colorized with charcoal, and crystallized from methylene dichloride–methanol, yielding 160 mg. (65%) of the amine VIIa, m.p. 187°. The analytical specimen was prepared by several crystallizations from methylene dichloride–ethanol and showed m.p. 190–192°; λ_{max} 258 mμ (ϵ 18,300) and 310–313 mμ (ϵ 2820); $[\alpha]_D$ +140°; ν_{max} 1363 (C–N), 1610, 1562, 1510 (aromatic ring), and 1739 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{22}H_{29}NO$: C, 81.69; H, 9.04; N, 4.33; O, 4.95. Found: C, 81.76; H, 9.22; N, 4.38; O, 5.07.

3-(N-Pyrrolidinyl)estra-1,3,5(10)-trien-17β-ol (VIIe).—A solution of 750 mg. of VIIa in 35 ml. of dioxane and 0.4 ml. of water was treated with 440 mg. of sodium borohydride. The reaction mixture was left at room temperature for 5 hr. and the excess of sodium borohydride was destroyed by careful addition of acetic acid. The mixture was diluted liberally with water, and the crystalline precipitate thus obtained was collected by filtration and washed with water to neutrality. Drying of the material then afforded 750 mg. of the 17β-alcohol VIIe, m.p. 175–178°. The analytical sample was obtained by recrystallizations from methanol and had m.p. 178–180°; λ_{max} 256 mμ (ϵ 17,800) and 312 mμ (ϵ 2750); $[\alpha]_D$ +78°; ν_{max} 1370 (C–N), 1525, 1562, 1612 (aromatic ring), and 3395 cm.$^{-1}$ (OH).

Anal. Calcd. for $C_{22}H_{31}NO$: C, 81.18; H, 9.60; N, 4.30; O, 4.92. Found: C, 80.79; H, 9.71; N, 4.25; O, 5.17.

3-(N-Pyrrolidinyl)estra-1,3,5(10)-trien-17β-ol Acetate (VIIf).—Acetylation of 600 mg. of the above 17β-alcohol with pyridine and acetic anhydride on the steam bath in the normal manner furnished the crude acetate VIIf. The analytical sample was prepared by several crystallizations from methylene dichloride–methanol and showed m.p. 137–138°; λ_{max} 258 mμ (ϵ 16,600) and 312 mμ (ϵ 2500); $[\alpha]_D$ +51°; ν_{max} 1350, 1380 (C—N), 1520, 1560, 1630 (aromatic ring), 1245 (C—O), and 1750 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{24}H_{33}NO_2$: C, 78.43; H, 9.05. Found: C, 78.85; H, 9.29.

3-Diethylaminoestra-1,3,5(10)-trien-17-one (VIIb).—A solution of 750 mg. of 10β-acetoxyestr-4-ene-3,17-dione (I) in 75 ml. of benzene and 4.5 ml. of diethylamine was treated with 0.1 ml. of acetic acid under reflux for 6 hr. The reaction mixture was concentrated under vacuum to 20 ml. and filtered through a short column of alumina, eluting with benzene. The material obtained after evaporation of the solvent was purified by further column chromatography on 36 g. of unwashed alumina (system: benzene–ether). The homogeneous, less polar fractions eluted with ether–benzene (85:15) were crystallized from methylene dichloride–hexane to give 230 mg. of the amine VIIb, m.p. 122–124°. Two crystallizations from methylene dichloride–methanol afforded the analytical sample: m.p. 131.5–132.5°; λ_{max} 263 mμ (ϵ 14,420) and 310 mμ (ϵ 2145); $[\alpha]_D$ +134°; ν_{max} 1370, 1379 (C—N), 1525, 1563, 1584 (aromatic ring), and 1754 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{22}H_{31}NO$: C, 81.18; H, 9.60; N, 4.30; O, 4.92. Found: C, 81.36; H, 10.19; N, 3.95; O, 4.98.

