive

(16) A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products," Pergamon Press, London, 1961, p 58.

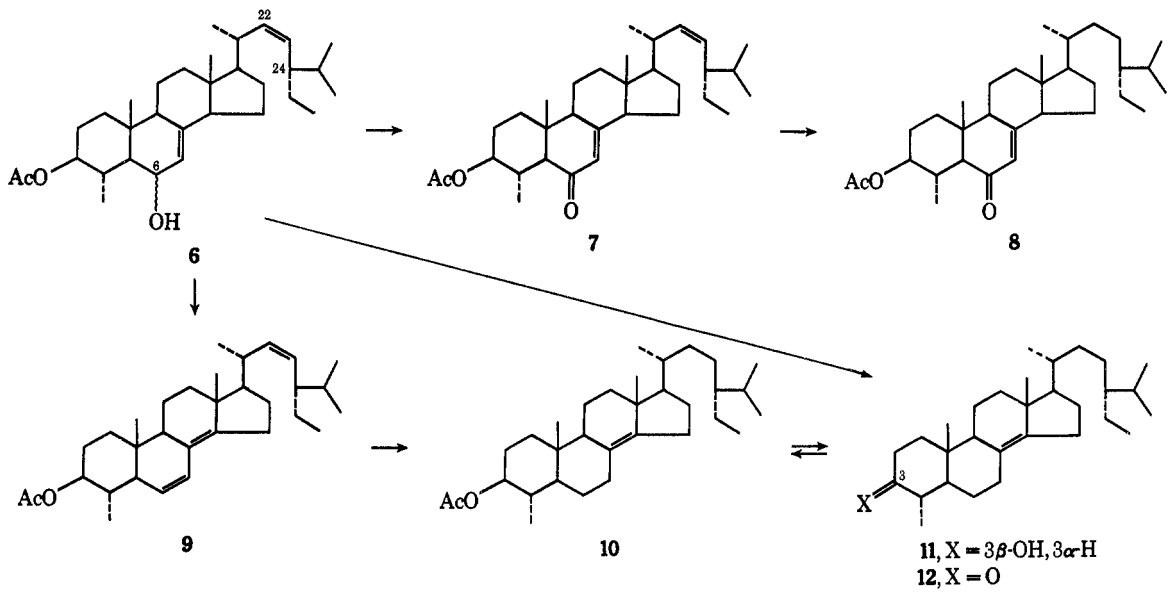
(17) We express our gratitude to Professor W. Lawrie, University of Strathclyde, Glasgow, for providing a sample of this compound.

(18) Carpesterol (1) does not have insect-metamorphosing hormonal activity. The authors thank M. J. Thompson, U. S. Department of Agriculture, Beltsville, Md., for providing this assay.

(19) H. Hikino, K. Nomoto, and T. Takemoto, *Tetrahedron*, **26**, 887 (1970).

(20) Y. Mazur, N. Danieli, and F. Sondheimer, *J. Amer. Chem. Soc.*, **82**, 5889 (1960).

