The organic solution was dried over sodium sulfate and filtered, and the solvent was evaporated leaving an oil (672 mg). The crude mixture of **1a** and **8a** was separated by preparative tlc. The plates (8 in.^{2}) were coated with a 500-μ layer of silica gel and activated overnight at 125°. The mixture (50 mg/plate) was deposited from methylene chloride solution as a 5-mm-wide band. The bands were detected by ultraviolet (R_f 0.65 and 0.73) and aspirated from the plates. The products were eluted from the adsorbant by washing with methylene chloride and filtering. The compound at R_f 0.73, 17β-acetoxy-5β-androst-1-en-3-one (**8a**), was crystallized from acetone–hexane (108 mg): mp 140–141°, $[\alpha]^{25}D$ +134° (*c* 0.53) (lit.[30] $[\alpha]D$ +141°), infrared ν_{max} 1667 cm^{-1} (>C=C—C=O), ultraviolet λ_{max} 232 mμ (log ϵ 4.22). The purity of the compound was verified by glpc (single peak at retention time 16 min).

The second tlc band (R_f 0.65) was isolated as described above and the compound crystallized from acetone–hexane: mp 139–141°. Glpc analysis and a mixture melting point with authentic 17β-acetoxy-androst-4-en-3-one (**1a**) prepared by the acetylation of **1b** were used to identify the compound.

(30) M. Pesez, J. Barlos, J. Mathieu, and J. Valls, *Bull. Soc. Chim. France*, 488 (1958).

The 17β-acetoxy-2β-bromo-5β-androstan-3-one (**9a**) (12 mg) obtained from the bromination of **7a** was subjected to the dehydrobrominating conditions described above and the crude product was analyzed by glpc. Three compounds were detected at retention times 13 (12.6% 17β-acetoxy-5β-androstan-3-one), 16 (78% 17β-acetoxy-5β-androst-1-en-3-one), and 21 min (9.5% 17β-acetoxy-androst-4-en-3-one). The identity of all peaks was verified by peak enhancement with authentic material and by infrared spectroscopy.

The dehydrobromination of 17β-acetoxy-4β-bromo-5β-androstan-3-one (**5a**, 80 mg) was carried out as described above and the crude product (64 mg) was analyzed by glpc. Three compounds were detected at retention times 13 (20% 17β-acetoxy-5β-androstan-3-one), 16 (14% 17β-acetoxy-5β-androst-1-en-3-one), and 21 min (65% 17β-acetoxy-androst-4-en-3-one). The identity of the peaks was verified by peak enhancement with authentic material and by infrared spectroscopy.

Acknowledgment.—The author wishes to thank Dr. O. E. Edwards and Dr. D. Vocelle of the National Research Council for the nmr spectra and Mr. A. J. Bayne for technical assistance.

Application of the Beckmann Rearrangement to the Preparation of A-Azapregnane Derivatives[1]

HAROLD R. NACE AND ARTHUR C. WATTERSON, JR.[2]

Metcalf Chemical Laboratories, Brown University, Providence, Rhode Island 02912

January 14, 1966

5α-Pregnane-3,20-dione 3-oxime and A-nor-5α-pregnane-2,20-dione 2-oxime were prepared in good yield by selective oximation of the corresponding diketones. The oximation studies showed that a six-membered A-ring 3-ketone is more reactive than a five-membered A-ring 2-ketone and that both of these are more reactive than the side-chain carbonyl group at C-20. Beckmann rearrangement of these oximes gave A-homo-4-aza-5α-pregnane-3,20-dione in 93% yield, and a mixture of 3-aza-5α-pregnane-3,20-dione and 2-aza-5α-pregnane-3,20-dione in 93% yield, thus providing an excellent route to A-azapregnane derivatives.

In recent years a number of examples of the partial synthesis of A-aza steroids by the Beckmann rearrangement of oximes have been reported.[3]

However, this route has not been utilized for the preparation of A-azapregnane and A-aza-A-homopregnane derivatives from simple pregnanediones. Several examples are now reported here.

Since 5α-pregnane-3,20-dione is readily available, and A-nor-5α-pregnane-2,20-dione is relatively readily available,[4] these compounds were chosen for study. If a method of selective oximation at the 2 or 3 position in the presence of the free 20-carbonyl group could be worked out, protection of the 20-carbonyl group could be avoided, thus simplifying the partial synthesis. Accordingly, a study of the relative reactivity of these three carbonyl groups toward hydroxylamine was undertaken (Scheme I).

When 5α-pregnane-3,20-dione (I) was treated with 1 equiv of hydroxylamine at ambient temperatures 5α-pregnane-3,20-dione 3-oxime (II) was formed in 75% yield. That oximation had taken place at the 3 position was shown in the following manner. 5α-Pregnan-3β-ol-20-one (III) was converted to the known 20-oxime IV,[5] and this was oxidized with Jones reagent[6] to 5α-pregnane-3,20-dione 20-oxime (V) (30%). This oxime was obviously different from the one obtained from the 3,20-dione, thus establishing the structure of the two oximes. As a further check, 5α-pregnane-3,20-dione dioxime (VI) was prepared and subjected to levulinic acid hydrolysis[7] under mild conditions, which gave the 20-oxime V (46%) along with unreacted dioxime. These experiments show that the 3-carbonyl group in the A ring is more reactive toward hydroxylamine (and presumably related compounds such as phenylhydrazine) than the 20-carbonyl group in the side chain. They also show that the 20-oximino group is more resistant to acidic hydrolysis than the 3-oximino group.

In order to obtain the oxime of A-nor-5α-pregnane-2,20-dione (VII) it was necessary to use higher temperatures (60°) and much longer reaction times (14 days). Under these conditions with 1 equiv of hydroxylamine, A-nor-5α-pregnane-2,20-dione 2-oxime (VIII) was obtained in 74% yield (90% based on recovered starting material). The structural assignment was made on the basis of the results of the Beckmann rearrangement of the oxime described below and by the infrared spectrum. The A-nor 2-oxime had a carbonyl stretching

(1) A portion of this work was supported by the U. S. Public Health Service under Grant AM 05249-02.

(2) Abstracted from the Ph.D. Thesis of A. C. W., Jr., Brown University, 1965. Jesse Metcalf Fellow, 1962–1964.

(3) (a) S. Hara, *Yakugaku Zasshi*, **78**, 1027 (1958); (b) C. W. Shoppee, R. E. Lack, and B. C. Newman, *J. Chem. Soc.*, 3388 (1964), and previous papers cited therein; (c) J. T. Edward and P. F. Morand, *Can. J. Chem.*, **38**, 1316 (1960); (d) J. C. Craig and A. R. Naik, *J. Am. Chem. Soc.*, **84**, 3410 (1962); (e) N. J. Doorenbos and R. E. Havranek, *J. Org. Chem.*, **30**, 2474 (1965), and previous papers cited therein.

