methyl N-(*trans*-2-iodocyclohexane)carbamate, 1199-15-1; phenyl N-(*trans*-2-iodocyclohexanecarbamate, 7480-11-7; methyl N-(*trans*-2-iodocycloheptane), 7480-12-8; methyl N-(*trans*-2-iodocyclooctane)carbamate, 7480-13-9; methyl N-(*cis*-2-iodocyclododecane)carbamate, 7492-93-5; **9**, 7480-14-0; **10**, 7480-15-1; **12**, 7480-16-2; **6**, 7480-17-3; **16**, 7480-18-4; **8a**, 7540-56-9; **8c**, 7480-19-5; **8b**, 7492-91-3; methyl N-(2-iodo-1-phenylpropane)carbamate, 7480-20-8; **1**, 7540-57-0; N-phenylcarbamoyl-1,2-iminocyclohexane, 4714-51-6; 1-(N-phenylcarbamoyl)-2,2-pentamethyleneaziridine, 7541-69-7; N-phenylcarbamoyl-1,2-iminocycloheptene, 7480-22-0; **20**, 7480-23-1; **28**, 7480-24-2; **29**, 1896-38-4; **29b**, 7480-26-4; **29c**, 1896-39-5; **31a**, 7480-28-6; **31b**, 7480-29-7; *cis*-cyclohexano[*d*]-2-oxazolidone, 7480-30-0; *trans*-cyclohexano[*d*]-2-oxazolidone, 7480-31-1; **4**, 7480-32-2; 4,4-diphenyl-2-oxazolidine, 7480-33-3; **25**, 7480-34-4; 2-hydroxy-1-phenylethylamine hydrochloride, 4561-44-8; **32a**, 7480-35-5; **32b**, 7480-36-6.

Acknowledgment.—Support of this work by Public Health Service Research Grant No. CA-04474 from the National Cancer Institute and by PRF Grant 2004-A1,4 from the American Chemical Society is gratefully acknowledged.

The Reaction of Bromo Epoxides and Acetoxy Epoxides with Amines[1]

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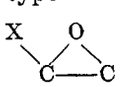
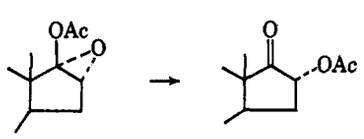
The synthesis of negatively substituted epoxides, such as 3β-acetoxy-17β-bromo-16α,17α-oxidoandrostane (I), and their reactions with amines are described. The resulting amino ketones (II) were identical with those obtained in a substitution reaction from the 16α-bromo 17-ketone IV with amines. Reduction of amino ketones II leads to the corresponding amino alcohols. 16β-Alkylamino 17-ketones (II) also resulted from the interaction of acetoxy epoxide VIII with amines. The opening of the three-membered ring is interpreted as a concerted process. The synthesis of 2-alkylamino-3-cholestanones cannot be effected *via* 2-bromo-3-cholestanone but was accomplished by ring opening of acetoxy epoxide IX with amines.

Little is known about the chemistry of negatively substituted epoxides of type

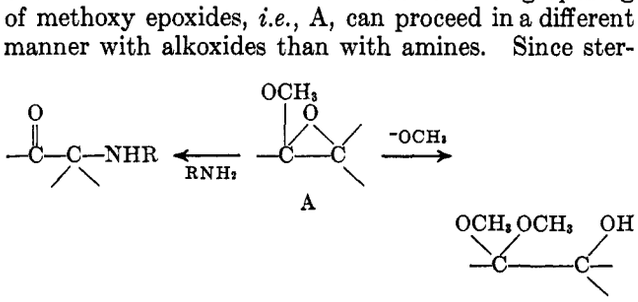


in particular about the stereochemistry of their reactions. Such compounds are of theoretical interest as possible precursors of highly strained oxirenes, as well as of synthetic interest leading to stereospecific introduction of functional groups. Acetoxy epoxides, such as VIII, are known to rearrange on heating or in the



VIII

presence of catalysts[2] and chloro epoxides apparently undergo similar transformations.[3] The investigations of Stevens and co-workers[4] indicate that ring opening of methoxy epoxides, *i.e.*, A, can proceed in a different manner with alkoxides than with amines. Since steroids provide an excellent testing ground for stereochemical principles and because of our interest in steroidal small-ring compounds[5] and amino ketones,[6] we investigated the reaction of bromo epoxides I and Ia and of acetoxy epoxides VIII and IX with amines.



Epoxide I was readily prepared by per acid oxidation of 3β-acetoxy-17-bromo-16-androstene, which was in turn obtained from epiandrosterone hydrazone as outlined by Mori and Tsuneda.[7] The assignment of the α configuration for epoxide I is based on the well-known approach of reagents from the α side of steroids and has analogy in the formation of other 16α,17α-oxido compounds on epoxidation of steroid 16-enes.[2,8]

The reaction of bromo epoxides such as I with amines can potentially proceed by a variety of pathways which include elimination to oxirene intermediates B or C. (See Scheme I.)

