after recrystallization from 1-butanol, mp 221–222°, mixture melting point with an authentic sample 220–221°. The infrared spectrum was identical with that of the known.

3D-Carbomethoxy-2,2-dimethyl-5-oxo-6D-phenylacetamidoperhydro-1,4-thiazepine (XV) from 6D-Amino-3D-carboxy-2,2-dimethyl-5-oxoperhydro-1,4-thiazepine (VIII).—With 60 mg (0.28 mmole) of VIII and following the same procedure described for the L,D isomer VII, a mixture of VI and phenylacetic acid was obtained. Solution in ether and standing, however, gave no crystalline material. The ether was then evaporated, and the acid mixture was dissolved in 10 ml of chloroform and treated with a slight excess of ethereal diazomethane. The solution was evaporated to give an oily mixture of esters. Compound XV readily crystallized as needles upon addition of ether: yield 80 mg (83% over-all), mp 170–172°. After one recrystallization from ethanol, it had mp 172–173° and was identical with the known compound; mixture melting point was 172–173°. The infrared spectra of the two were identical.

Acknowledgment.—The authors thank Mr. Josef Nemeth and his associates for microanalyses and Mr. Dick H. Johnson and his associates for some of the nmr and infrared spectra.

Heterocyclic Steroids. VIII. Steroidal Oxazines and 2-Aza-A-nor Steroids[1,2]

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Received June 21, 1966

The use of 17β-hydroxy-4-oxo-1,3-seco-2-nor-5α-estran-1-oic acid (**1a**) has been extended for the synthesis of additional heterocyclic steroids having 4-aza-2-oxa moieties. Introduction of a nitrogen replacing C-4 was accomplished *via* Beckmann rearrangement of the acetyl moiety. In addition, 2-benzyl-2-aza-A-nor steroids have been formed from acetyl acid **1a** and diacid **1i**.

Thus far the 17β-hydroxy-4-oxo-1,3-seco-2-nor-5α-estran-1-oic acid[5] (**1a**) (Chart I) has proved to be a versatile intermediate for the syntheses of a variety of heterocyclic steroids. By condensation with hydrazine, 2,3-diaza steroids[5,6] (steroidal pyridazinones) were prepared. Conversion of the acetyl moiety to a C-5 ketone gave a β-keto ester which was utilized for the construction of 2,4-diaza steroids[7] (steroidal pyrimidines). Functionalization[1] of the acetyl methyl by the introduction of a hydroxyl and subsequent ring closure led to a 2-oxa steroid **7**. During these latter studies certain interesting observations on the course of bromination of the acetyl group were made.

In the previous syntheses of steroid analogs having two heteroatoms in ring A, only nitrogens were introduced. It appeared that by appropriate modifications the intermediate **1a** can also be used for the construction of analogs having different heteroatoms in ring A. To create molecules of this type we undertook the syntheses of analogs having an oxygen atom at C-2 and a nitrogen at C-4. The projected route involved using the carboxylic acid group as the source of the oxygen atom which was to replace C-2 and introducing a nitrogen at C-4. Then ring A could be reconstructed. Although various approaches can be employed to introduce a nitrogen at C-4, we chose to explore the Beckmann rearrangement.[8]

The acetyl ester **1b** was therefore condensed with hydroxylamine to yield a mixture of oximes (see below), which was rearranged by phosphorous oxychloride–pyridine. The major product, acetamide **1c**, was identified by its elemental analysis, infrared spectrum, and nmr spectrum. In the nmr spectrum a singlet for the methyl of the acetamide moiety was observed at 115 cps. In addition, the nitrogen proton was coupled to the 5α proton and gave a doublet at 350.5 cps (J = 9.0 cps). Upon thin layer chromatography of the mother liquors a minor amount of the alternate amide **1d** was found. Although this product has an infrared spectrum similar to acetamide **1c**, its structure was deduced from its nmr spectrum. The absence of an acetamide methyl signal and the appearance of a doublet at 164 cps (J = 5.0 cps) for a methyl on a nitrogen clearly established the structure. In addition, a broad multiplet centered at 339 cps for the proton on the nitrogen was found. Upon exchange of the nitrogen proton for deuterium the signal at 339 cps vanished and the doublet collapsed into a singlet, as expected. These results indicate the presence of two oximes, the major being the isomer *syn* to the acetyl methyl. A similar sequence was performed on the corresponding 17-nitrate **1e** to yield **1f**.

