The infrared spectra (KBr pellet) of the two preparations were identical and had a band at 12.3 μ not present in the infrared spectrum of the 1α-epimer. The 1α-epimer, on the other hand, absorbed at 12.5 μ. These bands probably are the result of C–H out-of-plane deformation at position 6.

2β-Acetoxy-4-androstene-3,17-dione (XIII).—A solution of 51 mg. of 2β-hydroxy-4-androstene-3,17-dione in 1 ml. of pyridine and 1 ml. of acetic anhydride was allowed to stand at room temperature for 1.5 hours. It then was diluted with ice and water and the precipitate was separated by filtration. Crystallization of this material from aqueous acetone yielded 42.5 mg. of 2β-acetoxy-4-androstene-3,17-dione, m.p. 157–158°, $[\alpha]D$ −5.9°, λ_{max} 243 mμ (ϵ 15,300).

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19. Found: C, 73.47; H, 8.04.

2α-Acetoxy-4-androstene-3,17-dione (XIV).—The 2β-acetoxy-4-androstene-3,17-dione, obtained from 48 mg. of 2β-hydroxy-4-androstene-3,17-dione by the procedure described above, was heated under reflux for 4 hours in a solution of 2.00 g. of anhydrous potassium acetate in 10 ml. of acetic acid. The excess acetic acid was removed under vacuum, the residue was diluted with 40 ml. of water, and the resulting suspension was extracted with 50 ml. of ether in three portions. The ether solution was washed with water, dilute aqueous sodium carbonate, then water. The ether solution then was dried over sodium sulfate and evaporated to dryness. Crystallization of the residue (34 mg.) from acetone–cyclohexane, then aqueous acetone gave 13.8 mg. of 2α-acetoxy-4-androstene-3,17-dione (XIV), m.p. 209–211°, $[\alpha]D$ +147°, λ_{max} 239.5 mμ (ϵ 15,500). The reported constants[23b] are m.p. 209–210°, $[\alpha]D$ +146° ($CHCl_3$), λ_{max} 241 mμ (log ϵ 4.21).

CHICAGO, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES, CALIF.]

The Introduction of Oxygen and Nitrogen into the B Ring of the Steroid Nucleus[1]

BY THOMAS L. JACOBS AND ROBERT B. BROWNFIELD

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The degradation of cholesterol to suitable intermediates open in the B ring was accomplished by the ozonization of 7-ketocholesteryl acetate to give either 5-keto-5,7-seco-6-nor-3-cholesten-7-oic acid or 3β-acetoxy-5-keto-5,7-seco-6-norcholestan-7-oic acid depending upon the method of isolation employed. Treatment of either of the δ-keto acids with ethanolic ammonia afforded 6-aza-2,4-cholestadien-7-one. The reaction of 5-keto-5,7-seco-6-norcholestan-7-oic acid with ethanolic ammonia under pressure or with benzylamine gave 6-aza-4-cholesten-7-one and the corresponding N-benzylated enamine lactam, respectively. Treatment of these enamine lactams with N-bromosuccinimide resulted in C_4-vinyl rather than C_3-allyl bromides. Lithium aluminum hydride reduction of 6-aza-4-cholesten-7-one and its hydrogenation product, 6-aza-cholestan-7-one, gave 6-aza-5-cholestene and 6-aza-cholestane, respectively. 6-Oxacholestan-7-one was obtained by sodium borohydride reduction of methyl 5-keto-5,7-seco-6-norcholestan-7-oate. 6-Oxacholestane was prepared by the cyclodehydration of 5,7-seco-6-norcholestane-5β,7-diol.

The synthetic modification of naturally occurring steroids during the past decade has resulted in the discovery of a number of potent, highly specific, commercially important therapeutic agents. Excepting for the 19-nor- and 18,19-bisnor-series, none of these has involved modification of the basic carbon skeleton of the steroid nucleus itself. Actual examples of the substitution of nitrogen or oxygen for carbon in the otherwise intact ring system are comparatively few. Although no attempt will be made here to name individually all of the oxa- and aza-steroids in the literature, it does seem appropriate to give a reasonably complete list of general types. These are: 2-aza-,[2] 3-aza-,[2,3] 3-aza-A-homo-,[3–5] 3,4-diaza-,[6] 3-oxa-A-homo-,[4,5,7] 3-oxa-A-nor-,[6,8] 4-aza-,[3,9–12a] 4-aza-A-homo-,[3] 4-oxa-,[5,9,13–17] 4-oxa-A-homo-,[4,5,18] 6-oxa-B-homo-,[19] 7-aza-B-homo-,[20] 7-oxa-B-homo-,[20,21] 7a-aza-B-homo-,[20,22] 7a-oxa-B-homo-,[20,23] 12a-aza-C-homo-,[24] 15-aza-D-homo-,[25] 16-aza-,[26] 16-aza-D-homo-,[25] 17-aza-D-homo-,[25,27,28] 17a-aza-D-homo-[27,29,30] and 17a-oxa-D-homo-.[16,31] Inspection of this list re-

(1) Taken from a Dissertation submitted by Robert B. Brownfield to the University of California, Los Angeles, in partial fulfillment of the requirements for the Ph.D. in Chemistry, August, 1958.

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(3) S. Hara, *Pharm. Bull. (Japan)*, **3**, 209, 297 (1955).

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(12a) M. Uskoković and M. Gut, *Helv. Chim. Acta*, **42**, 2258 (1959).

(13) (a) R. B. Turner, *ibid.*, **69**, 726 (1947); (b) **72**, 579 (1950).

(14) A. H. Soloway and D. K. Fukushima, *ibid.*, **75**, 5442 (1953).

(15) C. C. Bolt, *Rec. trav. chim.*, **70**, 940 (1951).

(16) A. Salamon, *Z. physiol. Chem.*, **272**, 61 (1942).

(17) See ref. 2 for references to other 4-oxa-steroids.

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(20) S. Hara, *J. Pharm. Soc. (Japan)*, **78**, 1030 (1958).

(21) A. Windaus and O. Dalmer, *Ber.*, **52**, 162 (1919); A. Windaus, *ibid.*, **53**, 488 (1920); C. W. Shoppee, *J. Chem. Soc.*, 1032 (1948); H. Wieland and E. Dane, *Z. physiol. Chem.*, **210**, 268 (1932), and **212**, 41 (1932); A. Windaus and J. Brunken, *ibid.*, **140**, 52 (1924).

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(23) H. Heusser, A. Segre and Pl. A. Plattner, *ibid.*, **31**, 1183 (1948); K. Block, *ibid.*, **36**, 1611 (1953).

(24) R. H. Mazur, THIS JOURNAL, **81**, 1454 (1959); British Patent 815,692 (Oct. 7, 1957).

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(28) R. D. H. Heard, M. T. Ryan and H. I. Bolker, *J. Org. Chem.*, **24**, 172 (1959).

