treated with 0.105 ml of a 7.5 *N* HCl solution in dimethoxyethane (0.79 mmol) and 0.043 ml (0.375 mmol) of *tert*-butyl nitrite. The mixture was stirred at −15° for 20 min, then cooled to −30° and treated with 0.11 ml (0.79 mmol) of triethylamine.

A cooled solution of 167 mg (0.35 mmol) of H-Cys(Trt)-Asn-OH in 3 ml of DMF was added to this azide solution. The pH was adjusted to 7 with 10% Et_3N–DMF, and the solution was left for 3 days at 4°. The mixture was then diluted with 200 ml of 1-butanol–methanol–water (1:1:1) and added to an AG1-X2 column (1.6 × 22 cm). The column was eluted with 1-butanol–methanol–dilute acetic acid (1:1:1) mixtures in which the concentration of the acetic acid used was gradually raised: 0% (100 ml), 0.3% (300 ml), 1% (100 ml), 3% (200 ml), 15% (400 ml). Absorbancy measurements (254 nm) and tlc revealed that the excess of dipeptide was eluted with the 0.3% acetic acid mixture, while the desired product was located in the 15% acetic acid eluate.

Fractions containing the product were collected and evaporated. The residue was dissolved in 5 ml of DMF and precipitated with methanol–water, yielding 242 mg (58%) of XX, mp 253° dec, $[\alpha]^{23}D$ −20.2° (*c* 1, DMF), homogeneous (systems B and F).

Anal. Calcd for $C_{68}H_{83}N_{11}O_{20}S_2 \cdot H_2O$: C, 56.07; H, 5.88; N, 10.58. Found: C, 55.9; H, 5.8; N, 10.5.

Amino acid ratios in acid hydrolysate (in the presence of phenol): Asp, 1.9; Glu, 2.0; Leu, 1.1; Tyr, 1.95.

L-Tyrosyl-L-glutaminyl-L-leucyl-L-glutamyl-L-asparaginyl-L-tyrosyl-*S*-trityl-L-cysteinylasparagine (XXI). A suspension of 105 mg (0.073 mmol) of XX in water was treated with 0.35 ml (0.14 mmol) of 4 *N* NaOH. After 4 min the clear solution was acidified with a few drops of 2 *N* $KHSO_4$ solution and water was added. The precipitate was filtered, washed with water, and dried, yielding 85 mg (90.5%) of XXI, mp ~300° dec, $[\alpha]^{23}D$ −15.0° (*c* 1, DMF), homogeneous (system B).

Anal. Calcd for $C_{64}H_{77}N_{11}O_{16}S \cdot 2H_2O$: C, 58.04; H, 6.16; N, 11.63. Found: C, 57.9; H, 5.9; N, 11.5.

Amino acid analysis in acid hydrolysate, oxidized with performic acid: Asp, 2.0; Cys(SO_3H), 1.0; Glu, 1.9; Leu, 1.0; Tyr, 1.5.

Registry No.—XIX, 52278-85-0; XX, 52278-86-1; XXI, 52278-87-2; methylsulfonylethyl phthalimidocarbonate, 52278-88-3; 2-methylmercaptoethanol 5271-38-5; *N*-methylsulfonylethyloxycarbonyl-*O*-*tert*-butyltyrosine, 52278-89-4; *p*-nitrophenyl chloroformate, 7693-46-1; *N*-2-(*p*-biphenylyl)isopropyloxycarbonyl-*O*-*tert*-butyl-L-tyrosyl-L-glutamine, 52278-90-7; Bpoc-Tyr(*t*-Bu)-ONSu, 33527-03-6; *N*-*tert*-butyloxycarbonyl-*S*-trityl-L-cysteinyl-L-asparagine, 52278-91-8; *S*-trityl-L-cysteinyl-L-asparagine, 52278-92-9.

References and Notes

(1) The following abbreviations have been employed in the text: DCC = *N,N*-dicyclohexylcarbodiimide; HOBt = *N*-hydroxybenzotriazole; TFA = trifluoroacetic acid; THF = tetrahydrofuran; DCHA = dicyclohexylamine; TOSOH = *p*-toluenesulfonic acid; DIEA = *N*-ethyldiisopropylamine; Im = imidazole; DMF = *N,N*-dimethylformamide; DMSO = dimethyl sulfoxide; BOC = *tert*-butyloxycarbonyl; Bzh = benzhydryl; *t*-Bu = *tert*-butyl; Bpoc = 2-(*p*-biphenylyl)isopropyloxycarbonyl; Trt = triphenylmethyl; Tmb = 2,4,6-trimethylbenzyl; Bmv = 2-benzoyl-1-methylvinyl; Msc = 2-(methylsulfonyl)ethyloxycarbonyl; Pht = phthalimido; NSu = succinimido.

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(16) Incorporation of Bmv amino acids (*Y*) can be measured in a similar way by suspending a sample in 25 ml of 0.4 *N* HCl (aqueous)–THF, and measuring the optical density at 307 nm after 30 min. From the molar extinction of benzoylacetone it can be derived that $Y = 1.67\ d/x$ (milliequivalents of Bmv residues per gram of substituted resin).

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Isolation and Structure Determination of One of the Toxic Constituents from *Tetradymia glabrata*

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Tetradymol (I) isolated from *Tetradymia glabrata*, has been shown to be 4β,5β-dimethyl-10β-hydroxyfuranoermophilane. The combined results and relationships of chemical, nmr, and X-ray analyses of I are discussed. The mercuric chloride derivative of tetradymol crystallized in a space group $P2_12_12_1$ with cell dimensions $a = 7.371$ (5) Å, $b = 10.304$ (9) Å, $c = 19.759$ (17) Å with $Z = 4$. Counter data were refined by full-matrix least-squares to a residual of 5.4%. Tetradymol has been shown to effect hepatodysfunction and has an LD_{50} (mice) of 250 mg/kg.