We found that I reacts readily at room temperature with primary or secondary amines to give amino ketones. These products are identical with those obtained upon heating of 16α-bromo-17-keto steroid IV with amines and are assigned 16β-amino-17-keto structure II. The structures of IIc and IId have been recently established.[9] It was disquieting to find that 16β-bromoandrostan-17-on-3β-ol acetate reacted with piperidine to give IIc, the same product obtained from I or IV. Attempts to isolate a 16α-amino 17-ketone intermediate under milder reaction conditions were unsuccessful. Nevertheless, we feel that the 16β configuration for the amino group in II, though not unequivocally established, can be considered correct in view of the recent work of Hewett and Savage.[9]

(1) Stereochemistry. XXI. Small-Ring Compounds. For paper XX, see A. Hassner, M. E. Lorber, and C. Heathcock, *J. Org. Chem.*, **32**, 540 (1967).

(2) N. S. Leeds, D. K. Fukushima, and T. F. Gallagher, *J. Am. Chem. Soc.*, **76**, 2943 (1954).

(3) R. N. McDonald and P. A. Schwab, *ibid.*, **85**, 4004 (1963).

(4) C. L. Stevens, J. J. Beereboom, and K. G. Rutherford, *ibid.*, **77**, 4590 (1955); C. L. Stevens and C. H. Chang, *J. Org. Chem.*, **27**, 4392 (1962).

(5) A. Hassner and C. Heathcock, *ibid.*, **30**, 1748 (1965).

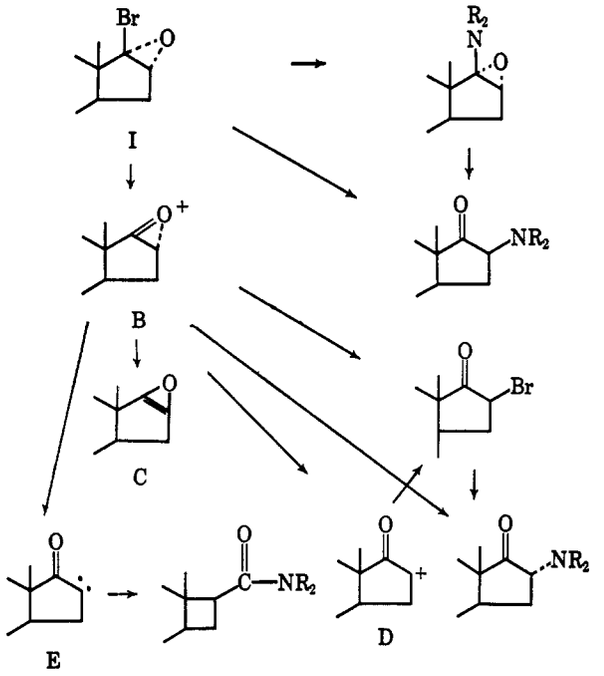
(6) A. Hassner and A. W. Coulter, *Steroids*, **4**, 281 (1964).

(7) H. Mori and K. Tsuneda, *Chem. Pharm. Bull.* (Tokyo), **11**, 1413 (1963).

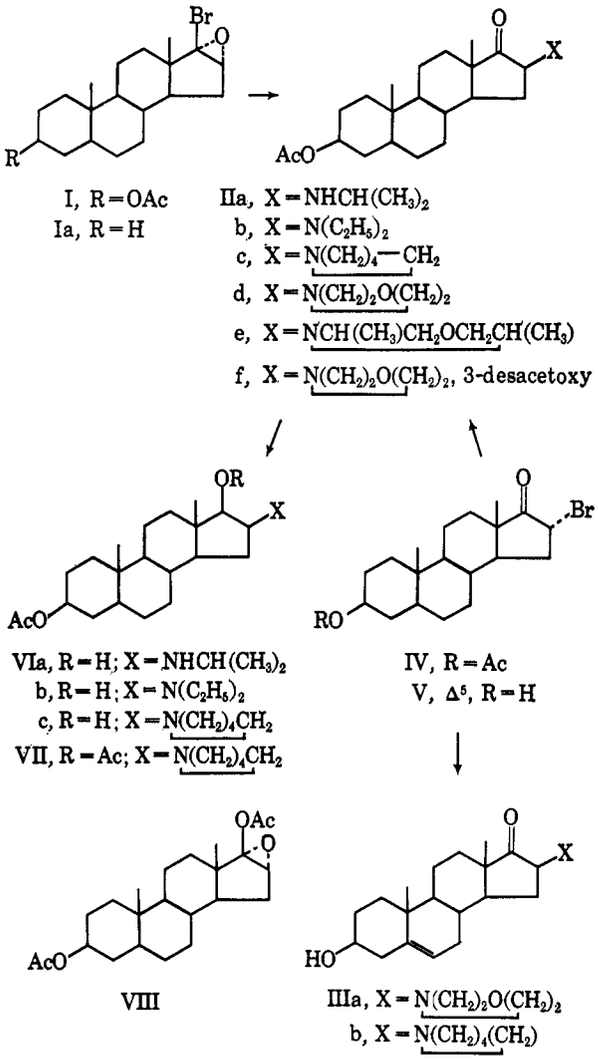
(8) J. Fajkos, *Collection Czech. Chem. Commun.*, **20**, 312 (1955).

