TABLE VI
DISTRIBUTION OF PRODUCTS IN THE PHE-ARG REACTION[a]

Product	From Phe-NTA, %	From Phe-NCA, %
Arginine	2.2	3.5
H-Phe-Arg·OH	94.2	89.2
H-Phe-Phe-Arg·OH	0.3	4.0
Hydantoic acid	2.7	2.8

[a] Traces of radioactivity between these spots bring the total to 100%.

layer was washed three times with 5% aqueous $NaHCO_3$, three times with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated to give 33 g (21%) of crude proline NTA. One recrystallization from ether gave material with a rotation of $[\alpha]_{589}$ −155.1° (*c* 1, $CHCl_3$) and three further crystallizations gave proline NTA of constant rotation, $[\alpha]_{589}$ −157 ±0.5° (*c* 1, $CHCl_3$). The final recrystallized proline NTA was used for the following racemization study.

Racemization in the Preparation of Prolylphenylalanine. A. In Tritiated Water.—A solution of 0.826 g (5.0 mmol) of phenylalanine in 50 ml of 0.5 *M* potassium borate in tritiated water was adjusted to pH 9.35 at 0°. Proline NTA (0.807 g, 5.8 mmol) was added while the pH was maintained at 9.35. The peptide was precipitated at pH 4.5 and recrystallized from water to constant activity. This product corresponded by tlc to peptide prepared *via* proline NCA.[1] A similar experiment was carried out at pH 10.0. At pH 9.35, 0.114% of 1 equiv of tritium was incorporated, and at pH 10.0, 0.129%.

B. In D_2O.—A solution of 0.66 g (4.0 mmol) of phenylalanine in 40 ml of 0.5 *M* borate buffer in D_2O which was prepared from boric acid anhydride and sodium deuterioxide was adjusted to a pH of 10.0 using a combination glass–calomel electrode set for a meter reading of 9.6.[37] A sample of the dipeptide was repeatedly recrystallized to free it of labile deuterium. This product was burned, and the water was reduced to hydrogen and then examined by mass spectroscopy.[38] Deuterium appeared at 0.0275% above natural abundance, which would correspond to an excess of 0.495% deuterium for one hydrogen position in the dipeptide.

A sample of L-proline NTA was hydrolyzed in dilute hydrochloric acid to proline, which was identified by tlc. The solution was concentrated and the product was assayed for D-proline by D-amino acid oxidase using a Warburg manometric technique[39] with an increased ratio of enzyme to substrate. Controls containing 0.5, 1.0, and 2.9% D-proline showed 0.34, 0.94, and 2.88% D-proline, whereas the above sample showed 2.08% D-proline (each an average of two runs).

Registry No.—Table I—L-Ala, 19777-64-1; D-alloisoleu, 26686-26-0; L-Arg, 26686-27-1; Gly, 26686-28-2; L-His, 19777-65-2; L-Ileu, 26686-30-6; L-Leu, 26686-31-7; L-Phe, 26686-32-8; L-Pro, 26686-33-9; L-Val, 26686-34-0; Table II—L-Ala, 16964-94-6; L-Arg, 26731-59-9; Gly, 16874-97-8; L-His, 26731-60-2; L-Leu, 26607-56-7; L-Phe, 26686-38-4; L-Pro, 26686-39-5; L-Val, 26731-61-3; **3** (R = *i*-Bu; R′ = Et), 26686-40-8; **9** (R = $C_6H_5CH_2$), 26686-41-9; **11**, 26686-47-5; glycyl-L-phenylalanyl-L-leucine, 15373-56-5; L-alanyl-L-phenylalanyl-L-leucine, 26686-43-1; L-Ala-*O*-benzyl-L-Ser-L-Val, 26731-62-4; L-Val-L-His-L-Phe-L-Asp-L-Ala-*O*-benzyl-L-Ser-L-Val, 6169-58-0; L-histidyl-L-alanylglycine, 26731-63-5; L-alanyl-L-phenylalanine, 3061-90-3; L-Arg-L-Phe, 2047-13-4.

Acknowledgments.—We wish to acknowledge the capable technical assistance of Messrs. James E. Deak, Victor Garsky, and John Sondey. We are indebted to Mr. R. Boos and associates for the elemental analyses, Mr. C. Homnick for the amino acid analyses, Dr. C. Rosenblum and his associates for assistance with the radiochemical measurements, and Miss D. L. Keller and Dr. T. Devlin for the D-amino acid oxidase studies.

