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Original article

# Synthesis, characterization and biological evaluation of some 16β-azolyl-3β-amino-5α-androstane derivatives as potential anticancer agents

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ABSTRACT

A series of new 16β-azolyl-3β-amino-5α-androstane derivatives were synthesized and characterized. The new compounds were screened for their anticancer activity against the human cancer cell lines SW480, A549, HepG2, HeLa and SiHa in vitro using the MTT assay. The results of the in vitro study showed that a number of compounds have shown $IC_{50}$ values lower than 20 μM against the five cancer cell lines.



## 1. Introduction

According to the World Health Organization (WHO), cancer is presently the second most important disease leading to death in both developing and developed countries. Drugs that are currently available for the treatment of cancer include bioalkylating agents (chlormethine) [1,2], antimetabolic agents (fluorouracil) [3,4], anticancer antibiotics (doxorubicin) [5], and compounds from plants and their derivatives (paclitaxel) [6]. However, sufficient doses of anticancer drugs to kill tumor cells are often toxic to normal tissues, thus leading to numerous side effects, which, in turn, limits treatment efficacy. Long term effectiveness is often limited by dose-related cumulative cardiotoxicity and development of acquired drug resistance [7–9]. Therefore, development of new therapeutic agents for the treatment of cancer that are more active and less side effects producing is of utmost importance.

Steroids elicit diverse biological actions via various functional groups located around the periphery of their rigid tetracyclic core. Nitrogen containing steroids are an important type of steroids, including natural products, and semi-synthetic compounds and synthetic compounds, all of which have been studied intensively. Most modifications are aimed at the A- and D-rings by incorporation of amino groups to the steroids backbone [10–15].

Nitrogen containing steroids have the ability to regulate a variety of biological processes and thus are potential drug candidates for the treatment of a large number of diseases including breast cancer [16], prostate cancer [17,18], leukemia [19–21], autoimmune diseases [22], and osteoporosis [23]. A series of 16-, 20-, and 21-aminosteroids have been synthesized, and these novel class of compounds have shown excellent anticancer or antioxidant activities [24–26]. It has been reported that some tertiary aminosteroids, such as 2β, 16β-dipiperidino-5α-androstane-3α, 17β-diol dipivalate(**DAP**) (Fig. 1) [27] exhibit significant antitumor activity against transplantable tumors in three animal species, including mice, hamsters, and rats. In an effort to find the new analogs of this type of novel steroid molecule, some 16E-arylidene androstene derivatives have emerged as potent anticancer agents, such as compound **DPJ-RG-1110** (Fig. 1). Further, a structure–activity relationship study has indicated that incorporation of a heterocyclic ring into the steroid backbone at position C-3 and

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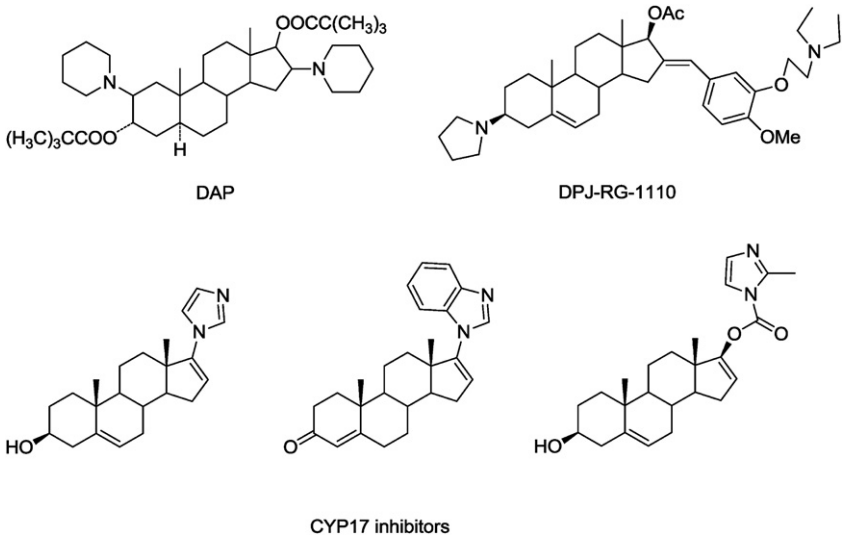



**Fig. 1.** Structures of DAP, DPJ-RG-1110 and CYP17 inhibitors.

variation of the substituent groups at position C-16 bring about important impacts to the activity of a steroid backbone [28–30].

Azoles, a versatile group of heterocycles often show some special biological activities when they are introduced to biologically active compounds. Some 1,2,4-triazole, 1,2,3-triazole, 1,3,4-thiadiazole, benzimidazole and benzotriazole derivatives have been reported to possess antibacterial [31,32], antivirus [33], antimicrobial [34], anti-inflammatory [35,36], antiglaucoma [37], antiprotozoal [38,39] and anticancer activities [40,41]. Moreover, when azole groups were introduced to the steroids backbone, some resulting C-21 and C-17 azolylsteroids were found to be potent inhibitors of 17α-hydroxylase-$C_{17,20}$-lyase(CYP17 inhibitors) (Fig. 1) which is the key enzyme for androgen biosynthesis [42–46]. Inhibitors of such enzymes are useful for the treatment of androgen dependant prostate cancer. Much work has been done on C-21 and C-17 azolylsteroids in searching for new potential CYP17 inhibitors [47–49]. An increasing numbers of publications had recently reported the anticancer activities of a wide range of natural [50,51], semi-synthetic [52,53] and synthetic aminosteroidal compounds [54,55]. However, to the best of our knowledge, little attention has been given to 16-azolyl-3-amino-androstanes.

On the basis of the above details, we synthesized a series of androstane-based aminosteroids to screen their anticancer activity against different cancer cell lines in vitro in order to get more potent anticancer agents.

## 2. Chemistry

The routes utilized for the synthesis of our target compounds **16a–g**, **17a–g**, **18a–g**, **19a–g** are outlined in Scheme 1. 5α-androstan-16α-bromo-3β-ol-17-one **2** was prepared with epiandrosterone and $CuBr_2$. The adol product was then oxidized with Jones reagent to obtain the compound **3** [56–58]. The 16β-azolyl derivatives **4**, **5**, **6**, **7** were prepared with appropriate azoles. Then the C-3 amino derivatives **8a–g**, **9a–g**, **10a–g**, **11a–g** were obtained via reductive amination of the carbonyl group at the C-3 position using pyrrolidine, piperidine, morpholine, N-methylpiperazine, diethylamine, N-methylaniline and N-benzylmethylamine respectively. Compounds **12a–g**, **13a–g**, **14a–g**, **15a–g** were prepared by reduction with sodium borohydride in methanol. Next, the esterification of the 17β-ol derivatives with acetic anhydride and 4-dimethylaminopyridine (DMAP) refluxed in $CHCl_2$ provided the desired ester **16a–g**, **17a–g**, **18a–g**, **19a–g**.

The chemical structures of the compounds synthesized were elucidated on the basis of $^1$H NMR, $^{13}$C NMR, MS and elemental analysis. The detailed physical and analytical data are given in experimental part.

## 3. Results and discussion

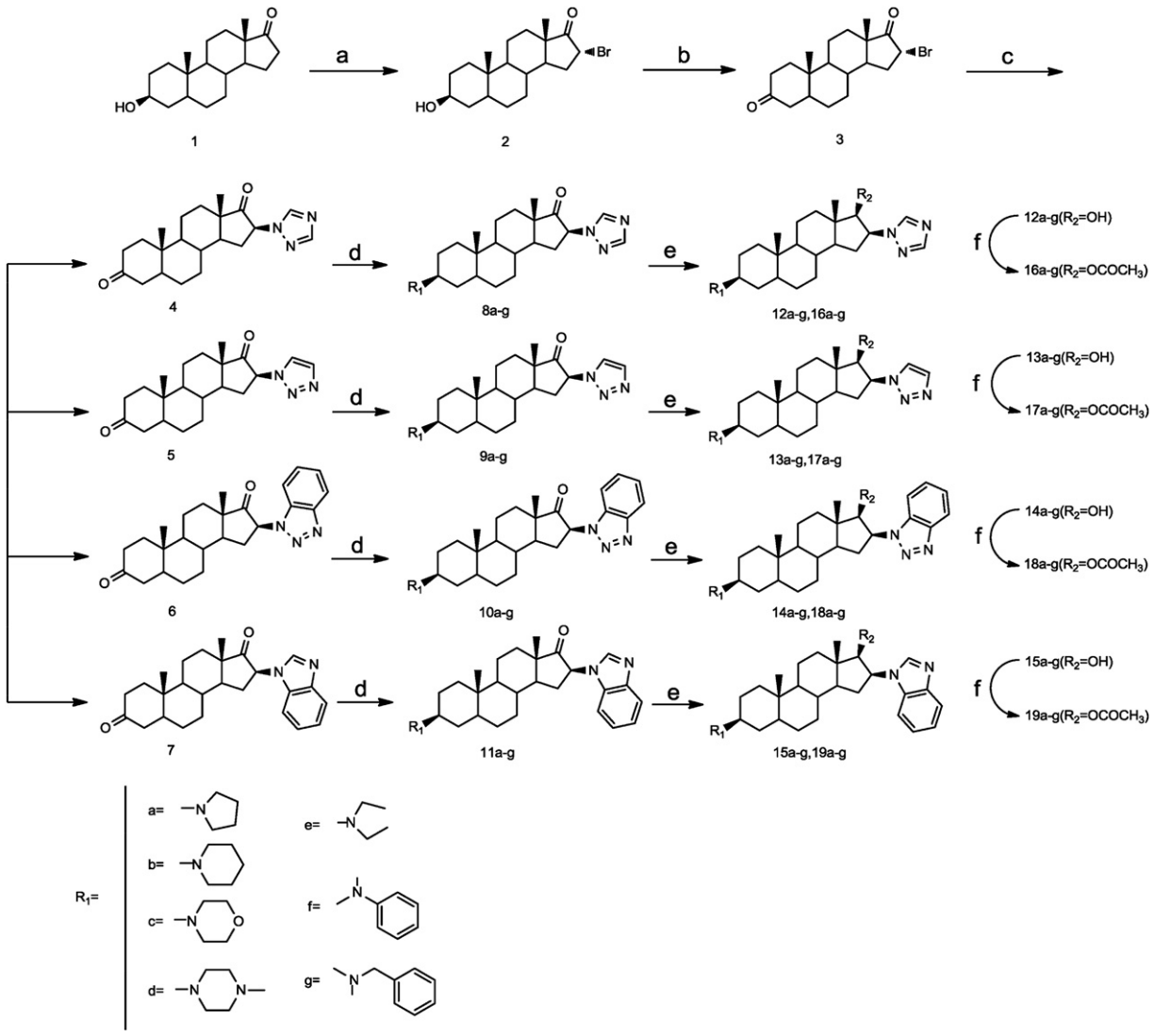
### 3.1. Chemistry

X-ray crystal structure of **16f** and **18d** were obtained and are presented in Figs. 2 and 3 respectively. These structures confirm the β-stereochemistry of the heterocycles at C-3, the azoles at C-16 and the acetoxy group at C-17. Crystallographic data for **16f** and **18d** have been deposited with the Cambridge Crystallographic Data Centre with the deposition number CCDC 805534 and CCDC 805535. These data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax(+44) 1223 336033, e-mail: deposit@ccdc.cam.ac.uk].

### 3.2. Anticancer activity

The newly synthesized compounds **16a–g**, **17a–g**, **18a–g**, **19a–g** were evaluated for their anticancer activities against human cancer cell lines derived from various human cancer types, including HeLa (human cervical cancer cells), SW480 (human colon adenocarcinoma cells), A549 (human lung carcinoma cells), HepG2 (human hepatic carcinoma cells) and SiHa (human cervical cancer cells). 293 (human embryonic cells) is non-cancer cell line. In vitro evaluation of the anticancer activities of the synthesized compounds was carried out using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Doxorubicin was employed as the positive control. The anticancer potency of these compounds was indicated by $IC_{50}$ values that were calculated by linear regression analysis of the concentration–response curves obtained for each compound. The results are summarized in Table 1.

As shown in Table 1, some of the tested compounds showed moderate to potent anticancer activities against all the tested cells. Six of the twenty-eight new compounds showed strong anticancer activities against more than three cell lines ($IC_{50} < 20$ μM). Compounds **18f** and **19g** were the most promising compounds amongst the tested derivatives, with $IC_{50}$ values of 5.12–18.63 μM and 4.22–15.76 μM, respectively.




**Scheme 1.** Preparation of target compounds (**16a**–**g**, **17a**–**g**, **18a**–**g**, **19a**–**g**). Reagents and Conditions: (a) $CuBr_2$, Methanol, 65°C, 12h; (b) Jones Reagent, acetone, Icebath; (c) appropriate azoles, $K_2CO_3$, $CH_3CN$, 65-80°C; (d) appropriate amine, $NaBH_3CN$, Methanol, 40°C, 24h; (e) $NaBH_4$, Methanol, Icebath, 4h; (f) Acetic Anhydride, 4-Dimethylaminopyridine, $CH_2Cl_2$, 40°C.

