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Synthesis of Two Benzamide-Androgen Derivatives

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In this study, two benzamide-androgen derivatives (N-(3-butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-N´-[2-(17-hydroxy-10,13-dimethyl-hexadecahydro-cyclo penta[a]phenanthren-3-ylideneamino)ethyl]-4-(naphtalen-2-yloxy)benzamide and N-(3-butyl-1-cyclohexyl-4-cyclohexyliminoazetidin-2-ylidene)-N´-[2-(3-hydroxy-10,13-dimethyl-hexadecahydro-cyclopenta[a]phenanthren-17-ylideneamino)ethyl]-4-(naphtalen-2-yloxy)benzamide were synthesized using some strategies. The structure of the compounds was confirmed by elemental analysis, spectroscopy and spectrometry data. The proposed method offers some advantages such as simple procedure, low cost and ease of workup.

Keywords: Dihydrotestosterone androsterone, Boric acid.

INTRODUCTION

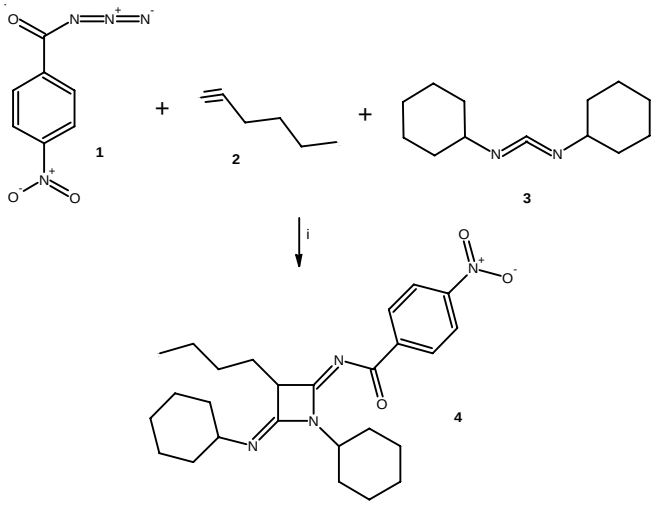
Since years ago, several androgen derivatives have been developed for example, synthesis of 17β-[N-methyl-N-(amino ethyl)amino-5α-androsterone by reduction of oxime-androsterone derivative using lithium aluminium hydride[1]. Literature reported the preparation of 17α-(tributylstannylethynyl)-4-androsten-17-ol-3-one by the reaction of 17-ethynyl-4-androsten-17-ol-3-one with Bu_3SnOMe[2]. In addition, other study described the synthesis of (17S)-spiro-3,3-(dimethoxy)-5α-androstan-17β,2´-oxirane by the reaction of 3,3-(dimethoxy)-5α-androstan-17-one with trimethylsulfonium iodide in DMF[3]. A synthesis of dehydroisoandrosterone derivative by the reaction between brucine derivative and dehydroisoandrosterone 3-sulfate using boric acid as catalyst is also reported[4]. Additionally, a study showed the preparation of a steroid-vitamin B1 derivatives by the reaction of dihydrotestosterone hemisuccinate with vitamin B1 using a carmodimide derivative as catalyst[5]. Also, other report showed the synthesis of an androsterone derivative by the reaction of androsterone with montelukast in presence of a carbodiimide derivative[6]. Additionally, other report[7] indicate the preparation of 17-(N-acetyl-4-imidazolyl)-3β-acetoxyandrost-5-ene by the reaction of 17β-(4-imidazolyl)androst-5-en-3-ol in pyridine/Ac_2O. Other studies made by Acs *et al.*[8] showed the synthesis of 11-carboxamidoandrostan-4,9-diene using palladium as catalyst. All these experimental results show several procedures which are available for synthesis of diverse androgen derivatives. Nevertheless, in some experimental methods expensive reagents and special conditions are required. Therefore, in this study, two androgen derivatives were synthesized using some strategies.

