Synthesis and *in Vitro* Activity of 17β-(*N*-Alkyl/arylformamido)- and 17β-[(*N*-Alkyl/aryl)alkyl/arylamido]-4-methyl-4-aza-3-oxo-5α-androstan-3-ones as Inhibitors of Human 5α-Reductases and Antagonists of the Androgen Receptor

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A number of 17β-(*N*-alkyl/arylformamido)- and 17β-[(*N*-alkyl/aryl)alkyl/arylamido]-3-oxo-4-aza-5α-steroids were prepared from 17β-hydroxy-4-azasteroids and evaluated as inhibitors of human 5α-reductase and antagonists of the androgen receptor. Jones' oxidation of 17β-hydroxy compounds gave the 17-keto-4-azasteroids, which were treated with amines and $NaBH(OAc)_3$/$NaBH_3CN$ to give 17β-(*N*-alkyl/arylamino)-4-azasteroids **10**–**27**. Alternatively, the above-indicated compounds were prepared from amines and 17-keto-4-azasteroids to form imines, which were then reduced with $NaBH_4$. Formylation of amines **10**–**27** gave 17β-(*N*-alkylformamides) **28**–**41**; however, acylation afforded 17β-[(*N*-alkyl/aryl)alkyl/arylamides] **42**–**53**. In comparison to *N*,*N*-diethyl-4-methyl-3-oxo-4-aza-5α-androstane-17β-carboxamide (4-MA; IC_{50} = 4.15 nM), 17β-(*N*-alkylformamido)-4-azasteroids were potent inhibitors of human type I 5α-reductase, IC_{50} values of compounds **29**, **30**, **36**, and **37** being measured as 3.05, 0.91, 2.19, and 2.35 nM, respectively. The structure–activity relationships suggest that the type I enzyme has preference for N-substituted straight alkyl side chains of four to five carbon atoms. On the other hand, formamides **32** (*N*-heptyl) and **33** (*N*-octyl), in addition to inhibiting the type I enzyme (IC_{50}s = 9.57 and 16.9 nM, respectively), showed also strong inhibitory activity (IC_{50}s = 14.0 and 18.4 nM, respectively) for human type II 5α-reductase, in comparison to *N*-(1′,1′-dimethylethyl)-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide (MK-906; IC_{50} = 4.53 nM). Other compounds in this series showed moderate activities (IC_{50} > 100 nM) on the type II enzyme. 17β-[(*N*-Alkyl/aryl)alkyl/arylamides] **45**, **46**, **48**, and **51** exhibited highly potent inhibitory activity for human type I 5α-reductase with IC_{50}s of 1.77, 2.42, 2.93, and 5.44 nM, respectively, while moderate to no effect was observed on the type II enzyme (100 < IC_{50}s < 1000 nM), except for compound **48** (IC_{50} = 3.75 nM). In another substitution pattern, *N*-aryl/alkylamides were studied; an electron-donating group increased the potency of compound **51**, whereas an electron-withdrawing group decreased the potency of compounds **52** and **53** compared to parent compound **50**. In addition to their 5α-reductase activities, 17β-(*N*-alkylformamides) were also studied for their inhibitory activities on dihydrotestosterone (DHT)-stimulated proliferation of androgen-sensitive Shionogi mouse mammary carcinoma cells (clone SEM-107). The inhibition of DHT action on the proliferation of the androgen-sensitive cancer cells by formamido compounds showed moderate to good activity, IC_{50} values ranging from 45 to 100 nM as compared to hydroxyflutamide (IC_{50} = 52.5 nM).

Introduction

The prostate[1] and skin[2] are not only major sites of androgen action but also important sites of androgen metabolism. Androgens are well known to play a predominant role in prostate cancer[3] and benign prostatic hyperplasia (BPH).[4] Excessive androgen action in the skin causes common disorders such as acne,[5] female hirsutism,[6] and male pattern baldness.[7]

The enzyme 5α-reductase[8] plays an important function in many androgen-sensitive tissues by converting the major circulating androgenic hormone, testosterone, into the more potent intracellular androgenic 5α-reduced metabolite dihydrotestosterone (DHT).[1,9] Two types of human 5α-reductase, chronologically identified as type I[10] and type II,[11] have been isolated from human prostatic cDNA libraries, and the structure of the two isoenzymes has been elucidated. The type I isoenzyme is expressed in the skin,[11] while type II is responsible for male pseudohypermaphroditism and is the main type expressed in the human prostate.

Several pharmacological approaches are under evaluation to treat androgen-sensitive diseases. These include inhibition of androgen action by androgen receptor antagonists[12,13] and inhibition of the conversion of testosterone to DHT by 5α-reductase inhibitors[14,15] (Figure 1).

Among numerous nonsteroidal[14] or steroidal compounds[15] prepared as competitive or uncompetitive inhibitors of 5α-reductase during the last two decades, 17β-carboxamide-4-azasteroids[15a,b] have been investigated *in vitro*[15,16] in different tissues, different species, and different disease states.[17] Two inhibitors of this series, *N*,*N*-diethyl-3-oxo-4-methyl-4-aza-5α-androstane-17β-carboxamide (4-MA)[15a,b,16] and *N*-(1′,1′-dimethylethyl)-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide (MK-906), have been extensively studied.[15a,b,16c,d,17] 4-MA shows high potency as an inhibitor of rat and

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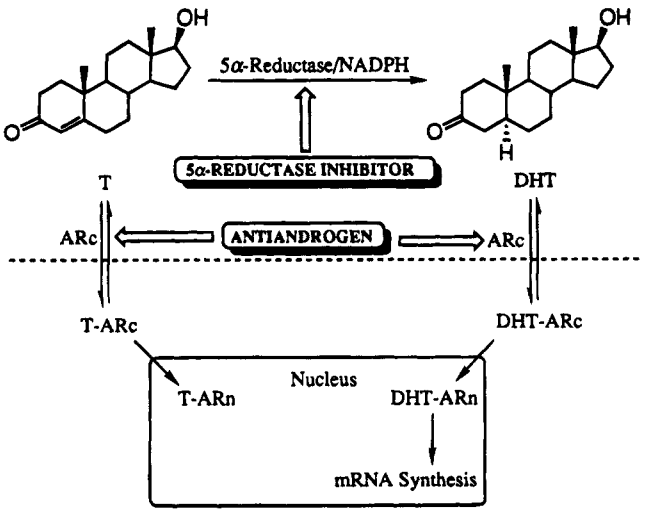
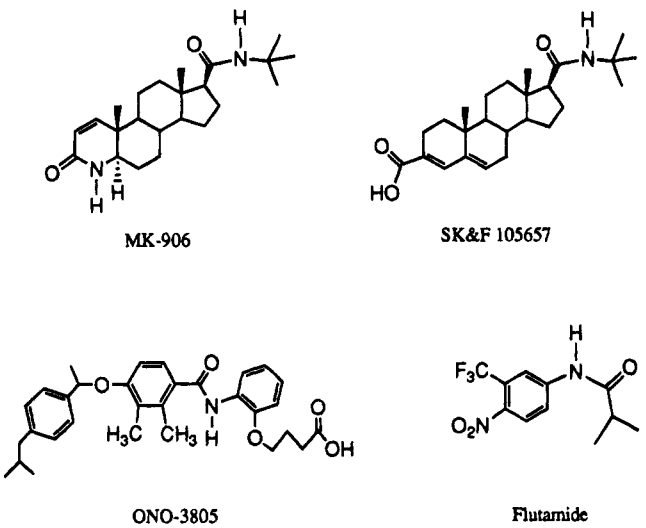


Figure 1. Intracellular events of testosterone and dihydrotestosterone action.

Chart 1



human prostate enzymes with IC_{50} values of 11.0 and 10.0 nM, respectively. MK-906 also shows high potency for the human (5.5 nM) and rat (6.8 nM) prostatic enzymes.[15b] MK-906 has demonstrated its biochemical efficacy with an 80% reduction of intraprostatic DHT and a 28% reduction in prostate size in patients with BPH, and this compound is currently used for the treatment of BPH[17] (Chart 1). Other inhibitors, which look promising, are the steroidal SK&F 105687[15d] and the nonsteroidal compound ONO-3805.[14b]

In addition to 5α-reductase activity, many 4-azasteroids exhibit antiandrogenic activity.[15b] The androgen receptor activity of the 4-azasteroids varies markedly depending upon the nature of the substitution on the A-ring. When a hydrogen was attached to the 4-position, receptor activity was greatly diminished relative to the corresponding methyl derivative. A range of 17-substituted 4-azasteroids were also studied for their receptor binding activities. These include 17β-OH, 17β-$CO(CH_3)R$, 17β-$COCH_3$, and 17β-$CONR_2$ derivatives. Out of these, the 17β-hydroxy group enhances potency more than any known other group.

Among pure systemic antiandrogens, the nonsteroidal flutamide[12] has been widely studied and has exhibited high androgen receptor activity *in vitro*. Its metabolite, hydroxyflutamide, is considered as the active species *in vivo*. Furthermore, flutamide has also been proved to be very effective in the treatment of prostate cancer. In contrast, an ideal topical antiandrogen would possess its activity limited to the immediate area of application. Win 17665 (17β-hydroxy-17α-propyl-4-androsten-3-one),[18a,b] SH-434 (17β-hydroxy-1α-methyl-17α-propyl-5α-androstan-3-one),[18c] and RU-38882 ([3S-(3α,3aα,-9aα,9bβ)]-6-ethyl-3a-methyl-1,2,3,3a,4,5,8,9,9a,9b-decahydro-7*H*-ben[*e*]linden-7-one acetate)[18d] are such compounds under investigation.

From the study of C-17-substituted 4-azasteroids, it thus appears that substituents at the C-17-position have pronounced effect on the activity of 5α-reductase and possess androgen receptor activities. 17β-Carboxamides are among these substituents. Study of other substituents are likely to provide more information with respect to their structure–activity relationships. In this paper, we describe the synthesis and *in vitro* activity of 17β-(*N*-alkyl/arylformamido)- and 17β-[(*N*-alkyl/aryl)-alkyl/arylamido]-4-methyl-4-aza-3-oxo-5α-androstanes as inhibitors of type I and II 5α-reductases and as antiandrogens.

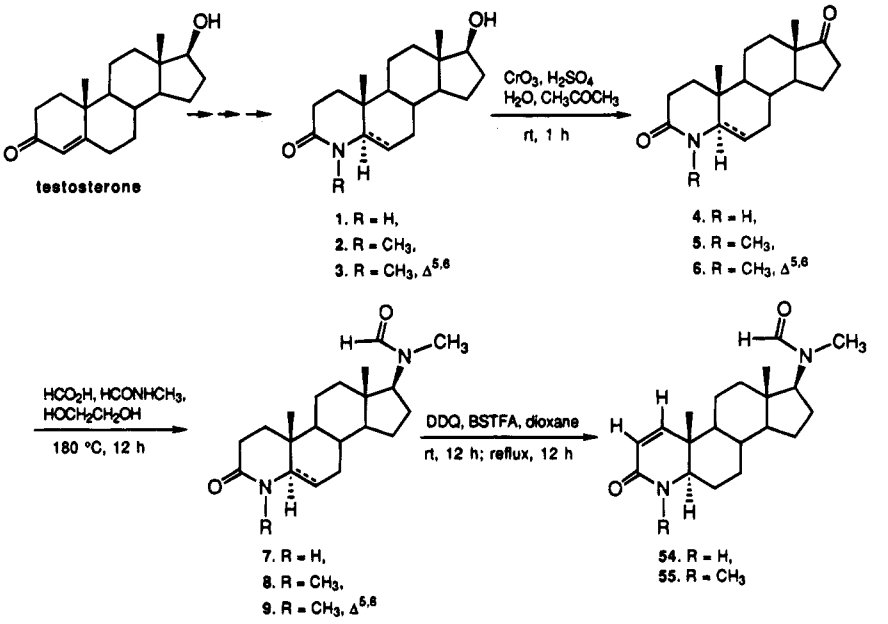
Results and Discussion

Chemistry. 17β-(*N*-Alkylformamido)-4-azasteroids were prepared from the commercially available testosterone. Thus, the 17β-hydroxy-4-azaandrostan-3-ones **1**–**3** were prepared following the method of Rasmusson *et al.* The 17β-hydroxy group of the 4-azasteroid derivatives was oxidized either with Jones' reagent or PCC[19] to give the corresponding 4-aza, 3,17-diones **4** and **5**. Oxidation of the 5-ene lactam **3** gave 17-keto 5-ene lactam **6**.

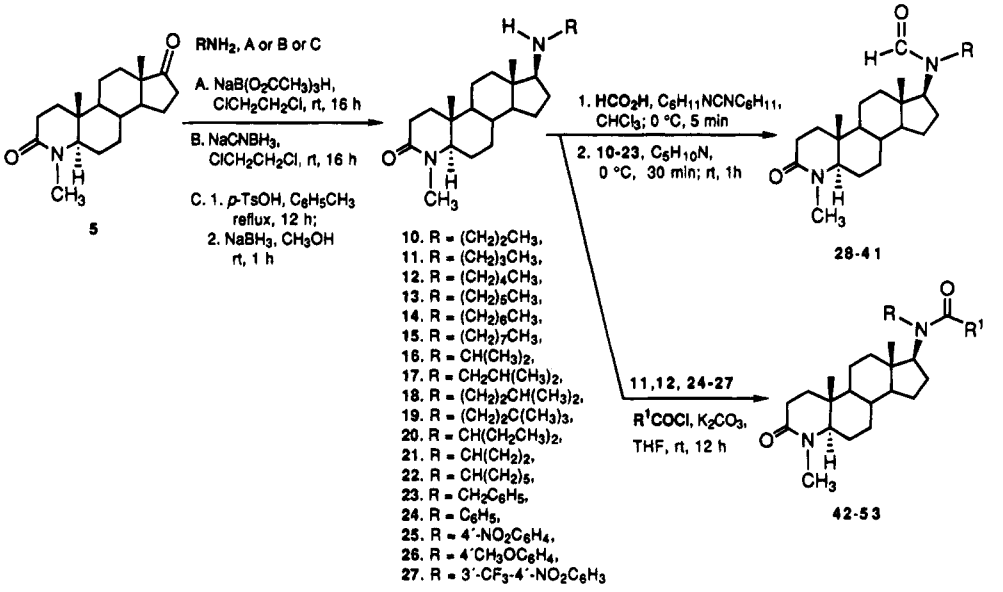
Reductive amination of the ketones **4** and **5** with formic acid[20] and *N*-methylformamide[21] under the conditions of Leuchart–Wallach[22] gave the corresponding 17β-(*N*-methylformamides) **7** and **8** in good yields, respectively. However, when the 5-ene ketone **6** was subjected to the above-indicated reaction conditions, 37% of the desired product **8** along with 24% of compound **9** was obtained (Scheme 1). Extension of the above reaction to various *N*-alkylformamides failed to give the desired products.

The reaction of ketone **5** with *N*-ethylurethane or 1,3-dimethylurea also failed to give reduction products. Therefore, other approaches were investigated to circumvent the above-indicated problem. Thus, in a two-step process, at first reductive amination[23] of ketone **4** and **5** with various alkylamines in the presence of sodium triacetoxyborohydride ($NaB(OCOCH_3)_3H$)[23c] or sodium cyanoborohydride ($NaCNBH_3$)[23a,b] and acetic acid gave the corresponding amines **10**–**23** in moderate to good yields, which were then formylated with formic acid[20] and 1,3-dicyclohexylcarbodiimide (DCC)[24] to give the *N*-alkylformamides **28**–**41** in excellent yields. Out of two reducing agents used, $NaCNBH_3$ gave the best results. However, in a two-step process, the reductive amination step was not satisfactory. This problem was circumvented when a high-boiling amine was used. Thus, a two-step approach was used to prepare amines **24**–**27**. At first, the amines were treated with ketone **5** to provide imines which were then reduced with sodium borohydride ($NaBH_4$) to give secondary amines in high yields. Furthermore, extension of this process to hindered amines such as *tert*-butylamine and adamantanamine failed to give the desired products. Reac-

Scheme 1



Scheme 2



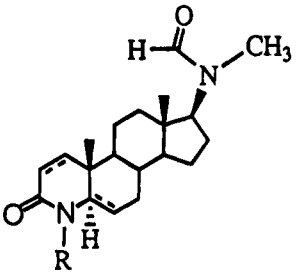
tion of amines **11**, **12**, and **24**–**27** with appropriate alkyl/arylcarboxylic chlorides[25] provided (*N*-alkyl/aryl)alkyl/arylamides **42**–**53** in good to excellent yields (Scheme 2).

The 1,2-double bond in 4-azasteroids was introduced with benzeneseleninic anhydride[15b,26] in refluxing chlorobenzene. Since the yields were not satisfactory, an alternate method was investigated. Thus, the reaction of 4-azasteroids with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[27] and bis(trimethylsilyl)trifluoroacetamide (BSTFA) in 1,4-dioxane gave the 4-aza 1-ene steroids **54** and **55** in high yields (Scheme 1).

Inhibition Study. The *in vitro* inhibition studies of human type I and II 5α-reductases and DHT action on the proliferation of the androgen-sensitive cancer Shionogi cells are summarized in Tables 1–3. The purpose of this study is to define the molecular changes which influence their activity in each of these assays in order to optimize the activity as 5α-reductase inhibitors and antiandrogens and thus provide information on the structure–activity relationships of these compounds.

Inhibition of Human 5α-Reductase (Types I and II). In the inhibition studies, 4-MA and MK-906 were used as the internal references. In comparison to 4-MA (IC_{50} = 4.15 nM), the IC_{50} values of 17β-(*N*-methylformamido)-4-methyl-4-aza-5α-steroids showed moderate to high inhibitory activity on human 5α-reductases. The results of the first series of compounds are summarized in Table 1. Compound **8** has an IC_{50} value of 29 nM for type I 5α-reductase. Introduction of the Δ^1-double bond in compound **8** reduced the potency as shown by compound **55** (IC_{50} = 124 nM). Moreover, introduction of the Δ^5-double bond in **8** gave compound **9** which completely lost activity (IC_{50} = 1900 nM). In contrast, 4-azasteroid **54** having a 1,2-double bond showed improved activity[10b] (IC_{50} = 207 nM) over its parent compound **7** (IC_{50} = 3700 nM). All the derived 4-azasteroids were thus less active than the 4-methyl analogues. However, both analogues showed no inhibitory

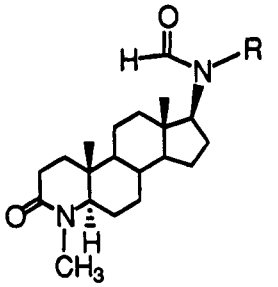
Table 1. *In Vitro* Activity of 17β-(*N*-Methylformamido)-4-methyl-/4-aza-5α-androstan-3-ones



entry	substituent R	substituent Δ	*in vitro* bioactivity[a] (IC_{50}, nM) human type I 5α-R (DU-145 cells)	human type II 5α-R (SW-13-transfected cells)	DHT[c]-stimulated Shionogi cell proliferation
4-MA[b]			4.14 ± 0.416	7.48 ± 0.285	463
MK-906[b]			26.3 ± 4.784	4.53 ± 0.906	ND[e]
Flu-OH[d]					52 ± 1.7
7	H		3700	>1000	ND
8	CH_3		29 ± 7.258	1000	1476
9	CH_3	Δ^5	1900	>1000	ND
54	H	Δ^1	>100	>1000	ND
55	CH_3	Δ^1	>100	>1000	ND

[a] The results of the inhibition of 5α-reductase (type I and type II) and DHT-stimulated proliferation of Shionogi cells were obtained by following standard procedures described in the Experimental Section. The concentration of the compounds required to inhibit 5α-reductase activity or 5α-dihydrotestosterone-induced stimulation of proliferation of Shionogi cells by 50% is represented as IC_{50} values. [b] 4-MA and MK-906 were used as standard references for the inhibition of 5α-reductases. [c] 5α-Dihydrotestosterone (DHT; 0.3 nM) was used as a standard substrate for the growth assay. [d] Hydroxyflutamide was added as a standard control for the antiandrogen test. [e] Not detected.