Most of the 16β-triazole derivatives, including **16a**, **16b**, **17a** and **17b** which have pyrrolidine and piperidine groups, respectively, at the C-3 position exhibited no activity against all the tested cells ($IC_{50} > 50$ μM). Compounds **16c** and **17c**, which have a morpholine moiety at the C-3 position, and compounds **16d** and **17d** which have a methylpiperazine moiety at the C-3 position, have slightly better activities (**16c** for HeLa 22.32 μM, for HepG2 19.47 μM; **16d** for HepG2 23.52 μM). When the nitrogenous heterocycles were replaced by diethylamine, **16e** and **17e** exhibited no activity (>50 μM). This result suggested that an aliphatic amine at the C-3 position was not beneficial for anticancer activity. On the other hand, the introduction of aromatic amines to the C-3 position

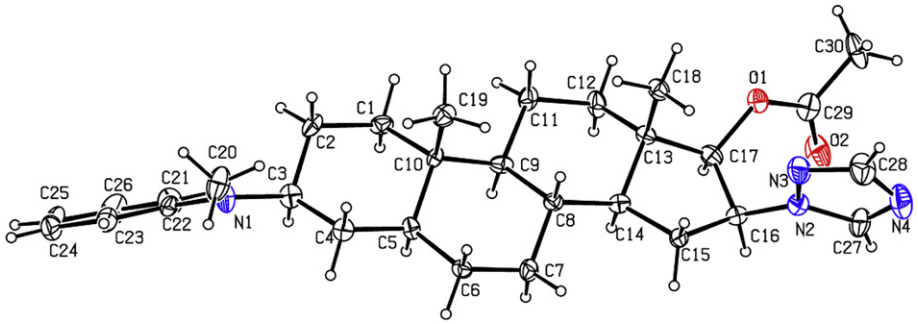



**Fig. 2.** X-ray crystal structure of **16f**.

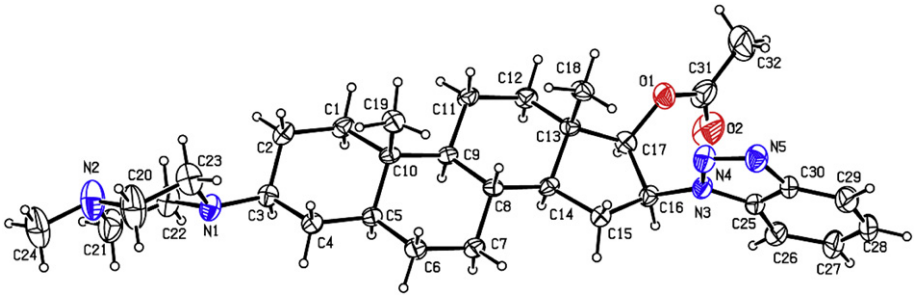



**Fig. 3.** X-ray crystal structure of **18d**.

resulted in increased anticancer activity. Compounds **16f** and **17f** which have N-methylaniline moiety at the C-3 position and compounds **16g** and **17g**, which have N-benzylmethylamine moiety at the C-3 position, showed potent activity against most of the five cancer cell lines (**16f** for A549 12.34 μM; **17f** for HepG2 9.35 μM, for SiHa 11.74 μM; **16g** for HepG2 10.56 μM; **17g** for A549 11.41 μM, HepG2 8.43 μM).

A comparison of the results obtained from the 16β-triazole, 16β-benzimidazole and 16β-benzotriazole derivatives, showed that compounds **18a**–**g** and **19a**–**g** which possess benzimidazole and benzotriazole moieties displayed good activities. Compared with 16β-triazolyl-3β-heterocyclic derivatives **16b** and **17b**, compounds **18b** and **19b** were active against some cancer cell lines (**18b** for A549 22.72 μM; **19b** for SiHa 18.74 μM). Similar findings were observed amongst the 3β-aromatic amine and the 3β-aliphatic amine derivatives. Among all the tested compounds, the N-methylaniline and N-benzylmethylamine analogs **19f** and **19g** exhibited the most potent anticancer activities, with $IC_{50}$ values ranging from 4.22 μM to 15.76 μM against most of the five cancer cell lines. These findings indicated that incorporation of benzimidazole or benzotriazole to the steroid scaffolds at the C-16 position together with the aromatic amine at C-3 position played an important role for the activity. Furthermore, it appeared that introducing proper azoles at the C-16 position could serve as a promising launch point for further design of this type of steroidal anticancer agent. All the active compounds did not show obvious cell line selectivity.

Compounds **18f**, **18g**, **19f** and **19g** were selected for further in vitro evaluation using 293 cell line which is a non-cancer cell line. The results are summarized in Table 2. As shown in Table 2, among the four tested compounds, only compound **18g** showed little cytotoxicity ($IC_{50}$ 48.70 μM). Compounds **18f**, **19f** and **19g** exhibited no cytotoxicity ($IC_{50}$ > 80 μM). It is apparent from the results depicted in Table 2 that compounds **18f**, **19f** and **19g** exhibit obvious selectivity between cancer cell line and non-cancer cell line.

In an overall view, aromatic amines at the C-3 position and aryl azoles at the C-16 position appeared to play a critical role for the anticancer activity. General structure–activity relationship of compounds for anticancer activity in vitro based on the $IC_{50}$ results on the five cancer cells lines is presented schematically in Fig. 4.

**Table 1**
Anticancer activity data for compounds **16a**–**g**, **17a**–**g**, **18a**–**g**, **19a**–**g** against HeLa, SW480, A549, HepG2, and SiHa.

| Compounds | $IC_{50}$/(μmol $L^{-1}$)[a] | | | | |
|---|---|---|---|---|---|
| | HeLa | SW480 | A549 | HepG2 | SiHa |
| **16a** | >50 | >50 | >50 | >50 | >50 |
| **16b** | >50 | >50 | >50 | >50 | >50 |
| **16c** | 22.32 | >50 | >50 | 19.47 | >50 |
| **16d** | >50 | >50 | 39.70 | 23.52 | >50 |
| **16e** | >50 | >50 | >50 | >50 | >50 |
| **16f** | 19.77 | >50 | 12.34 | 21.85 | 37.13 |
| **16g** | 18.71 | >50 | >50 | 10.56 | 22.43 |
| **17a** | >50 | >50 | >50 | >50 | >50 |
| **17b** | >50 | >50 | >50 | >50 | >50 |
| **17c** | >50 | 31.78 | 40.29 | >50 | 47.81 |
| **17d** | 38.12 | >50 | >50 | >50 | >50 |
| **17e** | >50 | >50 | >50 | >50 | >50 |
| **17f** | 72.12 | >50 | 18.86 | 9.35 | 11.74 |
| **17g** | >50 | >50 | 11.41 | 8.43 | 15.17 |
| **18a** | >50 | >50 | >50 | >50 | >50 |
| **18b** | 29.62 | >50 | 22.72 | >50 | >50 |
| **18c** | 19.82 | >50 | 12.18 | >50 | >50 |
| **18d** | >50 | 18.85 | 8.99 | 31.71 | 22.03 |
| **18e** | >50 | >50 | >50 | >50 | 37.22 |
| **18f** | 10.41 | 18.63 | 5.12 | 6.36 | 9.83 |
| **18g** | 11.33 | >50 | 7.72 | 5.54 | 26.18 |
| **19a** | >50 | >50 | 39.65 | >50 | 37.14 |
| **19b** | >50 | >50 | >50 | 29.57 | 18.74 |
| **19c** | >50 | >50 | 16.12 | >50 | 12.27 |
| **19d** | >50 | >50 | 22.40 | 11.71 | 14.92 |
| **19e** | >50 | >50 | >50 | 22.11 | 29.83 |
| **19f** | 4.51 | 9.22 | 28.43 | >50 | 6.67 |
| **19g** | 6.04 | 15.76 | 4.22 | 5.14 | 11.9 |
| Doxorubicin | 0.23 | 0.06 | 0.36 | 0.5 | 0.45 |

Exponentially growing cells were treated with the compounds at different concentrations for 48 h. Cell-growth inhibition was analyzed by the MTT assay.
[a] $IC_{50}$ is the concentration of compound that inhibits 50% of cell growth.

## 4. Conclusion

In summary, a series of new 16β-azolyl-3β-amino-5α-androstane derivatives were synthesized and evaluated for their anticancer activities. Some of the synthesized compounds exhibited potent anticancer activities against the five tested cancer cell lines in vitro. In particular, compound **18f** and **19g** were the most promising derivatives, with $IC_{50}$ values ranging from 5.12 μM to 18.63 μM, 4.22 μM–15.76 μM, against all the five cancer cell lines respectively. Aromatic amines at the C-3 position and aryl azoles at the C-16 position are beneficial for the activity. Substituent changes to the A- and D-rings of the androstane skeleton can affect potency against different kinds of cancer cell lines. In an overall view,

**Table 2**
Cytotoxic activity data for compounds **18f**, **18g**, **19f**, **19g** against 293 cell line.

| Compounds | $IC_{50}$/(μM $L^{-1}$)[a] |
|---|---|
| | 293 |
| **18f** | >80 |
| **18g** | 48.70 |
| **19f** | >80 |
| **19g** | >80 |

Exponentially growing 293 cells were treated with the compounds at different concentrations for 48 h. Cell-growth inhibition was analyzed by the MTT assay.
[a] $IC_{50}$ is the concentration of compound that inhibits 50% of cell growth.

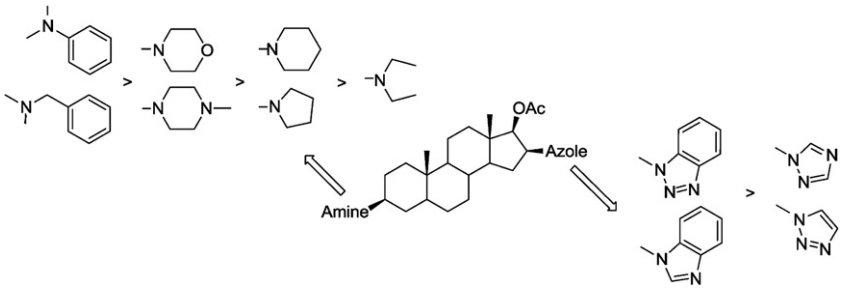



**Fig. 4.** General SAR of compounds for anticancer activity in vitro based on the $IC_{50}$ results on the five cancer cells lines.

aromatic amines at the C-3 position and aryl azoles at the C-16 position appeared to play a critical role for the anticancer activity. Preliminary structure–activity relationships were put forward based on the biological results. Future work will focus on the synthesis of additional candidate structures to address specific cancer cell lines.

## 5. Experimental protocols

### 5.1. Chemistry

All the chemicals and solvent were purchased from commercial sources. Solvents and reagents were dried and purified according to the literature methods. Melting points were determined on a XT-4 apparatus (uncorrected). $^1$H NMR and $^{13}$C NMR spectra were obtained on a Varian Mercury VX400 apparatus in $CDCl_3$ with TMS as internal standard. Mass spectra were recorded on a Shimadzu LCMS-2020 spectrometer. X-ray diffraction data were collected on Bruker SMART APEX CCD diffractometer. Elemental analysis was carried out on a VarioEL III (German) instrument. Silica gel was used for analytical and flash chromatography.

#### 5.1.1. General procedure for the synthesis of compounds **2**

To a stirred solution of epiandrosterone (1.45 g, 5.00 mmol) in methanol was added the $CuBr_2$ (2.23g, 10.00 mmol, 2.0 equiv). The resulting solution was stirred for 12 h at 65 °C until the reaction was completed (monitored by TLC). The reaction was quenched and concentrated in reduced pressure. Then 20 ml $CH_2Cl_2$ and 10 ml water was added to the residue. The organic layer was washed with brine and dried over anhydrous $Na_2SO_4$, filtered. The filtrate was concentrated in reduced pressure to afford a crude product. The products were purified by flash column chromatography to yield compound **2**.

*5.1.1.1. 5α-Androstan-16α-bromo-3β-ol-17-one (**2**).* White solid. yield 91%. m.p. 164–165 °C; $^1$H NMR(400 MHz,$CDCl_3$): $\delta$ 0.82 (s, 3H, $CH_3$-19), 0.89 (s, 3H, $CH_3$-18), 3.59 (m, 1H, H-3), 4.52 (d, 1H, $J$ = 6.34 Hz, H-16). $^{13}$C NMR(150 MHz,$CDCl_3$): $\delta$ 12.26, 14.20, 20.39, 28.23, 30.72, 31.36, 32.33, 34.07, 34.29, 35.63, 36.84, 37.97, 44.47, 46.41, 47.82, 47.93, 54.23, 71.05, 213.60. Anal. Calcd. for $C_{19}H_{29}BrO_2$: C 61.79, H 7.91; Found C 61.58, H 7.88.

#### 5.1.2. General procedure for the synthesis of compounds **3**

To a solution of aldol products (5.00 mmol) **2** in acetone, Jones reagent was added drop wise. The mixture was stirred at 0 °C until the reaction was completed (monitored by TLC). The reaction was quenched with ethanol (3 ml) and concentrated in reduced pressure. The crude product was dissolved in $CH_2Cl_2$, the organic layer was washed with brine and dried over anhydrous $Na_2SO_4$, filtered. The filtrate was concentrated in reduced pressure to afford a crude product. The products were purified by flash column chromatography to yield compound **3**. The Jones reagent was prepared according to previous study [56–58].

*5.1.2.1. 16α-Bromo-5α-androstan-3,17-dione (**3**).* White solid. yield 97%. m.p. 170–171 °C; $^1$H NMR(400 MHz,$CDCl_3$): $\delta$ 0.93 (s, 3H, $CH_3$-19), 1.04 (s, 3H, $CH_3$-18), 4.54 (d, 1H, $J$ = 3.32 Hz, H-16). $^{13}$C NMR(150 MHz,$CDCl_3$): $\delta$ 6.89, 9.65, 16.05, 23.92, 25.84, 27.74, 29.54, 29.67, 31.26, 33.46, 33.77, 39.96, 41.65, 41.93, 43.24, 49.14, 206.80, 208.64. Anal. Calcd. for $C_{19}H_{27}BrO_2$: C 62.13, H 7.41; Found C 62.32, H 7.52.

#### 5.1.3. General procedure for the synthesis of compounds **4**, **5**, **6**, **7**

To a suspension of 16α-bromo-5α-androstan-3,17-dione **3** 0.37 g (1.00 mmol) in 20 ml of $CH_3CN$ was added 0.21g (3.00 mmol, 3.0 equiv) of 1,2,4-triazole and 0.27g (2.00 mmol, 2.0 equiv) of $K_2CO_3$. The resulting solution was stirred for 24 h at 80 °C until the reaction was completed (monitored by TLC). The $CH_3CN$ was removed under reduced pressure, 20 ml $CH_2Cl_2$ was added to the residue, the organic layer was washed with saturated $NaHCO_3$, brine and dried over anhydrous $Na_2SO_4$, filtered. The filtrate was concentrated in reduced pressure to afford a crude product. The products were purified by flash column chromatography to yield compound **4**. Compounds **5**, **6** and **7** were obtained with 1,2,3-triazole, 1H-benzotriazole and benzimidazole respectively by using the same method that described above.