EXPERIMENTAL

The compounds evaluated in this study were purchased from Sigma-Aldrich Co. Ltd. The melting points for the different compounds were determined on an electrothermal (900 model). Infrared spectra (IR) were recorded using KBr pellets on a Perkin Elmer Lambda 40 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-300/5 FT NMR spectrometer at 300 and 75.4 MHz in $CDCl_3$ using TMS as internal standard. EIMS spectra were obtained with a Finnigan Trace GC Polaris Q. spectrometer. Elementary analysis data were acquired from a Perkin Elmer Ser. II CHNS/0 2400 elemental analyzer.

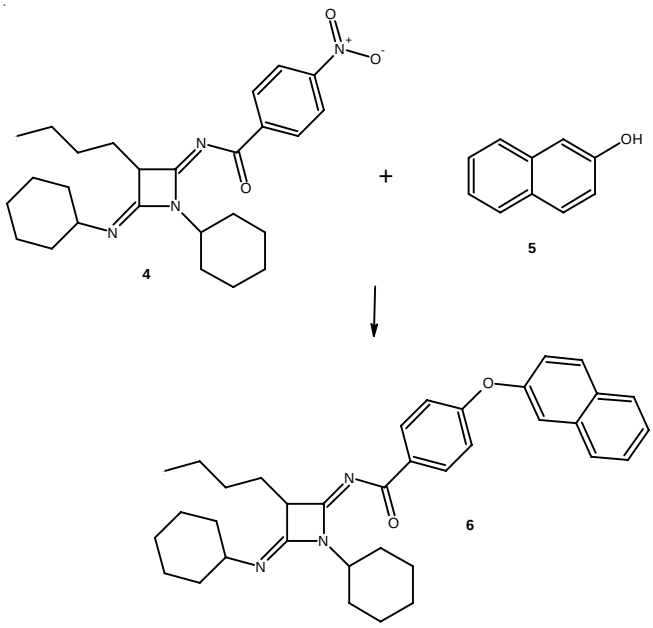
Synthesis of N-(3-butyl-1-cyclohexyl-4-cyclohexyl-imino-azetidin-2-ylidene)-4-nitrobenzamide (4): A solution

of 4-nitrobenzoyl azide (100 mg, 0.52 mmol), alkyne-1 (70 μL, 0.61 mmol), N,N'-dicyclohexylcarbodiimide (110 mg, 0.53 mmol) and anhydrous cupric chloride (100 mg, 0.74 mmol) in 5 mL of methanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform (**Scheme-I**). The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (3:1) yielding 69 % of product, m.p. 240-242 °C; IR (KBr, ν_{max}, cm^{-1}): 3338, 1648 and 1350; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 0.86 (s, 3H), 1.10-1.42 (m, 14H), 1.48 (m, 2H), 1.52-1.54 (m, 3H), 1.58 (t, 2H, *J* = 6.96 Hz), 1.62-1.66 (m, 3H), 1.80-1,90 (m, 2H), 3.16-3.22 (m, 2H), 4.70 (m, 1H), 8.00-8.10 (m, 4H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ_C: 14.12, 23.00, 23.12, 24.38, 25.38, 26.06, 26.30, 29.06, 29.70, 32.20, 38.64, 57.86, 59.70, 124.10, 131.12, 131.15, 134.46, 142.00, 152.50, 164.02, 175.80 ppm. EI-MS *m/z*: 452.24 (M^+ 12). Anal. Calcd. for $C_{26}H_{36}N_4O_3$: C, 69.00; H, 8.02; N, 2.38; O, 10.61; found: C, 68.98; H, 8.00.



