one acetate, 1164-91-6; cholestanone dimethyl ketal, 16159-03-8; 17β-acetoxy-3-ethoxy-2-(5α-androstene), 16159-04-9; 17β-acetoxy-3-ethoxy-3-(5α-androstene), 16159-05-0; 3-ethoxy-3-cholestene, 16159-06-1.

Acknowledgment.—Assistance from Dr. Fortune Kohen and Dr. A. P. Shroff in obtaining and interpreting the nmr spectra was extremely helpful during this investigation.

Steroids. VIII. The Beckmann Rearrangement of 2-Oximinocholesta-4,6-dien-3-one. The Synthesis of Some 2,3-Secocholesta-4,6-dienes[1a]

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The structure of an unusual dimeric Beckmann rearrangement product (III) derived from 2-oximinocholesta-4,6-dien-3-one (I) has been elucidated. A number of 2,3-secocholesta-4,6-dienes have been synthesized from I, making use of the Beckmann rearrangement as the ring-cleavage step.

The Beckmann rearrangement has been employed in the synthesis of a wide variety of aza steroids from various simple saturated and unsaturated steroidal ketoximines.[2] The Beckmann rearrangement of steroidal α-oximino ketones has been much less thoroughly investigated. This reaction appears to have been examined only with 16-oximino 17-ketones[3] and with 2,4-bisoximino 3-ketones;[4] it serves as a useful route to 16,17-seco steroids[3] and 2,3-seco-A-nor steroids,[4] respectively. We now report the behavior of the conjugated α-oximino ketone, 2-oximinocholesta-4,6-dien-3-one,[1a] (I) under Beckmann rearrangement conditions.

As reported previously, oximino ketone I reacts with acetic anhydride in pyridine to give an acetate (II) which can be hydrolyzed back to I without rearrangement or ring cleavage.[1a] On the other hand, the reaction of I with tosyl chloride in pyridine afforded a crystalline product, mp 197–198°, which was not the tosylate of I. It was assigned the unusual dimeric structure III on the basis of the spectral and chemical evidence discussed below.

The dimeric formula $C_{54}H_{82}O_3N_2$ fitted well with the results of both elemental analysis and molecular weight determinations. The infrared spectrum of III showed carbonyl bands at both 5.70 and 5.97 μ, as well as a series of bands at 6.17, 6.23, and 6.33 μ attributable to conjugated olefinic and imine functions; significantly, no nitrile absorption in the 4.4–4.5-μ region was observed.

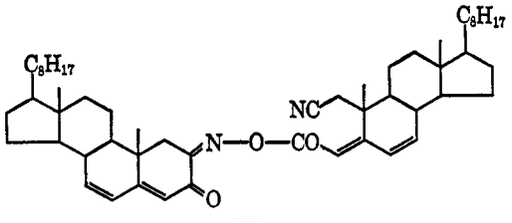
In the course of determining whether or not the dimer contained a readily reduced carbonyl group, it was allowed to react with sodium borohydride in methanol solution. Two crystalline products, mp 167 and 235°, were isolated in 41 and 37% yield, respectively, after preparative thin layer chromatography. It was soon shown that the reagent in this reaction was acting not as a reducing agent, but simply as a source of methoxide ion. The same products were obtained in approximately the same yields when dimer III was treated with a solution of sodium methoxide in methanol.

The product, mp 235°, was identified readily as the original oximino ketone I. The second product, mp 167°, analyzed for $C_{28}H_{43}O_3N$; it was assigned structure IV on the basis of its spectral and chemical properties. The infrared spectrum of IV showed an ester carbonyl at 5.78, a cyano group at 4.40, and conjugated olefin bands at 6.14 and 6.25 μ; no hydroxyl absorption in the 3-μ region was observed. The nmr spectrum of IV showed the methoxyl of the ester function as a singlet at τ 6.27, as well as a multiplet at 3.29–4.31 corresponding to three olefinic protons. Reaction of dimer III with sodium hydroxide yielded a mixture of oximino ketone I and the cyano acid V, mp 218°. Acid V was converted by diazomethane into the cyano ester IV.