Investigations reported in the literature on the components of *Tetradymia glabrata* are both long-standing and limited. The presented paper deals with the isolation of one of its toxic components, tetradymol (I),[2] and proof of its stereochemical structure.

Because of the work of Fleming,[3] Clawson and Huffman[4] prior to 1937, this plant was known to contain toxic components fatal to sheep and was further suspected to contain a component causing the maladay "bighead" in the same animal. These investigators suspected that at least two toxic compounds were present, one apparently effecting heptodysfunction, and the other effecting cardiac failure. We have not been successful in repeating the conditions necessary for the development of the "bighead" symptom,[5] and have found that the plant extract fraction reportedly containing the cardiac toxin actually contains another hepatotoxin which will be reported later. Tetradymol (I) has been shown to be a moderate hepatotoxin in several animals including sheep, mice, rats, rabbits, guinea pigs, and gerbils [oral LD_{50} (mice) is 250 mg/kg].

Results and Discussion

Isolation of Tetradymol. During the isolation procedure (Figure 1) we concluded that the toxin was located near the surface of the plant as we obtained similar amounts of I from either ground or unground plant. To

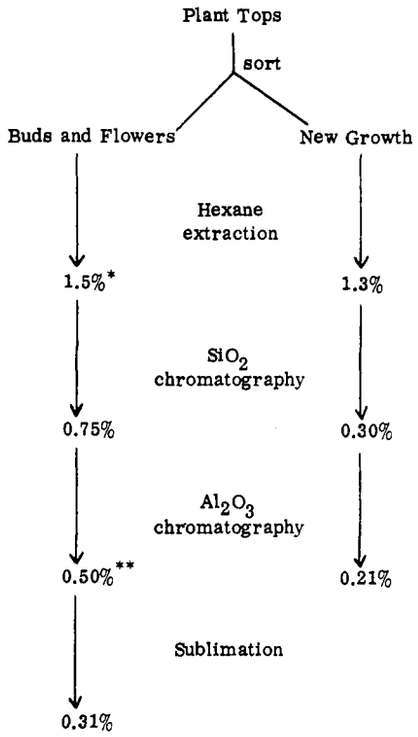


Figure 1. * Percentages based on isolated material at each step relative to the whole green plant material. ** A base extract was needed at this point for correct analyses.

monitor the isolation procedure, mice were used as the assay.[6]

Tetradymol was obtained from the extract of new growth stems and flower buds as colorless crystals, $C_{15}H_{22}O_2$, mp 92–92.5°, $[\alpha]^{25}D$ + 56°. From its uv [λ_{max} (MeOH) 222 nm (log ϵ 3.83)] and from its positive Ehrlich's color test, tetradymol (I) was assumed to contain a furan ring.

Presence of the furan ring was further confirmed by spectra and chemical data. The nmr spectrum of I (Figure 2) shows a single furan proton resonance at 7.00[7] which is coupled to a three-proton resonance (doublet J = 1.1 Hz) at 1.9 which was assigned to a furan methyl group. Such assignments are consistent with the following methyl furano compounds.

Compd	Furan methyl	Furan proton	J, Hz
Euryopsol[8]	7.12	2.04	1
Petasalbiene[9]	7.05	2.03	1.1
Menthofuran[10]	6.84	1.85	1.0

Tetradymol readily reacted with buffered mercury(II) chloride to form the 2-chloromercury derivative, mp 205–205.5°. Treatment of this derivative with H_2S regenerated tetradymol.

Hydrogenation Studies. Inspection of the formula for I ($C_{15}H_{22}O_2$) revealed that any structure proposed should incorporate five unsaturations and two oxygens. The furan ring described three unsaturations, and, from ir evidence, the second oxygen was assigned to a hydroxyl group (3400 cm^{-1}). The two remaining unsaturations were sorted out by catalytic hydrogenation (*vide infra*).

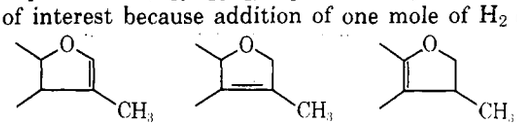
Catalytic hydrogenation of I resulted in several products, the relative concentrations of which were contingent upon the catalytic conditions (Table I). Products having incorporated 1, 2, and 3 mol of hydrogen were found (Figure 3). Structure IV is in fact a mixture of at least six components all having parent ions in the mass spectrum of 222, consistent with loss of H_2O and the addition of 3 mol of hydrogen. Ir spectra confirmed the loss of H_2O. New nmr resonances occurred in the fully hydrogenated products at 3.5 and 4.5 accounting for three protons adjacent to the ether linkage of the newly formed tetrahydrofuran moiety. Concluding that 3 mol of H_2 saturated the system of I, further characterization of constituents was terminated.

Table I

Product[a]	Catalyst: Rh on alumina in MeOH	Catalyst: Pd on charcoal in EtOH
IV	6	18
IIA	22	52
IIB	52	18
III	19	12

[a] Yields were based on isolated products.

Compound III ($C_{15}H_{24}O_2$, mp 145–146°, M^+ 236 m/e) was of interest because addition of one mole of H_2 could

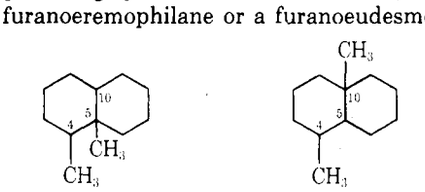


IIIa IIIb IIIc

yield three different structures, IIIa–c. The nmr spectrum of III showed three new proton resonances in the 4.7–5.5 region which is consistent with IIIb in which these protons are allylic to an olefin and adjacent to an ether oxygen. Further, the furan methyl did not move into the saturated methyl region which excluded structure IIIc. Structure IIIa was also eliminated as a possibility by the nmr spectrum since there is no single olefinic proton resonance, coupled to the furan methyl. An interesting fact is that further hydrogenation of IIIb yields only one of the tetrahydro compounds, IIB.

