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.

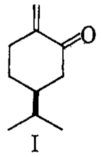
On the Occurrence of the Santolinenones. Terpenes. XV[1]

L. H. ZALKOW, D. R. BRANNON, AND J. W. UECKE

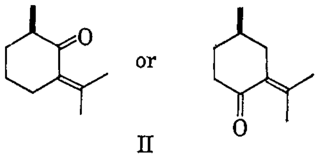
Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma

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



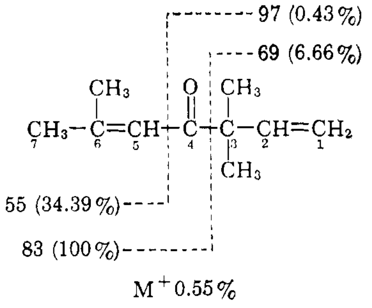
II

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.

was synthesized by a procedure similar to that previous described.[4] N.m.r. and mass spectral analyses were used to confirm the structure of IV.

Ketone III has been previously isolated only from *Artemisia annua* L.,[5,6] a plant not closely related botanically to *Santolina chamaecyparissus* L. It is interesting, however, that *Santolina chamaecyparissus* L. has been used as an anthelmintic agent[2] and that santonin, a well-known anthelmintic agent, is found in a species of *Artemisia.*[5]

We were unable to detect the presence of any substances of structures I or II in the oil investigated. In addition to III, two other compounds were isolated from the oil (comprising 15 and 10%, respectively, of the oil) but their infrared and n.m.r. spectra were not consistent with structures I or II. It thus seems unlikely that α- and β-santolinenones have been isolated from naturally occurring substances.

Experimental

Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were recorded on a Beckman IR-5 spectrophotometer; n.m.r. spectra were determined with the Varian A-60 spectrometer using carbon tetrachloride as solvent and tetramethylsilane as an internal standard (δ 0). Preparative gas chromatography was accomplished with the Aerograph A-700 Autoprep using a 0.5-in.-diameter by 20-ft. column of 20% Ucon Polar on Chromosorb W, a column temperature of 150°, and a helium flow rate of 200 cc. per min. Analytical gas chromatographs were obtained with Aerograph's Hy-Fi and Model A-350B gas chromatographs. Mass spectra were obtained with a Consolidated Electrodynamics Corporation Model 21-103C mass spectrometer.

Steam Distillation of *Santolina chamaecyparissus* L.—The coarsely chopped, air-dried, above-ground plant material (800 g.), collected in early winter, was steam distilled for 2 hr. to give 3.8 l. of distillate, which was extracted with 500 ml. of ether. After drying over magnesium sulfate, the ether was removed with a fractionating column, leaving a residue of 5.74 g. (0.72% based on dry plant) of light yellow oil, $n^{25}\mathrm{D}$ 1.4705. Analytical gas chromatography using several columns and thermal and hydrogen flame detectors indicated that the oil contained predominantly one major and three minor components.

Isolation of III.—Preparative gas chromatography gave four components with the retention time, yields, and properties shown below.

Component A had a retention time of 2.4 min., yield 4%, $n^{26.5}\mathrm{D}$ 1.4811.

Component B had a retention time of 25.6 min., yield 15%, $n^{26.5}\mathrm{D}$ 1.4679; infrared spectrum showed bands at $\nu_{\max}^{\text{film}}$ 1650, 1600, and 895 cm.$^{-1}$; n.m.r. showed a quartet (J = 11 c.p.s.) centered at δ 6.30, strong signal at 4.95, several weaker signals in region 4.5–5.3, and strong sharp signals at δ 0.72, 1.24, 1.60, 1.69, and 2.18.

Component C had a retention time of 37.5 min., yield 10%, $n^{26.5}\mathrm{D}$ 1.4832; infrared spectrum showed bands at $\nu_{\max}^{\text{film}}$ 1742, 1650, 1600, and 880 cm.$^{-1}$; n.m.r. showed a quartet (J = 11 c.p.s.) centered at δ 5.87 and sharp signals at δ 4.66, 0.95, and 0.87.

3,3,6-Trimethyl-1,5-heptadien-4-one (III) had a retention time of 50.1 min., yield 65%, $n^{25}\mathrm{D}$ 1.4670 (lit.[5b] $n^{25}\mathrm{D}$ 1.4631), b.p. 180–182° (lit.[5b] b.p. 182°); ultraviolet spectrum showed $\lambda_{\max}^{\text{alc}}$ 238 mμ (ϵ 11,275); infrared showed $\nu_{\max}^{\text{film}}$ 1675, 1635, 910, and 890 cm.$^{-1}$; for n.m.r., see text.