SCHEME II



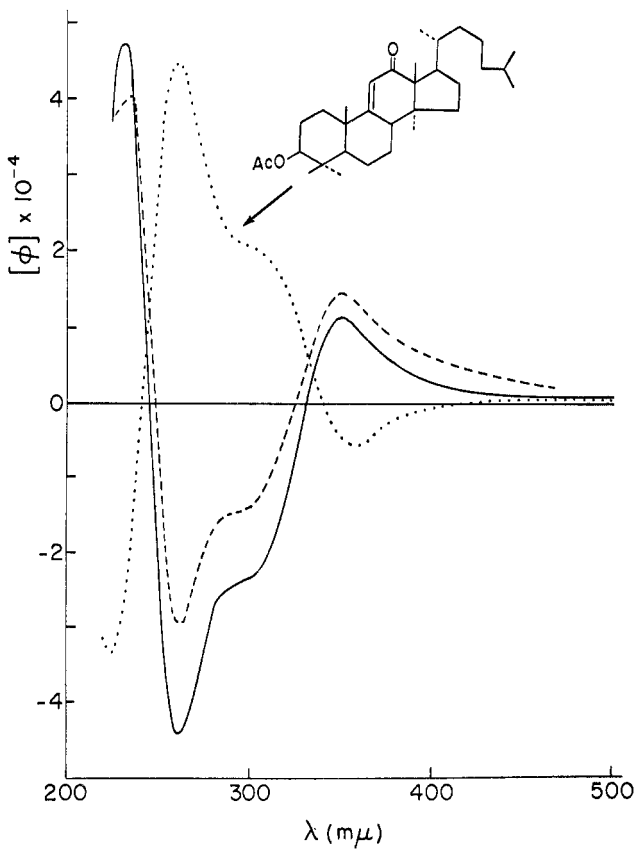


Figure 2.—ORD spectra of carpesterol (1, a = +570, solid line), debenzoylcarpesterol diacetate (2, a = +450, broken line), and 12-oxolanost-9(11)-en-3β-yl acetate (a = −515, dotted line).

treatments with DDQ and acetic anhydride converted 6 to debenzoylanhydrocarpesterol acetate (7). That the newly formed double bond in 6 and 7 occupies the 22 position was shown by the absence of a signal in the nmr attributable to a methyl group substituted on a sp^2-hybridized carbon atom (excepting the acyl methyl) and by the appearance of three protons in the olefinic region of the spectrum. Catalytic uptake of 1 mol equiv of hydrogen by 7 gave debenzoyldeoxycarpesterol acetate (8), the ORD spectrum (a = 499) of which was similar to those of 1 and 2.

By applying a different sequence of reactions to intermediate 6, known compounds were obtained from which it was possible to compare the absolute configuration of the C-24 ethyl groups of carpesterol and stigmasterol. Accordingly, acetylation of 6 followed by mild acid treatment produced a 6,8(14),22-triene acetate (9) which showed a maximum in the uv at 250 mμ (ε 19,400) comparable to ergosta-6,8(14),22-trien-3β-yl, acetate (ϵ_{252}^{max} 24,000).[21a] Both the latter compound[21b] and 9 exhibited negative Cotton effects in their ORD curves.[22] Hydrogenation of 9 results in uptake of 2 mol equiv of hydrogen to afford 4α-methyl-5α-stigmast-8(14)-en-3β-yl acetate (10, mp 131–132°, $[\alpha]_D$ +39°). Direct hydrogenation of intermediate 6 leads to hydrogenolysis of the allylic alcohol, saturation of the side-chain double bond, and isomerization of the nuclear double bond to the 8(14) position to give alcohol 11 (mp 147–148°, $[\alpha]_D$ +18°). Chromic acid oxidation of 11 provided the 3-keto derivative (12), which gave a positive Zimmerman reaction[24] and the anticipated positive Cotton effect in the ORD indicative of 4α-methyl-A/B trans steroids.[25] The ORD spectrum of 12, which requires the cholesterol absolute configuration at C-10, supports the validity of our earlier assumption in choosing the enantiomorph of carpesterol pipsylate from the two possibilities offered by the X-ray data. Hydride reduction of 12 returned alcohol 11, and acetylation of the latter gave an acetate that was identical (mixture melting point, ir) with acetate 10 prepared by the alternate route described above.

For the purpose of a structure determination, Mazur,

(21) (a) G. D. Laubach, E. C. Schreiber, E. J. Angello, and K. J. Brunings, *J. Amer. Chem. Soc.*, **78**, 4743 (1956); (b) E. Charney, H. Ziffer, and U. Weiss, *Tetrahedron*, **21**, 3121 (1965).