Scheme-I: Synthesis of N-(3-butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-4-nitrobenzamide (**4**) using three components system (4-nitrobenzoyl azide (**1**) alkyne-1 (**2**) and N,N'-dicyclohexylcarbodiimide (**3**)); (i) = anhydrous cupric chloride

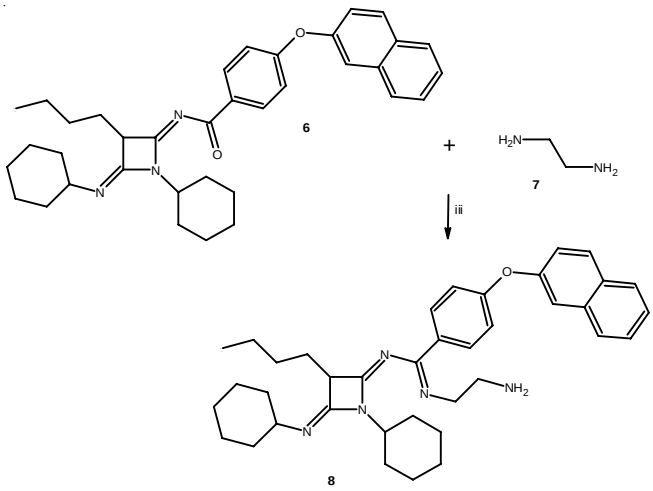
Synthesis of N-(3-butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-4-(naphthalen-2-yloxy)benzamide (6): A solution of **4** (100 mg, 0.22 mmol), β-naphthol (40 mg, 0.27 mmol) and anhydrous potassium carbonate (50 mg, 0.36 mmol) in 5 mL of dimethyl sulfoxide was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform (**Scheme-II**). The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (3:2) yielding 48 % of product, m.p. 274-276 °C; IR (KBr, ν_{max}, cm^{-1}): 3334, 1648 and 1250; H NMR (300 MHz, $CDCl_3$) δ_H: 0.86 (s, 3H), 1.02-1.42 (m, 14H), 1.44 (m, 2H), 1.50-1.54 (m, 3H), 1.59 (t, 2H, *J* = 6.00 Hz), 1.62-1.66 (m, 3H), 1.78-1.90 (m, 2H), 3.14-3.18 (m, 2H), 4.70 (m, 1H), 6.90-8.36 (m, 11H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ_C: 14.00, 23.00, 23.12, 24.38, 25.4, 26.00, 26.30, 29.02, 29.70, 32.18, 38.70, 57.78, 59.74, 110.90, 118.60, 119.44, 120.70, 123.04, 124.08, 125.95, 127.67, 130.36, 131.00, 132.56, 134.36, 151.86, 164.10, 164.56, 175.84 ppm.



Scheme-II: Synthesis of N-(3-butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-4-(naphthalen-2-yloxy)benzamide (**6**) by the reaction of **4** with β-naphthol (**5**); (ii) = K_2CO_3/DMSO

EI-MS *m/z*: 549.32 (M^+ 12). Anal. Calcd. for $C_{36}H_{43}N_3O_2$: C, 78.65; H, 7.88; N, 7.64; O, 5.82; found: C, 78.62; H, 7.86.

Synthesis of N-(2-aminoethyl)-N´-(butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-4-(naphthalen-2-yloxy)benzamide (8): A solution of **6** (100 mg, 0.17 mmol), ethylenediamine (40 μL, 0.60 mmol) and boric acid (40 mg, 0.64 mmol) in 5 mL of methanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform (**Scheme-III**). The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (4:2) yielding 78 % of product, m.p. 260-262 °C; IR (KBr, ν_{max}, cm^{-1}): 3382, 3332 and 1244; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 0.86 (s, 3H), 1.02-1, 42 (m, 14H), 1.48 (m, 2H), 1.50-1.53 (m, 3H), 1.56) m, 2H), 1.62-1.66 (m, 3H), 1.74-1.90 (m, 2H), 3.12 (m, 1H),

