Constituents of *Casimiroa Edulis Llave et Lex.* V.[1] Identity of Casimirolid and Obacunone

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The isolation of the lactone casimirolid (m.p. 229–231°, $[\alpha]_D$ −49°) from the seeds of *Casimiroa edulis Llave et Lex* was described in 1911 by Power and Callan[3] and recently by our group.[4] The lactone obacunone (m.p. 229–230°, $[\alpha]_D$ −51°) was first isolated by Kaku and Ri[5] from the bark of *Phellodendron amurense;* it was later obtained from citrus oil by Emerson,[6] who suspected it to be identical with casimirolid. We have now carried out a direct comparison between casimirolid and obacunone. The complete identity of the characteristic infrared spectra, as well as the fact that no melting point depression was observed on admixture, conclusively proves the two substances to be identical.

Casimirolid had been assigned the formula $C_{24}H_{28}O_6$ by Power and Callan[3] and $C_{28}H_{32}O_8$ by ourselves,[4] whereas obacunone undoubtedly possesses the formula $C_{26}H_{30}O_7$.[6,7] A series of new analyses of casimirolid has now shown the previously proposed formulas to be incorrect and favors the $C_{26}H_{30}O_7$ formulation also for this substance.

Although the name casimirolid has priority,[3] the structural investigations by Emerson[6] and especially by Dean and Geissman[7] have been carried out with obacunone, yielding degradation products the names of which have been derived from this substance. We propose therefore that the name obacunone be retained and casimirolid be abandoned.

EXPERIMENTAL

Comparison of casimirolid with obacunone. A sample of casimirolid[4] was crystallized repeatedly from ethanol and was then dried for 24 hr. at 120° (0.1 mm.). It showed m.p. 230–231°, $[\alpha]_D$ −49.6° ($CHCl_3$).

Anal. Calcd. for $C_{26}H_{30}O_7$: C, 68.70; H, 6.65; O, 24.64; Calcd. for $C_{28}H_{32}O_8$: C, 67.73; H, 6.50; O, 25.78. Found: C, 68.90, 68.79; H, 6.76, 6.83; O, 24.57, 24.33.

The infrared spectrum (potassium bromide pellet, determined on a Baird double-beam spectrophotometer) showed more than 20 well defined bands, the main ones being at 2.87, 3.31, 5.78, 5.88, 6.68, 6.85, 7.20, 7.45, 7.63, 7.83, 8.17, 8.62, 8.95, 9.35, 9.40, 9.75, 10.16, 10.24, 10.92, 11.46, 12.17, and 12.48μ.

An authentic sample of obacunone showed m.p. 229–231°, $[\alpha]_D$ −49.8° ($CHCl_3$). There was no depression in m.p. on admixture with a sample of casimirolid. The infrared spectrum was completely identical with that of casimirolid.

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Beckmann Rearrangement of 4-Trimethylsilylacetophenone Oxime

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Few reports of aminoaryltrialkylsilanes occur in the literature[2] as these compounds readily undergo fission of the aromatic carbon-silicon bond, particularly in acidic media. Those amines which have been reported were prepared by hydrogenation of the corresponding nitro compounds over a Raney nickel catalyst.[3–5]

Since 4-trimethylsilylacetophenone oxime (I) has recently become available[6] an attempt has been made to prepare 4-trimethylsilylacetanilide (II), by a Beckmann rearrangement, and then to hydrolyze this compound to 4-trimethylsilylaniline. Treatment of an ethereal solution of I with thionyl chloride or phosphorus pentachloride gave good yields of II. With sulfuric acid the yields of II were lower. The anticipated cleavage of the aromatic carbon-silicon bond of I did not occur under the conditions employed.[7] Analysis for nitrogen and silicon, and the infrared spectrum, confirmed the structure of II.

On heating the anilide under reflux with 40 or 70% aqueous-alcoholic potassium hydroxide for 30 minutes, then neutralizing, unreacted II was quantitatively recovered. The anilide is thus extremely difficult to cleave under basic conditions.

Heating II under reflux for 15 minutes with 10% aqueous-alcoholic sulfuric acid liberated a dark-brown oil (III). On distilling this oil and examining

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its infrared absorption spectrum no evidence was found for the presence of the trimethylsilyl group, and the spectrum resembled in every way that of aniline. This was confirmed by forming derivatives of III with phenyl isocyanate and 2,4-dinitrochlorobenzene. It thus appears that the Beckmann rearrangement of 4-trimethylsilylacetophenone oxime occurs in good yield; however, conditions for the preparation of 4-trimethylsilylaniline from this Beckmann product have not been found.