Table 2. *In Vitro* Activity of 17β-(*N*-Alkylformamido)-4-methyl-4-aza-5α-androstan-3-ones[a]



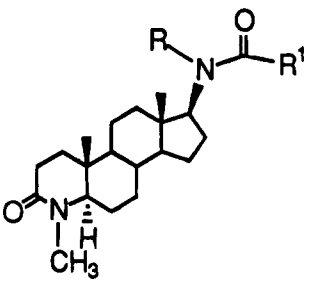
entry	substituent (R)	*in vitro* bioactivity (IC_{50}, nM) human type I 5α-R (DU-145 cells)	human type II 5α-R (SW-13-transfected cells)	DHT-stimulated Shionogi cell proliferation
28	$(CH_2)_2CH_3$	5.08 ± 0.595	>100	989
29	$(CH_2)_3CH_3$	3.05 ± 0.296	>100	166
30	$(CH_2)_4CH_3$	0.91 ± 0.236	>100	96
31	$(CH_2)_5CH_3$	7.25 ± 0.818	>100	89
32	$(CH_2)_6CH_3$	9.57 ± 1.745	14 ± 1.11	58
33	$(CH_2)_7CH_3$	16.9 ± 3.911	18.4 ± 1.541	50
34	$CH(CH_3)_2$	9.53 ± 1.728	>100	162
35	$CH_2CH(CH_3)_2$	7.31 ± 0.305	>100	994
36	$(CH_2)_2CH(CH_3)_2$	2.19 ± 0.476	>100	46
37	$(CH_2)_2C(CH_3)_3$	2.35 ± 0.421	>100	171
38	$CH(CH_2CH_3)_2$	10.6 ± 1.532	>100	90
39	$CH(CH_2)_2$	11.2 ± 0.375	>100	ND
40	$CH(CH_2)_5$	11.9 ± 1.142	>100	110
41	$CH_2C_6H_5$	5.63 ± 0.702	>100	ND

[a] Assay conditions were the same as those reported in Table 1.

effect (IC_{50}s ≥ 1000 nM) on type II 5α-reductase in comparison to MK-906 (IC_{50} = 4.53 nM).

The above results suggest that the 4-methyl 4-aza analogues give better results than the 4-aza analogues. We thus chose the 4-methyl-4-azasteroidal skeleton for further evaluation of the effect of various chains. The results are summarized in Tables 2 and 3. The inhibitory activity increased to a maximum as the length of the alkyl chain increased to a maximum, and then the activity dropped as the chain length increased further (Figure 2). For instance, compound **28** having a *N*-propyl substituent had an IC_{50} value of 5.08 nM that was about 6 times more potent than the *N*-methyl substituent and was as active as 4-MA. Addition of one more methylene carbon, *i.e.*, a *N*-butyl substituent (**29**), gave even better results (IC_{50} = 3.05 nM). Addition of one more methylene carbon to the *N*-butyl substituent gave the *N*-amyl compound **30** which showed very high inhibitory potency (IC_{50} = 0.91 nM) and is one of most potent inhibitors of human type I 5α-reductase known

Table 3. *In Vitro* Activity of 17β-[(*N*-Alkyl/aryl)alkyl/arylamido]-4-methyl-4-aza-5α-androstan-3-ones[a]



entry	substituent R	substituent R^1	*in vitro* inhibitory activity (IC_{50}, nM) human type I 5α-R (DU-145 cells)	human type II 5α-R (SW-13-transfected cells)
42	$(CH_2)_3CH_3$	CH_3	11.8 ± 1.647	1000 > IC_{50} > 100
43	$(CH_2)_4CH_3$	CH_2CH_3	4.56 ± 1.334	1000 > IC_{50} > 100
44	$(CH_2)_4CH_3$	$(CH_2)_2CH_3$	3.31 ± 0.689	1000 > IC_{50} > 100
45	$(CH_2)_4CH_3$	$(CH_2)_3CH_3$	1.77 ± 0.343	1000 > IC_{50} > 100
46	$(CH_2)_4CH_3$	$(CH_2)_3CH_2Br$	2.42 ± 0.409	1000
47	$(CH_2)_4CH_3$	C_6H_5	3.22 ± 0.405	>100
48	C_6H_5	C_6H_5	2.93 ± 2.158	3.75 ± 1.977
49	4″-$CH_3OC_6H_4$	C_6H_5	2.11 ± 0.874	>1000
50	C_6H_5	$CH(CH_3)_2$	10.5 ± 2.739	582
51	4″-$CH_3OC_6H_4$	$CH(CH_3)_2$	5.44 ± 1.067	1000 > IC_{50} > 100
52	4″-$NO_2C_6H_4$	$CH(CH_3)_2$	32.8 ± 3.258	>1000
53	3″-CF_3-4″-$NO_2C_6H_3$	$CH(CH_3)_2$	59.8 ± 4.112	>1000

[a] Assay conditions were the same as those reported in Table 1.

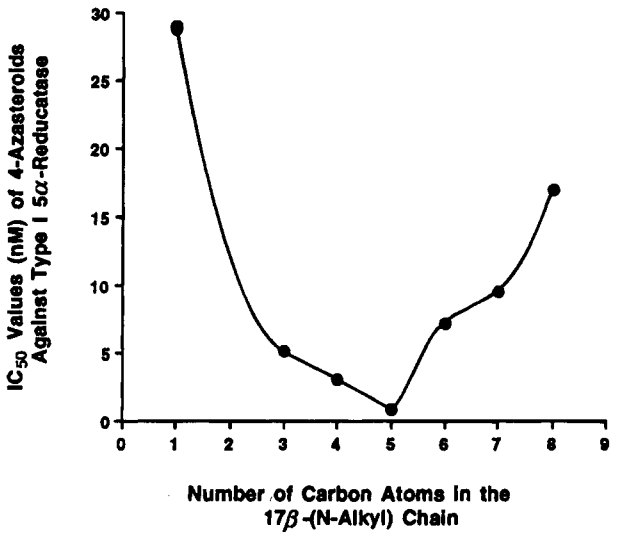


Figure 2. Plot of IC_{50} value versus number of carbon atoms in the 17β-*N*-alkyl chain.

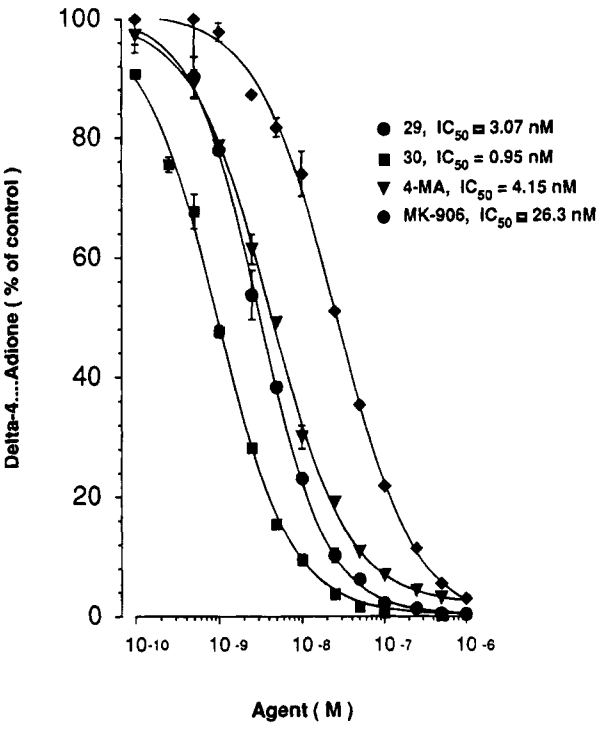


Figure 3. Inhibition of human type I 5α-reductase by 4-MA, MK-906, and 17β-(*N*-alkylformamido)-4-methyl-4-azasteroids **29** and **30**.

so far (Figure 3). Further extension of the chain did not improve the activity of the 4-methyl-4-azasteroids. Thus, the IC_{50} values of *N*-hexyl, *N*-heptyl, and *N*-octyl were 7.25, 9.57, and 16.9 nM, respectively. However, 4-azasteroids having a branched *N*-alkyl chain exhibited high potency. The potency of the compounds increased as the branching of the chain was carried out away from the nitrogen atom. For instance, compounds **36** (IC_{50} = 2.19 nM) and **33** (IC_{50} = 2.35 nM) were better inhibitors than compound **35** (IC_{50} = 7.31 nM). Compound **34** (IC_{50} = 9.53 nM) was a weaker inhibitor of this series. The *N*-benzyl substituent which has the similar steric hindrance as ethyl showed similar potency (IC_{50} = 5.63 nM). Since 17β-(*N*-amyl) and 17β-[*N*-(3′-methylbutyl)] substituents in 4-methyl 4-aza analogues exert maximal potency on human type I 5α-reductase, 4-aza analogues with the above substituents at the 17β-position were also prepared and tested. These compounds were moderate inhibitors of the type I enzyme and weak inhibitors of the type II enzyme. Compared with effects on the type I enzyme, 17β-(*N*-alkylformamido)steroids were less active on the type II enzyme. The IC_{50} values were close to 100 nM, except for compounds **32** (14.0 nM) and **33** (18.4 nM) which were also potent against the type II enzyme.

The above study shows that the *N*-amyl chain has maximal effect on human type I 5α-reductase. We evaluated the effect of various amides while keeping the *N*-amyl chain. We also studied the effect of *N*-aryl- and

-alkylamide substituents. It can be seen that 4-azasteroid **42** with an acetamide group shows high activity on type I 5α-reductase whereas it shows no effect on type II 5α-reductase. An alkylamide group with a longer chain displays stronger activity on the type I enzyme. For instance, the IC_{50} values of propionamide **43**, butyramide **44**, and valeramide **45** were measured at 4.56, 3.31, and 1.77 nM, respectively. Introduction of a remote halogen atom in the butylamide chain had little effect on the inhibitory activity measured for compound **46**.

In another type of substitution, *N*-aryl/alkyl and aryl/alkylamide groups were introduced to see their effect on the 5α-reductase inhibitory activity. The benzamide **47** derivative showed high potency toward type I 5α-reductase. However, it was not active against the type II enzyme. Replacement of the *N*-amyl chain by a *N*-aryl chain (**48**) did not improve the activity on the type I enzyme. However, a marked difference in the activity against type II was observed. In fact, azasteroid **48** showed very high potency against the type II enzyme. Introduction of an electron-donating methoxy group decreased the inhibitory activity on the type I isoenzyme, and compound **49** became inactive against the type II enzyme. In another combination, where the effect of *N*-aryl and alkylamide substituents was studied, introduction of an electron-withdrawing group on the C-4″-position of the aromatic ring made the compounds **52** and **53** less active compared to parent compound **50**. However, an electron-donating group in compound **51** increased the activity 5 times for the type I enzyme. All azasteroids of this family were inactive against the type II enzyme.

Inhibition of the Proliferation of Androgen-Sensitive Shionogi Carcinoma Cells (Clone SEM-107). The antiandrogenic activity of 17β-(*N*-alkylformamido)-4-aza/4-methyl-4-aza-5α-androstan-3-ones was determined by inhibiting DHT action on the proliferation of the androgen-sensitive Shionogi mouse mammary carcinoma cells (clone SEM-107). Hydroxyflutamide was used as the standard reference, with an IC_{50} value of 52.5 ± 1.7 nM. All compounds in Table 1 had little or no inhibitory effect on the cells. However, compounds having a longer chain than methyl at the 17β-position (Table 2) gave better results. For instance, 17β-(*N*-propylformamido)-4-azasteroid **28** (IC_{50} = 989 nM) was 1.5 times more active than compound **8**. Addition of one more methylene carbon to a 17β-(*N*-propyl) chain gave a significant increase in the inhibitory potency as illustrated by compound **29** (166.2 nM). The inhibitory potency went on increasing as the *N*-alkyl chain length increased. Compounds having *N*-amyl (**30**, IC_{50} = 95.5 nM), *N*-hexyl (**31**, IC_{50} = 89.3 nM), *N*-heptyl (**32**, IC_{50} = 57.5 nM), and *N*-octyl (**33**, IC_{50} = 50.3 nM) chains displayed high activities in the indicated increasing order. More data suggest that a lipophilic straight alkyl chain has preference over a short one for inhibiting the androgen receptor. In contrast, study of branched *N*-alkyl chains did not provide any clear cut trends of structure–activity relationships. 17β-(*N*-Isopropylformamido) compound **34** had an IC_{50} value of 162 nM which was 6 times more potent than the *N*-propyl isomer **28** and equally potent as the *N*-butyl compound **29**. However, when an isobutyl chain was introduced, the inhibitory activity of compound **35** sharply decreased to 994 nM, while an *N*-isopentyl chain in compound **36** exhibited the best activity (IC_{50} = 45.5 nM). However, 17β-[(*N*-alkyl/aryl)-alkyl/arylamido]-4-azasteroids showed no antiandrogenic activity.

In conclusion, the 17β-(*N*-alkylformamido)-4-azasteroids having C_4 and C_5 carbon atoms were potent inhibitors of type I 5α-reductase and very weak inhibitors of the type II enzyme and the androgen receptor. On the other hand, 17β-(*N*-branched alkyl)-4-azasteroids **36** and **37** were selective for the type I enzyme. Two azasteroids with C_7 and C_8 carbon atoms were potent inhibitors of both type I and type II enzymes and the androgen receptor. In the class of 17β-[(*N*-alkyl/aryl)-alkyl/arylamides], longer chain aliphatic amides show increased activity compared to shorter chains. In a substitution pattern, where both substitutions were aromatic, azasteroid **48** was active on both type I and type II isoenzymes. In another substitution pattern, an electron-donating group improved the activity of azasteroids whereas an electron-withdrawing group decreased their activity. All azasteroids of this family were selective inhibitors of the type I enzyme except for compound **48**, whereas MK-906 is only selective to the type II enzyme, but 4-MA is active on both isozymes. Finally, the present study provides selective inhibitors of the type I enzyme as well as inhibitors which are very active against both enzymes and have high antiandrogenic activities.

Experimental Section

General. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Diethyl ether and tetrahydrofuran (THF) were distilled from sodium/benzophenone immediately prior to use. All reactions except those involving water as a reagent were conducted under argon atmosphere. Melting points were measured on a Gallenkamp capillary melting point apparatus and are uncorrected. IR spectra were determined with a Perkin-Elmer 1600 Series FT infrared spectrometer. ^1H NMR spectra were determined on a Bruker Aspect-3000 spectrometer (300.13 MHz). ^{13}C NMR spectra were measured at 75.47 MHz with a Bruker Aspect-3000 spectrometer. Low-resolution mass spectra were obtained with a Varian Model 3700 gas chromatography/micromass 16F mass spectrometer. High-resolution mass spectra were measured at the Department of Chemistry, University of Montreal, Montreal, Québec, Canada. Combustion analyses (C, H, N) were performed by Galbraith Laboratories Inc., Knoxville, TN. All the final products were at least 98.0% pure, and the purity was determined by high-performance liquid chromatography (HPLC) on a Waters Model 600E instrument (Millipore). 17β-Hydroxy-4-aza-5α-androstan-3-ones **1**–**3** were prepared by following the method of Rasmusson *et al.*[15a,b]

General Procedure for Oxidation of 17β-Hydroxy Compounds. Method A. To a stirred solution of 17β-hydroxy-4-methyl/4-aza-5α-androstan-3-ones (25.09 mmol, 1.0 equiv) in CH_2Cl_2 (260 mL) were added pyridinium chlorochromate (37.63 mmol, 1.5 equiv), sodium acetate (75.27 mmol, 3.0 equiv), and activated molecular sieves (3 Å) (10% of the alcohol), and the mixture was stirred at room temperature for 3 h. The reaction mixture was passed through Celite 521 to remove the precipitates. The precipitates were washed with acetone (400 mL). The combined filtrate was evaporated to give the residue, which was purified by flash column chromatography (CH_2Cl_2:CH_3OH, 9:1 and then C_6H_{14}:CH_3COCH_3, 7:3).

Method B. To a solution of 17β-hydroxy-4-methyl/4-aza-5α-androstan-3-one (65.57 mmol, 1.0 equiv) in acetone (1000 mL) was added chromium(IV) oxide (98.36 mmol, 1.5 equiv) in 10% aqueous H_2SO_4 (v/v) (200 mL) dropwise for 1 h. Ater

addition, the reaction mixture was stirred for an additional hour. 2-Propanol (4.0 mL, 0.8 equiv) was added into the mixture and stirred for 15 min to reduce the excess of CrO_3. The mixture was filtered through a bed of silica gel (230 g), and the filtrate was concentrated to one-sixth of its volume. Water (300 mL) was added, and the aqueous solution was extracted with CH_2Cl_2 (3 × 300 mL). The combined organic phase was washed with saturated NaCl solution, dried ($MgSO_4$), filtered, and concentrated to give a white residue which was purified by flash silica gel chromatography (C_6H_{14}:CH_3COCH_3, 7:3).

4-Aza-5α-androstane-3,17-dione (4). The compound **4** (6.09 g, 84% yield) was prepared from its corresponding alcohol **1** (7.3 g, 25.09 mmol) by method A: mp >260 °C dec; IR (KBr, cm^{-1}) 3180, 3046, 2940, 2905, 2842, 1718, 1652, 1454, 1370, 1282, 1112, 1064; ^1H NMR ($CDCl_3$) δ 0.82 (s, 3 H, 18-CH_3), 0.87 (s, 3 H, 19-CH_3), 0.93–1.03 (m, 1 H), 1.28 (dd, J = 13.8, 14.6 Hz, 4 H), 1.41–1.60 (m, 6 H), 1.62–1.93 (m, 3 H), 1.90 (dd, J = 5.6, 12.0 Hz, 1 H), 2.01 (dd, J = 9.2, 18.9 Hz, 1 H), 2.24–2.41 (m, 2 H), 2.39 (dd, J = 8.9, 19.3 Hz, 1 H), 3.01 (dd, J = 3.6, 12.3 Hz, 1 H, 5α-H), 6.9 (br s, 1 H, 4-NH); ^{13}C NMR ($CDCl_3$) δ 220.4, 172.3, 60.5, 51.3, 50.8, 47.7, 35.6, 35.1, 34.5, 33.2, 31.2, 28.4, 28.3, 26.8, 21.6, 20.3, 13.7, 11.2; EI-MS m/s (rel intensity) 289 (M^+, 87), 274 (27), 261 (7), 246 (9), 232 (12), 218 (9), 189 (5), 174 (10), 164 (17), 145 (8), 127 (22), 105 (61), 91 (19), 79 (100), 67 (17), 56 (55); HRMS calcd for $C_{18}H_{27}O_2N_1$ 289.2042, found 289.2047.