The two major products, IIA and IIB, analyzed correctly for $C_{15}H_{26}O_2$ with m/e 238. Ir data indicated that the hydroxyl group (3400 cm^{-1}) was still intact. In the nmr spectra, both IIA (mp 75–77°) and IIB (mp 104–105°) showed the loss of furan proton resonance and new resonances at 3.0–4.1, consistent with protons adjacent to an ether function. Other than the possibility that these two compounds are two of six possible tetrahydrotetradymol isomers, further speculation on their stereochemical structure shall be deferred until additional data are obtained. The conclusion reached from these hydrogenation data is that 2 mol of H_2 saturated I, indicating that the furan ring accounted for all the olefins.

Proof of Ring System and Hydroxyl Position. Several sesquiterpene ring systems can be envisioned, but usually either a furanoeremophilane or a furanoeudesmone skeleton can be postulated. To distinguish between these two choices, additional interpretation of the nmr spectrum of I was necessary. The tentative assignments from Figure 2 are given in Table II and discussed below.



eremophilane A eudesmane B

Hydroxyl groups are usually found at positions 1,[12] 3,[13] and 6.[8,11] Euryopsol[8] is the only compound exhibiting this group at C-10. Based upon the fact that I would not esterify under a variety of conditions, that I eliminated H_2O under hydrogenation, and that the nmr spectrum of I

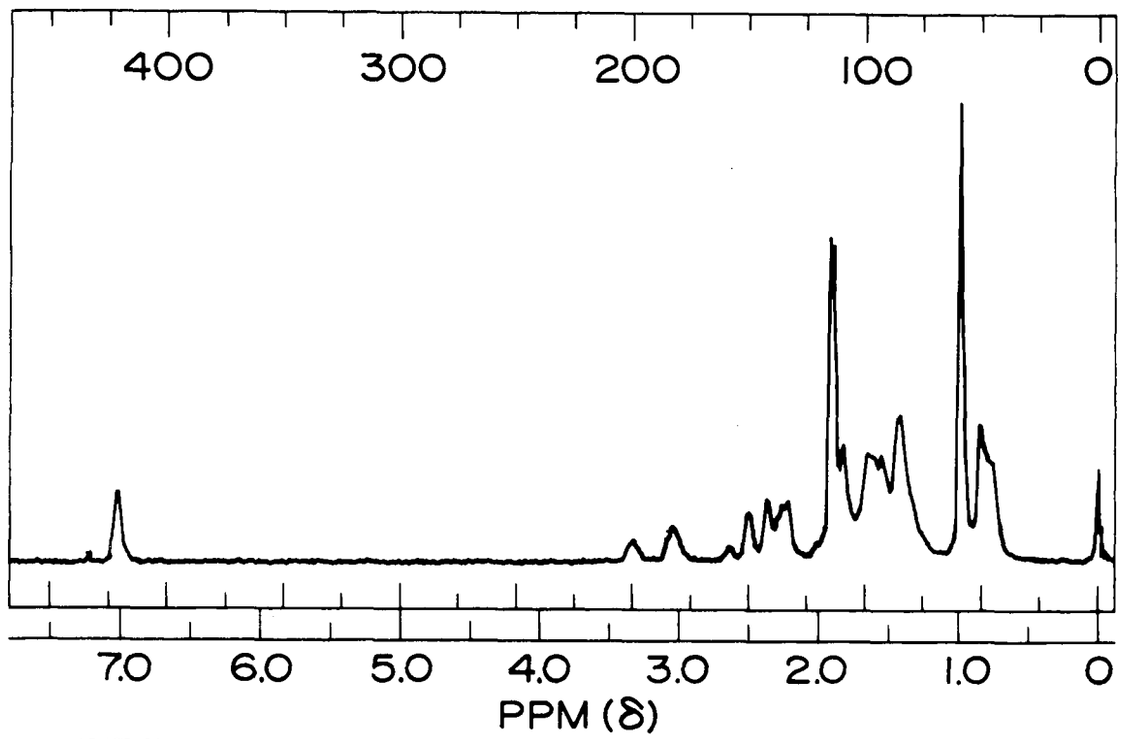


Figure 2. Nmr of I ($CDCl_3$).

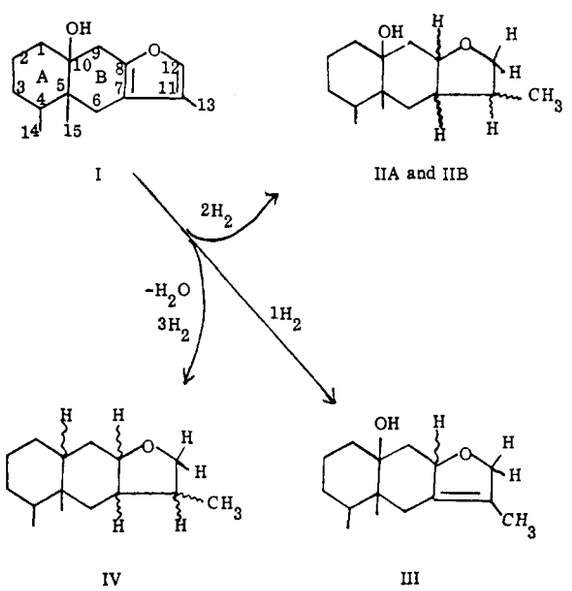
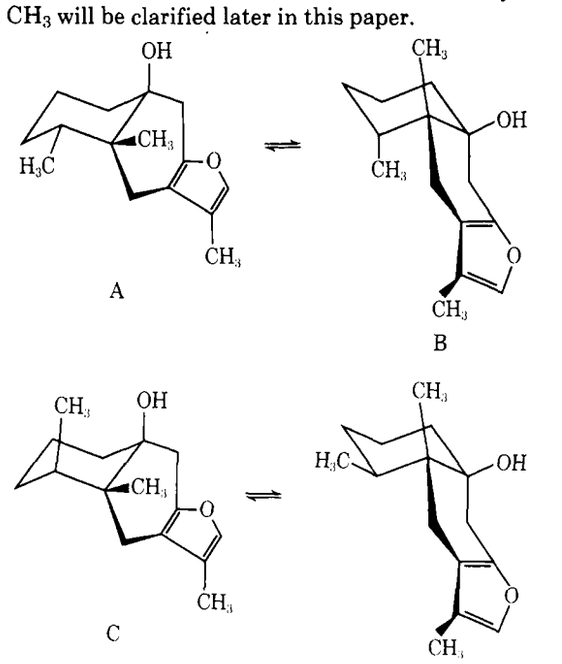