(22) The ergostatriene and 9 do not follow the transoid diene rule[22a] for prediction of the Cotton effect sign, perhaps due to the small skew angles required by their structures (see ref 21b, p 3124). This being true, the two additional methyl groups at C-4 and C-28 of 9 are not sufficient to change the skew sense of the diene with a concomitant change in the sign of the Cotton effect. The CD spectrum of the ergostatriene, however, conforms to theoretical predictions.[23]

(23) See ref 20 in A. W. Burgstahler and R. C. Barkhurst, *J. Amer. Chem. Soc.*, **92**, 7601 (1970).

(24) D. H. R. Barton and P. deMayo, *J. Chem. Soc.*, 887 (1954), and references cited therein.

(25) P. Crabbé, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, San Francisco, Calif., 1965, p 46.

et al.,[26] hydrogenated citrostadienol and its acetyl derivative to give isocitrostenol (mp 152–153°, $[\alpha]_D$ +23°) and isocitrostenol acetate (mp 129–130°, $[\alpha]_D$ +41°), respectively. Complete saturation of isocitrostenol occurred by hydrogenation under acidic conditions to yield 4α-methyl-5α-stigmastan-3β-ol. The identity of the last mentioned derivative was established by synthesis from stigmasterol. Thus, the adequate agreement of the melting points and rotations of **10** and **11** with isocitrostenol acetate and isocitrostenol, respectively, indicates an identity between the corresponding pairs, and it follows that the absolute configuration of the C-24 ethyl group is the same in stigmasterol, isocitrostenol,[27] and carpesterol.

The absolute configuration of the side-chain ethyl group of stigmasterol was determined by Tsuda and coworkers[28] by ozonolysis of the 22 double bond and conversion of the resulting fragment into a compound of known absolute configuration. The chemical degradation of **1** in conjunction with our X-ray study of carpesterol pipsylate confirms the 24*R* configurational assignment for stigmasterol ethyl group.

Experimental Section

Melting points were determined on a Kofler micro hot stage and were not corrected. Ir and uv spectra were recorded with a Perkin-Elmer Model 421 and a Cary Model 15 spectrophotometer, respectively. Rotations were measured in a 1-dm microcell in $CHCl_3$ solutions with a Perkin-Elmer Model 141 polarimeter. ORD curves were determined with a Cary Model 60 spectropolarimeter. Nmr spectra were measured in $CDCl_3$ solutions with a Varian Model A-60 spectrometer using TMS as an internal standard. The Hitachi Perkin-Elmer RMU-6 double-focusing mass spectrometer was used at 80 eV to record mass spectra.

Isolation of Carpesterol (1).—The dried and ground fruit from *S. xanthocarpum*[29] (7.7 kg) was extracted with 7 l. of *n*-hexane in a Soxhlet apparatus for 24 hr. The extract was concentrated to 1.5 l. by distillation of the solvent, allowed to stand at room temperature for 3 days, and then filtered. After washing thoroughly with fresh portions of hexane, 3.87 g of a tan powder was obtained. The powder was taken up in benzene–pentane and chromatographed on 110 g of Woelm alumina (neutral, activity II). After washing oils from the column with 500 ml of benzene–pentane mixtures, colorless crystals were eluted with benzene and benzene–Et_2O. Recrystallization from acetone gave 3.37 g (0.044% based on dried plant material) of **1** as glistening plates, mp 248–251°. The pure sterol was obtained from acetone–EtOH: mp 251° (lit.[3] mp 248°); $[\alpha]^{27}_D$ +67° (*c* 0.716); ORD (*c* 0.014, MeOH) $[\phi]_{600}$ +400°, $[\phi]_{350}$ +11,500°, $[\phi]_{295}$ −24,500° (sh), $[\phi]_{261}$ −44,500°, $[\phi]_{230}$ +47,600°; uv max (EtOH) 233 mμ (ε 19,400); ir ($CHCl_3$) 3590 (OH), 1710 (C=O, benzoate), 1677 (enone), 1632, 1607, 1587 cm^{-1}; nmr δ 8.2–7.3 (m, 5 H, aromatic protons), 5.71 (s, 1 H, C-7 proton), 4.71 (broad, 1 H, C-3 proton), and 3.76 (very broad doublet, 1 H, C-22 proton); mass spectrum *m/e* (rel intensity) 562 (9, M^+), 544 (16, M − H_2O), 529 (10, M − H_2O − Me), 501 (10), 440 (65, M − PhCOOH), 422 (22), 403 (19), 312 (100), 297 (18), 257 (69), 109 (45) 105 (88).