4-Methyl-4-aza-5α-androstane-3,17-dione (5). 3,17-Dione **5** (18.01 g, 91% yield) was prepared by method B as described above, starting from compound **2** (20.0 G, 65.57 mmol): mp 126–128 °C; IR (KBr, cm^{-1}) 2910, 2824, 1626, 1439, 1380, 1240, 1026; ^1H NMR ($CDCl_3$) δ 0.88 (s, 3 H, 18-CH_3), 0.91 (s, 3 H, 19-CH_3), 0.93–1.10 (m, 1 H), 1.22–1.40 (m, 6 H), 1.41–1.61 (m, 3 H), 1.66–1.72 (m, 1 H), 1.81–1.88 (m, 1 H), 1.91–1.99 (m, 2 H), 2.02–2.12 (m, 2 H), 2.42–2.51 (m, 3 H), 2.93 (s, 3 H, 4-NCH_3), 3.05 (dd, J = 3.5, 12.5 Hz, 1 H, 5α-H); ^{13}C NMR ($CDCl_3$) δ 220.3, 170.6, 65.6, 52.0, 50.9, 47.7, 36.5, 35.7, 33.9, 32.8, 31.3, 29.1, 29.0, 28.9, 25.1, 21.6, 20.3, 13.8, 12.3; EI-MS m/s (rel intensity) 303 (M^+, 100), 288 (36), 274 (19), 216 (4), 138 (4), 124 (18), 112 (13), 93 (6), 79 (6), 70 (82), 57 (18); HRMS calcd for $C_{19}H_{29}O_2N_1$ 303.2198, found 303.2198.

4-Methyl-4-aza-5-androstene-3,17-dione (6). 5-Ene 3,-17-dione **6** (0.30 g, 61% yield) was prepared from the corresponding 17β-alcohol **3** (0.50 g, 1.65 mmol) by method A (pyridine was used as the solvent): mp 151–153 °C; IR (KBr, cm^{-1}) 2936, 2920, 1725, 1630, 1442, 1368, 1235, 1118, 1036; ^1H NMR ($CDCl_3$) δ 0.92 (s, 3 H, 18-CH_3), 1.08 (s, 3 H, 19-CH_3), 1.15–1.38 (m, 4 H), 1.43–1.60 (m, 4 H), 1.61–1.79 (m, 2 H), 1.83–1.93 (m, 1 H), 1.95–2.15 (m, 3 H), 2.17–2.42 (m, 1 H), 2.46 (d, J = 6.4 Hz, 1 H), 2.54 (dd, J = 4.6, 10.3 Hz, 1 H), 3.13 (s, 3 H, 4-NCH_3), 5.08 (dd, J = 2.1, 5.5 Hz, 1 H, 6-H); ^{13}C NMR ($CDCl_3$) δ 220.2, 169.1, 144.6, 104.6, 51.2, 49.2, 42.8, 36.5, 36.4, 32.7, 32.1, 31.1, 30.2, 29.1, 27.1, 24.1, 20.5, 13.5, 12.4; EI-MS m/s (rel intensity) 301 (M^+, 100), 286 (68), 272 (7), 258 (9), 190 (6), 176 (4), 151 (9), 141 (5), 122 (9), 108 (12), 91 (12), 79 (12), 68 (16), 55 (14); HRMS calcd for $C_{19}H_{27}O_2N_1$ 301.2042, found 301.2046.

17β-(*N*-Methylformamido)-4-methyl-4-aza-5α-androstan-3-one (8). A mixture of dione **5** (0.8 g, 2.62 mmol), 99% formic acid (0.2 mL, 5.25 mmol) and *N*-methylformamide (7.74 g, 131.15 mmol) in a Schlenk tube was heated at 170–180 °C for 16 h. After cooling, the reaction mixture was dissolved in chloroform (80 mL), washed with water (3 × 80 mL), dried, and then filtered to give the residue, which was purified by flash silica gel chromatography to give (0.71 g, 78% yield) **8** as white crystals. The NMR analysis showed a mixture of two isomers (4.3:1): mp 194–196 °C; IR (KBr, cm^{-1}) 2920, 2838, 2824, 1650, 1630, 1402, 1385, 1306, 1222, 1052; ^1H NMR ($CDCl_3$) δ 0.74 (s, 2.44 H, 18-CH_3), 0.75 (s, 0.56 H, 18-CH_3), 0.88 (s, 0.57 H, 19-CH_3), 0.90 (s, 2.43 H, 19-CH_3), 0.93–1.15 (m, 3 H), 1.27–1.48 (m, 6 H), 1.63 (dd, J = 3.2, 13.7 Hz, 1 H), 1.75–1.91 (m, 5 H), 2.02–2.07 (m, 2 H), 2.44 (dd, J = 4.6, 9.5 Hz, 1 H), 2.91 (s, 2.44 H, 4-NCH_3), 2.96 (s, 0.56 H, 4-NCH_3), 3.04 (dd, J = 3.3, 12.6 Hz, 1 H, 5α-H), 3.33 (t, J = 9.4 Hz, 0.81 H, 17α-H), 4.21 (t, J = 9.5 Hz, 0.19 H, 17α-H), 8.16 (s, 0.81 H, 17β-NCHO), 8.19 (s, 0.19 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.6, 164.3, 163.4, 69.1, 65.5, 61.5, 51.9, 51.5, 51.2, 45.6, 44.3, 37.2, 36.8, 36.4, 33.9, 32.8, 30.1, 29.7, 29.6, 29.0, 28.9, 25.1, 22.9, 22.8, 21.6, 20.5, 13.3, 12.7, 12.3; EI-MS m/s (rel intensity) 346 (M^+, 77), 331 (13), 287 (9), 272 (8), 260 (23), 248 (21), 234 (7), 138 (11), 124 (24), 112 (34), 98 (86), 70 (100), 57 (44); HRMS calcd for $C_{21}H_{34}O_2N_3$ 346.2620, found 346.2645.

17β-(*N*-Methylformamido)-4-methyl-4-aza-5-androsten-3-one (9). Reductive aminoformylation of ene dione **6** (1.2 g, 3.966 mmol) with *N*-methylformamide in formic acid gave compound **9** (0.33 g, 24% yield) together with **8** (37% yield). The NMR analysis gave a mixture of two conformers (3.4:1): mp 213–215 °C; IR (KBr, cm^{-1}) 2902, 2832, 1650, 1590, 1402, 1368, 1306, 1114, 1042; ^1H NMR ($CDCl_3$) δ 0.77 (t, J = 4.3, 4.6 Hz, 3 H, 18-CH_3), 1.06 (s, 3 H, 19-CH_3), 1.11–1.23 (m, 2 H), 1.27 (d, J = 6.5 Hz, 1 H), 1.31–1.55 (m, 3 H), 1.57–2.07 (m, 9 H), 2.28 (dt, J = 5.3, 5.4, 15.6 Hz, 0.7 H), 2.53 (dd, J = 4.0, 9.1 Hz, 0.7 H), 2.70–2.76 (m, 0.6 H), 2.92 (s, 2.3 H, 4-NCH_3), 2.97 (s, 0.7 H, 4-NCH_3), 3.12 (s, 3 H, 17β-NCH_3), 3.04 (dd, J = 3.3, 12.6 Hz, 1 H, 5α-H), 3.30 (t, J = 9.4 Hz, 0.78 H, 17α-H), 4.22 (t, J = 9.3 Hz, 0.22 H, 17α-H), 5.04 (dd, J = 2.4, 5.7 Hz, 1 H, 6-H), 8.01 (s, 0.77 H, 17β-NCHO), 8.20 (s, 0.23 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 168.2, 164.3, 163.5, 144.3, 104.1, 103.9, 69.1, 61.5, 52.1, 51.8, 48.9, 45.3, 44.1, 37.0, 36.6, 35.4, 33.6, 31.6, 31.1, 30.7, 30.1, 28.8, 23.3, 23.0, 20.3, 18.8, 13.1, 12.6; EI-MS m/s (rel intensity) 344 (M^+, 40), 324 (9), 305 (100), 290 (17), 276 (12), 262 (10), 209 (10), 149 (15), 124 (13), 86 (17), 70 (52), 55 (29); HRMS calcd for $C_{21}H_{32}O_2N_2$ 344.2464, found 344.2468.

17β-(*N*-Methylformamido)-4-aza-5α-androstan-3-one (7). Reduction of dione **4** (0.30 g, 1.038 mmol) gave *N*-methylformamide **7** (0.20 g, 58% yield). The NMR analysis gave a mixture of two conformers (4.6:1): mp 251–253 °C, IR (KBr, cm^{-1}) 3184, 3062, 2920, 2836, 1654, 1462, 1394, 1226, 1112, 1052; ^1H NMR ($CDCl_3$) δ 0.63 (s, 2.39 H, 18-CH_3), 0.65 (s, 0.61 H, 18-CH_3), 0.77 (s, 0.55 H, 19-CH_3), 0.78 (s, 2.45 H, 19-CH_3), 0.91–1.01 (m, 3 H), 1.14–1.39 (m, 7 H), 1.41–1.57 (m, 2 H), 1.60–1.65 (m, 3 H), 1.66–1.79 (m, 2 H), 1.82–1.97 (m, 1 H), 2.28 (dd, J = 3.1, 6.9 Hz, 2 H), 2.79 (s, 2.45 H, 4-NCH_3), 2.87 (s, 0.55 H, 4-NCH_3), 2.95 (dd, J = 3.8, 12.6 Hz, 1 H, 5α-H), 3.22 (t, J = 9.5 Hz, 0.82 H, 17α-H), 4.08 (t, J = 9.6 Hz, 0.18 H, 17α-H), 8.0 (s, 0.82 H, 17β-NCHO), 8.03 (s, 0.18 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 173.2, 165.1, 163.8, 69.2, 62.2, 60.3, 51.3, 51.1, 48.2, 44.2, 36.5, 35.4, 34.5, 32.8, 30.1, 28.9, 28.0, 26.5, 22.7, 21.6, 20.3, 12.5, 11.0; EI-MS m/s (rel intensity) 332 (M^+, 76), 318 (9), 273 (14), 258 (10), 246 (27), 234 (24), 167 (9), 149 (100), 129 (58), 98 (78), 69 (59), 57 (42); HRMS calcd for $C_{20}H_{32}O_2N_2$ 332.2464, found 332.2446.

17β-(*N*-Propylamino)-4-methyl-4-aza-5α-androstan-3-ones (10). Method A.[23c] The following method is a representative. To a stirred mixture of the 3,17-dione **5** (0.20 g, 0.66 mmol), propylamine (0.12 g, 1.98 mmol), and acetic acid (0.12 g, 1.98 mmol) in 1,2-dichloroethane was added sodium triacetoxyborohydride (0.42 g, 1.98 mmol) (in the case of hindered amines, 3 equiv of sodium cyanoborohydride was used)[23a,b] under argon at room temperature. After stirring for 24 h, the solvent was removed under reduced pressure, the resulting residue was dissolved in EtOAc (25 mL) and washed with 4 N HCl solution (2 × 25 mL), and the aqueous acidic solution was basified with 4 N NaOH solution to pH 13. The basic solution was then extracted with CH_2Cl_2 (3 × 50 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated under vacuum. The crude product was purified by silica gel flash column chromatography (C_6H_{14}:EtOAc:Et_2NH, 20:80:1.5).

Method B. To a stirred mixture of the 3,17-dione **5** (0.20 g, 0.66 mmol), 3,3-dimethylbutylamine (0.20 g, 1.98 mmol), and acetic acid (0.12 g, 1.98 mmol) in 1,2-dichloroethane was added sodium cyanoborohydride (0.12 g, 1.98 mmol) under argon. The mixture was stirred at room temperature for 48 h, and the disappearance of starting material and the formation of amine were confirmed by TLC. After the reaction was complete, the mixture was worked up and purified as described in the method A.

Method C. A round flask equipped with an Allihn condenser and a Dean–Stark trap filled with molecular sieves (4 Å) was charged with 3,17-dione **5** (2.0 g, 6.60 mmol), *n*-

butylamine (4.83 g, 66.01 mmol), *p*-toluenesulfonic acid monohydrate (0.02 g), and benzene (50 mL, toluene was used as the solvent when the boiling point of an amine was higher than 111 °C), and the mixture was refluxed for 16 h. The disappearance of starting material and the formation of imine were confirmed by TLC. The reaction mixture was cooled, and the solvent was removed under reduced pressure. The resulting residue in CH_3OH (30 mL) was cooled to 0 °C, and sodium borohydride (0.38 g, 9.90 mmol) was added in small portions. After addition, the mixture was stirred for 1 h and then the solvent was concentrated *in vacco*. The resulting residue was dissolved in water (20 mL), and the aqueous solution was basified to pH 13 with 2 N NaOH. The basic solution was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was washed with brine, dried ($MgSO_4$), filtered, and concentrated under vacuum. The crude product was purified by flash column chromatography (CH_2Cl_2:CH_3OH, 100–50:1).

17β-(*N*-Propylamino)-4-methyl-4-aza-5α-androstan-3-one (10). The 17β-(*N*-propylamino) derivative **10** was prepared by method A (0.21 g, 90% yield): mp 109–111 °C; IR (KBr, cm^{-1}) 3264, 2910, 2844, 1626, 1432, 1376, 1292, 1216, 1092, 1022; ^1H NMR ($CDCl_3$) δ 0.59 (s, 3 H, 18-CH_3), 0.70 (br d, J = 11.7 Hz, 1 H), 0.77 (s, 3 H, 19-CH_3), 0.78 (t, J = 7.3 Hz, 3 H, 3′-CH_3), 0.88 (dd, J = 4.7, 11.9 Hz, 1 H), 1.0–1.19 (m, 3 H), 1.20–1.39 (m, 5 H), 1.34 (t, J = 7.3 Hz, 2 H), 1.41–1.57 (m, 2 H), 1.64–1.83 (m, 3 H), 1.86–1.92 (m, 2 H), 2.31 (dd, J = 4.6, 9.6 Hz, 2 H), 2.39–2.48 (m, 3 H), 2.80 (s, 3 H, 4-NCH_3), 2.91 (dd, J = 3.5, 12.4 Hz, 1 H, 5α-H), 6.21 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.4, 68.7, 65.4, 52.6, 51.8, 50.6, 42.6, 37.7, 36.1, 34.1, 32.6, 32.1, 29.7, 29.5, 28.8, 25.0, 23.4, 23.3, 20.6, 12.1, 11.7, 11.6; EI-MS *m/s* (rel intensity) 346 (M^+, 21), 331 (5), 317 (44), 303 (6), 288 (8), 262 (5), 249 (18), 234 (11), 138 (10), 124 (23), 112 (28), 98 (100), 84 (36), 70 (89); HRMS calcd for $C_{22}H_{38}O_1N_2$ 346.2984, found 346.3006.

17β-(*N*-Butylamino)-4-methyl-4-aza-5α-androstan-3-one (11). The 17β-(*N*-butylamino) analogue **11** (3.32 g, 92% yield) was prepared from the dione **5** (3.0 g, 9.9 mmol) by method B: mp 57–58 °C; IR (KBr, cm^{-1}) 3270, 2936, 2852, 1662, 1442, 1382, 1294, 1224, 1095, 1020; ^1H NMR ($CDCl_3$) δ 0.64 (s, 3 H, 18-CH_3), 0.82 (s, 3 H, 19-CH_3), 0.84 (t, J = 7.1 Hz, 3 H, 4′-CH_3), 0.88–1.41 (m, 10 H), 1.48–1.61 (m, 3 H), 1.64–1.84 (m, 4 H), 1.85–1.97 (m, 2 H), 2.01–2.14 (m, 1 H), 2.36 (dd, J = 4.8, 9.9 Hz, 2 H), 2.44–2.56 (m, 4 H), 2.85 (s, 3 H, 4-NCH_3), 2.96 (dd, J = 3.5, 12.4 Hz, 1 H, 5α-H), 6.27 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.6, 68.9, 65.6, 52.7, 52.0, 48.6, 42.8, 37.9, 36.3, 34.2, 32.8, 32.5, 29.8, 29.6, 29.5, 28.9, 25.2, 23.5, 20.8, 20.4, 13.9, 12.3, 11.8; EI-MS *m/s* (rel intensity) 360 (M^+, 22), 317 (62), 303 (5), 288 (12), 249 (14), 234 (7), 138 (5), 124 (13), 112 (100), 84 (44), 70 (57); HRMS calcd for $C_{23}H_{40}O_1N_2$ 360.3141, found 360.3129.

17β-(*N*-Amylamino)-4-methyl-4-aza-5α-androstan-3-one (12). The 17β-(*N*-amylamino) analogue **12** (0.22 g, 90% yield) was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method B: mp 96–98 °C; IR (KBr, cm^{-1}) 3226, 2904, 2820, 1638, 1438, 1378, 1292, 1216, 1090, 1022; ^1H NMR ($CDCl_3$) δ 0.62 (s, 3 H, 18-CH_3), 0.73 (dd, J = 3.9, 12.1 Hz, 1 H), 0.80 (s, 3 H, 19-CH_3), 0.81 (t, J = 6.7 Hz, 3 H, 5′-CH_3), 0.87 (dd, J = 3.8, 12.2 Hz, 1 H), 0.93–1.28 (m, 9 H), 1.30–1.42 (m, 6 H), 1.42–1.61 (m, 2 H), 1.69–1.82 (m, 3 H), 1.88–1.95 (m, 2 H), 2.34 (dd, J = 4.6, 9.6 Hz, 2 H), 2.42–2.54 (m, 3 H), 2.84 (s, 3 H, 4-NCH_3), 2.94 (dd, J = 3.5, 12.4 Hz, 1 H, 5α-H), 6.25 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.5, 68.9, 65.6, 52.7, 51.9, 48.8, 42.7, 37.8, 36.2, 34.2, 32.7, 30.1, 29.8, 29.6, 29.4, 29.3, 28.9, 25.1, 23.4, 22.4, 20.7, 13.9, 12.2, 11.7; EI-MS *m/s* (rel intensity) 374 (M^+, 28), 359 (6), 317 (52), 303 (12), 288 (16), 249 (13), 138 (9), 126 (100), 112 (34), 98 (61), 84 (36), 70 (88); HRMS calcd for $C_{24}H_{42}O_1N_2$ 374.3296, found 374.3275.

17β-(*N*-Hexylamino)-4-methyl-4-aza-5α-androstan-3-one (13). The 17β-(*N*-hexylamino) analogue **13** (0.21 g, 82% yield) was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method B: mp 83–85 °C; IR (KBr, cm^{-1}) 3236, 2902, 2824, 1628, 1436, 1378, 1292, 1216, 1092, 1022; ^1H NMR ($CDCl_3$) δ 0.63 (s, 3 H, 18-CH_3), 0.73 (dd, J = 4.0, 11.4 Hz, 1 H), 0.81 (t, J = 7.6 Hz, 3 H, 6′-CH_3), 0.82 (s, 3 H, 19-CH_3), 0.89 (dd, J = 3.9, 12.6 Hz, 1 H), 0.94–1.29 (m, 11 H), 1.31–1.40 (m, 6 H), 1.48–1.55 (m, 2 H), 1.70–1.83 (m, 3 H), 1.89–1.96 (m, 2 H), 2.36 (dd, J = 4.6, 12.5 Hz, 2 H), 2.42–2.55 (m, 3 H), 2.85 (s, 3 H, 4-NCH_3), 2.94 (dd, J = 3.5, 12.5 Hz, 1 H, 5α-H), 6.27 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.5, 68.9, 65.6, 52.7, 52.0, 48.9, 42.7, 37.9, 36.3, 34.2, 33.8, 31.6, 30.4, 29.8, 29.6, 29.4, 28.9, 26.9, 25.2, 23.4, 22.5, 20.7, 13.9, 12.2, 11.8; EI-MS *m/s* (rel intensity) 388 (M^+, 12), 373 (4), 330 (2), 317 (48), 303 (9), 288 (10), 249 (8), 140 (98), 124 (19), 112 (44), 83 (28), 70 (100); HRMS calcd for $C_{25}H_{44}O_1N_2$ 388.3453, found 388.3455.