(37) A correction factor of 0.4 pH units is required: P. K. Glasoe and F. A. Long, *J. Phys. Chem.*, **64**, 188 (1960).
(38) Gollob Analytical Service, Inc., Berkeley Heights, N. J.
(39) Worthington Biochemical Corp., Freehold, N. J., Data Sheet 1.4.3.1, 1967.

Steroidal β-Lactams.[1] II. Synthesis of Pregnane and *D*-Homo Compounds

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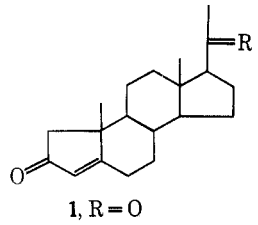
The conversion of *A*-norprogesterone (**1**) into 3,4-dinor-5-aza-*B*-homopregnane-2,20-dione (**20**) and its *D*-homo isomer, 17α-methyl-3,4-dinor-*B*-homo-*D*-homo-5-azaandrostane-2,17a-dione (**16**) is described.

The synthesis of a new steroidal ring system possessing a fused β-lactam as ring A has been recently described.[1] In that case, the substituent at C_{17} was a hydroxyl group, and we then became interested, from both the chemical and biological points of view, in the synthesis of a steroidal β-lactam bearing a pregnane side chain at C-17.[2] In this paper, we wish to describe the results of our efforts to convert *A*-norprogesterone (**1**)[3] into such a compound.

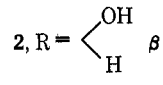
Our initial step in the synthesis was protection of the C-20 carbonyl of **1** as a hydroxyl function. We expected that treatment of **1** with sodium borohydride would lead to selective reduction at C-20, since α,β-unsaturated ketones reduce more slowly than saturated ketones (unhindered).[4] Indeed, reduction of **1** with sodium borohydride in methanol at 0° gave **2** in 80–90% yield. This compound has been previously prepared during the synthesis of **1**, by the ring A contraction method starting with 20β-hydroxy-4-pregnen-3-one.[3] Treatment of **2** with the permanganate–periodate combination[5] transformed the ring A α,β-unsaturated ketone system into a keto acid that cyclized and was isolated as the lactonol **3**. Room temperature acetylation selectively esterified the 20β-hydroxy group to give **4**. The methyl ester **5**, prepared by treatment of **4** with

* To whom correspondence should be addressed.
(1) Part I: S. D. Levine, *J. Org. Chem.*, **35**, 1064 (1970).
(2) Presented at the MetroChem 1969 Meeting of the American Chemical Society, New York, N. Y., May 1969.
(3) F. L. Weisenborn and H. E. Applegate, *J. Amer. Chem. Soc.*, **81**, 1960 (1959).
(4) J. K. Norymberski and G. F. Woods, *J. Chem. Soc.*, 3426 (1955).
(5) M. E. Wall and S. Serota, *J. Org. Chem.*, **24**, 741 (1959).

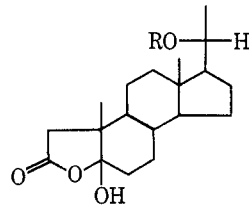
diazomethane, was reacted with hydroxylamine hydrochloride in pyridine to prepare the 5-oximino derivative. This oxime was not obtained in crystalline form, but was treated directly with thionyl chloride in dioxane to effect the ring B Beckmann rearrangement and give, after hydrolysis with base, the high-melting, very insoluble lactam acid **6**. Esterification with diazomethane gave the methyl ester **7**, which was reduced with lithium aluminum hydride in tetrahydrofuran to the amino diol **8**. Reaction of **8** with acetic anhydride in pyridine and purification of the product by alumina chromatography gave the *N*-acetyl diacetate **9** as an oil, which was characterized by its nmr spectrum.