Figure 3.

showed no peaks assignable to a proton on a carbon bearing a hydroxyl, we concluded that the OH group was at a tertiary position and most likely at C-10 in A or at C-5 in B. The only other tertiary position would have been at C-4, but the methyl already assigned to that position would have been seen as a singlet rather than a doublet in the nmr spectrum.

It was extremely fortuitous to have the OH in such unique positions as it was properly disposed to yield a great deal of structural evidence when coupled with solvent-induced chemical shifts[14] from nmr spectroscopy: $\Delta_{C_5H_5N}$ ($CDCl_3$) −0.18 ppm for the tertiary methyl of tetradymol, −0.22 ppm for the tertiary methyl of the 2-chloromercury derivative, −0.03 ppm for the secondary methyl of tetradymol. As a result of these data, tetradymol was assumed to have the eremophilane skeleton with the hydroxyl at position 10. Further the dihedral angle between the 10-OH and the tertiary methyl was estimated to be 60°. Additional data on the position of the C-4 secondary methyl and the confirmation of the cyclohexane ring was obtained from the mass spectrum.

If the C-4, or secondary CH_3 is cis and axial to the hydroxyl at C-10, a six-membered-ring transition state can be envisioned for the facile loss of H_2O during mass spectral analysis. In fact, the parent ion is 23% of the base peak which suggests that a route for facile loss of H_2O is not present. Of the four possibilities shown below only C could be eliminated from these data. The stereochemistry of the C-4 CH_3 will be clarified later in this paper.



Proof of the Furan Position. Except for the C-4 methyl group stereochemistry, the remaining step in the structure proof was the proper placement of the furano ring on the perhydronaphthalene skeleton. Two general models were

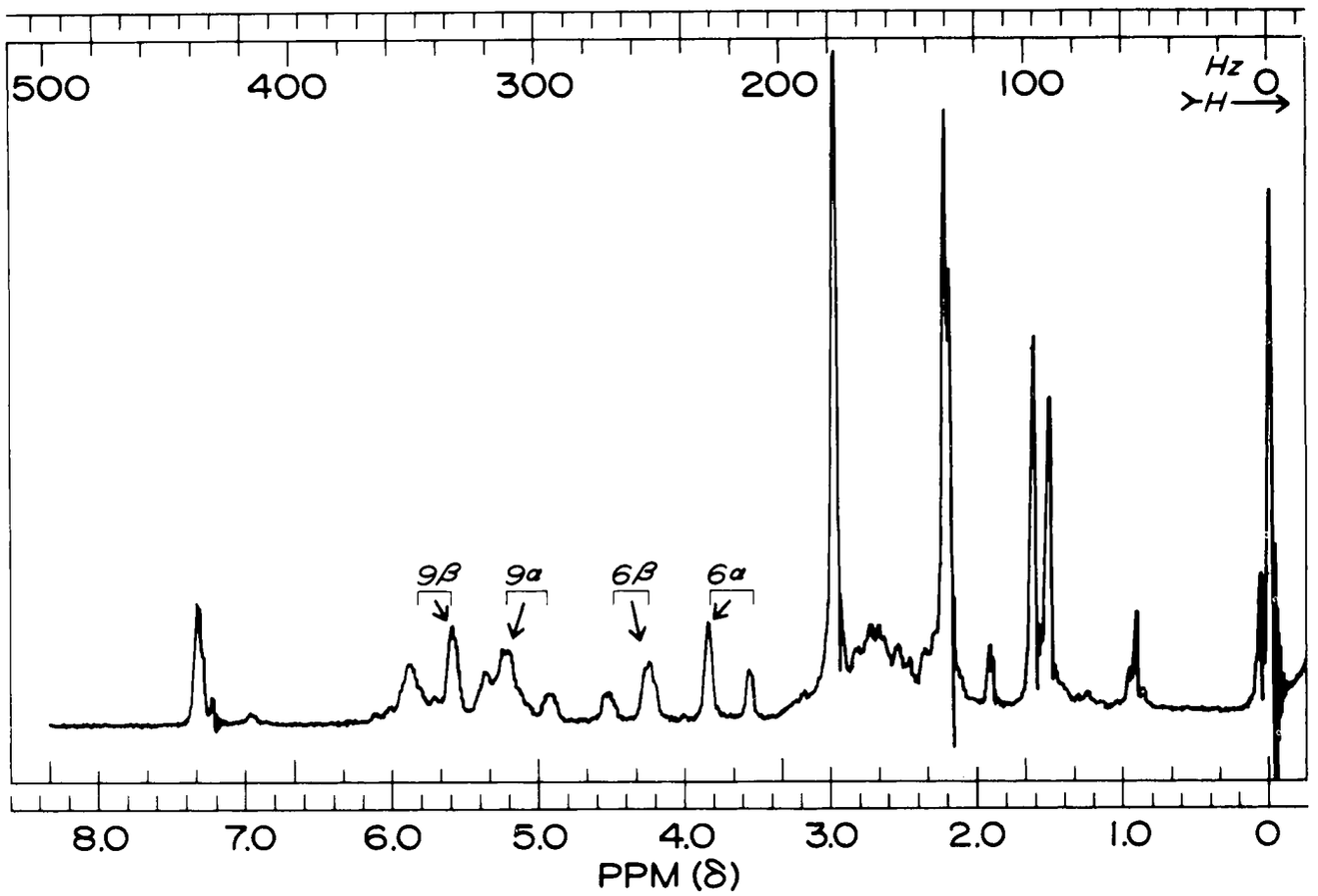
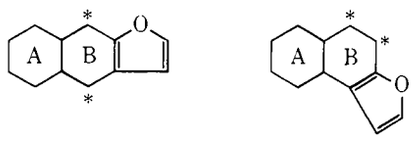