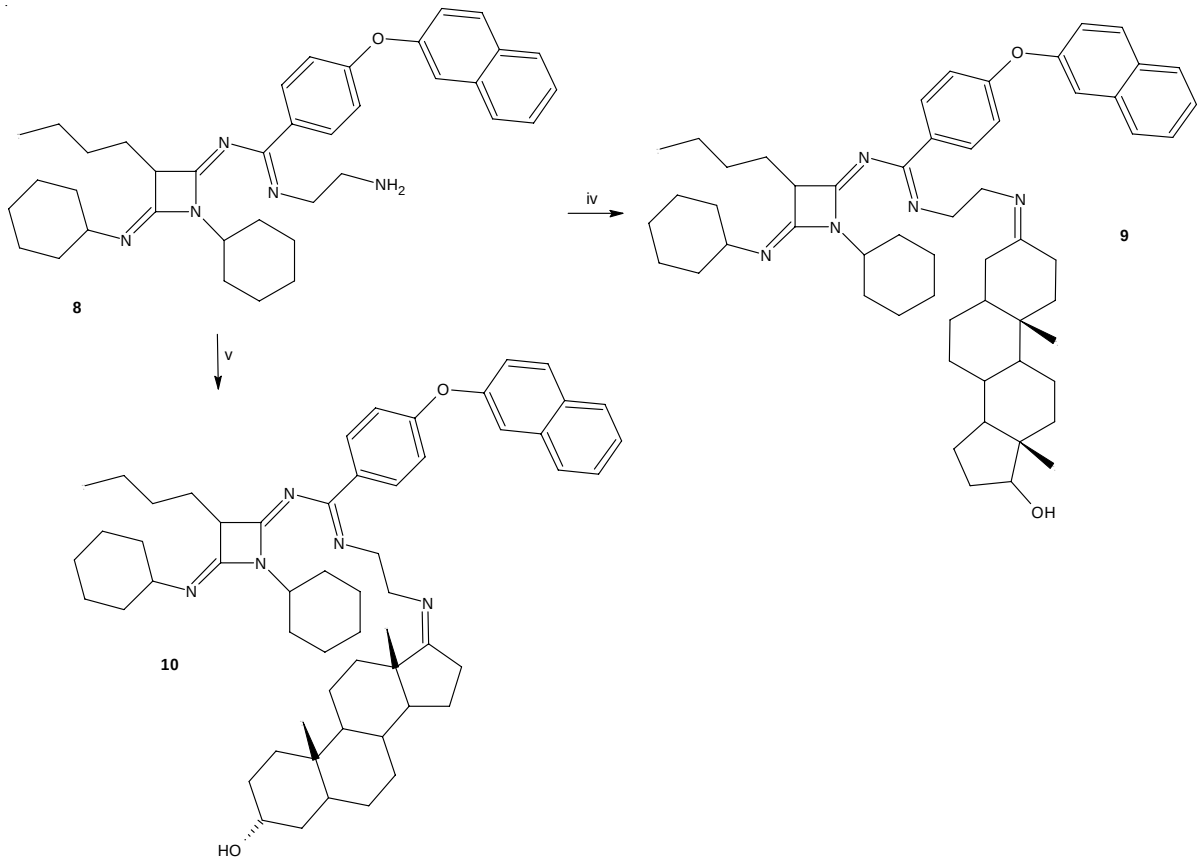


Scheme-III: Synthesis of N-(2-amino-ethyl)-N´-(butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-4-(naphthalen-2-yloxy)-benzamide (**8**) by the reaction of **6** with ethylenediamine; (iii) = boric acid

3.16 (t, 2H, *J* = 6.44), 3.22 (m, 1H), 3.60 (t, 2H, *J* = 6.44 Hz), 4.30 (broad, 2H), 5.10 (m, 1H), 7.00-7.90 (m, 11H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ_C: 14.12, 23.00, 23.10, 23.07, 24.38, 25.40, 26.00, 26.30, 28.88, 29.84, 32.20, 41.06, 41.90, 53.00, 59.36, 59.70, 110.90, 119.50, 120.56, 120.79, 123.00, 124.10, 125.95, 127.64, 129.42, 130.36, 131.04, 133.19, 137.48, 155.20, 156.38, 157.76, 161.36 ppm. EI-MS *m/z*: 591.38 (M^+ 12). Anal. Calcd. for $C_{38}H_{49}N_5O$: C, 77.12; H, 8.35; N, 11.83; O, 2.70; found: C, 77.10; H, 8.34.