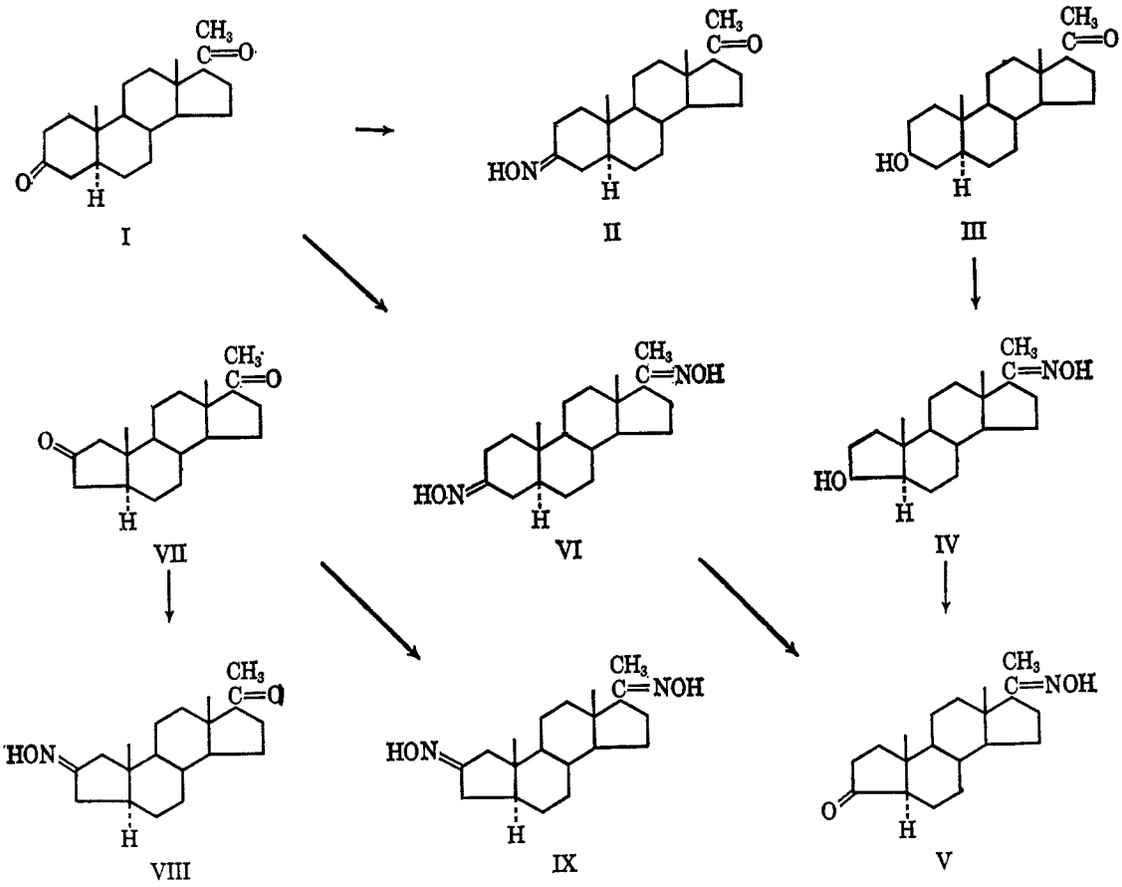
(4) H. R. Nace and D. H. Nelander, *ibid.*, **29**, 1677 (1964).

(5) A. Butenandt, V. Westphal, and W. Hohlweg, *Z. Physiol. Chem.*, **222**, 84 (1934).

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

(7) C. H. DePuy and B. W. Ponder, *J. Am. Chem. Soc.*, **81**, 4629 (1959).

SCHEME I
PREPARATION OF OXIMES



band at 5.85 μ characteristic of the 20-carbonyl group, and readily distinguishable from the band for the 2-carbonyl group at 5.74 μ. The 2,20-dioxime IX was also prepared and subjected to the levulinic acid hydrolysis, but no selectivity was observed and a mixture of the two monoximes was obtained.

An attempt was made to prepare A-nor-5α-pregnane-2,20-dione 20-oxime. A-Nor-5α-pregnan-2-ol-20-one-2-carboxylic acid[4] was converted to the 20-oxime, but treatment of this with lead tetraacetate in an attempt to generate the 2-carbonyl group did not give any of the desired product.

These oximation studies show that the 3-carbonyl group (cyclohexanone type) is more reactive to hydroxylamine than the 2-carbonyl group (cyclopentanone type), which in turn is more reactive than the 20-carbonyl group (open-chain type). These relative reactivities are in agreement with those obtained from kinetic studies[8] on simple ketones in which it was found that cyclohexanone was more reactive than cyclopentanone. Both cyclic ketones were more reactive than branched methyl ketones, and, since the 17-acetyl group constitutes part of a branched methyl ketone, the results for the 20-carbonyl group are also in agreement with the kinetic studies.

Further confirmation of the structures of the above oximes was obtained from an examination of the nuclear magnetic resonance (nmr) spectra of the compounds.[9]

The methyl resonances in steroid nmr spectra are sensitive to nearby substitution,[10] and comparison of the methyl resonances of the oximes with the methyl resonances of the parent ketones is in agreement with the structures assigned (Table I). In the 3-oxime II the C-19 methyl resonance is changed, while in the 20-oxime V the neighboring C-21 methyl resonance is changed. Similarly, in the A-nor-2-oxime VIII the C-19 methyl resonance is shifted.

TABLE I
COMPARISON OF THE METHYL RESONANCE FREQUENCIES OF VARIOUS OXIMES WITH THE PARENT KETONES

Compound	Methyl resonances in cps downfield from TMS C-18	C-19	C-21
5α-Pregnane-3,20-dione (I)	38	60	127
5α-Pregnane-3,20-dione 3-oxime (II)	38	55	127
5α-Pregnane-3,20-dione 20-oxime (V)	39	62	114
A-Nor-5α-pregnane-2,20-dione (VII)	38	52	128
A-Nor-5α-pregnane-2,20-dione 2-oxime (VIII)	37	45	127

Attention was next turned to the Beckmann rearrangement of the A-ring oximes. 5α-Pregnane-3,20-dione 3-oxime (II) was rearranged by the procedure of

authors thank Dr. G. O. Dudek for his cooperation in determining the spectra and Harvard University for the use of the spectrometer. All other nmr spectra were obtained on a Varian Model HR-60 and calibrated *vs.* TMS using a side-banding technique. The authors thank Henry Klos and Rebecca Bruce for their help in obtaining these spectra.