(29) S. Kaufmann, THIS JOURNAL, **73**, 1779 (1951).

(30) R. H. Mazur, U. S. Patent 2,738,350 (March 13, 1956).

(31) H. Levy and R. P. Jacobsen, *J. Biol. Chem.*, **171**, 71 (1947); R. P. Jacobsen, *ibid.*, **171**, 61 (1947); R. P. Jacobsen, G. M. Picha and H. Levy, *ibid.*, **171**, 81 (1947); G. M. Picha, THIS JOURNAL, **74**, 703 (1952); J. Fried, R. W. Thoma and A. Klingsberg, *ibid.*, **75**, 5764 (1953).

veals that most of the types represent steroid analogs in which one of the rings of the carbon skeleton has been expanded from a 6- to a 7-membered ring or in the case of ring D from a 5- to 6-membered ring. Further, it is apparent that no steroid analog has been prepared in which a six-membered B-ring contains oxygen or nitrogen substituted for carbon. This paper describes the preparation of several 6-oxa- and 6-aza-steroids of the cholestane series.

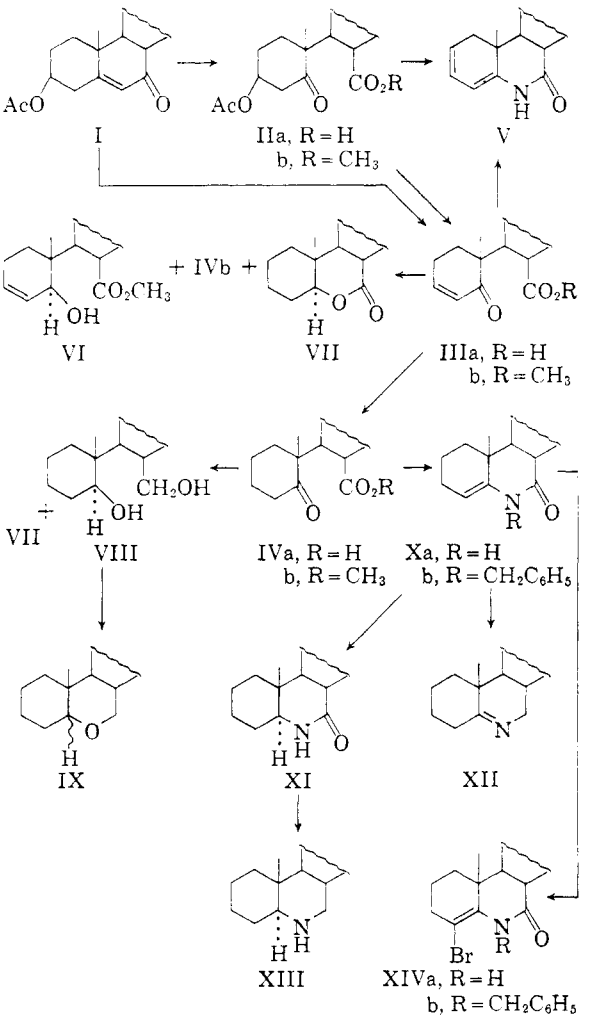
The ozonization of α,β-unsaturated keto steroids has resulted in steroidal δ-keto acids open in the $A^{6,8,10-15}$ and B^{32} rings. Since the ozonization of cyclic α,β-unsaturated ketones proceeds with the elimination of the α-carbon atom and since the removal of one carbon atom in the B ring was desirable, the ozonization of 7-ketocholesteryl acetate (I) was investigated.

Ozonization of I followed by oxidative decomposition of the ozonide with hydrogen peroxide gave crystalline 3β-acetoxy-5-keto-5,7-seco-6-norcholestan-7-oic acid (IIa) if care was taken to exclude base. This acid readily loses acetic acid; on titration, 2 equivalents of alkali was required and 5-keto-5,7-seco-6-nor-3-cholesten-7-oic acid (IIIa) was isolated from the titrated solution. When the ozonization product was isolated by the usual sodium hydroxide extraction only IIIa was obtained.

Both IIa and IIIa gave the corresponding methyl esters IIb and IIIb with diazomethane, but an attempted chromatographic purification of IIb on "neutral" alumina gave only IIIb.

Hydrogenation of IIIb gave crystalline methyl 5-keto-5,7-seco-6-norcholestan-7-oate (VIb). Saponification of IVb gave 5-keto-5,7-seco-6-norcholestan-7-oic acid (IVa). The preparation of IVa by the ozonization of 5-cholesten-7-one has been reported[32] but a comparison of physical properties was not possible since the investigators were interested in IVa only as a degradation intermediate. Because IVa proved to be a key intermediate it was more expedient to carry out the reactions I → IIIa → IIIb → IVb → IVa without the isolation of crystalline intermediates. In this way IVa was obtained in an over-all yield of 27% based on 7-ketocholesteryl acetate (I). The yield of crude acids in the initial ozonization step (I → IIIa) was improved considerably by treatment of the crude neutral fraction with periodic acid.[13]

The conversion of one or more of these cholestane derivatives to 6-oxacholestanes was next investigated. Sodium borohydride reduction of IVb at room temperature gave the δ-lactone VII in 58.5% yield; in addition 40.5% of the starting ester was recovered as the free acid IVa. At refluxing temperature VII was obtained in 21.5% yield and the same yield of the more completely reduced 5,7-seco-6-norcholestane-5β,7-diol (VIII) also was obtained. Reduction of a vicinal keto-carbethoxy compound to the corresponding diol by sodium borohydride has been reported.[33] Finally, the diol VIII was converted to 6-oxacholestane (IX) by treatment with hydrogen chloride in benzene. Although the B ring ether IX was not completely characterized, its infrared spectrum was consistent with the proposed structure.



Early in the work the keto ester IIIb was treated with sodium borohydride in methanol with the intention of obtaining 6-oxa-3-cholesten-7-one. Several such experiments resulted in inconsistent yields of VII, the saturated keto ester IVb and in one case a low yield of methyl 5β-hydroxy-5,7-seco-6-nor-3-cholesten-7-oate (VI). In no case was 6-oxa-3-cholesten-7-one obtained. The course of this apparently anomalous reaction of sodium borohydride is not clear. Few precedents for the reduction of a double bond α,β- to a carbonyl function either with or without the simultaneous reduction of the carbonyl group by sodium borohydride are readily found in the literature.[34-36]

The availability of the δ-keto acid IVa provided a suitable intermediate for the preparation of a 6-azacholestane compound. The method used by Bolt[11] for the formation of A ring δ-lactams, that is, reduction of the corresponding δ-oximino acid followed by spontaneous ring closure, was of no value

(32) W. G. Dauben and K. H. Takemura, THIS JOURNAL, **75**, 6302 (1953).

(33) N. J. Leonard, K. Conrow and R. W. Fulmor, *J. Org. Chem.*, **22**, 1445 (1957).

(34) C. Djerassi and W. Rittel, THIS JOURNAL, **79**, 3528 (1957).