Synthesis of N-(3-butyl-1-cyclohexyl-4-cyclohexyl-imino-azetidin-2-ylidene)-N´-[2-(17-hydroxy-10,13-dimethyl-hexadecahydro-cyclopenta[a]phenanthren-3-ylidene amino)ethyl]-4-(naphthalen-2-yloxy)benzamide (9): A solution of **8** (200 mg, 0.34 mmol), dihydrotestosterone (100 mg, 0.34 mmol) and boric acid (40 mg, 0.64 mmol) in 5 mL of methanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform. The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (3:2) yielding 52 % of product, m.p. 248-250 °C; IR (KBr, ν_{max}, cm^{-1}): 3420, 3336 and 1252; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.76 (s, 3H), 0.86 (s, 3H), 0.90 (s, 3H), 0.98-1.04 (m, 3H), 1.08 (m, 2H), 1.10 (m, 1), 1.14 (m, 2H), 1.16 (m, 1H), 1.20 (m, 2H), 1.25 (m, 1H), 1.30 (m, 1H), 1.32-1.36 (m, 3H), 1.38 (m, 2H), 1.39 (m, 1H), 1.42-1.46 (m, 4H), 1.47 (m, 1H), 1.48 (m, 1H), 1.50 (m, 2H), 1.51 (m, 1H), 1.53 (m, 1H), 1.59 (m, 2H), 1.61 (m, 1H), 1.64 (m, 1H), 1.65 (m, 2H), 1.68-1.74 (m, 4H), 1.80 (m, 1H), 1.92 (m, 1H), 1.98-2.30 (m, 3H), 3.14-3.20 (m, 2H), 3.50 (t, 2H, *J* = 6.54 Hz), 3.54 (t, 2H, *J* = 6.54 Hz), 3.60 (m, 1H), 5.10 (m, 1H), 6.20 (broad, 1H), 7.00-7.90 (m, 11H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ_C: 11.36, 14.12, 15.70, 20.80, 23.00, 23.10, 23.90, 24-00, 24.45, 25.40, 26.00, 28.50, 28.68, 29.64, 30.37, 30.55, 31.40, 32.27, 32-65, 35.10, 35.38, 36.25, 36.70, 37.71, 44.50, 44.88, 47.89, 51.60, 51.70, 52.08, 53.20, 54.10, 59.74, 82.33, 110.88, 119.58, 120.66, 120.79, 123.00, 124.13, 125.95, 127.64, 130.36, 131.00, 131.73, 133.21, 137.50, 153.38, 155.16, 156.38, 157.80, 161.22 ppm. EI-MS *m/z*: 863.60 (M^+ 12). Anal. Calcd. for $C_{57}H_{77}N_5O_2$: C, 79.21; H, 8.98; N, 8.10; O, 3.70; found: C, 79.20; H, 8.94.

Synthesis of N-(3-butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-N´-[2-(3-hydroxy-10,13-dimethylhexa-decahydro-cyclopenta[a]phenanthren-17-ylidene amino)-ethyl]-4-(naphtalen-2-yloxy)benzamide (10): A solution of **8** (200 mg, 0.34 mmol) androsterone (100 mg, 0.34 mmol) and boric acid (40 mg, 0.64 mmol) in 5 mL of methanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform (**Scheme-IV**). The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (3:1) yielding 46 % of product, m.p. 158-160 °C; IR (KBr, ν_{max}, cm^{-1}): 3406, 3330 and 1254; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.86 (s, 3H), 0.90 (s, 3H), 0.96 (m, 1H), 1.02 (s, 3H), 1.04 (m, 1H), 1.07 (m, 2H), 1.12 (m, 1H), 1.16-1.24 (m, 5H), 1.26 (m 1H), 1.30-1.36 (m, 3H), 1.37-1.38 (m, 4H), 1.42 (m, 2H), 1.45-1.46 (m, 2H), 1.47 (m, 2H), 1.48 (m, 2H), 1.51-1.54 (m,