Figure 4. Tetradymol with 60 mg of $Eu(THD)_3$.

Table II

Proton	Shift (J in Hz)
4-Me	0.80 (7), "filled-in" doublet, secondary
5-Me	0.95, tertiary
1,2,3-CH_2	1.1–1.75
10-OH	1.81
13-Me	1.88 (1.1)
6,9-CH_2	2.1–3.5
12-H	7.04 (1.1)

postulated: anthranoid and phenanthranoid. These two skeletons could be easily distinguished if resonance peaks



anthranoid phenanthranoid

for the methylenes (starred) in ring B were properly sorted out in the nmr spectrum. These protons were previously assigned (Table II) to the area of 2.1–3.5 ppm in Figure 2. To sort out these peaks, their resolution was improved by using a paramagnetic shift reagent (Figure 4). $Eu(thd)_3$ was chosen rather than $Eu(fod)_3$ as the latter is known to be a stronger acid and hence might complex with both the hydroxy and the furan oxygens.[15] As will be shown, $Eu(thd)_3$ complexes solely with the hydroxyl oxygen.

Following the movement of the methylene resonances through the spectral series of increasing concentrations of shift reagent, one observes finally, in Figure 4, a clear indication of two AB or AX quartets. Decoupling experiments revealed that each quartet was independent of the other indicating that the two methylene groups were not cross-coupled as would be the case in the phenantroid skeleton. Thus it was concluded that tetradymol should be assigned the anthranoid skeleton. The AB or AX quartet arises from the fact that the β protons are in different environments than the α protons, probably owing to inflexibility of the ring system. We have tentatively[16] assigned the narrower quartet with peaks at 2.63, 2.35, 2.30, and 2.02 (J = 16.5 Hz) to the 6α and β protons. Graphical presentation of how a few of the protons of I shift *vs.* shift reagent and substrate concentrations is shown in Figure 5. Since the furan methyl and proton resonances shift only slightly and did not show any upward curvature at high concentrations of $Eu(thd)_3$, we have concluded that the reagent complexes exclusively with the hydroxyl oxygen.

Table III

Position	Portion of quartet	$\Delta_{C_5H_5N(CDCl_3)}$
9α	Downfield	−0.05
9β	Upfield	−0.25
6α	Downfield	−0.09
6β	Upfield	−0.20

One additional feature of interest in the europium work deals with the fact that the upper half of each methylene quartet shifts downfield faster than the lower half (Figure 5). This suggests that the upper portion of each quartet can be assigned predominantly to a β proton cis to the hydroxyl group. This is further corroborated by the solvent induced chemical shift data shown in Table III.

Except for the stereochemistry of the C-4 methyl group,

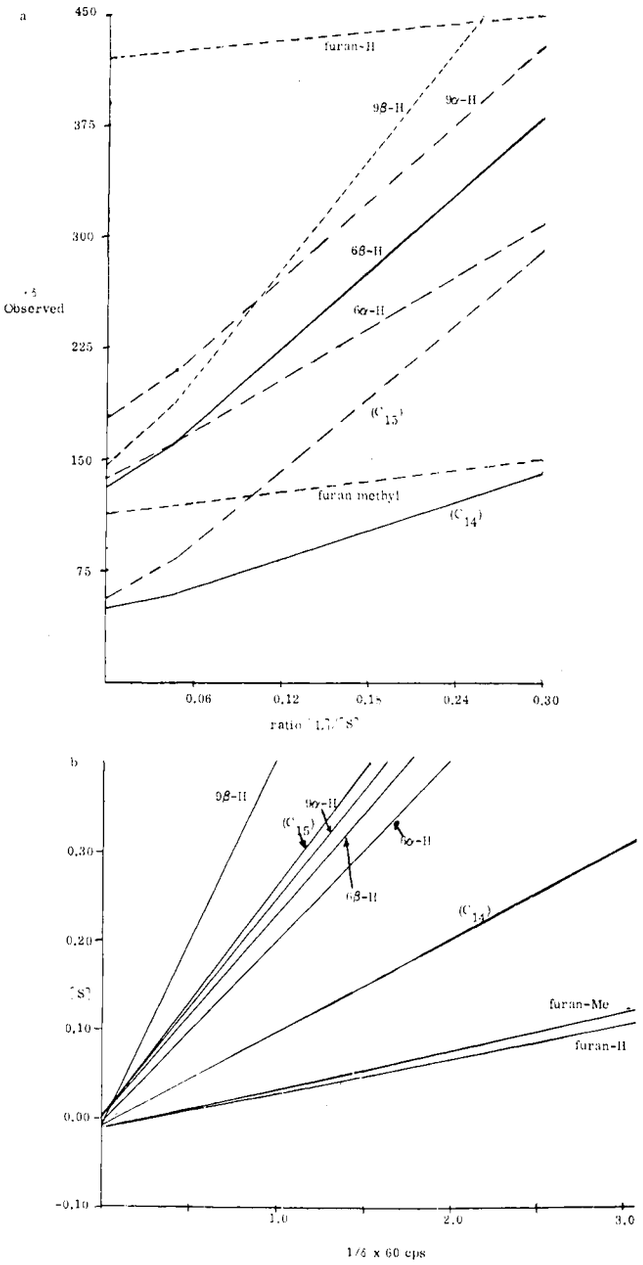


Figure 5.