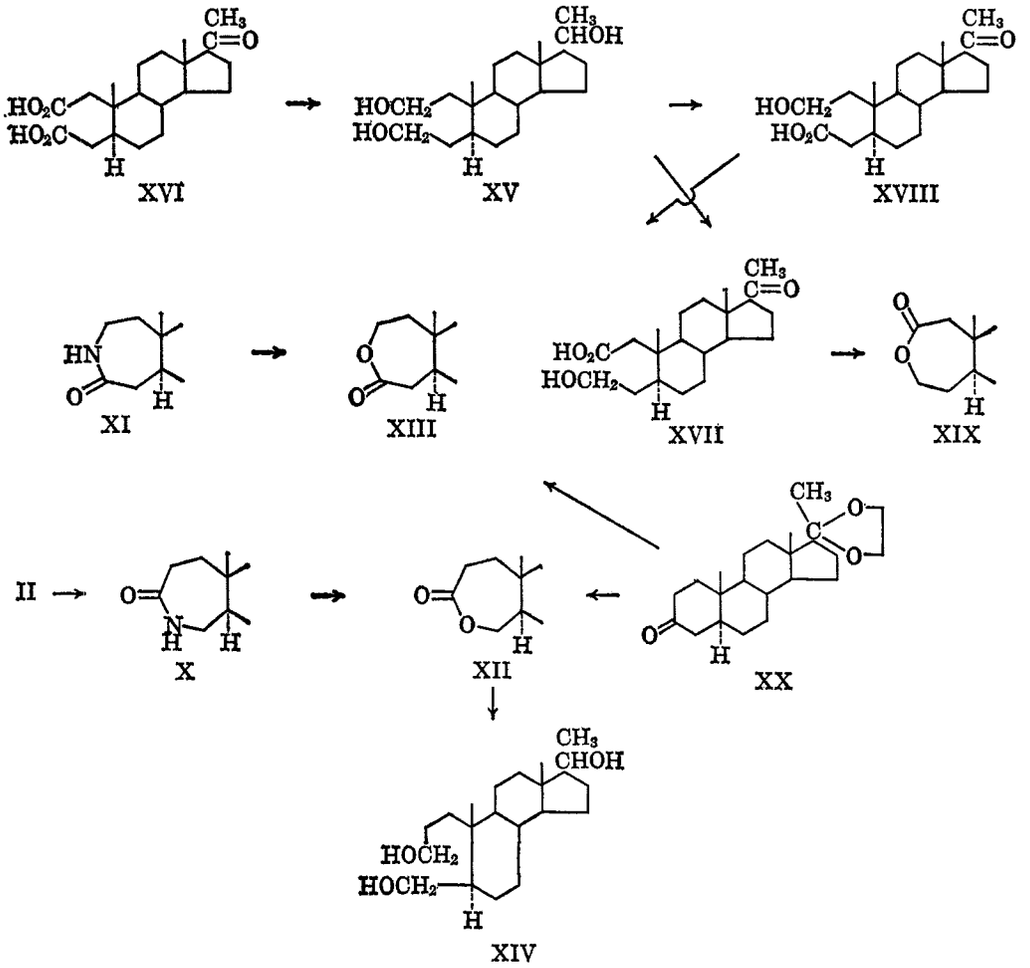
(8) F. W. Fitzpatrick and J. D. Gettler, *J. Am. Chem. Soc.*, **78**, 530 (1956).

(9) Methyl resonances were determined on a Varian Model A-60 spectrometer and peak positions are given in cycles per second from an internal standard, tetramethylsilane (TMS). For convenience, the chemical shifts are given positive values, although they are *downfield* from TMS. The

(10) J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958); N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964.

SCHEME II

BECKMANN REARRANGEMENT PRODUCT AND DERIVATIVES IN THE A-HOMO SERIES



Craig and Naik.[3d] The oxime was treated with benzenesulfonyl chloride and the crude benzenesulfonate ester, without isolation, was chromatographed on an alumina column to give the previously unknown rearranged product, A-homo-4-aza-5α-pregnane-3,20-dione (X), in 93% yield, based on recovered starting material. The product was homogeneous on tlc and no evidence could be obtained for the presence of isomers such as XI. The rearrangement was also conducted using thionyl chloride in dioxane under standard Beckmann conditions and again the product was a single isomer, but the yield of X was only 39%. Further evidence that a single rearrangement product was formed was obtained from nmr data, in which the C-19 methyl resonance at 55.5 cps was a single sharp peak. A mixture of two isomers would be expected to show two peaks in this region. The degradation and proof of structure experiments described below also gave further evidence that a single isomer was obtained (Scheme II).

In order to determine the structure of the lactam, it was converted to the lactone XII by the method of White.[11]

The lactone was obtained in 90% yield by treatment of the lactam with nitrogen dioxide in pyridine–carbon tetrachloride solution. This reaction has been shown[12] to proceed without rearrangement, and only one isomer was obtained, as shown by tlc, vpc, and the single C-19 methyl peak at 56 cps. There were also seven peaks between 240 and 290 cps (243, 255, 263, 268, 271, 278, 285 cps).

Since the lactone was also a new compound, it was necessary to establish its identity. It could have either structure XII or XIII, depending upon which lactam, X or XI, was obtained from the Beckmann rearrangement. Reduction of the lactone with lithium aluminum hydride would give a secotriol, either XIV or XV. Reduction of the known seco acid XVI in the same manner would give secotriol XV, which could then be compared with the one obtained from the lactone. Unfortunately, reduction of the seco acid XVI gave two secotriols XV in 35% yield, isomeric at C-20, which were detectable by vpc and nmr, but could not be obtained free of each other. They were produced in nearly equal amounts, as shown by vpc, which gave two peaks of relative retention times 0.33 and 0.45, and areas of 48 and 42%, respectively. The nmr showed methyl resonance peaks (C-18, -19, and -21) at 49, 59, 68, 83, and 128 cps.

However, it was possible to use this mixture to establish the structure of the unknown lactone. Oxidation with chromium trioxide restored the 20-carbonyl group, and in addition oxidation took place at C-2 and independently at C-3, to give two seco hydroxy acids XVII and XVIII, which immediately lactonized to give a

(11) E. H. White, *J. Am. Chem. Soc.*, **77**, 6011 (1955).
(12) E. H. White and C. A. Aufdermarsh, Jr., *ibid.*, **83**, 1179 (1961).

mixture of lactones, XIX and XIII. It should be noted at this point that one of these lactones is one of the possible ones XIII derived from the Beckmann rearrangement product. The isomers could not be separated by vpc and insufficient material was available for chromatographic isolation. However, the nmr spectrum proved to be quite informative. In addition to the C-18 methyl resonance at 37 cps, there were two C-19 methyl resonances at 53.5 and 56 cps and a C-21 methyl resonance at 126 cps. Multiple peaks were observed in the region of 240–260 cps, but *none* in the region of 260–290 cps. Therefore, the unknown lactone, which has peaks between 260 and 290 cps, was not present in the mixture, and, since one of the possible ones, XIII, must be present, the lactone from the lactam must be XII and the Beckmann rearrangement product must be X.

In order to gain further information about the lactone, 20,20-ethylenedioxy-5α-pregnan-3-one[4] (XX) was subjected to Baeyer–Villiger oxidation with peroxyacetic acid, and an 82% yield of a 1:1 mixture of the expected two lactones, A-homo-4-oxa-5α-pregnane-3,20-dione (XII) and A-homo-3 oxa-5α-pregnane-4,20-dione (XIII), were obtained. The presence of two isomers was shown by tlc and the appearance of two C-19 methyl resonances at 56 and 58 cps. It was not determined whether the ketal group came off during the rearrangement reaction or in the subsequent work-up. The mixture should contain the lactone XII and this was borne out by the presence of peaks between 260 and 290 cps, in the nmr spectrum. (All of the peaks listed above for the lactone were present.)

