SYNTHESIS OF 16α-BROMOACETOXY ANDROGENS AND 17β-BROMOACETYLAMINO-4-ANDROSTEN-3-ONE: POTENTIAL AFFINITY LABELS OF HUMAN PLACENTAL AROMATASE.

Mitsuteru Numazawa[1] and Yoshio Osawa

Medical Foundation of Buffalo, Inc.
73 High Street, Buffalo, New York 14203

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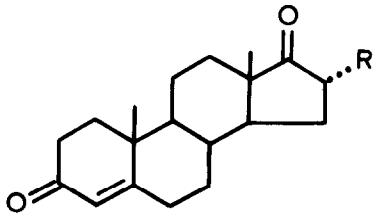
ABSTRACT

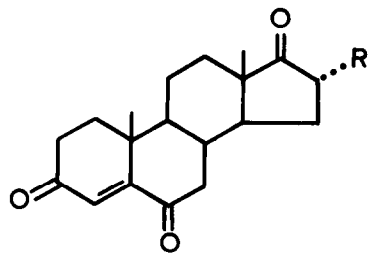
A novel synthesis of 16α-hydroxy-4-androstene-3,17-dione (3), 16α-hydroxy-4-androstene-3,6,17-trione (4), 17β-amino-5-androsten-3β-ol (10) and 17β-amino-4-androsten-3-one (14) is described. 16α-Bromoacetoxy-4-androstene-3,17-dione (5), 16α-bromoacetoxy-4-androstene-3,6,17-trione (6) and 17β-bromoacetylamino-4-androsten-3-one (15) were synthesized as potentially selective irreversible inhibitors of androgen aromatases. 16α-Bromo-4-androstene-3,17-dione (1) and 16α-bromo-4-androstene-3,6,17-trione (2) were converted to compounds 3 and 4 in 80-90% yield by controlled stereospecific hydrolysis using sodium hydroxide in aqueous pyridine. Reductive amination of 3β-hydroxy-5-androsten-17-one and 3-methoxy-3,5-androstadien-17-one (11) using ammonium acetate and sodium cyanohydridoborate ($NaBH_3CN$) and a subsequent treatment with acid gave the amines 10 and 14 respectively, as a salt. The corresponding 17-imino compounds 9 and 13 were also isolated from the reaction mixtures when methanol was used as a solvent for the reaction. The 16α-hydroxyl compounds 3 and 4 and the 17β-amino compound 14 were converted to the corresponding bromoacetyl derivatives, 5, 6, and 15, with bromoacetic acid and N,N'-dicyclohexylcarbodiimide.

INTRODUCTION

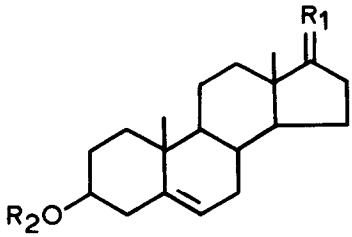
Two distinctive androgen aromatases which have different substrate specificity and cytochrome P-450 have recently been separated from human term placenta in our laboratory [2-5]. Some bromoandrogens have been shown to be effective as the active-site-directed irreversible inhibitors of placental aromatase in subcellular particulates and sliced tissue [6,7]. Since the difference in the substrate specificity of the two aromatases lie in the D-ring structure, we planned to synthesize several 16α-bromoacetoxy and 17β-bromoacetylamino derivatives of ster-



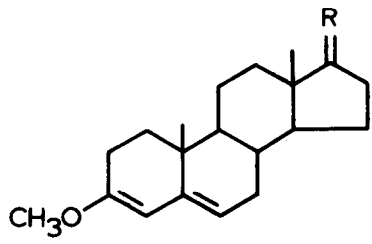
1, R = Br
3, R = OH
5, R = OCO CH_2Br



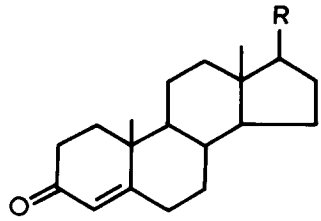
2, R = Br
4, R = OH
6, R = $OCOCH_2Br$



7, R_1 = O, R_2 = H
8, R_1 = $NOCH_3$, R_2 = H
9a, R_1 = NH, R_2 = H
9b, R_1 = NH, R_2 = $COCH_3$
10, R_1 =  $\cdot AcO^-$, R_2 = H