Anal. Calcd for $C_{37}H_{54}O_4$: C, 78.96. H, 9.67. Found: C, 78.70; H, 9.68.

Stirring **1** at room temperature for 24 hr in pyridine solution with excess *p*-iodobenzenesulfonyl chloride gave carpesterol pipsylate in quantitative yield as plates, mp 126–127°. Slow evaporation of a MeOH–CH_2Cl_2 solution provided crystals suitable for X-ray diffraction analysis.

Anal. Calcd for $C_{43}H_{57}O_6IS$: C, 62.31; H, 6.94; I, 15.32. Found: C, 62.05; H, 6.70; I, 15.36.

Debenzoylcarpesterol Diacetate (2).—Carpesterol (**1**) was reduced with $LiAlH_4$ in refluxing (3 hr) THF to give a quantitative yield of colorless needles after recrystallization from benzene.

A solution of 190 mg of the reduction product in 4 ml of dioxane treated with a solution of 200 mg of DDQ in 4 ml of dioxane and allowed to stand at room temperature for 44 hr. The reaction solution was poured into dilute NaOH solution and ether extracted, and the extracts were shaken twice with dilute NaOH and washed with water. Removal of the solvent gave a crystalline residue which was acetylated directly in the usual way with acetic anhydride–pyridine. A cyclohexane solution of the crude acetylated product was chromatographed on 13 g of Woelm (neutral, activity II) alumina. Elution with pentane–PhH mixtures afforded 131 mg of crystalline **2**: mp 205–206°; ORD (*c* 0.013, MeOH) $[\phi]_{600}$ +366°, $[\phi]_{348}$ +15,000°, $[\phi]_{295}$ −14,600°, $[\phi]_{263}$ −30,000°, $[\phi]_{231}$ +40,000; uv max (EtOH) 245 mμ (ε 12,500); ir (CS_2) 2875, 1768, 1686, 1634, 1245, 1142 cm^{-1}; mass spectrum *m/e* (rel intensity) 542 (4, M^+ requires 542.3971, found 542.3994), 482 (100, M − HOAc), 467 (12), 372 (22), 341 (23), 317 (23), 257 (57).

Anal. Calcd for $C_{34}H_{54}O_5$: C, 75.23; H, 10.03. Found: C, 75.24; H, 9.85.

Ketocarpesterol (3).—A modified Kiliani reagent[30] was prepared such that the concentration of the chromic acid provided 4 mequiv/ml. A microburet was used to drop 0.58 ml of the oxidant into a solution of 500 mg of **1** in 60 ml of acetone[31] stirred at room temperature. Stirring was continued for 15 min after the addition, then excess oxidant was destroyed with a few drops of *i*-PrOH and water was added dropwise until green droplets separated from solution. The solution was decanted, the decantate was evaporated, and the residue in ether solution was washed with 2% $NaHCO_3$ and water. The ether solution yielded 464 mg of crystalline **3**, which melted at 228–229° after recrystallization from acetone–MeOH: $[\alpha]^{20}_D$ +47° (*c* 0.9); ORD (*c* 0.013, MeOH) $[\phi]_{600}$ +200°, $[\phi]_{350}$ + 13,800°, $[\phi]_{300}$ −19,700° (sh), $[\phi]_{265}$ −38,100°, $[\phi]_{235}$ +50,300°; ir ($CHCl_3$) 2879, 1710, 1674, 1631, 1605, 1585 cm^{-1}; nmr δ 8.2–7.3 (m, 5 H, aromatic protons), 5.71 (s, 1 H, C-7 proton), and 4.75 (broad, 1 H, C-3 proton); mass spectrum *m/e* (rel intensity) 560 (28, M^+ requires 560.3865, found 560.3840), 545 (5), 518 (10), 477 (21), 438 (91), 354 (100).