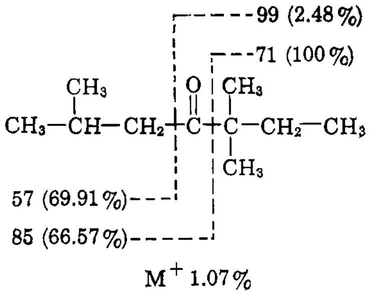
Anal. Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.60. Found: C, 78.51; H, 10.71.

The semicarbazide adduct (addition of semicarbazide across conjugated double bond) was prepared as previously described[5b] and gave m.p. 71–72° (lit.[5b] m.p. 68–75°).

Preparation of 3,3,6-Trimethylheptan-4-one (IV).—When 0.745 g. of ketone III was hydrogenated in 15 ml. of methanol in the presence of 0.08 g. of 10% palladium on carbon at room temperature and atmospheric pressure, 218 ml. (1.98 molar equiv.) was rapidly absorbed. The catalyst was removed by filtration, and 50 ml. of water was added to the methanolic filtrate. The aqueous methanol solution was extracted with ether and, after drying over anhydrous magnesium sulfate, the ether was removed with a fractionating column. The residue was distilled to give ketone IV, b.p. 70–75° (25 mm.), $n^{25.2}\mathrm{D}$ 1.4245; infrared showed $\nu_{\max}^{\text{film}}$ 1715 cm.$^{-1}$; n.m.r. showed δ 0.85 (doublet, J = 7 c.p.s.), 0.90 (doublet, J = 7 c.p.s.), and 1.07 (six-proton singlet). G.l.c. on several columns showed IV to be homogeneous. The mass spectrum of IV showed fragmentation as indicated in Scheme II.

SCHEME II

MASS SPECTRAL FRAGMENTATION OF IV



Ketone IV was synthesized by a procedure similar to that used by Colonge and Dumont for the synthesis of III[4]. 2,2-Dimethylbutyrolylchloride (2.5 g.), prepared by the reaction of 2,2-dimethylbutyric acid with thionyl chloride, was added to a stirred suspension of 1.0 g. aluminum chloride in 60 cc. of dry chloroform at 0°. Dry isobutylene was passed slowly through this suspension for 3 hr. and, after filtration, the solution was washed with a cold aqueous sodium hydroxide solution. The organic layer was washed with water, then dried over magnesium sulfate, and finally concentrated to give a viscous oil, which without further purification was heated at 100° with 20 ml. of N,N-dimethylaniline for 2 hr. The solution was then partitioned between 5% hydrochloric acid and chloroform, and the chloroform layer was washed with water, then dried over magnesium sulfate, and finally evaporated to yield 810 mg. of oily product. This oily product was hydrogenated in 10 ml. of methanol in the presence of 80 mg. of 10% palladium on carbon. After removal of the catalyst by filtration, the methanolic solution was added to 50 ml. of water and the aqueous solution was extracted with ether. After drying, the ether layer was concentrated to give an oily residue which was chromatographed on 100 g. of Merck acid-washed alumina (activity III). The benzene–ether eluent (1:1) gave 325 mg. of 3,3,6-trimethylheptan-4-one, identical in all respects with that obtained from III isolated from *Santolina chamaecyparissus* L. as described above.

Acknowledgment.—We wish to thank Messrs. M. C. Hamming and H. T. Ford of Continental Oil Company, Ponca City, Oklahoma, for mass spectral analysis and interpretation. We also wish to thank Messrs. J. Martin and G. Cabat for assistance in plant collection and preliminary work and Mr. W. R. Kays, Department of Horticulture, Oklahoma State University, for plant identification.

---

[4] J. Colonge and P. Dumont, *Compt. rend.*, **220**, 500 (1945).

[5] This work is reviewed in the following references: (a) J. L. Simonsen and L. N. Owen, ref. 2d, p. 105; (b) D. Merkel, "E. Gildemeister/Fr. Hoffmann," Die Ätherischen Öle, Band IIIc, Akademie-Verlag, Berlin, 1963, p. 193; (c) E. Guenther, ref. 2a, Vol. II, p. 386; (d) W. Karrer, "Konstitution und Vorkommen der Organischen Pflanzenstoffe," Birkhäuser Verlag, Basel, 1958, p. 174.

[6] There is confusion in the literature regarding the name given to ketone III. In some cases it is called artemisia ketone and in other cases it is referred to as isoartemisia ketone and likewise the isomeric ketone, 3,3,6-trimethyl-1,6-heptadien-4-one, also isolated from *Artemisia annua* L., is referred to by one or the other of these names.