Scheme-IV: Synthesis of two benzamide-steroid derivatives. First stage: Reaction of **8** with dihydrotestosterone to form the compound **9**. Second stage: Synthesis of **10** by the reaction of **8** with androsterone; (iv) and (v) = boric acid

3H), 1.59 (t, 2H, *J* = 1.09 Hz), 1.60 (m, 1H), 1.61 (m, 1H), 1.64 (m, 3H), 1.65 (m, 2H), 1.68-1.74 (m, 2H), 1.76 (m, 1H), 1.88 (m, 1H), 1.90 (m, 1H), 1.92-2.62 (m, 5H), 2.90 (broad, 1H), 3.12-3.20 (m, 2H), 3.50 (t, 2H, *J* = 10.00 Hz), 3.54 59 (t, 2H, *J* = 10.00 Hz), 3.74 (m, 1H), 5.10 (m, 1H), 7.00-7.90 (m, 11H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ_C: 14.12, 15.68, 18.38, 19.40, 21.83, 23.00, 23.12, 24.45, 25.34, 26.06, 27.58, 28.59, 29.68, 29.70, 30.37, 32.26, 32.27, 33.68, 33.93, 34.21, 34.64, 34.97, 36.23, 41.08, 41.59, 44.88, 50.28, 51.56, 52.78, 54.10, 55.63, 59.74, 69.24, 110.90, 119.58, 120.66, 120.73, 123.00, 124.13, 125.95, 127.64, 130.36, 131.00, 131.70, 133.18, 137.50, 155.18, 156.40, 157.78, 161.34, 176.76 ppm. EI-MS *m/z*: 863.60 (M^+ 12). Anal. Calcd. for $C_{57}H_{77}N_5O_2$: C, 79.21; H, 8.98; N, 8.10; O, 3.70; found: C, 79.20; H, 8.94.

RESULTS AND DISCUSSION

Many procedures for formation of benzamide derivatives are available in the literature. Nevertheless, despite their wide scope, these procedures suffer from several drawbacks. Some reagents are of limited stability and preparation can be dangerous[9-11]. Therefore, in this study we report a straight forward route for the synthesis of two new benzamide-androgen derivatives. The first step involves preparation of N-(3-butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-4-nitrobenzamide (**4**) using the three component system (*p*-nitrobenzoylazide, N,N'-dicyclohexylcarbodiimide and 1-hexyne) in presence of anhydrous cupric chloride. It is important to mention that the reaction mechanism involved may be through a [2 + 2] cycloaddition such as happening with other type of compounds[12]. ^{1}H NMR spectrum of **4** shows signals at 0.86 ppm for methyl group at 1.10-1.42, 1.52-1.54, 1.62-1.66 and 3.16-3,22 ppm for both cyclohexane rings; at 1.48, 1.58 and 1.80-1.90 ppm for methylene groups of arm bound to azetidine ring; at 4.70 ppm for proton involved in the azetidine ring at 8.00-8.10 ppm for phenyl group. The ^{13}C NMR spectra displays chemical shifts at 14.12 for methyl group 23.00, 24.38-26.30, 32,20, 57.86 and 59.70 ppm for both cyclohexane rings; at 23.12, 29.06-29.70 ppm for methylene groups involved in the arm bound to azetidine ring; at 38.64 ppm for azetidine ring at 134.46 and 164.02 ppm for both imino groups at 124.10-131.12 and 142.00-152.50 ppm for phenyl group; at 175.80 ppm for amide group. Finally, the presence of **4** was further confirmed from mass spectrum which showed a molecular ion at *m/z* 452.24.