*5.1.3.1. 16β-(1H-1,2,4-triazol-1-yl)-5α-androstan-3,17-dione (**4**).* White solid. yield 60%. m.p. 157–159 °C; $^1$H NMR(400 MHz,$CDCl_3$): $\delta$ 1.00 (s, 3H, $CH_3$-19), 1.08 (s, 3H, $CH_3$-18), 4.52 (t, 1H, $C_{16}$-αH), 7.88 (s, 1H), 8.10 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): $\delta$ 11.43,14.20, 20.48, 28.40, 29.26, 30.63, 31.79, 34.05, 35.83, 37.97, 38.28, 44.44, 46.46, 46.89, 47.37, 53.85, 63.86, 144.03, 152.13, 211.34, 211.70. Anal. Calcd. for $C_{21}H_{29}N_3O_2$: C 70.95, H 8.22, N 11.82; Found C 70.80, H 8.34, N 11.76.

*5.1.3.2. 16β-(1H-1,2,3-triazol-1-yl)-5α-androstan-3,17-dione (**5**).* White solid. yield 62%. m.p. 178–180 °C; $^1$H NMR(400 MHz,$CDCl_3$): $\delta$ 1.07 (s, 3H, $CH_3$-19), 1.15 (s, 3H, $CH_3$-18), 4.59 (t, 1H, $C_{16}$-αH), 7.95 (s, 1H), 8.17 (1H, s). $^{13}$C NMR(150 MHz,$CDCl_3$): $\delta$ 11.41,14.32, 20.50, 28.29, 29.25, 30.61, 31.80, 34.03, 35.82, 37.97, 38.18, 44.39, 46.44, 46.90, 47.37, 53.83, 63.85, 144.00, 152.10, 211.33, 211.72. Anal. Calcd. for $C_{21}H_{29}N_3O_2$: C 70.95, H 8.22, N 11.82; Found C 70.89, H 8.41, N 11.70.

*5.1.3.3. 16β-(1H-benzotriazol-1-yl)-5α-androstan-3,17-dione (**6**).* White solid. yield 55%. m.p. 209–211 °C; $^1$H NMR(400 MHz,$CDCl_3$): $\delta$ 1.10 (s, 3H, $CH_3$-19), 1.27 (s, 3H, $CH_3$-18), 4.99 (t, 1H, $C_{16}$-αH), 7.33 (t, 1H), 7.40–7.51 (m, 2H), 8.07 (d, 1H, $J$ = 8.36Hz). $^{13}$C NMR(150 MHz,$CDCl_3$): $\delta$ 11.50, 14.68, 20.56, 28.48, 29.33, 30.76, 31.94, 34.24, 35.93, 38.04, 38.39, 44.51, 46.59, 47.39, 47.77, 54.03, 62.53, 109.42, 120.01, 124.15, 127.68, 133.98, 145.69, 211.43, 211.87. Anal. Calcd. for $C_{25}H_{31}N_3O_2$: C 74.04, H 7.70, N 10.36; Found C 73.88, H 7.61, N 10.40.

*5.1.3.4. 16β-(1H-benzimidazol-1-yl)-5α-androstan-3,17-dione (**7**).* White solid. yield 58%. m.p. 195–197 °C; $^1$H NMR(400 MHz,$CDCl_3$):

δ 1.07 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 4.74 (t, 1H, $C_{16}$-αH), 7.28–7.32 (m,2H), 7.39 (d, 2H, $J$ = 8.40Hz), 7.80 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 11.46, 14.64, 20.54, 28.39, 30.30, 31.74, 34.09, 35.89, 37.99, 38.29, 44.45, 46.50, 47.11, 47.70, 53.97, 60.71, 109.76, 120.44, 122.60, 123.27, 134.17, 140.58, 143.40, 211.37, 213.12. Anal. Calcd. for $C_{26}H_{32}N_2O_2$: C 77.19, H 7.97, N 6.92; Found C 77.08, H 8.09, N 6.87.

*5.1.4. General procedure for the synthesis of compounds* ***8a–g, 9a–g, 10a–g, 11a–g***

To a suspension of dione **4** (1.00 mmol) in 20 ml of absolute methanol was added 0.5 ml of pyrrolidine and 60 mg (1.20 mmol, 1.2 equiv) of $NaBH_3CN$, then the solution was acidified to pH ≈ 6 with acetic acid. The resulting mixture was stirred at 40 °C for 24 h. The methanol was removed under reduced pressure, 20 ml $CH_2Cl_2$ was added to the residue, the organic layer was washed with saturated $NaHCO_3$, brine and dried over anhydrous $Na_2SO_4$, filtered. The filtrate was concentrated in vacuum to afford a crude product. The product was purified by flash column chromatography to yield compound **8a**. Compounds **8b–g** were obtained with piperidine, morpholine, N-methylpiperazine, diethylamine, N-methylaniline and N-benzylmethylamine respectively. Compounds **9a–g**, **10a–g**, **11a–g**,were prepared by using the same method that described above.

*5.1.4.1. 16β-(1H-1,2,4-triazol-1-yl)-3β-pyrrolidino-5α-androstan-17-one (**8a**).* White solid. yield 57%. m.p. 188–192 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.94 (s, 1H), 8.16 (s, 1H). Anal. Calcd. for $C_{25}H_{38}N_4O$: C 73.13, H 9.33, N 13.65; Found C 73.02, H 9.18, N 13.55.

*5.1.4.2. 16β-(1H-1,2,4-triazol-1-yl)-3β-piperidino-5α-androstan-17-one (**8b**).* White solid. yield 51%. m.p. 184–187 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.94 (s, 1H), 8.15 (s, 1H). Anal. Calcd. for $C_{26}H_{40}N_4O$: C 73.54, H 9.49, N 13.19; Found C 73.36, H 9.58, N 13.03.

*5.1.4.3. 16β-(1H-1,2,4-triazol-1-yl)-3β-morpholino-5α-androstan-17-one (**8c**).* White solid. yield 54%. m.p. 165–168 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.56 (s, 4H, $NCH_2$), 3.72 (s, 4H, $OCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.94 (s, 1H), 8.16 (s, 1H). Anal. Calcd. for $C_{25}H_{38}N_4O_2$: C 70.39, H 8.98, N 13.13; Found C 70.21, H 8.89, N 13.02.

*5.1.4.4. 16β-(1H-1,2,4-triazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17-one (**8d**).* White solid. yield 54%. m.p. 179–181 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.86 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.27(s, 3H, N–$CH_3$), 2.39–2.53 (br, 8H, $NCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.94 (s, 1H), 8.16 (s,1H). Anal. Calcd. for $C_{26}H_{41}N_5O$: C 71.03, H 9.40, N 15.93; Found C 71.17, H 9.28, N 15.86.

*5.1.4.5. 16β-(1H-1,2,4-triazol-1-yl)-3β-diethylamino-5α-androstan-17-one (**8e**).* White solid. yield 52%. m.p. 228–230 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.94 (s, 1H), 8.15 (s, 1H). Anal. Calcd. for $C_{25}H_{40}N_4O$: C 72.77, H 9.77, N 13.58; Found C 72.61, H 9.66, N 13.70.

*5.1.4.6. 16β-(1H-1,2,4-triazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17-one (**8f**).* White solid. yield 51%. m.p. 173–175 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.83 (s, 3H, N–$CH_3$), 4.57 (t, 1H, $C_{16}$-αH), 6.69 (t, 1H), 6.79 (d, 2H, $J$ = 8.28Hz), 7.24(t, 2H), 7.95 (s, 1H), 8.16 (s, 1H). Anal. Calcd. for $C_{28}H_{38}N_4O$: C 75.30, H 8.58, N 12.54; Found C 75.19, H 8.70, N 12.44.

*5.1.4.7. 16β-(1H-1,2,4-triazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17-one (**8g**).* White solid. yield 51%. m.p. 169–172 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.86 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.20 (s, 3H, N–$CH_3$), 3.57 (s, 2H, $PhCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.31 (s, 5H), 7.95 (s, 1H), 8.16 (s, 1H). Anal. Calcd. for $C_{29}H_{40}N_4O$: C 75.61, H 8.75, N 12.16; Found C 75.51, H 8.68, N 12.31.

*5.1.4.8. 16β-(1H-1,2,3-triazol-1-yl)-3β-pyrrolidino-5α-androstan-17-one (**9a**).* White solid. yield 51%. m.p.152–156 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.87 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.93 (s, 1H), 8.14 (s, 1H). Anal. Calcd. for $C_{25}H_{38}N_4O$: C 73.13, H 9.33, N 13.65; Found C 73.22, H 9.40, N 13.51.

*5.1.4.9. 16β-(1H-1,2,3-triazol-1-yl)-3β-piperidino-5α-androstan-17-one (**9b**).* White solid. yield 62%. m.p.170–173 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.93 (s, 1H), 8.14 (s, 1H). Anal. Calcd. for $C_{26}H_{40}N_4O$: C 73.54, H 9.49, N 13.19; Found C 73.36, H 9.58, N 13.31.

*5.1.4.10. 16β-(1H-1,2,3-triazol-1-yl)-3β-morpholino-5α-androstan-17-one (**9c**).* White solid. yield 55%. m.p.181–184 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.87 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 3.75 (s, 4H, $OCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.94 (s, 1H), 8.14 (s, 1H). Anal. Calcd. for $C_{25}H_{38}N_4O_2$: C 70.39, H 8.98, N 13.13; Found C 70.50, H 8.87, N 13.10.

*5.1.4.11. 16β-(1H-1,2,3-triazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17-one (**9d**).* White solid. yield 65%. m.p.169–173 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.87 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.27(s, 3H, N–$CH_3$), 2.40–2.56 (br, 8H, $NCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.94 (s, 1H), 8.16 (s,1H). Anal. Calcd. for $C_{26}H_{41}N_5O$: C 71.03, H 9.40, N 15.93; Found C 71.10, H 9.25, N 15.87.

*5.1.4.12. 16β-(1H-1,2,3-triazol-1-yl)-3β-diethylamino-5α-androstan-17-one (**9e**).* White solid. yield 61%. m.p.198–201 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 4.57 (t, 1H, $C_{16}$-αH), 7.94 (s, 1H), 8.14 (s, 1H). Anal. Calcd. for $C_{25}H_{40}N_4O$: C 72.77, H 9.77, N 13.58; Found C 72.60, H 9.63, N 13.68.

*5.1.4.13. 16β-(1H-1,2,3-triazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17-one (**9f**).* White solid. yield 56%. m.p. 169–173 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.82 (s, 3H, N–$CH_3$), 4.57 (t, 1H, $C_{16}$-αH), 6.69 (t, 1H), 6.79 (d, 2H, $J$ = 8.30Hz), 7.23(t, 2H), 7.96 (s, 1H), 8.16 (s, 1H). Anal. Calcd. for $C_{28}H_{38}N_4O$: C 75.30, H 8.58, N 12.54; Found C 75.22, H 8.63, N 12.39.

*5.1.4.14. 16β-(1H-1,2,3-triazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17-one (**9g**).* White solid. yield 57%. m.p. 155–158 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.85 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.21 (s, 3H, N–$CH_3$), 3.57 (s, 2H, $PhCH_2$), 4.56 (t, 1H, $C_{16}$-αH), 7.31 (s, 5H), 7.95 (s, 1H), 8.16 (s, 1H). Anal. Calcd. for $C_{29}H_{40}N_4O$: C 75.61, H 8.75, N 12.16; Found C 75.51, H 8.68, N 12.21.

*5.1.4.15. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-pyrrolidino-5α-androstan-17-one (**10a**).* White solid. yield 56%. m.p. 182–185 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.87 (s, 3H, $CH_3$-19), 1.24 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 4.98 (t, 1H, $C_{16}$-αH), 7.37 (t, 1H), 7.48–7.58(m, 2H), 8.07 (d, 1H, $J$ = 8.24Hz). Anal. Calcd. for $C_{29}H_{40}N_4O$: C 75.61, H 8.75, N 12.16; Found C 75.49, H 8.60, N 12.25.

*5.1.4.16. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-piperidino-5α-androstan-17-one (**10b**).* White solid. yield 60%. m.p. 242–245 °C; $^1$H

NMR(400 MHz,$CDCl_3$): δ 0.84 (s, 3H, $CH_3$-19), 1.23 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 4.98 (t, 1H, $C_{16}$-αH), 7.37 (t, 1H), 7.46–7.58(m, 2H), 8.07 (d, 1H, $J$ = 8.36Hz). Anal. Calcd. for $C_{30}H_{42}N_4O$: C 75.91, H 8.92, N 11.80; Found C 75.80, H 8.77, N 11.92.

*5.1.4.17. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-morpholino-5α-androstan-17-one (**10c**).* White solid. yield 60%. m.p. 218–220 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.86 (s, 3H, $CH_3$-19), 1.24 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 3.73 (s, 4H, $OCH_2$), 4.98 (t, 1H, $C_{16}$-αH), 7.37 (t, 1H), 7.47–7.58(m, 2H), 8.07 (d, 1H, $J$ = 8.36Hz). Anal. Calcd. for $C_{29}H_{40}N_4O_2$: C 73.07, H 8.46, N 11.75; Found C 73.19, H 8.60, N 11.63.

*5.1.4.18. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17-one (**10d**).* White solid. yield 60%. m.p. 215–218 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.85 (s, 3H, $CH_3$-19), 1.23 (s, 3H, $CH_3$-18), 2.28(s, 3H, N–$CH_3$), 2.47–2.63 (br, 8H, $NCH_2$), 4.98 (t, 1H, $C_{16}$-αH), 7.37 (t, 1H), 7.48–7.58(m, 2H), 8.06 (d, 1H, $J$ = 8.36Hz). Anal. Calcd. for $C_{30}H_{43}N_5O$: C 73.58, H 8.85, N 14.30; Found C 73.44, H 8.78, N 14.19.

*5.1.4.19. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-diethylamino-5α-androstan-17-one (**10e**).* White solid. yield 60%. m.p. 130–132 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.89 (s, 3H, $CH_3$-19), 1.24 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 4.98 (t, 1H, $C_{16}$-αH), 7.37 (t, 1H), 7.48–7.58(m, 2H), 8.06 (d, 1H, $J$ = 8.36Hz). Anal. Calcd. for $C_{29}H_{42}N_4O$: C 75.28, H 9.15, N 12.11; Found C 75.18, H 9.30, N 12.01.

*5.1.4.20. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17-one (**10f**).* White solid. yield 64%. m.p. 220–222 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s, 3H, $CH_3$-19), 1.24 (s, 3H, $CH_3$-18), 2.83 (s, 3H, N–$CH_3$), 4.97 (t, 1H, $C_{16}$-αH), 6.69 (t, 1H), 6.79 (d, 2H, $J$ = 8.28Hz), 7.24(t, 2H), 7.37 (t, 1H), 7.48–7.58(m, 2H), 8.06 (d, 1H, $J$ = 8.34Hz). Anal. Calcd. for $C_{32}H_{40}N_4O$: C 77.38, H 8.12, N 11.28; Found C 77.26, H 8.08, N 11.31.

