3-Chloro-3,5-cholestadiene Using Acetyl Chloride.—As a comparison with the phosphorus trichloride reaction above, a similar procedure was followed using acetyl chloride. A solution of 3.53 g. (9.16 mmoles) of 4-cholesten-3-one, 25 ml. of glacial acetic acid, and 3.5 ml. (49 mmoles) of acetyl chloride was allowed to stand at room temperature in a stoppered flask. After 3 hr., the solution was seeded with 3-chloro-3,5-cholestadiene, but no crystallization occurred. After standing for 20 hr., the now brownish solution was again seeded with the chlorodiene, whereupon the product crystallized from the solution. Filtration of this mixture gave 1.14 g. (31%) of crude 3-chloro-3,5-cholestadiene, m.p. 61–63°.

3-Chloro-3,5-androstadien-17β-ol Acetate.—The general procedure was followed using 4.68 g. (14.2 mmoles) of testosterone acetate, 25 ml. of glacial acetic acid, and 2.0 ml. (3.2 g., 23 mmoles) of phosphorus trichloride. Two recrystallizations of the crude product from ether afforded 2.78 g. (53%) of 3-chloro-3,5-androstadien-17β-ol acetate, m.p. 143.5–152.5° (m.p. 163–165° in an evacuated capillary), $[\alpha]^{26}D$ −155° (*c* 2.76, $CHCl_3$), λ_{max} 242 mμ (log ε 4.5); lit.[2] m.p. 148–152°, $[\alpha]D$ −172° λ_{max} 242 mμ (log ε 4.4).

3-Bromo-3,5-cholestadiene.—The general procedure was followed using 5.02 g. (13.0 mmoles) of 4-cholesten-3-one, 25 ml. of glacial acetic acid, and 2.0 ml. (5.7 g., 21 mmoles) of phosphorus tribromide. A yield of 5.12 g. (88%) of crude 3-bromo-3,5-cholestadiene, m.p. 62–66°, $[\alpha]^{27}D$ −112°, was obtained. Recrystallization of this product from ether–methanol afforded material with m.p. 65–72°, $[\alpha]^{27}D$ −115° (*c* 1.84, $CHCl_3$), λ_{max} 240 mμ (log ε 4.6).

Anal. Calcd. for $C_{27}H_{43}Br$: C, 72.46; H, 9.68; Br, 17.86. Found[13]: C, 72.40; H, 9.78; Br, 17.95.

3-Bromo-3,5-androstadien-17β-ol Acetate.—The general procedure was followed using 5.01 g. (15.2 mmoles) of testosterone acetate, 25 ml. of glacial acetic acid, and 3.0 ml. (8.5 g., 32 mmoles) of phosphorus tribromide. Two recrystallizations of the crude product from acetone afforded 4.12 g. (69%) of 3-bromo-3,5-androstadien-17β-ol acetate, m.p. 162–168° (m.p. 178–179.5° in an evacuated capillary), $[\alpha]^{27}D$ −141° (*c* 2.86, $CHCl_3$), λ_{max} 240 mμ (log ε 4.4).

Anal. Calcd. for $C_{21}H_{29}BrO_2$: C, 64.09; H, 7.46; Br, 20.32. Found[14]: C, 63.96; H, 7.30; Br, 20.56.

3-Acetoxy-3,5-cholestadiene.—To a suspension of 0.82 g. (2.1 mmoles) of 4-cholesten-3-one in 8 ml. of acetic anhydride was added 0.4 ml. (0.6 g., 5 mmoles) of phosphorus trichloride. The steroid dissolved upon slight warming and swirling. The product began to precipitate after 10 min. The mixture was allowed to stand at room temperature for 1 hr., then it was cooled in an ice bath and filtered to give 0.69 g. (76%) of white crystals, m.p. 74–78°. Recrystallization of this material from 95% ethanol, then methanol afforded 0.30 g. (33%) of 3-acetoxy-3,5-cholestadiene, m.p. 80–81°, $[\alpha]^{27}D$ −99.9° (*c* 1.87, $CHCl_3$); lit.[15] m.p. 81°, $[\alpha]^{23}D$ −100.4°.