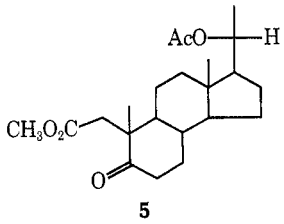
1, R = O



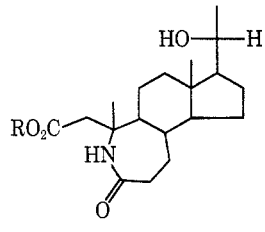
2, R = β-OH



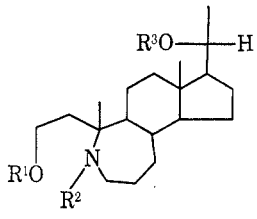
3, R = H
4, R = Ac



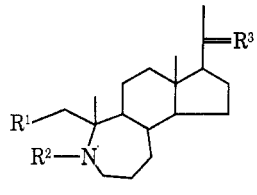
5



6, R = H
7, R = CH_3



8, $R^1 = R^2 = R^3 = H$
9, $R^1 = R^2 = R^3 = Ac$
10, $R^1 = H$; $R^2 = R^3 = Ac$
17, $R^1 = R^3 = H$; $R^2 = Ac$



11, $R^1 = CHO$; $R^2 = Ac$; $R^3 = \beta$-OAc
12, $R^1 = CO_2H$; $R^2 = Ac$; $R^3 = \beta$-OAc
18, $R^1 = CHO$; $R^2 = Ac$; $R^3 = O$
19, $R^1 = CO_2H$; $R^2 = Ac$; $R^3 = O$

We next sought to hydrolyze the C-2 and C-20 acetates in **9** to provide an *N*-acetyl diol that would, upon Jones oxidation, provide the C-17 progesterone side chain and an aldehyde at C-2, which could then be transformed into the desired β-lactam by following the same route employed in the androstane series.[1] Hydrolysis of **9** with refluxing methanolic potassium hydroxide solution for a few minutes gave, however, a product that contained only one hydroxyl group. An examination of the nmr spectrum of the product demonstrated that it was the C-2 alcohol. The signals for the C-18 Me, C-21 Me, and the 20α H were almost the same as those in **9**; therefore, the product was assigned structure **10**. At this stage, we decided to continue the synthesis as outlined above, because we felt that we could hydrolyze the 20β-acetate later, during the acid hydrolysis of the *N*-acetyl function. The desired ring A β-lactam, with a 17β-acetyl side chain, could then be prepared by cyclization to the β-lactam, followed by Jones oxidation of the 20β-ol.

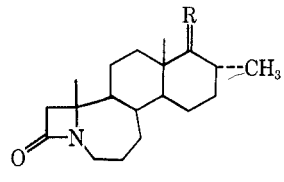
Stepwise oxidation at C-2 of **10**, first to the aldehyde **11** with Jones reagent at low temperature, and then to the carboxylic acid **12** with silver oxide proceeded uneventfully. Acid hydrolysis of **12** gave the crude amino acid that was cyclized with dicyclohexylcarbodiimide (DCC) in methylene chloride–nitromethane to provide a steroidal β-lactam having the expected molecular formula, $C_{19}H_{31}NO_2$. An inspection of the nmr spectrum of the product, however, revealed that we were no longer dealing with a 20β-hydroxypregnane derivative. This β-lactam has been assigned the *D*-homo structure **13** resulting from a uranediol type rearrangement.[6] The relevant nmr signals that enabled us to make the structural and stereochemical assignment are shown for **13**, uranediol **14**, and 17a-epiuranediol **15** in Table I.

TABLE I
NMR SIGNALS

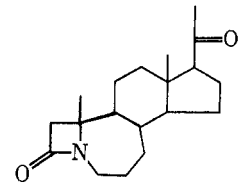
Compd	18-Me	17α Me	17α H
13	9.15	9.03 d, J = 5.5 Hz	7.28 d, J = 9 Hz
14[a]	9.19	9.06 d, J = 5 Hz	7.30 d, J = 9 Hz
15[a]	9.19	9.08 d, J = 7 Hz	6.69, W_H = 5 Hz

[a] See ref 6.

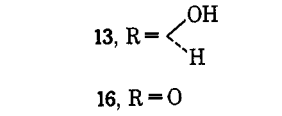
The rearrangement of the 20β-hydroxypregnane to the *D*-homo structure no doubt took place during the acid hydrolysis of **12**. The mechanism of this reaction has been discussed previously in detail[6] and will not be dealt with here. Jones oxidation of **13** provided the 17a-keto compound **16**.