*5.1.4.21. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17-one (**10g**).* White solid. yield 64%. m.p. 140–143 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.87 (s, 3H, $CH_3$-19), 1.24 (s, 3H, $CH_3$-18), 2.21 (s, 3H, N–$CH_3$), 3.58 (s, 2H, $PhCH_2$), 4.98 (t, 1H, $C_{16}$-αH), 7.24 (s, 1H), 7.31–7.37 (m, 4H), 7.46–7.58 (m, 2H), 7.86 (d, 2H, $J$ = 2.76Hz), 8.07 (d, 2H, $J$ = 8.32Hz). Anal. Calcd. for $C_{33}H_{42}N_4O$: C 77.61, H 8.29, N 10.97; Found C 77.80, H 8.41, N 10.88.

*5.1.4.22. 16β-(1H-benzimidazol-1-yl)-3β-pyrrolidino-5α-androstan-17-one (**11a**).* White solid. yield 64%. m.p. 133–136 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s, 3H, $CH_3$-19), 1.09 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 4.73 (t, 1H, $C_{16}$-αH), 7.29–7.32(m, 3H), 7.40–7.42 (m, 3H), 7.80 (s, 1H). Anal. Calcd. for $C_{30}H_{41}N_3O$: C 78.39, H 8.99, N 9.14; Found C 78.41, H 8.82, N 9.30.

*5.1.4.23. 16β-(1H-benzimidazol-1-yl)-3β-piperidino-5α-androstan-17-one (**11b**).* White solid. yield 60%. m.p. 219–222 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.85 (s, 3H, $CH_3$-19), 1.08 (s, 3H, $CH_3$-18), 2.53 (s, 4H, $NCH_2$), 4.74 (t, 1H, $C_{16}$-αH), 7.29–7.31(m, 3H), 7.40–7.42 (m, 3H), 7.81 (s, 1H). Anal. Calcd. for $C_{31}H_{43}N_3O$: C 78.60, H 9.15, N 8.87; Found C 78.50, H 9.24, N 8.98.

*5.1.4.24. 16β-(1H-benzimidazol-1-yl)-3β-morpholino-5α-androstan-17-one (**11c**).* White solid. yield 58%. m.p. 209–212 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s, 3H, $CH_3$-19), 1.09 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 3.73 (s, 4H, $OCH_2$), 4.74 (t, 1H, $C_{16}$-αH), 7.29–7.31(m, 3H), 7.41–7.42 (m, 3H), 7.81 (s, 1H). Anal. Calcd. for $C_{30}H_{41}N_3O_2$: C 75.75, H 8.69, N 8.83; Found C 75.62, H 8.88, N 8.78.

*5.1.4.25. 16β-(1H-benzimidazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17-one (**11d**).* White solid. yield 58%. m.p. 177–180 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.86 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.26(s, 3H, N–$CH_3$), 2.40–2.54 (br, 8H, $NCH_2$), 4.73 (t, 1H, $C_{16}$-αH), 7.29–7.31(m, 3H), 7.41–7.42 (m, 3H), 7.81 (s, 1H). Anal. Calcd. for $C_{31}H_{44}N_4O$: C 76.19, H 9.07, N 11.46; Found C 76.31, H 9.20, N 11.38.

*5.1.4.26. 16β-(1H-benzimidazol-1-yl)-3β-diethylamino-5α-androstan-17-one (**11e**).* White solid. yield 58%. m.p. 203–206 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.87 (s, 3H, $CH_3$-19), 1.10 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 4.98 (t, 1H, $C_{16}$-αH), 7.29–7.31(m, 3H), 7.41–7.42 (m, 3H), 7.82 (s, 1H). Anal. Calcd. for $C_{30}H_{43}N_3O$: C 78.05, H 9.39, N 9.10; Found C 78.13, H 9.51, N 9.22.

*5.1.4.27. 16β-(1H-benzimidazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17-one (**11f**).* White solid. yield 58%. m.p. 212–214 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.89 (s, 3H, $CH_3$-19), 1.03 (s, 3H, $CH_3$-18), 2.79 (s, 3H, N–$CH_3$), 5.02 (t, 1H, $C_{16}$-αH), 6.69 (t, 1H), 6.79 (d, 2H, $J$ = 8.24Hz), 7.20–7.30 (m, 5H), 7.77 (d, 2H, $J$ = 6.96Hz), 8.06 (s, 1H). Anal. Calcd. for $C_{33}H_{41}N_3O$: C 79.96, H 8.34, N 8.48; Found C 79.88, H 8.21, N 8.54.

*5.1.4.28. 16β-(1H-benzimidazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17-one (**11g**).* White solid. yield 58%. m.p. 248–251 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.85 (s, 3H, $CH_3$-19), 1.01 (s, 3H, $CH_3$-18), 2.21 (s, 3H, N–$CH_3$), 3.58 (s, 2H, $PhCH_2$), 4.73 (t, 1H, $C_{16}$-αH), 7.29–7.30(m, 3H), 7.31 (s, 5H), 7.40–7.42 (m, 3H), 7.80 (s, 1H). Anal. Calcd. for $C_{34}H_{43}N_3O$: C 80.11, H 8.50, N 8.24; Found C 80.01, H 8.39, N 8.12.

### *5.1.5. General procedure for the synthesis of compounds **12a–g**, **13a–g**, **14a–g**, **15a–g***

To the suspension of compounds **8a–g**, **9a–g**, **10a–g**, **11a–g** (1.00 mmol) in 20 ml of absolute methanol at 0 °C, sodium borohydride (1.20 mmol, 1.2 equiv) was added in small amounts over a period of 4 h. The methanol was removed under reduced pressure, 20 ml $CH_2Cl_2$ was added to the residue, the organic layer was washed with saturated $NaHCO_3$, brine and dried over anhydrous $Na_2SO_4$, filtered. The filtrate was concentrated in vacuum to afford a crude product. The product was purified by flash column chromatography to yield compound **12a–g**, **13a–g**, **14a–g**, **15a–g**.

*5.1.5.1. 16β-(1H-1,2,4-triazol-1-yl)-3β-pyrrolidino-5α-androstan-17β-ol (**12a**).* White solid. yield 58%. m.p. 236–239 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s, 3H, $CH_3$-19), 0.99 (s, 3H, $CH_3$-18), 2.53 (s, 4H, $NCH_2$), 3.83 (t, 1H, $C_{17}$-αH, $J$ = 9.40Hz), 4.82 (q, 1H, $C_{16}$-αH), 7.96 (s, 1H), 8.10 (s, 1H). Anal. Calcd. for $C_{25}H_{40}N_4O$: C 72.77, H 9.77, N 13.58; Found C 72.61, H 9.82, N 13.66.

*5.1.5.2. 16β-(1H-1,2,4-triazol-1-yl)-3β-piperidino-5α-androstan-17β-ol (**12b**).* White solid. yield 58%. m.p. 162–165 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.80 (s, 3H, $CH_3$-19), 0.99 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 3.85 (d, 1H, $C_{17}$-αH,), 4.82 (q, 1H, $C_{16}$-αH), 7.95 (s, 1H), 8.09 (s, 1H). Anal. Calcd. for $C_{26}H_{42}N_4O$: C 73.20, H 9.92, N 13.13; Found C 73.11, H 9.86, N 13.28.

*5.1.5.3. 16β-(1H-1,2,4-triazol-1-yl)-3β-morpholino-5α-androstan-17β-ol (**12c**).* White solid. yield 58%. m.p. 162–165 °C; $^1$H NMR (400 MHz,$CDCl_3$): δ 0.80 (s, 3H, $CH_3$-19), 0.83 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 3.71 (s, 4H, $OCH_2$), 3.88 (d, 1H, $C_{17}$-αH, $J$ = 5.04Hz), 5.06 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 8.14 (s, 1H). Anal. Calcd. for $C_{25}H_{40}N_4O_2$: C 70.06 H 9.41, N 13.07; Found C 70.18, H 9.29, N 13.12.

*5.1.5.4. 16β-(1H-1,2,4-triazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17β-ol (**12d**).* White solid. yield 49%. m.p. 259–262 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.80 (s, 3H, $CH_3$-19), 0.99 (s, 3H, $CH_3$-

18), 2.27 (s, 3H, N–$CH_3$), 2.43–2.61 (br, 8H, $NCH_2$), 3.84 (d, 2H, $C_{17}$-αH, $J$ = 9.08Hz), 4.82 (q, 1H, $C_{16}$-αH), 7.96 (s, 1H), 8.11 (s, 1H). Anal. Calcd. for $C_{26}H_{43}N_5O$: C 70.71, H 9.81, N 15.86; Found C 70.66, H 9.73, N 15.71.

*5.1.5.5. 16β-(1H-1,2,4-triazol-1-yl)-3β-diethylamino-5α-androstan-17β-ol (**12e**).* White solid. yield 60%. m.p. 215–219 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s, 3H, $CH_3$-19), 0.99 (s, 3H, $CH_3$-18), 2.62 (q, 4H, $NCH_2$), 3.83 (s, 1H, $C_{17}$-αH), 4.82 (q, 1H, $C_{16}$-αH), 7.95 (s, 1H), 8.09 (s, 1H). Anal. Calcd. for $C_{25}H_{42}N_4O$: C 72.42, H 10.21, N 13.51; Found C 72.33, H 10.04, N 13.62.

*5.1.5.6. 16β-(1H-1,2,4-triazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17β-ol (**12f**).* White solid. yield 61%. m.p. 198–202 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s, 3H, $CH_3$-19), 1.01 (s, 3H, $CH_3$-18), 2.78 (s, 3H, N–$CH_3$), 3.85 (s, 1H, $C_{17}$-αH), 4.83 (q, 1H, $C_{16}$-αH), 6.68 (t, 1H), 6.78 (d, 2H, $J$ = 8.20Hz), 7.21 (t, 2H), 7.97 (s, 1H), 8.10 (s, 1H). Anal. Calcd. for $C_{28}H_{40}N_4O$: C 74.96, H 8.99, N 12.49; Found C 74.88, H 8.83, N 12.60.

*5.1.5.7. 16β-(1H-1,2,4-triazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17β-ol (**12g**).* White solid. yield 53%. m.p. 206–208 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s, 3H, $CH_3$-19), 1.00 (s, 3H, $CH_3$-18), 2.20 (s, 3H, N–$CH_3$), 3.57 (s, 2H, $PhCH_2$), 3.86 (s, 1H, $C_{17}$-αH), 4.84 (t, 1H, $C_{16}$-αH), 7.31 (t, 5H), 7.97 (s, 1H), 8.10 (s, 1H). Anal. Calcd. for $C_{29}H_{42}N_4O$: C 75.28, H 9.15, N 12.11; Found C 75.09, H 9.23, N 12.01.

*5.1.5.8. 16β-(1H-1,2,3-triazol-1-yl)-3β-pyrrolidino-5α-androstan-17β-ol (**13a**).* White solid. yield 58%. m.p. 236–239 °C; $^1$H NMR (400 MHz,$CDCl_3$): δ 0.82 (s, 3H, $CH_3$-19), 0.99 (s, 3H, $CH_3$-18), 2.53 (s, 4H, $NCH_2$), 3.83 (t, 1H, $C_{17}$-αH, $J$ = 9.40Hz), 4.82 (q, 1H, $C_{16}$-αH), 7.96 (s, 1H), 8.10 (s, 1H). Anal. Calcd. for $C_{25}H_{40}N_4O$: C 72.77, H 9.77, N 13.58; Found C 72.61, H 9.82, N 13.66.

*5.1.5.9. 16β-(1H-1,2,3-triazol-1-yl)-3β-piperidino-5α-androstan-17β-ol (**13b**).* White solid. yield 58%. m.p. 162–165 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.80 (s, 3H, $CH_3$-19), 0.99 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 3.85 (d, 1H, $C_{17}$-αH,), 4.82 (q, 1H, $C_{16}$-αH), 7.95 (s, 1H), 8.09 (s, 1H). Anal. Calcd. for $C_{26}H_{42}N_4O$: C 73.20, H 9.92, N 13.13; Found C 73.11, H 9.86, N 13.18.

*5.1.5.10. 16β-(1H-1,2,3-triazol-1-yl)-3β-morpholino-5α-androstan-17β-ol (**13c**).* White solid. yield 58%. m.p. 162–165 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.80 (s, 3H, $CH_3$-19), 0.83 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 3.71 (s, 4H, $OCH_2$), 3.88 (d, 1H, $C_{17}$-αH, $J$ = 5.04Hz), 5.06 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 8.14 (s, 1H). Anal. Calcd. for $C_{25}H_{40}N_4O_2$: C 70.06 H 9.41, N 13.07; Found C 70.18, H 9.29, N 13.12.

*5.1.5.11. 16β-(1H-1,2,3-triazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17β-ol (**13d**).* White solid. yield 49%. m.p. 259–262 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.80 (s, 3H, $CH_3$-19), 0.99 (s, 3H, $CH_3$-18), 2.27 (s, 3H, N–$CH_3$), 2.43–2.61 (br, 8H, $NCH_2$), 3.84 (d, 2H, $C_{17}$-αH, $J$ = 9.08Hz), 4.82 (q, 1H, $C_{16}$-αH), 7.96 (s, 1H), 8.11 (s, 1H). Anal. Calcd. for $C_{26}H_{43}N_5O$: C 70.71, H 9.81, N 15.86; Found C 70.66, H 9.73, N 15.71.

*5.1.5.12. 16β-(1H-1,2,3-triazol-1-yl)-3β-diethylamino-5α-androstan-17β-ol (**13e**).* White solid. yield 60%. m.p. 215–219 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s, 3H, $CH_3$-19), 0.99 (s, 3H, $CH_3$-18), 2.62 (q, 4H, $NCH_2$), 3.83 (s, 1H, $C_{17}$-αH), 4.82 (q, 1H, $C_{16}$-αH), 7.95 (s, 1H), 8.09 (s, 1H). Anal. Calcd. for $C_{25}H_{42}N_4O$: C 72.42, H 10.21, N 13.51; Found C 72.33, H 10.04, N 13.62.