17β-(*N*-Heptylamino)-4-methyl-4-aza-5α-androstan-3-one (14). The 17β-(*N*-heptylamino) analogue **14** (0.55 g, 83% yield) was prepared from the 3,17-dione **5** (0.50 g, 1.65 mmol) by method B: mp 54–56 °C; IR (KBr, cm^{-1}) 3319, 2927, 2852, 1644, 1468, 1444, 1392, 1305, 1229, 1104, 1038, 751; ^1H NMR ($CDCl_3$) δ 0.73 (s, 3 H, 18-CH_3), 0.81 (dd, J = 3.4, 8.3 Hz, 1 H), 0.81 (t, J = 6.8 Hz, 3 H, 7′-CH_3), 0.82 (s, 3 H, 19-CH_3), 0.95 (dd, J = 4.1, 14.5 Hz, 2 H), 1.01–1.66 (m, 18 H), 1.72–2.08 (m, 6 H), 2.42 (dd, J = 4.7, 9.5 Hz, 2 H), 2.45–2.72 (m, 3 H), 2.85 (s, 3 H, 4-NCH_3), 2.94 (dd, J = 3.4, 12.5 Hz, 1 H, 5α-H), 6.25 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.7, 68.9, 65.7, 52.7, 52.2, 48.9, 42.9, 38.0, 36.5, 34.4, 33.0, 32.3, 31.8, 30.1, 30.0, 29.3 (2C), 29.2, 29.1, 27.3, 25.3, 23.6, 22.6, 20.9, 14.1, 12.4, 12.0; EI-MS *m/s* (rel intensity) 402 (M^+, 4), 317 (33), 288 (2), 249 (4), 154 (100), 126 (9), 70 (14); HRMS calcd for $C_{26}H_{46}O_1N_2$ 402.3610, found 402.3592.

17β-(*N*-Octylamino)-4-methyl-4-aza-5α-androstan-3-one (15). The 17β-(*N*-octylamino) compound **15** (0.64 g, 93% yield) was prepared from the 3,17-dione **5** (0.50 g, 1.65 mmol) by method B: mp 58–60 °C; IR (KBr, cm^{-1}) 3320, 2922, 2850, 1643, 1469, 1443, 1381, 1297, 1226, 1109, 1032; ^1H NMR ($CDCl_3$) δ 0.73 (s, 3 H, 18-CH_3), 0.83 (d, J = 2.1 Hz, 1 H), 0.86 (t, J = 7.1 Hz, 3 H, 8′-CH_3), 0.87 (s, 3 H, 19-CH_3), 0.94 (dd, J = 4.1, 14.6 Hz, 2 H), 1.0–1.65 (m, 20 H), 1.73–2.01 (m, 6 H), 2.42 (dd, J = 4.7, 9.5 Hz, 2 H), 2.50–2.65 (m, 3 H), 2.90 (s, 3 H, 4-NCH_3), 3.0 (dd, J = 3.3, 12.5 Hz, 1 H, 5α-H), 6.21 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.7, 68.9, 65.8, 52.9, 52.1, 48.9, 42.9, 38.0, 36.5, 34.4, 33.0, 31.8, 30.1, 30.0, 29.5 (2C), 29.3 (2C), 29.1, 27.4, 25.3, 23.6, 22.6, 20.9, 14.1, 12.4, 12.0; EI-MS *m/s* (rel intensity) 416 (M^+, 4), 317 (32), 235 (6), 201 (5), 168 (100), 151 (17), 113 (12), 84 (5), 70 (16); HRMS calcd for $C_{27}H_{48}O_1N_2$ 416.3776, found 416.3746.

17β-[*N*-(1′-Methylethyl)amino]-4-methyl-4-aza-5α-androstan-3-one (16). The 17β-(*N*-isopropylamino) compound **16** (0.14 g, 61% yield) was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method A: mp 134–136 °C; IR (KBr, cm^{-1}) 3276, 2914, 2844, 1625, 1432, 1366, 1294, 1218, 1160, 1092, 1022; ^1H NMR ($CDCl_3$) δ 0.61 (s, 3 H, 18-CH_3), 0.63–0.75 (m, 2 H), 0.80 (s, 3 H, 19-CH_3), 0.94 (t, J = 6.7 Hz, 6 H, 1′,2′-CH_3), 0.85–0.96 (m, 1 H), 1.04 (dd, J = 0.88, 10.7 Hz, 2 H), 1.09–1.18 (m, 2 H), 1.21–1.41 (m, 5 H), 1.46–1.56 (m, 2 H), 1.69–1.81 (m, 3 H), 1.82–1.96 (m, 2 H), 2.35 (dd, J = 4.6, 9.9 Hz, 2 H), 2.55 (t, J = 8.3 Hz, 1 H, 17α-H), 2.84 (s, 3 H, 4-NCH_3), 2.93 (dd, J = 3.4, 12.3 Hz, 1 H, 5α-H), 6.12 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.8, 77.2, 65.8, 52.9, 52.2, 46.7, 42.9, 37.9, 36.5, 34.5, 33.0, 30.5, 30.0, 29.8, 29.1, 25.3, 23.6, 23.3, 20.9, 20.7, 12.4, 11.7; EI-MS *m/s* (rel intensity) 346 (M^+, 28), 331 (39), 317 (6), 303 (6), 289 (8), 274 (2), 262 (5), 249 (10), 234 (7), 138 (26), 124 (36), 112 (38), 98 (100), 84 (67), 70 (86); HRMS calcd for $C_{22}H_{38}O_1N_2$ 346.2984, found 346.2981.

17β-[*N*-(2′-Methylpropyl)amino]-4-methyl-4-aza-5α-androstan-3-one (17). The 17β-(*N*-isobutylamino) compound **17** (0.23 g, 97% yield) was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method A: mp 78–80 °C; IR (KBr, cm^{-1}) 3278, 2914, 2844, 1628, 1454, 1380, 1368, 1292, 1218, 1092, 1024; ^1H NMR ($CDCl_3$) δ 0.60 (s, 3 H, 18-CH_3), 0.66–0.72 (m, 1 H), 0.77–0.82 (m, 9 H, 19,2′,3′-CH_3), 0.83–0.91 (m, 2 H), 0.93–1.02 (m, 2 H), 1.03–1.17 (m, 2 H), 1.19–1.39 (m, 4 H), 1.49 (dd, J = 9.0, 18.1 Hz, 2 H), 1.60 (dd, J = 6.7, 13.3 Hz, 1 H), 1.67–1.80 (m, 3 H), 1.88–1.92 (m, 2 H), 2.25–2.36 (m, 4 H), 2.41 (t, J = 7.8 Hz, 1 H, 17α-H), 2.82 (s, 3 H, 4-NCH_3), 2.94 (dd, J = 3.2, 12.1 Hz, 1 H, 5α-H), 6.02 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.7, 68.9, 65.7, 56.9, 52.8, 52.1, 42.9, 38.0, 36.4, 34.3, 32.9, 29.9, 29.7, 29.0 (2 C), 28.6, 25.3, 23.5, 20.8, 20.6 (2 C), 12.3, 11.8; EI-MS *m/s* (rel intensity) 360 (M^+, 4), 345 (3), 317 (42), 303 (10), 288 (11), 274 (5), 138 (11), 124 (29), 112 (96), 100 (38), 81 (27), 70 (100); HRMS calcd for $C_{23}H_{40}O_1N_2$ 360.3140, found 360.3108.

17β-[*N*-(3′-Methylbutyl)amino]-4-methyl-4-aza-5α-androstan-3-one (18). The 17β-(*N*-isoamylamino) derivative **18** (0.24 g, 96% yield) was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method B: mp 64–66 °C; IR (KBr, cm^{-1}) 3274, 2924, 2842, 1625, 1452, 1372, 1354, 1292, 1218, 1094, 1026; ^1H NMR ($CDCl_3$) δ 0.62 (s, 3 H, 18-CH_3), 0.80 (s, 3 H, 19-CH_3), 0.81 (t, J = 6.6 Hz, 6 H, 3′,4′-CH_3), 0.85–0.97 (m, 1 H), 1.05 (ddd, J = 4.7, 12.8, 13.1 Hz, 1 H), 1.12–1.21 (m, 2 H), 1.23–1.41 (m, 6 H), 1.50 (dd, J = 6.3, 12.9 Hz, 2 H), 1.54 (dd, J = 6.4, 13.0 Hz, 2 H), 1.69–1.82 (m, 3 H), 1.93 (dd, J = 3.2, 18.6 Hz, 2 H), 2.34 (dd, J = 4.7, 10.3 Hz, 2 H), 2.45 (t, J = 8.3 Hz, 1 H, 17α-H), 2.83 (s, 3 H, 4-NCH_3), 2.99 (dd, J = 3.5, 12.4 Hz, 1 H, 5α-H), 3.12 (dd, J = 5.7, 7.6 Hz, 1 H), 6.08 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.6, 69.0, 65.7, 52.7, 52.0, 47.0, 42.8, 39.6, 37.9, 36.3, 34.2, 32.8, 29.9, 29.6, 28.0, 26.1, 25.2, 23.5, 22.6, 22.5, 22.3, 20.8, 12.3, 11.8; EI-MS *m/s* (rel intensity) 374 (M^+, 15), 359 (4), 317 (17), 303 (5), 288 (6), 249 (9), 163 (7), 151 (16), 126 (83), 113 (11), 98 (13), 84 (27), 69 (100); HRMS calcd for $C_{24}H_{42}O_1N_2$ 374.3296, found 374.3278.

17β-[*N*-(3′,3′-Dimetylbutyl)amino]-4-methyl-4-aza-5α-androstan-3-one (19). The 17β-[*N*-(3′,3′-dimethylbutyl)-amino] derivative **19** (0.24 g, 83% yield) was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method B: mp 73–75 °C; IR (KBr, cm^{-1}) 3236, 2916, 2842, 1627, 1428, 1380, 1352, 1294, 1218, 1092, 1024; ^1H NMR ($CDCl_3$) δ 0.60 (s, 3 H, 18-CH_3), 0.78 (s, 9 H, 3′,3′,4′-CH_3), 0.81 (s, 3 H, 19-CH_3), 0.93 (ddd, J = 3.3, 12.7, 14.7 Hz, 1 H), 1.03–1.21 (m, 1 H), 1.24–1.38 (m, 10 H), 1.49 (dd, J = 8.2, 9.4 Hz, 2 H), 1.69 (dd, J = 3.1, 12.9 Hz, 2 H), 1.72 (dd, J = 4.4, 15.9 Hz, 2 H), 1.84–1.98 (m, 2 H), 2.32 (dd, J = 4.2, 9.6 Hz, 2 H), 2.44 (dd, J = 8.1, 13.6 Hz, 2 H), 2.49 (t, J = 8.2 Hz, 1 H), 2.81 (s, 3 H, 4-NCH_3), 2.92 (dd, J = 3.2, 12.0 Hz, 1 H, 5α-H), 3.12 (ddd, J = 3.1, 5.4, 5.7 Hz, 1 H), 6.22 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.5, 69.0, 65.5, 52.6, 51.9, 44.7, 44.4, 42.9, 42.6, 37.8, 36.2, 36.0, 34.1, 32.7, 29.7, 29.5, 29.4, 29.1, 28.8, 25.1, 23.4, 23.0, 20.7, 12.2, 11.7; EI-MS *m/s* (rel intensity) 388 (M^+, 4), 371 (16), 357 (3), 329 (17), 317 (46), 303 (5), 288 (7), 180 (12), 140 (100), 124 (22), 112 (20), 96 (16), 84 (43), 70 (83); HRMS calcd for $C_{25}H_{44}O_1N_2$ 388.3423, found 388.3443.

17β-[*N*-(1′-Ethylpropyl)amino]-4-methyl-4-aza-5α-androstan-3-one (20). The 17β-[*N*-(1′-ethylpropyl)amino] analogue **20** (0.14 g, 57% yield) was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method B: mp 135–137 °C; IR (KBR, cm^{-1}) 3320, 2906, 2844, 1624, 1448, 1382, 1352, 1294, 1220, 1094, 1024; ^1H NMR ($CDCl_3$) δ 0.64 (s, 3 H, 18-CH_3), 0.69–0.72 (m, 1 H), 0.79 (dd, J = 6.8, 7.3 Hz, 3 H, 3′-CH_3), 0.81 (dd, J = 3.6, 4.9 Hz, 3 H, 3′-CH_3), 0.82 (s, 3 H, 19-CH_3), 0.86–1.19 (m, 2 H), 1.21–1.39 (m, 12 H), 1.48–1.54 (m, 2 H), 1.71–1.83 (m, 3 H), 1.93 (dd, J = 3.3, 8.7 Hz, 2 H), 2.35 (dd, J = 5.1, 6.0 Hz, 1 H), 2.37 (dd, J = 4.6, 9.7 Hz, 2 H), 2.53 (t, J = 8.3 Hz, 1 H, 17α-H), 2.86 (s, 3 H, 4-NCH_3), 2.96 (dd, J = 3.5, 12.5 Hz, 1 H, 5α-H), 6.15 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.6, 65.6, 58.4, 52.7, 52.1, 50.4, 42.8, 37.6, 36.3, 34.3, 33.8, 30.3, 30.2, 29.8, 29.0, 26.5, 26.4, 25.2, 23.4, 20.7, 12.3, 11.6, 10.0, 9.9; EI-MS *m/s* (rel intensity) 374 (M^+, 8), 359 (5), 345 (60), 331 (32), 315 (16), 305 (30), 288 (27), 138 (18), 126 (89), 112 (48), 98 (66), 84 (52), 70 (100); HRMS calcd for $C_{24}H_{42}O_1N_2$ 374.3296, found 374.3272.

17β-(*N*-Cyclopropylamino)-4-methyl-4-aza-5α-androstan-3-one (21). The 17β-(*N*-cyclopropylamino) analogue **21** (1.70 g, 99% yield) was prepared from 3,17-dione **5** (1.5 g, 4.95 mmol) by method A: mp 165–167 °C; IR (KBr, cm^{-1}) 3292, 2924, 2842, 1654, 1436, 1402, 1381, 1226, 1094; ^1H NMR ($CDCl_3$) δ 0.27 (dd, J = 3.5, 7.2 Hz, 2 H), 0.36 (d, J = 6.6 Hz, 2 H), 0.67 (s, 3 H, 18-CH_3), 0.85 (s, 3 H, 19-CH_3), 0.94 (ddd, J = 2.1, 3.4, 5.2 Hz, 2 H), 1.10–1.50 (m, 8 H), 1.52–1.75 (m, 3 H), 1.78–2.08 (m, 5 H), 2.09–2.15 (m, 1 H), 2.40 (dd, J = 4.7, 10.2 Hz, 2 H), 2.62 (t, J = 8.6 Hz, 1 H, 17α-H), 2.89 (s, 3 H, 4-NCH_3), 2.99 (dd, J = 3.6, 12.3 Hz, 1 H, 5α-H), 5.87 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.7, 68.9, 65.7, 52.7, 52.1, 42.7, 37.9, 36.4, 34.4, 32.9, 29.9, 29.7, 29.6, 29.0, 25.3, 23.5, 20.8, 20.3, 12.3, 11.8, 7.2, 6.4; EI-MS *m/s* (rel intensity) 344 (M^+, 42), 329 (72), 315 (44), 303 (7), 288 (9), 272 (5), 260 (7), 234 (6), 149 (17), 129 (28), 121 (100), 91 (28), 70 (84), 57 (55); HRMS calcd for $C_{22}H_{36}O_1N_2$ 344.2822, found 344.2794.

17β-(*N*-Cyclohexylamino)-4-methyl-4-aza-5α-androstan-3-one (22). The 17β-(*N*-cyclohexylamino) compound **22** (0.17 g, 77% yield) was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method B: mp 103–105 °C; IR (KBr, cm^{-1}) 3260, 2908, 2830, 1632, 1436, 1375, 1224, 1028; ^1H NMR ($CDCl_3$) δ 0.65 (s, 3 H, 18-CH_3), 0.69–0.82 (m, 1 H), 0.84 (s, 3 H, 19-CH_3), 0.97–1.26 (m, 10 H), 1.28–1.41 (m, 4 H), 1.51–1.57 (m, 3 H), 1.59–1.69 (m, 2 H), 1.71–1.85 (m, 5 H), 1.92–1.99 (m, 2 H), 2.39 (dd, J = 4.7, 10.1 Hz, 2 H), 2.37–2.48 (m, 1 H), 2.61 (dd, J = 7.2, 12.9 Hz, 1 H, 17α-H), 2.88 (s, 3 H, 4-NCH_3), 2.96 (dd, J = 3.5, 12.6 Hz, 1 H, 5α-H), 5.92 (br s, 1 H, 17β-NH); ^{13}C NMR ($CDCl_3$) δ 170.7, 77.2, 65.7, 65.2, 55.1, 52.1, 42.8, 37.7, 36.3, 34.3, 34.1, 33.9, 32.8, 30.6, 29.9, 29.2 (2C), 28.9, 26.1, 25.2, 25.1, 23.5, 20.8, 12.3, 11.7; EI-MS *m/s* (rel intensity) 386 (M^+, 31), 343 (30), 152 (10), 138 (100), 124 (5), 110 (6), 96 (9), 70 (11), 57 (13); HRMS calcd for $C_{25}H_{42}O_1N_2$ 386.3297, found 386.3289.

17β-(*N*-Benzylamino)-4-methyl-4-aza-5α-androstan-3-one (23). The 17β-(*N*-benzylamino) analogue **23** (0.23 g, 87% yield) was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method B: mp 139–141 °C; IR (KBr, cm^{-1}) 3234, 2908, 2838, 1624, 1438, 1380, 1294, 1218, 1092, 1028; ^1H NMR ($CDCl_3$) δ 0.69 (s, 3 H, 18-CH_3), 0.81 (s, 3 H, 19-CH_3), 0.90–1.08 (m, 1 H), 1.14 (dd, J = 5.6, 11.9 Hz, 1 H), 1.20–1.42 (m, 7 H), 1.52 (dd, J = 7.8, 9.0 Hz, 2 H), 1.71–1.95 (m, 6 H), 2.35 (dd, J = 4.3, 9.6 Hz, 2 H), 2.51 (t, J = 8.5 Hz, 1 H, 17α-H), 2.84 (s, 3 H, 4-NCH_3), 2.92 (dd, J = 3.0, 12.5 Hz, 1 H, 5α-H), 3.73 (d, J = 2.7 Hz, 2 H, $ArCH_2$), 4.37 (br d, J = 3.1 Hz, 1 H, 17β-NH), 7.17 (dd, J = 3.4, 3.8 Hz, 1 H, ArH), 7.21–7.25 (m, 4 H, ArH); ^{13}C NMR ($CDCl_3$) δ 170.3, 140.7, 128.2, 128.0 (2C), 127.6, 126.4, 67.8, 65.7, 52.4, 51.8, 43.2, 42.7, 37.6, 36.1, 34.0, 32.6, 29.6, 29.3, 28.8, 25.0, 23.3, 21.8, 20.6, 12.1, 11.78; EI-MS *m/s* (rel intensity) 394 (M^+, 4), 377 (16), 363 (2), 315 (3), 303 (3), 289 (10), 186 (34), 170 (9), 146 (87), 132 (36), 124 (17), 106 (75), 91 (100), 79 (54); HRMS calcd for $C_{26}H_{38}O_1N_2$ 394.2928, found 394.2898.