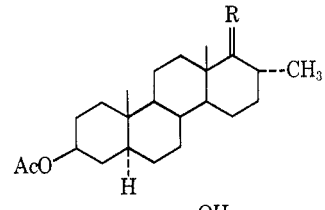
13, R = β-OH



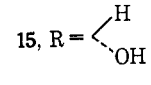
20



16, R = O



14, R = β-OH



15, R = α-OH

The unstable nature of the 20β-hydroxy side chain, under the acid conditions employed for the hydrolysis of the *N*-acetyl function, necessitated hydrolysis of the 20β-acetoxy group under alkaline conditions at some point in the synthesis. We were fortunate to observe that the 20β-acetoxy function could be slowly hydro-

(6) H. Hirschmann, F. B. Hirschmann, and A. P. Zala, *J. Org. Chem.*, **31**, 375 (1966), and references contained therein.

lyzed when the alkaline treatment of **9** was allowed to proceed at room temperature for an extended period of time (4–6 days). In this manner, we were able to obtain the desired *N*-acetyl diol **17**. Jones oxidation of **17** to the 2-aldehydo compound **18**, followed by further oxidation with silver oxide, afforded the *N*-acetyl acid **19**. The synthesis of the β-lactam bearing a 17β-acetyl side chain **20** was completed by acid hydrolysis of the *N*-acetyl group and cyclization of the resulting crude amino acid with DCC in nitromethane and chloroform.

Experimental Section

Melting points were determined in a Thomas–Hoover capillary melting-point apparatus and are uncorrected. Values of $[\alpha]D$ have been approximated to the nearest degree and were taken on a Perkin-Elmer 141 polarimeter in 95% EtOH. Ir spectra were determined on a Perkin-Elmer 21 spectrometer in pressed KBr pellets (unless otherwise indicated), and nmr spectra on a Varian A-60 spectrometer, employing TMS as the internal standard. The organic solutions were dried over sodium sulfate and all evaporations were carried out *in vacuo*. Alumina refers to neutral alumina, activity V, and silica gel refers to silica gel $HF_{254+366}$. Compounds were detected on the plates with iodine vapor. IPE stands for isopropyl ether.

20β-Hydroxy-*A*-nor-3-pregnen-2-one (2).—A solution of *A*-norprogesterone (2.0 g) in MeOH (200 ml) was treated at 0° with $NaBH_4$ (380 mg) and stirred at that temperature for 1 hr. Acetic acid (3 drops) was added and the solution was evaporated, diluted with H_2O, and extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with 8% NaCl solution, dried, and evaporated. Crystallization from $CHCl_3$–IPE gave **2** [1.68 g, mp 210–212° (lit.[3] mp 213–214°)].

5β,20β-Dihydroxy-3-oxa-*A*-norpregnan-2-one (3).—A solution of **2** (1.0 g) in *tert*-BuOH (150 ml) was treated with a suspension of K_2CO_3 (1.38 g), $KMnO_4$ (0.18 g), and $NaIO_4$ (5.72 g) in H_2O (150 ml) and stirred overnight at room temperature. The mixture was diluted with H_2O and extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with 8% NaCl solution, dried, and evaporated. Crystallization of the residue from $CHCl_3$–acetone gave **3** (413 mg, mp 192–193°). Recrystallization from $CHCl_3$ gave the analytical sample: mp 192–193°; $[\alpha]D$ +29°; ir 2.79, 2.82, 2.95, 5.64, and 5.79 μ; nmr ($CDCl_3$) τ 9.21 (s, 18-Me), 8.89 (s, 19-Me), 8.86 (d, J = 6 Hz, 21-Me), and 6.28 (m, 20α H).

Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.67; H, 9.15.

3-Oxa-5β-hydroxy-20β-acetoxy-*A*-norpregnan-2-one (4).—A solution of **3** (10.0 g) in Ac_2O (13 ml) and pyridine (25 ml) was left at room temperature for 4 hr. The mixture was diluted with H_2O and extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with 2 *N* HCl and 8% NaCl solution, dried, and evaporated. Crystallization of the residue from $CHCl_3$–IPE gave **4** (9.4 g, mp 167–168°). Recrystallization from acetone–IPE gave the analytical sample: mp 168–169°; $[\alpha]D$ +57°; ir 2.97, 5.71, and 5.79 μ; nmr ($CDCl_3$) τ 9.33 (s, 18-Me), 8.87 (s, 19-Me), 8.85 (d, J = 6 Hz, 21-Me), 7.97 (s, 20β-OAc), and 5.11 (m, 20α H).

Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 69.09; H, 8.69.

5-Oxo-20β-acetoxy-3,4-dinor-2,5-secopregnan-2-oic Acid 2-Methyl Ester (5).—A solution of **4** (3.57 g) in MeOH (8 ml) and ether (8 ml) was treated with an excess of diazomethane in ether at room temperature for 12 min. Acetic acid was added and the solvents were evaporated. The residue was dissolved in $CHCl_3$ and this solution was washed with 8% NaCl solution, dried, and evaporated to afford **5** (3.85 g) as a homogeneous oil (tlc): nmr ($CDCl_3$) τ 9.29 (s, 18-Me), 8.84 (d, J = 6 Hz, 21-Me), 8.83 (s, 19-Me), 7.99 (s, 20β-OAc), 6.34 (s, 2-CO_2CH_3), and 5.10 (m, 20α H).

6-Oxo-20β-hydroxy-3,4-dinor-2,5-seco-5-aza-*B*-homopregnan-2-oic Acid (6).—A solution of **5** (3.85 g) and $NH_2OH \cdot HCl$ (4 g) in pyridine (40 ml) was left at room temperature for 40 hr. The mixture was diluted with H_2O and extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with 2 *N* HCl and 8% NaCl solution, dried, and evaporated to give the crude oxime (3.6 g).

The oxime (3.6 g) in dioxane (60 ml) was cooled to 12° in an ice bath. Thionyl chloride (4 ml) was added, the ice bath was removed, and the mixture was stirred for 9 min. The reaction mixture was then added to 25% KOH solution (170 ml) and heated to 80°. After cooling, the mixture was extracted with ether. The aqueous portion was acidified and extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with 8% NaCl solution, dried, and evaporated, Crystallization of the residue from MeOH–IPE gave **6** (1.39 g, mp 266–267.5°). Recrystallization from MeOH gave the analytical sample: mp 270–271.5°; ir 2.86, 3.04, 3.11, 5.83, and 6.16 μ.

Anal. Calcd for $C_{19}H_{31}NO_4$: C, 67.62; H, 9.26; N, 4.15. Found: C, 67.84; H, 9.59; N, 4.09.

6-Oxo-20β-hydroxy-3,4-dinor-2,5-seco-5-aza-*B*-homopregnan-2-oic Acid 2-Methyl Ester (7).—Methylation of **6** (370 mg) by the procedure described for **5** gave **7** (277 mg, mp 151.5–152.5°) from EtOAc–IPE. Recrystallization from EtOAc–IPE gave the analytical sample: mp 154–155°; $[\alpha]D$ +22°; ir 2.87, 2.97, 5.81, and 6.10 μ; nmr ($CDCl_3$) τ 9.20 (s, 18-Me), 8.87 (d, J = 6 Hz, 21-Me), 8.58 (s, 19-Me), 6.3 (m, 20α H), and 6.27 (s, 2-CO_2CH_3).

Anal. Calcd for $C_{20}H_{33}NO_4$: C, 68.34; H, 9.46; N, 3.99. Found: C, 68.21; H, 9.36; N, 3.80.

2,20β-Dihydroxy-3,4-dinor-2,5-seco-5-aza-*B*-homopregnane (8).—A solution of **7** (2.5 g) in THF (250 ml) was treated with $LiAlH_4$ (2.6 g) for 67 hr. The cooled mixture was treated with EtOAc and H_2O and the organic layer separated. The aqueous layer was extracted with $CHCl_3$. The combined organic fractions were washed with 8% NaCl solution, dried, and evaporated. Crystallization of the residue from EtOAc–IPE gave **8** (1.05 g, mp 158–159°). Recrystallization from EtOAc–IPE gave the analytical sample: mp 159–160.5°; $[\alpha]D$ −20°; ir 2.96 and 3.03 μ; nmr ($CDCl_3$) τ 9.24 (s, 18-Me), 8.87 (d, J = 6 Hz, 21-Me), and 8.81 (s, 19-Me).