*5.1.5.13. 16β-(1H-1,2,3-triazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17β-ol (**13f**).* White solid. yield 61%. m.p. 198–202 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s, 3H, $CH_3$-19), 1.01 (s, 3H, $CH_3$-18), 2.78 (s, 3H, N–$CH_3$), 3.85 (s, 1H, $C_{17}$-αH), 4.83 (q, 1H, $C_{16}$-αH), 6.68 (t, 1H), 6.78 (d, 2H, $J$ = 8.20Hz), 7.21 (t, 2H), 7.97 (s, 1H), 8.10 (s, 1H). Anal. Calcd. for $C_{28}H_{40}N_4O$: C 74.96, H 8.99, N 12.49; Found C 74.88, H 8.83, N 12.60.

*5.1.5.14. 16β-(1H-1,2,3-triazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17β-ol (**13g**).* White solid. yield 53%. m.p. 220–223 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s, 3H, $CH_3$-19), 1.00 (s, 3H, $CH_3$-18), 2.20 (s, 3H, N–$CH_3$), 3.57 (s, 2H, $PhCH_2$), 3.86 (s, 1H, $C_{17}$-αH), 4.84 (t, 1H, $C_{16}$-αH), 7.31 (t, 5H), 7.97 (s, 1H), 8.10 (s, 1H). Anal. Calcd. for $C_{29}H_{42}N_4O$: C 75.28, H 9.15, N 12.11; Found C 75.09, H 9.23, N 12.01.

*5.1.5.15. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-pyrrolidino-5α-androstan-17β-ol (**14a**).* White solid. yield 60%. m.p. 259–262 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s, 3H, $CH_3$-19), 1.11 (s, 3H, $CH_3$-18), 2.56 (s, 4H, $NCH_2$), 4.03 (t, 1H, $C_{17}$-αH), 5.20 (q, 1H, $C_{16}$-αH), 7.37 (t, 1H,), 7.47–7.54 (m, 2H), 8.05 (d, 1H, $J$ = 8.40Hz). Anal. Calcd. for $C_{29}H_{42}N_4O$: C 75.28, H 9.15, N 12.11; Found C 75.17, H 9.21, N 11.98.

*5.1.5.16. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-piperidino-5α-androstan-17β-ol (**14b**).* White solid. yield 61%. m.p. 263–266 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.86 (s, 3H, $CH_3$-19), 1.08 (s, 3H, $CH_3$-18), 2.53 (s, 4H, $NCH_2$), 4.02 (t, 1H, $C_{17}$-αH), 5.18 (q, 1H, $C_{16}$-αH), 7.37 (t, 1H,), 7.47–7.54 (m, 2H), 8.03 (d, 1H, $J$ = 8.36Hz). Anal. Calcd. for $C_{30}H_{44}N_4O$: C 75.59, H 9.30, N 11.75; Found C 75.67, H 9.14, N 11.69.

*5.1.5.17. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-morpholino-5α-androstan-17β-ol (**14c**).* White solid. yield 57%. m.p. 257–259 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.57 (s, 4H, $NCH_2$), 3.72 (s, 4H, $OCH_2$), 4.03 (t, 1H, $C_{17}$-αH), 5.20 (q, 1H, $C_{16}$-αH), 7.36 (t, 1H,), 7.47–7.54 (m, 2H), 8.05 (d, 1H, $J$ = 8.36Hz). Anal. Calcd. for $C_{29}H_{42}N_4O_2$: C 72.77, H 8.84, N 11.70; Found C 72.84, H 8.85, N 11.64.

*5.1.5.18. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17β-ol (**14d**).* White solid. yield 65%. m.p. 292–295 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.27 (s, 3H, N–$CH_3$), 2.42–2.61 (br, 8H, $NCH_2$), 4.03 (s, 1H, $C_{17}$-αH), 5.20 (q, 1H, $C_{16}$-αH), 7.35 (t, 1H,), 7.46–7.54 (m, 2H), 8.02 (d, 1H, $J$ = 8.36Hz). Anal. Calcd. for $C_{30}H_{45}N_5O$: C 73.28, H 9.22, N 14.24; Found C 73.19, H 9.09, N 14.21.

*5.1.5.19. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-diethylamino-5α-androstan-17β-ol (**14e**).* White solid. yield 70%. m.p. 240–243 °C; $^1$H NMR (400 MHz,$CDCl_3$): δ 0.83 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 4.02 (t, 1H, $C_{17}$-αH), 5.20 (q, 1H, $C_{16}$-αH), 7.36 (t, 1H,), 7.47–7.54 (m, 2H), 8.04 (d, 1H, $J$ = 8.40Hz). Anal. Calcd. for $C_{29}H_{44}N_4O$: C 74.96, H 9.54, N 12.06; Found C 74.88, H 9.62, N 12.03.

*5.1.5.20. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17β-ol (**14f**).* White solid. yield 70%. m.p. 243–246 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.85 (s, 3H, N–$CH_3$), 4.04 (t, 1H, $C_{17}$-αH), 5.21 (q, 1H, $C_{16}$-αH), 6.69 (t, 1H), 6.68–6.77 (m, 1H), 6.85–6.96 (m, 2H), 7.24(t, 2H), 7.36 (t, 1H), 7.47–7.55(m, 2H), 8.05 (d, 1H, $J$ = 8.32Hz). Anal. Calcd. for $C_{32}H_{42}N_4O$: C 77.07, H 8.49, N 11.23; Found C 77.14, H 8.37, N 11.32.

*5.1.5.21. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17β-ol (**14g**).* White solid. yield 52%. m.p. 231–234 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.85 (s, 3H, $CH_3$-19), 1.12 (s, 3H, $CH_3$-18), 2.22 (s, 3H, N–$CH_3$), 3.59 (s, 2H, $PhCH_2$), 4.05 (s, 1H, $C_{17}$-αH), 5.21 (t, 1H, $C_{16}$-αH), 7.31 (t, 5H), 7.37 (t, 1H,), 7.47–7.54 (m, 2H), 8.06 (d, 1H, $J$ = 8.40Hz).

Anal. Calcd. for $C_{33}H_{44}N_4O$: C 77.30, H 8.65, N 10.93; Found C 77.41, H 8.58, N 10.82.

*5.1.5.22. 16β-(1H-benzimidazol-1-yl)-3β-pyrrolidino-5α-androstan-17β-ol (**15a**).* White solid. yield 59%. m.p. 279–282 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s, 3H, $CH_3$-19), 0.93 (s, 3H, $CH_3$-18), 2.55 (s, 4H, $NCH_2$), 4.01 (d, 1H, $C_{17}$-αH, $J$ = 9.16Hz), 4.79 (q, 1H, $C_{16}$-αH), 7.24 (t, 2H), 7.33 (d, 1H, $J$ = 7.28Hz), 7.67 (d, 1H, $J$ = 7.32Hz), 8.04 (s, 1H). Anal. Calcd. for $C_{30}H_{43}N_3O$: C 78.05, H 9.39, N 9.10; Found C 78.12, H 9.56, N 9.24.

*5.1.5.23. 16β-(1H-benzimidazol-1-yl)-3β-piperidino-5α-androstan-17β-ol (**15b**).* White solid. yield 56%. m.p. 273–275 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.81 (s, 3H, $CH_3$-19), 0.93 (s, 3H, $CH_3$-18), 2.52 (s, 4H, $NCH_2$), 4.01 (d, 1H, $C_{17}$-αH, $J$ = 9.20Hz), 4.82 (q, 1H, $C_{16}$-αH), 7.22 (t, 2H), 7.35 (d, 1H, $J$ = 7.32Hz), 7.70 (d, 1H, $J$ = 7.30Hz), 8.05 (s, 1H). Anal. Calcd. for $C_{31}H_{45}N_3O$: C 78.27, H 9.53, N 8.83; Found C 78.41, H 9.36, N 8.71.

*5.1.5.24. 16β-(1H-benzimidazol-1-yl)-3β-morpholino-5α-androstan-17β-ol (**15c**).* White solid. yield 56%. m.p. 278–280 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s, 3H, $CH_3$-19), 0.94 (s, 3H, $CH_3$-18), 2.55 (s, 4H, $NCH_2$), 3.71 (s, 4H, $OCH_2$), 4.02 (d, 1H, $C_{17}$-αH, $J$ = 9.20Hz), 4.79 (q, 1H, $C_{16}$-αH), 7.21 (t, 2H), 7.35 (d, 1H, $J$ = 7.20Hz), 7.66 (d, 1H, $J$ = 7.48Hz), 8.03 (s, 1H). Anal. Calcd. for $C_{30}H_{43}N_3O_2$: C 75.43, H 9.07, N 8.80; Found C 75.32, H 9.16, N 8.68.

*5.1.5.25. 16β-(1H-benzimidazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17β-ol (**15d**).* White solid. yield 56%. m.p. 279–281 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.81 (s, 3H, $CH_3$-19), 0.94 (s, 3H, $CH_3$-18), 2.24 (s, 3H, N–$CH_3$), 2.43–2.59 (br, 8H, $NCH_2$), 4.02 (d, 1H, $C_{17}$-αH, $J$ = 9.16Hz), 4.79 (q, 1H, $C_{16}$-αH), 7.21 (t, 2H), 7.33 (d, 1H, $J$ = 7.36Hz), 7.66 (d, 1H, $J$ = 7.32Hz), 8.06 (s, 1H). Anal. Calcd. for $C_{31}H_{46}N_4O$: C 75.87, H 9.45, N 11.42; Found C 75.72, H 9.31, N 11.60.

*5.1.5.26. 16β-(1H-benzimidazol-1-yl)-3β-diethylamino-5α-androstan-17β-ol (**15e**).* White solid. yield 56%. m.p. 227–230 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s, 3H, $CH_3$-19), 0.93 (s, 3H, $CH_3$-18), 2.56 (q, 4H, $NCH_2$), 4.02 (d, 1H, $C_{17}$-αH, $J$ = 9.22Hz), 4.78 (q, 1H, $C_{16}$-αH), 7.20 (t, 2H), 7.40 (d, 1H, $J$ = 7.96Hz), 7.64 (d, 1H, $J$ = 7.76Hz), 7.97 (s, 1H). Anal. Calcd. for $C_{30}H_{45}N_3O$: C 77.71, H 9.78, N 9.06; Found C 77.64, H 9.89, N 9.17.

*5.1.5.27. 16β-(1H-benzimidazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17β-ol (**15f**).* White solid. yield 59%. m.p. 264–266 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s, 3H, $CH_3$-19), 0.94 (s, 3H, $CH_3$-18), 2.79 (s, 3H, N–$CH_3$), 4.01 (d, 1H, $C_{17}$-αH, $J$ = 9.22Hz), 4.82 (q, 1H, $C_{16}$-αH), 6.79 (t, 1H), 6.96 (d, 2H, $J$ = 8.20Hz), 7.21 (t, 2H), 7.24 (t, 2H), 7.35 (d, 1H, $J$ = 7.62Hz), 7.70 (d, 1H, $J$ = 7.44Hz), 8.07 (s, 1H). Anal. Calcd. for $C_{33}H_{43}N_3O$: C 79.63, H 8.71, N 8.44; Found C 79.80, H 8.65, N 8.52.

*5.1.5.28. 16β-(1H-benzimidazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17β-ol (**15g**).* White solid. yield 56%. m.p. 214–216 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s, 3H, $CH_3$-19), 0.94 (s, 3H, $CH_3$-18), 2.20 (s, 3H, N–$CH_3$), 3.57 (s, 2H, $PhCH_2$), 4.01 (d, 1H, $C_{17}$-αH, $J$ = 9.16Hz), 4.82 (q, 1H, $C_{16}$-αH), 7.21 (t, 2H), 7.31 (m, 6H), 7.66 (d, 1H, $J$ = 7.28Hz), 8.07 (s, 1H). Anal. Calcd. for $C_{34}H_{45}N_3O$: C 79.80, H 8.86, N 8.21; Found C 79.70, H 8.93, N 8.08.

### *5.1.6. General procedure for the synthesis of compounds **16a–g**, **17a–g**, **18a–g**, **19a–g***

To a solution of compounds **12a–g**, **13a–g**, **14a–g**, **15a–g** (2.00 mmol) in $CH_2Cl_2$ was added acetic anhydride (4.00 mmol, 2.0 equiv) and 4-dimethylaminopyridine (2.00 mmol, 1.0 equiv). The mixture was stirred at 40 °C until the reaction was completed (monitored by TLC). The reaction was concentrated in reduced pressure. The crude product was dissolved in $CH_2Cl_2$, the organic layer was washed with brine and dried over anhydrous $Na_2SO_4$, filtered. The filtrate was concentrated in reduced pressure to afford a crude product. The products were purified by flash column chromatography to yield compound **16a–g**, **17a–g**, **18a–g**, **19a–g**.

*5.1.6.1. 16β-(1H-1,2,4-triazol-1-yl)-3β-pyrrolidino-5α-androstan-17β-yl acetate (**16a**).* White solid. Yield 96%. m.p. 167–170 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s,3H, $CH_3$-19), 1.11 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.56 (s,4H, $NCH_2$), 4.70 (d, 1H, $C_{17}$-αH, $J$ = 9.12Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.92 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.28, 12.57, 20.08, 20.34, 23.13, 27.74, 28.60, 31.30, 31.86, 34.24, 34.46, 35.84, 37.34, 37.78, 42.13, 45.15, 48.41, 51.69, 54.31, 58.12, 64.17, 81.57, 145.02, 151.13, 170.88. Anal. Calcd. for $C_{27}H_{42}N_4O_2$: C 71.33, 9.31, N 12.32; Found C 71.18, H 9.55, N 12.24. MS ($m/z$):455[M + 1]$^+$.

*5.1.6.2. 16β-(1H-1,2,4-triazol-1-yl)-3β-piperidino-5α-androstan-17β-yl acetate (**16b**).* White solid. Yield 93%. m.p. 197–200 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.81 (s,3H, $CH_3$-19), 1.11 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.51 (s,4H, $NCH_2$), 4.69 (d, 1H, $C_{17}$-αH, $J$ = 9.08Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.92 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.38, 12.60, 20.11, 20.43, 23.95, 24.73, 26.21, 28.69, 30.49, 31.88, 34.28, 36.05, 37.80, 37.94, 42.17, 45.97, 48.43, 50.28, 54.34, 58.16, 64.50, 81.61, 145.05, 151.16, 170.92. Anal. Calcd. for $C_{28}H_{44}N_4O_2$: C 71.76, H 9.46, N 11.95; Found C 71.69, H 9.60, N 11.87. MS ($m/z$):469[M + 1]$^+$.