(35) C. Djerassi, F. W. Donovan, S. Burstein and R. Mauli, *ibid.*, **80**, 1972 (1958).

(36) F. Sondheimer, M. Velasco, E. Batres and G. Rosenkranz, *Chemistry & Industry*, 1482 (1954).

here in view of the unreactivity of the keto acids IIIa and IVa and their methyl esters IIIb and IVb under a variety of oxime-forming reaction conditions. Success, however, was achieved by another route. When an ethanolic solution of the δ-keto acid IVa saturated with ammonia was heated in a sealed tube, 6-aza-4-cholesten-7-one (Xa) resulted. The vinylog of Xa, 6-aza-2,4-cholestadien-7-one (V), was obtained upon similar treatment of IIIa or IIa.

The reintroduction of an oxygen function at C_3 in the enamine lactam Xa was investigated. Using conditions suitable for allylic bromination, Xa and N-bromosuccinimide gave 6-aza-4-bromo-4-cholesten-7-one (XIVa) in high yield. The same compound was obtained when Xa was treated with bromine in carbon tetrachloride. The vinyl disposition of the bromine atom in XIVa is supported by its unreactivity toward a wide variety of solvolytic reagents ranging from aqueous acetone to silver nitrate in refluxing ethanol as well as toward the powerful dehydrohalogenating agent, refluxing collidine. The very remote possibility that XIVa was actually an N-bromoenamine lactam was dispelled when the N-benzylenamine lactam Xb (prepared from IVa) gave an ill defined but equally inert bromo derivative, presumably XIVb, upon treatment with N-bromosuccinimide.

The ultraviolet spectra of the enamine lactams V, Xa, Xb and XIVa are worthy of note because ultraviolet data for structurally analogous chromophores are not to be found in the literature. Two examples of less spacially rigid acylated enamines are available, however, and are listed in Table I along with the enamine lactams described herein. The close correspondence of maxima positions and intensities of the enamine lactams Xa, Xb and XIVa with those of the two "model" compounds is to be expected in view of the non-ambiguity of the structural assignments. The substituents on the basic acylated enamine chromophore exhibit the expected small bathochromic shifts (*e.g.*, bromo, 5 mμ, and benzyl, 3 mμ). The rather large bathochromic shift observed in the vinylogous enamine lactam V (65 mμ) represents not only the extension of conjugation to a seven center system but also the introduction of a homoannular diene.

TABLE I[c]

	Solvent	λ_{max}, mμ	log ε
6-Aza-2,4-cholestadiene-7-one (V)	EtOH	299	4.11
6-Aza-4-cholestene-7-one (Xa)	EtOH	234	4.11
N-Benzyl-6-aza-4-cholestene-7-one (Xb)	EtOH	237	4.05
6-Aza-4-bromo-4-cholestene-7-one (XIVa)	EtOH	239	4.04
N-Vinylpyrrolidone[a]	HOH	235	4.13
3β-Acetoxy-17-acetylamino-5,16-androstadiene[b]	EtOH	240	3.82

[a] G. Oster and E. H. Immergut, THIS JOURNAL, 76, 1393 (1954). [b] G. Rosenkranz, O. Mancera, F. Sondheimer and C. Djerassi, *J. Org. Chem.*, 21, 520 (1956). [c] Several ring enamine lactams have been reported recently (ref. 12a); these include 17β-acetoxy-4-aza-5-androsten-3-one and related compounds having hydroxyl, aceto, or C_8H_{17} instead of acetoxy in position 17. All show λ_{max} 233 mμ, log ε 4.12–4.14.

Catalytic hydrogenation of the enamine lactam Xa in glacial acetic acid gave 6-azacholestane-7-one (XI) in 85% yield. Although rear-side addition of hydrogen to give an α-C_5-hydrogen (A/B *trans*) is to be expected on the basis of steric considerations, other arguments will be presented below to confirm the assignment of XI to the cholestane series. Finally lithium aluminum hydride reduction of XI gave 6-azacholestane (XIII). Although the infrared spectrum of XIII showed no N–H stretching band, it was consistent in every other respect with the expected reduction product. It is quite possible that the band due to N–H stretching in XIII is weak enough and shifted just enough to be obscured by the strong C–H stretching band. The total transparency of the amine in the region 2500 to 1480 cm.$^{-1}$ reflects the absence of the lactam carbonyl as was expected. The amine also was characterized satisfactorily as its picric acid salt.

In an alternate approach to the conversion of Xa to XIII, the lithium aluminum hydride reduction of Xa was carried out, but the product was 6-aza-5-cholestene (XII) rather than the expected 6-aza-4-cholestene. The infrared spectrum of XII showed no N–H stretching band but did show a moderately strong sharp band at 1650 cm.$^{-1}$ which can be attributed to >C=N— stretching. Meyers[37] reported the range 1653 to 1639 cm.$^{-1}$ for >C=N— in several 1-pyrrolines, while 1650 cm.$^{-1}$ was reported for the >C=N— grouping contained in a seven-membered ring.[38] The ultraviolet spectrum also supports the structure shown for XII; whereas enamines generally show maxima in the region 230–240 mμ,[39] XII showed no maximum.

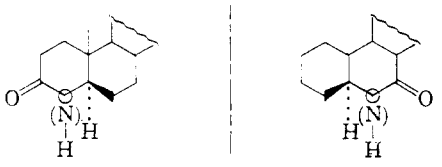
Up to now the ring B oxa- and aza-steroids described herein have been assigned the *allo* (A/B *trans*) configuration without justification other than the assumed back-side attack of hydride ion at C_5 in the δ-keto ester IVb and of hydrogen at C_4 and C_5 in the enamine lactam Xa. Since the method of molecular rotation differences has been used successfully to distinguish between 4-oxacoprostan-3-one (XIX) and 4-oxacholestan-3-one (XV)[40] (thus corroborating the original work of Turner[13b]) it was of interest to see whether assignments could be made for the lactam XI and the lactone VII by the use of this method. Table II lists three A ring steroid lactones and two A ring steroid lactams obtained from the literature. The steroids assigned the *allo* (A/B *trans*) configuration (XV, XVI, XVII and XVIII) were originally prepared *via* chemical conversions generally assumed to give the most thermodynamically stable products, that is, sodium–alcohol reductions of δ-keto acids or δ-oximino acids. The intermediate reduction products (not isolated) therefore should have contained equatorial hydroxy or amino groups at C_5 and hence would have cyclized to the corresponding A/B *trans*-lactones or lactams, respectively. It will be observed that the ΔM_D values [M_D (lactone or lactam) − M_D (parent δ-keto acid)] for the A ring lactones and lactams assigned the A/B *trans* configuration (cholestane or androstane) are always positive while the corre-

(37) A. I. Meyers, *J. Org. Chem.*, **24**, 1233 (1959).
(38) J. H. Boyer and F. C. Cantor, THIS JOURNAL, **77**, 3287 (1955).
(39) N. J. Leonard and D. M. Locke, *ibid.*, **77**, 437 (1955).
(40) W. Klyne, *J. Chem. Soc.*, 3072 (1953).