11, R = O
12, R = 
13, R = NH



14, R = $NH_3^+ \cdot Cl^-$
15, R = $NHCOCH_2Br$

oidal 4-en-3-ones as potentially selective irreversible inhibitors.

We previously reported the improved synthesis of 16α-hydroxy-4-androstene-3,17-dione (3) which involves 3 steps from 16α-bromo-4-androstene-3,17-dione (1) [8]. Recently we also reported one-step synthesis of 16α-hydroxydehydroepiandrosterone from 16α-bromodehydroepiandrosterone by controlled alkaline hydrolysis [9]. Umino *et al* [10] reported the usefulness of sodium trifluoroacetoxyhydridoborate ($NaBH_3(OCOCF_3)$) in reduction of oxime ethers which overcomes the low yield of other metal hydride reductions [11-13]. On the other hand, Borch *et al* [14] reported a reductive amination of ketones with ammonia and sodium cyanohydridoborate ($NaBH_3CN$) to the corresponding amines.

This paper describes one-step synthesis of 16α-hydroxy-4-androstene-3,17-dione (3) and 16α-hydroxy-4-androstene-3,6,17-trione (4) from the corresponding 16α-bromo compounds 1 and 2 using the controlled alkaline hydrolysis, and a convenient synthesis of 17β-amino-3β-hydroxy-5-androsten-17-one (10) and 17β-amino-4-androsten-3-one (14). Synthesis of the bromoacetyl derivatives (5, 6 and 15) of compounds 3, 4 and 14 is also described.

RESULTS AND DISCUSSION

16α-Bromo-4-androstene-3,17-dione (1) and 16α-bromo-4-androstene-3,6,17-trione (2) were synthesized according to known methods [6,15]. Treatment of the α-bromoketones 1 and 2 with 1.2 equivalent of sodium hydroxide in aqueous pyridine at room temperature for 8 hr [9] gave stereospecifically 16α-hydroxy-4-androstene-3,17-dione (3) and 16α-hydroxy-4-androstene-3,6,17-trione (4) in 80-90% yield without formation of other ketols. The ketol 3 was identical in every respect with the standard sample. The NMR spectrum of 4 showed two angular methyl

groups at δ 1.02 (18-CH_3) and 1.24 (19-CH_3), the 16β-H at 4.37 (multiplet), and the 4-H at 6.22 (singlet). The IR spectrum of the hydroxy triketone 4 showed characteristic absorptions of the conjugated ketones at 1690 and 1675 cm^{-1} and of the 5-membered ring ketone at 1742 cm^{-1}. Kinetic analysis of the controlled alkaline hydrolysis of 16α-bromodehydroepiandrosterone has previously shown that equilibrium between the 16α-bromoketone and its 16β-bromo isomer precedes the formation of 16α-hydroxydehydroepiandrosterone in which the true intermediate is the 16β-isomer and that the ketol is formed by the direct S_N2 displacement of bromine with hydroxide ion [9]. Treatment of the diketobromide 1 with 0.012 equivalent of sodium hydroxide in aqueous pyridine did not cause any change, but a ten-fold increment of sodium hydroxide gave an approximate 1:1.5 equilibrium between bromide 1 and its 16β-bromo isomer in favor of the 16β-isomer with 20% yield of the hydroxy diketone 3, while an approximate 1:1.3 equilibration between 16α-bromodehydroepiandrosterone and its 16β-bromo isomer with 9% yield of 16α-hydroxydehydroepiandrosterone was observed under the same condition (Table I). The results indicate that bromides 1 and 2 are converted to the hydroxy derivatives 3 and 4, respectively, through the same reaction mechanism as that observed in the formation of 16α-hydroxydehydroepiandrosterone [9] and that this hydrolysis may be applicable for conversion of other steroidal α-bromoketones to α-ketols without ketol rearrangement. It should be noted, however, that there is a difference in the rate of ketol formation between 16α-bromodehydroepiandrosterone and the diketobromide 1 (Table I). Although the detailed conformational analysis by X-ray crystallography is not yet available, a conformational transmission of distortion through B-C-D rings might be in operation.