3-N-Piperidinylestra-1,3,5(10)-trien-17-one (VIIc).—A solution of 500 mg. of I in 50 ml. of benzene, 1 ml. of piperidine, and 0.4 ml. of acetic acid was refluxed for 2.5 hr. Dilution and product isolation as described above for the 3-(N-pyrrolidinyl)-amine furnished 240 mg. of the amine VIIc, m.p. 138–140°. The analytical sample was prepared by recrystallization from methylene dichloride–methanol and showed m.p. 143–143.5°; λ_{max} 250–252 mμ (ϵ 11,000) and 322 mμ (ϵ 1620); $[\alpha]_D$ +135°; ν_{max} 1389, 1370 (C—N), 1510, 1563, 1613 (aromatic ring), and 1724 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{23}H_{31}NO$: C, 81.85; H, 9.26; N, 4.15; O, 4.74. Found: C, 82.33; H, 9.36; N, 4.02; O, 4.60.

3-(2-Diethylamino)ethylaminoestra-1,3,5(10)-trien-17-one (VIId).—A solution of 720 mg. of I in 70 ml. of benzene, 0.7 ml. of N,N-diethylethylenediamine, and 0.1 ml. of acetic acid was refluxed (with water separator) for 1 hr. The mixture was concentrated to a final volume of 20 ml. and worked up further as described above to yield 550 mg. of crude amine VIId. The analytical sample was prepared by recrystallization from methylene dichloride–pentane and had m.p. 90–100°; $[\alpha]_D$ +121°; λ_{max} 248 mμ (ϵ 13,820) and 300–302 mμ (ϵ 2050); ν_{max} 1370, 1385 (C—N), 3350 (N—H), 1508, 1570, 1615 (aromatic ring), and 1738 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{24}H_{36}NO_2$: C, 78.21; H, 9.85; N, 7.60; O, 4.34. Found: C, 78.49; H, 9.81; N, 7.54; O, 4.22.

Isolation and Structure of Aeneadiol[*]

XORGE ALEJANDRO DOMÍNGUEZ AND VÍCTOR BARRAGÁN

Departamento de Química, Escuela de Ciencias,
Instituto Tecnológico y de Estudios Superiores de Monterrey,
Monterrey, N.L., Mexico

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Most *Argemone* species are native to the dry regions of North and Central America.[1] Several parts of these plants have been used medicinally even in prehispanic times.[2-4] Alkaloids of the berberine and protopine group have been isolated from these plants.[5-7] Flavones have been isolated from the flowers of *A. mexicana.*[8] As part of our study of flowers used in Mexican folk medicine, several substances present in *Argemone aenea* G. B. Ownb. were investigated. From the nonsaponifiable portion of the petroleum ether extract three compounds were isolated. The most abundant, A, m.p. 115–116°, had the empirical formula $C_{30}H_{62}O_2$. Its infrared spectrum showed hydroxyl bands. It gave positive tests for a vicinal glycol and a linear aliphatic compound. A Kuhn–Roth determination gave two terminal C-methyl groups. Oxidation with periodic acid furnished two aldehydes. The steam-volatile component was identified as *n*-decanal; the nonvolatile component, m.p. 77–79°, $C_{20}H_{40}O$, as *n*-eicosanal. Therefore, A, which we have named aeneadiol, is the previously unreported 10,11-triacontanediol.[9]

Compound B, m.p. 73–74°, $C_{26}H_{52}O$, showed infrared bands of a linear aliphatic ketone. A Kuhn–Roth determination gave two C-methyl groups. The Zimmermann and other tests for carbonyl groups agreed with the infrared information. Its n.m.r. spectrum showed a methyl peak at τ 8.9 (6H) and a methylene peak at 8.75 (50–54H).

Compound C, m.p. 134–136°, $C_{26}H_{46}O$ (acetate m.p. 120–122°, $C_{28}H_{48}O_2$), gave a positive Liebermann–Burchard test and a negative tetranitromethane test. It must be a sterol which was not further investigated.