*5.1.6.3. 16β-(1H-1,2,4-triazol-1-yl)-3β-morpholino-5α-androstan-17β-yl acetate (**16c**).* White solid. Yield 92%. m.p. 183–186 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s,3H, $CH_3$-19), 1.12 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.56 (s,4H, $NCH_2$), 3.72 (s, 4H, $OCH_2$), 4.69 (d, 1H, $C_{17}$-αH, $J$ = 9.12Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.92 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.33, 12.59, 20.10, 20.40, 24.37, 28.67, 31.00, 31.30, 31.84, 34.24, 35.96, 37.64, 37.76, 42.14, 45.61, 48.39, 49.97, 54.28, 58.12, 63.98, 67.26, 81.56, 145.04, 151.13, 170.90. Anal. Calcd. for $C_{27}H_{42}N_4O_3$: C 68.90, H 8.99, N 11.90; Found C 68.78, H 9.16, N 11.83. MS ($m/z$):471[M + 1]$^+$.

*5.1.6.4. 16β-(1H-1,2,4-triazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17β-yl acetate (**16d**).* White solid. Yield 92%. m.p. 208–210 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.81 (s,3H, $CH_3$-19), 1.12 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.28 (s, 3H, N–$CH_3$), 2.46–2.61 (br, 8H, $NCH_2$), 4.69 (d, 1H, $C_{17}$-αH, $J$ = 9.12Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.92 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.38, 12.60, 20.13, 20.42, 24.45, 28.69, 31.22, 31.33, 31.87, 34.27, 35.98, 37.79, 42.16, 45.76, 46.00, 48.42, 49.25, 54.32, 55.46, 58.15, 63.74, 81.61, 145.06, 151.19, 170.95. Anal. Calcd. for $C_{28}H_{45}N_5O_2$: C 69.53, H 9.38, N 14.48; Found C 69.62, H 9.33, N 14.63. MS ($m/z$):484[M + 1]$^+$.

*5.1.6.5. 16β-(1H-1,2,4-triazol-1-yl)-3β-diethylamino-5α-androstan-17β-yl acetate (**16e**).* White solid. Yield 92%. m.p. 115–118 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s,3H, $CH_3$-19), 1.12 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.64 (q, 4H, $NCH_2$), 4.70 (d, 1H, $C_{17}$-αH, $J$ = 9.12Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.93 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.38, 12.60, 13.20, 20.10, 20.43, 24.20, 28.69, 30.80, 31.33, 31.85, 34.27, 36.04, 37.79, 37.88, 42.16, 43.57, 45.97, 48.42, 54.31, 58.16, 59.64, 81.59, 145.04, 151.14, 170.93. Anal. Calcd. for $C_{27}H_{44}N_4O_2$: C 71.01, H 9.71, N 12.27; Found C 71.20, H 9.66, N 12.09. MS ($m/z$):457[M + 1]$^+$.

*5.1.6.6. 16β-(1H-1,2,4-triazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17β-yl acetate (**16f**).* White solid. Yield 92%. m.p. 179–182 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.88 (s,3H, $CH_3$-19), 1.13

(s,3H, $CH_3$-18), 1.73 (s, 3H, $OCOCH_3$), 2.78 (s, 3H, N–$CH_3$), 4.71 (d, 1H, $C_{17}$-αH, $J = 9.12$Hz), 5.00 (q, 1H, $C_{16}$-αH), 6.68 (t, 1H), 6.79 (d, 2H, $J = 8.20$Hz), 7.22 (t, 2H), 7.91 (s, 1H), 7.95 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.45, 12.61, 20.11, 20.46, 24.91, 28.50, 31.31, 31.40, 31.52, 31.79, 34.27, 35.84, 37.76, 37.89, 42.17, 46.12, 48.37, 54.26, 58.21, 58.32, 81.55, 113.32, 116.42, 129.07, 145.08, 150.14, 150.91, 170.95. Anal. Calcd. for $C_{30}H_{42}N_4O_2$: C 73.43, H 8.63, N 11.42; Found C 73.31, H 8.59, N 11.52. MS (*m*/*z*): 491[M + 1]$^+$.

*5.1.6.7. 16β-(1H-1,2,4-triazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17β-yl acetate (**16g**).* White solid. Yield 88%. m.p. 98–100 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s,3H, $CH_3$-19), 1.12 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.21 (s, 3H, N–$CH_3$), 3.59 (s, 2H, $PhCH_2$), 4.69 (d, 1H, $C_{17}$-αH, $J = 9.08$Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.16–7.37(m, 6H), 7.92 (d, 2H, $J = 8.60$Hz). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.41, 12.63, 20.16, 20.47, 23.66, 28.70, 30.20, 31.35, 31.85, 34.28, 36.07, 37.48, 37.76, 37.80, 42.17, 45.83, 48.42, 54.26, 57.75, 58.16, 62.34, 81.62, 126.29, 127.02, 128.28, 129.09, 138.98, 145.10, 151.19, 170.97. Anal. Calcd. for $C_{31}H_{44}N_4O_2$: C 73.77, H 8.79, N 11.10; Found C 73.83, H 8.62, N 11.25. MS (*m*/*z*):505[M + 1]$^+$.

*5.1.6.8. 16β-(1H-1,2,3-triazol-1-yl)-3β-pyrrolidino-5α-androstan-17β-yl acetate (**17a**).* White solid. Yield 85%. m.p. 177–180 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s,3H, $CH_3$-19), 1.11 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.60 (s, 4H, $NCH_2$), 4.70 (d, 1H, $C_{17}$-αH, $J = 9.12$Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.92 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.30, 12.62, 20.14, 20.39, 23.19, 27.14, 28.59, 31.34, 31.85, 33.81, 34.26, 35.86, 37.28, 37.80, 42.18, 45.19, 48.45, 51.56, 54.27, 58.18, 64.24, 81.60, 145.04, 151.19, 171.00. Anal. Calcd. for $C_{27}H_{42}N_4O_2$: C 71.33, H 9.31, N 12.32; Found C 71.19, H 9.42, N 12.18. MS (*m*/*z*):455[M + 1]$^+$.

*5.1.6.9. 16β-(1H-1,2,3-triazol-1-yl)-3β-piperidino-5α-androstan-17β-yl acetate (**17b**).* White solid. Yield 88%. m.p. 189–192 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.81 (s,3H, $CH_3$-19), 1.11 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.53 (s, 4H, $NCH_2$), 4.69 (d, 1H, $C_{17}$-αH, $J = 9.08$Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.92 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.37, 12.60, 20.11, 20.43, 23.82, 24.63, 26.04, 28.67, 30.36, 31.33, 31.86, 34.27, 36.03, 37.79, 37.89, 42.17, 45.92, 48.42, 50.21, 54.31, 58.16, 64.49, 81.60, 145.05, 151.16, 170.93. Anal. Calcd. for $C_{28}H_{44}N_4O_2$: C 71.76, H 9.46, N 11.95; Found C 71.67, H 9.54, N 11.88. MS (*m*/*z*):469 [M + 1]$^+$.

*5.1.6.10. 16β-(1H-1,2,3-triazol-1-yl)-3β-morpholino-5α-androstan-17β-yl acetate (**17c**).* White solid. Yield 93%. m.p. 168–170 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s,3H, $CH_3$-19), 1.12 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.56 (s, 4H, $NCH_2$), 3.72 (s, 4H, $OCH_2$), 4.70 (d, 1H, $C_{17}$-αH, $J = 9.16$Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.92 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.36, 12.62, 20.14, 20.44, 24.40, 28.70, 31.03, 31.35, 31.87, 34.28, 36.00, 37.68, 37.80, 42.18, 45.65, 48.43, 50.01, 54.32, 58.18, 64.05, 67.29, 81.61, 145.06, 151.18, 170.99. Anal. Calcd. for $C_{27}H_{42}N_4O_3$: C 68.90, H 8.99, N 11.90; Found C 68.72, H 8.85, N 11.99. MS (*m*/*z*):471[M + 1]$^+$.

*5.1.6.11. 16β-(1H-1,2,3-triazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17β-yl acetate (**17d**).* White solid. Yield 93%. m.p. 211–214 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.81 (s,3H, $CH_3$-19), 1.12 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.28 (s, 3H, N–$CH_3$), 2.46–2.62 (br, 8H, $NCH_2$), 3.72 (s, 4H, $OCH_2$), 4.70 (d, 1H, $C_{17}$-αH, $J = 9.12$Hz), 5.00 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.92 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.36, 12.61, 20.14, 20.42, 24.46, 28.70, 31.22, 31.34, 31.85, 34.26, 35.97, 37.79, 42.15, 45.76, 46.00, 48.42, 49.24, 54.31, 55.46, 58.14, 63.73, 81.60, 145.07, 151.19, 170.95. Anal. Calcd. for $C_{28}H_{45}N_5O_2$: C 69.53, H 9.38, N 14.48; Found C 69.70, H 9.29, N 14.54. MS (*m*/*z*):484[M + 1]$^+$.

*5.1.6.12. 16β-(1H-1,2,3-triazol-1-yl)-3β-diethylamino-5α-androstan-17β-yl acetate (**17e**).* White solid. Yield 90%. m.p. 140–143 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s,3H, $CH_3$-19), 1.11 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.63 (q, 4H, $NCH_2$), 4.71 (d, 1H, $C_{17}$-αH, $J = 9.14$Hz), 5.01 (q, 1H, $C_{16}$-αH), 7.90 (s, 1H), 7.93 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.37, 12.60, 13.21, 20.08, 20.43, 24.21, 28.70, 30.81, 31.32, 31.86, 34.27, 36.04, 37.80, 37.89, 42.15, 43.57, 45.97, 48.42, 54.30, 58.16, 59.64, 81.61, 145.01, 151.15, 170.93. Anal. Calcd. for $C_{27}H_{44}N_4O_2$: C 71.01, H 9.71, N 12.27; Found C 71.09, H 9.80, N 12.40. MS (*m*/*z*):457[M + 1]$^+$.

*5.1.6.13. 16β-(1H-1,2,3-triazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17β-yl acetate (**17f**).* White solid. Yield 92%. m.p. 187–190 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s,3H, $CH_3$-19), 1.13 (s,3H, $CH_3$-18), 1.72 (s, 3H, $OCOCH_3$), 2.78 (s, 3H, N–$CH_3$), 4.71 (d, 1H, $C_{17}$-αH, $J = 9.16$Hz), 5.01 (q, 1H, $C_{16}$-αH), 6.68 (t, 1H), 6.79 (d, 2H, $J = 8.20$Hz), 7.22 (t, 2H), 7.91 (s, 1H), 7.95 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.40, 12.60, 20.09, 20.46, 24.92, 28.50, 31.30, 31.42, 31.52, 31.80, 34.27, 35.85, 37.74, 37.89, 42.20, 46.12, 48.38, 54.27, 58.20, 58.32, 81.53, 113.33, 116.43, 129.09, 145.08, 150.14, 150.91, 170.94. Anal. Calcd. for $C_{30}H_{42}N_4O_2$: C 73.43, H 8.63, N 11.42; Found C 73.29, H 8.55, N 11.57. MS (*m*/*z*):491[M + 1]$^+$.

*5.1.6.14. 16β-(1H-1,2,3-triazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17β-yl acetate (**17g**).* White solid. Yield 92%. m.p. 139–142 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s,3H, $CH_3$-19), 1.12 (s,3H, $CH_3$-18), 1.71 (s, 3H, $OCOCH_3$), 2.22 (s, 3H, N–$CH_3$), 3.60 (s, 2H, $PhCH_2$), 4.70 (d, 1H, $C_{17}$-αH, $J = 9.06$Hz), 5.00 (q, 1H, $C_{16}$-αH), 7.13–7.35(m, 6H), 7.91 (d, 2H, $J = 8.64$Hz). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.41, 12.62, 20.15, 20.48, 23.66, 28.70, 30.20, 31.35, 31.85, 34.28, 36.07, 37.48, 37.76, 37.78, 42.17, 45.83, 48.41, 54.26, 57.75, 58.14, 62.33, 81.62, 126.26, 127.04, 128.28, 129.10, 138.97, 145.10, 151.15, 170.95. Anal. Calcd. for $C_{31}H_{44}N_4O_2$: C 73.77, H 8.79, N 11.10; Found C 73.60, H 8.86, N 11.07. MS (*m*/*z*):505[M + 1]$^+$.

*5.1.6.15. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-pyrrolidino-5α-androstan-17β-yl acetate (**18a**).* White solid. Yield 87%. m.p. 243–246 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.86 (s,3H, $CH_3$-19), 1.18 (s,3H, $CH_3$-18), 1.23 (s, 3H, $OCOCH_3$), 2.58 (s, 4H, $NCH_2$), 5.02 (d, 1H, $C_{17}$-αH, $J = 9.08$Hz), 5.28 (q, 1H, $C_{16}$-αH), 7.33 (t, 1H), 7.40–7.47 (m, 2H), 8.03 (d, 1H, $J = 8.28$Hz). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.34, 12.70, 19.79, 20.36, 23.16, 27.76, 28.67, 31.35, 31.98, 34.41, 34.49, 35.91, 37.41, 37.84, 42.77, 45.23, 48.76, 51.67, 54.42, 56.74, 64.18, 80.51, 109.97, 119.56, 123.70, 126.95, 134.07, 145.48, 170.56. Anal. Calcd. for $C_{31}H_{44}N_4O_2$: C 73.77, H 8.79, N 11.10; Found C 73.68, H 8.81, N 11.21. MS (*m*/*z*):505[M + 1]$^+$.

*5.1.6.16. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-piperidino-5α-androstan-17β-yl acetate (**18b**).* White solid. Yield 93%. m.p. 271–273 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s,3H, $CH_3$-19), 1.18 (s,3H, $CH_3$-18), 1.23 (s, 3H, $OCOCH_3$), 2.54 (s, 4H, $NCH_2$), 5.01 (d, 1H, $C_{17}$-αH, $J = 9.08$Hz), 5.28 (q, 1H, $C_{16}$-αH), 7.33 (t, 1H), 7.40–7.47 (m, 2H), 8.03 (d, 1H, $J = 8.28$Hz). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.43, 12.72, 19.81, 20.43, 23.84, 24.64, 26.05, 28.72, 30.36, 31.38, 31.96, 34.42, 36.09, 37.84, 37.93, 42.79, 45.99, 48.75, 50.23, 54.40, 56.75, 64.58, 80.52, 109.98, 119.59, 123.73, 126.98, 134.09, 145.51, 170.58. Anal. Calcd. for $C_{32}H_{46}N_4O_2$: C 74.09, H 8.94, N 10.80; Found C 74.13, H 8.80, N 10.91. MS (*m*/*z*):519[M + 1]$^+$.