The proposed mechanism for the conversion of oximino ketone I into the oxime imidate ester III, and fragmentation of III into I and IV by methoxide ion, is shown in Scheme I.

The interception of imino derivatives in the course of Beckmann rearrangements is well known.[5] An example of a Beckmann rearrangement in which an equivalent of unrearranged oxime is incorporated into the isolated product has been provided by Hill, who described the conversion of A into B shown in Scheme II.[6]

A rather analogous process can be envisaged for the Beckmann rearrangement of oximino ketone I to give a dimeric product of structure IIIa. The latter struc-



IIIa

(1) (a) Part VII: M. P. Cava, E. J. Glamkowski, and Q. A. Ahmed, *J. Org. Chem.*, **32**, 2644 (1967). (b) To whom all inquiries should be addressed: Department of Chemistry, Wayne State University, Detroit, Mich. 48202.

(2) (a) T. A. Jacobs and R. B. Brownfield [*J. Amer. Chem. Soc.*, **82**, 4033 (1960)] cover the literature up to 1960; (b) C. W. Shoppee and G. Kruger, *J. Chem. Soc.*, 3641 (1961); (c) C. W. Shoppee, G. Kruger, and R. N. Mirrington, *ibid.*, 1050 (1962); (d) C. W. Shoppee, R. E. Lack, and B. C. Newman, *ibid.*, 3388 (1964); (e) C. W. Shoppee, R. W. Killick, and G. Kruger, *ibid.*, 2275 (1962); (f) C. W. Shoppee, R. E. Lack, and S. K. Roy, *ibid.*, 3767 (1963); (g) C. W. Shoppee, R. E. Lack, R. N. Mirrington, and C. R. Smith, *ibid.*, 5868 (1965); (h) C. W. Shoppee, M. I. Akhtar, and R. E. Lack, *ibid.*, 3392 (1964); (i) N. J. Doorenbos and R. E. Havranek, *J. Org. Chem.*, **30**, 2474 (1965); (j) R. Mazur, *ibid.*, **28**, 248 (1963); (k) L. Knof, *Ann.*, **642**, 194 (1961); (l) J. A. Zderic and J. Iriarte, *J. Org. Chem.*, **27**, 1756 (1962); (m) P. Bladon and W. McMeekin, *J. Chem. Soc.*, 3504 (1961); (n) R. T. Blickenstaff and E. L. Foster, *J. Org. Chem.*, **26**, 5029 (1961); (o) H. Singh and V. V. Parashar, *Tetrahedron Lett.*, 983 (1966).

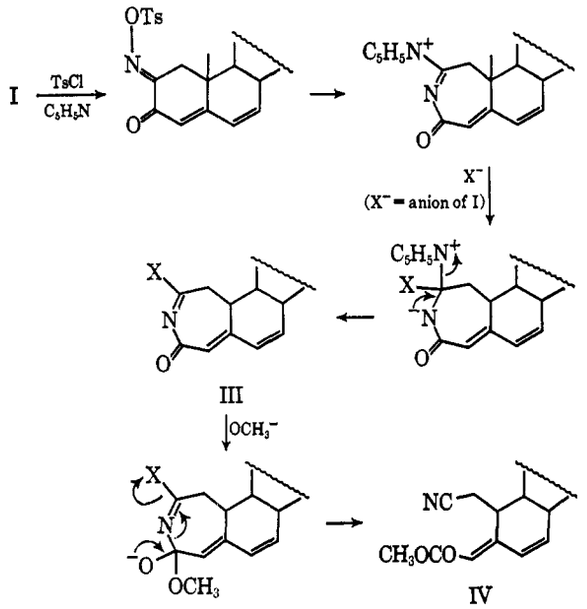
(3) (a) F. Litvan and R. Robinson, *J. Chem. Soc.*, 1997 (1938); and, more recently, (b) A. Hassner and I. H. Pomerantz, *J. Org. Chem.*, **27**, 1760 (1962).

(4) (a) M. P. Cava, E. J. Glamkowski, and P. M. Weintraub, *ibid.*, **31**, 2755 (1966); (b) G. Ohta, T. Takegoshi, K. Ueno, and M. Shimizu, *Chem. Pharm. Bull.* (Tokyo), **13**, 1445 (1965).