From the acetone extract two alkaloids were isolated: berberine and α-allocryptopine. Six unidentified alkaloids were detected by thin layer chromatography (t.l.c.) on silica gel, R_f 0.18, 0.21, 0.25, 0.57, 0.62, and 0.70. From the alcoholic extracts, berberine, α-

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[*] To Professor Louis F. Fieser.

(1) G. B. Ownbey, *Mem. Torrey Botan. Club*, **21**, 50 (1958).

(2) P. C. Standley, "Trees and Shrubs of México," Part 1, Smithsonian Institution, Washington, D. C., 1920, p. 299.

(3) M. Martínez, "Plantas medicinales de México," 3rd Ed., Editorial Botas, Mexico, 1959, p. 108.

(4) F. Hernández, "Historia de las plantas de Nueva España," Imprenta Universitaria México, Mexico, 1942, p. 805.

(5) A. Santos and P. Adkilen, *J. Am. Chem. Soc.*, **54**, 2923 (1932).

(6) L. Slavikova and J. Slavik, *Collection Czech. Chem. Commun.*, **21**, 211 (1955).

(7) J. Schermerhorn and T. Soine, *J. Am. Pharm. Assoc.*, **40**, 20 (1951).

(8) W. Rahman and M. Ilyas, *J. Org. Chem.*, **27**, 153 (1962).

(9) The only previous reference to a triacontanediol is the 1,2-diol from the insect *Tenebro molitor* [W. Schulz and M. Becker, *Biochem. Z.*, **232**, 189 (1931)]. This structure would appear to be rather tenuous owing to the paucity of data used to substantiate it. It is reported to melt at the same temperature as our glycol which suggests that they may be the same. The great difference in the two sources, one animal and the other plant, however, suggests that they are different. Very few other long-chain aliphatic diols have been described [W. Karrer, "Konstitution und vorkommen der organischen Pflanzenstoffe," Birkhaeuser Verlag, Basel, 1958]; most of them are α,ω-diols.

allocryptopine, and protopine were isolated and five unidentified alkaloids were detected by t.l.c. T.l.c. comparison with authentic samples of argemonine and bisnorargemonine indicted the absence of these alkaloids in the acetonic and alcoholic extracts.

Experimental[10]

The flowers of *A. aenea* G. B. Ownb. were collected south of Monterrey, Mexico, in June 1963. The sun-dried whole flowers were pulverized in a Wiley mill. A 1400-g. sample of the powder in a Soxhlet apparatus was extracted successively with petroleum ether (b.p. 30–60°), acetone, and ethanol. Each extract was filtered before concentration. From the yellow petroleum ether extract 3.76 g. (0.27%) of a white precipitate (A) melting about 100° was collected. Three crystallizations from methanol afforded 2.84 g. of white crystals of A: m.p. 115–116°; infrared bands at 3579 (nonbonded hydroxyl), 3000 (C–H), 1470 (methylene), 1390 (methyl), 1210, and 1045 cm.$^{-1}$; no absorption in the ultraviolet. It gave a positive periodic acid test for *vic*-glycol and a xanthate test for alcohols. A formed a complex with a methanolic urea. On Kuhn–Roth determination two C-methyl groups were found.

Anal. Calcd. for $C_{30}H_{62}O_2$: C, 79.59; H, 13.36; O, 7.07; mol. wt., 454.8. Found: C, 79.09; H, 13.53; O, 7.4; mol. wt. (Rast in camphor), 446.

On evaporation of the petroleum ether extract 8.9 g. (0.64%) of a yellow resin was left. This residue was saponified with methanolic potassium hydroxide. The nonsaponifiable portion was extracted with ethyl ether which on concentration afforded 269 mg. (0.019%) of a yellowish solid (B), which on crystallization from methanol afforded 237 mg. of small white needles: m.p. 73–74°; infrared bands at 2920 (C–H), 2840 (C–H), 1716 (carbonyl), 1460 (methylene), and 1380 (methyl) cm.$^{-1}$; no absorption in the ultraviolet; n.m.r. methyl peak at τ 8.9 (6H) and methylene peak at 8.75 (50–54H). 2,4-Dinitrophenylhydrazine gave a yellow precipitate with a sample. The Zimmermann test for methylene ketones was positive. The haloform and the tetranitromethane tests were negative. Reduction with sodium borohydride B gave a white solid, m.p. 124–126°. The Kuhn–Roth determination showed two C-methyl groups.

