



Design and Synthesis of Two Steroid-Pyrrolo Derivatives using Estrone and Pregnenolone as Chemical Tools

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ABSTRACT

Several steroid-pyrrolo derivatives have been prepared using different protocols; nevertheless, have some drawbacks such as the use of some reagents that have limited stability and require special conditions. The aim of study involved the synthesis of two steroid-pyrrolo-triazecin derivatives using a series of reactions that involve; cycloaddition [2 + 2], displacement of nitro group, formation of shift base, amidation/cyclization using boric acid (Method A) or carbodiimide derivative (Method B). The results showed that there is a higher yielding with the method A in comparison with the method B. In addition, chemical structure of compounds was confirmed by NMR spectroscopic data.

Keywords: Estrone, pregnenolone, pyrrol, triazecin, steroid.

INTRODUCTION

For several years there has been interest on the preparation of some substituted pyrroles;

for example, the synthesis of the reaction of 1,4-diols with amines to form substituted pyrroles was developed¹. Other data² showed the synthesis of aryl-substituted pyrroles using the three-component

system (arylketones, 1,2-diols and amines) in presence of ruthenium. In addition, a pyrrole-steroid derivative³ was prepared by reaction of androsterone-arylidine with acenaphthylene-1,2-dione and 1,3-thiazolane-4-carboxylic acid. Other study showed a reaction regioselective palladium-catalyzed cyclization of internal alkynes and 2-amino-3-iodoacrylates to form some substituted pyrroles⁴. Also, another report indicated that the cationic N-heterocyclic carbene-gold(I) complex catalyzes the formation of tri- and tetra substituted pyrroles via the amino-Claisen rearrangement of *N*-propargyl α -enaminone derivatives and the cyclization of α -allenyl α -enaminone as intermediates⁵. Additionally, a study showed that a Lewis acid can activate to cyclopropanes which react with aliphatic, aromatic, and α,β -unsaturated nitriles via dipolar cycloaddition [3 + 2], following by dehydration, and a tautomerization sequence for preparation of pyrroles⁶. Another report indicated that the Dirhodium(II) reagent can be used in the three-component system (imine, diazoacetone, and an activated alkynyl) as catalyst to form substituted 1,2-diarylpyrroles⁷. In addition, a study showed that Au(I) reagent catalyzed the reaction of aryl-substituted with *N*-tosyl alkynyl aziridines to give 2,5-substituted

pyrroles⁸. Another study showed a rearrangement reaction of a propargylic-aziridine, catalyzed by $\text{PPh}_3\text{AuCl/AgOTf}$, forming some pyrrole derivatives⁹. Additionally, a report showed a direct synthesis of pyrroles by the reaction of imines, acid chlorides, and alkynes catalyzed by isocyanides is reported¹⁰. Other data showed the functional homologation of a α -ketoester with an aldehyde followed by an oxidation to form a series of different substituted 1,4-dicarbonyl compounds that can be rapidly cyclized with the Paal-Knorr procedure for synthesis some pyrrole derivatives¹¹. All these experimental results show different methods for the preparation of unsubstituted pyrrole; never the less. It is important to mention that there are some protocols that require hazardous reagents as well as different experimental conditions for the preparation of these compounds. Therefore, in this study two steroid-pyrrolo-triazecin derivatives were prepared using some chemical tools.

MATERIAL AND METHODS

General Chemical

The compounds evaluated in this study were purchased from Sigma-Aldrich Co., Ltd. The melting point of compounds was determined on

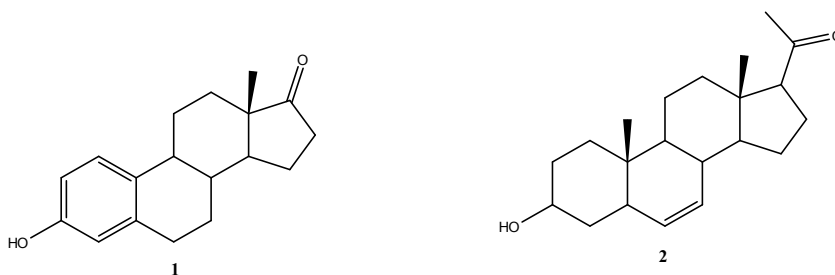


Fig. 1: Chemical structure of estrone (1) and pregnenolone (2)

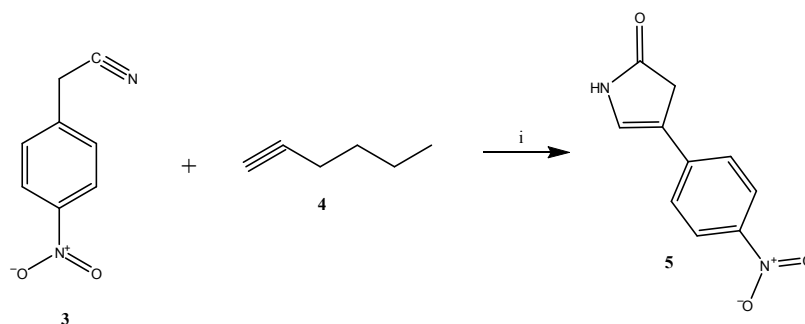


Fig. 2: Synthesis of 4-(4-nitrophenyl)1,3-dihydro-2H-pyrrol-2-one⁵. Reaction of 4-nitrophenylacetone nitrile³ with 6-chloro-1-hexyne⁴ to form 5. $i = \text{Et}_3\text{N/CHCl}_3$

an Electrothermal (900 model). Infrared spectra (IR) were recorded using KBr pellets on a Perkin Elmer Lambda 40 spectrometer. ^1H and ^{13}C NMR (nuclear magnetic resonance) spectra were recorded on a Varian VXR-300/5 FT NMR spectrometer at 300 and 75.4 MHz (megahertz) in CDCl_3 (deuteratedchloroform) using TMS (tetramethylsilane) as internal standard. EIMS (electron impact mass spectroscopy) spectra were obtained with a Finnigan Trace Gas Chromatography Polaris Q Spectrometer. Elementary analysis data were acquired from a Perkin Elmer Ser. II CHNS/O 2400 elemental analyzer.