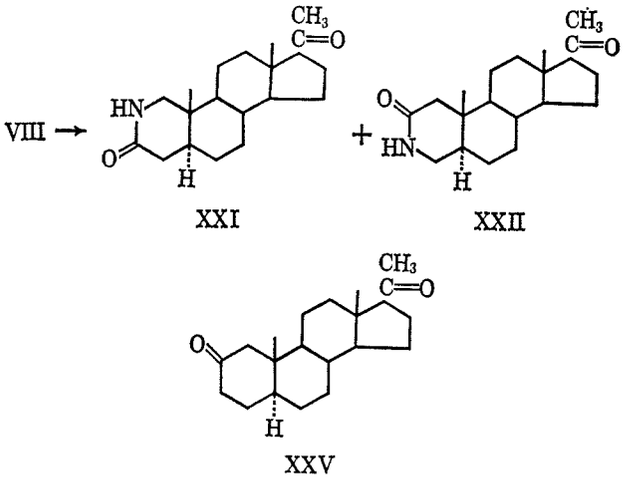
Comparison of the results obtained here with those from the rearrangement of the 3-oxime in the cholestane series is of interest. In the cholestane series, it appears that an inseparable mixture of the 3-aza-4-keto and 4-aza-3-keto compound, analogous to XI and X, was obtained.[3,13] If, as is generally the case, exclusive *trans* migration occurs in the rearrangement, and no prior isomerization of the oxime takes place, the *anti* configuration (with respect to C-4) can be assigned to the 5α-pregnane-3,20-dione 3-oxime, and the cholestane 3-oxime must be a mixture of the *syn* and *anti* forms. The pregnane oxime was prepared at room temperature, while in all cases,[3] the cholestane oxime was prepared at the temperature of boiling ethanol–pyridine mixtures, which could account for the different results. It is also possible that the 20-carbonyl group in the pregnane series may in some manner favor the *anti* instead of the *syn* isomer. The C-19 methyl resonance of the pregnane-3-oxime was sharp, while that of the A-norpregnane-2-oxime, which gave two lactams (see below), was broad, indicating a mixture of *syn* and *anti* forms for the latter oxime.

Rearrangement of A-nor-5α-pregnane-2,20-dione 2-oxime (VIII) (Scheme III) using the Craig and Naik procedure gave a mixture of lactams in 93% yield. The nmr spectrum of the product indicated that it was a 1:1 mixture of 2-aza-5α-pregnane-3,20-dione (XXI) and 3-aza-5α-pregnane-2,20-dione (XXII). Two C-19 methyl resonances, of equal intensity, appeared at 54 and 59 cps. Examination of models shows that the shielding effect of a carbonyl group in the 2 position

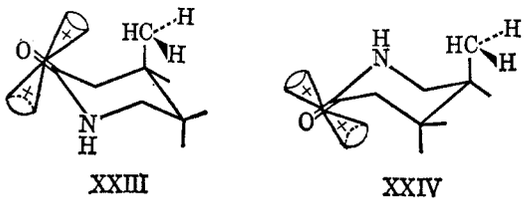
(13) C. W. Shoppee, G. Krüger, and R. N. Mirrington, *J. Chem. Soc.*, 1050 (1962).

SCHEME III

BECKMANN REARRANGEMENT OF THE A-NOROXIME



(XXIII) is to place the conical region above the group closer to the protons of the C-19 methyl group than when the carbonyl group is in the 3 position (XXIV).



If such is the case, the C-19 methyl resonance of the 2-carbonyl isomer XXII would appear at higher field than that of the 3 isomer XXI. It is possible, however, that the unshared electron pair on the nitrogen atom may have some effect on the C-19 methyl resonance. It seems unlikely that this unshared pair would reverse the effect of the carbonyl group on the methyl resonance for several reasons.

The first is illustrated by a comparison of the methyl resonances of 5α-pregnane-2,20-dione (XXV)[14] and 5α-pregnane-3,20-dione (I) shown in Table II.

TABLE II

COMPARISON OF METHYL RESONANCE FREQUENCIES OF STEROID KETONES AND LACTAMS

Compound	Methyl resonances in cps downfield from TMS C-18	C-19	C-21
5α-Pregnane-3,20-dione (I)	38	60	127
5α-Pregnane-2,20-dione (XXV)	37	43	124
2-Aza-5α-pregnane-3,20-dione (XXI)	38	59	128
3-Aza-5α-pregnane-2,20-dione (XXII)	38	54	128

An upfield shift of 17 cps is observed when the carbonyl group is changed from the 3 to the 2 position, in accord with the above considerations of the shielding effect of the carbonyl group. A similar, but smaller, shift of 5 cps is observed in going from the 3-keto to the

(14) The 5α-pregnane-2,20-dione, previously unreported, was prepared by the method developed by Clarke[15] in the androstane series. Treatment of 2α-bromo-5α-pregnane-3,20-dione with *n*-propyl mercaptan, followed by hydrolysis, gave a 1:1 mixture of the 2- and 3-ketones. The mixture was separated by treatment with sodium bisulfite and the 2-ketone was obtained in low yield. Although satisfactory analytical values for carbon and hydrogen content could not be obtained for it, satisfactory values were obtained for the dioxime, and other physical measurements indicated that the ketone was pure.

(15) R. L. Clarke, *J. Org. Chem.*, **28**, 2626 (1963).

2-keto aza compound. If the unshared pair on nitrogen were to reverse this effect, the nitrogen atom in the 3 position would have to shift the resonance *downfield* 16 cps, while the nitrogen in the 2 position would have to shift the resonance *upfield* 6 cps. It seems unreasonable that there should be such opposing effects in the different positions.

Separation of the isomers proved difficult, and only one of them was obtained in a pure state. Extensive work with tlc and column chromatography produced partial separation, and several recrystallizations of the partially separated products produced one isomer pure, 3-aza-5α-pregnane-2,20-dione (XXII) with a methyl resonance at 54 cps.

The formation of two isomers parallels the results obtained in the Beckmann rearrangement of A-norcholestan-2-one oxime.[3e] The C-19 methyl resonance of the A-noroxime described here was broad, indicating that the oxime was a mixture of *syn* and *anti* forms, which would give rise to two lactams.

In summary, the selective oximation of pregnanediones, followed by Beckmann rearrangement of the oxime, using the procedure of Craig and Naik, gives A-azapregnane derivatives in high yield, and offers an excellent route to the preparation of such compounds.

Experimental Section[16]

5α-Pregnane-3,20-dione (I).—This compound was prepared as described previously[4] and had mp 201–203°; $[\alpha]_{589}$ +119°, $[\alpha]_{578}$ +128°, $[\alpha]_{546}$ +149°, $[\alpha]_{436}$ +324°, $[\alpha]_{365}$ +766° (*c* 0.56, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 5.85 μ; R_f^{BE} 1.00; nmr, 38 (18-H), 60 (19-H), and 127 (21-H) cps; lit.[17] mp 202–202.5°, $[\alpha]_D$ +127° (EtOH).

5α-Pregnane-3,20-dione 3-Oxime (II).—A solution of 8.30 g (26.9 mmoles) of 5α-pregnane-3,20-dione (I) and 1.87 g (26.9 mmoles) of hydroxylamine hydrochloride in 500 ml of absolute ethanol and 125 ml of dry pyridine was stirred at room temperature for 90 hr. The solvent was removed under reduced pressure and the residue was triturated with 150 ml of water, collected, and recrystallized from ethanol. Two crops gave 7.87 g (75%) of 5α-pregnane-3,20-dione 3-oxime (II): mp 238–241° (dec); $[\alpha]_{589}$ +107°, $[\alpha]_{578}$ +112°, $[\alpha]_{436}$ +279°, $[\alpha]_{365}$ +632°, (*c* 0.49, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 2.96, 5.85, and 6.03 μ; R_f^{BE} 0.67, R_f^{BEA} 0.92; nmr, 38 (18-H), 55 (19-H), and 127 (21-H) cps.

An analytical sample was recrystallized from methanol and had mp 240–241.5°.