Now with the acetamide **1c** prepared we had a potential intermediate for the 4-aza-2-oxa steroids. For example, lithium aluminum hydride reduction of **1c** would lead to the 1-hydroxy-5-N-ethylamine (**2a**). Alternately, hydrolysis of the acetamide followed by lithium aluminum hydride reduction would provide the unsubstituted 1-hydroxy-5-amine (**2c**). The first route to be undertaken was the direct reduction of **1c**, which gave **2a** in good yield. In an nmr spectrum, *inter alia*, a triplet appeared at 65 cps (J = 7.0 cps) for the methyl of the ethylamine portion of the molecule. Acetylation of the ethylamine **2a** gave **2b**.

The synthesis of steroids containing a tetrahydro-1,3-oxazine ring required insertion of a carbon atom between the amine and the hydroxyl groups of **2a**.

(1) Part VII: D. M. Piatak and E. Caspi, *Tetrahedron*, **22**, 2823 (1966).

(2) This work was supported by Grants A-5326, CA-07137, and FR-05528 from the U. S. Public Health Service.

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(4) Recipient of a Research Career Program Award CA-K3-16614 from the National Cancer Institute.

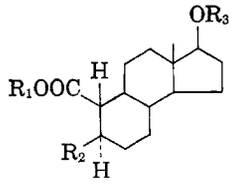
(5) (a) E. Caspi, P. K. Grover, D. M. Piatak, and Y. Shimizu, *J. Chem. Soc.*, 3052 (1965); (b) E. Caspi, P. K. Grover, and D. M. Piatak, *Chem. Ind.* (London), 1495 (1963).

(6) D. M. Piatak, R. I. Dorfman, D. Tibbetts, and E. Caspi, *J. Med. Chem.*, **7**, 590 (1964).

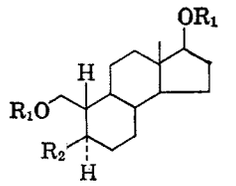
(7) D. M. Piatak and E. Caspi, *Steroids*, **3**, 631 (1964).

(8) This subject has been reviewed by C. G. Donaruma and W. Z. Heldt, *Org. Reactions*, **11**, 1 (1960). See C. W. Shoppee, R. Lack, R. N. Mirrington, and L. R. Smith, *J. Chem. Soc.*, 5868 (1965), for leading references to some recent observations on the Beckmann rearrangement of steroidal ketones.

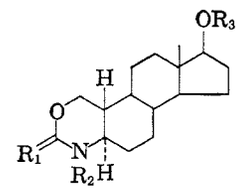
CHART I



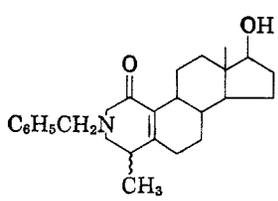
1a, $R_1 = H$; $R_2 = CH_3CO$; $R_3 = H$
b, $R_1 = CH_3$; $R_2 = R_3 = CH_3CO$
c, $R_1 = CH_3$; $R_2 = CH_3CONH$; $R_3 = CH_3CO$
d, $R_1 = CH_3$; $R_2 = CH_3NHCO$; $R_3 = CH_3CO$
e, $R_1 = CH_3$; $R_2 = CH_3CO$; $R_3 = NO_2$
f, $R_1 = CH_3$; $R_2 = CH_3CONH$; $R_3 = NO_2$
g, $R_1 = CH_3$; $R_2 = H_2N$; $R_3 = H$
h, $R_1 = CH_3$; $R_2 = C_6H_5NHCONH$; $R_3 = H$
i, $R_1 = H$; $R_2 = HOOC$; $R_3 = H$