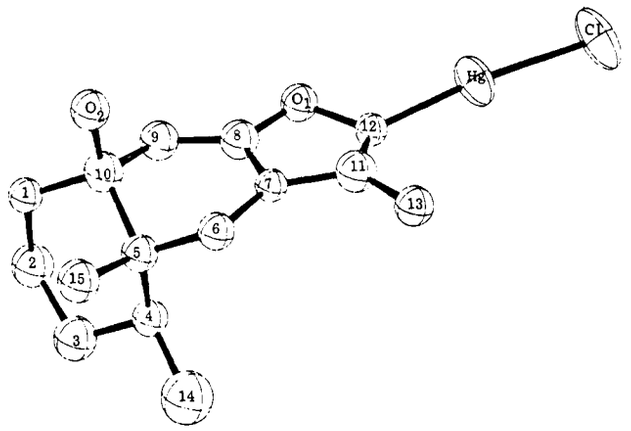


Figure 6. ORTEP drawing of tetradymol · HgCl.

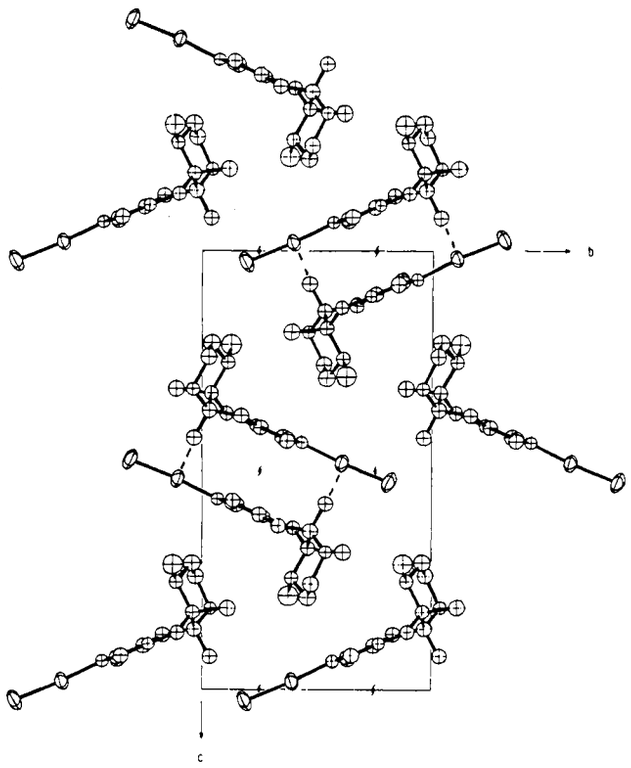


Figure 7.

the structure of tetradymol was complete. Because we could not sort this difficulty out and because there had never been an unambiguous structure proof for the furanoeremophilane system, a single-crystal X-ray analysis was performed on the 2-chloromercury derivative. The previous spectral and chemical evidence might ordinarily be regarded as penultimate to a X-ray study, but it is felt that the corroboration and correlation of these techniques may help other structural problems in this area if a single crystal X-ray facility is not available.

Discussion of X-Ray Analysis. Results of the single crystal X-ray study on the 2-chloromercury derivative of tetradymol (I) are depicted in an ORTEP drawing (Figure 6). The C(4) methyl group is equatorial in ring A and is in fact cis to both the C(5) methyl and the C(10) hydroxyl groups. Also the dihedral angle between the C(10) hydroxyl and the C(5) methyl is 57.3° which is very close to that predicted by the solvent-induced shift work. Similarity between the crystal structure and the solution structure is thus evident and would be consistent with the mass spectral data cited earlier.

Table IV

equation of plane[a] 0.0016X − 0.36276Y + 0.93188Z − 6.453 = 0

Atom	Distance to plane
Hg	0.16
Cl	0.20
C(13)	0.14
C(6)	−0.03
C(9)	−0.18

[a] The orthogonal coordinate system from which this plane is derived is defined by X along *a*, Y along *b*, and Z along *c*. The sum of the squares of the deviations of the atom from the least-squares plane is 0.005 Å².

The furan ring is nearly planar, the average deviation of the five atoms in the ring being 0.03 Å. Carbon 12 has the largest deviation of −0.05 Å. Table IV shows the distances of other atoms to the least-squares plane of the furan ring which substantiates the assumption that C(6) and C(9) are