TABLE II

	M_D	M_D' (parent δ-keto acid)	ΔM_D ($M_D - M_D'$)	A/B
4-Oxacholestane-3-one (XV)[13b,15]	+313°[13b]	+137.5°[13b]	+175.5°	*trans*
4-Oxa-17β-hydroxy-17α-methylandrostane-3-one (XVI)[15]	+189[15]	+ 51.2[15]	+137.8	*trans*
4-Azacholestane-3-one (XVII)[11]	+170[11]	+137.5[13b]	+ 32.5	*trans*
4-Aza-17β-hydroxyandrostane-3-one (XVIII)[11]	+ 96[11]	− 92.5[6]	+188.5	*trans*
4-Oxacoprostane-3-one (XIX)[13b]	+ 71.1[13b]	+137.5[13b]	− 66.4	*cis*
6-Oxacholestane-7-one (VII)	− 67	+376	−443	*trans*
6-Azacholestane-7-one (XI)	+ 81	+376	−295	*trans*

sponding ΔM_D value for the lactone XIX assigned the A/B *cis* configuration is negative. Since the ΔM_D value reflects only the asymmetry about C_5, one may visualize C_5 in the A ring lactones XV and XVI and lactams XVII and XVIII as being "epimeric" with respect to C_5 in the B ring lactone VII and the lactam XI if the latter compounds are of the A/B *trans* configuration. Accordingly, since



the above A/B *trans* A ring lactones and lactams exhibit positive ΔM_D values, VII and XI should be expected to exhibit negative ΔM_D values if they are of the A/B *trans* configuration. Since both VII and XI exhibit negative ΔM_D values they satisfy the requisite "epimeric" condition and have been assigned the A/B *trans* (cholestane) configuration. These arguments are entirely consistent with Hudson's well known lactone rules with respect to the absolute configuration about the asymmetric alkyl carbon of the sugar acid lactones. It necessarily follows that since the hydroxy ester VI and the diol (VIII) were obtained by the same hydride reduction which produced the lactone VII, the C_5-hydroxyl groups in VI and VIII are β (or equatorially) oriented and hence are named 5,7-secocholestanes. The conversion of the lactam XI to the amine XIII by hydride reduction would not be expected to alter the configuration about C_5 and hence XIII has been assigned to the cholestane series.

Experimental

Melting points are uncorrected and were determined in a Silicone-bath with total-immersion Anschütz thermometers unless otherwise noted. The notation "block" indicates that the melting point was determined on a Fisher–Johns melting point apparatus. All optical rotations were taken in chloroform solution. Infrared spectra were obtained with a Perkin–Elmer model 21 spectrophotometer equipped with sodium chloride optics. Analyses were carried out by Miss Heather King.

5-Keto-5,7-seco-6-nor-3-cholesten-7-oic Acid (IIIa).—A solution of 7-keto-cholesteryl acetate (I) (5.20 g., 11.7 mmoles) in 50 ml. of glacial acetic acid and 50 ml. of ethyl acetate was placed in an ozonization tube suspended in an ice–salt-bath. Ozone was passed through the solution for 2 hours at a rate of about 0.024 mole per hr. Water, 20 ml., and 30% hydrogen peroxide, 3 ml., then were added and the solution was transferred to a separatory funnel and shaken vigorously. After the reaction mixture had stood at room temp. for 24 hr. an equal volume of ether was added, and the solution was exhaustively extracted with water and finally once with a saturated sodium chloride solution. The combined washes were extracted once with ether and the ethereal solutions were combined and extracted with five 25-ml. portions of 5% sodium hydroxide solution. The combined alkaline extracts were acidified with 150 ml. of 5% hydrochloric acid solution and the organic phase which separated was taken up in ether. (In one experiment the acid separated from the aqueous solution in an easily filterable form and needed only to be recrystallized from ether-pentane.) The ethereal solution was washed with water, dried and evaporated to give 2.67 g. of slightly yellow oil. Upon standing overnight the acidic oil solidified; trituration with pentane produced a white solid. After standing in the refrigerator for several days in contact with pentane, the mixture was filtered to produce 600 mg. (1.49 mmoles, 12.7% yield) of white crystalline solid, m.p. 157–159° (block). Three recrystallizations from ether–pentane gave an analytical sample of 5-keto-5,7-seco-6-nor-3-cholesten-7-oic acid (IIIa), m.p. 164–165°, $\lambda_{max}^{ethanol}$ 227 mμ (log ε 3.89), $[\alpha]^{27}D$ +81 ± 1°; infrared (8% in carbon tetrachloride): carboxyl broadening of C–H stretching band, 1702 cm.$^{-1}$ (carboxyl carbonyl) with a shoulder at 1725 cm.$^{-1}$ and finally a shoulder at 1678 cm.$^{-1}$ (α,β-unsaturated ketone carbonyl).

Anal. Calcd. for $C_{26}H_{42}O_3$ (402.60): C, 77.56; H, 10.52. Found: C, 77.53; H, 10.74.

The methyl ester IIIb was prepared in ether by reaction of IIIa with diazomethane. It was purified by chromatography on neutral alumina but remained as a viscous, colorless oil, yield 62%; infrared (8% in carbon tetrachloride): 1730 (carbomethoxy carbonyl), 1681 cm.$^{-1}$ (α,β-unsaturated carbonyl).

Methyl 5-Keto-5,7-seco-6-norcholestan-7-oate (IVb).—Hydrogenation of 2.67 g. (6.4 mmoles) of IIIb in ethyl acetate over Adams catalyst gave an oil (hydrogen uptake 87.5 % of theor.) which crystallized from 80% alcohol to give IVb in 71.5% yield. Three crystallizations from aqueous alcohol gave an analytical sample, m.p. 71.2–72.6°, $[\alpha]^{25}D$ +84.9 ± 0.3°; infrared (8% in carbon tetrachloride): 1728 (carbomethoxy carbonyl) and 1703 cm.$^{-1}$ (saturated ketone carbonyl).

Anal. Calcd. for $C_{27}H_{46}O_3$ (418.64): C, 77.46; H, 11.08. Found: C, 77.59; H, 10.81.

5-Keto-5,7-seco-6-norcholestan-7-oic Acid (IVa).—If the oil obtained above directly from the hydrogenation of IIIb was saponified with aqueous ethanolic potassium hydroxide, IVa, m.p. 185° (block), could be isolated in 67% yield based on IIIb (crystallization induced by addition of petroleum ether (b.p. 66–68°) and cooling). Three recrystallizations from ether–pentane gave an analytical sample, m.p. 188.6–189.2°, $[\alpha]^{25}D$ +93 ± 2°; infrared (8% in chloroform): typical acid broadening of the C–H stretching band and 1701 cm.$^{-1}$ (broad, ketone and carboxyl carbonyls).