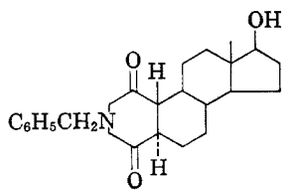
2a, $R_1 = H$; $R_2 = CH_3CH_2NH$
b, $R_1 = CH_3CO$; $R_2 = CH_3CH_2(CH_3CO)N$
c, $R_1 = H$; $R_2 = H_2N$



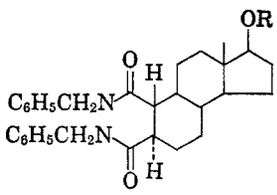
3a, $R_1 = H_2$; $R_2 = CH_3CH_2$; $R_3 = H$
b, $R_1 = H_2$; $R_2 = CH_3CH_2$; $R_3 = COCH_3$
c, $R_1 = O$; $R_2 = CH_3CH_2$; $R_3 = H$
d, $R_1 = O$; $R_2 = CH_3CH_2$; $R_3 = COCH_3$
e, $R_1 = H_2$; $R_2 = R_3 = COCH_3$
f, $R_1 = O$; $R_2 = H$; $R_3 = COCH_3$



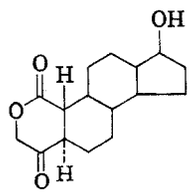
4



5



6a, R = H
b, R = $COCH_3$



7

This was first achieved by refluxing the amine with paraformaldehyde. The obtained tetrahydro-1,3-oxazine (**3a**) gave the correct analysis for $C_{18}H_{31}NO_2$ and its infrared and nmr spectra were consistent with the assigned structure (see Experimental Section). Upon acetylation of **3a** the corresponding 17β-acetate **3b** was formed. Its nmr spectrum was practically identical with that of the 17β-hydroxyoxazine (**3a**) except for the appearance of a sharp singlet at 121.5 cps for the 17-acetate methyl and a downfield shift of 3.0 cps for the 18-methyl. The nmr spectra of **3a** and **3b** are in full agreement with recent observations on the spectra of simple urethans and ureas.[9]

Having completed the incorporation of a tetrahydro-1,3-oxazine ring within a steroid ring system, we turned to the synthesis of a tetrahydro-1,3-oxazine-2-one. Such a molecule would have a 3-oxo group, a salient feature of many steroid hormones. By using phosgene with amine **2a** the desired 3-oxo oxazine **3c** was formed in one step, albeit in low yield. The structure was inferred from its elemental analysis and a 1680-cm^{-1} peak in the infrared spectrum. In an nmr spectrum the 18-methyl singlet at 48.5, the triplet for the methyl on the C-4 ethyl at 69 (J = 7.0 cps), and the quartet for the methylene of the C-4 ethyl at 205.5 cps (J = 7.0 cps) were discernible. Further identification of the 4-aza-2-oxa-3-oxo steroid **3c** was achieved by its acetylation to the corresponding 17-acetate **3d**.

For the synthesis of a steroid tetrahydrooxazine devoid of an N-alkyl group the acetamide of **1c** had to be removed prior to the reduction. The unsubstituted amine **2c** could then be used as before to generate tetrahydrooxazine **3e**. Acid hydrolysis of acetamide **1c** gave amino ester **1g** which resisted crystallization. For identification the amino ester **1g** was derivatized with phenyl isocyanate to yield the urea[9] **1h**. Reduction of amino ester **1g** with lithium aluminum hydride gave the unsubstituted amine **2c**.

The condensation of amine **2c** with paraformaldehyde gave a mixture which was acetylated to facilitate resolution. Upon chromatographic separation the acetate **3e** was isolated. Its structure follows from analysis and infrared bands at 1725 for the 17-acetate and at 1640 cm^{-1} for the C-4 amide carbonyl. A nmr spectrum confirmed the structure since it showed singlets at 121.5 for the 17-acetate and at 126 cps for the C-4 acetamide. In addition, there was present a pair of doublets at 197 and 209 (J = 9.5 cps) equivalent to two protons and a pair of doublets at 285.5 and 305.5 cps (J = 11.0 cps) also equivalent to two protons. These doublets are tentatively assigned to the C-3 and C-1 protons, respectively. Alternatively, condensation of **2c** with phosgene and subsequent acetylation gave **3f**.