(9) C. L. Hewett and D. S. Savage, *J. Chem. Soc.*, 484 (1966).

SCHEME I

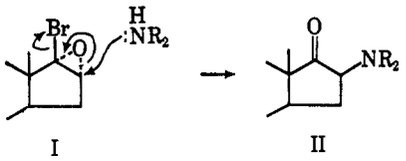


SCHEME II



It is reasonable to assume that displacement by piperidine on the 16β-bromo 17-ketone gives rise initially to a 16α-piperidino 17-ketone which isomerizes to the 16β epimer in the presence of the basic amine. The isomerization of 16α-bromo to 16β-bromo 17-ketones under basic conditions is well established.[9,10] Amino ketones II were readily reduced by sodium borohydride to amino alcohols VI which can be acetylated to VII. (See Scheme II.)

Since in reactions of negatively substituted epoxides[11a] the formation of intermediates such as B has been postulated[11b] and in view of the thermal conversion of bromo epoxide I to bromo ketone IV,[12] the possibility existed that the transformation of I to II proceeded *via* IV. That this is not the case was shown by the fact that bromo ketone IV could be recovered unchanged in the presence of piperidine at 25°, conditions under which bromo epoxide I was converted readily to amino ketone IIc. Two pathways appear most reasonable for the transformation I → II. One



involves ionization of I to B in analogy to the known behavior of α-halo ethers except that intermediate B, as well as the derivable C and D, is expected to be rather unstable. Conversion of B to an α-keto carbene (E) is feasible but this carbene is known to undergo ring contraction to a D-nor steroid system.[13]

The other plausible pathway for the conversion of I to II is a concerted process with ring opening of the epoxide by amine at C-16 proceeding more or less simultaneously with the expulsion of bromide ion. The following facts speak against an ionization of I to B and in favor of a concerted mechanism for I → II. Bromo epoxide I remains unaffected by silver nitrate in ethanol or by silver acetate in acetic acid at room temperature indicating that formation of bromide ion is not a facile process. On the other hand sodium iodide reacts readily with I in acetone leading to an iodo ketone.[12] Consistent with both pathways is the fact that acetoxy epoxide VIII reacts much more slowly with amines than does bromo epoxide I (bromide being a better leaving group than acetate). For instance, while I is converted to IId by morpholine in 25 min at 25°, acetoxy epoxide VIII remains unchanged on contact with morpholine for 24 hr at 25°. *trans*-2,6-Dimethylmorpholine reacts with the bromo epoxide I about one-third as fast as morpholine, but 2,2,-6,6-tetramethylpiperidine does not react with I even on heating, indicating that the reaction has definite steric requirements.

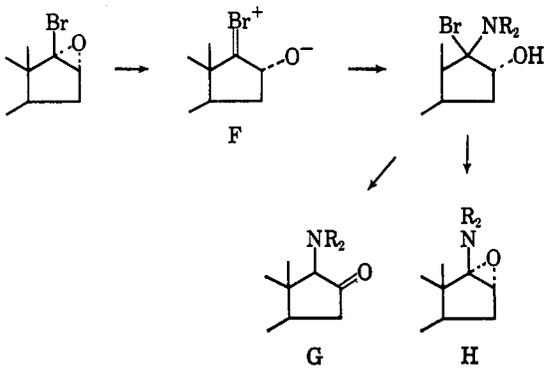
A concerted process with attack by the amine from the β side at C-16 would also be stereochemically consistent with the formation of a 16β-amino 17-ketone. In addition, 17β-acetoxy-16α,17α-oxidoandrostan-3β-ol

(10) J. Fajkos and F. Sorm, *Collection Czech. Chem. Commun.*, **24**, 766 (1959).

(11) (a) For reaction of such epoxides with phenylhydrazine, see A. Hassner and P. Catsoulacos, *Chem. Commun.*, in press; (b) A. Hassner and P. Catsoulacos, *J. Org. Chem.*, **31**, 3149 (1966).

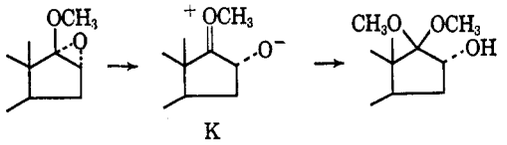
(12) Unpublished results from this laboratory.