Anal. Calcd. for $C_{26}H_{44}O_3$ (404.61): C, 77.17; H, 10.96. Found: C, 76.91; H, 10.98.

Compound IVa also was isolated in 27% yield based on 7-ketocholesteryl acetate (I) when the ozonization was performed as follows and the remaining steps carried through without isolation of intermediates. Ozonized oxygen (concentration ~ 3%) was passed through a solution of 6.06 g. (13.7 mmoles) of I in 140 ml. of 1:1 acetic acid–ethyl acetate for 2 hr. at ice–salt temperature. The cold solution was treated with 20 ml. of water containing 3 ml. of 30% hydrogen peroxide and left at room temp. for 24 hr. A large quantity of water was added and the solution was exhaustively extracted with ether. The acidic components of the reaction product were removed from the ethereal solution by extraction with 5% sodium hydroxide solution. After acidification of the alkaline extracts the acidic organic material was taken up in ether and the ethereal solution was

washed with water, dried and evaporated to give 4.3 g. of yellow oily acids.

The ethereal solution of neutral material was washed with water, dried and evaporated to give 2.73 g. of neutral material as a yellow oil. The residue was taken up in 30 ml. of glacial acetic acid and after standing at room temp. for 36 hr. was filtered to remove a small amount of crystalline solid. To the clear filtrate was added 2.5 g. of periodic acid in 10 ml. of 80% acetic acid and the solution was stirred at room temperature for 5 hours. After the removal of a small amount of crystalline material, the solution was diluted largely with water and the reaction product was taken up in ether. The acidic material was extracted from the ethereal solution with 5% sodium hydroxide solution and the alkaline extracts were combined and acidified with concentrated hydrochloric acid. The organic phase was taken up in ether and the ethereal solution was washed with water, dried and evaporated to give 1.75 g. of acidic material as a yellow oil.

The combined acidic fractions in ether were treated with an ethereal solution of diazomethane prepared in the usual way from nitrosomethylurea, 4.22 g. (41.0 mmoles). The usual isolation procedure gave 5.2 g. of neutral product as a yellow oil which as a solution in pentane was adsorbed on 130 g. of neutral alumina. The column was eluted with pentane, various mixtures of pentane–ether and finally ether. The eluted fractions were combined and evaporated to give IIIb which was hydrogenated and saponified as above.

3β-Acetoxy-5-keto-5,7-seco-6-norcholestan-7-oic Acid (IIa).—7-Ketocholesteryl acetate (I) (21.0 g., 47.5 mmoles) in three 7-g. batches, each dissolved in 140 ml. of glacial acetic acid–ethyl acetate (1:1), was ozonized at ice–salt temperature. Each batch was ozonized for 90 min., diluted with 25 ml. of water and 5 ml. of 30% hydrogen peroxide, heated on the steam-bath for 0.5 hr. and finally allowed to stand at room temp. for 48 hr. The combined solutions, containing no solid, were concentrated under reduced pressure on the steam-bath to a small volume and then diluted with 70 ml. of methanol and enough water to produce turbidity. The solid which separated as white needles amounted to 2.4 g. The filtrate was diluted with water and extracted with ether. The ethereal solution was washed well with water, dried over magnesium sulfate, filtered, concentrated, diluted with pentane and seeded with some of the above solid whereupon three more crops of the same material were obtained, 4.5 g., m.p. 154.0–155.5°. The infrared spectra of each of the four crops in chloroform were identical and consistent with 3β-acetoxy-5-keto-5,7-seco-6-norcholestan-7-oic acid (IIa). Total yield of the unpurified acid was 6.95 g. (15 mmoles, 32%). Three crystallizations from ether–petroleum ether (b.p. 66–68°) gave an analytical sample, m.p. 159.0–159.5°, $[\alpha]^{26}D$ +71 ± 2°; infrared (6% in chloroform): carboxyl broadening of C–H stretching band 1728 (shoulder, acetate carbonyl), 1710 (carboxyl and ketone carbonyls) and 1245 cm.$^{-1}$ (acetate).

Anal. Calcd. for $C_{28}H_{46}O_5$ (462.65): C, 72.69; H, 10.02. Found: C, 72.96; H, 9.82.

Titration of a 72.6-mg. sample of the acid in hot ethanol–water (1:1) required 3.164 ml. of 0.0994 *N* sodium hydroxide; neut. equiv. calcd. 231, found 231. This value corresponds to the titration of the free carboxylic acid followed by the elimination and titration of acetic acid. The acid recovered from the titration, m.p. 165–167° (block), $\lambda_{max}^{ethanol}$ 227 mμ, was identical with 5,7-seco-6-nor-3-cholesten-5-on-7-oic acid (IIIa).

Methyl 3β-acetoxy-5-keto-5,7-seco-6-norcholestan-7-oate (IIb) was prepared by treating IIa in anhyd. ether with an ethereal solution of diazomethane, removing the ether and crystallizing from methanol, m.p. 85° (block), yield 67%. Three recrystallizations from aqueous ethanol gave an analytical sample, m.p. 91.0–92.0°, $[\alpha]^{26}D$ +67 ± 2°; infrared (6% in carbon tetrachloride): 1733 (acetate carbonyl and carbomethoxy carbonyl), 1714 (ketone carbonyl) and 1240 cm.$^{-1}$ (acetate).

Anal. Calcd. for $C_{29}H_{48}O_5$ (476.67): C, 73.07; H, 10.15. Found: C, 73.37; H, 9.89.

6-Oxacholestan-7-one (VII) was prepared by adding 1 g. (2.4 mmoles) of IVb in 15 ml. of anhyd. isopropyl alcohol to a suspension of 181 mg. (4.8 mmoles) of sodium borohydride in 30 ml. of the same solvent. The suspension (clear after 0.5 hr.) was stirred at room temp. for 11 hr. and concentrated to a small volume. One gram of sodium hydroxide in aqueous alcohol was added and the solution was boiled, cooled and acidified with concd. hydrochloric acid (gas evolution). The solution was diluted with water and exhaustively extracted with ether. After removal of acidic material with 5% sodium hydroxide, the ethereal solution was washed, dried and concentrated to give 457 mg. of white solid, m.p. 127–131° (block) after one recrystallization from methanol. The alkaline extract was acidified, extracted with ether and the extract partitioned again with 5% sodium hydroxide to yield an additional 85 mg. of neutral material (m.p. 131–133° from methanol). The final alkaline extracts were acidified to yield 392 mg. of IVa, m.p. 197–198° (block) after one recrystallization from petroleum ether (b.p. 66–68°); yield of crude acid 40.5%. The total yield of neutral material VII was 58.5%.