Synthesis of 4-(4-nitrophenyl)1,3-dihydro-2H-pyrrol-2-one⁵

A solution of 4-nitrophenyl acetonitrile (200 mg, 1.23 mmol), 6-chloro-1-hexyne (180 μl , 1.38 mmol), and triethyl amine (220 μL , 1.56 mmol)

in 5 mL of chloroform was stirred for 72 h at room temperature. The reaction mixture was evaporated to dryness under reduced pressure, the residue washed 3 times with water. Then the precipitate was separated and dried at room temperature. The product yield was 66 %; m.p. 44-46 $^\circ\text{C}$; 1670 and 1600; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 3.22 (m, 2H), 7.28 (d, 1H), 7.44 (m, 2H), 8.02 (broad, 1H), 8.10 (m, 2H) ppm. ^{13}C NMR (75.4 Hz, CDCl_3) δ_{C} : 42.20 (C-3), 117.32 (C-4), 121.54 (C-9, C-11), 124.63 (C-5), 132.54 (C-8, C-12), 144.30 (C-10), 144.76 (C-7), 176.98 (C-2) ppm. EI-MS m/z : 204.05. Anal. Calcd. for $\text{C}_{10}\text{H}_8\text{N}_2\text{O}_3$: C, 58.82; H, 3.95; N, 13.72; O, 23.51. Found: C, 58.74; H, 3.82.

Preparation of steroid-oxy-phenyl-acetonitrile derivatives

A solution of **1** or **2** (0.5 mmol), 4-nitrophenyl acetonitrile (90 mg, 0.55 mmol), potassium carbonate

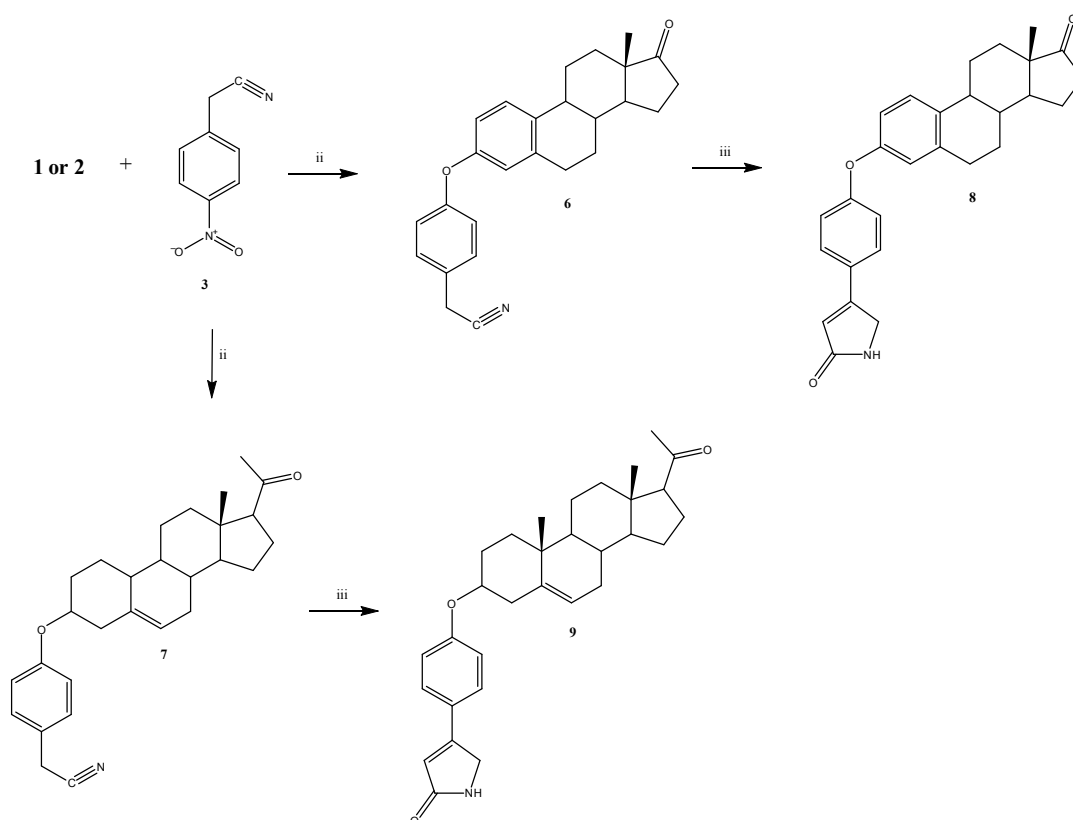


Fig. 3: Synthesis of two steroid-pyrrolone derivatives (**6** or **7**). The first stage involves the reaction of estrone¹ or pregnenolone² with 4-nitrophenylacetonitrile³ to form two steroid-oxy-phenyl-acetonitrile derivatives (**6** or **7**). The second stage was achieved by the reaction of **6** or **7** with 6-chloro-1-hexyne (iii) to synthesis of **8** or **9**. ii = $\text{K}_2\text{CO}_3/\text{DMSO}$

(40 mg, 0.30 mmol) in 5 mL of dimethyl sulfoxide was stirred for 72 h at room temperature. The reaction mixture was evaporated to dryness under reduced pressure, the residue washed 3 times with water. Then the precipitate was separated and dried at room temperature.

2 - (4 - (((1 3 S) - 1 3 - m e t h y l - 1 7 - o x o - 7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[*a*] phenanthren-3-yl)oxy)phenyl)acetonitrile⁶.

The product yield was 52 %; m.p. 202-204 °C; 2269, 1710 and 1246; ¹H NMR (300 MHz, CDCl₃) d_H: 1.00 (s, 3H), 1.22-1.36 (m, 4H), 1.54-1.94 (m, 3H), 2.08-2.20 (m, 4H), 2.48-3.00 (m, 4H), 3.66 (m, 2H), 6.70-6.78 (m, 2H), 6.98 (m, 2H), 7.14 (m, 1H), 7.36 (m, 2H). ¹³C NMR (75.4 Hz, CDCl₃) d_C: 13.60 (C-18), 21.78 (C-7), 23.50 (C-27), 25.72 (C-3), 26.32 (C-10), 29.40 (C-11), 30.92 (C-4), 35.70 (C-8), 37.56 (C-1), 44.70 (C-2), 48.00 (C-5), 48.62 (C-6),

114.26 (C-17), 114.51 (C-15), 117.10 (C-22, C-26), 117.40 (C-28), 122.50 (C-24), 124.60 (C-14), 128.30 (C-23, C-25), 132.61 (C-13), 139.54 (C-12), 155.00 (C-21), 155.94 (C-16), 219.80 (C-9) ppm. EI-MS *m/z*: 385.20. Anal. Calcd. for C₂₆H₂₇NO₂: C, 81.01; H, 7.06; N, 3.63; O, 8.30. Found: C, 81.00; H, 7.00.