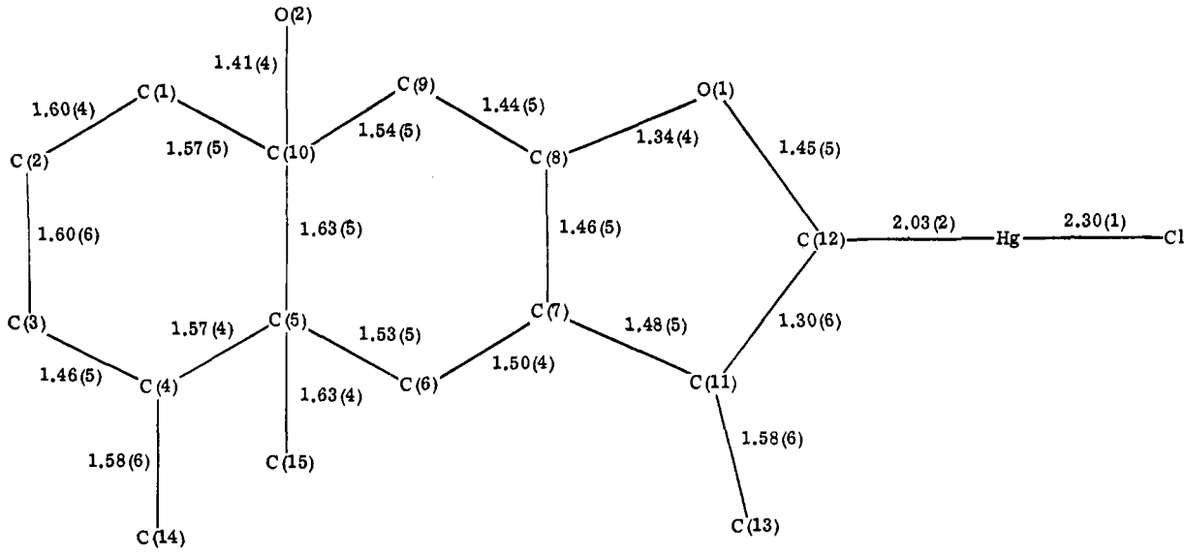


Figure 8. Bond distances.

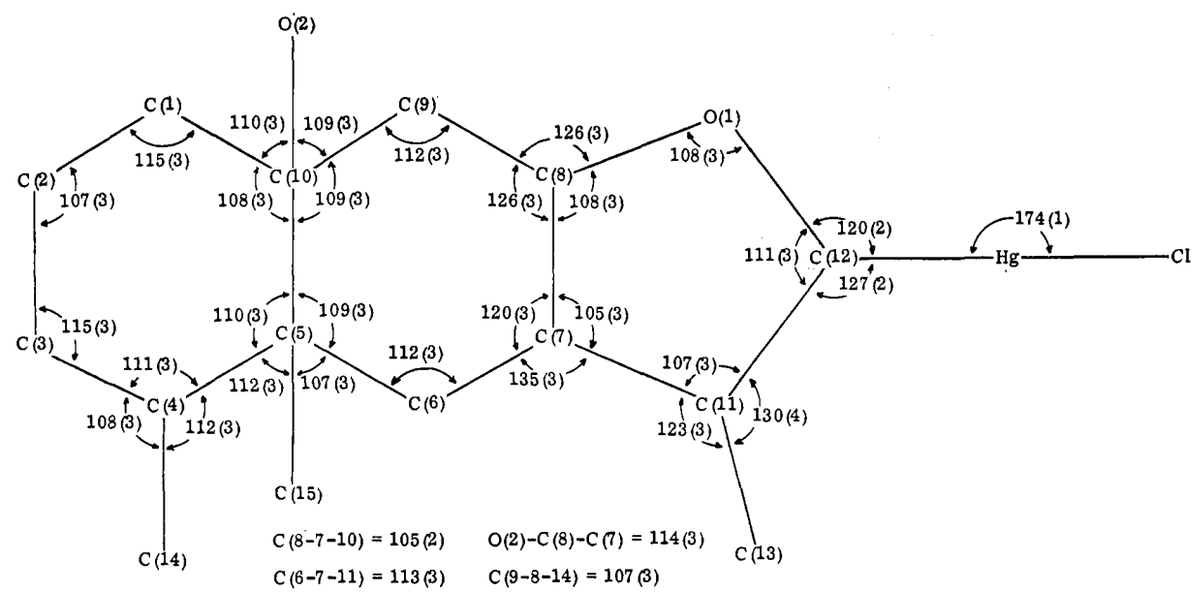


Figure 9. Bond angles.

fixed and flat resulting in the AB or AX quartet for the hydrogens.

It appears from the arrangement of the molecules within the crystal (Figure 7) that a hydrogen bond exists between the hydroxyl group, O(2), and the mercury atom, since the distance of 2.80 Å is 0.1 Å shorter than the sum of the van der Waals radii of mercury and oxygen. In fact, pairs of symmetry related molecules are hydrogen bonded by two such intermolecular interactions as shown by dotted lines in the figure. The next closest intermolecular distance was found to be 3.34 Å, between O(2) and C(13).

The bond distances and angles (Figures 8 and 9) of the light atoms differ somewhat from accepted values, but these differences are probably due primarily to small, systematic errors in the data caused by decomposition of the crystal in the X-ray beam, absorption, and the unusually large contribution of the heavy atom. The mercury–carbon and mercury–chlorine bond distances agree well with the published values.

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Registry No.—I, 52279-13-7; I HgCl, 52279-14-8; II, 52279-15-9; III, 52279-16-0; IV, 52340-24-6.

Supplementary Material Available. The Experimental Section and a listing of calculated and observed structure factors in electrons and a table of positional and thermal parameters will appear following these pages in the microfilm edition of this 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 Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $4.00 for photocopy or $2.00 for microfiche, referring to code number JOC-74-3392.

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(1) Abstracted in part from the Ph.D. Theses of S.K.R., 1971, Montana State University, and J.C.H., 1972, Montana State University.
(2) 4β,5β-Dimethyl-10β-hydroxyfuranoeremophilane.
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(5) There appears to be a certain sequence of events including *Tetradymia*, time, water, and possibly another plant which leads to the bighead syndrome.
(6) There may be some danger in characterizing a sheep toxin with mice, but symptoms and morphological slides were identical.
(7) When expanded this resonance is a quartet with J = 1.1 Hz. All nmr values are in δ (parts per million).
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(16) Since these quartets, especially the narrower one, are AB quartets, each doublet is not strictly one proton.