In exploring routes to other aza steroids we had occasion to prepare 2-aza-A-nor steroids from **1a** and **1i**. By refluxing acetyl acid **1a** in benzylamine we obtained the lactam **4** which showed a lactam band at 1660 cm^{-1}. An ultraviolet spectrum exhibited a pronounced end absorption with a distinct shoulder at about 240 mμ, suggestive of an α,β-unsaturated amide.[10] Proof of the structure was provided by an nmr spectrum which was devoid of a signal for a vinylic methyl and had instead a doublet at 69.5 cps (J = 7.0 cps) for a secondary methyl. This spectrum coupled with the ultraviolet data is consistent with the 5(10) location of the double bond. Presumably, during the reaction the initially formed enamine lactam rearranged to

(9) A. J. Bloodworth and A. G. Davies, *J. Chem. Soc.*, Ser B, 125 (1966).
(10) A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products," Pergamon Press Ltd., Oxford, 1964, p 79.

give **4**. Of interest are the doublets separated by about 64 cps at 238.5 and 302.0 cps (J = 15.0 cps) for the benzyl methylene protons. Clearly, the two protons are not equivalent as a result of differences in deshielding. This implies that the benzyl moiety assumes a preferred conformation in respect to the lactam ring. The lower field doublet is assigned to the proton *cis* to the carbonyl since this proton would be the one most deshielded. The nonequivalence of the two protons and their separation by about 60 cps has been observed previously for similar nonsteroidal systems.[11]

With benzylamine and diacid **1i** prepared from the bromoform oxidation[1] of acid **1a** we obtained two compounds, the imide **5** and the diamide **6a**. The imide **5** was identified by elemental analysis and its characteristic[12] infrared peaks at 1770 and 1700 cm^{-1}. In addition, a singlet at 274.5 cps was observed for the two protons of the benzyl methylene. In this instance the two protons of the benzyl methylene are equivalent since each is equally influenced by a carbonyl. The major product **6a** from this experiment was converted to its acetate **6b**. It was identified on the basis of elemental analysis and infrared bands at 1635 for the amide I band and at 1540 cm^{-1} for the amide II band.

Experimental Section[13]

Methyl 17β-Acetoxy-4-aza-3-oxo-1,2-seco-5α-estran-1-oate (1c).—To a solution of ester[5] **1b** (1.0 g) in methanol (35 ml) was added a solution of hydroxylamine hydrochloride (0.77 g) and sodium acetate·3H$_2$O (1.54 g) in water (7.5 ml). After storage of the reaction at room temperature for 16 hr, it was diluted with water and the steroids were recovered by extraction with ether.

The above crude oxime was dissolved in anhydrous pyridine (8.0 ml) and added to a mixture of phosphorous oxychloride (4.6 ml) and anhydrous pyridine (11.5 ml) at 0°. The mixture was stirred for 4 hr at 0°, then decomposed by adding ice (*CAUTION*). The amides were taken up in ethyl acetate and washed with 2 N hydrochloric acid and saline. Crystallization from methanol gave 560 mg of acetamide **1c**. Tlc of the mother liquor gave two products. An additional amount of **1c** (280 mg) was obtained from the less mobile zone. The slightly more polar zone gave **1d** (90 mg).

Repeated recrystallization of **1c** from methanol gave an analytical sample: mp 243–245°; ν_{max} 3280, 3090, 1730, 1650, and 1560 cm^{-1}; nmr spectrum, 48.5 (18 methyl) 115 (acetamide methyl), 122 (17 acetate), 220 (carbomethoxy), 276.5 (triplet, J = 7.5 cps, 17α-hydrogen), 350.5 cps (doublet, J = 9.0 cps, NH).

Anal. Calcd for $C_{20}H_{31}NO_5$: C, 65.73; H, 8.55. Found: C, 65.51; H, 8.47.