[4-(17-acetyl-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*] phenanthren-3-yl)oxy)phenyl]acetonitrile⁷

The product yield was 52 %; m.p. 168-170 °C; 2258, 1712 and 1248; ¹H NMR (300 MHz, CDCl₃) d_H: 0.64 (s, 3H), 1.00 (s, 3H), 1.04-1.38 (m, 5H), 1.44-2.08 (m, 11H), 2.10 (s, 3H), 2.20-2.54 (m, 4H), 3.66 (t, 2H, J = 18.24 Hz), 4.20 (m, 1H), 5.46 (d, 1H, J = 2.00 Hz), 6.84-7.28 (m, 4H). ¹³C NMR (75.4 Hz, CDCl₃) d_C: 13.23 (C-25), 23.42 (C-28), 24.00 (C-15), 25.66 (C-3), 26.15 (C-10), 30.22 (C-31), 31.40 (C-14), 32.56 (C-2), 32.66 (C-16), 36.20 (C-6), 36.88 (C-9), 41.58 (C-11), 43.76 (C-5),

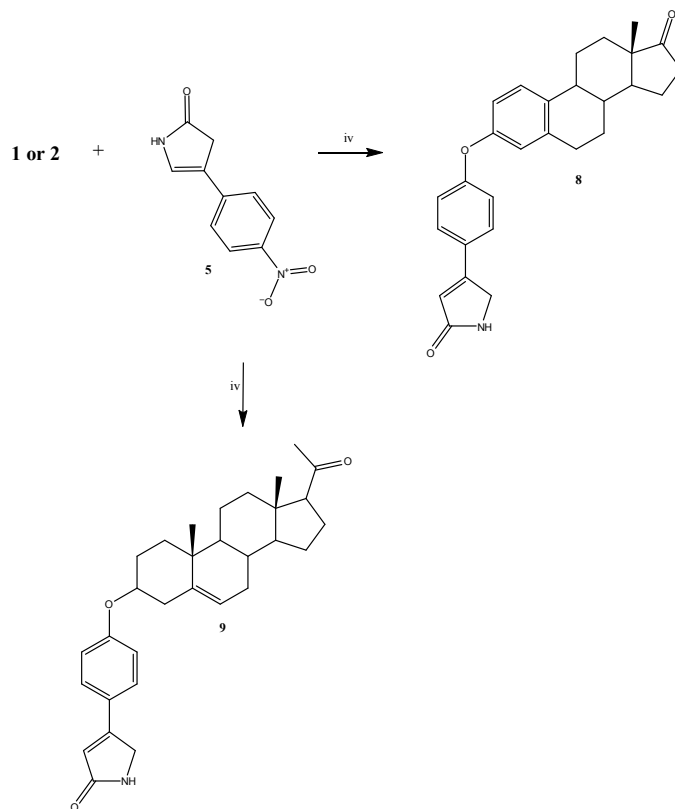


Fig. 4: Synthesis of two steroid-pyrrolone derivatives (6 or 7). Reaction of estrone (1) or pregnenolone (2) with 5 to form 6 or 7. iv = K₂CO₃/DMSO

44.60 (C-8), 47.43 (C-4), 54.50 (C-7), 63.70 (C-17), 80.32 (C-1), 115.20 (C-20, C-24), 117.40 (C-29), 122.24 (C-13), 122.80 (C-22), 127.10 (C-21, C-23), 139.00 (C-12), 156.32 (C-19), 209.23 (C-26) ppm. EI-MS *m/z*: 417.26. Anal. Calcd. for $C_{30}H_{37}NO_3$: C, 80.53; H, 8.45; N, 3.35; O, 7.86. Found: C, 80.44; H, 8.36.

Preparation of steroid-phenyl-pyrrolone derivatives

Method A: A solution of **6** or **7** (0.5 mmol), 6-chloro-1-hexyne (94 ml, 0.77 mmol), potassium carbonate anhydride (50 mg, 0.36) in 5 mL of dimethyl sulfoxide was stirred for 72 h at room temperature. The reaction mixture was evaporated to dryness under reduced pressure, the residue washed 3 times with water. Then the precipitate was separated and dried at room temperature.

4 - (4 - (((1 3 S) - 1 3 - m e t h y l - 1 7 - o x o - 7 , 8 , 9 , 1 1 , 1 2 , 1 3 , 1 4 , 1 5 , 1 6 , 1 7 - d e c a h y d r o - 6 H - c y c l o p e n t a [a] p h e n a n t h r e n - 3 - y l) o x y) p h e n y l) 1 , 5 - d i h y d r o - 2 H - p y r r o l - 2 - o n e ⁸

The product yield was 45 %; m.p. 202-204 °C; 1705, 1672 and 1600; ¹H NMR (300 MHz, CDCl₃) *d_H*: 1.00 (s, 3H), 1.22-1.36 (m, 4H), 1.54-1.94 (m, 3H), 2.08-2.20 (m, 4H), 2.48-3.00 (m, 4H), 4.56 (m, 2H), 5.50 (d, 1H, *J* = 2.10 Hz), 6.70 (m, 1H), 6.74 (m, 2H), 6.78-7.14 (m, 2H), 7.28 (m, 2H), 8.01 (broad, 1H). ¹³C NMR (75.4 Hz, CDCl₃) *d_C*: 13.60 (C-31), 21.78 (C-25), 25.72 (C-21), 26.32 (C-18), 29.40 (C-17), 30.92 (C-22), 35.70 (C-26), 37.56 (C-19), 44.70 (C-20), 48.00 (C-23), 48.62 (C-24), 50.70 (C-5), 114.26 (C-15), 114.51 (C-28), 117.58 (C-9, C-1), 118.00 (C-3), 124.60 (C-29), 128.60 (C-8, C-12), 130.00 (C-7), 132.61 (C-30), 139.54 (C-16), 154.82 (C-14), 156.91 (C-10), 168.60