Anal. Calcd for $C_{37}H_{52}O_4$: C, 79.24; H, 9.35. Found: C, 79.40; H, 9.09.

Carpesterol Tosylate (4).—A solution of 2.79 g of **1** in 20 ml of dry pyridine was combined with 2.92 g of *p*-toluenesulfonyl chloride and stirred at room temperature for 70 hr. The product was ether extracted from dilute HCl solution. While concentrating the dried ether extracts on a steam bath, *n*-hexane was slowly added until a saturated solution was obtained. On cooling, a quantitative yield of the tosylate was collected as colorless needles: mp 126–127°; ir (CS_2) 1715, 1682, 1627, 1365, 1267, 1173 cm^{-1}.

Anal. Calcd for $C_{44}H_{60}O_6S$: C, 73.70; H, 8.44; S, 4.47. Found: C, 74.00; H, 8.38; S, 4.31.

Borohydride Reduction of Ketocarpesterol (3).—Ketocarpesterol (74 mg), dissolved in 20 ml of THF–EtOH (1:1), was treated with 155 mg of $NaBH_4$ and stirred for 30 hr at room temperature. Concentration under vacuum gave a residue, 2% $NaHCO_3$ solution was added, and the solution was extracted with CH_2Cl_2. The evaporated extracts produced a gum that crystallized on standing. Recrystallization (acetone–water) gave 66 mg of **5**: mp 188–191°; ir ($CHCl_3$) 3620, 2960, 1711, 1607, 1120, 1072, 1027, 966 cm^{-1}.

Anal. Calcd for $C_{37}H_{54}O_4$: C, 78.96; H, 9.67. Found: C, 78.82; H, 9.51.

Using methanol as the reaction solvent gave the same product.

Ketocarpesterol (3) from 5.—To a solution of 66 mg of **5** in 4 ml of dioxane was added a solution of 90 mg of DDQ in 4 ml of dioxane, and the resulting clear yellow solution was stirred at

(26) Y. Mazur, A. Weizmann, and F. Sondheimer, *J. Amer. Chem. Soc.*, **80**, 6293 (1958).

(27) In the synthesis of 4α-methyl-5α-stigmastan-3β-ol, asymmetric centers were generated at the 4 and 5 positions in the reduction of 4-methylstigmast-4-en-3-one with H_2/Pd or Li/NH_3.[26] Not only does the present study confirm the 4α-methyl-5α-hydrogen assignment for the reduction product, but also confirms the correct stereochemical assignments at C-4 and C-5 of citrostadienol itself.

(28) K. Tsuda, Y. Kishida, and R. Hayatsu, *J. Amer. Chem. Soc.*, **82**, 3396 (1960).

(29) We are indebted to Dr. Quentin Jones, New Crops Research Branch, U. S. Department of Agriculture, Beltsville, Md., for making a generous supply of plant material available to us.

(30) H. Kiliani, *Chem. Ber.*, **46**, 676 (1913).

(31) R. G. Curtis, I. Heilbron, E. R. H. Jones, and G. F. Woods, *J. Chem. Soc.*, 457 (1953).

room temperature for 3 days. Work-up as for **2** gave a yellow solid which yielded 40 mg of white needles by crystallization from acetone–MeOH. The product (mp 221–225°) was identical with **3** (mixture melting point, ir, mass spectrum).

$LiAlH_4$ Reduction of Carpesterol Tosylate (4).—To a stirring mixture of 6.4 g of $LiAlH_4$ and 225 ml of dry THF was added dropwise a solution of 6.65 g of **4** in 75 ml of THF. The mixture was stirred and refluxed for 5 hr, cooled, and hydrolyzed with water. The reaction solution was poured into saturated Rochelle salt solution and ether extracted. Evaporation of the extracts and recrystallization of the residue from EtOAc gave 4.04 g of **6** as a crystalline solid which melted over a broad range and which showed no carbonyl absorption in the infrared. Repeated recrystallization (EtOAc) gave small prisms, mp 197–209°.