17β-(*N*-Phenylamino)-4-methyl-4-aza-5α-androstan-3-one (24). **24** was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method C in 74% yield: mp 95–97 °C; IR (KBr, cm^{-1}) 3234, 2908, 2838, 1624, 1438, 1380, 1294, 1218, 1092, 1028; ^1H NMR ($CDCl_3$) δ 0.69 (s, 3 H, 18-CH_3), 0.81 (s, 3 H, 19-CH_3), 0.90–1.08 (m, 1 H), 1.14 (dd, J = 5.6, 11.9 Hz, 1 H), 1.20–1.42 (m, 7 H), 1.52 (dd, J = 7.8, 9.0 Hz, 2 H), 1.71–1.95 (m, 6 H), 2.35 (dd, J = 4.3, 9.6 Hz, 2 H), 2.51 (t, J = 8.4 Hz, 1 H, 17α-H), 2.84 (s, 3 H, 4-NCH_3), 2.92 (dd, J = 3.0, 12.5 Hz, 1 H, 5α-H), 3.73 (d, J = 2.7 Hz, 2 H, $ArCH_2$), 4.37 (br d, J = 3.1 Hz, 1 H, 17β-NH), 7.17 (dd, J = 3.4, 3.8 Hz, 1 H, ArH), 7.21–7.25 (m, 4 H, ArH); ^{13}C NMR ($CDCl_3$) δ 170.3, 140.7, 128.2, 128.0 (2C), 127.6, 126.4, 67.8, 65.7, 52.4, 43.2, 42.7, 37.6, 36.1, 34.0, 32.6, 29.6, 29.3, 28.8, 25.0, 23.3, 21.8, 20.6, 12.1, 11.78; EI-MS *m/s* (rel intensity) 380 (M^+, 19), 363 (2), 351 (2), 317 (2), 288 (4), 249 (10), 149 (9), 132 (69), 119 (20), 106 (12), 91 (73), 76 (21), 62 (100); HRMS calcd for $C_{25}H_{36}O_1N_2$ 380.2827, found 380.2813.

17β-[*N*-(4′-Nitrophenyl)amino]-4-methyl-4-aza-5α-androstan-3-one (25). **25** was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method C in 49% yield: mp 154–156 °C; IR (KBr, cm^{-1}) 3387, 2940, 2858, 1638, 1598, 1472, 1309, 1108, 825; ^1H NMR ($CDCl_3$) δ 0.76 (s, 3 H, 18-CH_3), 0.86 (s, 3 H, 19-CH_3), 0.97 (dt, J = 3.4, 12.2 Hz, 1 H), 1.09–1.44 (m, 8 H), 1.45–1.59 (m, 1 H), 1.60–1.84 (m, 4 H), 2.0 (dd, J = 3.3, 12.9 Hz, 1 H), 2.11–2.28 (m, 2 H), 2.40 (dd, J = 4.6, 9.4 Hz, 2 H), 2.90 (s, 3 H, 4-NCH_3), 3.03 (dd, J = 3.3, 12.4 Hz, 1 H, 5α-H), 3.47 (dd, J = 8.5, 17.1 Hz, 1 H), 4.73 (d, J = 8.5 Hz, 1 H), 6.53 (d, J = 9.3 Hz, 2 H, 2′,6′-H), 7.99 (d, J = 9.2 Hz, 2 H, 3′,5′-H); ^{13}C NMR ($CDCl_3$) δ 170.7, 153.8 (1′-C), 137.3 (4′-C), 126.4 (2C, 3′,5′-C), 111.3 (2C, 2′,6′-C), 65.6, 62.9, 52.3, 51.9, 44.2, 38.0, 36.4, 32.9, 30.9, 30.1, 29.8, 29.1, 29.1, 25.3, 23.4, 20.8, 12.4, 12.2; EI-MS *m/s* (rel intensity) 425 (M^+, 45), 317 (22), 288 (48), 249 (18), 235 (30), 210 (100), 167 (59), 124 (27), 114 (33), 85 (36), 70 (42); HRMS calcd for $C_{25}H_{35}O_3N_3$ 425.2678, found 425.2658.

17β-[*N*-(4′-Methoxyphenyl)amino]-4-methyl-4-aza-5α-androstan-3-one (26). **26** was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method C in 99% yield: mp 132–134 °C; IR (KBr, cm^{-1}) 3349, 2945, 2868, 1637, 1510, 1459, 1413,

1394, 1306, 1236, 1103, 1040; ^{1}H NMR ($CDCl_3$) δ 0.76 (s, 3 H, 18-CH_3), 0.88 (s, 3 H, 19-CH_3), 0.79–1.06 (m, 2 H), 1.08–1.45 (m, 9 H), 1.47–1.85 (m, 7 H), 1.99 (dd, J = 3.4, 12.9 Hz, 1 H), 2.01–2.24 (m, 1 H), 2.42 (dd, J = 4.7, 9.5 Hz, 2 H), 2.92 (s, 3 H, 4-NCH_3), 3.02 (dd, J = 3.5, 12.5 Hz, 1 H, 5α-H), 3.31 (t, J = 8.5 Hz, 1 H), 3.72 (s, 3 H, 4′-OCH_3), 6.60 (dd, J = 2.5, 8.9 Hz, 2 H, 2′,6′-H), 6.72 (dd, J = 2.5, 8.9 Hz, 2 H, 3′,5′-H), 7.99 (d, J = 9.1 Hz, 1 H, 5′-H); ^{13}C NMR ($CDCl_3$) δ 170.7, 152.1 (4′-C), 142.8 (1′-C), 114.9 (2C, 2′,6′-C), 114.3 (2C, 3′,5′-C), 65.7, 64.5, 55.5 (4′-OCH_3), 52.4, 51.6, 43.3, 38.1, 36.7, 34.9, 32.6, 31.6, 30.0, 29.8, 29.4, 25.2, 23.5, 20.9, 12.5, 12.3; EI-MS m/s (rel intensity) 410 (M^+, 100), 234 (4) 162 (82), 149 (31), 134 (10), 91 (4), 70 (7); HRMS calcd for $C_{26}H_{38}O_2N_2$ 410.2933, found 410.2927.

17β-[N-[3′-(Trifluoromethyl)-4′-nitrophenyl]amino]-4-methyl-4-aza-5α-androstan-3-one (27). **27** was prepared from the 3,17-dione **5** (0.20 g, 0.66 mmol) by method C in 66% yield: mp 158–160 °C; IR (KBr, cm^{-1}) 3295, 2943, 2849, 1625, 1601, 1508, 1468, 1325, 1261, 1155, 1038, 830; ^{1}H NMR ($CDCl_3$) δ 0.80 (s, 3 H, 18-CH_3), 0.90 (s, 3 H, 19-CH_3), 1.01 (dt, J = 3.7, 12.1 Hz, 1 H), 1.14–1.53 (m, 8 H), 1.61–1.88 (m, 7 H), 2.05 (dd, J = 3.7, 13.0 Hz, 1 H), 2.28 (dq, J = 4.5, 11.5, 17.3 Hz, 1 H), 2.46 (dd, J = 4.8, 9.5 Hz, 2 H), 2.94 (s, 3 H, 4-NCH_3), 3.06 (dd, J = 3.6, 12.4 Hz, 1 H, 5α-H), 3.49 (t, J = 7.8 Hz, 1 H), 4.59 (br s, 1 H), 6.68 (dd, J = 2.5, 9.2 Hz, 1 H, 6′-H), 6.90 (d, J = 2.4 Hz, 1 H, 2′-H), 7.99 (d, J = 9.1 Hz, 1 H, 5′-H); ^{13}C NMR ($CDCl_3$) δ 170.7, 152.1 (1′-C), 136.1 (4′-C), 129.2 (6′-C), 128.8 (5′-C), 112.8 (2′-C), 111.5 (3′-C), 65.6, 63.0, 52.3, 51.9, 44.3, 38.0, 36.5, 35.8, 34.6, 32.9, 31.4, 29.8, 29.2, 29.0, 25.3, 23.4, 20.8, 12.4, 12.3; EI-MS m/s (rel intensity) 493 (M^+, 100), 476 (39), 463 (44), 367 (5), 288 (9), 262 (25), 245 (92), 235 (36), 215 (22), 167 (58), 124 (26), 112 (48), 91 (6), 70 (42); HRMS calcd for $C_{26}H_{34}O_3N_3F_3$ 493.2552, found 493.2545.

17β-(N-Propylformamido)-4-methyl-4-aza-5α-androstan-3-one (28). The following method is a representative.[24a] To a 2 M solution of formic acid (0.05 g, 1.16 mmol) in chloroform (3.0 mL) was added dicyclohexylcarbodiimide (DCC) (0.238 g, 1.156 mmol) dropwise in chloroform (3.0 mL). After 5 min, the above mixture was added into an ice-cold solution of compound **10** (0.20 g, 0.58 mmol) in pyridine (2 mL) over a period of 30 min. The reaction mixture was stirred for 1 h at room temperature. Evaporation of solvent followed by addition of Et_2O precipitated dicyclohexylurea which was removed by filtration. The combined filtrate was concentrated to an oil, which was purified by silica gel flash column chromatography (C_6H_{14}:CH_3COCH_3, 9:1–7:3) to give the formamido compound **28** (0.18 g, 82% yield). The NMR analysis gave a mixture of two conformers (4.5:1): mp 127–129 °C; IR (KBr, cm^{-1}) 2912, 2822, 1632, 1402, 1386, 1294, 1218, 1088; ^{1}H NMR ($CDCl_3$) δ 0.65 (s, 3 H, 18-CH_3), 0.83 (t, J = 7.2 Hz, 3 H, 3′-CH_3), 0.85 (s, 3 H, 19-CH_3), 0.86–1.12 (m, 2 H), 1.20–1.42 (m, 8 H), 1.56 (dd J = 2.2, 7.4 Hz, 2 H), 1.68–1.93 (m, 4 H), 1.94–2.02 (m, 3 H), 2.39 (dd, J = 4.5, 9.6 Hz, 2 H), 2.86 (s, 3 H, 4-NCH_3), 2.99 (dd, J = 3.5, 12.4 Hz, 1 H, 5α-H), 3.14–3.28 (m, 0.82 H), 3.24 (dd, J = 5.7, 19.7 Hz, 2 H) 4.12 (t, J = 9.9 Hz, 0.18 H), 8.11 (s, 0.82 H, 17β-NCHO), 8.11 (s, 0.18 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.5, 164.4, 163.0, 68.5, 65.5, 51.9, 51.6, 48.3, 45.8, 44.2, 36.3, 34.0, 32.8, 29.6, 28.9, 25.1, 24.3, 23.5, 22.8, 21.6, 20.5, 12.3 (2C), 11.2, 11.6; EI-MS m/s (rel intensity) 374 (M^+, 34), 360 (9), 345 (36), 331 (6), 317 (5), 287 (11), 261 (15), 248 (17), 126 (100), 112 (29), 98 (60), 83 (27), 70 (78); HRMS calcd for $C_{23}H_{38}O_2N_2$ 374.2933, found 374.2903. Anal. ($C_{23}H_{38}O_2N_2$) C, H, N.

17β-(N-Butylformamido)-4-methyl-4-aza-5α-androstan-3-one (29). The 17β-(*N*-butylformamido) compound **29** (2.20 g, 73% yield) was prepared from the 17β-(*N*-butylamino) compound **11** (2.80 g, 7.778 mmol). The NMR analysis gave a mixture of two conformers (4:1): mp 128–130 °C; IR (KBr, cm^{-1}) 2912, 2844, 1628, 1402, 1382, 1292, 1218, 1088, 1022; ^{1}H NMR ($CDCl_3$) δ 0.66 (s, 3 H, 18-CH_3), 0.69–0.82 (m, 1 H), 0.84 (s, 3 H, 19CH_3), 0.86 (t, J = 7.0 Hz, 3 H, 4′-CH_3), 0.89–1.19 (m, 2 H), 1.21–1.41 (m, 9 H), 1.43–1.64 (m, 2 H), 1.66–1.84 (m, 4 H), 1.86–2.07 (m, 3 H), 2.39 (dd, J = 3.7, 9.9 Hz, 2 H), 2.87 (s, 3 H, 4-NCH_3), 3.02 (dd, J = 3.4, 12.3 Hz, 1 H, 5α-H), 3.17–3.38 (m, 3 H), 8.12 (s, 0.80 H, 17β-NCHO), 8.24 (s, 0.20 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.5, 164.5, 163.0, 68.6, 65.6, 52.0, 51.7, 46.6, 44.3, 44.2, 36.9, 36.5, 34.1, 32.9, 29.7, 29.4, 29.0, 28.9, 25.2, 24.4, 23.2, 22.9, 20.6, 20.2, 13.8, 12.3; EI-MS m/s (rel intensity) 388 (M^+, 12), 345 (22), 287 (8), 264 (5), 247 (9), 149 (7), 129 (9), 114 (7), 101 (44), 85 (13), 72 (26), 59 (100); HRMS calcd for $C_{24}H_{40}O_2N_2$ 388.3171, found 388.3148. Anal. ($C_{24}H_{40}O_2N_2$) C, H, N.

17β-(N-Amylformamido)-4-methyl-4-aza-5α-androstan-3-one (30). The 17β-(*N*-amylformamido) compound **30** (2.50 g, 93% yield) was prepared from the 17β-(*N*-amylamino) compound **12** (2.50 g, 6.69 mmol). The NMR analysis gave a mixture of two conformers (4:1): mp 149–151 °C; IR (KBr, cm^{-1}) 2904, 2822, 1642, 1389, 1294, 1218, 1088, 1016; ^{1}H NMR ($CDCl_3$), δ 0.68 (s, 3 H, 18-CH_3), 0.71–0.81 (m, 1 H), 0.86 (s, 3 H, 19-CH_3), 0.86 (t, J = 4.6 Hz, 3 H, 5′-CH_3), 0.94–1.19 (m, 2 H), 1.21–1.42 (m, 11 H), 1.52–1.64 (m, 2 H), 1.66–1.92 (m, 4 H), 1.93–1.98 (m, 3 H), 2.41 (dd, J = 4.6, 9.8 Hz, 2 H), 2.89 (s, 3 H, 4-NCH_3), 3.01 (dd, J = 3.4, 12.3 Hz, 1 H, 5α-H), 3.22–3.28 (m, 3 H), 8.14 (s, 0.80 H, 17β-NCHO), 8.20 (s, 0.20 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.6, 164.8, 163.0, 68.5, 65.6, 52.0, 51.7, 51.2, 46.7, 44.3, 37.2, 36.8, 36.4, 34.1, 32.8, 32.1, 29.6, 29.1, 29.0, 28.8, 25.2, 24.3, 23.2, 22.8, 22.4, 20.5, 13.9, 12.8, 12.3; EI-MS m/s (rel intensity) 402 (M^+, 58), 387 (9), 373 (6), 345 (56), 331 (8), 317 (8), 287 (24), 261 (20), 248 (24), 154 (100), 126 (72), 112 (56), 98 (25), 81 (29), 70 (84); HRMS calcd for $C_{25}H_{42}O_2N_2$ 402.3245, found 402.3242. Anal. ($C_{25}H_{42}O_2N_2$) C, H, N.

17β-(N-Hexylformamido)-4-methyl-4-aza-5α-androstan-3-one (31). The 17β-(*N*-hexylformamido) compound **31** (0.15 g, 70% yield) was prepared from the 17β-(*N*-hexylamino) compound **13** (0.20 g, 0.52 mmol). The NMR analysis gave a mixture of two conformers (4:1): mp 101–103 °C; IR (KBr, cm^{-1}) 2904, 2826, 1634, 1442, 1402, 1382, 1294, 1228, 1090, 1022; ^{1}H NMR ($CDCl_3$) δ 0.68 (s, 3 H, 18-CH_3), 0.85 (t, J = 6.5 Hz, 3 H, 6′-CH_3), 0.86 (s, 3 H, 19-CH_3), 0.92–1.09 (m, 2 H), 1.24–1.43 (m, 12 H), 1.44–1.57 (m, 2 H), 1.61–1.83 (m, 5 H), 1.89–2.03 (m, 4 H), 2.41 (dd, J = 4.5, 9.7 Hz, 2 H), 2.90 (s, 3 H, 4-NCH_3), 3.0 (dd, J = 3.3, 12.2 Hz, 1 H, 5α-H), 3.18–3.28 (m, 2.8 H), 4.12 (t, J = 10.0 Hz, 0.2 H), 8.14 (s, 0.80 H, 17β-NCHO); 8.20 (s, 0.20 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.6, 164.8, 163.0, 68.5, 65.6, 62.0, 52.0, 51.7, 51.3, 46.7, 45.7, 44.3, 44.2, 37.2, 36.8, 36.4, 34.1, 32.8, 32.4, 31.3, 29.6, 29.2, 29.0, 28.9, 28.5, 26.6, 26.4, 25.2, 24.3, 23.2, 22.8, 22.5, 20.5, 13.9, 12.5, 12.3; EI-MS m/s (rel intensity) 416 (M^+, 10), 402 (3), 373 (2), 345 (14), 331 (3), 317 (3), 219 (25), 168 (34), 149 (31), 140 (18), 125 (24), 111 (27), 97 (54), 85 (67), 70 (100); HRMS calcd for $C_{26}H_{44}O_2N_2$ 416.3382, found 416.3355. Anal. ($C_{26}H_{44}O_2N_2$) C, H, N.

17β-(N-Heptylformamido)-4-methyl-4-aza-5α-androstan-3-one (32). The 17β-(*N*-heptylformamido) analogue **32** (0.53 g, 98% yield) was prepared from the 17β-(*N*-heptylamino) compound **14** (0.50 g, 1.24 mmol). The NMR analysis gave a mixture of two conformers (5.3:1): mp 73–75 °C; IR (KBr, cm^{-1}) 2928, 2846, 1660, 1628 1470, 1396, 1310, 1230, 1106, 1042; ^{1}H NMR (CDCl3, δ 0.69 (s, 3 H, 18-CH_3), 0.70–0.77 (m, 1 H), 0.86 (t, J = 6.8 Hz, 3 H, 7′-CH_3), 0.88 (s, 3 H, 19-CH_3), 0.91–1.14 (m, 2 H), 1.24–1.49 (m, 18 H), 1.49–1.68 (m, 1 H), 1.69–1.85 (m, 3 H), 1.89–2.04 (m, 2 H), 2.41 (dd, J = 4.6, 9.5 Hz, 2 H), 2.91 (s, 3 H, 4-NCH_3), 3.02 (dd, J = 3.4, 12.5 Hz, 1 H, 5α-H), 3.18–3.36 (m, 2.84 H), 4.13 (t, J = 9.8 Hz, 0.16 H), 8.16 (s, 0.84 H, 17β-NCHO), 8.22 (s, 0.16 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.6, 164.5, 163.0, 68.6, 65.7, 62.1, 52.1, 51.8, 51.4, 46.8, 45.7, 44.4, 44.3, 37.3, 36.9, 36.5, 34.2, 32.9, 32.5, 31.8, 29.7, 29.0, 28.6, 27.0, 26.7, 25.5, 24.4, 23.3, 23.2, 22.9, 22.6, 20.6, 14.0, 12.9, 12.4; EI-MS m/s (rel intensity) 430 (M^+, 44), 415 (7), 345 (58), 287 (19), 261 (13), 201 (8), 182 (100), 168 (34), 150 (33), 124 (16), 112 (21), 70 (28); HRMS calcd for $C_{27}H_{46}O_2N_2$ 430.3559, found 430.3536. Anal. ($C_{27}H_{46}O_2N_2$) C, H, N.