Sterol Metabolism. XXXII. Radiation-Induced Oxidation of Isomeric Cholesten-3β-ols[1]

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The air oxidation induced by ^{60}Co γ radiation of cholest-4-en-3β-ol, 5α-cholest-6-en-3β-ol, and 5α-cholest-7-en-3β-ol yielded allylic hydroperoxides and other oxidized derivatives. The Δ^4-sterol gave cholest-4-en-3-one, 6β-hydroperoxycholest-4-en-3-one, 3β-hydroxycholest-4-ene 6α-hydroperoxide, and cholest-4-ene-3β,6α-diol. The Δ^6-sterol gave cholesterol 7α- and 7β-hydroperoxides, the epimeric cholest-5-ene-3β,7-diols, 3β-hydroxycholest-5-en-7-one, and 5α-cholest-6-ene-3β,5-diol but no 3β-hydroxy-5α-cholest-6-ene 5-hydroperoxide. The Δ^7-sterol gave the epimeric 3β-hydroxy-5α-cholest-7-ene 6-hydroperoxides, the epimeric 5α-cholest-7-ene-3β,6-diols, 3β-hydroxy-5α-cholest-7-en-6-one, and cholesta-5,7-dien-3β-ol. Pyrolysis of either Δ^7-6-hydroperoxide gave the corresponding 5α-cholest-7-ene-3β,6-diol, 3β-hydroxy-5α-cholest-7-en-6-one, and cholesta-5,7-dien-3β-ol. Reaction pathways for oxidations by radiation-induced processes of the isomeric Δ^4-, Δ^5-, Δ^6-, and Δ^7-sterols and for their photosensitized oxidations in which singlet molecular oxygen is implicated were compared.

We have recently demonstrated that radiation-induced oxidation of the Δ^5-sterol cholesterol (**1a**) by air afforded the epimeric 7-hydroperoxides **1b** and **1c**,[3] with the quasi-equatorial[4] 7β-hydroperoxide **1c** predominating. In contrast oxidation of cholesterol by excited-stage (singlet) molecular oxygen yielded the 5α-hydroperoxide **3b** as major product, with small amounts of the epimeric 3β-hydroxycholest-4-ene 6-hydroperoxides **2b** and **2c** but with neither 7-hydroperoxide **1b** nor **1c** formed.[5] This distinction in major products formed provides a means of differentiation between participation of ground-state or of singlet molecular oxygen in chemical and enzymic[6] reactions.

Although the mechanism of attack of singlet molecular oxygen on steroid olefins has been extensively studied, free-radical oxidations by ground-state molecular oxygen have not received systematic attention. In order to determine whether additional distinctions between free-radical and singlet molecular oxygen oxidations of sterol olefins existed, as well as to provide additional substrates for use as probes in reactions in which cholesterol was unsuited, we examined the oxidation of cholest-4-en-3β-ol (**2a**), 5α-cholest-6-en-3β-ol (**3a**), and 5α-cholest-7-en-3β-ol (**4a**) induced by γ radiation of ^{60}Co for comparison with their previously reported behavior toward singlet molecular oxygen.

Oxidation of the Δ^4-3β-alcohol **2a** yielded cholest-4-en-3-one (**5a**) as major product, with 6β-hydroperoxycholest-4-en-3-one (**5b**) as the major hydroperoxide product. Small amounts of the 6α-hydroperoxide **2b** were also formed. The Δ^4-3-ketone **5a** was stable to ^{60}Co γ radiation, but irradiation of the pure Δ^4-6β-hydroperoxide **2c** yielded **5b** along with previously recognized thermal decomposition products cholest-4-ene-3β,6β-diol (**2e**) and 3β-hydroxycholest-4-en-6-one (**6**).[5] Accordingly, the 6β-hydroperoxide **5b** did not derive from **5a** but must have derived from **2c**. Inadequate amounts of the 6α-hydroperoxide **2b** precluded study of its radiation stability.

Formation of the 6-ketone **6** as a thermal decomposition product from **2c** was previously supported by detection of its pyrolysis products cholest-4-ene-3,6-dione (**7**) and 5α-cholestane-3,6-dione (**8**) among pyrolysis products from **2c**.[5] Direct observation of **6** following irradiation of **2c** now clearly establishes this reaction pathway of the 6β-hydroperoxide **2c**. However, pyrolysis of the 6β-hydroperoxide **5b** also gave the 3,6-diketones **7** and **8** as prominent products, a point previously suggested but not examined.[5] Derivation from **5b** of the saturated 3,6-diketone **8** must involve intermediate formation of 6β-hydroxycholest-4-en-3-one (**5c**) which then rearranges to **8**. Formation from **2c** of the Δ^4-3,6-diketone **7** may occur by three pathways— **2c** to **5b** to **7**, **2c** to **5b** to **5c** to **7**, or **2c** to **6** to **7**—whereas that of the saturated 3,6-diketone **8** may be by two pathways—**2c** to **5b** to **5c** to **8** and **2c** to **6** to **8**.

Oxidation of the Δ^6-3β-alcohol **3a** gave unexpectedly the epimeric cholesterol 7-hydroperoxides **1b** and **1c** as major products, the 7β-hydroperoxide **1c** predominating. The secondary oxidation products cholest-5-ene-3β,7α-diol (**1d**), cholest-5-ene-3β,7β-diol (**1e**), 5α-cholest-6-ene-3β,5-diol (**3c**), and 3β-hydroxycholest-5-en-7-one (**9**) were also formed. However, no 5α-hydroperoxide **3b** was detected. The 5α-hydroperoxide **3b** was fairly stable to ^{60}Co γ radiation in air, with less than 10% being converted to a mixture of **1b**, **1c**, **1d**, **1e**, and **3c**. Accordingly, were **3b** formed from **3a** initially, **3b** would have survived and been detected. Thus, initial formation of **3b** with complete allylic rearrangement to **1b**, epimerizatior of **1b**, and thermal decomposition of **1b**, **1c**, and **3b** cannot account for the presence of **1b**, **1c**, **1d**, **1e**, and **3c** as products from **3a**. Residual parent sterol **3a** recovered after ^{60}Co irradiation was not contaminated with detectable amounts of cholesterol; so the product 7-hydroperoxides **1b** and **1c** did not derive by initial isomerization of the Δ^6-double bond to the Δ^5 position, followed by oxidation of cholesterol thereby formed. Rath-