Anal. Calcd for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38. Found: C, 81.09; H, 11.26.

Debenzoylanhydrocarpesterol Acetate (7).—Diol **6** (914 mg) was oxidized with 1.0 g of DDQ, and the crude product was acetylated as described for the preparation of **2**. From the crude acetylation product 536 mg of **7** was obtained by crystallization from MeOH: mp 200–201°; uv max (EtOH) 246 mμ (ε 13,000); ir (CS_2) 1735, 1682, 1630 cm^{-1}; nmr δ 5.76 (br s, 1 H, C-7 proton), 5.21 (m, 2 H, CH=CH), 4.5 (very broad, 1 H, C-3 proton), and 2.08 (s, 3 H, COMe); mass spectrum *m/e* (rel intensity) 482 (58, M^+ requires 482.3760, found 482.3769), 439 (36), 422 (41), 379 (32), 370 (20), 341 (100).

Anal. Calcd for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.32; H, 10.57.

Debenzoyldeoxycarpesterol Acetate (8).—At room temperature and pressure, 225 mg of **7** was hydrogenated in EtOAc solution (10 ml) to which 123 mg of 10% palladium/charcoal catalyst had been added. Hydrogen uptake was complete after 30 min. After filtration and evaporation of the reaction solution, 167 mg of **8** was obtained by recrystallization from MeOH: mp 188–189°; $[\alpha]^{23}D$ +26° (*c* 1.01); ORD (*c* 0.014 MeOH) $[\phi]_{348}$ +9700°, $[\phi]_{263}$ −40,200°; uv max (EtOH) 246 mμ (ε 12,500); ir (CS_2) 1743, 1690, 1636 cm^{-1}; mass spectrum *m/e* (rel intensity) 484 (12, M^+), 424 (100), 409 (37), 356 (67), 343 (14), 283 (22), 257 (37).

Anal. Calcd for $C_{32}H_{52}O_3$: C, 79.28; H, 10.81. Found: C, 79.13; H, 10.87.

4α-Methyl-5α-stigmast-6,8(14),22-trien-3β-yl Acetate (9).—Diol **6** (275 mg), obtained from the reduction of carpesterol tosylate, in 10 ml of dry pyridine was combined with 5 ml of acetic anhydride, stirred at room temperature for 15 hr, and then heated to 70–75° for 4 hr. After hydrolyzing the reaction solution with ice chips the product was isolated in the usual way to give a noncrystallizable gum which was homogeneous by tlc (PhH–EtOAc).

Dissolving the gum in 4 ml of glacial HOAc containing 0.1 ml of concentrated HCl caused crystals to separate slowly from solution (150 mg, mp 132–144°) (recrystallization from MeOH–CH_2Cl_2 raised the melting point to 154–155°): ORD (*c* 0.015, MeOH) $[\phi]_{400}$ −990°, $[\phi]_{300}$ −3800°, $[\phi]_{264}$ −17,700°, $[\phi]_{250}$ −4600°; uv max (EtOH) 250 mμ (ε 19,400); ir (CS_2) 3045, 2868, 1745, 1245, 1024, 973, 800, 689 cm^{-1}; nmr δ 5.39–5.06 (m, 4 H, olefinic protons), 4.38 (broad, 1 H, C-3 proton); mass spectrum *m/e* (rel intensity) 466 (56, M^+), 451 (31), 391 (19), 353 (13), 326 (100), 311 (34).

Anal. Calcd for $C_{32}H_{50}O_2$: C, 82.34; H, 10.80. Found: C, 82.45; H, 10.68.