(13) A. Hassner, A. W. Coulter, and W. S. Seese, *Tetrahedron Letters*, 759 (1962).



acetate (VIII) reacted with morpholine to yield 16β-morpholino 17-ketone IId identical with the one obtained from I or IV.

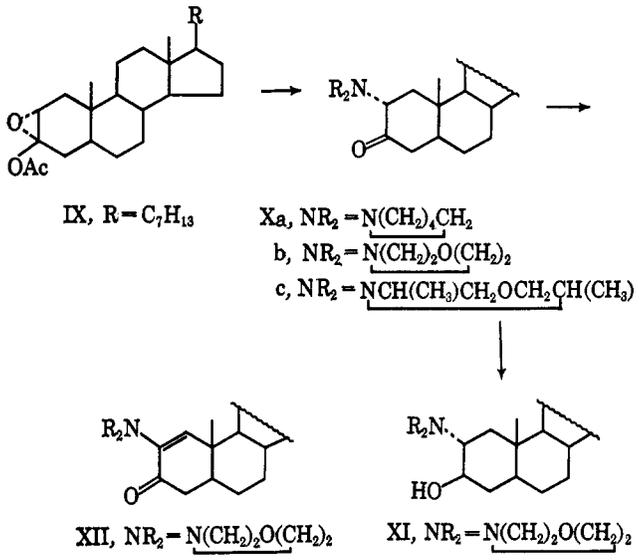
It is noteworthy that, among the pathways available to bromo epoxide in its reaction with amines, ring opening leading to intermediate F is apparently not involved here since none of the logical products (G and H) of such an intermediate was observed. This can be contrasted to the behavior of methoxy epoxides which prefer ring opening presumably through intermediate K.[4,11]



Since the same products are obtained from the reaction of amines with either bromo epoxide I or bromo ketone IV and the latter does not undergo hydrogen bromide elimination readily, the preferred route to ring D amino ketones and amino alcohols is through bromo ketone IV. By this method we synthesized some 16β-amino 17-ketones in the 5-androstene series (*cf.* III).[14] On the other hand ring-A bromo ketones, such as 2α-bromo-3-cholestanone, are known to dehydrobrominate readily even in the presence of weak bases (*e.g.*, 2,4-dinitrophenylhydrazine)[15] and are therefore unsuitable as sources of amino ketones.

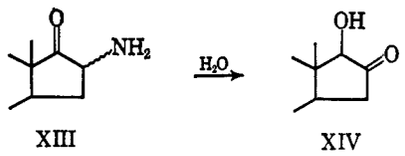
We succeeded in the synthesis of 2-amino-3-keto steroids by employing the reaction of negatively substituted epoxides with amines. 3β-Acetoxy-2α,3α-oxidocholestane (IX) was prepared from cholestanone enol acetate with *m*-chloroperbenzoic acid. On heating with piperidine, morpholine, or 2,6-dimethylmorpholine, IX gave amino ketones Xa, b, and c, respectively. The morpholino ketone Xb was very sensitive to air oxidation and became contaminated with its dehydro derivative 2-morpholino-1-cholesten-3-one (XII) even on crystallization from ethanol. Compound Xc behaved similarly. The conversion of the saturated amino ketone Xb (C=O absorption at 1710 cm^{-1}) to unsaturated amino ketone XII (C=O absorption at 1675 cm^{-1}) was easily accomplished on bubbling oxygen through a solution of Xb in morpholine. The structure of XII was confirmed by its analytical and spectral data [λ_{max} 297 mμ (ε 2820)]. The singlet for the vinyl proton in the nmr spectrum of XII is consistent with its structure and precludes an alternate 3-amino-2-keto structure for X or XII. Air oxidations of amino ketones have been reported earlier[16] and are now under study in this laboratory.

Reduction of Xa with sodium borohydride led to amino alcohol XI. Since reduction of the 3-keto function always gives the equatorial 3β-alcohol in high



yield, the hydroxy function in XI is assigned 3β. The configuration of the amino group in X–XI was deduced as 2α (equatorial) on the following basis. Equilibration experiments showed that X did not epimerize in base and therefore must possess an equatorial amino substituent. The nmr spectrum of X is consistent with this assignment; the proton at C-2 appears at τ 6.9 with a half-width of 18 cps indicative of an axial hydrogen.[17] This implies that in the reaction of IX an initially formed 2β-piperidino 3-ketone has been isomerized on heating with piperidine to the 2α isomer.[18]

It was of interest to show whether 16-alkylamino-17-keto steroids would enolize and/or rearrange as did 16-amino-5-androsten-17-on-3β-ol (XIII),[6] which could be transformed by water to ketol XIV. We found that alkylamino ketones II were stable in boiling water



and therefore behaved more analogously to the acetamide of XIII rather than like XIII itself. Whether this behavior is related to the configuration at C-16 in these compounds (the configuration at C-16 in XIII is not known yet) remains to be determined.