17β-(N-Octylformamido)-4-methyl-4-aza-5α-androstan-3-one (33). The 17β-(*N*-octylformamido) analogue **33** (0.62 g, 98% yield) was prepared from the 17β-(*N*-octylamino) compound **15** (0.59 g, 1.42 mmol). The NMR analysis gave a mixture of two conformers (5.3:1): mp 106–108 °C; IR (KBr, cm^{-1}) 2926, 2840, 1662, 1623, 1469, 1412, 1393, 1310, 1230, 1103, 1044; ^{1}H NMR ($CDCl_3$) δ 0.68 (s, 3 H, 18-CH_3), 0.72–0.78 (m, 1 H), 0.84 (t, J = 7.2 Hz, 3 H, 8′-CH_3), 0.88 (s,

3 H, 19-CH_3), 0.93–1.10 (m, 2 H), 1.24–1.48 (m, 20 H), 1.49–1.66 (m, 1 H), 1.68–1.89 (m, 3 H), 1.92–2.04 (m, 2 H), 2.41 (dd, J = 4.6, 9.4 Hz, 2 H), 2.90 (s, 3 H, 4-NCH_3), 3.0 (dd, J = 3.3, 12.5 Hz, 1 H, 5α-H), 3.15–3.33 (m, 2.84 H), 4.12 (t, J = 9.8 Hz, 0.16 H), 8.14 (s, 0.84 H, 17β-NCHO), 8.20 (s, 0.16 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.6, 164.5, 163.0, 68.6, 65.6, 62.0, 52.0, 51.7, 51.3, 46.7, 45.7, 44.4, 44.2, 37.3, 36.8, 36.4, 34.2, 32.9, 32.4, 31.7, 29.0, 28.5, 27.0, 26.7, 25.2, 24.4, 23.2, 23.1, 22.8, 22.5, 20.5, 14.0, 12.8, 12.3; EI-MS m/s (rel intensity) 444 (M^+, 46), 429 (6), 345 (62), 287 (120), 261 (16), 248 (13), 196 (100), 168 (38), 151 (22), 124 (16), 112 (23), 70 (37); HRMS calcd for $C_{28}H_{48}O_2N_2$ 444.3715, found 444.3705. Anal. ($C_{28}H_{48}O_2N_2$) C, H, N.

17β-[*N*-(1′-Methylethyl)formamido]-4-methyl-4-aza-5α-androstan-3-one (34). The 17β-(*N*-isopropylformamido) compound **34** (0.08 g, 66% yield) was prepared from the 17β-(*N*-isopropylamino) compound **16** (0.12 g, 0.33 mmol). The NMR analysis gave a mixture of two conformers (1.4:1): mp 177–179 °C; IR (KBr, cm^{-1}) 2912, 2826, 1632, 1434, 1382, 1294, 1218, 1088, 1022; ^1H NMR ($CDCl_3$) δ 0.72 (s, 1.26 H, 18-CH_3), 0.77 (s, 1.74 H, 18-CH_3), 0.85 (1.26 H, 19-CH_3), 0.88 (s, 1.74 H, 19-CH_3), 0.94–1.08 (m, 2 H), 1.20 (d, J = 6.5 Hz, 1.35 H, 1′-CH_3), 1.21 (d, J = 7.8 Hz, 1.63 H, 2′-CH_3), 1.23 (d, J = 7.7 Hz, 1.55 H, 2′-CH_3), 1.24 (d, J = 6.8 Hz, 1.37 H, 1′-CH_3), 1.16–1.45 (m, 8 H), 1.58–1.61 (m, 1 H), 1.69–1.83 (m, 4 H), 1.99 (ddd, J = 3.5, 7.4, 8.2 Hz, 2 H), 2.42 (dd, J = 4.2, 9.9 Hz, 2 H), 2.90 (s, 3 H, 4-NCH_3), 3.01 (dd, J = 3.0, 12.4 Hz, 1 H, 5α-H), 3.17 (t, J = 9.9 Hz, 0.58 H), 3.59 (dq, J = 6.5, 6.7, 6.9, 7.1 Hz, 0.42 H), 4.14 (dq, J = 6.6, 7.0 Hz, 0.58 H), 4.25 (t, J = 9.8 Hz, 0.42 H), 8.24 (s, 0.58 H, 17β-NCHO), 8.40 (s, 0.42 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.5, 163.4, 162.7, 66.3, 65.5, 61.9, 52.2, 51.9, 51.8, 51.2, 46.6, 46.2, 44.6, 43.0, 37.0, 36.7, 36.3, 34.1, 33.9, 32.8, 29.7, 29.6, 29.0, 28.9, 27.2, 25.2, 25.1, 23.1, 22.8, 22.7, 20.5, 20.4, 20.2, 12.8, 12.7, 12.3; EI-MS m/s (rel intensity) 374 (M^+, 45), 359 (42), 345 (10), 331 (15), 317 (4), 305 (3), 287 (25), 261 (31), 248 (28), 126 (87), 112 (65), 98 (77), 84 (55), 70 (100); HRMS calcd for $C_{23}H_{38}O_2N_2$ 374.2933, found 374.2945. Anal. ($C_{23}H_{38}O_2N_2$) C, H, N.

17β-[*N*-(2′-Methylpropyl)formamido]-4-methyl-4-aza-5α-androstan-3-one (35). The 17β-[*N*-(2′-methylpropyl)formamido] compound **35** (0.18 g, 90% yield) was prepared from the 17β-[*N*-(2′-methylpropyl)amino] compound **17** (0.18 g, 0.50 mmol). The NMR analysis gave a mixture of two conformers (4:1): mp 52–54 °C; IR (KBr, cm^{-1}) 2916, 2842, 1696 (sh), 1628, 1448, 1398, 1382, 1294, 1216, 1092, 1024; ^1H NMR ($CDCl_3$) δ 0.68 (s, 3 H, 18-CH_3), 0.80 (s, 3 H, 19-CH_3), 0.84 (d, J = 5.0 Hz, 3 H, 2′-CH_3), 0.86 (d, J = 5.3 Hz, 3 H, 3′-CH_3), 0.77–0.89 (m, 3 H), 0.89–1.10 (m, 2 H), 1.21–1.39 (m, 6 H), 1.49–1.70 (m, 1 H), 1.71–1.82 (m, 4 H), 1.93–1.99 (m, 3 H), 2.40 (dd, J = 4.2, 10.1 Hz, 2 H), 2.89 (s, 3 H, 4-NCH_3), 3.0 (dd, J = 3.5, 12.5 Hz, 1 H, 5α-H), 3.12 (dd, J = 5.7, 13.2 Hz, 0.20 H), 3.34 (t, J = 9.9 Hz, 0.8 H), 3.34 (dd, J = 6.6, 13.2 Hz, 0.80 H), 4.05 (t, J = 10.0 Hz, 0.20 H), 8.15 (s, 0.20 H, 17β-NCHO), 8.29 (s, 0.80 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.6, 164.7, 162.8, 69.2, 65.6, 52.3, 51.9, 51.8, 51.2, 46.0, 46.2, 44.3, 43.0, 37.2, 36.3, 32.8, 29.0, 28.9, 28.0, 27.1, 26.8, 25.1, 24.9, 23.1, 22.8, 20.2, 20.0, 19.8, 12.8, 12.3; EI-MS m/s (rel intensity) 388 (M^+, 20), 373 (3), 359 (3), 345 (32), 317 (5), 287 (6), 262 (9), 248 (7), 140 (60), 129 (17), 112 (29), 101 (89), 85 (34), 69 (100); HRMS calcd for $C_{24}H_{40}O_2N_2$ 388.3171, found 388.3169. Anal. ($C_{24}H_{40}O_2N_2$) C, H, N.

17β-[*N*-(3′-Methylbutyl)formamido]-4-methyl-4-aza-5α-androstan-3-one (36). The 17β-[*N*-(3′-methylbutyl)formamido] compound **36** (0.13 g, 66% yield) was prepared from the 17β-[*N*-(3′-methylbutyl)amino] compound **18** (0.18 g, 0.48 mmol). The NMR analysis gave a mixture of two conformers (4:1): mp 87–89 °C; IR (KBr, cm^{-1}) 2918, 2842, 1634, 1452, 1406, 1382, 1368, 1294, 1218, 1091, 1022; ^1H NMR ($CDCl_3$) δ 0.68 (s, 3 H, 18-CH_3), 0.85 (d, J = 5.9 Hz, 3 H, 3′-CH_3), 0.86 (s, 3 H, 19-CH_3), 0.87 (d, J = 6.4 Hz, 3 H, 4′-CH_3), 0.94–1.07 (m, 2 H), 1.22–1.43 (m, 8 H), 1.48 (dd, J = 5.2, 5.9 Hz, 2 H), 54 (dd, J = 6.5, 12.6 Hz, 2 H), 1.70–1.80 (m, 4 H), 72 (dd, J = 5.2, 12.0 Hz, 2 H), 1.80 (dd, J = 4.3, 8.6 Hz, 2 H), 1.93 (dd, J = 9.7, 10.4 Hz, 2 H), 1.94 (dd, J = 8.8, 9.6 Hz, 1 H), 2.41 (dd, J = 4.5, 9.4 Hz, 2 H), 2.89 (s, 3 H, 4-NCH_3), 2.99 (dd, J = 3.3, 12.4 Hz, 1 H, 5α-H), 3.20–3.29 (m, 1.8 H), 4.16 (t, J = 10.0 Hz, 0.20 H), 8.13 (s, 0.80 H, 17β-NCHO), 8.20 (s, 0.20 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.6, 164.5, 162.9, 68.5, 65.6, 51.9, 51.6, 44.2, 42.7, 37.2, 36.8, 36.4, 34.1, 32.8, 29.6, 29.2, 29.0, 28.9, 28.0, 26.3, 25.9, 25.2, 24.3, 22.8, 22.5, 20.5, 12.8, 12.3; EI-MS m/s (rel intensity) 402 (M^+, 24), 387 (4), 374 (3), 359 (3), 345 (25), 317 (2), 287 (7), 264 (9), 248 (7), 219 (13), 192 (27), 154 (66), 126 (27), 101 (100), 85 (54), 71 (86); HRMS calcd for $C_{25}H_{42}O_2N_2$ 402.3245, found 402.3230. Anal. ($C_{25}H_{42}O_2N_2$) C, H, N.

17β-[*N*-(3′,3′-Dimethylbutyl)formamido]-4-methyl-4-aza-5α-androstan-3-one (37). The 17β-[*N*-(3′,3′-dimethylbutyl)formamido] compound **37** (0.12 g, 66% yield) was prepared from the 17β-[*N*-(3′,3′-dimethylbutyl)amino] compound **19** (0.23 g, 0.59 mmol). The NMR analysis gave a mixture of two conformers (4:1): mp 150–152 °C; IR (KBr, cm^{-1}) 2922, 2846, 1632, 1612, 1452, 1382, 1380, 1352, 1294, 1218, 1132, 1094, 1022; ^1H NMR ($CDCl_3$) δ 0.66 (s, 3 H, 18-CH_3), 0.82 (s, 0.62 H, 19-CH_3), 0.84 (s, 2.38 H, 19-CH_3), 0.87 (s, 9 H, 3′,3′,4′-CH_3), 0.96–1.05 (m, 2 H), 1.20–1.47 (m, 7 H), 1.48–1.64 (m, 3 H), 1.88–1.81 (m, 4 H), 1.92 (t, J = 9.7 Hz, 2 H), 1.89–1.95 (m, 1 H), 2.38 (dd, J = 4.6, 10.5 Hz, 2 H), 2.87 (s, 3 H, 4-NCH_3), 2.97 (dd, J = 3.5, 12.6 Hz, 1 H, 5α-H), 3.18–3.34 (m, 3 H), 8.10 (s, 0.80 H, 17β-NCHO), 8.17 (s, 0.20 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.5, 164.6, 162.8, 68.4, 65.5, 62.4, 51.8, 51.5, 46.7, 44.1, 43.8, 41.4, 40.5, 36.7, 36.3, 34.0, 32.8, 29.7, 29.6, 29.1 (3C), 29.0, 28.9, 25.1, 24.1, 22.8, 20.5, 12.3 (2C); EI-MS m/s (rel intensity) 416 (M^+, 20), 401 (11), 387 (7), 371 (5), 345 (53), 331 (11), 315 (13), 287 (18), 260 (21), 246 (16), 168 (100), 140 (34), 124 (39), 112 (52), 84 (28), 70 (81). HRMS calcd for $C_{26}H_{44}O_2N_2$ 416.3382, found 416.3361. Anal. ($C_{26}H_{44}O_2N_2$) C, H, N.

17β-[*N*-(1′-Ethylpropyl)formamido]-4-methyl-4-aza-5α-androstan-3-one (38). The 17β-[*N*-(1′-ethylpropyl)formamido] compound **38** (0.08 g, 50% yield) was prepared from the corresponding 17β-[*N*-(1′-ethylpropyl)amino] compound **20** (0.14 g, 0.37 mmol). The NMR analysis gave a mixture of two conformers (2.3:1): mp 111–113 °C; IR (KBr, cm^{-1}) 2908, 2824, 1632, 1442, 1406, 1384, 1368, 1295, 1218, 1092, 1022; ^1H NMR ($CDCl_3$) δ 0.82 (s, 3 H, 18-CH_3), 0.86 (t, J = 7.5 Hz, 3 H, 2″-CH_3), 0.89 (s, 3 H, 19-CH_3), 0.89 (t, J = 7.3 Hz, 3 H, 3′-CH_3), 0.99–1.19 (m, 2 H), 1.24–1.45 (m, 7 H), 1.50 (t, J = 2.7 Hz, 1 H), 1.53–1.59 (m, 2 H), 1.67 (dd, J = 9.8, 10.1 Hz, 1 H), 1.68 (t, J = 12.6 Hz, 2 H), 1.77 (dd, J = 3.6, 7.7 Hz, 2 H), 1.82 (dd, J = 3.3, 9.2 Hz, 2 H), 2.42 (dd, J = 4.7, 9.9 Hz, 2 H), 2.92 (s, 3 H, 4-NCH_3), 3.01 (dd, J = 3.5, 12.1 Hz, 1 H, 5α-H), 2.99–3.10 (m, 0.7 H), 3.95 (t, J = 10.0 Hz, 0.3 H), 8.24 (s, 0.30 H, 17β-NCHO), 8.48 (s, 0.70 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.6, 163.9, 163.5, 66.3, 65.7, 65.6, 63.8, 52.9, 52.0, 51.9, 51.8, 44.9, 43.2, 37.2, 36.4, 34.2, 32.9, 29.8, 29.7, 29.1, 29.0, 28.9, 28.6, 28.5, 26.2, 25.3, 25.2, 23.3, 23.1, 23.0, 20.8, 20.6, 13.3, 13.1, 12.4, 11.8, 11.4, 10.6; EI-MS m/s (rel intensity) 402 (M^+, 20), 387 (4), 373 (24), 359 (7), 345 (62), 331 (26), 315 (5), 290 (21), 274 (9), 260 (15), 154 (57), 126 (100), 112 (36), 98 (37), 84 (28), 70 (84); HRMS calcd for $C_{25}H_{42}O_2N_2$ 402.3246, found 402.3265. Anal. ($C_{25}H_{42}O_2N_2$) C, H, N.

17β-(*N*-Cyclopropylformamido)-4-methyl-4-aza-5α-androstan-3-one (39). The 17β-(*N*-cyclopropylformamido) compound **39** (1.34 g, 78% yield) was prepared from the corresponding 17β-(*N*-cyclopropylamino) compound **21** (1.60 g, 4.65 mmol). The NMR analysis gave a mixture of two conformers (1.5:1): mp 163–165 °C; IR (KBr, cm^{-1}) 2914, 2842, 2738, 1652, 1434, 1382, 1294, 1216, 1080, 1018; ^1H NMR ($CDCl_3$) δ 0.39–0.44 (m, 0.8 H), 0.67–0.71 (m, 1.60 H), 0.72 (s, 3 H, 18-CH_3), 0.74–0.82 (m, 1.60 H), 0.88 (s, 3 H, 19-CH_3), 0.86–0.91 (m, 1 H), 0.92–1.16 (m, 1 H), 1.18–1.38 (m, 7 H), 1.41–1.57 (m, 1 H), 1.62–1.66 (m, 2 H), 1.67–1.79 (m, 3 H), 1.98 (dd, J = 3.3, 10.9 Hz, 1 H), 2.35 (dd, J = 4.5, 10.2 Hz, 2 H), 2.43–2.59 (m, 2 H), 2.85 (s, 3 H, 4-NCH_3), 2.97 (dd, J = 3.4, 12.6 Hz, 1 H, 5α-H), 3.24 (t, J = 8.8 Hz, 0.4 H), 3.99 (t, J = 8.7 Hz, 0.6 H), 8.27 (s, 0.40 H, 17β-NCHO), 8.33 (s, 0.60 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.6, 165.4, 163.5, 69.9, 65.6, 64.4, 51.9, 51.8, 51.3, 45.7, 44.2, 37.9, 37.5, 36.4, 34.2, 29.7, 29.3, 29.1, 29.0, 28.8, 25.3, 22.2, 20.7, 13.6, 12.3, 9.9, 8.1, 6.4, 6.2; EI-MS m/s (rel intensity) 372 (M^+, 74), 357 (10), 344 (26), 329 (26), 315 (47), 287 (34), 272 (26), 260 (8), 246 (5), 224 (12), 203 (5), 192 (72), 177 (13), 149 (21), 126 (34), 112 (35), 95 (41),

81 (50), 69 (54), 55 (100); HRMS calcd for $C_{23}H_{36}O_2N_2$ 372.2797, found 372.2820. Anal. ($C_{23}H_{36}O_2N_2$) C, H, N.

17β-(N-Cyclohexylformamido)-4-methyl-4-aza-5α-androstan-3-one (40). The 17β-(N-cyclohexylformamido) compound **40** (0.92 g, 78% yield) was prepared from the 17β-(N-cyclohexylamino) compound **22** (1.10 g, 2.82 mmol). The NMR analysis gave a mixture of two conformers (1:1): mp 144–146 °C; IR (KBr, cm^{-1}) 2904, 2822, 2764, 1632, 1432, 1382, 1290, 1220, 1092, 1016; ^1H NMR ($CDCl_3$) δ 0.70 (s, 1.50 H, 18-CH_3), 0.77 (s, 1.50 H, 18-CH_3), 0.85 (s, 1.50 H, 19-CH_3), 0.87 (s, 1.50 H, 19-CH_3), 0.90–1.16 (m, 2 H), 1.18–1.41 (m, 10 H), 1.42–1.83 (m, 13 H), 1.89–2.04 (m, 2 H), 2.40 (dd, J = 4.6, 10.2 Hz, 2 H), 2.90 (s, 3 H, 4-NCH_3), 2.99 (dd, J = 3.1, 12.4 Hz, 1 H, 5α-H), 3.16 (t, J = 9.8 Hz, 0.50 H, 17α-H), 3.70–3.82 (m, 0.50 H), 4.28 (t, J = 9.8 Hz, 0.5 H, 17α-H), 8.30 (s, 0.50 H, 17β-NCHO), 8.38 (s, 0.50 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.7, 163.5, 163.1, 77.2, 69.9, 66.3, 65.7, 61.9, 55.4, 54.4, 52.4, 52.1, 51.4, 44.7, 43.1, 37.2, 36.8, 36.5, 34.2, 34.1, 33.7, 32.9, 30.9, 30.6, 29.8, 29.7, 29.3, 29.1, 29.0, 27.9, 26.9, 26.2, 26.0, 25.4, 25.3, 23.2, 22.9, 20.7, 20.5, 13.0, 12.6, 12.4; EI-MS m/s (rel intensity) 414 (M^+, 8), 307 (2), 249 (9), 186 (4), 166 (4), 149 (11), 125 (4), 111 (9), 101 (43), 83 (16), 69 (23), 59 (100); HRMS calcd for $C_{26}H_{42}O_2N_2$ 414.3247, found 414.3270. Anal. ($C_{26}H_{42}O_2N_2$) C, H, N.