Anal. Calcd for $C_{19}H_{35}NO_2$: C, 73.73; H, 11.40; N, 4.53. Found: C, 73.94; H, 11.45; N, 4.37.

***N*-Acetyl-2,20β-diacetoxy-3,4-dinor-2,5-seco-5-aza-*B*-homopregnane (9).**—A solution of **8** (0.9 g) in Ac_2O (9 ml) and pyridine (9 ml) was left at room temperature overnight. The mixture was diluted with H_2O and extracted with ether. The ether extracts were washed with 8% NaCl solution, dried, and evaporated. Plate chromatography of the residue on alumina, using $CHCl_3$–hexane (5:1) as the developing solvent, and elution of the major band with EtOAc gave **9** (0.9 g) as an oil: nmr ($CDCl_3$) τ 9.33 (s, 18-Me), 8.87 (d, J = 6 Hz, 21-Me), 8.63 (s, 19-Me), 7.98 (s, 2 and 20β-OAc), 7.93 (s, 5-NAc), and 5.13 (m, 20α H).

***N*-Acetyl-2-hydroxy-20β-acetoxy-3,4-dinor-2,5-seco-5-aza-*B*-homopregnane (10).**—A solution of **9** (1.4 g) in 12.5% KOH solution (4 ml) and MeOH (40 ml) was refluxed for 8 min and then left at room temperature for 0.5 hr. The mixture was concentrated and diluted with H_2O. The precipitate was collected by filtration to give **10** (1.07 g, mp 167–168.5°). Recrystallization from ether–IPE gave the analytical sample: mp 169.5–170.5°; $[\alpha]D$ −9°; ir 2.83, 2.84, 5.84, and 6.12 μ; nmr ($CDCl_3$) τ 9.35 (s, 18-Me), 8.85 (d, J = 6 Hz, 21-Me), 8.6 (s, 19-Me), 7.99 (s, 20β-OAc), 7.92 (s, 5-NAc), and 5.15 (m, 20α H).

Anal. Calcd for $C_{23}H_{39}NO_4$: C, 70.19; H, 9.99; H, 3.56. Found: C, 70.06; H, 10.04; H, 3.41.

***N*-Acetyl-20β-acetoxy-3,4-dinor-2,5-seco-5-aza-*B*-homopregnan-2-al (11).**—A solution of **10** (535 mg) in acetone (40 ml) at 3° was treated with an excess of Jones reagent and stirred at 3° for 1.75 hr. The mixture was treated with MeOH, filtered through Hy-flo, and evaporated. Plate chromatography of the residue on alumina, using $CHCl_3$–hexane (4:1) as the developing solvent, gave a major band which was eluted with EtOAc. Evaporation gave a residue (367 mg) that was crystallized from acetone–IPE to give **11** (75 mg, mp 159.5–160.5°). Recrystallization from acetone–IPE gave the analytical sample: mp 159.5–160.5°; $[\alpha]D$ +19°; ir 5.79, 5.84, and 6.09 μ; nmr ($CDCl_3$) τ 9.36 (s, 18-Me), 8.85 (d J = 6 Hz, 21-Me), 8.59 (s, 19-Me), 8.01 (s, 20β-OAc), 7.94 (s, 5-NAc), 5.16 (m, 20α H), and 0.27 (t, J = 1.6 Hz, 2-CHO).

Anal. Calcd for $C_{23}H_{37}NO_4$: C, 70.55; H, 9.53; N, 3.58. Found: C, 70.75; H, 9.49; N, 3.60.

***N*-Acetyl-20β-acetoxy-3,4-dinor-2,5-seco-5-aza-*B*-homopregnan-2-oic Acid (12).**—A solution of $AgNO_3$ (2.2 g) in H_2O (23 ml) was added to a solution of **11** (2.1 g) in EtOH (45 ml). A solution of NaOH (2.2 g) in H_2O (45 ml) was then added to the reaction mixture and the resulting suspension was stirred in the dark for 4 hr. The mixture was filtered and the solid was washed with H_2O. The filtrate was extracted with $CHCl_3$ and then acidified with 2 *N* HCl. The acidic phase was extracted with

$CHCl_3$ and the $CHCl_3$ extracts were washed with 8% NaCl solution, dried, and evaporated. Crystallization of the residue from acetone–IPE gave **12** (957 mg, mp 172–173°). Recrystallization from acetone–IPE gave the analytical sample: mp 177–177.5°; $[\alpha]D$ −21°; ir 5.80 and 6.30 μ; nmr ($CDCl_3$) τ 9.35 (s, 18-Me), 8.86 (d, J = 6 Hz, 21-Me), 8.47 (s, 19-Me), 7.99 (s, 20β-OAc), 7.91 (s, 5-NAc), and 5.17 (m, 20α H).