Compound IVa also was reduced with sodium borohydride in methanol (15 min. at room temp.); acidification of the alkaline reduction mixture with 5% hydrochloric acid gave crude VII directly, m.p. 128° (block), 48% yield. Three crystallizations from methanol gave an analytical sample, m.p. 133.2–134.0°, $[\alpha]^{23.5}D$ −17.2 ± 0.5°; infrared (8% in chloroform). no ketone carbonyl; δ-lactone carbonyl at 1726 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{44}O_2$ (388.61): C, 80.35; H, 11.41. Found: C, 80.21; H, 11.60.

5,7-Seco-6-norcholestane-5β,7-diol (VIII) was obtained along with VII when the reduction of 2 g. of IVb was carried out in isopropyl alcohol with 2-hr. refluxing and 19 hr. at room temp. The neutral material obtained after removal of the acidic portion with 5% sodium hydroxide as described above was a mixture of broad m.p. It was refluxed for 45 min. with 2 g. of potassium hydroxide in 45 ml. of aqueous alcohol (10 to 35 by volume) and after standing at room temp. for 8 hr. the solution was diluted with water; a crystalline solid separated, was collected, washed and air-dried to give 406 mg. (21.5% yield) of VIII, m.p. 163° (block). Two recrystallizations from acetone and one from petroleum ether (b.p. 66–68°) gave an analytical sample of VIII, m.p. 160.2–161.0°; infrared (8% in chloroform): 3608 (free–OH), 3396 cm.$^{-1}$ (associated–OH) and no carbonyl absorption.

Anal. Calcd. for $C_{26}H_{48}O_2$ (392.64): C, 79.53; H, 12.32. Found: C, 79.80; H, 11.90.

The aqueous alkaline filtrates from above were combined and acidified with concentrated hydrochloric acid and the organic material was extracted into ether. Extraction of the ethereal solution with 5% sodium hydroxide produced no acidic material. The ethereal solution of the neutral material was washed with water, dried and finally evaporated. The residue crystallized from methanol giving 6-oxacholestan-7-one (VII), 779 mg. (1.03 mmoles, 21.5% yield), m.p. 130–131° (block), in two crops.

6-Oxacholestane (IX).—5,7-Seco-6-norcholestan-5β,7-diol (VIII, 335 mg., 0.855 mmole) in 10 ml. of dry benzene was treated with anhyd. hydrogen chloride at room temp. for 15 min. The solvent was removed under reduced pressure leaving a slightly yellow oil. Infrared (8% in carbon tetrachloride): no hydroxyl or carbonyl absorption; 1134, 1085 and 1045 cm.$^{-1}$ (tetrahydropyran type ether absorption). The product was chromatographed on neutral alumina (activity I/II), eluting with pentane and 50% ether-in-pentane. The colorless viscous oil (247 mg., 0.660 mmole, 77.2% yield) could not be induced to crystallize.

Methyl 5β-Hydroxy-5,7-seco-6-nor-3-cholesten-7-oate (VI).—The methyl ester obtained from 1.5 g. (3.7 mmoles) of IIIa was reduced with 250 mg. (7 mmoles) of sodium borohydride in methanol (room temp., 14 hr.). The solution was acidified with concd. hydrochloric acid, diluted with much water and extracted with ether. The ether extract was washed, dried and concentrated to yield an oil which deposited a little 6-oxacholestan-7-one (VII) when taken up in acetone. The crystals were separated, the filtrate concentrated and the residual oil chromatographed on neutral alumina (activity I/II) in pentane. Fractional elution with 40% ether–60% pentane allowed separation of 712 mg. (1.7 mmoles, 45% yield) of methyl 5-keto-5,7-seco-6-norcholestan-7-oate (IVb), m.p. 65 to 70° depending on the fraction. Two recrystallizations from methanol and one from aqueous ethanol gave pure IVb, m.p. 71.2–72.6°. Elution with ether gave material which would not crystallize, but further elution with ether containing a little methanol gave 60 mg. (0.143 mmole, 3.8% yield) of VI as a white solid, m.p. 180° (block). Several recrystallizations from ether gave an ana-

ytical sample, m.p. 193.6–194.2°; infrared (8% in chloroform): 3577 (free hydroxyl), 3416 (associated hydroxyl) and 1726 cm.$^{-1}$ (carbomethoxy carbonyl).

Anal. Calcd. for $C_{27}H_{46}O_3$ (418.64): C, 77.46; H, 11.08. Calcd. for $C_{27}H_{48}O_3$ (420.66): C, 77.09; H, 11.50. Found: C, 77.23; H, 10.85.

6-Aza-4-cholesten-7-one (Xa).—Ammonia was bubbled through 250 mg. (0.62 mmole) of IVa for 45 min. at 0° in 20 ml. of 96% ethanol in a heavy-walled glass tube. The tube was cooled to −78°, sealed under reduced pressure, and heated for 13 to 27 hr. at 105–115°. After slow cooling, finally in ice, the product separated in long, fine, white needles. The tube was opened and a total of 200 mg. (0.52 mmole, 84% yield) of Xa was obtained in several crops after successive concentrations on a steam-bath. The product was insoluble in alkali. Three recrystallizations from methanol gave an analytical sample, m.p. 168.0–169.5°, $\lambda_{max}^{ethanol}$ 234 mμ (log ε 4.108), $[\alpha]^{23}D$ +86 ± 1°; infrared (8% in chloroform): 3375 (lactam N–H stretching), 3170 (lactam N–H stretching) and 1653 cm.$^{-1}$ (lactam carbonyl).

Anal. Calcd. for $C_{26}H_{43}ON$ (385.61): C, 80.89; H, 11.24; N, 3.63. Found: C, 80.81; H, 11.00; N, 3.83.

6-Aza-2,4-cholestadien-7-one (V).—The reaction of IIIa with ammonia was carried out as with IVa, but the product was isolated by concentrating the ethanolic solution, diluting with water and extracting with ether. Two runs (400 and 412 mg.) of IIIa gave a total of 677 mg. of a yellow, amorphous solid by evaporation of the ether. This material was placed on 40 g. of neutral alumina (activity I/II) in chloroform; elution with pentane or ether failed, but ether containing 2% methanol gave 187 mg. (0.49 mmole, 24% yield) of V. Further elution with increasing concentrations of methanol in ether gave mixtures which were discarded; V was recrystallized three times from 95% ethanol to give colorless rods, m.p. 188–189° dec. (introduced into the bath near the melting point), $\lambda_{max}^{ethanol}$ 299 mμ (log ε 4.11), $[\alpha]^{27}D$ +49 ± 3°; infrared (8% in chloroform): 3173 (lactam N–H stretching), 3027 (lactam N–H stretching), 1661 (lactam carbonyl) and 1586 cm.$^{-1}$ (conjugated unsaturation).

Anal. Calcd. for $C_{26}H_{41}ON$ (383.60): C, 81.40; H, 10.77; N, 3.65. Found: C, 81.30; H, 10.89; N, 3.79.