Anal. Calcd. for $C_{26}H_{52}O$: C, 82.03; H, 13.77. Found: C, 81.89; H, 13.91.

The ethereal filtrate on concentration afforded 320 mg. of a white solid (C) which, after several recrystallizations from methanol, melted at 134–136°. It gave a positive Liebermann–Burchard test (pink–violet–green) and a negative tetranitromethane test. The infrared spectrum showed bands at 3520 (hydroxyl), 2926, 2850 (C–H), 1435, 1380, and 1138 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{46}O$: C, 83.03; H, 12.44. Found: C, 83.35; H, 12.38.

Acetylation of C.—A mixture of 30 mg. of C, 5 ml. of acetic anhydride, and 1 ml. of pyridine was refluxed 1 hr. and diluted with water, the precipitate was recrystallized from methanol, and white crystals melting at 120–122° were obtained. The infrared spectrum showed bands at 1735 (carbonyl) and 1244 cm.$^{-1}$ (acetoxy).

Anal. Calcd. for $C_{28}H_{48}O_2$: C, 80.71; H, 11.61. Found: C, 81.09; H, 11.54.

Oxidation of Aeneadiol with Jones Reagent.—A solution of 100 mg. of A in acetone was oxidized with an excess of Jones reagent.[11] The product was separated in the usual way and was recrystallized twice from methanol, yielding 66 mg. of white crystals, m.p. 69–70°, infrared band at 1724 cm.$^{-1}$ (aliphatic carbonyl).

Anal. Calcd. for $C_{30}H_{58}O_2$: C, 79.93; H, 12.97. Found: C, 79.70; H, 12.95.

Acetylation of Aeneadiol.—A mixture of 150 mg. of A, 5 ml. of acetic anhydride, and 2 ml. of pyridine was refluxed 2 hr. and worked up as usual. Recrystallization from methanol furnished the diacetate, m.p. 39–40°, infrared bands at 1720 (carbonyl) and 1236 cm.$^{-1}$ (acetoxy).

Anal. Calcd. for $C_{34}H_{66}O_4$: C, 75.78; H, 12.35; O, 11.88. Found: C, 75.76; H, 12.21; O, 12.06.

Cleavage of Aeneadiol with Periodic Acid.—A mixture of 250 mg. of aeneadiol and periodic acid solution was magnetically stirred for 34 hr. The oxidized material was distilled with steam; from the distillate a coriander-smelling oil was separated. It was identified as *n*-decanal, b.p. 208–210,° lit.[12] m.p. 208–209°, n^{30}_D 1.4216, lit.[12] n^{15}_D 1.4297. It gave positive Schiff and Tollens tests. The following derivatives were prepared: 2,4-dinitrophenylhydrazone, m.p. 106–107°, lit[12] m.p. 105–107°; semicarbazone, m.p. 108°, lit[12] m.p. 102°; decanaldimethone, m.p. 108–110°, lit[13] m.p. 92°.

Extraction of the steam-distillation residue with ethyl ether afforded a white solid (eicosanal) which, on recrystallization from methanol, melted at 77–79°. It gave the usual positive tests for aldehydes.

Anal. Calcd. for $C_{20}H_{40}O$: C, 81.00; H, 13.60; O, 5.39. Found: C, 79.88; H, 13.76; O, 5.47.

The 2,4-dinitrophenylhydrazone prepared by the usual procedure[13] gave yellow crystals, m.p. 89–91°.

Anal. Calcd. for $C_{26}H_{44}N_4O_4$: C, 65.51; H, 9.31; N, 11.76. Found: C, 65.47; H, 9.18; N, 11.59.