Table I. Epimerization of the 16α-Bromo-17-ketones and Formation of the 16α-Hydroxy-17-ketones in Sodium Hydroxide-Aqueous Pyridine Systems.

	Conditions		Relative Amount of Product (%)*		
	NaOH (equiv)	Time (min)	16α-Bromo Isomer	16β-Bromo Isomer	16α-Hydroxy Compound
1) 16α-Bromodehydroepiandrosterone					
A	0.012	10	100	0	0
B	0.12	10	39	52	9
C	1.20	480	<5†		>95
2) 16α-Bromo-4-androstene-3,17-dione (1)					
C	0.012	10	100	0	0
D	0.12	10	26	34	20
E	1.20	480	<1†		>99

*Relative amount of product was obtained by peak areas corresponding to both the C-16 proton and C-18 angular methyl by NMR spectra of the reaction mixtures without isolation.

†16α-Bromo isomer plus 16β-bromo isomer.

The 16α-hydroxylated compounds 3 and 4 were converted to the 16α-bromoacetoxy derivatives 5 and 6 with bromoacetic acid and N,N'-dicyclohexylcarbodiimide (DCC). The structures of compounds 5 and 6 were identified by IR and NMR spectroscopy.

For the purpose of developing a synthetic method for the preparation of 17β-amino-4-androsten-3-one (14) with high yield, we tried first two different types of reactions which convert ketones to amines by using dehydroepiandrosterone (7) as a model compound. When the 17-methoxime 8 was submitted to a reaction with $NaBH_3(OCOCF_3)$ in THF, 17β-amino-5-androsten-3β-ol acetate (10) [16] was obtained in 82% yield. The IR spectrum of amine 10 showed characteristic absorptions of the ammonium acetate at 3050-3400 (OH, NH_3^+), 2650 and 2180 (NH_3^+) and 1630 (COO^-) cm^{-1}. The reductive amination of 7 with ammonium acetate and $NaBH_3CN$ in absolute methanol gave a precipitate in the reaction mixture which was identified as 17-imino-5-androsten-3β-ol (9a) (65% yield) by

the IR [ν_{max} 3300-3400 (OH), 1450 (C=N)] and NMR [δ 0.67 (18-CH_3), 1.03 (19-CH_3), 2.02 (3β-acetyl), 4.60 (3α-H), 5.33 (6-H)] spectra of the 3-acetate 9b of imine 9a. The imine 9a was hydrolyzed back to ketone 7 with AcOH. On the other hand, the reductive amination in absolute THF-methanol (3:1) gave the desired 17β-amino compound 10 in 60% yield. The imine 9a is considered to be an intermediate in the formation of the amine 10 [14] and to be isolable because of its low solubility in methanol. The results suggested that the reductive amination, using an appropriate solvent, would be suitable for the synthesis of 17β-amino-4-androsten-3-one (14).

