ride at 0° for 2 days.[27] After the usual work-up procedure[27] the crude product was recrystallized from ether–ligroin mixture (82%): mp 119–121° (lit.[28] mp 120–122°); NMR δ 4.4 (m, 1, >CHOTs), 7.66 (m, 4, C_6H_4).

3β-Cholestanyl-4β-d_1 Brosylate (9). The mixture containing 3β-cholesterol-4β-d_1 and freshly distilled acetic anhydride was refluxed in dry pyridine for 20 hr.[29] After addition of ether (200 ml) the resulting solution was washed with water until neutral reaction. The organic layer was dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure and crude 3β-acetoxycholesterol-4β-d_1 was recrystallized from EtOH (91%): mp 113–115.5° (lit.[29] mp 114.5–116.5°); NMR δ 2.00 (s, 3, $-CH_3$), 4.70 (m, 1, >CHOAc).

Acetylated 3β-cholesterol-4β-d_1 was catalytically hydrogenated over Pt (Adams catalyst) in glacial acetic acid at 65° for 36 hr. This method does not lead to deuterium scrambling.[30] After the usual work-up the crude product was refluxed in an alkaline ethanol solution for 1 hr.[30] Purification and recrystallization from acetone yielded 3β-cholestanol-4β-d_1 (80%): mp 142–144°; $[\alpha]_D$ +23.4°; ir ν 2140 cm^{-1} (C–D).[23] The alcohol was converted to the corresponding brosylate **9** by the known procedure[27] (53%), mp 121–122°. Mass spectral data did not indicate deuterium scrambling. The deuterium content was determined as 0.91 atom D per molecule. The ir spectrum supported the presence of a 4β C–D bond in the substrate.[23]

3β-Cholestanyl-5α,6α-d_2 Brosylate (10). 3β-Acetoxycholesterol[29] was catalytically deuterated over Pt in AcOH-d_1 as previously described.[30] The reaction mixture was treated as usual,[30] yielding 3β-cholesterol-5α,6α-d_2 (91%): mp 142.5–144°; $[\alpha]_D$ +23.1°; ^1H NMR spectrum did not show the signal corresponding to a vinyl proton (δ 5.35). The deuterium distribution according to the mass spectrum was d_3, 3%; d_2, 96%; d_1, 1%; total 2.02 atoms D per molecule. The deuterated alcohol was converted to the brosylate **10** in a described manner[27] (67%), mp 120.5–122°.

Kinetic Measurements. The titrimetric rates were obtained using the automatic potentiometric titration method by means of a pH-stat, Radiometer, Copenhagen, SBR-2/TTT 11, maintaining a constant "pH setting" of 6.8. The substrate concentration was 1.5 mmol in all experiments. Six to eight solvolyses were performed for each sulfonate ester, alternating the measurement of the labeled and unlabeled derivative. The rate data were calculated from the standard integrated first-order law and evaluated using a nonlinear least-squares program. No trend was observed in the rate constants between 15 and 80% of the solvolysis completion.

Acknowledgment. We are indebted to Professor V. J. Shiner, Jr., Indiana University, for helpful and stimulating discussions.

Registry No.—**1**, 1182-65-6; **2**, 56227-24-8; **5**, 55913-52-5; **6**, 55913-53-6; **7**, 55954-48-8; **8**, 55913-54-7; **9**, 55954-49-9; **10**, 55954-50-2; **11**, 3381-56-4; **12**, 35596-32-8; 3β-cholesterol, 57-88-5; 3α-cholesterol, 474-77-1; 3β-cholesteryl benzoate, 604-32-0; 3β-cholesterol-4β-d_1, 1973-68-8; 3β-cholesterol-6-d, 16374-87-1; 3β-cholestanol, 80-97-7; 3β-acetoxycholesterol-4β-d_1, 1973-64-4; 3β-cholestanol-4β-d_1, 55954-51-3; 3β-cholestanol-5α,6α-d_2, 55954-52-4.

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Configuration of 5-Cholestene Hydrochloride

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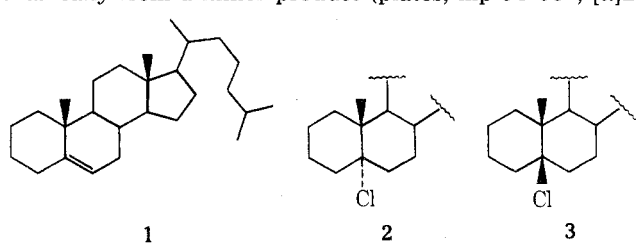
The addition of hydrogen chloride to 5-cholestene (**1**) was reported long before the constitution of the steroid nucleus was established.[2] The major product (prisms, mp 97°, $[\alpha]_D$ +4.7°) has been described as 5α-chlorocholestane (**2**), rather than the 5β isomer (**3**),[3] and reference has been made[4] to a structure determination using X-ray diffraction techniques.[5]

The structure of the major product ("Mauthner's hydrochloride") was, however, not solved. The crystallographic investigation was limited to the determination of the point group and dimensions of the unit cell. As pointed out by Bernal,[5] these data are not sufficient to be considered diagnostic as to the stereochemistry of the ring junction.