6-Aza-4-bromo-4-cholesten-7-one (XIVa) was obtained when 100 mg. (0.26 mmole) of Xa in 30 ml. of petroleum ether (b.p. 66–68°) was refluxed with 51 mg. (0.29 mmole) of N-bromosuccinimide for 5 min. with the heat and light of a photospot lamp (G. E. RSP-2). The suspension was filtered while warm and the filtrate concentrated (reduced pressure) to give 132 mg. of an oil that solidified on standing. Chromatography on neutral alumina (activity I/II) from pentane gave no eluate until ether was used alone, followed by 10% methanol in ether. The product (102 mg., 0.22 mmole, 85% yield) gave a positive Beilstein test. Three recrystallizations from aqueous acetone gave an analytical sample of the bromide XIVa, m.p. 134.0–135.5°, $\lambda_{max}^{ethanol}$ 239 mμ (log ε 4.040), $[\alpha]^{24}D$ +90 ± 2°; infrared (8% in carbon tetrachloride): 3370 (lactam N–H stretching), 1681 (lactam carbonyl) and 692 cm.$^{-1}$ (vinyl bromide).

Anal. Calcd. for $C_{26}H_{42}ONBr$ (464.52): C, 67.22; H, 9.11; N, 3.02. Found: C, 67.43; H, 9.14; N, 3.17.

N-Benzyl-6-aza-4-cholesten-7-one (Xb).—Acid IVa (500 mg., 1.24 mmoles) in 10 ml. of freshly distilled benzylamine was refluxed for 5 hours. After standing at room temp. overnight the solution was diluted with water, the water-insoluble material extracted into ether, and the ethereal solution washed repeatedly with water and then 5% hydrochloric acid to remove the last traces of benzylamine. Extraction of the ethereal solution with 5% sodium hydroxide and acidification of the alkaline extracts gave essentially no acidic organic material. The ethereal solution was washed well with water and saturated saline solution, dried (magnesium sulfate) and evaporated to give 644 mg. of yellowish oil which solidified when methanol was added. Recrystallization from methanol gave 486 mg. (1.02 mmoles, 82.8% yield) of fine white needles in three crops. Two recrystallizations from methanol gave an analytical sample of Xb, m.p. 136.3–137.3°, $\lambda_{max}^{ethanol}$ 237 mμ (log ε 4.053), $[\alpha]^{24}D$ +107 ± 1°; infrared (8% in carbon tetrachloride): 1665 (lactam carbonyl), 1640 cm.$^{-1}$ (double bond).

Anal. Calcd. for $C_{33}H_{49}ON$ (475.73): C, 83.31; H, 10.38; N, 2.94. Found: C, 83.53; H, 10.24; N, 3.20.

6-Azacholestan-7-one (XI).—Adams catalyst, 49 mg., in 40 ml. of glacial acetic acid was prereduced in a quantitative hydrogenation apparatus and 6-aza-4-cholesten-7-one (Xa), (599 mg., 1.55 mmoles) in 20 ml. of acetic acid was introduced into the system. Since the uptake of hydrogen at near atmospheric pressure was slow, an additional 24 mg. of platinum oxide in 10 ml. of acetic acid was introduced and the stirred suspension was kept under hydrogen at slightly greater than atmospheric pressure for an over-all total of 24 hours. The catalyst was removed and the filtrate diluted with water whereupon white solid began to form. The solid was removed by filtration, taken up in ether and the ethereal solution was washed with 5% sodium bicarbonate solution, water, dried and filtered. Upon successively concentrating the ethereal filtrate there were obtained five crops of white needles ranging in melting point from 235–238° (block) to 246° (block), totaling 512 mg. (1.32 mmoles, 85% yield). Three recrystallizations from acetone gave an analytical sample of 6-azacholestan-7-one (XI), m.p. 238.6–239.2°, $[\alpha]^{27}D$ + 21 ± 1°; infrared (8% in chloroform): 3397 and 3180 (lactam N–H stretching) and 1640 cm.$^{-1}$ (lactam carbonyl).

Anal. Calcd. for $C_{26}H_{45}ON$ (387.63): C, 80.56; H, 11.70. Found: C, 80.79; H, 11.56.

6-Azacholestane (XIII).—6-Azacholestan-7-one (XI, 595 mg., 1.535 mmoles) in a Soxhlet cup was continuously extracted with a refluxing solution of lithium aluminum hydride, 300 mg., in *ca.* 80 ml. of dioxane (freshly distilled from lithium aluminum hydride). After refluxing for 19 hr., 6 ml. of water was added dropwise and the resulting suspension was refluxed for an additional 0.5 hour. The hot suspension was filtered through Celite and the filter pack was washed well with hot dioxane. About one-third of the solvent was removed *in vacuo*, the concentrate was diluted largely with water and the aqueous dioxane mixture was exhaustively extracted with ether. After washing with water and drying over anhyd. magnesium sulfate, the ethereal solution was evaporated to give 518 mg. of slightly yellow oil which solidified upon standing. The product in pentane was adsorbed on 15 g. of neutral alumina (activity I/II) and the column was eluted in 15-ml. fractions with pentane, mixtures of ether in pentane and finally ether to give 20 fractions of colorless oil, 370 mg., all of which solidified upon standing. An early fraction recrystallized from aqueous acetone, m.p. 71° (block), and a later fraction recrystallized in the same way, m.p. 68° (block), showed no melting point depression upon admixture. Three recrystallizations from aqueous acetone gave an analytical sample of 6-azacholestane (XIII), m.p. 68.5–70.0° (Kofler hot-stage), $\lambda_{max}^{ethanol}$ only weak "end absorption", $[\alpha]^{25}D$ +19.1°; infrared (3% in carbon tetrachloride): no N–H stretching band, no bands in the >C=O, >C=N– or >C=C< regions.

Anal. Calcd. for $C_{26}H_{47}N$(373.65): C, 83.57; H, 12.68; N, 3.75. Found: C, 83.67; H, 12.42; N, 4.02.

The picrate of 6-azacholestane was formed by melting together, over a low flame, 20 mg. of the amine and 37 mg. of picric acid. The product which solidified upon cooling was recrystallized twice from 95% ethanol to give an analytical sample, m.p. 197–199° (Kofler hot-stage).

Anal. Calcd. for $C_{42}H_{50}N_4O_7$ (602.75): C, 63.76; H, 8.36; N, 9.30. Found: C, 63.99; H, 8.37; N, 9.13.

6-Aza-5-cholestene (XII).—6-Aza-4-cholestene-7-one (Xa) (1.12 g., 2.9 mmoles), in 40 ml. of anhyd. ether was added in a slow stream to a stirred suspension of 510 mg. (13.4 mmoles) of lithium aluminum hydride in 25 ml. of anhyd. ether. While being protected from atmospheric moisture, the mixture was refluxed with stirring for 9 hr. Water was added slowly until the inorganic salts coagulated to a gelatinous mass. The supernatant ethereal solution was drawn off and the residue was washed with several small portions of dry ether. The combined ethereal solutions were further dried over anhyd. magnesium sulfate and then evaporated to give 1.04 g. of colorless oil which solidified upon standing. Trituration of the product with cold acetone gave white solid, m.p. 89–90° (block).