(13) Elemental analysis were performed by Weiler and Strauss Laboratories, Oxford, England.

(14) Elemental analysis were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

(15) U. Westphal, *Chem. Ber.*, **70**, 2128 (1937).

Preparation of the γ-Lactone and γ-Lactam of 5-Methyl-4-oxo-2-hexenoic Acid

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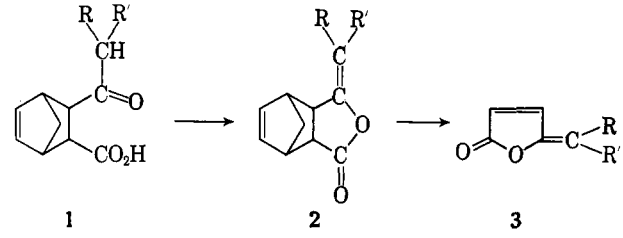
Received April 10, 1964

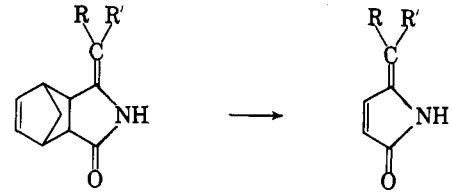
In a study of compounds related to the protoanemonin-type antibiotics, Walton[1] synthesized a number of 4-hydroxy-2,4-alkadienoic acid γ-lactones (**3**, R = alkyl, R′ = H) *via* cyclopentadiene Diels–Alder adducts (**1**). He was unable, though, to prepare the dialkyl unsaturated γ-lactones (**3**, R and R′ = alkyl). As an example, when R and R′ were methyl, the eno lactone **2** could not be formed using the usual methods (acetic anhydride and either sodium acetate or hydrochloric acid). Walton concluded, therefore, that branching in the position α to the carbonyl group interfered with lactonization. We have been able, by a change in reagents, to accomplish the lactonization and lactamization of **1** despite the α-branching.



1 **2** **3**

In our study we have found that when cyclopentadiene adduct **1** (R = R′ = CH_3) is treated with thionyl chloride followed by ammonium hydroxide, the product is not the expected ketoamide but rather the enol lactone **2**. Pyrolytic distillation of this lactone yields 5-methyl-4-hydroxy-2,4-hexadienoic acid γ-lactone (**3**, R = R′ = CH_3), characterized from its infrared, n.m.r., and mass spectra.

Since for our purposes we were interested not only in the γ-lactone but also in the γ-lactam (**5**), we set about to prepare it also. Ammonolysis of lactone **3** (R = R′ = CH_3) with aqueous ammonia or liquid ammonia failed to give the lactam; fusion of the lactone with ammonium carbonate also failed to give a new product. We were, however, able to prepare the desired lactam by a retro Diels–Alder decomposition of lactam **4**. Lactam **4** was prepared by fusion of keto acid **1** with ammonium carbonate, and this lactam was then pyrolyzed at 400° in a nitrogen atmosphere.



4 **5**

The product after purification by liquid chromatography was identified from its spectral properties as 5-methyl-4-amino-2,4-hexadienoic acid γ-lactam (**5**).

Experimental[2]

3-Isobutyryl-5-norbornene-2-carboxylic Acid (**1**).—Isopropylmagnesium bromide, prepared from 41 g. of isopropyl bromide, 7.3 g. of magnesium, and 250 ml. of ether, was added dropwise to 50 g. of 5-norbornene-2,3-dicarboxylic anhydride[3] dissolved in 100 ml. of benzene and 200 ml. of ether. After the addition was complete, the reaction mixture was stirred at room temperature for 2 hr., then hydrolyzed with 300 ml. of 3 *N* hydrochloric

(1) H. M. Walton, *J. Org. Chem.*, **22**, 312 (1957).