Anal. Calcd for $C_{21}H_{33}NO_2$: C, 76.15; H, 9.97. Found: C, 76.25; H, 9.83.

5α-Pregnan-3β-ol-20-one 20-Oxime (IV).—A solution of 2.42 g (7.6 mmoles) of 5α-pregnan-3β-ol-20-one (III)[18] and 2.5 g (35 mmoles) of hydroxylamine hydrochloride in 100 ml of 1:1 dry pyridine and absolute ethanol was boiled under reflux for 2 hr. The solvent was removed with a stream of air and the residue was triturated with 25 ml of water. The white solid was collected, recrystallized from methanol, and 1.97 g (78%) of 5α-pregnan-3β-ol-20-one 20-oxime (IV) was obtained: mp 227–229°; $[\alpha]_{589}$ +34.2°, $[\alpha]_{578}$ +41.4°, $[\alpha]_{546}$ +41.0°, $[\alpha]_{436}$ +81.7°, $[\alpha]_{365}$ +158°, (*c* 0.58, C_5H_5N); λ_{max}^{KBr} 2.99, 3.10, and 6.10 μ; R_f^{BE} 0.41, R_f^{BEA} 0.96; lit.[5] mp 227°.

5α-Pregnane-3,20-dione Dioxime (VI).—This compound was prepared in 57% yield from 5α-pregnane-3,20-dione in the same manner as the 5α-pregnan-3β-ol-20-one 20-oxime and had mp 250–252° (dec); $[\alpha]_{589}$ +62.0°, $[\alpha]_{578}$ +67.5°, $[\alpha]_{546}$ +70.7°, $[\alpha]_{436}$ +132°, $[\alpha]_{365}$ +236° (*c* 0.50, C_5H_5N); λ_{max}^{KBr} 3.01 and 6.05 μ; R_f^{BEA} 0.96; lit.[5] mp 260°.

Anal. Calcd for $C_{21}H_{34}N_2O_2$: C, 72.83; H, 9.83. Found: C, 72.69; H, 9.58.

5α-Pregnane-3,20-dione 20-Oxime (V) *via* Levulinic Acid Hydrolysis of 5α-Pregnane-3,20-dione Dioxime (VI).—Levulinic acid reagent (88 g)[7] was added to 2.93 g (8.5 mmoles) of 5α-pregnane-3,20-dione dioxime (VI) and the resulting slurry was stirred at room temperature until all of the solid was dissolved (*ca.* 4 hr). The solution was diluted with 200 ml of water and extracted with ether (10 × 80 ml). The ether extracts were combined, washed with 10% sodium bicarbonate solution (5 × 80 ml) and water, and then dried over anhydrous sodium sulfate. The ether solution was filtered, the solvent was removed under reduced pressure, and the residue was taken up in chloroform and chromatographed on 60 g of silica gel. Elution with 0–10% ether in benzene produced 1.30 g (46%) of 5α-pregnane-3,20-dione 20-oxime (V), mp 229.5–231.0°, after recrystallization from ethanol: $[\alpha]_{589}$ +48.0°, $[\alpha]_{578}$ +50.6°, $[\alpha]_{546}$ +59.7°, $[\alpha]_{436}$ +122°, $[\alpha]_{365}$ +269° (*c* 0.51, $CHCl_3$); λ_{max}^{KBr} 3.01, 5.85, and 6.01 μ; R_f^{BE} 0.83, R_f^{BEA} 1.11; nmr, 39 (18-H), 62 (19-H), and 114 (21-H) cps.

Anal. Calcd for $C_{21}H_{33}NO_2$: C, 76.13; H, 9.96. Found: C, 76.07; H, 9.92.

Further elution with increasing amounts of ether in benzene produced 1.05 g of dioxime VI identified by comparison of the infrared spectrum and tlc R_f value with those of an authentic sample. After correcting for recovered starting material the yield of 5α-pregnane-3,20-dione 20-oxime (V) was 72%.

5α-Pregnane-3,20-dione 20-Oxime (V) *via* Oxidation of 5α-Pregnan-3β-ol-20-one 20-Oxime (IV).—To a solution of 3.00 g (9.00 mmoles) of 5α-pregnan-3β-ol-20-one 20-oxime (IV) in 150 ml of purified dioxane was added 3.00 ml of Jones chromium trioxide reagent[6] over a 1-min period. The solution was stirred for an additional 5 min and then poured into 3 l. of water. The precipitated white solid was collected, air dried, taken up in chloroform, and chromatographed on 40 g of silica gel. Elution with 0–5% ether in benzene produced 0.900 g (30%) of 5α-pregnane-3,20-dione 20-oxime (V): mp 229–232°; mixture melting point with the monoxime prepared from hydrolysis of 5α-pregnane-3,20-dione dioxime (VI), 228–231°. R_f values for tlc were identical for the two independently prepared oximes.

Further elution with increasing amounts of ether in benzene produced 1.35 g of 5α-pregnan-3β-ol-20-one 20-oxime (IV) identified by comparison of the infrared spectrum and tlc R_f with those of an authentic sample. After correcting for recovered starting material, the yield of V was 62%.

A-nor-5α-pregnane-2,20-dione (VII).—This compound was prepared by two previously described methods[4,19] and had mp 176–179°; $[\alpha]_{589}$ +248°, $[\alpha]_{578}$ +253°, $[\alpha]_{546}$ +292°, $[\alpha]_{436}$ +630°, $[\alpha]_{365}$ +1440° (*c* 0.51, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 5.74 and 5.87 μ; R_f^{BE} 1.30; R_f^{BEA} 1.30; nmr, 38.5 (18-H), 52 (19-H), and 128 (21-H) cps; lit.[20] mp 180°, $[\alpha]_D$ +255°. It was found that the over-all yield of the method of Nace and Nelander[4] could be substantially improved by not isolating the nitrone intermediate, but by hydrolyzing it directly to the diosphenol.

A-Nor-5α-pregnane-2,20-dione 2-Oxime (VIII).—A solution of 0.500 g (1.67 mmoles) of A-nor-5α-pregnane-2,20-dione (VII) and 0.116 g (1.67 mmoles) of hydroxylamine hydrochloride in 100 ml of 1:1 dry pyridine and abolute ethanol was kept at 60° for 2 weeks. The solvent was removed under reduced pressure and the residue triturated with 100 ml of water. The white solid was collected, taken up in 10 ml of chloroform, and chromatographed on 50 g of silica gel. Elution with 0–5% ether in benzene produced 0.090 g of A-nor-5α-pregnane-2,20-dione (VII), mp 177–179° after recrystallization from acetone–dilute hydrochloric acid, lit.[19] mp 180°.