When 3-methoxy-3,5-androstadien-17-one (11) obtained according to the method of Nussbaum *et al.* [17] was submitted to the reductive amination in absolute THF-methanol (3:1), the corresponding 17β-amino compound 12 was obtained in 65% yield. The amine 12 was identified by the IR [3300-3500 cm^{-1} (NH_2)] and NMR [δ 0.72 (18-CH_3), 0.98 (19-CH_3), 3.56 (3-OCH_3), 5.03-5.30 (4- and 6-H)] spectra. 17-Imino-3-methoxy-3,5-androstadiene (13) was also obtained in 50% yield by using a 1:1 mixture of THF and methanol as a solvent for the above reaction. The amine 12 was hydrolyzed to 17β-amino-4-androsten-3-one hydrochloride (14) by dilute HCℓ in methanol. The IR spectrum showed characteristic absorptions of an ammonium salt at 3400, 2650 and 2010 cm^{-1}. Elemental analysis and the NMR spectrum also supported the structure of the amine hydrochloride 14. The amine 14 was then converted to 17β-bromoacetylamino-4-androsten-3-one (15) with bromoacetic acid and DCC. The structure of the derivative 15 was identified by the IR [3350 (NH), 1680 (conjugated C=O), 1662 (amide C=O), 1545 (NH) cm^{-1}] and NMR [δ 0.79 (18-CH_3), 1.21 (19-CH_3), 3.42 (17α-H), 3.86 (17β-$NCOCH_2Br$), 5.74 (4-H)] spectra.

A preliminary inhibition study of partially purified human placental aromatase II by the bromo acetates 5 and 6 showed that both are active as competitive inhibitors of the aromatase and that their inhibitory effect is weaker than that of 17β-bromoacetoxy-4-androsten-3-one which was shown to act as an affinity label of aromatase (Higashiyama, T. and Osawa, Y., unpublished data). It has been shown that some 6-bromoandrogens synthesized in our laboratory [18] are active-site-directed irreversible inhibitors of the aromatases [6,7,19]. The results suggest that the isotope labeled bromoacetyl derivatives 5, 6 and 15, and the 6-bromoandrogens, when used appropriately as the affinity label, would play a critical role in characterization of the active site(s) of estrogen synthesizing systems.

EXPERIMENTAL

General methods. Melting points were measured on a Fisher-Jones melting point apparatus and were uncorrected. IR spectra were recorded on a Perkin-Elmer 267 spectrophotometer in KBr pellets. NMR spectra were obtained with a Varian EM-360 spectrometer at 60 MHz using tetramethylsilane as an internal standard.

16α-Bromo-4-androstene-3,17-dione (1) and 16α-bromo-4-androstene-3,6,17-trione (2). Compounds 1 and 2 were synthesized according to Bellino *et al.* [16].

Reaction to the bromoketones 1 and 2 with NaOH in aqueous pyridine. To a solution of 1 and 2 (4.1 mmol) in 75% aqueous pyridine (80 ml) was added 4.8 ml of a 1N NaOH solution and the mixture was allowed to stand under N_2 at room temperature for 8 hr. The reaction mixture was poured into a 1% HCℓ solution and then precipitates were collected by filtration and dried under vacuum to give 90-95% yield of the crude hydrolyzed product.

16α-Hydroxy-4-androstene-3,17-dione (3). The crude product obtained from 1 was recrystallized from acetone to give 3 (1.1 g, 89%) as colorless prisms, mp 188-190° (lit [8] 188-190°). IR (KBr): ν_{max} 3360 (OH), 1742 and 1650 (C=O). NMR ($CDC\ell_3$): δ 0.99 (3H, s, 18-CH_3), 1.21 (3H, s, 19-CH_3), 4.36 (1H, m, 16β-H), 5.72 (1H, s, 4-H).

16α-Hydroxy-4-androstene-3,6,17-trione (4). The crude solid obtained from 2 was recrystallized from aqueous MeOH to give 4 (1.0 g, 77%) as slightly yellow needles, mp 209-213° (decomp.). IR (KBr): ν_{max} 3350-

3450 (OH), 1742, 1690 and 1675 (C=O). NMR ($CDCl_3$-CD_3OD 3:1): δ 1.02 (3H, s, 18-CH_3), 1.24 (3H, s, 19-CH_3), 4.37 (1H, m, 16β-H), 6.22 (1H, s, 4-H).