(2) All melting points were determined using a Fisher-Johns melting point apparatus and are uncorrected. Elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. The n.m.r. spectra were run in deuterated chloroform solutions using a Varian Associates HR-60 instrument and are reported in τ-values with the number of protons in parenthesis. We are indebted to John J. Whalen and Johnnie L. Stewart for infrared spectra, to W. E. Walker, Jr., for n.m.r. spectra, to George W. Young for mass spectra, and to Richard F. Walsh for technical assistance.

(3) Nadic Anhydride, Allied Chemical Co.

acid. The ether layer was separated, and the aqueous layer was extracted with ether. The combined ether extracts were extracted four times with a total of 250 ml. of 10% sodium carbonate solution. Acidification of the carbonate solution gave 37 g. of 3-isobutyryl-5-norbornene-2-carboxylic acid, m.p. 82.5–83.5° (from hexane, lit.[1] m.p. 85–86°). Evaporation of the ether solution gave 23 g. of 5-norbornene-2,3-dicarboxylic anhydride; a quantitative yield of keto acid was obtained, based on recovered anhydride.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.37; H, 7.82.

4-Hydroxy-5-methyl-2,4-hexadienoic Acid γ-Lactone (3).—3-Isobutyryl-5-norbornene-2-carboxylic acid was warmed with excess thionyl chloride for 1 hr. Excess concentrated ammonium hydroxide was added to the cooled mixture. The solution was extracted with ether, the solvent was removed *in vacuo*, and the residue was chromatographed on silicic acid. The major product was identified as **2** (R = R′ = CH_3), m.p. 53–54° (from ethanol), by its infrared absorption, 1785 and 1709 cm.$^{-1}$, and n.m.r. spectrum, τ 3.84 (two), 6.62 (four), 8.28 (three), and 8.37 (three).

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.75; H, 7.47.

Distillation of **2** (R = R′ = CH_3) at 70 mm. and a pot temperature of 180–200° gave a crystalline product which was purified by chromatography. The product, 4-hydroxy-5-methyl-2,4-hexadienoic acid γ-lactone, m.p. 77–78°, was identified from its various spectra: ν 1810, 1740, and 1540 cm.$^{-1}$; τ 2.32 (one, doublet), 3.87 (one, doublet), 7.98 (three), and 8.04 (three); λ_{max}^{EtOH} 289 mμ (ε 18,700).

Anal. Calcd. for $C_7H_8O_2$: C, 67.73; H, 6.50; mol. wt., 122. Found: C, 67.75; H, 6.46; mass, 122.

4-Amino-5-methyl-2,4-hexadienoic Acid γ-Lactam (5).—3-Isobutyryl-5-norbornene-2-carboxylic acid (8 g.) was ground with one-half its weight of ammonium carbonate, and the mixture was fused. Recrystallization of the fusion product (7.5 g.) from ethanol–water gave a solid, m.p. 168–169°, characterized as imide **4** (R = R′ = CH_3) by the infrared and n.m.r. spectra: ν 3180, 1680, 1250, and 770 cm.$^{-1}$; τ 2.48 (N*H*), 4.18 (two), 6.82 (four), 8.30 (three), and 8.46 (three).

Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40. Found: C, 75.85; H, 7.92; N, 7.32.

Four grams of imide **4** (R = R′ = CH_3) was pyrolyzed at 400° in a nitrogen atmosphere, and the pyrolysate was chromatographed on silicic acid. Elution with 25% ether–pentane solution gave 1.2 g. of 4-amino-5-methyl-2,4-hexadienoic acid γ-lactam (**5**, R = R′ = CH_3), m.p. 183–184° (from water). The compound was identified from the following: λ_{max}^{EtOH} 300 mμ (ε 13,200); ν 3180, 1678, 1255, 1180, and 787 cm.$^{-1}$; τ 0.13 (N*H*), 2.73 (one, quadruplet), 3.85 (one, quadruplet), 7.98 (three), and 8.02 (three).

Anal. Calcd. for C_7H_9NO: C, 68.27; H, 7.37; mol. wt., 123. Found: C, 68.46; H, 7.53; mass, 123.