*5.1.6.17. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-morpholino-5α-androstan-17β-yl acetate (**18c**).* White solid. Yield 93%. m.p. 246–248 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s,3H, $CH_3$-19), 1.19 (s,3H, $CH_3$-18), 1.23 (s, 3H, $OCOCH_3$), 2.57 (s, 4H, $NCH_2$), 3.73 (s, 4H, $OCH_2$), 5.02 (d, 1H, $C_{17}$-αH, $J = 9.08$Hz), 5.30 (q, 1H, $C_{16}$-αH), 7.33 (t, 1H), 7.39–7.47 (m, 2H), 8.03 (d, 1H, $J = 8.32$Hz). $^{13}$C

NMR(150 MHz,$CDCl_3$): δ 12.41, 12.73, 19.82, 20.44, 24.44, 28.76, 31.08, 31.39, 31.98, 34.44, 36.06, 37.74, 37.85, 42.80, 45.73, 48.77, 50.04, 54.42, 56.76, 64.10, 67.35, 80.53, 109.97, 119.62, 123.74, 127.00, 134.10, 145.53, 170.61. Anal. Calcd. for $C_{31}H_{44}N_4O_3$: C 71.51, H 8.52, N 10.76; Found C 71.44, H 8.39, N 10.80. MS (*m*/*z*):521[M + 1]$^+$.

*5.1.6.18. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17β-yl acetate (**18d**).* White solid. Yield 91%. m.p. 267–270 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s,3H, $CH_3$-19), 1.19 (s,3H, $CH_3$-18), 1.23 (s, 3H, $OCOCH_3$), 2.29 (s, 3H, N–$CH_3$), 2.45–2.63 (br, 8H, $NCH_2$), 5.01 (d, 1H, $C_{17}$-αH, *J* = 9.12Hz), 5.28 (q, 1H, $C_{16}$-αH), 7.33 (t, 1H), 7.39–7.47 (m, 2H), 8.03 (d, 1H, *J* = 8.32Hz). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.41, 12.71, 19.81, 20.42, 24.36, 28.72, 31.12, 31.38, 31.96, 34.41, 36.02, 37.78, 37.83, 42.78, 45.80, 45.83, 48.74, 49.04, 54.39, 55.23, 56.74, 63.75, 80.51, 109.98, 119.59, 123.73, 126.99, 134.08, 145.49, 170.60. Anal. Calcd. for $C_{32}H_{47}N_5O_2$: C 72.01, H 8.88, N 13.12; Found C 72.13, H 8.91, N 13.08. MS (*m*/*z*):534[M + 1]$^+$.

*5.1.6.19. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-diethylamino-5α-androstan-17β-yl acetate (**18e**).* White solid. Yield 82%. m.p. 225–228 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.89 (s,3H, $CH_3$-19), 1.19 (s,3H, $CH_3$-18), 1.23 (s, 3H, $OCOCH_3$), 2.64 (q, 4H, $NCH_2$), 5.02 (d, 1H, $C_{17}$-αH, *J* = 9.08Hz), 5.30 (q, 1H, $C_{16}$-αH), 7.33 (t, 1H), 7.40–7.47 (m, 2H), 8.03 (d, 1H, *J* = 8.36Hz). $^{13}$C NMR(150 MHz,$CDCl_3$): δ. 12.41, 12.72, 13.70, 19.81, 20.43, 24.42, 28.75, 31.10, 31.38, 31.98, 34.42, 36.03, 37.80, 37.85, 42.80, 45.77, 48.77, 49.42, 54.42, 56.73, 64.02, 80.52, 109.97, 119.60, 123.73, 127.00, 134.09, 145.52, 170.60. Anal. Calcd. for $C_{31}H_{46}N_4O_2$: C 73.48, H 9.15, N 11.06; Found C 73.52, H 9.03, N 11.18. MS (*m*/*z*):507[M + 1]$^+$.

*5.1.6.20. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17β-yl acetate (**18f**).* White solid. Yield 91%. m.p. 277–280 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.91 (s,3H, $CH_3$-19), 1.20 (s,3H, $CH_3$-18), 1.24 (s, 3H, $OCOCH_3$), 2.79 (s, 3H, N–$CH_3$), 5.03 (d, 1H, $C_{17}$-αH, *J* = 9.08Hz), 5.30 (q, 1H, $C_{16}$-αH), 6.68 (t, 1H), 6.79 (d, 2H, *J* = 8.20Hz), 7.23 (t, 2H), 7.33 (t, 2H), 7.40–7.47 (m, 2H), 8.03 (d, 1H, *J* = 8.32Hz). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.53, 12.76, 19.84, 20.50, 25.01, 28.59, 29.71, 31.39, 31.62, 31.95, 34.47, 35.93, 37.87, 37.98, 42.82, 46.25, 48.78, 54.43, 56.77, 58.33, 80.54, 110.00, 113.24, 116.34, 119.64, 123.76, 127.02, 129.12, 134.12, 145.55, 150.23, 170.62. Anal. Calcd. for $C_{34}H_{44}N_4O_2$: C 75.52, H 8.20, N 10.36; Found C 75.40, H 8.09, N 10.51. MS (*m*/*z*):541[M + 1]$^+$.

*5.1.6.21. 16β-(benzo-1H-1,2,3-triazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17β-yl acetate (**18g**).* White solid. Yield 79%. m.p. 198–201 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.86 (s,3H, $CH_3$-19), 1.19 (s,3H, $CH_3$-18), 1.23 (s, 3H, $OCOCH_3$), 2.22 (s, 3H, N–$CH_3$), 3.59 (s, 2H, $PhCH_2$), 5.01 (d, 1H, $C_{17}$-αH, *J* = 9.04Hz), 5.29 (q, 1H, $C_{16}$-αH), 7.23 (t, 2H), 7.29–7.35 (m, 4H), 7.40–7.47 (m, 2H), 8.03 (d, 1H, *J* = 8.32Hz). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.47, 12.75, 19.85, 20.48, 23.96, 28.80, 30.47, 31.42, 32.00, 34.46, 36.18, 37.83, 37.89, 37.93, 42.81, 45.98, 48.79, 54.44, 56.77, 58.01, 62.62, 80.55, 110.00, 119.63, 123.74, 126.75, 127.00, 128.21, 128.86, 134.11, 145.55, 170.63. Anal. Calcd. for $C_{35}H_{46}N_4O_2$: C 75.78, H 8.36, N 10.10; Found C 75.61, H 8.50, N 10.22. MS (*m*/*z*):555[M + 1]$^+$.

*5.1.6.22. 16β-(1H-benzimidazol-1-yl)-3β-pyrrolidino-5α-androstan-17β-yl acetate (**19a**).* White solid. Yield 77%. m.p. 241–243 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.86 (s,3H, $CH_3$-19), 1.01 (s,3H, $CH_3$-18), 1.39 (s, 3H, $OCOCH_3$), 2.87 (s, 4H, $NCH_2$), 4.96–5.06 (m, 2H, $C_{16}$-αH, $C_{17}$-αH), 7.22–7.31 (m, 3H), 7.77 (d, 1H, *J* = 6.96Hz), 8.05 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.20, 13.48, 19.93, 20.38, 25.99, 28.38, 31.83, 32.30, 32.60, 34.20, 35.77, 37.07, 37.62, 42.88, 45.11, 48.54, 50.97, 51.62, 53.84, 54.05, 63.88, 79.03, 119.95, 122.13, 122.92, 134.71, 141.81, 142.87, 170.13. Anal. Calcd. for $C_{32}H_{45}N_3O_2$: C 76.30, H 9.00, N 8.34; Found C 76.09, H 8.91, N 8.40. MS (*m*/*z*):504 [M + 1]$^+$.

*5.1.6.23. 16β-(1H-benzimidazol-1-yl)-3β-piperidino-5α-androstan-17β-yl acetate (**19b**).* White solid. Yield 71%. m.p. 256–258 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s,3H, $CH_3$-19), 1.01 (s,3H, $CH_3$-18), 1.39 (s, 3H, $OCOCH_3$), 2.57 (s, 4H, $NCH_2$), 4.96–5.06 (m, 2H, $C_{16}$-αH, $C_{17}$-αH), 7.24–7.31 (m, 3H), 7.77 (d, 1H, *J* = 6.84Hz), 8.05 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.40, 13.51, 19.96, 20.45, 23.87, 24.71, 26.15, 28.66, 30.43, 31.98, 32.39, 34.31, 36.08, 37.71, 37.89, 42.93, 45.93, 48.62, 50.22, 53.88, 54.27, 64.41, 79.10, 109.93, 120.03, 122.13, 122.94, 134.78, 141.85, 142.99, 170.15. Anal. Calcd. for $C_{33}H_{47}N_3O_2$: C 76.55, H 9.15, N 8.12; Found C 76.48, H 9.03, N 8.20. MS (*m*/*z*):518[M + 1]$^+$.

*5.1.6.24. 16β-(1H-benzimidazol-1-yl)-3β-morpholino-5α-androstan-17β-yl acetate (**19c**).* White solid. Yield 80%. m.p. 235–238 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.83 (s,3H, $CH_3$-19), 1.02 (s,3H, $CH_3$-18), 1.39 (s, 3H, $OCOCH_3$), 2.58 (s, 4H, $NCH_2$), 3.73 (s, 4H, $OCH_2$), 4.96–5.06 (m, 2H, $C_{16}$-αH, $C_{17}$-αH), 7.22–7.31 (m, 3H), 7.77 (d, 1H, *J* = 6.84Hz), 8.05 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.37, 13.52, 19.97, 20.45, 24.38, 28.66, 31.00, 31.97, 32.39, 34.31, 36.02, 37.64, 37.70, 42.93, 45.63, 48.62, 50.00, 53.88, 54.26, 64.03, 67.28, 79.10, 109.92, 120.02, 122.17, 122.96, 134.75, 141.83, 142.93, 170.18. Anal. Calcd. for $C_{32}H_{45}N_3O_3$: C 73.95, H 8.73, N 8.09; Found C 73.88, H 8.67, N 8.14. MS (*m*/*z*):520[M + 1]$^+$.

*5.1.6.25. 16β-(1H-benzimidazol-1-yl)-3β-(4-Methylpiperazinyl)-5α-androstan-17β-yl acetate (**19d**).* White solid. Yield 80%. m.p. 288–290 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s,3H, $CH_3$-19), 1.01 (s,3H, $CH_3$-18), 1.39 (s, 3H, $OCOCH_3$), 2.28 (s, 3H, N–$CH_3$), 2.40–2.61 (br, 8H, $NCH_2$), 4.96–5.06 (m, 2H, $C_{16}$-αH, $C_{17}$-αH), 7.24–7.31 (m, 3H), 7.77 (d, 1H, *J* = 6.92Hz), 8.05 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.39, 13.51, 19.97, 20.43, 24.46, 28.65, 31.21, 31.97, 32.37, 34.29, 36.00, 37.69, 37.74, 42.91, 45.73, 46.02, 48.60, 49.27, 53.85, 54.26, 55.48, 63.74, 79.08, 109.91, 120.03, 122.12, 122.92, 134.75, 141.83, 142.99, 170.16. Anal. Calcd. for $C_{33}H_{48}N_4O_2$: C 74.40, H 9.08, N 10.52; Found C 74.29, H 9.16, N 10.44. MS (*m*/*z*):533[M + 1]$^+$.

*5.1.6.26. 16β-(1H-benzimidazol-1-yl)-3β-diethylamino-5α-androstan-17β-yl acetate (**19e**).* White solid. Yield 90%. m.p. 202–204 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.82 (s,3H, $CH_3$-19), 1.01 (s,3H, $CH_3$-18), 1.40 (s, 3H, $OCOCH_3$), 2.64 (s, 4H, $NCH_2$), 4.96–5.06 (m, 2H, $C_{16}$-αH, $C_{17}$-αH), 7.24–7.31 (m, 3H), 7.77 (d, 1H, *J* = 7.00Hz), 8.05 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ. 12.38, 13.50, 13.71, 19.98, 20.45, 24.38, 28.64, 31.14, 31.97, 32.38, 34.25, 36.01, 37.68, 37.70, 42.91, 45.71, 48.62, 49.33, 53.88, 54.25, 64.02, 79.10, 109.92, 120.02, 122.16, 122.94, 134.75, 141.83, 142.97, 170.16. Anal. Calcd. for $C_{32}H_{47}N_3O_2$: C 76.00, H 9.37, N 8.31; Found C 76.12, H 9.29, N 8.40. MS (*m*/*z*):506[M + 1]$^+$.

*5.1.6.27. 16β-(1H-benzimidazol-1-yl)-3β-(N-methylphenylamino)-5α-androstan-17β-yl acetate (**19f**).* White solid. Yield 79%. m.p. 236–240 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.89 (s,3H, $CH_3$-19), 1.03 (s,3H, $CH_3$-18), 1.40 (s, 3H, $OCOCH_3$), 2.79 (s, 3H, N–$CH_3$), 4.96–5.06 (m, 2H, $C_{16}$-αH, $C_{17}$-αH), 6.69 (t, 1H), 6.79 (d, 2H, *J* = 8.12Hz), 7.20–7.30 (m, 5H), 7.77 (d, 1H, *J* = 6.92Hz), 8.06 (s, 1H). $^{13}$C NMR(150 MHz,$CDCl_3$): δ 12.51, 13.56, 20.01, 20.52, 24.98, 28.50, 29.71, 31.41, 31.58, 31.95, 32.42, 34.35, 35.90, 37.73, 37.91, 42.94, 46.16, 48.63, 53.89, 54.27, 58.29, 79.10, 109.95, 113.27, 116.41, 120.07, 122.18, 122.99, 129.13, 141.85, 150.20, 170.20. Anal. Calcd. for $C_{35}H_{45}N_3O_2$: C 77.88, H 8.40, N 7.79; Found C 77.91, H 8.32, N 7.87. MS (*m*/*z*):540[M + 1]$^+$.