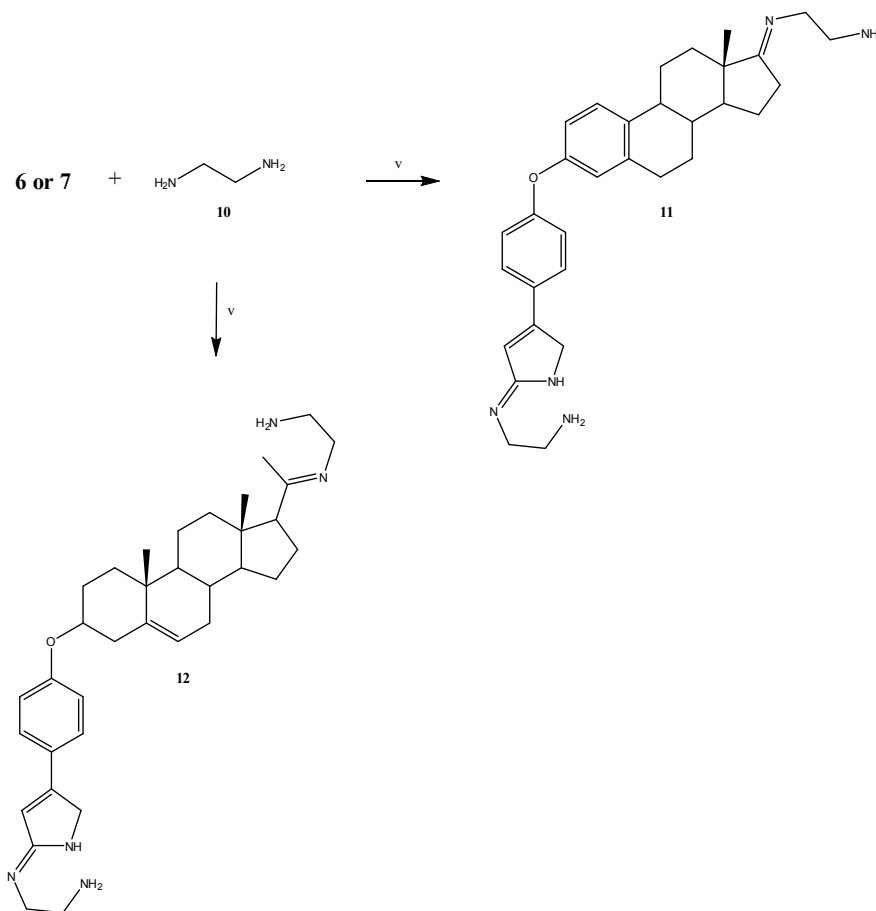


Fig. 5: Preparation of pyrrol-oxy-steroid-ethanediamine derivatives (**11** or **12**). Reaction of **6** or **7** with ethylenediamine to form **11** or **12**. *v* = boric acid/rt

(C-4), 174.38 (C-2), 219.80 (C-27) ppm. EI-MS *m/z*: 427.21. Anal. Calcd. for C₂₈H₂₉NO₃: C, 78.66; H, 6.84; N, 3.28; O, 11.23. Found: C, 78.54; H, 6.76.

4-[4-(17-acethyl-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)phenyl]1,5-dihydro-2*H*-pyrrol-2-one⁹

The product yield was 52 %; m.p. 168-170 °C; 1702, 1670 and 1246; ¹H NMR (300 MHz, CDCl₃) d_H: 0.64 (s, 3H), 1.00 (s, 3H), 1.04-1.46 (m, 7H), 1.60-2.08 (m, 9H), 2.10 (s, 3H), 2.20-4.20 (m, 5H), 4.56 (m, 2H), 5.44 (d, 1H, *J* = 2.00 Hz), 5.50 (d, 1H, *J* = 2.10 Hz), 6.84-7.14 (m, 4H), 8.02 (broad, 1H). ¹³C NMR (75.4 Hz, CDCl₃) d_C: 13.23 (C-32), 19.40 (C-31), 21.40 (C-23), 23.10 (C-35), 23.98 (C-28), 30.30 (C-15), 31.44 (C-29), 31.80 (C-19, C-27), 37.56 (C-16), 38.10 (C-17), 38.90 (C-22), 40.00 (C-24), 44.76 (C-21), 50.00 (C-18), 50.66 (C-5), 56.84 (C-20), 63.70 (C-30), 81.42 (C-14), 114.94 (C-9, C-11), 118.00 (C-3), 122.04 (C-26), 127.10 (C-8, C-12), 128.10 (C-7), 140.00 (C-25), 156.44 (C-10), 168.62 (C-4), 174.44 (C-2), 209.23 (C-32) ppm. EI-MS *m/z*: 473.29. Anal. Calcd. for C₃₁H₃₉NO₃: C, 78.61; H, 8.30; N, 2.96; O, 10.13. Found: C, 78.54; H, 8.24.

Method B

A solution of **1** or **2** (0.5 mmol), **5** (110 mg, 0.54 mmol), potassium carbonate anhydride (50 mg, 0.36) in 5 mL of dimethyl sulfoxide was stirred for 72 h at room temperature. The reaction mixture was evaporated to dryness under reduced pressure, the residue washed 3 times with water. Then the precipitate was separated and dried at room temperature. The yield for **8** was 65 % and for **9** of 72%. Similar ¹H NMR and ¹³C NMR data for the compound **8** or **9** were obtained compared with method A.

Preparation of pyrrol-ethanediamine derivatives

A solution of **8** or **9** (0.5 mmol), ethylene diamine (60 µl, 0.90 mmol), boric acid (50 mg, 0.80 mmol) in 5 mL of methanol was stirred for 72 h at room temperature. The reaction mixture was evaporated to dryness under reduced pressure, the residue washed 3 times with water. Then the precipitate was separated and dried at room temperature.

***N'*-(4-[4-[17-(2-amino-ethylimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yloxy]-phenyl]-1,5-dihydro-pyrrol-2-ylidene)-ethane-1,2-diamine¹¹**

The product yield was 52 %; m.p. 124-126 °C; 3380, 3320 and 1248; ¹H NMR (300 MHz, CDCl₃) d_H: 1.00 (s, 3H), 1.22-1.90 (m, 6H), 2.08-2.80 (m, 9H), 3.10 (t, 2H, *J* = 13.34 Hz), 3.16 (t, 2H, *J* = 13.34 Hz), 3.50 (t, 2H, *J* = 8.79 Hz), 3.66 (t, 2H, *J* = 8.79 Hz), 4.90 (m, 2H), 5.30 (broad, 5H), 6.68 (m, 1H), 6.70 (d, 1H, *J* = 2.10 Hz), 6.74 (m, 2H), 6.78 (m, 1H), 7.24 (m, 2H), 7.30 (m, 1H). ¹³C NMR (75.4 Hz, CDCl₃) d_C: 15.80 (C-34), 22.00 (C-28), 25.82 (C-21), 26.00 (C-24), 27.50 (C-29), 29.76 (C-20), 32.42 (C-25), 37.56 (C-22), 40.94 (C-8), 41.00 (C-37), 41.44 (C-26), 43.32 (C-23), 54.00 (C-7), 54.14 (C-36), 54.30 (C-27), 59.52 (C-5), 114.26 (C-18), 114.51 (C-31), 118.98 (C-12, C-14), 124.20 (C-3), 125.88 (C-32), 129.10 (C-11, C-15), 130.61 (C-10), 134.14 (C-33), 140.80 (C-19), 153.32 (C-4), 154.78 (C-2), 154.80 (C-17), 158.14 (C-13), 176.80 (C-30) ppm. EI-MS *m/z*: 511.33. Anal. Calcd. for C₃₂H₄₁N₅O: C, 75.11; H, 8.08; N, 13.69; O, 3.13. Found: C, 75.04; H, 8.00.