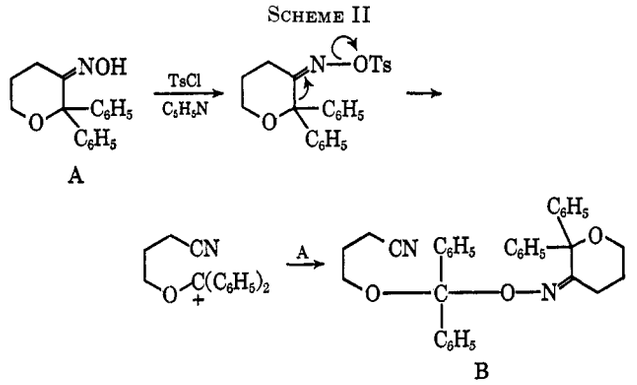
(5) For some examples, see W. Z. Heldt, *J. Amer. Chem. Soc.*, **80**, 5880 (1958), and references cited therein.

(6) R. K. Hill, *J. Org. Chem.*, **27**, 30 (1962).

SCHEME I



SCHEME II

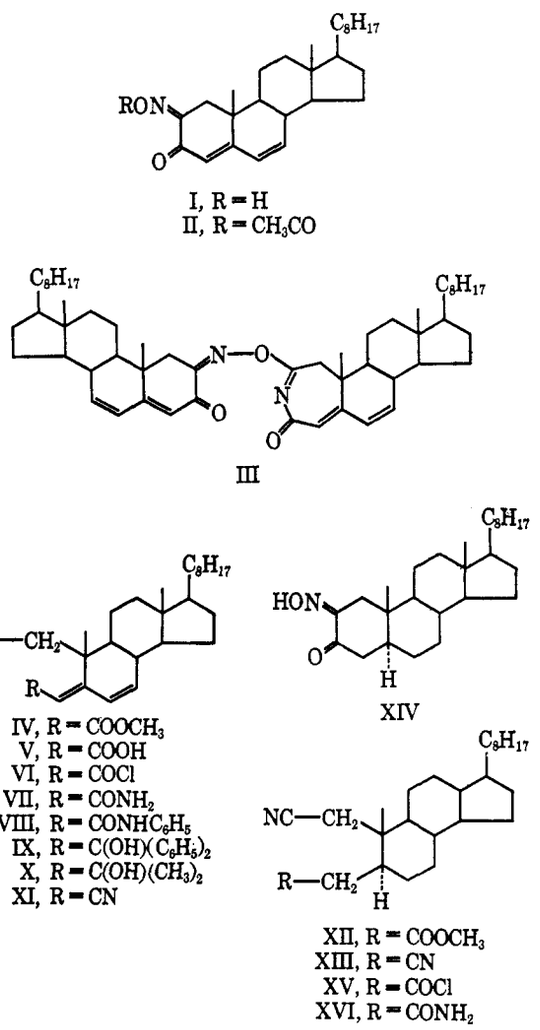


ture for the rearrangement product would be in accord with its transformation into compounds IV and V by base cleavage. It must be discarded in favor of III, however, since the infrared spectrum of the actual dimer unambiguously shows the absence of a cyano group in the molecule.

The reaction of oximino ketone I with thionyl chloride does not give the dimeric compound III. The product of second-order Beckmann cleavage, cyano acid chloride VI, is formed instead.[7] Although compound VI was not isolated in a state of purity, the crude material showed bands at 4.43 and 5.65 μ, characteristic of the cyano and the conjugated acid chloride functions, respectively. Furthermore, unpurified VI reacted with water and with methanol to give acid V and methyl ester IV, respectively, in yields based on I of well over 50%; no starting material was detected in these reactions.

Acid chloride VI was treated also with ammonia, aniline, phenylmagnesium bromide, and methylmagnesium bromide to give the corresponding 2,3-seco steroids (VII, VIII, IX, and X) in satisfactory yields. Dehydration of amide VII with refluxing thionyl chloride gave the dinitrile XI.