Anal. Calcd for $C_{23}H_{37}NO_5$: C, 67.78; H, 9.15; N, 3.44. Found: C, 67.82; H, 9.12; N, 3.40.

17α-Methyl-17a,β-hydroxy-3,4-dinor-*B*-homo-*D*-homo-5-aza-androstan-2-one (13).—A solution of **12** (1 g) in H_2O (1 ml), concentrated HCl (10 ml), and dioxane (80 ml) was refluxed overnight. Evaporation of the solvents gave a residue that was dissolved in H_2O; the pH was then adjusted to 5.1 The aqueous solution was extracted with $CHCl_3$. The aqueous phase was then adjusted to pH 5.1, 8% NaCl solution was added, and the solution was evaporated. The residue was extracted with warm $CHCl_3$ which was then evaporated to yield the crude amino acid (507 mg).

The amino acid was dissolved in CH_2Cl_2 (20 ml) and CH_3NO_2 (80 ml), treated with DCC (340 mg), and stirred at room temperature for 72 hr. The precipitate was removed by filtration and the filtrate was evaporated. The residue (496 mg) was plate chromatographed on silica gel, using $CHCl_3$–EtOAc (1:1) as the developing solvent. Elution of the major band with EtOAc–MeOH (3:1) gave a residue that was crystallized from acetone–IPE to give **13** (163 mg, mp 155–157°). Recrystallization from acetone–IPE gave the analytical sample: mp 158–159.5°; $[\alpha]D$ +27°; ir ($CDCl_3$) 2.87 and 5.79 μ; nmr ($CDCl_3$) τ 9.15 (s, 18-Me), 9.03 (d, J = 6 Hz, 17α-Me), 8.59 (s, 19-Me), and 8.22 (s, 17a β-OH).

Anal. Calcd for $C_{19}H_{31}NO_2$: C, 74.71; H, 10.23; N, 4.99. Found: C, 74.49; H, 10.29; N, 4.89.

17α-Methyl-3,4-dinor-*B*-homo-*D*-homo-5-aza-androstane-2,-17a-dione (16).—A solution of **13** (150 mg) in acetone (10 ml) was treated with a slight excess of Jones reagent while stirring at room temperature. Methanol was added and the mixture was filtered through Hy-flo. The filtrate was concentrated and then diluted with H_2O, and the precipitate was collected by filtration to obtain **16** (41 mg, mp 193.5–195.5°). Recrystallization from acetone–IPE gave the analytical sample: mp 199–201°; $[\alpha]D$ −12°; ir 5.73 and 5.90 μ; nmr ($CDCl_3$) τ 9.02 (d, J = 6 Hz, 17α-Me), 8.88 (s, 18-Me), 8.60 (s, 19-Me), and 7.37 (s, 1-CH_2).

Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.20; H, 9.63; N, 4.62. Found: C, 75.48; H, 9.83; N, 4.53.

***N*-Acetyl-2,20β-dihydroxy-3,4-dinor-2,5-seco-5-aza-*B*-homo-pregnane (17).**—A solution of **9** (4.9 g) in MeOH (125 ml) containing 12.5% KOH solution (20 ml) was refluxed for 15 min and then stirred at room temperature for 6 days. The mixture was concentrated, diluted with H_2O, and extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with 8% NaCl solution, dried, and evaporated to give crude **17** (4.07 g).