Subsequent experiments on the addition of hydrogen chloride to **1** substantiated Mauthner's observations but lacked rigorous proof of stereochemistry.[6] The major product (prisms, mp 96–97°, $[\alpha]_D$ +6.4°) was separated mechanically from a minor product (plates, mp 94–95°, $[\alpha]_D$



1 2 3

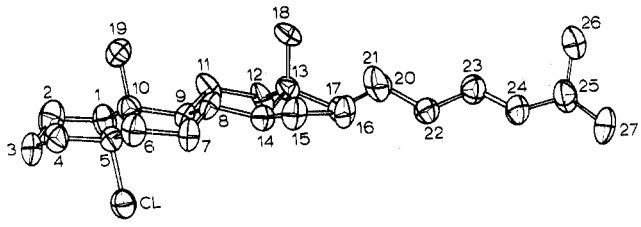


Figure 1. ORTEP view of 5α-chlorocholestane.

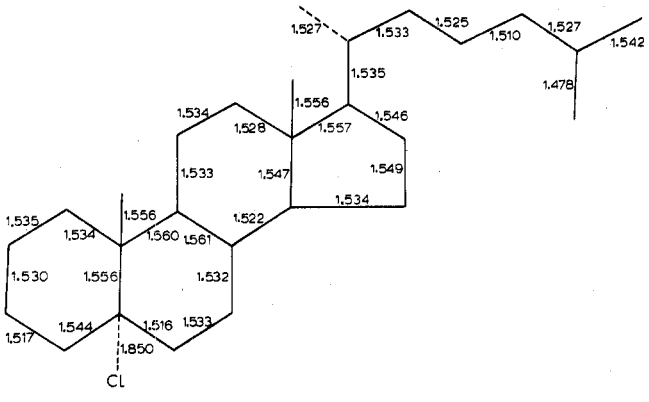


Figure 2. Bond lengths of 5α-chlorocholestane. The average standard deviation of a C–C bond is 0.008 Å.

+37°). The minor product was assigned the 5β configuration **3**.

Recent interest in the stereochemical and conformational aspects of decalyl cations[7] led us to question the structure of Mauthner's hydrochloride. The reasoning which prompts this reconsideration is based on the numerous observations of competitive, sometimes dominant capture of decalyl cations by nucleophiles to afford products having cis ring fusions.[7-9]

Addition of hydrogen chloride to **1** in chloroform at 25° afforded prisms, mp 96.0–96.5°, $[\alpha]D$ +3°, as the only crystallizable product. These constants correspond well to those reported and the physical appearance of the crystals matched those of a diagram of Mauthner's hydrochloride.[5]

Since the chemical shift of the 19-methyl group in steroids is sensitive to the presence of substituents elsewhere in the molecule and the stereochemistry of the A/B ring junction,[10] an attempt was made to deduce the structure of the product from its NMR spectrum. A singlet 1.04 ppm downfield from internal tetramethylsilane was readily assignable to the 19-methyl group. The chemical shift of 0.26 ppm to lower field relative to 5α-cholestane is in good agreement with the 0.21–0.27-ppm shift predicted from the Zurcher rules. In spite of the observed correspondence, the 5β-chloro stereochemistry could not be rigorously excluded because of the lack of data available with which to make a prediction for this substitution pattern. The observed signal is 0.12 ppm downfield from the 19-methyl signal of 5β-cholestane and a shift of this magnitude appears not unreasonable. It is relevant to note that the chemical shifts of the methyl groups of *cis*- and *trans*-9-chloro-10-methyldecalin are identical within experimental error (1.11 ppm).[11]

With only one isomer in hand, recourse was made to an unambiguous determination of structure by X-ray crystallographic methods. The structure was solved by standard Patterson heavy atom techniques, and refined by block-diagonal least-squares calculations. The coordinates of all hydrogen atoms were found in a Fourier difference map. The final conventional R factor was 4.6%, weighted R was 3.4%.