***N'*-(4-(4-[17-[1-(2-amino-ethylimino)-ethyl]-13-methyl-2,3,4,7,8,9,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yloxy]-phenyl)-1,5-dihydro-pyrrol-2-ylidene)-ethane-1,2-diamine¹²**

The product yield was 52 %; m.p. 120-122 °C; 3380, 3318 and 1246; ¹H NMR (300 MHz, CDCl₃) d_H: 0.90 (s, 3H), 0.98 (m, 1H), 1.22-1.70 (m, 9H), 1.80 (s, 3H), 1.82-2.50 (m, 10), 3.10 (t, 2H, *J* = 13.34 Hz), 3.16 (t, 2H, *J* = 13.34 Hz), 3.50 (t, 2H, *J* = 8.79 Hz), 3.66 (t, 2H, *J* = 8.79 Hz), 4.20 (m, 1H), 4.18 (m, 1), 4.90 (m, 2H), 5.28 (broad, 5H), 5.44 (d, 1H, *J* = Hz), 6.70 (d, 1H, *J* = 2.10 Hz), 6.78 (m, 2H), 7.14 (m, 2H). ¹³C NMR (75.4 Hz, CDCl₃) d_C: 13.30 (C-34), 16.70 (C-40), 19.40 (C-34), 21.22 (C-26), 26.40 (C-32), 26.60 (C-31), 30.30 (C-18), 30.78 (C-22), 31.90 (C-30), 37.56 (C-19), 38.10 (C-20), 38.18 (C-25), 40.00 (C-27), 40.94 (C-8), 41.00 (C-39), 42.82 (C-24), 50.40 (C-21), 53.10 (C-38), 54.02 (C-7), 55.30 (C-23), 59.52 (C-5), 63.10 (C-33), 81.40 (C-17), 116.26 (C-12, C-14), 122.11 (C-29), 124.20 (C-3), 127.58 (C-11, C-15), 128.80 (C-10), 140.02 (C-28), 153.32 (C-4), 154.78 (C-2), 156.70 (C-35), 157.74 (C-13) ppm. EI-MS *m/z*:

557.40. Anal. Calcd. for $C_{35}H_{51}N_5O$: C, 75.36; H, 9.22; N, 12.56; O, 2.87. Found: C, 75.22; H, 9.12.

Preparation of carboxy-propionylamino-steroid-succinamic acid

A solution of **11** or **12** (0.50 mmol), ethylenediamine (144 mg, 1.22 mmol) and N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide (90 mg, 0.58 mmol) in 10 mL of methanol was stirred for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. Then 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 (3:1)

N-{2-[3-(4-{5-[2-(3-carboxy-propionylamino)-ethylimino]pyrrolidin-3-yl}-phenoxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-cyclopenta[a]phenanthren-17-ylideneamino]-ethyl}-succinamic acid¹⁴

The product yield was 52 %; m.p. 164-166 °C; 3320, 1674 and 1248; ¹H NMR (300 MHz, CDCl₃) d_H: 1.00 (s, 3H), 1.22-1.90 (m, 6H), 2.06-2.28 (m, 5H), 2.50 (t, 2H, J = 13.34 Hz), 2.51 (t, 2H, J = 15.34 Hz), 2.54 (t, 2H, J = 16.80 Hz), 2.55 (t, 2H, J = 16.80 Hz), 2.60-2.80 (m, 4H), 3.32 (t, 2H, J = 15.00 Hz), 3.54 (t, 2H, J = 15.00 Hz), 3.55 (t, 2H, J = 15.00 Hz), 3.70 (t, 2H, J = 8.79 Hz), 4.90 (m, 2H), 6.68 (m, 1H), 6.70 (d, 1H, J = 2.10 Hz), 6.72 (m, 2H), 6.78 (m, 1H), 7.24 (m, 2H), 7.30 (m, 1H), 8.40 (broad, 5H) ppm. ¹³C NMR (75.4 Hz, CDCl₃) d_C: 15.80 (C-41), 22.00 (C-34), 25.82 (C-27), 26.00 (C-30), 27.50 (C-35), 28.84 (C-18, C-48), 29.76 (C-26), 30.00 (C-19, C-49), 32.42 (C-31), 36.00 (C-19), 36.08 (C-44), 37.56 (C-28), 41.44 (C-32), 43.32 (C-29), 54.10 (C-7), 54.24 (C-43), 54.30 (C-33), 59.52 (C-5), 114.26 (C-24), 114.51 (C-37), 118.98 (C-14, C-16), 124.20 (C-3), 125.88 (C-38), 129.10 (C-13, C-17), 130.61 (C-12), 134.14 (C-39), 140.80 (C-25), 153.32 (C-4), 154.78 (C-2), 154.80 (C-23), 158.14 (C-15), 166.80 (C-10, C-46), 173.56 (C-20, C-50), 176.88 (C-50) ppm. EI-MS *m/z*: 711.36. Anal. Calcd. for $C_{40}H_{49}N_5O_7$: C, 67.49; H, 6.94; N, 9.84; O, 15.73. Found: C, 67.37; H, 6.90.