Cyano ester IV and dinitrile XI both underwent catalytic reduction in the presence of palladium to yield single crystalline tetrahydro derivatives (XII and XIII) in good yield. These compounds were shown to have the 5α configuration, resulting from delivery of hydrogen at the less hindered side of the molecule, by direct correlation with a cholestane derivative of known configuration at C-5. Thus, reaction of pure 2-oximinocholestan-3-one (XIV)[1a,8] with thionyl chloride gave the cyano acid chloride (XV), which was treated directly with sodium methoxide to give ester XII, identical with the reduction product of the unsaturated cyano ester IV. Similarly, the reaction of acid chloride XV with ammonia gave the saturated amide XVI; dehydration of XVI with thionyl chloride gave dinitrile XIII, identical with the reduction product of the unsaturated dinitrile XI.



Experimental Section[9]

Reaction of 2-Oximinocholesta-4,6-dien-3-one (I) with Tosyl Chloride in Pyridine.—A solution of oximino ketone I[1a] (3.00 g)

(7) The reaction of 1-nitroso-2-naphthol with phosphorous pentachloride to give *o*-cyanocinnamoyl chloride is closely analogous to this reaction: W. Borsche and W. Sander, *Ber.*, **47**, 2815 (1914).

(8) M. P. Cava, P. M. Weintraub, and E. J. Glamkowski, *J. Org. Chem.*, **31**, 2015 (1966).

(9) Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 237 spectrophotometer (potassium bromide disks). Ultraviolet absorption spectra were determined in 95% ethanol using a Perkin-Elmer Model 4000 Spectracord. Optical rotations were measured in chloroform solution, unless otherwise indicated. Elemental analyses were performed by Midwest Microlab, Inc., Indianapolis, Ind., and by Dr. A. Bernhardt, Mülheim, Germany. The statement that a solution was worked up on the usual manner should be taken to mean that it was washed successively with water and aqueous sodium chloride, then dried over anhydrous sodium sulfate, and finally evaporated to dryness on a steam bath with the aid of a rotary evaporator. The identity of products with authentic samples was checked by mixture melting point determinations and infrared spectral comparisons.

and tosyl chloride (4.50 g) in dry pyridine (50 ml) was stirred for 24 hr at room temperature. The reaction mixture was poured into cold water (500 ml) and the precipitated product was extracted into two 350-ml portions of ether. The ether extract was washed with aqueous sodium bicarbonate and worked up in the usual manner. Crystallization from ether–methanol gave the Beckmann dimer III (1.90 g, 63%), mp 195–197°. The pure dimer (1.83 g, 61%), mp 197–198°, was obtained by recrystallization from the same solvent mixture: $[\alpha]^{25}D$ −131° (*c* 2.62); λ_{max} 5.70, 5.97, 6.17, 6.23, and 6.30 μ; λ_{max} (sh) 220 mμ (ε 20,900) and 308 mμ (ε 30,200).

Anal. Calcd for $C_{54}H_{82}O_3N_2$: C, 80.59; H, 9.95; N, 3.48; S, 0.00. Found: C, 80.54; H, 9.91; N, 3.42; S, 0.00.

Sodium Hydroxide Cleavage of Beckmann Dimer III. 2,3-Secocholesta-4,6-diene-2-nitril-3-oic Acid (V).—A solution of dimer III (0.100 g) in 1:1 ether–methanol (50 ml) was combined with 10% methanolic sodium hydroxide (15 ml), and the mixture was stirred for 20 hr at room temperature. The solution was evaporated, diluted with water (20 ml), and extracted with three 20-ml portions of ether. The ether extract was worked up in the usual manner to give crude oximino ketone I (0.041 g, 40%), mp 221–231°; recrystallization from ethanol afforded pure I (0.035 g, 34%), mp 235° dec, identical with an authentic sample.

Acidification (HCl) of the alkaline aqueous phase from the hydrolysis fraction gave crude acid V (0.040 g). Two recrystallizations from ethanol gave pure V (0.031 g, 31%): mp 218°; $[\alpha]^{26}D$ −32.3° (*c* 1.12, tetrahydrofuran); λ_{max} 3.80, 4.40, 5.89, 6.10, and 6.22 μ; λ_{max} 259 mμ (ε 16,400).