Experimental Section

All melting points are taken on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were determined in the solid phase (KBr) using a Beckman IR-5 spectrophotometer. Ultraviolet spectra were measured in methanol solution on

(14) Our studies were essentially completed when the work of Hewett and Savage[9] came to our attention.

(15) C. Djerassi, *J. Am. Chem. Soc.*, **71**, 1003 (1949).

(16) A. Hassner and N. H. Cromwell, *ibid.*, **80**, 901 (1958).

(17) A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 1350 (1964).

(18) An analogy to this epimerization is found in the formation of a 2α-pyridinium salt from 2α-bromo-3-cholestanone: E. W. Warnhoff, *ibid.*, **27**, 4587 (1962).

a Carey Model 14 instrument. Nmr spectra were run in deuteriochloroform on a Varian Associates A-60 instrument with tetramethylsilane as an internal standard. Elemental analysis were performed by A. Bernhardt, Mülheim, Germany, and by Huffman Laboratories, Denver, Colo.

17-Bromo-16-androsten-3β-ol Acetate.—17-Bromo-16-androsten-3β-ol, mp 127–129°, was obtained in 55% yield by the reaction of epiandrosterone hydrazone with N-bromosuccinimide in pyridine.[7]

17-Bromo-16-androsten-3β-ol (2.53 g) was acetylated with acetic anhyride and pyridine at room temperature and afforded 2.65 g of acetate, crystallized from methanol: mp 129–130°; ν_{max} 1730 (C=O), 1585 (C=C), 1240 cm^{-1}.

Anal. Calcd for $C_{21}H_{31}BrO_2$: C, 63.79; H, 7.84. Found: C, 63.80; H, 7.78.

17β-Bromo-16α,17α-oxidoandrostan-3β-ol Acetate (I).—To a solution of 2, 6 g of 17-bromo-16-androsten-3β-ol acetate in 120 ml of chloroform was added 3 g of *m*-chloroperbenzoic acid. The mixture was allowed to stand at room temperature for 20 hr. After this time the solution was washed with an ice cold solution of potassium hydroxide and then with water. After drying the organic layer with magnesium sulfate and removal of the solvent under reduced pressure, the residue was crystallized from methanol (2.06 g). One more crystallization brought the melting point of I to 129–131°; ν_{max} 1715 and 1225 (C=O) and four peaks between 850 and 750 cm^{-1} characteristic for I.

Anal. Calcd for $C_{21}H_{31}BrO_3$: C, 61.31; H, 7.54. Found: C, 61.20; H, 7.68.

General Procedure for the Preparation of 16β-Alkylamino-17-ketoandrostan-3β-ol Acetates (II). A. From 17β-Bromo-16α,17α-oxidoandrostan-3β-ol Acetate (I).—To a flask containing 1.0 g of bromo epoxide I was added an excess of amine (5 ml) and the reaction mixture was refluxed for 3–6 hr. The excess of amine was evaporated under reduced pressure to give the corresponding amino ketones in 45–70% yields after crystallization from methanol–water. All of the amino ketones obtained showed strong absorption at 1735–1740 and 1260 cm^{-1}.

3β-Acetoxy-16β-isopropylaminoandrostan-17-one (IIa) had mp 144–146°. *Anal.* Calcd for $C_{24}H_{39}NO_3$: C, 73.99; H, 10.09. Found: C, 73.89; H, 10.21.

3β-Acetoxy-16β-diethylaminoandrostan-17-one (IIb) had mp 83–87°; the material was not analytically pure, but sufficiently pure for the reduction to the corresponding amino alcohol.

3β-Acetoxy-16β-piperidinoandrostan-17-one (IIc) had mp 132–134°, α_D +97° (acetone). *Anal.* Calcd for $C_{26}H_{41}NO_3$: C, 75.13; H, 10.00. Found: C, 75.14; H, 10.11.

3β-Acetoxy-16β-morpholinoandrostan-17-one (IId) had mp 185–186°, α_D +108° (acetone). *Anal.* Calcd for $C_{25}H_{39}NO_4$: C, 71.94; H, 9.35. Found: C, 71.87; H, 9.37.

3β-Acetoxy-16β-(2′,6′-dimethylmorpholino)androstan-17-one (IIe) had mp 148–150°. *Anal.* Calcd for $C_{27}H_{43}NO_4$: C, 72.87; H, 9.73; N, 3.14. Found: C, 73.29; H, 9.74; N, 3.41.

The reaction of I with morpholine proceeds at 25°. It was followed by infrared and was found to require 25 min for completion. The reaction of I with *trans*-2,6-dimethylmorpholine required 60 min at 25°.