A small amount of the solidified oil was taken up in a small volume of 96% ethanol and treated dropwise with a saturated ethanolic solution of picric acid until the volume of the original solution had been doubled. Brief heating on the steam-bath followed by ice cooling gave the picrate. Three recrystallizations from 96% ethanol afforded an analytical sample, m.p. 157–158° (block).

Anal. Calcd. for $C_{32}H_{48}N_4O_7$ (600.74): C, 63.97; H, 8.05; N, 9.33. Found: C, 64.01; H, 8.16; N, 9.12.

The purified picrate, 140 mg., was taken up in ether and the yellow ethereal solution was washed with three small portions of aqueous ethanolamine[41] (*ca.* 5% v./v. ethanolamine). The combined yellow aqueous extracts were backwashed with two small portions of ether and the combined, colorless ethereal solutions were washed with water, saturated saline solution, dried (magnesium sulfate) and finally evaporated to give 65 mg. of colorless oil which solidified upon standing. Recrystallization from aqueous acetone afforded an analytical sample of 6-aza-5-cholestene (XII), m.p. 94.0–95.5° (Kofler hot-stage), $\lambda_{max}^{ethanol}$ none, $[\alpha]^{25}D$ −73.8; infrared (8% in carbon tetrachloride): no N–H stretching band, 1650 cm.$^{-1}$ (>C=N-stretching).

Anal. Calcd. for $C_{26}H_{45}N$ (371.63): C, 84.02; H, 12.21. Found: C, 84.15; H, 12.27.

(41) L. Goodman, A. Benitez, C. D. Anderson and B. R. Baker, THIS JOURNAL, **80**, 6582 (1958).

[CONTRIBUTION FROM THE MCPHERSON CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY, COLUMBUS 10, OHIO

The Synthesis of 8-Hydroxy-1-keto-4-methyl-1,2,3,5,6,7-hexahydronaphthalene[1]

BY MELVIN S. NEWMAN AND ARLEN B. MEKLER[2]

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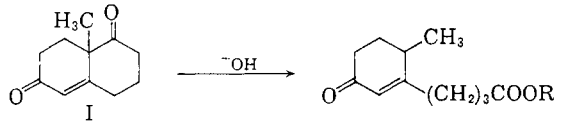
The conversion of 1,6-diketo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (I) to 8-hydroxy-1-keto-4-methyl-1,2,3,5,6,7-hexahydronaphthalene (III) by means of sodium methoxide in methanol is described; III forms a stable copper chelate with ease.

In connection with another problem, we wish ed to prepare a quantity of methyl γ-(6-methyl-3-keto-1-cyclohexen-1-yl)-butyrate (IIb). Since it was known[3] (and confirmed by us) that treatment of 1,6-diketo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (I) with aqueous alkali affords γ-(6-methyl-3-keto-1-cyclohexen-1-yl)-butyric acid (IIa), we sought to prepare IIb directly from I by treatment with sodium methoxide.

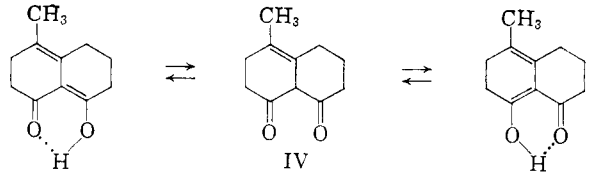


I

IIa, R = H
b, R = CH_3

When Compound I was treated with one equivalent of sodium methoxide in absolute methanol, the expected conversion to IIb was effected only in part. In addition there was obtained in over 90% yield a liquid compound, III, $C_{11}H_{14}O_2$, isomeric to I, which lacked absorption in the 3 and 5–6 μ regions.[4] The new compound absorbed at 233 and 344 mμ (log E 4.14 and 3.48, respectively) and formed a copper chelate derivative when treated with cupric acetate.

These facts suggested that III was best represented by the formulas III–IV–V.



III IV V

This formulation was supported by the following findings. Reduction of III with lithium aluminum hydride, followed by aromatization of the reduced product by heating with palladium-on-charcoal, afforded 1-methylnaphthalene in high yield. The lack of infrared absorption in the 5–6 μ region indicates that the diketonic form, IV, is present in minute amount, if at all. A study of the n.m.r. spectrum[5] indicated that either III or V are suitable structures but that it was not possible to distinguish between the two. Similarly, the ultraviolet absorption spectrum was of no aid in distinguishing between the two because of a lack of similar structures for comparison.[6] We believe our compound is best represented by structure 8-hydroxy-1-keto-4-methyl-1,2,3,5,6,7-hexahydronaphthalene (III) since treatment with excess methylmagnesium iodide followed by aromatization yielded almost pure 1,4-dimethylnaphthalene.

The crude product obtained from reaction of III with methylmagnesium iodide afforded a red 2,4-dinitrophenylhydrazone in high, but not exactly determined, yield. The red color indicates that the derivative is that of 5,8-dimethyl-8-hydroxy-1-keto-1,2,3,4,5,6,7,8-octahydronaphthalene (VIII), but no further structure proof was attempted.

When a solution of crude III was refluxed in xylene solution for 36 hours, a small amount of 8-keto-4-methyl-5,6,7,8-tetrahydro-1-naphthol (VI) was produced. This result, however, was not always obtained as all samples of crude III did not yield VI on similar treatment. Reduction of VI afforded 4-methyl-5,6,7,8-tetrahydro-1-naphthol[7] (VII).

The conversion of I to III (etc.), an intramolecular transacylation, by sodium methoxide is readily explained as shown.

(1) This work is taken from the Ph.D. Thesis of A.B.M., Ohio State University, 1959.

(2) Holder of a Charles F. Kettering Foundation Fellowship, 1956–1957, U. S. Industrial Co. Fellowship, 1957–1958, and Allied Chemical Co. Fellowship, 1958–1959. This work was also supported in part by funds donated to the Chemistry Department by the E. I. du Pont de Nemours Co.

(3) N. L. Wendler, H. L. Slates and M. Tishler, THIS JOURNAL, **73**, 3816 (1951).

(4) On treatment with sodium methoxide, IIb, prepared by acid-catalyzed esterification of IIa, affords III in high yield.

(5) We thank Dr. G. V. D. Tiers of the Minnesota Mining and Manufacturing Co., St. Paul, Minn., for this determination and interpretation of the result.

(6) The only other 1,8-diketohydronaphthalene structure known to us is 1,8-diketodecahydronaphthalene (also undoubtedly completely enolized); see H. Stetter and U. Milbers, *Ber.*, **91**, 977 (1958).

(7) R. B. Woodward and T. Singh, THIS JOURNAL, **72**, 494 (1950). We thank Dr. Woodward for sending us a sample which proved identical to VII.