EXPERIMENTAL

Beckmann rearrangements of I. A solution of I (20.7 g., 0.1 mole) in anhydrous diethyl ether (500 ml.) was treated with thionyl chloride (12 g., 0.1 mole). After the initially exothermic reaction had moderated, the mixture was heated at reflux for 0.5 hr. Water (500 ml.) was then added to decompose unreacted thionyl chloride. Excess powdered sodium bicarbonate was then cautiously added to the stirred mixture, the ether layer separated, washed three times with water, then dried over anhydrous sodium sulfate. On distilling off the ether a yellow crystalline solid remained, yield 18 g. (87%). After two treatments with charcoal, and a further recrystallization from alcohol, colorless flat crystalline plates were obtained of m.p. 171°,[8] in good agreement with the literature[5] value of 169–170°.

Anal. Calcd. for $C_{11}H_{17}NOSi$: N, 6.76; Si, 13.55. Found: N, 6.64; Si, 13.29.

Employing the same experimental conditions with phosphorus pentachloride (21 g., 0.1 mole) the yield of II was 18 g. With concentrated sulfuric acid (10 g., 0.1 mole) the yield of II was 15 g. (72.5%).

Infrared absorption spectrum of II. The spectrum was determined using a Perkin-Elmer Model 112 spectrophotometer with sodium bromide optics. Prominent bands included those assigned to NH stretching at 3257; aliphatic CH stretch at 2927; amide C:O at 1666; aromatic C:C at 1506 and 1592; NH bend at 1537; parasubstitution at 823; and three strong bands due to the trimethylsilyl group at 1248, 838, and 759 cm.$^{-1}$ [9,10]

Attempted alkaline hydrolysis of II. One-gram samples of II were dissolved in 20–30 ml. of 40% potassium hydroxide in dilute (1:1) alcohol. On heating at reflux for 30 min., cooling, and making slightly acid, II was quantitatively recovered, m.p. 170–171°. Similar results were obtained using 70% potassium hydroxide in dilute alcohol.

Acid hydrolysis of II. On heating II (10 g.) under reflux with excess dilute (1:10) sulfuric acid for 15 min. the solution turned dark brown. Heating was continued for a further 15 min. to ensure complete reaction. Excess 10% sodium hydroxide solution was then added to liberate the free base. The crude amine (approx. 7 g.) was extracted with ether, the extracts washed with water, dried, and the ether removed. Fractional distillation yielded 3.5 g. of a colorless oil, b.p. 100–120°/12–15 mm. The oil was redistilled and the fraction of b.p. 112–115°/12–15 mm. collected. Yield, 2.0 g.

Identification of hydrolysis product. The infrared absorption spectrum of the colorless oil obtained by acidic hydrolysis of II was identical with that of an authentic specimen of freshly distilled aniline.

Phenyl isocyanate reacted with the oil to give 1,3-diphenylurea, m.p. 238°; and 2,4-dinitrochlorobenzene reacted to give 2,4-dinitrodiphenylamine, m.p. 156°. Both these data are identical with those for the corresponding aniline derivatives.

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16-Hydroxylated Steroids. IX.[1] Synthesis of 12α-Bromo-16α-hydroxycortisone 21-Acetate and 16,21-Diacetate

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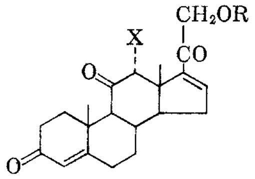
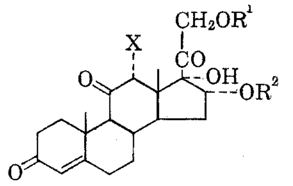
Recently described work from this Laboratory on 16α-hydroxycorticoids[2] has now been extended to include those containing a 12α-halogen group.[3] The present note describes the synthesis of 12α-bromo-16α-hydroxycortisone (12α-bromo-16α,17α-21-trihydroxy-4-pregnene-3,11,20-trione) in the form of its 21-acetate IIa and 16,21-diacetate IIb.



Ia. R = Ac; X = Br
Ib. R = Ac; X = H
Ic. R = X = H



IIa. R^1 = Ac; R^2 = H; X = Br
IIb. R^1 = R^2 = Ac; X = Br
IIc. R^1 = R^2 = Ac; X = H

Hydroxylation of 21-acetoxy-12α-bromo-4,16-pregnadiene-3,11,20-trione (Ia)[4] with potassium permanganate in aqueous acetone[5a,b] gave a mixture of products[6] from which the desired 21-acetoxy-12α-

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(6) The reaction mixture was shown by paper-strip chromatographic analysis to contain at least five products. No attempt was made to isolate and identify the byproducts.