B. From 3β-Acetoxy-16α-bromoandrostan-17-one (IV).—Bromo ketone IV[19] (0.5 g) was refluxed with 5 ml of morpholine or piperidine for 3 hr. Work-up as above produced the corresponding amino ketones IId and IIc in 50–60% yields. Bromo ketone IV was recovered unchanged on exposure to morpholine at 25° for 5 hr.

C. From 3β-Acetoxy-16β-bromoandrostan-17-one.—A solution of 0.5 g of 16β-bromo 17-ketone[9,10] in excess of piperidine was heated under reflux for 3 hr and worked up as above to yield 200 mg of IIc identical by a mixture melting experiment and infrared spectra with an authentic sample. Attempts to isolate an isomeric amino ketone under milder reaction conditions led to isolation of unchanged bromo ketone or of IIc.

D. From 16α,17α-Oxidoandrostane-3β,17β-diol Diacetate (VIII).—When 0.5 g of crude acetoxy epoxide VIII[2] was refluxed with 5 ml of morpholine for 18 hr, 0.25 g of amino ketone IId, mp 184–186°, was isolated upon normal work-up.

Hydrolysis of 3β-Acetoxy-16β-morpholinoandrostan-17-one (IId).—To a solution of 110 mg of IId in 3 ml of methanol was added 80 mg of sodium hydroxide. The mixture was refluxed for 2 hr. Evaporation of the solvent and two crystallizations from methanol–water yielded 3β-hydroxy-16β-morpholinoandrostan-17-one, mp 168–172°, identical by melting point and infrared spectra with the reaction product of 3β-hydroxy-16α-bromoandrostan-17-one with morpholine by the method of Hewett and Savage.[9]

16β-Morpholino- and 16β-Piperidino-5-androsten-3β-ol-17-one (IIIa and b).—16α-Bromo-3β-hydroxy-5-androsten-17-one[20] (450 mg) was refluxed with 3 ml of morpholine or of piperidine for 3 hr. Work-up as described for II yielded after recrystallization from methanol–water 180 mg of IIIa, mp 194–195° (for IIIa·0.5H_2O, lit.[9] mp 200°) (*Anal.* Calcd for $C_{23}H_{35}NO_3$: C, 73.95; H, 9.45. Found: C, 73.69; H, 9.48.), or, respectively, 210 mg of IIIb, mp 169–170° (for IIIb·0.5H_2O, lit.[9] mp 170°) (*Anal.* Calcd for $C_{24}H_{37}NO_2$: C, 77.58; H, 10.04. Found: C, 77.25; H, 10.00.).

Reduction of Amino Ketones II with Sodium Borohydride.—To a solution of 0.5 g of II in 30 ml of methanol was added an excess of sodium borohydride (0.4 g). The mixture was allowed to stand at room temperature for 2–3 hr. After this time the solution was poured into water and extracted with ether. The ether layer was washed with water and dried over magnesium sulfate. Evaporation of the solvent and crystallization from methanol–water yielded amino alcohols VI whose infrared spectra showed absorption near 3400 cm^{-1} and lack of absorption at 1740 cm^{-1}. Compound VIa was isolated as the hydrochloride or the picrate salt.

3β-Acetoxy-16β-isopropylaminoandrostan-17β-ol (VIa) hydrochloride was obtained by passing hydrogen chloride into an ether solution of IIa, mp >295°. *Anal.* Calcd for $C_{24}H_{40}ClNO_3$: Cl, 8.36. Found: Cl, 8.54. The **picrate** had mp 184–186° (from methanol). *Anal.* Calcd for $C_{30}H_{42}N_4O_{10}$: N, 9.03. Found: N, 8.93.

3β-Acetoxy-16β-diethylaminoandrostan-17β-ol (VIb) had mp 117–118°. *Anal.* Calcd for $C_{25}H_{43}NO_3$: C, 74.13; H, 10.69. Found: C, 74.42; H, 10.84.

3β-Acetoxy-16β-piperidinoandrostan-17β-ol (VIc) had mp 135–136°. *Anal.* Calcd for $C_{26}H_{43}NO_3$: C, 74.10; H, 10.38. Found: C, 74.42; H, 10.42.

16β-Piperidinoandrostane-3β,17β-diol Diacetate (VII).—Amino alcohol VIc (200 mg) was acetylated with excess pyridine and acetic anhydride at room temperature overnight. The solution was poured into ice–water and extracted with ether. The organic layer was washed with water and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue crystallized from methanol to yield 160 mg of VII: mp 195–197°; ν_{max} 1740, 1235 cm^{-1}.

Anal. Calcd for $C_{28}H_{45}NO_4$: C, 73.16; H, 9.87. Found: C, 73.02; H, 9.63.