*5.1.6.28. 16β-(1H-benzimidazol-1-yl)-3β-(N-benzylmethylamino)-5α-androstan-17β-yl acetate (**19g**).* White solid. Yield 72%. m.p. 201–203 °C; $^1$H NMR(400 MHz,$CDCl_3$): δ 0.84 (s,3H, $CH_3$-19), 1.00 (s,3H, $CH_3$-18), 1.41 (s, 3H, $OCOCH_3$), 2.29 (s, 3H, N–$CH_3$), 3.72 (s, 2H, $PhCH_2$), 4.96–5.06 (m, 2H, $C_{16}$-αH, $C_{17}$-αH), 6.70 (t, 1H), 6.79 (d, 2H, *J* = 8.14Hz), 7.23 (t, 2H), 7.21–7.31 (m, 4H), 7.77 (d, 1H, *J* = 6.96Hz), 8.05 (s, 1H). $^{13}$C

NMR(150 MHz,$CDCl_3$): $\delta$ 12.41, 13.74, 17.12, 19.18, 20.19, 23.54, 28.68, 29.26, 30.06, 30.94, 31.62, 35.48, 36.03, 37.27, 37.66, 45.25, 45.79, 49.89, 53.82, 55.93, 57.64, 62.25, 65.58, 79.84, 110.20, 120.23, 122.17, 122.90, 127.27, 128.37, 129.30, 130.94, 142.89, 169.38. Anal. Calcd. for $C_{36}H_{47}N_3O_2$: C 78.08, H 8.55, N 7.59; Found C 78.13, H 8.47, N 7.62. MS ($m/z$):554[M + 1]$^+$.

### 5.2. Biology

#### 5.2.1. Cell lines and culture conditions

Cell lines SW480, A549, HepG2, HeLa, SiHa and 293 used in this work, were purchased from China Centre for Type Culture Collection (Wuhan, China). SW480, A549 and HepG2 cells were grown in RPMI 1640 supplemented with 10% fetal bovine serum (FBS), 100U/ml penicillin and 100 μg/ml streptomycin at 37°Cwith 5% $CO_2$ in a humidified atmosphere. HeLa, SiHa and 293 cells were grown in Dulbecco's modified Eagle's medium (DMEM) supplanted with FBS and aitibiotics as described above for RPMI 1640. Fresh medium was given every second day and on the day before the experiments were done.

#### 5.2.2. Cell viability assay(MTT)

The anticancer activity in vitro was measured using the MTT assay. The assay was carried out according to previous study [59,60]. Exponentially growing cells were plated in 96-well plates at a concentration of $1 \times 10^4$ cells/well, and incubated for 24 h at 37 °C. The cells in the wells were respectively treated with target compounds at various concentrations for 48 h. Then, 20 μL MTT (5 mg/mL) was added to each well and incubated for 4 h at 37 °C. After the supernatant was discarded, 100 μL DMSO was added to each well, and the absorbance values were determined by a microplate reader (Bio-Rad Instruments) at 570 nm. Effects of the drug on cell viability were calculated using cells treated with DMSO as control. $IC_{50}$ values, determined in μM, were obtained by a linear regression analysis of the concentration-response curves obtained for each compound. Assays were performed in triplicate on three independent experiments.

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## References

[1] J.L. Everett, J.J. Roberts, W.C.J. Ross, J. Chem. Soc. (1953) 2386–2392.
[2] L.A. Shervington, N. Smith, E. Norman, T. Ward, R. Phillips, A. Shervington, Eur. J. Med. Chem. 44 (2009) 2944–2951.
[3] A. McLean, D. Newell, G. Baker, T. Connors, Biochem. Pharmacol. 29 (1980) 2039–2047.
[4] K. Loven, L. Stein, K. Furst, S. Levy, Clin. Ther. 24 (2002) 990–1000.
[5] A. Skladanowski, J. Konopa, Biochem. Pharmacol. 46 (1993) 375–382.
[6] M.C. Wani, H.L. Taylor, M.E. Wall, P. Coggon, A.T. McPhail, J. Am. Chem. Soc. 93 (1971) 2325–2327.
[7] A. Chugun, K. Temma, T. Oyamada, N. Suzuki, Y. Kamiya, Y. Hara, T. Sasaki, H. Kondo, T. Akera, Can. J. Physiol. Pharmacol. 78 (2000) 329–338.
[8] T. Ohga, T. Uchiumi, Y. Makino, K. Koike, M. Wada, M. Kuwano, K. Kohno, J. Bio. Chem. 273 (1998) 5997–6000.
[9] Y. Wang, M. Tamara, Biochem. Pharmacol. 68 (2004) 2031–2042.
[10] S.N. Khan, B.J. Kim, H. Kim, Bioorg. Med. Chem. Lett. 17 (2007) 5139–5142.
[11] G.A. Elmegeed, H.H. Ahmed, J.S. Hussein, Eur. J. Med. Chem. 40 (2005) 1283–1294.
[12] C. Salmi, C. Loncle, Y. Letourneux, J.M. Brunel, Tetrahedron 64 (2008) 4453–4459.
[13] E.J. Jacobsen, J.M. McCall, D.E. Ayer, F.J. VanDoornik, J.R. Palmer, K.L. Belonga, J.M. Braughler, E.D. Hall, D.J. Houser, et al., J. Med. Chem. 33 (1990) 1145–1151.
[14] C. Bubert, M.P. Leese, M.F. Mahon, E. Ferrandis, S. Regis-Lydi, P.G. Kasprzyk, S.P. Newman, Y.T. Ho, A. Purohit, M.J. Reed, B.V.L. Potter, J. Med. Chem. 50 (2007) 4431–4443.
[15] M.P. Leese, F.L. Jourdan, K. Gaukroger, M.F. Mahon, S.P. Newman, P.A. Foster, C. Stengel, S. Regis-Lydi, E. Ferrandis, A. Di Fiore, G. De Simone, C.T. Supuran, A. Purohit, M.J. Reed, B.V.L. Potter, J. Med. Chem. 51 (2008) 1295–1308.
[16] V. Kaklamani, R.M. O'Regan, Oncology 17 (2003) 335–342.
[17] X. Li, S.M. Singh, J. Cote, S. Laplante, R. Veilleux, F. Labrie, J. Med. Chem. 38 (1995) 1456–1461.
[18] H.J. Mitchell, W.P. Dankulich, G.D. Hartman, T. Prueksaritanont, A. Schmidt, R.L. Vogel, C. Bai, S. McElwee-Witmer, H.Z. Zhang, F. Chen, C. Leu, D.B. Kimmel, W.J. Ray, P. Nantermet, M.A. Gentile, M.E. Duggan, R.S. Meissner, J. Med. Chem. 52 (2009) 4578–4581.
[19] Q. He, D. Jiang, Leuk. Res. 23 (1999) 369–372.
[20] J. Roy, P. DeRoy, D. Poirier, J. Combin. Chem. 9 (2007) 347–358.
[21] R. Minorics, T. Szekeres, G. Krupitza, P. Saiko, B. Giessrigl, J. Woelfling, E. Frank, I. Zupko, Steroids 76 (2011) 156–162.
[22] K.A. Latham, A. Zamora, H. Drought, S. Subramanian, A. Matejuk, H. Offner, E.F. Rosloniec, J. Immunol. 171 (2003) 5820–5827.
[23] D. Hosking, C.E. Chilvers, C. Christiansen, P. Ravn, R. Wasnich, P. Ross, M. McClung, A. Balske, D. Thompson, M. Daley, A.J. Yates, N. Engl. J. Med. 338 (1998) 485–492.
[24] R.W. Hartmann, M. Hector, B.G. Wachall, A. Palusczak, M. Palzer, V. Huch, M. Veith, J. Med. Chem. 43 (2000) 4437–4445.
[25] M.A. Fousteris, U. Schubert, D. Roell, J. Roediger, N. Bailis, S.S. Nikolaropoulos, A. Baniahmad, A. Giannis, Bioorg. Med. Chem. Lett. 18 (2010) 6960–6969.
[26] E.J. Jacobsen, J.M. McCall, D.E. Ayer, F.J. VanDoornik, J.R. Palmer, K.L. Belonga, J.M. Braughler, E.D. Hall, D.J. Houser, M.A. Krook, T.A. Runge, J. Med. Chem. 33 (1990) 1145–1151.
[27] David S. Savage, Cancer Letters 2 (1977) 267–272.
[28] S. Dubey, P. Piplani, D.P. Jindal, Chem. Biodivers 1 (2004) 1529–1536.
[29] R. Bansal, S. Guleria, Steroids 73 (2008) 1391–1399.
[30] S. Dubey, P. Kaur, D.P. Jindal, Y.D. Satyanarayan, P. Piplani, Med. Chem. 4 (2008) 229–236.
[31] B.S. Holla, K.V. Malini, B.S. Rao, B.K. Sarojini, N.S. Kumari, Eur. J. Med. Chem. 38 (2003) 313–318.
[32] A. Khalaj, M. Nakhjiri, A.S. Negahbani, M. Samadizadeh, L. Firoozpour, S. Rajabalian, N. Samadi, M.A. Faramarzi, N. Adibpour, A. Shafiee, A. Foroumadi, Eur. J. Med. Chem. 46 (2011) 65–70.
[33] W. Zhao, J. Wang, Z. Li, Z. Yang, Bioorg. Med. Chem. Lett. 16 (2006) 6107–6111.
[34] K. Sztanke, T. Tuzimski, J. Rzymowska, K. Pasternak, M. Kandefer-Szerszen, Eur. J. Med. Chem. 43 (2008) 404–419.
[35] S.A.F. Rostom, I.M. El-Ashmawy, H.A. Abd El Razik, M.H. Badr, M.A. Hayam Ashour, Bioorg. Med. Chem. 17 (2009) 882–895.
[36] A.A. Bekhit, T. Abdel-Aziem, Bioorg. Med. Chem. 12 (2004) 1935–1945.
[37] M. Bulbul, N. Saracoglu, K.O. Irfan, M. Ciftci, Bioorg. Med. Chem. 10 (2002) 2561–2567.
[38] D. Valdez-Padilla, S. Rodriguez-Morales, A. Hernandez-Campos, F. Hernandez-Luis, L. Yepez-Mulia, A. Tapia-Contreras, Ra. Castillo, Bioorg. Med. Chem. 17 (2009) 1724–1730.
[39] F. Hernandez-Luis, A. Hernandez-Campos, R. Castillo, G. Navarrete-Vazquez, O. Soria-Arteche, M. Hernandez-Hernandez, L. Yepez-Mulia, Eur. J. Med. Chem. 45 (2010) 3135–3141.
[40] W. Li, D. Hwang, J. Song, C. Chen, J. Chuu, C. Hu, H. Lin, C. Huang, C. Huang, H. Tseng, C. Lin, T. Chen, C. Lin, H. Wang, C. Shen, C. Chang, Y. Chao, C. Chen, J. Med. Chem. 53 (2010) 2409–2417.
[41] M.M. Ramla, M.A. Omar, A.M. El-Khamry, H.I. El-Diwani, Bioorg. Med. Chem. 14 (2006) 7324–7332.
[42] J.P. Burkhart, P.M. Weintraub, C.A. Gates, R.J. Resvick, R.J. Vaz, D. Friedrich, M.R. Angelastro, P. Bey, N.P. Peet, Bioorg. Med. Chem. 10 (2002) 929–934.
[43] Y. Ling, J. Li, Y. Liu, K. Kato, G.T. Klus, A. Brodie, J. Med. Chem. 40 (1997) 3297–3304.
[44] V.C.O. Njar, K. Kato, I.P. Nnane, D.N. Grigoryev, B.J. Long, A.M.H. Brodie, J. Med. Chem. 41 (1998) 902–912.
[45] V.D. Handratta, T.S. Vasaitis, V.C.O. Njar, L.K. Gediya, R. Kataria, P. Chopra, D. Newman Jr., R. Farquhar, Z. Guo, Y. Qiu, A.M.H. Brodie, J. Med. Chem. 48 (2005) 2972–2984.
[46] V.M.A. Moreira, T.S. Vasaitis, V.C.O. Njar, J.A.R. Salvador, Steroids 72 (2007) 939–948.
[47] V.M.A. Moreira, T.S. Vasaitis, Z. Guo, V.C.O. Njar, J.A.R. Salvador, Steroids 73 (2008) 1217–1227.
[48] M.A.E. Pinto-Bazurco Mendieta, M. Negri, C. Jagusch, U. Mueller-Vieira, T. Lauterbach, R.W. Hartmann, J. Med. Chem. 51 (2008) 5009–5018.
[49] D. Ondre, J. Woelfling, I. Toth, M. Szecsi, J. Julesz, G. Schneider, Steroids 74 (2009) 1025–1032.
[50] T. Kam, K. Sim, T. Koyano, M. Toyoshima, M. Hayashi, K. Komiyama, J. Nat. Prod. 61 (1998) 1332–1336.
[51] B.R. Moser, J. Nat. Prod. 71 (2008) 487–491.
[52] J.J. Poza, R. Fernandez, F. Reyes, J. Rodriguez, C. Jimenez, J. Org. Chem. 73 (2008) 7978–7984.
[53] F. Leonessa, J. Kim, A. Ghiorghis, R.J. Kulawiec, C. Hammer, A. Talebian, R. Clarke, J. Med. Chem. 45 (2002) 390–398.

[54] A.H. Banday, B.P. Mir, I.H. Lone, K.A. Suri, H.M.S. Kumar, Steroids 75 (2010) 805–809.
[55] J. Provencher-Mandeville, C. Debnath, S.K. Mandal, V. Leblanc, S. Parent, E. Asselin, G. Berube, Steroids 76 (2011) 94–103.
[56] B.H. Walker, J. Org. Chem. 32 (1967) 1098–1103.
[57] K.E. Harding, L.M. May, K.F. Dick, J. Org. Chem. 40 (1975) 1664–1665.
[58] F.A. Luzzio, F.S. Guziec Jr., Org. Prep. Proced. Int. 20 (1988) 533–584.
[59] T. Mosmann, J. Immunol. Methods 65 (1983) 55–63.
[60] M. El-Far, G.A. Elmegeed, E.F. Eskander, H.M. Rady, M.A. Tantawy, Eur. J. Med. Chem. 44 (2009) 3936–3946.