A sample of **17** (276 mg) was plate chromatographed on alumina, using $CHCl_3$–MeOH (97:3) as the developing solvent. The major band was eluted with EtOAc, evaporated, and the residue was crystallized from acetone–IPE to give **17** (81 mg, mp 179–181.5°). Recrystallization from acetone–IPE gave the analytical sample: 184.5–185°; $[\alpha]D$ −51°; ir 2.90, 2.98, and 6.23 μ; nmr ($CDCl_3$) τ 9.24 (s, 18-Me), 8.87 (d, J = 6 Hz, 21-Me) 8.59 (s, 19-Me), and 7.92 (s, 5-NAc).

Anal. Calcd for $C_{21}H_{37}NO_3$: C, 71.75; H, 10.61; N, 3.99. Found: C, 71.71; H, 10.63; N, 3.96.

***N*-Acetyl-20-oxo-3,4-dinor-2,5-seco-5-aza-*B*-homopregnan-2-al (18).**—A solution of **17** (489 mg) in acetone (50 ml) at 3° was treated with an excess of Jones reagent and stirred at 3° for 1.75 hr. The mixture was treated with MeOH, concentrated, diluted with H_2O, and extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with 8% NaCl solution, dried, and evaporated. The residue was plate chromatographed on alumina, using $CHCl_3$ as the developing solvent. Elution of the major band with EtOAc and evaporation, gave **18** (221 mg) as an oil: nmr ($CDCl_3$) τ 9.38 (s, 18-Me), 8.59 (s, 19-Me), 7.94 (s, 5-NAc), 7.91 (s, 21-Me), and 0.34 (t, J = 1.6 Hz, 2-CHO).

***N*-Acetyl-20-oxo-3,4-dinor-2,5-seco-5-aza-*B*-homopregnan-2-oic Acid (19).**—A sample of **18** (220 mg) was oxidized as previously described for the preparation of **12**. Crystallization of the residue from acetone–IPE gave **19** (52 mg, mp 174–175°). Recrystallization from acetone–IPE gave the analytical sample: mp 176–177°; $[\alpha]D$ +1°; ir 5.78, 5.89, and 6.25 μ; nmr ($CDCl_3$) 9.35 (s, 19-Me), 8.46 (s, 18-Me), 7.88 (s, 5-NAc and 21-Me).

Anal. Calcd for $C_{21}H_{33}NO_4$: C, 69.39; H, 9.15; N, 3.85. Found: C, 69.72; H, 9.39; N, 3.75.

3,4-Dinor-5-aza-*B*-homopregnane-2,20-dione (20).—A solution of **19** (380 mg) in H_2O (0.4 ml), concentrated HCl (7 ml), and dioxane (20 ml) was refluxed overnight. Evaporation of the solvents gave a residue that was dissolved in water; the pH was then adjusted to 5.1. After the aqueous solution had been extracted with $CHCl_3$, the aqueous phase was adjusted to pH 5.5, 8% NaCl solution was added, and the solution was evaporated. The residue was extracted with warm $CHCl_3$, and the $CHCl_3$ evaporated to yield the crude amino acid (75 mg).

The amino acid was dissolved in CH_2Cl_2 (2 ml) and CH_3NO_2 (5 ml), treated with DCC (50 mg), and stirred at room temperature for 67 hr. The precipitate was removed by filtration and the filtrate was evaporated. The residue was chromatographed on silica gel, using EtOAc–$CHCl_3$ (1:1) as the developing solvent. Elution of the major band with EtOAc gave a residue which was crystallized from acetone–IPE to give **20** (17 mg, mp 169–170°). Recrystallization from acetone–IPE gave the analytical sample: mp 169.5–170.5°; $[\alpha]D$ +120°; ir 5.75 and 5.93 μ; nmr ($CDCl_3$) τ 9.34 (s, 18-Me), 8.61 (s, 19-Me), 7.89 (s, 21-Me), and 7.38 (s, 1-CH_2).

Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.20; H, 9.63; N, 4.62. Found: C, 75.20; H, 9.68; N, 4.60.

Registry No.—**3,** 26527-03-7; **4,** 26527-04-8; **5,** 26527-05-9; **6,** 26527-06-0; **7,** 26527-07-1; **8,** 26527-08-2; **9,** 26527-09-3; **10,** 26527-10-6; **11,** 26527-11-7; **12,** 26599-14-4; **13,** 26527-12-8; **16,** 26527-13-9; **17,** 26527-14-0; **18,** 26527-15-1; **19,** 26599-15-5; **20,** 26527-16-2.

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