Anal. Calcd for $C_{27}H_{41}O_2N$: C, 78.78; H, 10.04; N, 3.40. Found: C, 78.83; H, 10.15; N, 3.37.

Sodium Methoxide Cleavage of Beckmann Dimer III. Methyl Ester (IV) of Acid V.—A solution of dimer III (0.100 g) and sodium methoxide (0.013 g) in 1:1 ether–methanol (50 ml) was stirred under nitrogen for 20 hr at room temperature. Evaporation of the solvent gave a residue which was shaken with water and ether. Work-up of the ether extract in the usual manner gave a residue which was separated into two constituents by preparative tlc on a silica gel plate (1:1 benzene–ethyl acetate eluent). The slower moving band (R_f 0.59) afforded oximino ketone I (0.035 g, 34%), identical with an authentic sample. The faster moving band (R_f 0.91) gave crystals of methyl ester IV (0.045 g, 47%): mp 166° from ether–methanol; $[\alpha]^{26}D$ −3.3° (*c* 1.44); λ_{max} 4.44, 5.78, 6.12, and 6.25 μ; λ_{max} 268 mμ (ε 18,600).

Anal. Calcd for $C_{28}H_{43}O_2N$: C, 79.01; H, 10.18; N, 3.29. Found: C, 79.01; H, 10.37; N, 3.25.

When the reaction described above was run using sodium borohydride (0.100 g) instead of sodium methoxide, the same work-up yielded oximino ketone I (37%) and ester IV (41%) as the only products found.

Ester IV was also prepared (77% yield, recrystallized) by reaction of acid V with diazomethane in ether.

Cleavage of 2-Oximinocholesta-4,6-dien-3-one (I) to Acid Chloride VI.—Thionyl chloride (4 ml) was added to a solution of oximino ketone I (0.200 g) in methylene chloride (5 ml) and the mixture was stirred for 24 hr at room temperature. The solvent and excess thionyl chloride were then removed completely by evaporation under reduced pressure. The quantity of crude acid chloride VI obtained in this way was used directly in each of the reactions described below.

Reactions of Acid Chloride VI. A. Reaction of VI with Sodium Methoxide.—Acid chloride VI was stirred at room temperature for 15 min with a solution of sodium methoxide (0.10 g) in methanol (10 ml). The mixture was then diluted with water (10 ml) and the resulting precipitate was crystallized from 1:1 ether–methanol to give crude methyl ester IV (0.173 g, 96%), mp 157–164°. Recrystallization afforded the pure ester IV (0.160 g, 77%), mp 167°, identical with material prepared as described above.

B. Reaction of VI with Water.—Acid chloride VI was stirred with water for 5 hr at room temperature. Crystallization of the precipitate from ethanol afforded acid V, mp 218°, identical with material prepared from dimer III.

C. Reaction of VI with Ammonia. 2,3-Secocholesta-4,6-diene-2-nitril-3-amide (VII).—Dry gaseous ammonia was bubbled through a solution of acid chloride VI in dry ether (20 ml) at 0° for 10 min. The precipitate was filtered and washed well with ether. The combined filtrate and ether washings were worked up in the usual manner. The resulting crystalline residue (0.131 g) was recrystallized from petroleum ether (30–60°) to give amide VII (0.120 g, 65%): mp 209°; $[\alpha]^{25}D$ −3.2° (*c* 3.63); λ_{max} 3.01, 3.15, 4.51, 5.94, and 6.05 mμ; λ_{max} 249 mμ (ε 20,650).

Anal. Calcd for $C_{27}H_{42}ON_2$: C, 78.97; H, 10.31; N, 6.82. Found: C, 78.78; H, 10.35; N, 6.81.