4α-Methyl-5α-stigmast-8(14)-en-3β-yl Acetate (10) from 9.—Reduction of 38 mg of triene **9** in 4 ml of EtOAc with hydrogen at room temperature and pressure (47 mg of 10% palladium/charcoal catalyst) gave a quantitative yield of **10**: mp 131–132° (from MeOH–CH_2Cl_2); $[\alpha]^{24}D$ +39° (*c* 1.01); ir (CS_2) 2870, 1735, 1377, 1370, 1241, 1022 cm^{-1}; mass spectrum *m/e* (rel intensity) 470 (100, M^+), 455 (12), 410 (6), 395 (8), 329 (6), 287 (4), 269 (15), 243 (13), 227 (15), 147 (18), 135 (10), 133 (11); no olefinic protons appeared in the nmr.

Anal. Calcd for $C_{32}H_{54}O_2$: C, 81.64; H, 11.56. Found: C, 81.85; H, 11.51.

4α-Methyl-5α-stigmast-8(14)-en-3β-ol (11) from 6.—A solution of 510 mg of diol **6** in 15 ml of EtOAc was mixed with 285 mg of 10% palladium/charcoal catalyst and hydrogenated at room temperature and pressure for 4.5 hr. The catalyst was removed by filtration and thoroughly extracted (Soxhlet) with EtOAc, and the filtrate and extracts were combined and evaporated. Recrystallization of the product from MeOH–CH_2Cl_2 gave 379 mg of plates: mp 147–148°; $[\alpha]^{22}D$ +18° (*c* 1.02); ir (CS_2) 3620, 2870, 1378, 1368, 1212, 959 cm^{-1}; mass spectrum *m/e* (rel intensity) 428 (100, M^+ requires 428.4018, found 428.4017), 413 (25), 287 (20), 243 (17), 227 (19).

Anal. Calcd for $C_{30}H_{52}O$: C, 84.04; H, 12.23. Found: C, 84.15; H, 12.09.

Acetylation of **11** with pyridine/acetic anhydride gave acetate **10** (mp 131–132°), which was identical (mixture melting point, ir) with the hydrogenation product from triene **9**.

4α-Methyl-5α-stigmast-8(14)-en-3-one (12).—Alcohol **11** (257 mg), dissolved in 15 ml of acetone, was oxidized with 0.55 ml of the 4 *N* chromic acid reagent which was added dropwise to the stirred reaction solution. The product was isolated as described for ketocarpesterol (**3**). Accordingly, the extracts yielded 248 mg of a gum that spontaneously crystallized. Several recrystallizations from MeOH–CH_2Cl_2 gave pure ketone **12**: mp 110–112°; $[\alpha]^{22}D$ +18° (*c* 1.03); ORD (*c* 0.077, dioxane) $[\phi]_{400}$ +180°, $[\phi]_{312}$ +2400°, $[\phi]_{306}$ +2240° (sh), $[\phi]_{260}$ −8640°; ir (CS_2) 1709, 1374, 1365, 1174, 957 cm^{-1}; mass spectrum *m/e* (rel intensity) 426 (100), 412 (14), 411 (38), 285 (37), 272 (12), 259 (22), 258 (25), 243 (46).

Anal. Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.50; H, 11.59.

Addition of excess $LiAlH_4$ to an ethereal solution of ketone **12** (30 mg) gave, on work-up, 28 mg of alcohol **11**. Colorless plates (mp 143–147°) were obtained from MeOH–CH_2Cl_2 and a mixture melting point with **11** prepared from **6** showed no depression. The acetate (**10**) derivative (Ac_2O/py) had a melting point of 127–131° after one recrystallization from MeOH–CH_2Cl_2.

Registry No.—**1**, 31077-78-8; **1** pipsylate, 31077-79-9; **2**, 31893-26-2; **3**, 31893-27-3; **4**, 31893-28-4; **5**, 31893-29-5; **6**, 31893-30-8; **7**, 31893-31-9; **8**, 31893-32-0; **9**, 31893-33-1; **10**, 31893-34-2; **11**, 31893-35-3; **12**, 31893-36-4.

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