17β-(N-Benzylformamido)-4-methyl-4-aza-5α-androstan-3-one (41). The 17β-(N-benzylformamido) compound **41** (0.20 g, 80% yield) was prepared from the corresponding 17β-(N-benzylamino) compound **23** (0.23 g, 0.58 mmol). The NMR analysis gave a mixture of two conformers (4:1): mp 89–91 °C; IR (KBr, cm^{-1}) 2926, 2844, 2822, 1638, 1606, 1465, 1442, 1386, 1372, 1294, 1208, 1092; ^1H NMR ($CDCl_3$) δ 0.73 (s, 2.30 H, 18-CH_3), 0.75 (s, 0.70 H, 18-CH_3), 0.83 (s, 3 H, 19-CH_3), 0.88–1.08 (m, 1 H), 1.12 (dd, J = 9.5, 12.9 Hz, 1 H), 1.18–1.47 (m, 7 H), 1.60 (dd, J = 3.0, 16.0 Hz, 2 H), 1.71–1.84 (m, 4 H), 1.85–1.97 (m, 2 H), 2.38 (dd, J = 3.6, 9.8 Hz, 2 H), 2.86 (s, 3 H, 4-NCH_3), 2.96 (dd, J = 3.4, 12.3 Hz, 1 H, 5α-H), 3.27 (t, J = 9.8 Hz, 0.78 H, 17α-H), 4.21 (t, J = 9.9 Hz, 0.22 H, 17α-H), 4.39 (d, J = 15.7 Hz, 0.79 H, $ArCH_2$), 4.53 (d, J = 15.4 Hz, 0.21 H, $ArCH_2$), 4.74 (d, J = 15.2 Hz, 0.21 H, $ArCH_2$), 4.78 (d, J = 15.5 Hz, 0.79 H, $ArCH_2$), 7.13 (d, J = 7.2 Hz, 2 H, ArH), 7.25 (d, J = 6.5, 7.6 Hz, 3 H, ArH), 8.26 (s, 0.21 H, 17β-NCHO), 8.41 (s, 0.79 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 170.7, 165.2, 163.0, 137.3, 128.6, 128.4, 127.3, 127.0, 126.9, 125.8, 68.0, 65.4, 51.7, 51.6, 51.1, 50.3, 47.2, 45.8, 44.1, 37.3, 37.0, 36.2, 34.6, 34.0, 32.7, 30.7, 29.6, 29.5, 28.9, 28.8, 25.0, 24.6, 23.2, 22.7, 22.5, 20.5, 13.0, 12.4, 12.2; EI-MS m/s (rel intensity) 422 (M^+, 17), 407 (3), 393 (3), 377 (4), 331 (15), 287 (7), 260 (9), 174 (24), 146 (18), 124 (16), 112 (20), 91 (100), 70 (31); HRMS calcd for $C_{27}H_{38}O_2N_2$ 422.2933, found 422.2924. Anal. ($C_{27}H_{38}O_2N_2$) C, H, N.

Preparation of 17β-[(N-Alkyl/aryl)alkyl/arylamido]-4-methyl-4-aza-5α-androstan-3-ones 42–53.[25] The following method is a representative. To a solution of 17β-(N-butylamino)-4-methyl-4-aza-5α-androstan-3-one (**11**) (0.50 g, 1.39 mmol) in dry THF (25 mL) was added anhydrous powdered potassium carbonate (0.42, g, 3.06 mmol) followed by acetyl chloride (0.22 g, 2.78 mmol) dropwise, and the mixture was stirred overnight. Evaporation of solvent gave the residue which was treated with 5% aqueous $NaHCO_3$ for 15 min and then extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with brine, dried, and concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography (C_6H_{14}:CH_3COCH_3, 9:1–7:3) to give compound **42** (0.48 g, 85%). The NMR analysis gave a mixture of two conformers (1.85:1): mp 152–154 °C; IR (KBr, cm^{-1}) 2910, 2826, 1622, 1404, 1352, 1294, 1224, 1028; ^1H NMR ($CDCl_3$) δ 0.67 (s, 1.95 H, 18-CH_3), 0.74 (s, 1.05 H, 18-CH_3), 0.80–1.0 (m, 9 H, 19, 2′,4″-CH_3), 1.07–1.69 (m, 12 H), 1.71–1.91 (m, 5 H), 1.99–2.07 (m, 1 H), 2.12 (s, 1.05 H), 2.14 (s, 1.95 H), 2.38 (dd, J = 4.6, 10.2 Hz, 2 H), 2.89 (s, 3 H, 4-NCH_3), 3.0 (dd, J = 3.4, 12.3 Hz, 1 H, 5α-H), 2.84–3.0 (m, 0.35 H), 3.24–3.29 (m, 0.65 H), 3.68–3.71 (m, 0.70 H), 4.12 (t, J = 9.6 Hz, 0.65 H, 17α-H); ^{13}C NMR ($CDCl_3$) δ 171.4, 171.1, 170.5, 67.3, 65.5, 62.3, 51.1, 46.4, 45.6, 44.6, 44.3, 37.1, 36.3, 34.0, 32.8, 30.9, 29.7, 29.2, 29.0, 25.2, 24.6, 23.7, 23.2, 22.7, 22.3, 20.5, 20.0, 13.7, 12.9, 12.7, 12.3; EI-MS m/s (rel intensity) 402 (M^+, 31), 387 (16), 373 (3), 359 (15), 345 (9), 331 (6), 317 (34), 303 (4), 287 (30), 273 (8), 260 (12), 248 (11), 154 (64), 140 (34), 124 (28), 112 (86), 93 (15), 84 (40), 69 (100); HRMS calcd for $C_{25}H_{42}O_2N_2$ 402.3246, found 402.3234. Anal. ($C_{25}H_{42}O_2N_2$) C, H, N.

17β-[(N-Amyl)propionamido]-4-methyl-4-aza-5α-androstan-3-one (43). **43** was prepared in 56% yield. The NMR analysis gave a mixture of two conformers (3.5:1): oil; IR (KBr, cm^{-1}) 2918, 2832, 1608, 1446, 1402, 1370, 1294, 1222, 1990, 1022; ^1H NMR ($CDCl_3$) δ 0.63 (s, 0.66 H, 18-CH_3), 0.66 (s, 2.34 H, 18-CH_3), 0.70–1.0 (m, 9 H, 3 CH_3, 19,3′,5″-CH_3), 1.03–1.60 (m, 18 H), 1.64–1.89 (m, 4 H), 1.95 (dd, J = 2.5, 12.3 Hz, 1 H), 2.38 (dd, J = 4.3, 9.5 Hz, 2 H), 2.12–2.39 (m, 1 H), 2.46–2.57 (m, 1 H), 2.87 (s, 3 H, 4-NCH_3), 2.68–2.85 (m, 0.22 H), 2.98 (dd, J = 2.7, 9.9 Hz, 1 H, 5α-H), 3.04–3.14 (m, 0.78 H), 3.19–3.36 (m, 0.78 H), 3.57–3.79 (m, 0.44 H), 4.46 (t, J = 9.7 Hz, 0.78 H, 17α-H); ^{13}C NMR ($CDCl_3$) δ 173.5, 172.7, 170.9, 66.8, 65.6, 62.5, 51.9, 51.7, 51.1, 45.8, 45.6, 45.4, 45.2, 44.8, 37.3, 36.4, 34.0, 33.4, 33.0, 32.7, 32.4, 32.2, 32.0, 31.0, 29.7, 29.1, 28.9, 25.2, 24.7, 24.4, 23.6, 23.5, 22.9, 22.3, 20.5, 14.0, 12.8, 12.3; EI-MS m/s (rel intensity) 430 (M^+, 2), 401 (2), 374 (4), 330 (5), 317 (57), 288 (14), 249 (7), 182 (13), 126 (100), 97 (39), 80 (22), 63 (74); HRMS calcd for $C_{27}H_{46}O_2N_2$ 430.3559, found 430.3532. Anal. ($C_{27}H_{46}O_2N_2$) C, H, N.

17β-[(N-Amyl)butyramido]-4-methyl-4-aza-5α-androstan-3-one (44). **44** was prepared in 45% yield. The NMR analysis gave a mixture of two conformers (3:1): oil; IR (KBr, cm^{-1}) 2908, 2896, 1614, 1424, 1395, 1286, 1212, 1086, 1018; ^1H NMR ($CDCl_3$) δ 0.65 (s, 2.25 H, 18-CH_3), 0.73 (s, 0.75 H, 18-CH_3), 0.79–0.99 (m, 10 H), 1.04–1.59 (m, 16 H), 1.61–1.96 (m, 8 H), 2.0 (d, J = 9.7 Hz, 1 H), 2.16–2.34 (m, 1 H), 2.37–2.44 (m, 2 H), 2.84–2.92 (m, 0.25 H), 2.91 (s, 3 H, 4-NCH_3), 3.02 (dd, J = 3.4, 12.5 Hz, 1 H, 5α-H), 3.08–3.14 (m, 0.75 H), 3.24–3.38 (m, 0.75 H), 3.59–3.80 (m, 0.50 H), 4.51 (t, J = 9.5 Hz, 0.75 H, 17α-H); ^{13}C NMR ($CDCl_3$) δ 174.3, 174.0, 170.8, 66.2, 65.7, 62.4, 52.1, 51.8, 51.2, 45.9, 45.7, 37.4, 36.5, 35.9, 34.1, 32.9, 31.1, 29.8, 29.7, 29.6, 29.1, 25.3, 23.7, 23.3, 23.1, 23.0, 22.3, 20.6, 19.4, 18.9, 12.8, 12.4; EI-MS m/s (rel intensity) 444 (M^+, 4), 401 (5), 374 (11), 330 (10), 317 (87), 288 (26), 249 (17), 196 (24), 126 (100), 97 (68), 80 (57), 63 (91); HRMS calcd for $C_{28}H_{48}O_2N_2$ 444.3716.2904, found 444.3712. Anal. ($C_{28}H_{48}O_2N_2$) C, H, N.

17β-[(N-Amyl)valeramido]-4-methyl-4-aza-5α-androstan-3-one (45). **45** was prepared in 45% yield. The NMR analysis gave a mixture of two conformers (3.3:1): oil; IR (KBr, cm^{-1}) 2902, 2894, 2818, 1612, 1420, 1391, 1282, 1209, 1086, 1015; ^1H NMR ($CDCl_3$) δ 0.60 (s, 2.31 H, 18-CH_3), 0.68 (s, 0.69 H, 18-CH_3), 0.74–0.98 (m, 10 H), 1.01–1.53 (m, 17 H), 1.55–1.94 (m, 9 H), 1.94 (d, J = 9.5 Hz, 1 H), 2.10–2.30 (m, 1 H), 2.36 (dd, J = 7.0, 14.7 Hz, 2 H), 2.78–2.84 (m, 0.23 H), 2.85 (s, 3 H, 4-NCH_3), 2.96 (dd, J = 3.3, 12.5 Hz, 1 H, 5α-H), 2.99–3.12 (m, 0.77 H), 3.17–3.31 (m, 0.77 H), 3.56–3.77 (m, 0.46 H), 4.45 (t, J = 9.5 Hz, 0.77 H, 17α-H); ^{13}C NMR ($CDCl_3$) δ 174.4, 173.9, 170.7, 66.1, 65.6, 62.3, 52.0, 51.7, 51.2, 45.8, 45.6, 45.4, 44.7, 37.4, 36.4, 34.1, 33.7, 32.8, 31.1, 29.7, 29.5, 29.0, 28.6, 28.2, 27.8, 25.3, 24.7, 23.7, 23.4, 22.9, 22.6, 22.3, 20.6, 14.0, 13.9, 12.8, 12.3; EI-MS m/s (rel intensity) 458 (M^+, 4), 401 (5), 373 (37), 330 (2), 287 (11), 210 (26), 149 (12), 126 (79), 79 (14), 62 (100); HRMS calcd for $C_{29}H_{50}O_2N_2$ 458.3872, found 458.3843. Anal. ($C_{29}H_{50}O_2N_2$) C, H, N.

17β-[(N-Amyl)-5′-bromovaleramido]-4-methyl-4-aza-5α-androstan-3-one (46). **46** was prepared in 22% yield. The NMR analysis gave a mixture of two conformers (2.85:1): mp 59–61 °C; IR (KBr, cm^{-1}) 2904, 2826, 1622, 1402, 1378, 1294, 1214, 1088, 1018; ^1H NMR ($CDCl_3$) δ 0.63 (s, 2.22 H, 18-CH_3), 0.70 (s, 0.78 H, 18-CH_3), 0.76–0.93 (m, 8 H), 1.14–1.51 (m, 14 H), 1.61–1.90 (m, 10 H), 1.91–1.99 (m, 1 H), 2.18–2.44 (m, 4 H), 2.88 (s, 3 H, 4-NCH_3), 2.77–2.92 (m, 0.26 H), 2.99 (dd, J = 3.4, 12.5 Hz, 1 H, 5α-H), 2.79–3.16 (m, 0.74 H), 3.20–3.32 (m, 0.74 H), 3.35–3.39 (m, 1.48 H), 3.41–3.51 (m, 0.52 H), 3.53–3.74 (m, 0.52 H), 4.46 (t, J = 9.8 Hz, 0.74 H, 17α-H); ^{13}C NMR ($CDCl_3$) δ 173.5, 172.7, 170.9, 66.8, 65.6, 62.5, 51.9, 51.7, 51.1, 45.8, 45.6, 45.4, 45.2, 44.8, 37.3, 36.4, 34.0, 33.4, 33.0, 32.7, 32.4, 32.2, 32.0, 31.0, 29.7, 29.1, 28.9, 25.2, 24.7, 24.4, 23.6, 23.5, 22.9, 22.3, 20.5, 14.0, 12.8, 12.3; EI-MS m/s (rel intensity) 538/536 (M^+, 2), 456 (4), 401 (6), 373 (4), 317

(7), 287/285 (12), 244 (12), 170 (15), 126 (100), 97 (18), 76 (16), 62 (54); HRMS calcd for $C_{29}H_{49}O_2N_2{}^{79}Br$ 536.2904, found 536.2896. Anal. ($C_{29}H_{49}O_2N_2{}^{79}Br$) C, H, N, Br.

17β-[(*N*-Amyl)benzamido]-4-methyl-4-aza-5α-androstan-3-one (47). **47** was prepared in 76% yield: mp 84–86 °C; IR (KBr, cm^{-1}) 2908, 2832, 1614, 1572, 1432, 1402, 1384, 1294, 1218, 1088, 1020; ^1H NMR ($CDCl_3$) δ 0.73 (s, 3 H, 18-CH_3), 0.82 (s, 3 H, 19-CH_3), 0.56–0.96 (m, 4 H), 1.15–1.60 (m, 14 H), 1.63–1.76 (m, 5 H), 1.81–1.96 (m, 3 H), 2.36 (dd, J = 4.4, 9.1 Hz, 2 H), 2.86 (s, 3 H, 4-NCH_3), 2.91–3.06 (m, 3 H), 3.40–3.76 (m, 1 H), 7.26–7.32 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 173.2, 170.7, 138.8, 128.8, 128.3 (3C), 126.6, 68.6, 51.8, 51.3, 45.8, 45.5, 36.9, 36.4, 33.9, 32.8, 29.7, 29.0 (3C), 25.2 (2C), 24.0, 23.0, 22.2, 20.4, 13.9, 13.0, 12.3 (2C); EI-MS *m/s* (rel intensity) 478 (M^+, 5), 407 (4), 373 (2), 330 (2), 287 (15), 230 (51), 120 (53), 104 (100), 71 (82), 62 (90); HRMS calcd for $C_{31}H_{46}O_2N_2$ 478.3559, found 478.3534. Anal. ($C_{31}H_{46}O_2N_2$) C, H, N.

17β-[(*N*-Phenyl)benzamido]-4-methyl-4-aza-5α-androstan-3-one (48). **48** was prepared in 76% yield: mp 250–251 °C; IR (KBr, cm^{-1}) 2918, 2824, 1628, 1584, 1482, 1430, 1310, 1292, 1208; ^1H NMR ($CDCl_3$) δ 0.78 (s, 3 H, 18-CH_3), 0.87 (s, 3 H, 19-CH_3), 0.64–1.02 (m, 2 H), 1.16–1.46 (m, 6 H), 1.58–1.87 (m, 8 H), 1.89–1.99 (m, 1 H), 2.4 (dd, J = 4.7, 9.1 Hz, 2 H), 2.92 (s, 3 H, 4-NCH_3), 3.04 (dd, J = 3.4, 10.2 Hz, 1 H, 5α-H), 4.76 (t, J = 8.8 Hz, 1 H, 17α-H), 7.08–7.26 (m, 10 H, ArH); ^{13}C NMR ($CDCl_3$) δ 172.9, 170.9, 142.1, 137.9, 131.3 (2C), 128.7, 128.4 (2C), 127.9 (2C), 127.5 (2C), 127.1, 66.1, 65.7, 52.0, 51.9, 45.6, 38.2, 36.5, 34.3, 32.9, 29.8, 29.1 (2C), 25.3, 25.1, 23.0, 20.8, 13.8, 12.4; EI-MS *m/s* (rel intensity) 484 (M^+, 4), 430 (2), 379 (2), 288 (16), 236 (18), 197 (18), 126 (14), 104 (100), 91 (6), 71 (29), 62 (43); HRMS calcd for $C_{32}H_{40}O_2N_2$ 484.3090, found 484.3094. Anal. ($C_{32}H_{40}O_2N_2$) C, H, N.

17β-[*N*-(4″-Methoxyphenyl)benzamido]-4-methyl-4-aza-5α-androstan-3-one (49). **49** was prepared in 94% yield: mp 108–110 °C; IR (KBr, cm^{-1}) 2939, 2844, 2809, 1646, 1578 (sh), 1510, 1448, 1342, 1305, 1244, 1059, 775, 688; ^1H NMR ($CDCl_3$) δ 0.76 (s, 3 H, 18-CH_3), 0.86 (s, 3 H, 19-CH_3), 0.91–1.46 (m, 7 H), 1.55–1.90 (m, 9 H), 2.01 (dd, J = 4.6, 13.9 Hz, 1 H), 2.42 (dd, J = 4.2, 9.1 Hz, 2 H), 2.90 (s, 3 H, 4-NCH_3), 3.03 (dd, J = 2.8, 12.4 Hz, 1 H, 5α-H), 3.69 (s, 3 H, 4″-OCH_3), 4.73 (t, J = 9.6 Hz, 1 H, 17α-H), 6.63 (d, J = 8.5 Hz, 2 H, 2 ArH), 6.97–7.2 (m, 7 H, 7 ArH); ^{13}C NMR ($CDCl_3$) δ 173.0, 170.8, 158.1 (4″-C), 138.1 (1′-C), 134.6, 132.2, 128.5, 127.8 (3C), 127.4 (2C), 113.4 (2C), 65.9, 65.5, 55.2, 51.9, 51.8, 45.4, 38.1, 36.4, 34.2, 32.8, 29.7, 29.2, 29.0, 25.3, 25.0, 22.9, 20.8, 13.7, 12.3; EI-MS *m/s* (rel intensity) 514 (M^+, 16), 410 (487), 288 (7), 266 (14), 227 (25), 162 (44), 105 (100); HRMS calcd for $C_{33}H_{42}O_3N_2$ 514.3165, found 514.3139. Anal. ($C_{33}H_{42}O_3N_2$) C, H, N.