D. Reactions of VI with Aniline. N-Phenyl-2,3-secocholesta-4,6-diene-2-nitril-3-amide (VIII).—Acid chloride VI was stirred with redistilled aniline (2 ml) for 30 min at room temperature. The mixture was then heated on a steam bath for 15 min, cooled, and diluted with water. Crystallization of the precipitate from acetone afforded shining colorless crystals of VIII (0.130 g, 60%): mp 215°; $[\alpha]^{25}D$ −11.0° (*c* 1.43); λ_{max} 3.20, 4.45, 5.97, 6.15, 6.25, 6.51, 13.29, and 14.49 μ; λ_{max} 225 mμ (ε 7364) and 286 mμ (ε 21,030).

Anal. Calcd for $C_{33}H_{46}ON_2$: C, 81.43; H, 9.53; N, 5.76. Found: C, 81.44; H, 9.56; N, 5.78.

E. Reaction of VI with Phenylmagnesium Bromide. 3,3-Diphenyl-3-hydroxy-2,3-secocholesta-4,6-diene-2-nitrile (IX).—An ethereal solution containing phenylmagnesium bromide (0.265 g) was added to a solution of acid chloride VI in dry ether (10 ml), and the mixture was refluxed for 45 min. The reaction mixture was then decomposed by stirring for 2 hr at room temperature with saturated aqueous ammonium chloride (50 ml). The mixture was filtered, the precipitate being washed well with ether. The combined ether solutions were worked up in the usual manner to give, after crystallization from ether–petroleum ether, white rosettes of alcohol IX (0.150 g, 56%): mp 215°; $[\alpha]^{26}D$ +70.9° (*c* 1.18, tetrahydrofuran); λ_{max} 249 mμ (ε 20,640).

Anal. Calcd for $C_{39}H_{51}ON$: C, 85.19; H, 9.35; N, 2.55. Found: C, 84.99; H, 9.09; N, 2.64.

F. Reaction of VI with Methylmagnesium Bromide. 3,3-Dimethyl-3-hydroxy-2,3-secocholesta-4,6-diene-2-nitrile (X).—The reaction of acid chloride VI with methylmagnesium bromide (0.160 g) was carried out as in part E above, except that a 90-min reaction time was used; the work-up was similar. The crude product (0.070 g) was chromatographed in ether over neutral alumina (grade IV, 1 g) to give colorless crystals of alcohol X (0.056 g, 30%): mp 145°; $[\alpha]^{26}D$ +7.2° (*c* 1.42); λ_{max} 2.91, 4.43, 6.06, and 6.11 μ; λ_{max} 241 mμ (ε 16,360).

Anal. Calcd for $C_{29}H_{47}ON$: C, 81.82; H, 11.13; N, 3.29. Found: C, 82.02; H, 11.19; N, 3.32.

Dehydration of Amide VII. 2,3-Secocholesta-4,6-diene-2,3-dinitrile (XI).—Amide VII (0.200 g) was refluxed for 1 hr with thionyl chloride (0.6 ml). Evaporation of the excess thionyl chloride left a residue which was taken up in ether and worked up in the usual manner. The resulting crude dinitrile was triturated with petroleum ether to remove a brown impurity, and then crystallized twice from ether–petroleum ether to give the pure dinitrile (0.077 g, 40%): mp 116°; $[\alpha]^{26}D$ +6.5° (*c* 0.65); λ_{max} 4.43, 4.52, 6.14, and 6.33 μ; λ_{max} 265 mμ (ε 20,280).

Anal. Calcd for $C_{27}H_{40}N_2$: C, 82.59; H, 10.27; N, 7.14. Found: C, 83.04; H, 10.15; N, 7.01.

Methyl 2-3-Secocholestane-2-nitril-3-oate (XII). A. By Reduction of Ester IV.—A solution of ester IV (0.195 g) in pure ethyl acetate (30 ml) was stirred with 10% palladium-on-charcoal catalyst (0.10 g) for 7 min in an atmosphere of hydrogen (atmospheric pressure); during this time 2 molar equiv of hydrogen were absorbed. Work-up in the usual manner gave a product which was separated from a small amount of an oily polar impurity (R_f 0.11) by preparative tlc (silica, 1:1 benzene–methanol; R_f of major product = 0.85). Crystallization from methanol–ether gave the reduced ester XII as white rosettes (0.160 g, 81%): mp 91°; $[\alpha]^{25}D$ +23.6 (*c* 1.90); λ_{max} 4.42 and 5.72 μ; no uv maxima above 210 mμ.