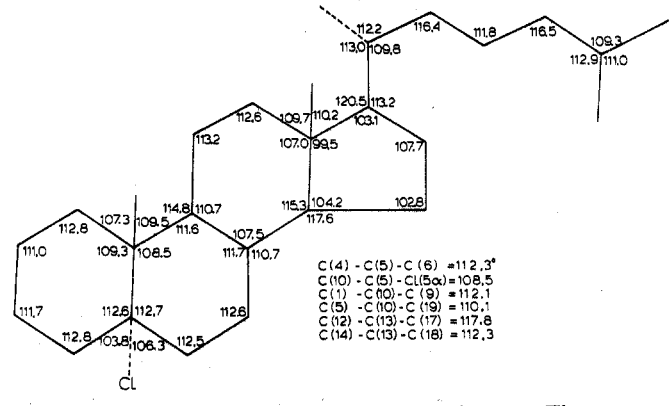


Figure 3. Valence angles of 5α-chlorocholestane. The average standard deviation in a valence angle is 0.6°.

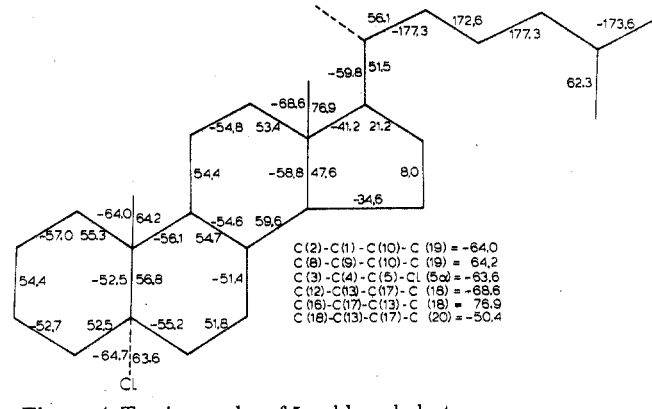


Figure 4. Torsion angles of 5α-chlorocholestane.

Final positional and thermal parameters are listed in Tables I and II (supplementary material). Figure 1 shows an ORTEP drawing (50% probability thermal ellipsoids) of the steroid skeleton. Figures 2, 3, and 4 depict the bond distances, angles, and torsion angles, respectively, of the steroid skeleton. *The chlorine is clearly in the α position on C(5).* Figures 5 and 6 show the packing in the 100 and 001 projections, respectively (supplementary material). The side chains pack over one another and the steroid skeletons pack over one another with normal van der Waals contacts.

Experimental Section

NMR spectra were recorded on a Jeol PS-FT spectrometer at 100 MHz in $CDCl_3$ and chemical shifts are reported in parts per million from internal tetramethylsilane. Melting points are corrected and were determined on a Thomas-Hoover apparatus.

Hydrochlorination of 5-Cholestene. Hydrogen chloride was passed through a solution of 1.02 g (2.77 mmol) of 5-cholestene in chloroform for 2 hr. The solution was allowed to stand at 25° for 2 days, the solvent was evaporated, and the resulting product was taken up in ether dried over magnesium sulfate. The ether was evaporated and the residue was then dissolved in the minimum quantity of anhydrous ether and allowed to stand at 25°. After 2 days the crystalline product (139 mg, 12%) was collected: mp 96–96.5°; $[\alpha]D$ +3° (chloroform); NMR ($CDCl_3$) 0.65 (s, 3, C-18 methyl), 0.86 (d, 6, J = 6 Hz, C-25 methyls), 0.90 (d, 3, J = 6 Hz, C-20 methyl), 1.04 (s, 3, C-19 methyl), and 1.0–2.1 ppm (m).

Crystal Data. $C_{27}H_{47}Cl$, mol wt 407.1, a = 14.444 (3) Å, b = 19.264 (6) Å, c = 8.976 (2) Å; space group, $P2_12_12_1$, orthorhombic, Z = 4, V = 2495.5 Å^3.

Crystallographic Measurements. The unit cell parameters were determined by a least-squares refinement of 20 values of 15 well-centered reflections with 30° < 2θ < 50°. An initial set of three-dimensional data (2444 reflections, 1056 observed) was collected with a GE-XRD-5 diffractometer. The data did not refine well, so another set of data was collected with an Enraf-Nonius CAD-4 automated diffractometer using Mo Kα (λ 0.71069 Å) ra-

diation with a graphite monochromator (4104 reflections, 1533 observed). Only the latter data set was used in the refinement reported here.

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Registry No.—**1**, 570-74-1; **2**, 56114-17-1; hydrogen chloride, 7647-01-0.