Preparation of 17β-[(*N*-Aryl)-2′-methylpropionamido]-4-methyl-4-aza-5α-androstan-3-ones 50–53. The following method is a representative. 17β-[*N*-(3′-Trifluoro-4′-nitrophenyl)amino]azasteroid **27** (0.50 g, 1.01 mmol) was dissolved in isobutyryl chloride[17c] (60 equiv), and the mixture was refluxed for 16 h. The reaction mixture was cooled to 0 °C. Water (300 equiv) was added dropwise to decompose the excess of isobutyryl chloride. Then, the reaction mixture was treated with 5% $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with brine, dried, and concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography (C_6H_{14}:CH_3COCH_3, 9:1–7:3) to give the 17β-[*N*-[3″-(trifluoromethyl)-4″-nitrophenyl]-2′-methylpropionamido] analogue **53** (0.32 g, 56% yield): mp 122–124 °C; IR (KBr, cm^{-1}) 2940, 2832, 1665, 1645, 1544, 1470, 1412, 1362, 1310, 1233, 1153, 1040; ^1H NMR ($CDCl_3$) δ 0.64 (s, 3 H, 18-CH_3), 0.84 (s, 3 H, 19-CH_3), 0.93 (d, J = 6.5 Hz, 3 H, 2′-CH_3), 1.06 (d, J = 6.7 Hz, 3 H, 3′-CH_3), 1.17–1.44 (m, 8 H), 1.51–1.85 (m, 8 H), 1.87–2.13 (m, 3 H), 2.41 (dd, J = 4.4, 9.6 Hz, 2 H), 2.89 (s, 3 H, 4-NCH_3), 3.0 (dd, J = 3.1, 12.7 Hz, 1 H, 5α-H), 4.58 (t, J = 9.5 Hz, 1 H, 17α-H), 7.28–7.71 (br m, 2 H, 2″,6″-H), 7.93 (d, J = 8.5 Hz, 1 H, 5″-H); ^{13}C NMR ($CDCl_3$) δ 177.9, 170.7, 146.7 (4″-C), 146.0 (1″-C), 135.4 (6″-C), 130.5 (2″-C), 126.0 (5″-C), 119.4 (3″-C), 65.6, 65.3, 51.8, 51.5, 45.7, 38.1, 36.4, 34.2 (2C), 33.0, 32.8, 29.6, 29.0 (2C), 25.4, 25.2, 22.8, 20.7, 20.4, 19.0, 13.7, 12.3; EI-MS *m/s* (rel intensity) 563 (M^+, 45), 546 (7), 493 (39), 476 (10), 288 (30), 249 (23), 215 (8), 112 (25), 71 (100); HRMS calcd for $C_{30}H_{40}O_4N_3F_3$ 563.2991, found 563.2954. Anal. ($C_{30}H_{40}O_4N_3F_3$) C, H, N, F.

17β-[(*N*-Phenyl)-2′-methylpropionamido]-4-methyl-4-aza-5α-androstan-3-one (50). **50** was prepared in 74% yield: mp 246–248 °C; IR (KBr, cm^{-1}) 2948, 2931, 2842, 2817, 1655, 1580, 1502, 1478, 1452, 1389, 1302, 1248, 719; ^1H NMR ($CDCl_3$) δ 0.67 (s, 3 H, 18-CH_3), 0.86 (s, 3 H, 19-CH_3), 0.91 (d, J = 6.6 Hz, 3 H, 2′-CH_3), 1.04 (d, J = 6.7 Hz, 3 H, 3′-CH_3), 1.16–1.47 (m, 8 H), 1.54–1.86 (m, 8 H), 1.99 (dd, J = 4.5, 12.9 Hz, 1 H), 2.13 (ddd, J = 6.4, 6.6, 6.7 Hz, 1 H), 2.42 (dd, J = 4.7, 9.6 Hz, 2 H), 2.92 (s, 3 H, 4-NCH_3), 3.03 (dd, J = 3.5, 12.4 Hz, 1 H, 5α-H), 4.59 (t, J = 9.3 Hz, 1 H, 17α-H), 6.97–7.0 (m, 1 H, 4″-H), 7.30–7.39 (m, 4 H, 2″,3″,5″,6″-H); ^{13}C NMR ($CDCl_3$) δ 179.2, 171.0, 141.5 (1″-C), 131.0, 130.6 (2C, 3″,5″-C), 130.0 (4″-C), 127.8 (2″-C), 65.7, 64.8, 52.0, 51.8, 45.5, 38.3, 36.5, 34.3, 32.8, 32.4, 29.7, 29.2, 29.0, 25.4, 25.3, 22.9, 20.8, 20.6, 19.2, 13.6, 12.4; EI-MS *m/s* (rel intensity) 450 (M^+, 27), 380 (14), 288 (34), 249 (7), 202 (26), 163 (24), 132 (100), 119 (18), 93 (12), 71 (24); HRMS calcd for $C_{29}H_{42}O_2N_2$ 450.2341, found 450.2346. Anal. ($C_{29}H_{42}O_2N_2$) C, H, N.

17β-[*N*-(4″-Methyoxyphenyl)-2′-methylpropionamido]-4-methyl-4-aza-5α-androstan-3-one (51). **51** was prepared in 99% yield: mp 186–188 °C; IR (KBr, cm^{-1}) 2945, 2932, 2868, 2829, 1652, 1575, 1511, 1463, 1386, 1293, 1169, 1100, 1028, 849; ^1H NMR ($CDCl_3$) δ 0.64 (s, 3 H, 18-CH_3), 0.83 (s, 3 H, 19-CH_3), 0.88 (d, J = 6.5 Hz, 3 H, 2′-CH_3), 1.0 (d, J = 6.7 Hz, 3 H, 3′-CH_3), 0.74–1.16 (m, 2 H), 1.17–1.44 (m, 6 H), 1.54–1.84 (m, 8 H), 1.96 (dd, J = 2.9, 12.4 Hz, 1 H), 2.23 (dd, J = 6.6, 6.6, 6.7 Hz, 1 H), 2.40 (dd, J = 4.5, 9.2 Hz, 2 H), 2.89 (s, 3 H, 4-NCH_3), 3.0 (dd, J = 3.0, 12.3 Hz, 1 H, 5α-H), 3.81 (s, 3 H, 4″-OCH_3), 4.54 (t, J = 9.2 Hz, 1 H, 17α-H), 6.80–6.88 (m, 3 H, 3″,5″,6″-H), 7.13 (d, J = 8.9 Hz, 1 H, 2″-H); ^{13}C NMR ($CDCl_3$) δ 179.6, 170.8, 158.8 (4″-C), 134.0 (1″-C), 131.9, 131.5 (2C, 3″,5″-C), 114.1, 113.8 (2C, 2″,6″-C), 65.6, 64.7, 55.4 (4″-OCH_3), 52.0, 51.8, 45.3, 38.3, 36.4, 34.3, 32.9, 32.2, 39.7, 29.1, 25.3, 22.9, 20.8, 20.6, 19.2, 13.6, 12.4; EI-MS *m/s* (rel intensity) 480 (M^+, 44), 410 (29), 288 (24), 232 (24), 193 (55), 162 (100), 149 (20), 123 (17), 71 (19); HRMS calcd for $C_{30}H_{44}O_3N_2$ 480.3352, found 480.3343. Anal. ($C_{30}H_{44}O_3N_2$) C, H, N.

17β-[*N*-(4″-Nitrophenyl)-2′-methylpropionamido]-4-methyl-4-aza-5α-androstan-3-one (52). **52** was prepared in 69% yield: mp 214–216 °C; IR (KBr, cm^{-1}) 2935, 2846, 1665, 1642, 1589, 1518, 1465, 1388, 1340, 1310, 1239; ^1H NMR ($CDCl_3$) δ 0.65 (s, 3 H, 18-CH_3), 0.85 (s, 3 H, 19-CH_3), 0.91 (d, J = 6.6 Hz, 3 H, 2′-CH_3), 1.05 (d, J = 6.6 Hz, 3 H, 3′-CH_3), 1.13–1.46 (m, 8 H), 1.50–1.86 (m, 8 H), 1.99 (dd, J = 2.8, 12.7 Hz, 1 H), 2.13 (dt, J = 6.6, 6.7 Hz, 1 H), 2.42 (dd, J = 4.7, 9.5 Hz, 2 H), 2.90 (s, 3 H, 4-NCH_3), 3.01 (dd, J = 3.5, 12.5 Hz, 1 H, 5α-H), 4.59 (t, J = 9.6 Hz, 1 H, 17α-H), 7.0–7.58 (br m, 2 H, 2″,6″-H), 8.24 (d, J = 8.8 Hz, 2 H, 3″,5″-H); ^{13}C NMR ($CDCl_3$) δ 178.2, 170.8, 147.8 (4″-C), 147.0 (1″-C), 131.8 (2C, 3″,5″-C), 124.4 (2C, 2″,6″-C), 65.6, 65.2, 51.9, 51.6, 48.7, 38.2, 36.4, 34.3, 32.9, 29.7 (2C), 29.1, 29.0, 25.4, 25.3, 22.9, 20.8, 20.5, 19.1, 13.7, 12.4; EI-MS *m/s* (rel intensity) 495 (M^+, 32), 425 (30), 408 (16), 288 (48), 249 (26), 177 (30), 151 (9), 124 (20), 112 (28), 81 (11), 71 (100); HRMS calcd for $C_{29}H_{41}O_4N_3$ 495.3087, found 495.3063. Anal. ($C_{29}H_{41}O_4N_3$) C, H, N.

17β-(*N*-Methylformamido)-4-methyl-4-aza-5α-androst-1-en-3-one (55). The following method is a representative.[15a,b,27] A three-neck round bottom flask (250 mL) equipped with an argon inlet, reflux condenser, addition funnel, mechanical stirrer, and immersion thermometer was charged with dioxane (50 mL) followed by 3.0 g (8.66 mmol) of formamide **8** portionwise with stirring. To this suspension was added portionwise 1.9 g (8.66 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ); the flask was evacuated (22 mmHg) and flushed with argon three times. To this stirred suspension was added bis(trimethylsilyl)trifluoroacetamide (BSTFA; 9.14 g, 35.50 mmol) via the addition funnel at a rate of 5 mL/min. The temperature slowly went up from 22 to 25 °C in a period of 30 min, as most of the solids dissolved within this period to afford a clear solution. The solution was stirred for 18 h at 22 °C (after which time formation of the two diastereomeric adducts was observed by TLC). Then, to this solution was added 0.08 g of cyclohexane-1,3-dione, and the reaction mixture was stirred at 22 °C for an additional 3 h to decompose

any residual DDQ. The solution was then heated in an oil bath so that very gentle reflux was maintained (bath temperature 120 °C, internal temperature 108 °C). After refluxing for 16 h, complete disappearance of the adducts and formation of the compound **55** were observed. The reaction mixture was cooled to 22 °C and poured into a stirred mixture of CH_2Cl_2 (50 mL) and 1% aqueous sodium bisulfite solution (9.2 mL). The heterogeneous mixture was filtered to remove precipitated hydroquinone. The dark red organic layer was separated and washed with 6 N HCl solution (20 mL) followed by saturated NaCl solution, dried, and concentrated. The crude residue was further purified by silica gel chromatography (C_6H_{14}:CH_3COCH_3, 95:5–70:30) to give the product **55** (2.14 g, yield 72%). The NMR analysis gave a mixture of two conformers (3.6:1): mp 176–178 °C; IR (KBr, cm^{-1}) 2918, 2842, 2820, 1645, 1590, 1420, 1388, 1205, 1042; ^1H NMR ($CDCl_3$) δ 0.73 (s, 2.34 H, 18-CH_3), 0.74 (s, 0.66 H, 18-CH_3), 0.90 (s, 0.67 H, 19-CH_3), 0.91 (s, 2.33 H, 19-CH_3), 0.99–1.20 (m, 2 H), 1.24–1.41 (m, 4 H), 1.57 (dd, J = 3.8, 12.9 Hz, 1 H), 1.73–1.89 (m, 6 H), 1.91–2.15 (m, 2 H), 2.89 (s, 2.34 H, 4-NCH_3), 2.90 (s, 0.66 H, 4-NCH_3), 2.94 (s, 3 H, 17β-NCH_3), 3.31 (t, J = 9.5 Hz, 0.78 H, 17α-H), 3.35 (dd, J = 3.7, 6.6 Hz, 1 H, 5α-H), 4.22 (t, J = 9.5 Hz, 0.22 H, 17α-H), 5.82 (dd, J = 3.2, 8.1 Hz, 0.22 H, 2-H), 5.84 (dd, J = 3.2, 8.2 Hz, 0.78 H, 2-H), 6.65 (d, J = 9.9 Hz, 1 H, 1-H), 8.15 (s, 0.78 H, 17β-NCHO), 8.24 (s, 0.22 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 165.7, 164.5, 163.6, 149.1, 148.8, 122.9, 122.8, 69.2, 63.7, 51.4, 51.2, 47.9, 44.4, 39.5, 37.1, 36.7, 34.3, 33.8, 30.2, 29.4, 27.6, 24.2, 22.9, 22.9, 20.7, 13.3, 12.7, 12.1; EI-MS *m/s* (rel intensity) 344 (M^+, 83), 329 (25), 285 (8), 270 (13), 259 (23), 246 (22), 150 (7), 137 (42), 124 (100), 108 (12), 98 (47), 70 (59), 57 (23); HRMS calcd for $C_{21}H_{32}O_2N_3$ 344.2464, found 344.2436. Anal. ($C_{21}H_{32}O_2N_2$) C, H, N.

17β-(*N*-Methylformamido)-4-aza-5α-androst-1-en-3-one (54). In a similar fashion, compound **54** (0.06 g, yield 68%) was prepared from compound **7** (0.09 g, 0.30 mmol). The NMR analysis gave a mixture of two conformers (4.3:1): mp >242 °C dec; IR (KBr, cm^{-1}) 3542–3320 (br), 3152, 3020, 2904, 2820, 1636, 1586, 1436, 1316, 1204, 1045; ^1H NMR ($CDCl_3$) δ 0.74 (s, 2.18 H, 18-CH_3), 0.75 (s, 0.82 H, 18-CH_3), 0.83–0.90 (m, 1 H), 0.96 (s, 0.65 H, 19-CH_3), 0.98 (s, 2.35 H, 19-CH_3), 1.03–1.17 (m, 3 H), 1.24–1.48 (m, 4 H), 1.56–1.63 (m, 2 H), 1.64–1.92 (m, 4 H), 2.00–2.17 (m, 1 H), 2.91 (s, 2.43 H, 4-NCH_3), 2.95 (s, 0.57 H, 4-NCH_3), 3.30 (dd, J = 2.6, 11.7 Hz, 1 H, 5α-H), 3.32 (t, J = 9.5 Hz, 0.81 H, 17α-H), 4.23 (t, J = 9.5 Hz, 0.19 H, 17α-H), 5.52–5.61 (br s, 1 H, 4-NH), 5.80 (dd, J = 1.9, 9.9 Hz, 1 H, 2-H), 6.77 (d, J = 9.9 Hz, 1 H, 1-H), 8.16 (s, 0.81 H, 17β-NCHO), 8.18 (s, 0.19 H, 17β-NCHO); ^{13}C NMR ($CDCl_3$) δ 166.4, 165.1, 163.5, 151.1, 150.7, 124.6, 124.3, 77.2, 69.1, 61.5, 59.6, 51.6, 51.3, 47.8, 45.9, 44.6, 36.8, 35.0, 33.8, 30.2, 29.7, 29.3, 29.0, 25.9, 23.3, 22.9, 22.7, 21.6, 20.7, 13.4, 12.9, 12.0; EI-MS *m/s* (rel intensity) 330 (M^+, 66), 315 (31), 293 (6), 271 (17), 256 (9), 246 (22), 232 (22), 219 (10), 195 (8), 185 (16), 167 (8), 149 (95), 123 (19), 98 (100), 83 (47), 71 (60), 57 (67); HRMS calcd for $C_{20}H_{30}O_2N_2$ 330.2309, found 330.2292. Anal. ($C_{20}H_{30}O_2N_2$) C, H, N.

Evaluation of the Inhibition of Human 5α-Reductase (Types I and II). The measurements of *in vitro* inhibitory activity of compounds **7–9** and **28–55** on human type I and type II 5α-reductases were carried according to the following procedure.

Type I 5α-Reductase.[28] DU-145 (human prostatic carcinoma metastasis to brain) cells between passages 60 and 90 (ATCC, HTB81) in culture were used as the source of type I 5α-reductase. DU-145 cells were plated in Falcon 24-well plates at a density of 100 000 cells/well and allowed to become adherent for a period of 24 h. Compounds to be tested were dissolved in ethanol and diluted with DMEM plus 2% charcoal-adsorbed fetal bovine serum. Inhibitors were first tested at two concentrations for inhibition of 5α-reductase activity: 1 and 0.1 μM. Products showing 50% or more inhibition at the 1 μM dose were subsequently tested at 12 doses ranging from 0.1 to 1.000 nM, for measurement of IC_{50} value. The compounds and 5 nM [^3H]androstenedione were added to the sample wells in a final volume of 1 mL of medium. Following a 24-h incubation in 5% CO_2 and 95% air at 37 °C, the media were extracted twice with ether after the addition of 25 μg each of nonradioactive steroid carriers (androstanedione, androstenedione, androsterone, and testosterone). Steroids were separated by TLC, and radioactivity was counted. Results are expressed as the amount of androstanedione, androsterone, and epiandrosterone formed as a percentage of control values. (To check other metabolites, 5 nM androstenedione (Δ^4-dione) was incubated with the cells for 24 h and then the medium was extracted with ethyl ether. The etheral layer was analyzed by HPLC to give the following metabolites: Δ^4-dione, 41.1%; androstanedione, 38.2%; androsterone, 4.8%; epiandrosterone, 4.0%; testosterone, 6.6%; dihydrotestosterone, 10%; and androstane-3α,17β-diol, 1.0%.) 5α-Reductase activity measured by this method in DU-145 cells is human type I.[27]

Type II 5α-Reductase.[11a,b] SW-13 cells (ATCC CCL 105) were transfected with human type II 5α-reductase cDNA[11b] and used as the source of type II 5α-reductase. After transfection, cells were homogenized for use in an *in vitro* assay. Compounds to be tested were dissolved in ethanol and diluted with 50 mM Tris HCl buffer containing inhibition of 20% glycerol and 1 mM EDTA at pH 7.5. Inhibitors were first tested at two concentrations for 5α-reductase activity: 1 and 0.1 μM. Products showing 50% or more inhibition at the 1 μM dose were subsequently tested at 12 doses ranging from 0.1 to 1.000 nM, for measurement of IC_{50} value. The compounds, 5 nM [^3H]androstenedione, 500 μM NADPH, and the homogenized cells were added to the sample tubes to a final volume of 1 mL. Following a 60-min incubation at 37 °C, the media were extracted twice with ether after the addition of 25 μg each of nonradioactive steroid carriers (androstanedione, androstenedione, androsterone, and testosterone). Steroids were separated by TLC, and radioactivity was counted. Results are expressed as the amount of androstanedione formed as a percentage of control values.

Inhibition of DHT Action on the Proliferation of the Androgen-Sensitive Shionogi Mouse Mammary Carcinoma Cells. An androgen-sensitive cell line (clone SEM-107) derived from Shionogi mouse mammary carcinoma cells[29] was used at passage 23. Cells were routinely grown as described previously.[30] For the measurement of cell proliferation and sensitivity to antiandrogens, cells were plated at a density of 17 000 cells/mL in minimal essential medium (MEM) supplemented with 2% dextran-coated charcoal-treated fetal calf serum, 1% nonessential amino acids, 10 IU/mL penicillin, and 50 μg/mL streptomycin. Steroids and antiandrogens were dissolved in ethanol, and stock solutions were chosen to yield a final ethanol concentration less than 0.01% in the culture medium. Twenty-four hours after plating, medium was changed and the indicated concentrations of antiandrogens and DHT were added to triplicate dishes. Cells were grown for 13 days with medium changes every 3–4 days. Cells were then fixed in methanol, and their number was evaluated by measurement of DNA content by a modification[31] of the method of Fiszer-Szafarz.[32] Dose–reponse curves and IC_{50} values were calculated using a weighted iterative nonlinear least squares regression.[33] Results are presented as means ± SEM.

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