Methyl 17β-Acetoxy-3-aza-4-oxo-1,2-seco-5α-estran-1-oate (1d).—The N-methyl amide **1d** isolated from the above experiment was recrystallized from methanol to mp 230–232°; ν_{max} 3260, 3090, 1730, 1635, and 1565 cm^{-1}; nmr 48.5 (18-methyl), 121 (17 acetate), 164 (doublet, J = 5.0 cps, N-methyl), 217 (carbomethoxy), 274.5 (triplet, J = 7.5 cps, 17α-hydrogen), and 339 cps (NH).

Anal. Calcd for $C_{20}H_{31}NO_5$: C, 65.73; H, 8.55. Found: C, 65.36; H, 8.33.

Methyl 4-Aza-3-oxo-1,2-seco-5α-estrane-17β-nitrate-1-oate (1f).—A solution of hydroxylamine hydrochloride (240 mg) and sodium acetate·3H$_2$O (485 mg) in water (2.5 ml) was added to a solution of nitrate ester[7] **1e** (315 mg) in methanol (8.0 ml). After 22 hr at room temperature the solution was diluted with water and the steroids were recovered with ether.

The oxime was dissolved in dry pyridine (4.0 ml) and added to a mixture of phosphorous oxychloride (2.4 ml) and dry pyridine (6.0 ml) at 0°. After stirring for 4 hr at 0° the mixture was decomposed with ice and the steroids were dissolved in ethyl acetate. The organic layer was washed with 2 N hydrochloric acid and water. Crystallization of the residue from methanol gave 240 mg of crystals: mp 189–190°; ν_{max} 3380, 1710, 1670, 1620, and 1530 cm^{-1}.

Anal. Calcd for $C_{18}H_{28}N_2O_6$: C, 58.68; H, 7.66; N, 7.60. Found: C, 58.50; H, 7.58; N, 7.56.

4-Aza-1,17β-dihydroxy-1,2-seco-5α-estrane (2a).—To a solution of acetamide **1c** (110 mg) in dry ether (10 ml) and anhydrous tetrahydrofuran (10 ml) was added lithium aluminum hydride (400 mg). The mixture was refluxed for 20 hr, then cautiously decomposed with water. The product was taken up in ether and washed with 2 N sodium hydroxide, then water. Evaporation of solvent gave 90 mg of crystalline amine **2a**. Repeated recrystallizations from ethyl acetate gave a pure sample: mp 143–145°; ν_{max} 3370, 3250, 1140, 1120, 1100, 1050, 1035, and 1005 cm^{-1}; nmr spectrum, 44 (18 methyl), 65 (triplet, J = 7.0 cps, methyl of N-ethyl), and 190–250 cps (series of multiplets).

Anal. Calcd for $C_{17}H_{31}NO_2$: C, 72.55; H, 11.10. Found: C, 72.55; H, 11.15.

A portion of amine **2a** was acetylated in the usual manner with acetic anhydride–pyridine to yield **2b**. Recrystallization of the product from ethyl acetate gave an analytical sample with mp 101–103°, ν_{max} 1730 and 1645 cm^{-1}.

Anal. Calcd for $C_{23}H_{37}NO_5$: C, 67.78; H, 9.15. Found: C, 67.81; H, 9.09.

4-Aza-4-ethyl-17β-hydroxy-2-oxa-5α-estrane (3a).—A mixture of amine **2a** (200 mg) and paraformaldehyde in benzene (10 ml) was refluxed for 16 hr. The water formed during the reaction was collected in a Dean–Stark tube. The solution was diluted with ether–chloroform (3:1) and washed with water. Removal of solvents and recrystallization of the residue from ethyl acetate gave 170 mg of colorless crystals: mp 158–161°; ν_{max} 3190, 1135, 1115, 1085, 1070, 1035, and 1020 cm^{-1}; nmr spectrum, 44.5 (18 methyl), 63 (triplet, J = 7.0 cps, methyl of N-ethyl), and 130–290 cps, (complex pattern of signals).