On the Occurrence of the Santolinenones. Terpenes. XV[1]

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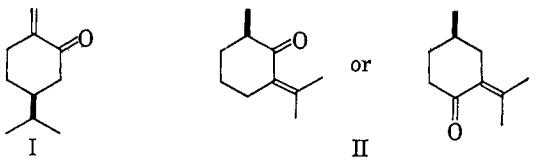
Received April 3, 1964

The steam-volatile oil of the ornamental shrub *Santolina chamaecyparissus* L. has been reported to contain three monoterpenic ketones, for two of which the structures I (α-santolinenone) and II (β-santolinenone) were suggested.[2] These unusual monoterpenoid structures were assigned on the basis of little chemical evidence and without any of the ketones being obtained in a pure form. The structures are, therefore, generally considered to be doubtful.[2]



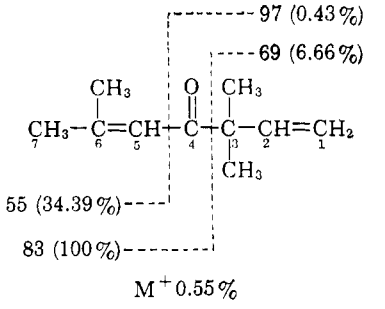
I II

We have reinvestigated the steam-volatile oil of this plant and by the use of gas–liquid chromatography (g.l.c.) have shown that it contains one major (65%) and three minor components. By the use of preparative g.l.c. the major component has been isolated and shown to be 3,3,6-trimethyl-1,5-heptadien-4-one (III) a monoterpene which does not obey the "isoprene rule." It is this compound which is responsible for the strong penetrating aromatic odor of the plant. The infrared spectrum of III showed the presence of an α,β-unsaturated carbonyl band at 1670 and a strong band at 1635 cm.$^{-1}$ indicating the presence of carbon–carbon double bonds. The n.m.r. spectrum of III showed a strong six-proton singlet at δ 1.18 (two methyl groups at C-3) and two three-proton singlets at δ 1.89 and 2.10 (two methyl groups at C-6); the vinylic region showed a typical ABX splitting pattern with the X proton (proton attached to C-2) giving a quartet centered at δ 5.94 with J_{AX} = 10 c.p.s. and J_{BX} = 18 c.p.s. and the AB protons (protons attached to C-1) appearing as an octet in the range δ 4.91–6.20 with $J_{AB} \sim 1.5$ c.p.s.; the C-5 proton gave a broad signal centered at δ 6.18.

The elemental analysis of III, together with its g.l.c. retention time and n.m.r. spectrum, indicated the molecular formula to be $C_{10}H_{16}O$, and the mass spectrum of III confirmed this by showing the molecular ion peak at mass 152. In addition, the most intense peak in the mass spectrum (39.4% of total ion yield) appeared at mass 83 and another intense peak appeared at mass 55 (see Scheme I). Both of these peaks arise from cleavage α to the carbonyl group, a process frequently encountered with saturated ketones.[3] Chemical evidence for structure III was obtained by its hydrogenation to 3,3,6-trimethylheptan-4-one (IV), which itself

SCHEME I

MASS SPECTRAL SPLITTING PATTERN OF III



(1) Terpenes. XIV: L. H. Zalkow and J. W. Ellis, *J. Org. Chem.*, submitted for publication.

(2) The earlier work is reviewed in the following references: (a) E. Guenther, "The Essential Oils," Vol. II, D. Van Nostrand Co., Inc., New York, N. Y., 1949, p. 409; (b) Vol. V, p. 475; (c) W. Treibs and K. Bournot, "E. Gildemeister/Fr. Hoffmann, Die Ätherischen Öle," Band VII, Akademie-Verlag, Berlin, 1961, p. 632; (d) J. L. Simonsen and L. N. Owen, "The Terpenes," Vol. I, Cambridge University Press, Cambridge, England, 1947, p. 390.

(3) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 1.