Anal. Calcd. for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65.
Found C, 71.84; H, 7.85.

16α-Bromoacetoxy-4-androstene-3,17-dione (5). To a solution of 3 (110 mg) and bromoacetic acid (100 mg) in 5 ml of CH_2Cl_2 containing one drop of pyridine was added 200 mg of DCC and the reaction mixture was stirred at 0° overnight. Solid was removed by filtration and the filtrate was washed with 5% $NaHCO_3$, 5% HCl and water. After the usual work up, a brown oily substance was obtained. The oily compound was purified by silica gel TLC (hexane-AcOEt, 2:1) to give 5 (105 mg, 68%). Crystallization from ether gave pure 5 (58 mg) as colorless needles, mp 141°. IR (KBr): ν_{max} 1760, 1740 and 1670 (C=O). NMR ($CDCl_3$): δ 1.04 (3H, s, 18-CH_3), 1.23 (3H, s, 19-CH_3), 3.89 (2H, s, 16α-$OCOCH_2Br$), 5.43 (1H, m, 16β-H), 5.76 (1H, s, 4-H).

Anal. Calcd. for $C_{21}H_{27}O_4Br$: C, 59.58; H, 6.43.
Found C, 59.51; H, 6.79.

16α-Bromoacetoxy-4-androstene-3,6,17-trione (6). Compound 4 (65 mg) and bromoacetic acid (60 mg) were dissolved in 15 ml of dioxane and 4 ml of CH_2Cl_2. To this solution was added 120 mg of DCC and the reaction mixture was stirred at 4° overnight. Solid was removed by filtration and the filtrate was diluted with 50 ml of CH_2Cl_2. The organic layer was washed with 5% $NaHCO_3$ and water. After usual work up an oily substance (93 mg) was obtained. The oily compound was purified by silica gel TLC (hexane-AcOEt, 2:1) to give 6 (81 mg, 90%). Crystallization from acetone-ether gave pure 6 (68 mg, 76%) as colorless plates, mp 189-192° (decomp.). IR (KBr): ν_{max} 1750, 1733, 1687 and 1675 (C=O). NMR ($CDCl_3$): δ 1.06 (3H, s, 18-CH_3), 1.22 (3H, s, 19-CH_3), 3.91 (2H, s, 16α-$OCOCH_2Br$), 5.49 (1H, m, 16β-H), 6.25 (1H, s, 4-H).

Anal. Calcd. for $C_{21}H_{25}O_5Br$: C, 57.67; H, 5.76.
Found C, 57.35; H, 5.99.

17-Imino-5-androsten-3β-ol (9a). A solution of dehydroepiandrosterone (7) (1 g), NH_4OAc (2.67 g) and $NaBH_3CN$ (155 mg) in 50 ml of absolute MeOH was stirred at room temperature for 3 days. The precipitates were collected by filtration, washed with MeOH and dried under vacuum. The crude solid (750 mg) was recrystallized from $CHCl_3$-MeOH to give 9a (680 mg, 68%) as colorless needles, mp 264-267° (decomp.). IR (KBr): ν_{max} 3300-3400 (OH), 1450 (C=N).

Anal. Calcd. for $C_{19}H_{29}ON$: C, 79.39; H, 10.17; N, 4.87.
Found C, 79.11; H, 10.23; N, 5.01.

3β-Acetoxy-17-imino-5-androstene (9b). Compound 9a (20 mg) was acetylated with Ac_2O (0.3 ml)-pyridine (0.5 ml) at room temperature. Crystallization of the crude acetate from AcOEt gave 9b (18 mg, 78%) as colorless leaflets, mp 263-265° (decomp.). IR (KBr): ν_{max} 1728 (C=O), 1450 (C=N).

NMR ($CDC\ell_3$): δ 0.67 (3H, s, 18-CH_3), 1.03 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 4.60 (1H, broad m, 3α-H), 5.33 (1H, m, 6-H).