Anal. Calcd for $C_{18}H_{31}NO_2$: C, 73.67; H, 10.65. Found: C, 73.36; H, 10.48.

17β-Acetoxy-4-aza-4-ethyl-2-oxa-5α-estrane (3b).—The steroidal tetrahydrooxazine **3a** was acetylated as usual with acetic anhydride–pyridine. The recovered steroids were chromatographed on an alumina thin layer plate (30% ethyl acetate–benzene). Recrystallization of the recovered material from ethyl acetate yielded colorless crystals: mp 94–96; ν_{max} 1730, 1150, 1135, 1105, 1065, 1040, and 1025 cm^{-1}; nmr spectrum, 47.5 (18 methyl), 63 (triplet, J = 7.0 cps, methyl of N-ethyl), 121.5 (17 acetate), and 145–285 cps (complex multiplets).

Anal. Calcd for $C_{20}H_{33}NO_3$: C, 71.60; H, 9.92. Found: C, 71.76; H, 9.71.

4-Aza-4-ethyl-17β-hydroxy-2-oxa-3-oxo-5α-estrane (3c).—To a solution of amine **2a** (140 mg) in anhydrous pyridine (1.0 ml) and benzene (5.0 ml) was added a saturated solution of phosgene in benzene (2.0 ml). The mixture was stored overnight, then decomposed with water. The steroids were taken up in ether–chloroform (3:1) and washed with 2 N hydrochloric acid, water, sodium bicarbonate solution, and water. Evaporation of the solvents gave 125 mg of crude material which was chromatographed on a thin layer silica plate [benzene–ethyl acetate (1:1)]. Rechromatography of the major zone on silica [ethyl acetate–chloroform (1:1)] gave **3c** (*ca.* 30 mg). Recrystallization from ethyl acetate yielded colorless crystals: sublimation occurred from 241°; $\nu_{max}^{CHCl_3}$ 1680 cm^{-1}; nmr spectrum, 48.5 (18 methyl), 69 (triplet, J = 7.0 cps, methyl of N-ethyl), 165–286 (series of complex signals), and 205.5 cps (quartet, J = 7.0 cps, methylene of N-ethyl).

Anal. Calcd for $C_{18}H_{29}NO_3$: C, 70.32; H, 9.51. Found: C, 69.77; H, 9.07.

17β-Acetoxy-4-aza-4-ethyl-2-oxa-3-oxo-5α-estrane (3d).—The mother liquor from the above experiment was acetylated as usual. Tlc of the product [chloroform–ethyl acetate (1:1)] on silica gave crystals (from ethyl acetate): mp 239–240°; ν_{max}

(11) (a) K. D. Barrow and T. M. Spotswood, *Tetrahedron Letters*, 3325 (1965); (b) P. L. Southwick, J. A. Fitzgerald, and G. E. Milliman, *ibid.*, 1247 (1965); (c) A. H. Lewin, J. Lipowitz, and T. Cohen, *ibid.*, 1241 (1965).

(12) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p 47.

(13) All melting points were taken on a micro hot stage and are corrected. The infrared spectra were taken on solids incorporated in KBr blotters unless otherwise noted. Nmr spectra were recorded at 60 Mc on deuteriochloroform solution on a Varian Associates HA-60 spectrometer, unless otherwise noted. For thin layer chromatography (tlc) silica gel HF$_{254}$ or alumina GF$_{254}$ (Brinkmann, Inc.) was used. The developing solvents are indicated in each case. Extracts were dried over anhydrous sodium sulfate before the solvent was removed *in vacuo*.

1730 and 1680 cm^{-1}; nmr spectrum, 49 (18 methyl), 67 (triplet, J = 7.0 cps, methyl of N-ethyl), 121.5 (17 acetate), and 170–290 cps (complex multiplets).

Anal. Calcd for $C_{20}H_{31}NO_4$: C, 68.74; H, 8.94. Found: C, 68.65; H, 8.73.