Elution with 30–50% ether in benzene gave 0.390 g (74%) of A-nor-5α-pregnane-2,20-dione 2-oxime (VIII): mp 224–225° (dec); $[\alpha]_{589}$ +125°, $[\alpha]_{578}$ +136°, $[\alpha]_{546}$ +158°, $[\alpha]_{436}$ +318°, $[\alpha]_{365}$ +664°, (*c* 0.51, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 3.02, 5.85, and 6.01 μ;

(16) Melting points were determined with a Hershberg apparatus and Anshutz thermometers and are corrected. Analyses were carried out by Micro-Tech Laboratories, Skokie, Ill., and by Dr. S. M. Nagy and associates, Microchemical Laboratory, Massachusetts Institute of Technology. Optical rotations were determined on a Perkin-Elmer 141 polarimeter using a jacketed cell kept at 25°. Infrared spectra were determined on a Perkin-Elmer Infracord spectrophotometer. Chromatographic separations were made using Baker chromatographic grade silica gel and Merck chromatographic grade alumina. For thin layer chromatography, R_f^{BE} and R_f^{BEA} are reported for solvents 3:1 benzene–ether and 30:10:1 benzene–ether–acetic acid, respectively, and are relative to the R_f value of 5α-pregnane-3,20-dione. The R_f values were determined on glass plates with a 500-μ coating of silica gel and developed by spraying with a solution of 2,4-dinitrophenylhydrazine in phosphoric acid and ethanol.

(17) N. L. Allinger and M. A. DaRooge, *J. Am. Chem. Soc.*, **83**, 4256 (1961).

(18) N. Pappas and H. R. Nace, *ibid.*, **81**, 4556 (1959).

(19) R. E. Marker, O. Kamm, and D. M. Jones, *ibid.*, **59**, 1595 (1937).

(20) C. T. Rull and G. Ourisson, *Bull. Soc. Chim. France*, 1573 (1958).

R_f^{BE} 0.45, R_f^{BEA} 0.80; nmr, 37 (18-H), 45.5 (br), (19-H), and 127 (21-H) cps.

Anal. Calcd for $C_{20}H_{31}NO_2$: C, 75.70; H, 9.78. Found: C, 76.16; H, 10.35.

After correcting for recovered starting material the yield of A-nor-5α-pregnane-2,20-dione 2-oxime (VIII) was 90%.

A-Nor-5α-pregnane-2,20-dione Dioxime (IX).—This compound was prepared in 81% yield in the same manner as 5α-pregnan-3β-ol-20-one 20-oxime (IV) and had mp 251–253° (dec); $[\alpha]_{589}$ +75°, $[\alpha]_{578}$ +83°, $[\alpha]_{546}$ +89°, $[\alpha]_{436}$ +168°, $[\alpha]_{365}$ +286°, (*c* 0.57, C_5H_5N); λ_{max}^{KBr} 3.02 and 6.02 μ; R_f^{BEA} 0.81.

Anal. Calcd for $C_{20}H_{32}N_2O_2$: C, 72.28; H, 9.64. Found: C, 71.63; H, 9.45.

Attempted Preparation of A-Nor-5α-pregnane-2,20-dione 20-Oxime *via* Levulinic Acid Hydrolysis of A-Nor-5α-pregnane-2,20-dione Dioxime (IX).—Levulinic acid reagent (1.5 g)[7] was added to 0.050 g (0.15 mmole) of A-nor-5α-pregnane-2,20-dione dioxime (IX). The resulting slurry was stirred at 60° for 2 hr, then diluted with 50 ml of water. The aqueous mixture was extracted with methylene chloride (3 × 30 ml) and chloroform (3 × 30 ml). The extracts were combined, washed with half-saturated sodium bicarbonate (4 × 50 ml) solution, and water (2 × 50 ml), and then dried over anhydrous sodium sulfate. The solution was filtered and the solvent was removed under reduced pressure. An infrared spectrum of the residue showed two peaks in the carbonyl region at 5.74 and 5.85 μ with the peak at 5.85 μ being about one-third the intensity of the 5.74-μ peak. Tlc showed two spots with R_f values intermediate between the dioxime IX and the dione VII.

A-Nor-5α-pregnan-2-ol-20-one-2-carboxylic Acid 20-Oxime.—This compound was prepared from A-nor-5α-pregnan-2-ol-20-one-2-carboxylic acid[4] in 44% yield and had mp 232–235°; $[\alpha]_{578}$ +45°, $[\alpha]_{546}$ +52°, $[\alpha]_{436}$ +95° (*c* 0.40, C_5H_5N); λ_{max}^{KBr} 2.90 and 5.75–5.85 μ.

Anal. Calcd for $C_{21}H_{33}NO_4$: C, 69.39; H, 9.06. Found: C, 69.41; H, 9.42.

Attempted Preparation of A-Nor-5α-pregnane-2,20-dione 20-Oxime by Lead Tetraacetate Oxidation of A-Nor-5α-pregnan-2-ol-20-one-2-carboxylic Acid 20-Oxime.—A solution of 0.050 g (0.13 mmole) of A-nor-5α-pregnan-2-ol-20-one-2-carboxylic acid 20-oxime and 0.088 g of lead tetraacetate in 5 ml of glacial acetic acid was stirred at room temperature for 2 days. The solution developed a bright blue-green color upon addition of the lead tetraacetate, and then faded to a light green at the end of the 2-day period. The solution was heated on a steam bath for 0.5 hr, then diluted with 10 ml of water. The aqueous layer was extracted with ether (5 × 20 ml) and the extracts were combined, washed with water (3 × 20 ml), half-saturated potassium bicarbonate solution (4 × 20 ml), and water (2 × 30 ml), and then dried over sodium sulfate. After filtration and removal of the solvent under reduced pressure, tlc of the residue showed four spots, one with R_f values identical with those of starting material, one with R_f values identical with those of A-nor-5α-pregnane-2,20-dione (VII), and two trace spots with greater R_f values than those of the 2,20-dione. The infrared spectrum was very similar to that of A-nor-5α-pregnane-2,20-dione and showed no evidence that any oxime was present.

A-Homo-4-aza-5α-pregnane-3,20-dione (X) *via* Rearrangement of 5α-Pregnane-3,20-dione 3-Oxime Benzenesulfonate.—To a solution of 5.75 g (10.7 mmoles) of 5α-pregnane-3,20-dione 3-oxime (II) in 150 ml of dry pyridine, cooled to 0°, was added 2.4 ml of benzenesulfonyl chloride, and then the solution was stirred for 0.5 hr. The solvent was removed under reduced pressure and the remaining red oil was taken up in 100 ml of chloroform and chromatographed on 240 g of alumina. Elution with 0–40% ether–benzene gave 0.61 g of unreacted starting material II: mp 238–240° after recrystallization from ethanol; with an authentic sample, mmp 238–241°. Elution with 50–100% ether–benzene produced 4.80 g (93% after correction for recovered starting material) of A-homo-4-aza-5α-pregnane-3,20-dione (X), which was recrystallized from methanol–methylene chloride, and had mp 275–277° (dec); $[\alpha]_{589}$ +85° $[\alpha]_{578}$ +89°, $[\alpha]_{546}$ +105°, $[\alpha]_{436}$ +230°, $[\alpha]_{365}$ +543° (*c* 0.56, $CHCl_3$); R_f^{BEA} 0.65; λ_{max}^{KBr} 3.04, 5.85, 5.94, and 6.07 μ; nmr, 36.5 (18-H), 55.5 (19-H), and 129 (21-H) cps.

Anal. Calcd for $C_{21}H_{33}NO_2$: C, 76.13; H, 9.97. Found: C, 76.11; H, 10.01.

The red oil obtained after evaporation of the pyridine was assumed to be the benzenesulfonate ester of the oxime. The infrared spectrum was consistent with this assumption and the oil could be converted to the lactam X by heating in ether. This red oil was also obtained by elution of the alumina column with methanol–ether, and could be recycled to give the lactam X.