Anal. Calcd. for $C_{21}H_{31}O_2N$: C, 76.55; H, 9.84; N, 4.25.
Found C, 77.00; H, 9.59; N, 4.11.

Hydrolysis of the imine 9a with acetic acid. A solution of 9a (30 mg) in 200 ml of 50% aqueous acetic acid was heated under reflux for 4 hr. The solvent was then condensed to 20 ml under reduced pressure. Precipitate obtained by addition of water to the condensed reaction mixture was collected by filtration and dried under vacuum. The crude solid (18 mg) was recrystallized from aqueous MeOH to give 7 (13 mg, 43%) as colorless leaflets, mp 140-142°. 7 obtained by hydrolysis was identical with authentic sample in every respect.

17β-Amino-5-androsten-3β-ol acetate (10). (A) *$NaBH_3(OCOCF_3)$ method:* To a stirred solution of $NaBH_3(OCOCF_3)$, which was prepared from 600 mg of $NaBH_4$ according to Umino *et al.* [10], in 10 ml of THF was added 1 g of 17-methoxime of 7 (8) in 50 ml of THF dropwise and stirring was continued at room temperature for 2 hr and then heated under reflux for 2 hr. The excess reagent was cautiously decomposed with water below 10° and resulting mixture was poured into ice-water. Solid was collected by filtration and dried under vacuum. To a solution of the solid (895 mg) in 100 ml of $CHC\ell_3$ was added 5 ml of glacial AcOH to precipitate a crude 10 (855 mg) which was recrystallized from MeOH to give a pure 10 (660 mg, 60%) as colorless needles, mp 225-227° (lit [16] 227°). IR (KBr): ν_{max} 3050-3400 (OH and NH_3^+), 2650 and 2180 (NH_3^+), 1630 (COO^-).

(B) *$NaBH_3CN$ method:* 7 (1 g) and NH_4OAc (2.7 g) was dissolved in 60 ml of THF and 30 ml of MeOH. To this solution was added 350 mg of $NaBH_3CN$ and the solution was stirred at room temperature for 4 days. Precipitates were removed by filtration and the filtrate was poured into a chilled 1N NH_4OH solution. Solid was collected by filtration and dried under vacuum. The solid (565 mg) was converted to an acetate salt 10 as described above. The crude 10 was recrystallized from MeOH to give a pure 10 (320 mg, 29%) as colorless leaflets, mp 224-226°. This compound was identical with 10 obtained above.

3-Methoxy-3,5-androstadien-17-one (11). 11 was synthesized according to Nussbaum *et al.* [17].

17β-Amino-3-methoxy-3,5-androstadiene (12). To a solution of 11 (2 g) and NH_4OAc (5.3 g) in 150 ml of THF and 50 ml of MeOH was added 820 mg of $NaBH_3CN$ and the mixture was stirred at room temperature for 4 days. The mixture was poured into a chilled 5% $NaHCO_3$ solution. Precipitates were collected by filtration and dried under vacuum. The solid (1.91 g) was recrystallized from MeOH-$CDC\ell_3$ to give 12 (1.34 g, 67%) as colorless needles, mp 265-268° (decomp.). IR (KBr): ν_{max} 3300-3500 (NH_2), 1653 and 1628 (C=C). NMR ($CDC\ell_3$-CD_3OD, 9:1): δ 0.72 (3H, s, 18-CH_3), 0.98 (3H, s, 19-CH_3), 3.56 (3H, s, 3-OCH_3), 5.05-5.30 (2H, m, 4- and 6-H).

Anal. Calcd. for $C_{20}H_{31}ON$: C, 75.19; H, 10.41; N, 4.38.
Found C, 75.51; H, 10.16; N, 4.51.