Methyl 17β-Hydroxy-2,4-diaza-2-phenyl-1,2-seco-5α-estran-3-on-1-oate (1h).—A solution of acetamide **1c** (350 mg) in methanol (40 ml) was treated with concentrated hydrochloric acid (15 ml) and the solution was refluxed for 16 hr. Most of the methanol was evaporated in a stream of nitrogen and the mixture was diluted with water. The neutral fraction (105 mg) was removed by extraction with ethyl acetate, then the aqueous phase was made basic by the addition of concentrated ammonium hydroxide (15 ml). The acid-soluble fraction was recovered with ether and washed with water. Evaporation of the solvents gave 145 mg of an oil which resisted crystallization.

The above oil was dissolved in dry methylene chloride (5.0 ml) and phenyl isocyanate (0.13 ml) was added. After 1.5 hr water was added and the steroid was recovered with chloroform. The crude material was then chromatographed on a tlc silica plate [ethyl acetate–benzene (3:1)] to yield 130 mg of urea **1h**. Repeated recrystallization from methanol–ethyl acetate gave colorless crystals: mp 202–204°; ν_{max} 3340, 1730, 1670, 1590, 1640, and 1495 cm^{-1}; nmr spectrum (in deuteriodimethyl sulfoxide), 39.5 (18 methyl), 213 (carbomethoxy), 266 (doublet, J = 5.0 cps, 17 hydroxyl hydrogen), 359.5 (doublet, J = 9.0 cps), (4-NH), and 504 cps (2-NH).

Anal. Calcd for $C_{23}H_{32}N_2O_4$: C, 68.97; H, 8.05; N, 7.00. Found: C, 68.87; H, 7.92; N, 7.45.

1,17β-Dihydroxy-5β-amino-1,5-seco-2,3,4-trisnorestrane (2c).—Acetamide **1c** (840 mg) was hydrolyzed in methanol (80 ml) with concentrated hydrochloric acid (35 ml) as above to yield 580 mg of acid-soluble oil.

The oil was dissolved in tetrahydrofuran (30 ml) and ether (20 ml), lithium aluminum hydride (1.0 g) was added and the mixture was refluxed for 16 hr. The excess hydride was destroyed by cautiously adding water. The steroids were extracted into ether, then washed with 2 N sodium hydroxide and water. Removal of the solvent gave 400 mg of crystalline amine, which was recrystallized from methanol–ethyl acetate to mp 152–154°; ν_{max} 3390, 3280, 3160, 1130, 1075, 1065, 1040, and 1020 cm^{-1}.

Anal. Calcd for $C_{15}H_{27}NO_2$: C, 71.10; H, 10.74. Found: C, 71.23; H, 10.45.

17β-Acetoxy-4-acetyl-4-aza-2-oxa-5α-estrane (3e).—A mixture of amine **2c** (150 mg) and paraformaldehyde (18.5 mg) in benzene (10 ml) was heated at reflux for 20 hr. The water formed during the reaction was removed by a Dean–Stark tube. The benzene was removed by a stream of nitrogen and the insoluble residue was acetylated as usual. Work-up of the acetylation mixture gave 90 mg of residue which was chromatographed on a tlc silica plate [chloroform–ethyl acetate (1:1)]. The most mobile zone gave crystalline **3e**, which was recrystallized from ethyl acetate–pentane to mp 166–168°; ν_{max} 1725 and 1640 cm^{-1}; nmr spectrum, 48.5 (18 methyl), 121.5 (17 acetate), 126 (N-acetyl), 197 and 209 (pair of doublets, J = 9.5 cps, 2 hydrogens), 248.5 (quartet, J = 5.0 cps, 1 hydrogen), and 285.5 and 305.5 (pair of doublets, J = 11.0 cps, 2 hydrogens).

Anal. Calcd for $C_{20}H_{31}NO_4$: C, 68.74 H, 8.94. Found: C, 68.58; H, 8.78.