N-(2-[4-[4-(17-{1-[2-(3-carboxy-propionylamino)-ethylimino]-ethyl}-13-methyl-2,3,4,5,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yloxy)-

phenyl]1,5-dihydro-pyrrol-2-ylideneamino]-ethyl)-succinamic acid¹⁵

The product yield was 52 %; m.p. 178-180; 3318, 1700, 1674 and 1248; ¹H NMR (300 MHz, CDCl₃) d_H: 0.78 (s, 3H), 0.90 (s, 3H), 1.30-1.56 (m, 5H), 1.68 (s, 3H), 1.70-1.94 (m, 6H), 2.00-2.42 (m, 8H), 2.50 (t, 2H, J = 13.34 Hz), 2.51 (t, 2H, J = 13.34 Hz), 2.55 (t, 2H, J = 8.79 Hz), 2.56 (t, 2H, J = 8.79 Hz), 3.46 (t, 2H, J = 13.34 Hz), 3.54 (t, 2H, J = 13.34 Hz), 3.60 (t, 2H, J = 13.34 Hz), 3.74 (t, 2H, J = 13.34 Hz), 4.00 (m, 1H), 4.88 (m, 2H), 5.40-5.60 (m, 2H), 6.70 (d, 1H, J = 2.10 Hz), 6.80 (m, 2H), 7.12 (m, 2H), 8.14 (broad 5H) ppm. ¹³C NMR (75.4 Hz, CDCl₃) d_C: 14.64 (C-41), 16.36 (C-42), 21.22 (C-32), 22.58 (C-50), 26.20 (C-38), 28.90 (C-18, C-24, C-51), 30.00 (C-19, C-52), 34.08 (C-33), 34.56 (C-26), 35.00 (C-25), 35.70 (C-46), 36.00 (C-8), 37.46 (C-28), 37.96 (C-31), 43.56 (C-30), 45.54 (C-34), 51.08 (C-27), 53.00 (C-29), 53.30 (C-45), 54.10 (C-7), 57.00 (C-39), 59.52 (C-5), 82.66 (C-23), 116.00 (C-14, C-16), 124.21 (C-3), 127.58 (C-13, C-17), 128.80 (C-12), 129.48 (C-35), 130.80 (C-36), 153.32 (C-4), 154.78 (C-2), 157.40 (C-15), 162.70 (C-43), 166.80 (C-10, C-48), 173.64 (C-20, C-53) ppm. EI-MS *m/z*: 757.44. Anal. Calcd. for $C_{42}H_{57}N_5O_7$: C, 68.14; H, 7.85; N, 9.24; O, 14.78. Found: C, 68.06; H, 7.78.

Preparation of Pyrrolo-steroid-triazecin-oxobutanoic acids complex

Method A: A solution of **14** or **15** (0.50 mmol), N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide (90 mg, 0.58 mmol) in 10 mL of methanol was stirred for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. Then 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 (3:1).

4-((2-(((13S,E)-3-(4-((Z)-5,8-dioxo-2,3,4,5,6,7,8,10,11,12-decahydropyrrolo [1,2-a] [1,3, 6]triazecin-11-yl)-phenoxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-ylidene)amino)ethyl)amino)-4-oxobutanoic acid¹⁶

The product yield was 40 %; m.p. 116-118 °C; 3320, 1702, 1672 and 1246; ¹H NMR (300 MHz, CDCl₃) d_H: 1.02 (s, 3H), 1.22-2.18 (m, 9H), 2.22 (t, 2H, J = 13.34 Hz), 2.25-2.28 (m, 2H),

2.40 (t, 2H, J = 13.34 Hz), 2.52 (t, 2H, J = 15.34 Hz), 2.56 (t, 2H, J = 16.80 Hz), 2.62-2.80 (m, 4H), 3.32 (t, 2H, J = 15.00 Hz), 3.52 (t, 2H, J = 15.00 Hz), 3.55 (t, 2H, J = 15.00 Hz), 3.88 (t, 2H, J = 8.79 Hz), 4.88-5.16 (m, 2H), 6.68 (m, 1H), 6.75 (m, 2H), 6.76 (m, 1H), 7.24 (m, 1H, J = Hz), 7.28 (m, 1H), 7.29 (m, 2H), 7.76 (broad, 1H, -NHCO), 8.58 (broad, 5H, -NHCO and -COOH) ppm. ^{13}C NMR (75.4 Hz, CDCl_3) δ_c : 15.80 (C-40), 22.00 (C-34), 25.82 (C-27), 26.00 (C-30), 27.50 (C-35), 28.84 (C-47), 29.76 (C-26), 30.00 (C-48), 31.60 (C-7), 32.42 (C-31), 33.50 (C-6), 36.08 (C-43), 37.56 (C-28), 37.79 (C-3), 41.44 (C-32), 43.32 (C-29), 54.24 (C-42), 54.30 (C-33), 58.92 (C-13), 62.12 (C-2), 114.26 (C-24), 114.51 (C-37), 119.20 (C-18, C-20), 124.90 (C-11), 125.88 (C-38), 129.10 (C-17, C-21), 130.00 (C-16), 134.14 (C-39), 140.80 (C-25), 147.50 (C-10), 150.66 (C-12), 154.78 (C-23), 158.14 (C-19), 166.80 (C-45), 170.60 (C-5), 173.56 (C-49), 176.88 (C-36), 178.40 (C-8) ppm. EI-MS m/z : 693.35. Anal. Calcd. for $\text{C}_{40}\text{H}_{47}\text{N}_5\text{O}_6$: C, 69.24; H, 6.83; N, 10.09; O, 13.84. Found: C, 69.12; H, 6.71.

4-((2-(((Z)-1-((10S,13S)-3-(4-((Z)-5,8-dioxo-2,3,4,5,6,7,8,10-decahydropyrrolo[1,2-a][1,3,6]triazecin-11-yl)-phenoxy)-10,13-dimethyl-2,3,4,5,8,,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)ethylidene)amino)ethyl)amino-4-oxobutanoic acid¹⁷

The product yield was 38 %; m.p. 164-166 °C; 3322, 1700, 1676 and 1248; ^1H NMR (300 MHz, CDCl_3) δ_H : 0.78 (s, 3H), 1.00 (s, 3H), 1.28-1.56 (m, 5H), 1.68 (s, 3H), 1.70-2.14 (m, 11H), 2.20 (t, 2H, J = 13.34 Hz), 2.30-2.40 (m, 2H), 2.42 (t, 2H, J = 13.34 Hz), 2.43 (m, 1H), 2.50 (t, 2H, J = 13.34 Hz), 2.56 (t, 2H, J = 13.34 Hz), 3.08-3.30 (m, 2H), 3.48 (t, 2H, J = 13.34 Hz), 3.58 (t, 2H, J = 8.79 Hz), 3.62 (t, 2H, J = 13.34 Hz), 3.80 (m, 1H), 3.96 (t, 2H, J = 8.79 Hz), 3.98 (m, 1H), 4.00 (m, 1H), 4.22 (m, 1H), 5.36-5.58 (m, 2H), 6.80-7.00 (m, 3H), 7.74 (broad, 1H, -NHCO), 7.90 (broad, 2H, -NHCO and -COOH) ppm. ^{13}C NMR (75.4 Hz, CDCl_3) δ_c : 14.60 (C-40), 16.30 (C-41), 21.22 (C-32), 22.60 (C-49), 26.20 (C-38), 26.25 (C-37), 28.88 (C-24), 28.90 (C-50), 30.00 (C-51), 31.60 (C-7), 33.50 (C-6), 34.08 (C-33), 34.56 (C-26), 35.00 (C-25), 35.70 (C-45), 37.40 (C-28), 37.94 (C-31), 37.98 (C-3), 43.36 (C-11), 43.40 (C-12), 43.60 (C-30), 45.58 (C-34), 51.00 (C-27), 51.70 (C-10), 53.00 (C-29), 53.32 (C-44), 57.00 (C-39), 62.16 (C-2),