Anal. Calcd for $C_{28}H_{47}O_2N$: C, 78.27; H, 11.03; N, 3.26. Found: C, 78.50; H, 10.70; N, 3.14.

B. From 2-Oximinocholestan-3-one (XIV) by Beckmann Cleavage.—Thionyl chloride (4 ml) was added to a solution of oximino ketone XIV[1a,6] (0.200 g) in methylene chloride (5 ml), and the mixture was stirred for 24 hr at room temperature. The solution was then evaporated and kept under reduced pressure until all thionyl chloride was removed. A solution of sodium methoxide (0.10 g) in methanol (10 ml) was added. After a short time the neutral product was worked up in the usual manner to give the cyano ester XII (0.176 g, 85%), mp 91–91.5°, identical with material obtained from ester IV as described above (section A).

2,3-Secocholestane-2,3-dinitrile (XIII). A. By Reduction of Dinitrile XI.—A solution of dinitrile XI (0.093 g) in pure ethyl acetate (20 ml) was stirred with 10% palladium-on-charcoal catalyst (0.05 g) for 23 min under hydrogen at atmospheric pressure;

2 molar equiv of hydrogen were absorbed. Work-up in the usual manner gave a product which was separated from a small amount of an oily polar impurity (R_f 0.12) by preparative tlc (silica, 1:1 benzene–ethyl acetate, R_f (major product) 0.90). Crystallization from petroleum ether gave nitrile XIII (0.067 g, 71%), mp 116°. Recrystallized XIII had mp 118–119°; $[\alpha]^{26}D$ +19.9° (*c* 1.00); λ_{max} 4.42, 6.81, 6.91, 7.20, and 7.25 μ.

Anal. Calcd for $C_{27}H_{44}N_2$: C, 81.75; H, 11.18; N, 7.06. Found: C, 81.87; H, 11.25; N, 6.94.

B. From 2-Oximinocholestan-3-one (XIV) by Beckmann Cleavage.—Oximino ketone XIV (0.200 g) was cleaved with thionyl chloride exactly as described for the synthesis of cyano ester XII. The resulting acid chloride XV was dissolved in methylene chloride (20 ml) and the solution was saturated with gaseous ammonia at 0°. Work-up in the usual manner, followed by crystallization from 1:1 chloroform–petroleum ether, gave brilliant colorless crystals of the cyano amide XVI (0.170 g, 86%): mp 261°; $[\alpha]^{26}D$ +33.6° (*c* 1.03); no uv maxima above 210 mμ.

Anal. Calcd for $C_{27}H_{46}ON_2$: C, 78.20; H, 11.18; N, 6.76. Found: C, 78.30; H, 11.02; N, 6.80.

A solution of amide XVI (0.100 g) in thionyl chloride (3 ml) was refluxed for 18 hr. Evaporation of the excess thionyl chloride, followed by crystallization of the residue from petroleum ether, afforded dinitrile XIII (0.060 g, 66%), mp 118–119°, identical with material obtained from dinitrile XI as described above (section A).

Registry No.—I, 13341-55-4; III, 16426-16-7; IV, 16426-17-8; V, 16426-18-9; VII, 16426-19-0; VIII, 16426-20-3; IX, 16426-21-4; X, 16426-22-5; XI, 16426-23-6; XII, 16426-24-7; XIII, 16426-25-8; XVI, 16426-26-9.

Acknowledgment.—This investigation was supported by Public Health Service Research Grants CY-4498 and CA-04498, National Institutes of Health.

The Alkaloids of *Cassytha americana* (*C. filiformis* L.)[1]

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Received January 10, 1968

Thirteen alkaloids have been isolated from Brazilian *Cassytha americana* (*C. filiformis* L., Lauraceae). The structures of 1,2,9,10-bismethylenedioxy-3-methoxydibenzo[*de,g*]quinolin-7-one and 1,2,9,10-bismethylenedioxydibenzo[*de,g*]quinolin-7-one are suggested for the new oxoaporphine bases cassamedine and cassameridine. The plant also yielded ten previously known aporphine bases.