17β-Acetoxy-4-aza-2-oxa-3-oxo-5α-estrane (3f).—To a olution of **2c** (210 mg) in pyridine (2 ml) and chloroform (10 ml) a saturated solution of phosgene in benzene (4 ml) was added and the mixture was stored for 16 hr at room temperature. The steroids were recovered as described for **3c** to yield 150 mg of an acid-insoluble (neutral) residue. The residue was chromatographed on plates, [silica, benzene–ethyl acetate (1:1)]. The product of intermediate mobility (30 mg) was acetylated to yield **3f**. Crystallization from ethyl acetate–pentane gave a sample: sintering occurred at 250° dec; ν_{max} 3300, 1735, 1710, 1670, and 1250 cm^{-1}. Mass spectrum showed a molecular ions at 321 ($C_{18}H_{27}O_4N$, 321.40).

17β-Hydroxy-2-aza-2-benzyl-3ζ-methyl-1-oxo-A-norestr-5(10)-ene (4).—A solution of acid **1a** (100 mg) in benzylamine (1.1 ml) was heated at reflux for 18 hr. The reaction was cooled, diluted with ether, and washed with 2 N hydrochloric acid, water, saturated sodium bicarbonate solution, and water. Removal of the solvent gave 80 mg of crystalline product **4**, which was recrystallized from ethyl acetate–pentane to mp 192–197°; ν_{max} 3420, 1660, and 710 cm^{-1}; λ_{max}^{MeOH} end absorption with a shoulder at 240 mμ; nmr spectrum, 47.5 (18 methyl), 69.5 (doublet, J = 7.0 cps, C-3 methyl), and 238.5 and 302 (pair of doublets, J = 15.0 cps, methylene of N-benzyl).

Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55. Found: C, 78.82; H, 8.17.

17β-Hydroxy-2-aza-2-benzyl-1,3-dioxo-A-nor-5α-estrane (5).—A solution of diacid[1] **1i** (100 mg) in benzylamine (1.1 ml) was refluxed for 17 hr. The solution was diluted with ether–chloroform (3:1) and washed with 2 N hydrochloric acid, water, sodium bicarbonate, and water. Evaporation of the solvents gave a yellow residue which was chromatographed on a tlc silica plate [ethyl acetate–benzene (1:1)]. The most mobile zone was eluted to give 33 mg of imide **5**. Repeated recrystallizations from acetone gave an analytical sample: mp 183–186°; ν_{max} 3550, 1770, and 1700 cm^{-1}; nmr spectrum, 45 (18 methyl), 274.5 (methylene of N-benzyl), and 435.5 cps (aromatic hydrogens).

Anal. Calcd for $C_{23}H_{29}NO_3$: C, 75.17; H, 7.95. Found: C, 75.30; H, 7.77.

N,N′-Dibenzyl-17β-acetoxy-1,4-*seco*-2,3-bisnor-5α-estradioic Diamide (6b).—The least mobile zone from the above experiment was eluted to give 75 mg of hydroxy diamide **6a**. Attempts to recrystallize this material resulted in gels. The compound was acetylated as usual to **6b**, which was recrystallized from chloroform–acetone to mp 241–242°; ν_{max} 3300, 1730, 1635, and 1540 cm^{-1}.

Anal. Calcd for $C_{32}H_{40}N_2O_4$: C, 74.39; H, 7.80. Found: C, 73.92; H, 7.53.

Photochemical Cycloaddition Reactions with Norbornene

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Received July 28, 1966

The photochemical addition of dimethyl maleate, dimethyl fumarate, and maleic anhydride to norbornene has been studied. Stereochemistry has been deduced for the adducts and a revised structure has been assigned the one isomer recorded by Hara, Odaira, and Tsutsumi.[2]

Direct irradiation of a solution of norbornene in dimethyl maleate has been reported to yield a single 1:1 adduct assigned the structure **2**.[2] The *exo* nature of the cyclobutane ring was securely established by degradation of the adduct to the known *exo*-2,3-bishydroxymethylbicyclo[2.2.1]heptane, while the assignment of the *cis,trans,cis*-substitution pattern of the

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(2) M. Hara, Y. Odaira, and S. Tsutsumi, *Tetrahedron*, **22**, 95 (1966).