The second stage was achieved by the synthesis of N-(3-butyl-1-cyclohexyl-4-cyclohexyl imino-azetidin-2-ylidene)-4-(naphthalen-2-yloxy)benzamide (**6**) *via* displacement of nitro group from the compound **4**. It is important to mention that there are several methods for displacement of nitro groups[13,14] using a dipolar aprotic solvent such as DMSO[15]. In general, dipolar solvents are used to attain high yield of ether groups; therefore, in this study the compound **6** was synthetized by the reaction of **4** with ß-naphthol in presence of dimethylsulfoxide at mild conditions. The ^{1}H NMR spectrum of **4** shows signals at 0.86 ppm for methyl group at 1,02-1.42, 1.50-1.54, 1.62-1.66 and 3.18 ppm for both cyclohexane rings at 1.44, 1.59 and 1.78-1.90 ppm for methylene groups involved in the arm bound to azetidine ring at 4.70 ppm for azetidine group; at 6.90-8.36 ppm for phenyl groups. The ^{13}C NMR spectra displays chemical shifts at 14 ppm for methyl group; at 23, 24.38-26.30, 32.18 and 57.78-59.74 ppm for both cyclohexane rings; at 23.12 and 29.02-29.70 ppm for methylene groups of arm bound to azetidine ring; at 38.70 for azetidine ring; at 134.36 and 164.10 ppm for both imino groups; at 110.90-132.56, ppm for phenyl groups; at 151.86 and 164.56 ppm for ether group; at 175.84 ppm for amide group. Finally, the presence of **6** was further confirmed from mass spectrum which showed a molecular ion at *m/z* 549.32.

The third stage was achieved by the formation of new imino group involved in the chemical structure of N-(2-aminoethyl)-N´-(butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-4-(naphthalen-2-yloxy)benzamide (**8**). It is noteworthy that there are several reports for the synthesis of imino groups; nevertheless, expensive reagents and special conditions are required[16,17]. In this study, boric acid was used as catalyst to formation of imino group involved in the chemical structure of **8**. ^{1}H NMR spectrum of **8** shows signals at 0.86 ppm for methyl group; at 1.02-1.42, 1.50-1.53, 1.62-1.66, 3.12 and 3.22 ppm for both cyclohexane rings; at 1.48, 1.56 and 1.74-1.90 ppm for methylene groups involved in the arm bound to azetidine ring; at 3.16 and 3.60 ppm for methylene group bound to both amino and imino groups; at 4.30 ppm for amino group; at 5.10 ppm for azetidine group; at 7.00-7.90 for phenyl groups. The ^{13}C NMR spectra displays chemical shifts at 14.12 ppm for methyl group; at 23.00, 24.38-26.30, 32.20 and 59.36-59.70 ppm for both cyclohexane rings; at 23.00, 28.88-29.84 ppm for methylene group involved in the arm bound to azetidine ring; at 41.06 and 53 ppm for methylene groups of arm bound to both amino and imino groups; at 41.90 ppm for azetidine ring; at 110.90-133.19 ppm for phenyl groups; at 155.20 and 161.36 ppm for ether group; at 137.48, 156.38 and 157.76 ppm for imino groups. Finally, the presence of **8** was further confirmed from mass spectrum which showed a molecular ion at *m/z* 591.38.