Supplementary Material Available. Tables of coordinates, thermal parameters, structure factors, and packing diagrams (Figures 5 and 6) will appear following these pages in the microfilm edition of the volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Business Office, Books and Journals Division, American Chemical Society, 1155 16th Street, N.W., Washington, D.C. 20036. Remit check or money order for $4.50 for photocopy or $2.50 for microfiche, referring to code number JOC-75-2956.

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Isolation and Structure of 1-Hydroxy-7-methoxy-4-isopropyl-1,6-dimethyl-2(1*H*)-naphthalenone from Cotton

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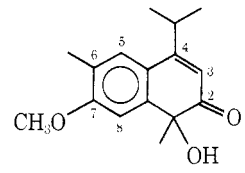
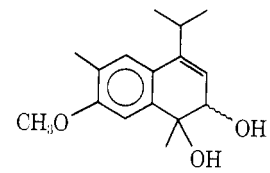
Previous work from this laboratory has been concerned with attempts to identify the components in the cotton plant *Gossypium hirsutum* which are implicated in producing the clinical symptoms of the disease byssinosis.[1] In this earlier study we reported preliminary characterization of a column chromatographic fraction from cotton dust or cotton bracts which exhibited chemotactic activity with human polymorphonucleur cells. Purification of this fraction by preparative layer chromatography afforded 70 μg of a compound exhibiting a strong yellow-green fluorescence under 254-nm ultraviolet light which was tentatively assigned a molecular weight of 260 from mass spectral examination.

Reisolation of 20 mg of this compound has now permitted its characterization as 1-hydroxy-7-methoxy-4-isopropyl-1,6-dimethyl-2(1*H*)-naphthalenone (**1**).



1



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The initial isolation studies of the fluorescent component were directed toward examination of the volatile fraction on the basis that steam treatment of cotton is reported to reduce or destroy the byssinosis factor when measured by the response of susceptible workers.[2] The yields of the fluorescent fraction obtained by this procedure were extremely low (~10 μg/kg) and alternative sources and methods of isolation were examined. Using the fluorescence properties as a guide to the presence of active material, it was found that aged cotton bracts contained more than fresh bracts and that fresh leaves and stems contained only insignificant amounts of this material.

Extensive purification of an aqueous acetone extract of aged cotton bracts by column chromatography afforded a crude fraction containing the yellow-green fluorescent component. Preparative layer chromatography of this fraction on silica gel in chloroform–5% methanol gave a pure compound, mp 100–102°, which proved identical in its chromatographic and mass spectral characteristics with that previously obtained.

An exact mass measurement of the molecular ion, *m/e* 260, from the electron impact (EI) spectrum established the molecular formula as $C_{16}H_{20}O_3$. Verification that the ion *m/e* 260 was indeed the molecular ion was obtained from the chemical ionization (CI) spectrum, which showed a quasimolecular ion at *m/e* 261 (100).

The CI spectrum was remarkably simple in that in addition to the QM^+ ion the only ions of significant intensity appear at $(QM^+ + 1)$, $(QM^+ - OH)$, and $(QM^+ - H_2O)$ and account for 90% of the total ion current. In contrast, the high-resolution EI spectrum contained many ions of which those corresponding to $M^+ - CH_3$ at *m/e* 245 and $M^+ - CO$ at *m/e* 232 were present. The loss of CH_3 from the *m/e* 232 ion to a fragment ion of *m/e* 217, when taken in conjunction with the appearance of an ion at *m/e* 202, suggested the presence of two methyl groups and a ketone. In addition, the base peak at *m/e* 189 ($C_{12}H_{13}O_2$) and an ion at *m/e* 175 ($C_{11}H_{11}O_2$) were the only other ions of any significance at high mass. The occurrence of absorption bands at 1670 and 3490 cm^{-1} in the ir spectrum of **1** confirmed the presence of an unsaturated carbonyl and hydroxyl functions, respectively.[3] The invariance of the OH band at 3490 cm^{-1} with increasing dilution in CCl_4 solution demonstrated that the OH group was intramolecularly hydrogen bonded and the frequency of the absorption was consistent with that expected for an α-hydroxy ketone.[4]

In agreement with the fluorescence properties of **1**, the uv spectrum in cyclohexane showed evidence for extended conjugation with bands at 222 nm (ε 9100), 227 (10,400), 252 (10,800), 258 (11,300), 335 (4730), and 365 (2730). An indication that the latter was consistent with a β-aryl-α,β-unsaturated ketone chromophore was supported by a comparison of its spectrum in ethanol, which was much less detailed than in cyclohexane, with the uv of other 2(1*H*)-naphthalenones[5] and by the marked change in the uv spec-