The semicarbazone was obtained as white crystals, m.p. 88–90°.

Anal. Calcd. for $C_{21}H_{43}N_3O$: C, 71.33; H, 12.26; N, 11.89. Found: C, 71.27; H, 12.40; N, 11.65.

Eicosanaldimethone was obtained as white crystals, m.p. 127–129°.

Anal. Calcd. for $C_{36}H_{62}O_4$: C, 77.36; H, 11.18. Found: C, 77.30; H, 11.01.

Acetonic Extract.—This yellow extract gave positive Mayer and Dragendorff tests for alkaloids. Evaporation gave 20.1 g. (1.48%) of yellow residue which was mixed with calcium hydroxide and extracted repeatedly with chloroform. The chloroform layer was extracted with 1 *N* hydrochloric acid; the acid solution was made basic with ammonium hydroxide and extracted with chloroform followed by distillation to dryness, leaving 1.8 g. (0.12%) of the alkaloid mixture. T.l.c. showed eight spots, R_f 0.18, 0.21, 0.25, 0.29, 0.37, 0.57, 0.62, and 0.70. The alkaloids with R_f 0.29 and 0.37 (layer spots) were isolated on a preparative t.l.c. The yellow substance (14 mg., R_f 0.29) was identified as berberine, by comparison of melting point, ultraviolet spectrum, and t.l.c. (R_f with an authentic sample) and its conversion to berberine nitrate. The alkaloid (18 mg., R_f 0.37) was identified as α-allocryptopine by comparison of its melting point, ultraviolet spectrum, and t.l.c. (R_f with an authentic sample). T.l.c. analysis of a sample of the alkaloid mixture and authentic specimens[14] of berberine (R_f 0.26), α-allocryptopine (R_f 0.33), protopine (R_f 0.32), bisnorargemonine (R_f 0.27), norargemonine (R_f 0.25), and argemonine (R_f 0.24), and observation of their behavior under ultraviolet light, iodine vapor, and modified Dragendorff[15] reagent, indicated the presence of the first three and absence of the last three alkaloids.

Ethanolic Extract.—The black solution gave positive alkaloid tests. It was evaporated, the residue was treated with ammonia, and the free alkaloids were extracted and separated as described above. Evaporation of the chloroform afforded 1.0 g. of a blackish mixture of alkaloids which was dissolved in chloroform and chromatographed on neutral alumina. The elution was followed with t.l.c. Berberine, α-allocryptopine, and protopine were isolated and identified.

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[10] All melting points were observed on a Kofler micro hot stage. Infrared spectra were observed on a Beckman IR-5 double-beam spectrophotometer in chloroform solution. Ultraviolet spectra were observed on a Beckman DU spectrophotometer. We are indebted to Dr. R. Ketcham of the School of Pharmacy, University of California, San Francisco, Calif., for revising this paper and for the n.m.r. spectrum, which was obtained on a Varian 60-A n.m.r. spectrometer operating at 60 Mc. with tetramethylsilane as an internal standard and deuteriochloroform as solvent. Analyses were performed by Dr. A. Bernhard of Mülheim, Germany. The thin layer chromatograms were run on silica gel G (Merck) on 20 × 20 cm. glass plates and developed with butanol-acetic acid-water (75:10:15 v./v.). Positions of the spots were ascertained with ultraviolet light and iodine vapor. We thank Dr. Paulino Rojas from the Botany Department for the identification of the *A. aenea*.

[11] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

[12] I. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Vol. I, Oxford University Press, London, 1953, p. 421.

[13] N. D. Cheronis, "Semimicro Qualitative Organic Analysis," 2nd Ed., Interscience Publishers, Inc., New York, N. Y., 1958.

[14] We are indebted to Dr. T. Soine of the School of Pharmacy, University of Minnesota, for generous gifts of argemonine, norargemonine, and bisnorargemonine.

[15] R. Munier and M. Macheboeuf, *Bull. soc. chim. France*, 852 (1952).