Attempted Reaction of Bromo Epoxide I with Silver Salts.—Bromo epoxide (100 mg) was dissolved in the minimum amount warm ethanol. To this was added 45 mg of silver nitrate in ethanol, and the mixture was allowed to stand at room temperature for 2 hr. The white precipitate which formed was unchanged starting material I. Unchanged bromo epoxide was also obtained on exposure of I to an acetic acid solution of silver acetate at room temperature for 2 hr.

3β-Acetoxy-2α,3α-oxidocholestane (IX) was prepared in 80% yield from 3-acetoxy-2-cholestene[21] with *m*-chloroperbenzoic acid (2 equiv) in chloroform and recrystallized from ether, mp 133–135° (lit.[21] mp 133–134.5°), ν_{max} 1740 cm^{-1}.

2α-Piperidinocholestan-3-one (Xa).—A solution of 1.0 g of 2α,3α-oxido-3β-acetoxycholestane (IX) in 5 ml of piperidine was heated under reflux for 18 hr. Unreacted piperidine was removed under reduced pressure, and the product was worked up as described for II to yield 630 mg of Xa after recrystallization from acetone–chloroform: mp 139–141°; ν_{max} 1715 cm^{-1} (C=O); nmr τ 6.82 (1 H, $W_{1/2}$ = 18 cps).

Anal. Calcd for $C_{32}H_{55}NO$: C, 81.81; H, 11.80. Found: C, 81.62; H, 11.81.

2α-Morpholinocholestan-3-one (Xb).—When 1.0 g of 3β-acetoxy-2α,3α-oxidocholestane (IX) was refluxed with 5 ml of morpholine for 18 hr there was isolated a mixture of saturated and unsaturated amino ketones, mp 142–146° (ν_{max} 1710 for the saturated, 1675 cm^{-1} for the unsaturated ketones) in 45–50% yield, after recrystallization from acetone. Thin layer chromatography of this product indicated two spots. Attempts to separate the components of the mixture by crystallization were unsuccessful.

(19) E. R. Glazier, *J. Org. Chem.*, **27**, 2937 (1962).

(20) E. R. Glazier, *ibid.*, **27**, 4396 (1962).

(21) K. L. Williamson and W. S. Johnson, *ibid.*, **26**, 4563 (1961).

3β-Acetoxy-2α,3α-oxidocholestane (IX, 850 mg) was heated with morpholine as above except under a nitrogen atmosphere. Evaporation of the solvent and careful crystallization from acetone yielded 550 mg of Xb. One further recrystallization from Skellysolve F (bp 40–50°) gave ketone Xb: mp 148–150°; ν_{max} 1710, 1280 cm^{-1}.

Anal. Calcd for $C_{31}H_{53}NO_2$: C, 78.92; H, 11.32. Found: C, 79.14; H, 11.06.

Crystallization of Xb from 95% ethanol or bubbling air through a solution of Xb led to products containing variable amounts of Xb and XII as indicated by infrared absorption at 1710 and 1675 cm^{-1}.

2α-(2′,6′-Dimethylmorpholino)cholestan-3-one (Xc) was prepared as described for Xb using 2,6-dimethylmorpholine. The product was crystallized from acetone (850 mg), mp 147–150°. Its infrared spectrum showed peaks at 1720 and 1675 cm^{-1} indicative of a mixture of saturated and unsaturated amino ketone.

Anal. Calcd for $C_{33}H_{57}NO_2$ (saturated ketone): C, 79.30; H, 11.50. Found: C, 79.54; H, 11.58.

2-Morpholino-1-cholesten-3-one (XII).—Amino ketone Xb (180 mg) in 3 ml of morpholine was heated on a steam bath for 60 min. During this time oxygen was passed through the solution. Work-up as above and crystallization of the product from methanol yielded 100 mg of pure, unsaturated amino ketone XII: mp 171–172°; λ_{max} 297 mμ (ε 2820); ν_{max} 1675 (conjugated C=O), 1612 (conjugated C=C); nmr τ 4.5 (broadened singlet).

Anal. Calcd for $C_{31}H_{51}NO_2$: C, 79.26; H, 10.94. Found: C, 79.26; H, 11.03.

2α-Morpholinocholestan-3β-ol (XI).—To a solution of 350 mg of crude amino ketone Xb in 30 ml of methanol at 30° was added sodium borohydride in large excess (*ca.* 700 mg). After 3.5 hr the solution was poured into ice–water and extracted with ether. Evaporation and crystallization from acetone gave 290 mg of XI, mp 179–180°.

Anal. Calcd for $C_{31}H_{55}NO_2$: C, 78.59; H, 11.70. Found: C, 78.75; H, 11.67.