A-Homo-4-aza-5α-pregnane-3,20-dione (X) *via* Thionyl Chloride-Catalyzed Rearrangement of 5α-Pregnane-3,20-dione 3-Oxime (II).—A solution of 1.73 g (5.21 mmoles) of 5α-pregnane-3,20-dione 3-oxime (II) in 200 ml of purified dioxane was cooled to 0° and a solution of 15 ml of thionyl chloride in 40 ml of dioxane was added slowly while the temperature was kept at 0°. After the addition was complete, the solution was allowed to come to room temperature and then was decomposed by adding 100 ml of water, followed by 60 ml of concentrated aqueous ammonia. The solution was then extracted with 350 ml of methylene chloride in three portions. The extracts were combined, filtered through sodium sulfate, and evaporated to a volume of 60 ml. This solution was diluted with 200 ml of methanol and the precipitated solid was collected and recrystallized from methanol. Two crops gave 0.970 g of material, mp 220–270°. The material was then chromatographed on 32 g of silica gel. Elution with 0–20% ether–benzene gave 0.087 g of starting material II. Elution with 30–100% ether–benzene and 0–100% methanol–ether gave 0.635 g (39%) of A-homo-4-aza-5α-pregnane-3,20-dione (X), mp 270–276°. The physical properties of this product were identical in all respects with the lactam prepared by rearrangement of the oxime benzenesulfonate.

A-Homo-4-oxa-5α-pregnane-3,20-dione (XII).—A solution of 0.500 g (1.5 mmoles) of A-homo-4-aza-5α-pregnane-3,20-dione (X) in 50 ml of dry pyridine and 50 ml of carbon tetrachloride was cooled to 0°. A slow stream of nitrogen dioxide was bubbled through the solution for a period of 1 hr. The solution was then poured into a mixture of ice and water and extracted with chloroform (3 × 50 ml). The chloroform solution was then washed with water (2 × 50 ml), 5% sodium bicarbonate solution, and again with water. The solvent was then removed under reduced pressure and the residue was recrystallized from ether–hexane. Two crops gave 0.445 g (90%) of A-homo-4-oxa-5α-pregnane-3,20-dione (XII): mp 197–199°; $[\alpha]_{589}$ +84.5°, $[\alpha]_{578}$ +87.5°, $[\alpha]_{546}$ +102°, $[\alpha]_{436}$ +218°, $[\alpha]_{365}$ +465° (*c* 0.64, $CHCl_3$); retention time 0.31 (sharp);[21] R_f^{BE} 0.60, R_f^{BEA} 0.80; λ_{max}^{KBr} 5.77 and 5.85 μ; nmr, 37 (18-H), 56 (19-H), 126 (21-H), and 243, 255, 263, 268, 271, 278, and 285 cps.

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.90; H, 9.64. Found: C, 75.42; H, 9.78.

20,20-Ethylenedioxy-5α-pregnan-3-one (XX).—This compound was prepared as described previously[4] and had mp 186.5–189.0°; $[\alpha]_{589}$ +38°, $[\alpha]_{578}$ +40.5°, $[\alpha]_{546}$ +47.5°, $[\alpha]_{436}$ +96°, $[\alpha]_{365}$ +210° (*c* 0.51, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 5.85 μ; R_f^{BE} 1.21, R_f^{BEA} 1.08; nmr, 48 (18-H), 61.5 (19-H), 78 (21-H), and 232–240 (quartet) (ketal) cps; lit.[4] mp 187–188°, $[\alpha]^{25}D$ +35°.

A-Homo-4-oxa-5α-pregnane-3,20-dione (XII) and A-Homo-3-oxa-5α-pregnane-4,20-dione (XIII).—A solution of 6 ml of 40% peroxyacetic acid (Becco Chemicals) and 10 ml of chloroform was made up and dried over sodium sulfate. To a solution of 0.18 g (0.50 mmole) of 20,20-ethylenedioxy-5α-pregnane-3-one in 15 ml of chloroform was added 3 ml of the peroxyacetic acid solution and the resulting solution was kept at 40° for 18 hr. The solution was then washed with half-saturated potassium bicarbonate solution (5 × 50 ml) and water (2 × 50 ml), and then dried over anhydrous sodium sulfate. After filtration and removal of the solvent under reduced pressure the residue was recrystallized from methanol. Two crops gave 0.132 g (82%) of a 1:1 mixture (based on nmr 19-H peak heights) of A-homo-4-oxa-5α-pregnane-3,20-dione (XII) and A-homo-3-oxa-5α-pregnane-4,20-dione (XIII): mp 191–206°; $[\alpha]_{589}$ +45°, $[\alpha]_{578}$ +48.5°, $[\alpha]_{546}$ +56°, $[\alpha]_{436}$ +124°, $[\alpha]_{365}$ +294° (*c* 0.59, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 5.77 and 5.85 μ; R_f^{BE} 0.50, 0.59; nmr, 38 (18-H), 56, 58 (19-H), 126 (21-H), (multiple peaks in the region of 240–290 cps including the seven given above for the lactone XII.

2,3-Seco-5α-pregnane-2,3,20-triol (XV).—To a solution of 0.500 g of lithium aluminum hydride in 75 ml of anhydrous ether was slowly added, with stirring, a solution of 0.500 g of 2,3-seco-5α-pregnan-20-one-2,3-dioic acid[20] (XVI) in 75 ml of ether. After the addition was complete, the solution was boiled under reflux for 6 hr and cooled; then 100 ml of a 10% aqueous sulfuric acid solution was added. The layers were separated and the aqueous layer was extracted further with ether (2 × 100 ml). The ether extracts were combined, washed with half-saturated

(21) Retention time relative to 5α-pregnane-3β-ol-20-one on vpc using a 4-ft column containing a 1% QF-1 coating on Gas Chrom-Z support.

sodium bicarbonate solution and water, and filtered through anhydrous sodium sulfate. After evaporation of the solvent under reduced pressure, the residue was recrystallized from ether-cyclohexane, and 0.140 g (30%) of 2,3-seco-5α-pregnane-2,3,20-triol (XV) was obtained: mp 165–170°; nmr, 49, 59, 68, 83, and 128 cps. Vpc showed two major peaks, 49 and 43% of the total, with relative retention times of 0.33 and 0.45, respectively.

A-Homo-4-oxa-5α-pregnane-2,20-dione (XIX) and A-Homo-3-oxa-5α-pregnane-4,20-dione (XIII).—A solution of 0.100 g (1.0 mmole) of chromium trioxide and 0.100 g (0.29 mmole) of 2,3-seco-5α-pregnan-2,3,20-triol (XV) in 3 ml of glacial acetic acid was kept at 52.4° for 5 hr with occasional shaking. The solution was then diluted with 10 ml of water and extracted with ether (12 × 50 ml). The ether extracts were combined, washed with water (2 × 150 ml), and dried over sodium sulfate. After filtration and removal of the ether under reduced pressure, the residue was treated with 10% potassium carbonate solution and extracted with 1:1 ether–methylene chloride (2 × 100 ml). The extracts were combined, dried over anhydrous sodium sulfate, filtered, and evaporated to dryness under reduced pressure. The residue was recrystallized from ether–hexane and 0.032 g of a 1:1 mixture (based on nmr 19-H peak heights) of A-homo-3-oxa-5α-pregnane-2,20-dione (XIX) and A-homo-3-oxa-5α-pregnane-4,20-dione (XIII) was obtained: mp 172–198°; $\lambda_{max}^{CHCl_3}$ 5.77 and 5.85 μ; retention time 0.51 (br); R_f^{BE} 0.58, 0.45; nmr, 37 (18-H), 53.5, 56 (19-H), 126 (21-H), 240–260 (multiplet) cps.