82.70 (C-23), 114.54 (C-18, C-20), 125.90 (C-38), 127.50 (C-16), 128.74 (C-17, C-21), 129.44 (C-35), 130.80 (C-36), 156.08 (C-19), 156.30 (C-13), 162.66 (C-42), 166.80 (C-47), 170.60 (C-5), 173.64 (C-52), 180.98 (C-8) ppm. EI-MS m/z : 741.44. Anal. Calcd. for $\text{C}_{43}\text{H}_{59}\text{N}_5\text{O}_6$: C, 69.61; H, 8.02; N, 9.44; O, 12.94. Found: C, 69.52; H, 8.00.

Method B

A solution of **14** or **15** (0.50 mmol), boric acid (50 mg, 0.80 mmol) in 10 mL of methanol was stirred for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. Then 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 (3:1). The yield for **8** was 36 % and for **9** of 32%. Similar ^1H NMR and ^{13}C NMR data for the compounds **16** or **17** were obtained compared with method A.

RESULTS AND DISCUSSIONS

There are several methods for preparation of pyrroles; however, despite its wide scope, have some drawbacks such as the use of some reagents that have limited stability and require special conditions; for example, basic medium¹², $\text{Ru}_3(\text{CO})_{12}$ ¹³, ammonia/ HCl ¹⁴ and others. In this work two pyrrole derivatives were prepared using several strategies.

Synthesis of 4-(4-nitrophenyl)1,3-dihydro-2H-pyrrol-2-one⁵.

The first stage was achieved by the reaction of 4-nitrophenylacetonitrile with 6-chloro-1-hexyne to form a pyrrolone derivative⁵ in presence of triethylamine. The ^1H NMR spectrum of **5** showed several signals at 3.22-7.28, and 8.02 ppm for pyrrole ring; at 7.44 and 8.10 ppm for phenyl group. The ^{13}C NMR spectrum exhibits the following signals at 42.20-117.32 and 124.63 ppm for pyrrole ring; at 121.54 and 132.54-144.76 ppm for phenyl group; at 176.98 ppm for ketone group. In addition, the mass spectrum of **5** exhibited molecular ion peak at m/z 204.05.

Preparation of steroid-oxy-phenyl-acetonitrile derivatives

The second stage was achieved by preparation of two steroid-3-oxy-phenylacetonitrile

derivatives via displacement of nitro group of nitrophenylacetonitrile³ to form two steroid-oxyphenyl-acetonitrile derivatives (**6** or **7**). It is important to mention that there are several methods for displacement of nitro groups which use dipolar aprotic solvents to attain a high yield of ether groups^{15,16}. In this study the estrone and pregnenolone were reacted with **3** in medium basic to form **6** or **7**. The ¹H NMR spectrum of **6** showed several signals at 1.00 ppm for methyl group; at 1.22-3.00, 6.78-6.78 and 7.14 ppm for steroid moiety; at 3.66 ppm for methylene group bound to both phenyl and nitrile groups; at 6.98 and 7.36 ppm for phenyl group. The ¹³C NMR spectrum exhibits the following signals at

13.60 ppm for methyl group; at 21.78, 25.72-114.51, 124.60, 132.61-139.84 and 155.94 ppm for steroid moiety; at 23.50 ppm for methylene group bound to both phenyl and nitrile groups; at 117.10, 122.50, 128.30 and 155.00 ppm for phenyl group; at 117.40 ppm for carbon of nitrilomethane; at 219.80 for ketone group. In addition, the mass spectrum of **6** exhibited molecular ion peak *atm/z* 385.20.

On the other hand, the ¹H NMR spectrum of **7** showed several signals at 0.64 ppm for methyl group bound to steroid nucleus; at 2.10 ppm for methyl bound to ketone; at 1.00-2.04, 4.20-5.40 and 2.20-2.58 ppm for steroid nucleus; at 3.66 ppm