Recent investigations have shown the parasitic genus *Cassytha* (Lauraceae) to be a rich source of aporphine alkaloids. Aporphines have been reported from the following species: *Cassytha filiformis*,[2] *C. melantha*,[3] *C. glabella*,[3] *C. pubescens*,[4] and *C. racemosa*.[5] The vine, *C. filiformis*, is a species which is widely distributed throughout the tropics. Plant material from Taiwan yielded the new aporphine cassyfiline (I),[1,6] whereas material from New Guinea and Australia gave cassythidine (III).[2] We now report the results of an investigation of the alkaloids of *Cassytha americana* of Brazilian origin. After the study was essentially complete, we learned that *C. americana* was apparently synonomous with *C. filiformis*.[7] Our work has resulted in the isolation of thirteen tertiary bases, two of which, cassamedine (IV) and cassameridine (V), are new oxoaporphines.

Separation of the Bases.—As described in detail in the Experimental Section, the bases were separated first into alkali-soluble and alkali-insoluble fractions. The latter were further fractionated by differential acid buffer extraction and chromatography. The yields of pure compounds were generally low, owing to experimental difficulties encountered in the separation steps. Thin layer chromatography indicated, however, the absence of significant quantities of alkaloids other than those identified.

The Alkali-Soluble Aporphines.—The largest portion of the total alkaloids was alkali soluble and consisted of a mixture of cassyfiline (I), actinodaphnine (VI), and N-methylactinodaphnine (VII). Compound VI was the major component of the mixture, although an efficient procedure for its separation was not devised. Compound VII has been described as a transformation product of VI,[8] but it had not been encountered as a naturally occurring alkaloid prior to the completion of our investigation. Very recently, however, it has been reported to be the major alkaloid of both *Cassytha melantha* and *C. glabella* and has been given the name cassythicine.[3]

The Alkali-Insoluble Aporphines.—The alkali-insoluble alkaloids consisted mainly of a mixture of seven aporphines. These included the cryptophenolic bases launobine (VIII) and bulbocapnine (IX), as well as the closely related nonphenolic bases O-methylcassyfiline (II), cassythidine (III), dicentrine (X), neolitsine (XI), and (+)-nornuciferine (XII). Compound XII could be separated from the natural alkaloid mixture only in the form of (+)-nuciferine (XIII) after N-methylation with formaldehyde and sodium borohydride. Thin layer chromatography showed definitely that no XIII was present before N-methylation.

(1) The plant material used in this investigation was collected near Porto Seguro in the State of Bahia, Brazil, by Dr. Aparicio Duarte whose assistance is gratefully acknowledged. A reference specimen, R. B. 130345, has been filed in the Herbarium of the Botanical Garden at Rio de Janeiro.

(2) (a) M. Tomita, S. T. Lu, and S. J. Wang, *J. Pharm. Soc. Jap.*, **85**, 827 (1965); (b) S. R. Johns, J. A. Lamberton, and A. A. Sioumis, *Aust. J. Chem.*, **19**, 297 (1966).

(3) S. R. Johns, J. A. Lamberton, and A. S. Sioumis, *ibid.*, **19**, 2339 (1966).

(4) S. R. Johns, J. A. Lamberton, and A. A. Sioumis, *ibid.*, **19**, 2331 (1966).

(5) S. R. Johns, J. A. Lamberton, and A. A. Sioumis, *ibid.*, in press.

(6) Alkaloid I is named cassyfiline in ref 1a and cassythine in ref 1b in which an independent isolation and structure determination are described. In view of the earlier publication of ref 1a, the name cassyfiline will henceforth be used in this paper.

(7) The preferred binomial is *Cassytha filiformis* L. with *C. americana* Nees. and *C. capillaris* F.-Vill. occasionally given as synonyms.

(8) M. Tomita, M. Kozuka, E. Nakagawa, and Y. Mitsunori, *J. Pharm. Soc. Jap.*, **83**, 763 (1963).