2-Aza-5α-pregnane-3,20-dione (XXI) and 3-Aza-5α-pregnane-2,20-dione (XXII).—A solution of 0.600 g (1.9 mmoles) of A-nor-5α-pregnane-2,20-dione 2-oxime (VIII) and 2.0 ml of benzenesulfonyl chloride in 20 ml of dry pyridine was stirred at 65° for 1 hr. The pyridine was removed under reduced pressure and the red oil which remained was taken up in chloroform and chromatographed on 50 g of alumina. Elution with 0.5% ether–benzene gave 0.050 g (8.5%) of A-nor-5α-pregnane-2,20-dione 2-oxime (VIII), identified by comparison of the infrared spectrum with that of an authentic sample. Elution with 50–100% ether–benzene produced 0.510 g (85%) of a 1:1 mixture (based on nmr 19-H peak heights) of 2-aza-5α-pregnane-3,20-dione (XXI) and 3-aza-5α-pregnane-2,20-dione (XXII): mp 277–281° (dec); $[\alpha]_{578}$ +72°, $[\alpha]_{546}$ +84°, $[\alpha]_{436}$ +166°, $[\alpha]_{365}$ +391° (*c* 0.079, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 2.90, 5.85 and 6.01 μ; nmr, 38 (18-H), 54, 59 (19-H), and 128 (21-H) cps. After correction for recovered starting material the yield of lactams was 93%.

The mixture of azapregnanes was taken up in chloroform and chromatographed on 50 g of silica gel. The column was eluted with chloroform (technical grade, with 0.75% ethanol stabilizer) and 46 100-ml cuts were taken and evaporated. These fractions were divided into two approximately equal parts, A and B. Part A was chromatographed on 50 g of silica gel, using specially prepared chloroform (ethanol stabilizer replaced by 0.25% of methanol) as the eluent. When product started coming off the column, the percentage of methanol in the eluent was increased to 0.50% and 500-ml cuts were taken. Fractions (20) were collected, and the first 10 were combined and evaporated. The residue was recrystallized eight times from methanol, and 0.040 g of 3-aza-5α-pregnane-2,20-dione (XXII) was obtained: mp 278–280° (dec); $[\alpha]_{578}$ +97°, $[\alpha]_{546}$ +111°, $[\alpha]_{436}$ +216°, $[\alpha]_{365}$ +465° (*c* 0.143, $CHCl_3$); R_f^{BEA} 0.29; nmr, 38 (18-H), 54 (19-H), and 128 (21-H) cps.

Anal. Calcd for $C_{20}H_{31}NO_2 \cdot 0.5CH_3OH$: C, 73.87; H, 9.91. Found: C, 74.37; H, 9.85.

The last five fractions of the above chromatogram were combined and recrystallized several times from methanol, and methanol–water, and 0.005 g of a product containing 75% of 2-aza-5α-pregnane-3,20-dione (XXI) was obtained, as indicated by relative heights of the C-19 methyl resonances: $[\alpha]_{578}$ +77°, $[\alpha]_{546}$ +89°, $[\alpha]_{436}$ +166°, $[\alpha]_{365}$ +396°, (*c* 0.070, $CHCl_3$); R_f^{BEA} 0.24.

2α-Bromo-5α-pregnane-3,20-dione.—This compound was prepared as described previously[13,22] and had mp 199–201°; $[\alpha]_{589}$ +106°, $[\alpha]_{578}$ +111°, $[\alpha]_{546}$ +130°, $[\alpha]_{436}$ +279°, $[\alpha]_{365}$ +653°, (*c* 0.49, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 5.76 and 5.85 μ; R_f^{BE} 1.99, R_f^{BEA} 1.32; nmr, 38 (18-H), 72 (19-H), and 128 (21-H) cps; lit.[18] mp 199–202°, $\lambda_{max}^{CCl_4}$ 5.77 and 5.86 μ, $[\alpha]^{24}D$ +104°.[22]

5α-Pregnane-2,20-dione (XXV).—A solution of 12.0 g (30.4 mmoles) of 2α-bromo-5α-pregnane-3,20-dione and 25 ml of *n*-propyl mercaptan in 150 ml of chloroform was boiled under reflux under nitrogen for 17 hr. The solution was evaporated under reduced pressure to give a brown viscous oil. The oil was taken up in 500 ml of methanol and 50 ml of dilute (1:1) hydrochloric acid was added. The solution was boiled under reflux for 5 hr with 2–3 ml of water being added at 15-min intervals. Water (200 ml) was then added and the solution was steam distilled under aspirator pressure while 5% hydrochloric acid solution was added to keep the level of the solution constant. After 1500 ml of distillate had been collected, the distillation was stopped. The solid product remaining in the pot was collected, dissolved in 400 ml of ethanol and heated to boiling, and a solution of 36 g of sodium metabisulfite in 160 ml of water was added. The solution was stirred for 2 hr, then 200 ml of methylene chloride and 100 ml of water were added, and the solution was stirred for an additional 0.5 hr. The layers were separated and the methylene chloride solution was dried over sodium sulfate. After filtration and removal of the solvent, the residue was treated in the manner above with sodium bisulfite four additional times. The methylene chloride solution thus obtained was evaporated and the residue was recrystallized from methanol. One crop gave 0.350 g (36%) of 5α-pregnane-2,20-dione (XXV): mp 132–135°; $[\alpha]_{589}$ +93°, $[\alpha]_{578}$ +97°, $[\alpha]_{546}$ +114°, $[\alpha]_{436}$ +244°, $[\alpha]_{365}$ +563° (*c* 0.57, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 5.85 μ; R_f^{BE} 0.96, R_f^{BEA} 0.97; nmr, 36.5 (18-H), 43 (19-H), and 124 (21-H) cps.

An analytical sample was recrystallized from methanol and had mp 135–136°.

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.74; H, 10.12. Found: C, 80.76; H, 9.28.

5α-Pregnane-2,20-dione Dioxime.—A solution of 0.033 g (0.1 mmole) of 5α-pregnane-2,20-dione (XXV) and 0.038 g of hydroxylamine hydrochloride in 20 ml of 1:1 absolute ethanol–pyridine was boiled under reflux 4 hr. The solvent was removed under reduced pressure and the residue was triturated with 10 ml of water, collected, and recrystallized from methanol. One crop gave 0.015 g (41%) of 5α-pregnane-2,20-dione dioxime: mp 236–238°; $[\alpha]_{578}$ +41°, $[\alpha]_{546}$ +46°, $[\alpha]_{436}$ +81°, $[\alpha]_{365}$ +132° (*c* 0.195, C_5H_5N); λ_{max}^{KBr} 3.00 and 6.03 μ; R_f^{BEA} 0.77.

Anal. Calcd for $C_{21}H_{34}N_2O_2$: C, 72.83; H, 9.83' Found: C, 73.11; H, 10.15.

(22) M. Rubin, H. Wishinsky, and F. Bompard, *J. Am. Chem. Soc.*, **73**, 2338 (1951).