Androstan-17-one Hydrazone.—A solution of 2.1 g of androstan-17-one, mp 118–118.5°, in 20 ml of ethanol, 10 ml of triethylamine, and 15 ml of hydrazine hydrate was refluxed for 90 min, after which time it was poured into ice–water. The precipitate was collected by filtration, washed with water, and dried (2.2 g). Crystallization of the product from methanol–water furnished white crystals: mp 154–156°; ν_{max} 3350 (NH), 1670 (C=N), 930 cm^{-1}.

Anal. Calcd for $C_{19}H_{32}N_2$: C, 79.16; H, 11.11. Found: C, 79.26; H, 11.26.

17-Bromo-16-androstene.—A solution of N-bromosuccinimide (3 g) in 30 ml of dry pyridine was added, dropwise, to a cold solution of the androstan-17-one hydrazone (2.10 g) in dry pyridine (40 ml) with agitation. Nitrogen gas was evolved during the reaction. After the addition, the mixture was stirred for an additional 15 min. The solution was poured into ice–water and extracted with chloroform. After washing with 10% of hydrochloric acid, water and drying over magnesium sulfate, the solvent was evaporated and the residue was crystallized from acetone (1.4 g). Two more crystallizations brought the melting point to 122–124°; ν_{max} 1600 cm^{-1} (C=C).

Anal. Calcd for $C_{19}H_{29}Br$: C, 67.65; H, 8.60. Found: C, 67.56; H, 8.71.

17β-Bromo-16α,17α-oxidoandrostane (Ia).—Bromo epoxide Ia (1.0 g) was obtained from 1.4 g of 17-bromo-16-androstene as described for I. It melted at 164–165° after one recrystallization from methanol–acetone: ν_{max} 850–750 cm^{-1} (four peaks characteristic for the bromooxidoandrostane).

Anal. Calcd for $C_{19}H_{29}BrO$: C, 64.58; H, 8.21. Found: C, 64.75; H, 8.32.

16β-Morpholinoandrostan-17-one (IIf).—Bromo epoxide Ia (0.6 g) was heated under reflux for 4 hr with an excess of morpholine and worked up as before to yield 330 mg of IIf after recrystallization from methanol: mp 174–176°; ν_{max} 1740 cm^{-1}.

Anal. Calcd for $C_{23}H_{37}NO_2$: C, 76.83; H, 10.37. Found: C, 76.91; H, 10.40.

Registry No.—17-Bromo-16-androsten-3β-ol acetate, 7481-29-0; I, 7541-70-0; IIa, 7458-96-0; IIb, 7458-97-1; IIc, 7458-98-2; IId, 7541-71-1; IIe, 7491-66-9; 3β-hydroxy-16β-morpholinoandrost-17-one, 3000-34-8; IIIa, 5986-91-4; IIIb, 5986-90-3; VIa, 7547-75-3; VIa hydrochloride, 7548-18-7; VIa picrate, 7548-19-8; VIb, 7541-73-3; VIc, 5986-98-1; VII, 7541-74-4; IX, 7459-00-9; Xa, 7459-01-0; Xb, 7459-02-1; Xc, 7541-75-5; XII, 7459-03-2; XI, 7459-04-3; androst-17-one hydrazone, 7459-05-4; 17-bromo-16-androstene, 7459-06-5; Ia, 7481-31-4; IIf, 7459-07-6.

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Preparation and Solvolysis of *trans*-3-Vinylcyclopentyl Bromide

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Norcamphor was oxidized under Baeyer–Villiger conditions to its lactone (**3**) which on reaction with dimethylamine gave N,N-dimethyl-*cis*-3-hydroxycyclopentylacetamide (**4**). Reduction of **4** to the corresponding amine (**5**) followed by oxidation with hydrogen peroxide and pyrolysis produced *cis*-3-vinylcyclopentanol (**6**) which was converted to *trans*-3-vinylcyclopentyl bromide (**1**) by reaction with triphenylphosphine dibromide. Solvolysis of **1** and of the tosylate of **6** under a variety of conditions gave only derivatives of **6** and its epimer and the solvolysis of **1** was found to be unassisted. Stereoelectronic factors responsible for these observations are evaluated and discussed.

Bartlett[1-5] and his associates have recently published the results of a comprehensive study of the solvolyses of 1-(Δ^3-cyclopentenyl)-2-ethyl arenesulfonates and some related compounds and have used their data to support arguments for the intervention of a "non-classical" norbornyl cation during the solvolytic process. This contention is based upon the observation of enhanced rates of solvolysis and the formation of bicyclic products for compounds in which interaction between the unsaturated center and the incipient carbonium ion is stereoelectronically favorable. A factor which complicates this interpretation of their data is that in the reactions of 1-(Δ^3-cyclopentenyl)-2-ethyl tosylate, considerable driving force for both participation and cyclization must arise from the conversion of a primary to a secondary cation. In fact, as Bartlett[2] pointed out, in the solvolysis of 1-(Δ^3-cyclo-

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