17-Imino-3-methoxy-3,5-androstadiene (13). When a 1:1 mixture of THF to MeOH (100 ml) was used as a solvent in the above experiment, the imino compound 13 was precipitated in the reaction mixture and collected by filtration. Recrystallization of the crude 13 from MeOH-$CHCl_3$ gave 13 (930 mg, 47%) as colorless needles, mp 221-224° (decomp.). IR (KBr): ν_{max} 1650, 1626 (C=C). NMR ($CDCl_3$): δ 0.70 (3H, s, 18-CH_3), 0.98 (3H, s, 19-CH_3), 3.55 (3H, s, 3-OCH_3), 5.05-5.30 (2H, m, 4- and 6-H).

Anal. Calcd. for $C_{20}H_{29}ON$: C, 80.22; H, 9.76; N, 4.68.
Found C, 79.98; H, 9.55; N, 4.37.

Hydrolysis of 13 with HCl. To a solution of 13 (50 mg) in 100 ml of MeOH was added 20 ml of 1N HCl and the mixture was heated under reflux for 30 min. The mixture was condensed to 20 ml under reduced pressure and then poured into water. Precipitates were collected by filtration and then recrystallized from acetone to give 4-androstene-3,17-dione (11 mg, 23%) as colorless plates, mp 142-145°. The product was identical with the authentic sample in every respect.

17β-Amino-4-androsten-3-one hydrochloride (14). To a solution of 12 (1 g) in 40 ml of MeOH was added 25 ml of 2N HCl and the mixture was heated under reflux for 30 min. The solvent was removed under reduced pressure to give a crude 14 (1.15 g). The solid was recrystallized from MeOH-ether to give pure 14 (635 mg, 56%) as colorless needles, mp 265-270° (decomp.). IR (KBr): ν_{max} 3400, 2650 and 2010 (NH_3+), 1670 (C=O), 1611 (C=C). NMR (CD_3OD): δ 0.88 (3H, s, 18-CH_3), 1.24 (3H, s, 19-CH_3), 3.09 (1H, t, J=9Hz, 17α-H), 5.67 (1H, s, 4-H).

Anal. Calcd. for $C_{19}H_{30}ONCl \cdot H_2O$: C, 66.73; H, 9.43; N, 4.10.
Found C, 67.04; H, 9.33; N, 4.00.

17β-Bromoacetylamino-4-androsten-3-one (15). To a solution of 14 (160 mg) and bromoacetic acid (400 mg) in 15 ml of dioxane and 5 ml of CH_2Cl_2 was added 900 mg of DCC and the mixture was stirred at 0° overnight. Solid was removed by filtration and the filtrate was diluted with 50 ml of $CHCl_3$ and then washed with 5% $NaHCO_3$ and water and dried (Na_2SO_4). After the usual work up, an oily substance obtained was purified by silica gel TLC (hexane-AcOEt, 1:1) to give a solid (123 mg). The solid was recrystallized from acetone to give 15 (95 mg, 50%) as colorless plates, mp 196-198°. IR (KBr): ν_{max} 3350 (NH), 1680 and 1662 (C=O), 1610 (C=C), 1545 (NH). NMR ($CDCl_3$-CD_3OD, 9:1): δ 0.79 (3H, s, 18-CH_3), 1.21 (3H, s, 19-CH_3), 3.42 (1H, t, J=9Hz, 17α-H), 3.86 (2H, s, 17β-$OCOCH_2Br$), 5.74 (1H, s, 4-H).

Anal. Calcd. for $C_{21}H_{30}O_2NBr$: C, 61.76; H, 7.40; N, 3.43.
Found C, 61.54; H, 7.60; N, 3.22.

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REFERENCES

The following trivial names have been used in this paper:

Dehydroepiandrosterone = 3β-hydroxy-5-androsten-17-one
16α-Bromodehydroepiandrosterone = 16α-bromo-3β-hydroxy-5-androsten-17-one
16α-Hydroxydehydroepiandrosterone = 3β,16α-dihydroxy-5-androsten-17-one
DCC = N,N'-dicyclohexylcarbodiimide

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