The fourth stage was achieved by the reaction of **8** with dihydrotestosterone to formation of N-(3-butyl-1-cyclo hexyl-4-cyclohexylimino-azetidin-2-ylidene)-N´-[2-(17-hydroxy-10,13-dimethyl-hexadecahydro-cyclopenta[a]phenanthren-3-ylideneamino)ethyl]-4-(naphthalen-2-yloxy)benzamide (**9**) using boric acid as catalyst. ^{1}H NMR spectrum of **9** shows signals at 0.76-0.86 ppm for methyl groups bound to steroid nucleus; at 0.90 ppm for methyl group involved in the arm bound to azetidine ring at 0.98-1.04, 1.10, 1.16, 1.25, 1.32-1.36, 1.39, 1.48, 1. 51, 1.64, 1.68-1.74, 1.80, 1.98-2.30 and 3.60 ppm for steroid moiety; at 1.08, 1.14, 1.20, 1.30, 1.38, 1.42-1.46, 1.50, 1.53, 1.61, 1.65 and 3.14-3.20 ppm for both cyclohexane rings; at 1.47, 1.59, 1,76 and 1.92 ppm for methylene groups of arm bound to azetidine ring; at 3.50 and 3.54 ppm for methylene groups bound to both imino and amino groups; at 5.10 ppm for azetidine ring; at 6.20 ppm for hydroxyl group; at 7.00-7.90 ppm for phenyl groups. The ^{13}C NMR spectra displays chemical shifts at 11.36 and 15.70 ppm for methyl groups bound to steroid nucleus: at 14.12 ppm for methyl group involved in the arm bound to azetidine ring; at 20.80, 23.90-240.00, 28.68, 31.40, 32.65-44.50, 47.89, 52-08-53.20 and 82.33 ppm for steroid moiety; at 23.00, 24.45-26.00, 30.37, 32.27 and 54.10-59.74 ppm for both cyclohexane rings; at

23.18, 28.50 and 29.64 ppm for methylene groups of arm bound to azetidine ring; at 51.60 and 51.70 ppm for methylene groups bound to imino groups, at 44.88 ppm for azetidine ring; at 137.50, 153.38, 156.38 and 157.80 ppm for imino groups; at 155.16 and 161.22 ppm for ester group; at 110.88-133.21 ppm for phenyl groups. In addition, the presence of **9** was further confirmed from mass spectrum which showed a molecular ion at *m/z* 863.60.

Finally, the last stage was achieved with the synthesis of N-(3-butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidene)-N´-[2-(3-hydroxy-10,13-dimethyl-hexadecahydrocyclopenta-[a]phenanthren-17-ylideneamino)ethyl]-4-(naphthalen-2-yloxy)benzamide (**10**) by the reaction of **8** with androsterone using boric acid as catalyst. ^{1}H NMR spectrum of **10** shows signals at 0.86 and 1.02 ppm for methyl groups bound to steroid nucleus; at 0.90 ppm for methyl group involved in the arm bound to azetidine ring; at 0.96, 1.04, 1.12, 1.26, 1.37-1.38, 1.45-1.46, 1.60, 1,64, 1.68-1.74, 1.88, 1.92-2.62 and 3.74 ppm for steroid moiety; at 1.07, 1.16-1.24, 1.30-1.36, 1.42, 1.47, 1.51-1.54, 1.61, 1.65 and 3.12-3.20 ppm for both cyclohexane rings; at 1.48, 1.59 and 1.90 ppm for methylene groups involved in the arm bound to azetidine ring; at 2.90 ppm for hydroxyl group; at 3.50 and 3.54 ppm for methylene groups bound to both imino groups; at 5.10 ppm for azetidine ring; at 7.00-7.90 ppm for phenyl groups. The ^{13}C NMR spectra displays chemical shifts at 14.12 ppm for methyl group involved in the arm bound to azetidine ring; at 15.68 and 18.38 ppm for methyl groups bound to steroid nucleus; at 19.40-21.83, 27.58, 29.68, 32.26, 33.68-41.59, 50.28, 55.63 and 69.24 ppm for steroid moiety; at 23.00, 24.45-26.06, 30.57, 32.27 and 54.10 ppm for both cyclohexane rings; at 23.12, 28.59 and 28.70 ppm for methylene groups involved in the arm bound to azetidine ring; at 44.88 ppm for azetidine ring; at 51.56 and 52.78 ppm for methylene groups bound to both imino groups; at 59.74, 137.50, 156.40, 157.78 and 176.76 ppm for imino groups; at 155.18 and 161.34 ppm for ether group; at 110.90-133.18 ppm for phenyl groups. Finally, the presence of **10** was further confirmed from mass spectrum which showed a molecular ion at *m/z* 863.60.

Conclusion

This study reported some strategies for the synthesis of two benzamide-androgen derivatives. The proposed method offers some advantages such as simple procedure, low cost and ease of workup.

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