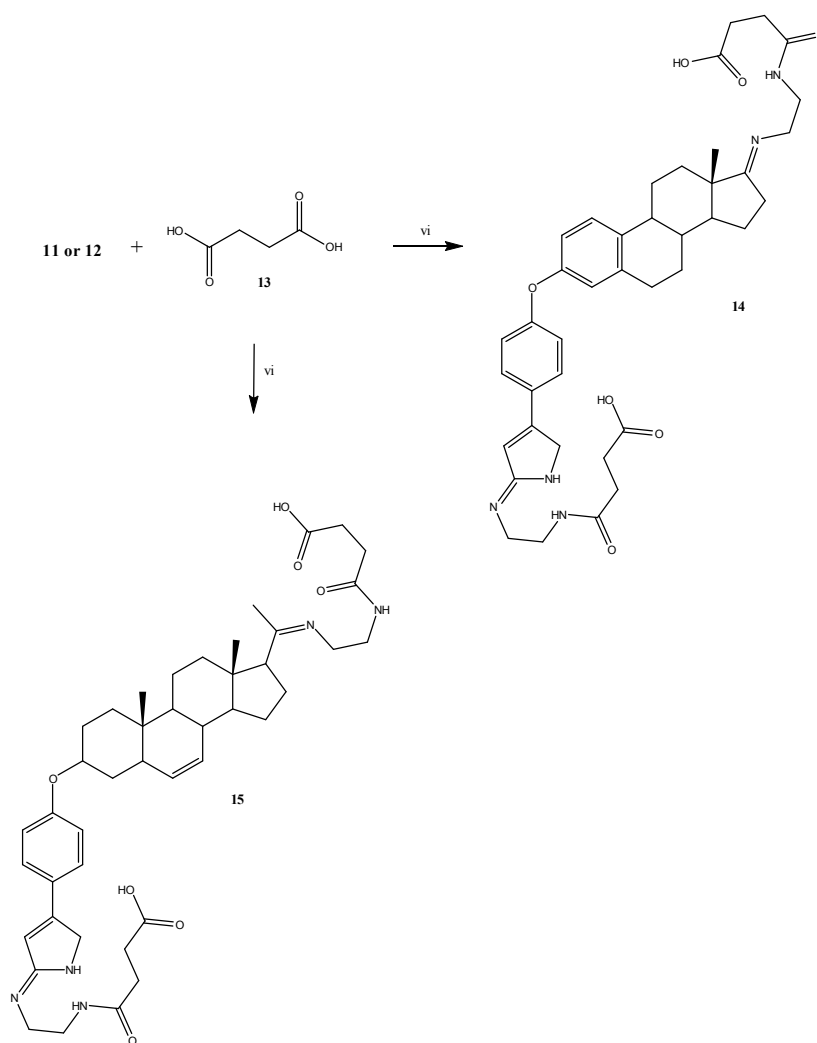


Fig. 6: Preparation of twocarboxyl-propionylamino-steroid- succinamic acids (14** or **15**). Reaction of **11** or **12** with succinic acid using carbodiimide derivative as catalyst (**vi**)**

for methylene bound to nitrile; at 6.84-7.28 ppm for phenyl group. The ^{13}C NMR spectrum exhibits the following signals at 13.23 ppm for methyl group bound to steroid nucleus; 30.22 ppm for methyl group bound to ketone; 23.42 ppm for methylene bound to nitrile; at 24.00-26.15, 31.40-80.32, 122.24 and 139.00 ppm for steroid moiety; at 115.20, 122.80-127.10 and 156.32 ppm for steroid moiety; at 117.40 ppm for nitrile group; at 209.23 ppm for ketone group. Finally, the mass spectrum of **7** exhibited molecular ion peak at m/z 417.26.

Preparation of steroid-phenyl-pyrrolone derivatives

The second stage involved the preparation of two steroid-phenyl-pyrrolone derivatives (**8** and **9**). It is important to mention that these compounds were prepared using two methods the first step (Method A) was achieved by reaction of **6** or **7** with with 6-chloro-1-hexyne to form **8** or **9** in mild conditions. The second step (method B) was achieved by the reaction of estrone or pregnenolone with **5** to form **8** or **9**. It is important to mention that with the method B

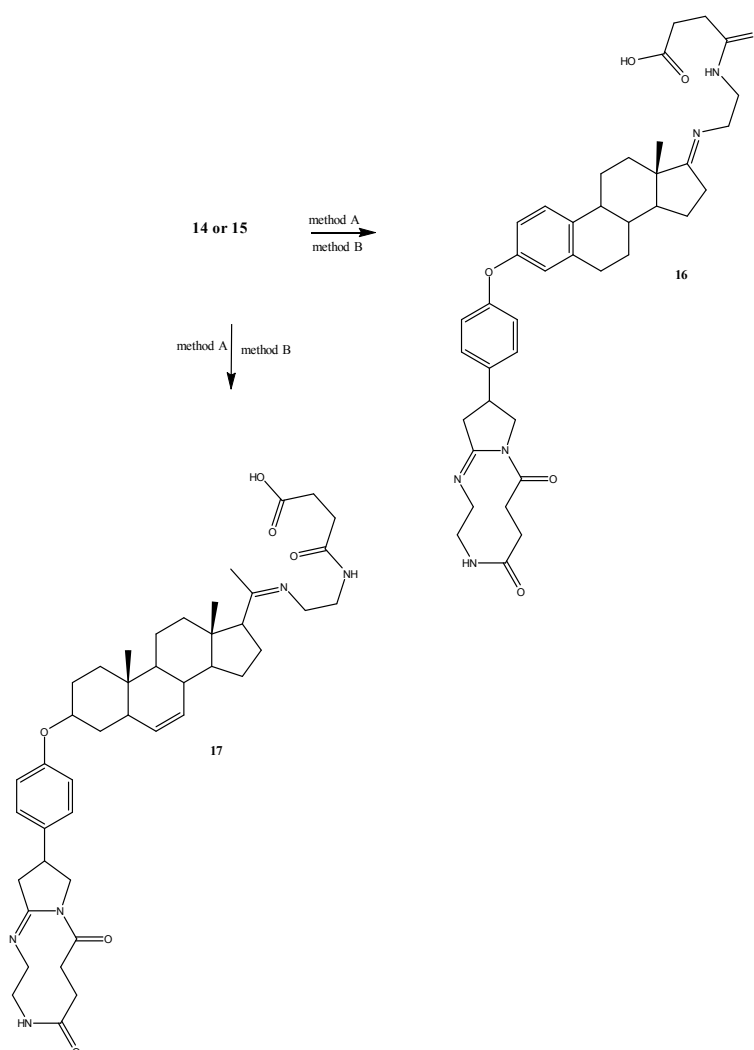


Fig. 7: Preparation of two pyrrolo-steroid-triazecin-oxobutanoic acids complex (**16** or **17**) via cyclization of **14** or **15** in presence of a carbodiimidederivative (Method A) or boric acid (Method B)

the production was higher in comparison with method A. This phenomenon possibly is due to conditions of reaction involved in each method. The ^1H NMR spectrum of **8** showed several signals at 1.00 ppm for methyl group; at 1.22-3.00, 6.70 and 6.78-7.14 ppm for steroid moiety; at 4.50-5.50 ppm for pyrrole ring; at 6.74 and 7.28 ppm for phenyl group; at 8.01 ppm for amino group. The ^{13}C NMR spectrum exhibits the following signals at 13.60 ppm for methyl group; at 21.78-48.62, 114.26-114.51, 124.60, 130.00 and 132.61-154.82 ppm for steroid moiety; at 50.70, 118.50, 168.60 and 174.38 ppm for pyrrole ring; at 117.58, 128.60, 156.91 ppm for phenyl group; at 219.80 for ketone group. Finally, the mass spectrum of **8** exhibited molecular ion peak at m/z 427.21.

On the other hand, the ^1H NMR spectrum of **9** showed several signals at 0.64 and 1.00 ppm for methyl groups bound to steroid nucleus; at 2.10 ppm for methyl group bound to ketone; at 1.04-2.08, 2.20-4.20 and 5.44 ppm for steroid moiety; at 4.56 and 5.50 ppm for pyrrole ring; at 6.84-7.14 ppm for phenyl group; at 8.02 ppm for amino group. The ^{13}C NMR spectrum exhibits the following signals at 13.23 and 19.40 ppm for methyl groups bound to steroid nucleus; at 23.10 ppm for methyl group bound to ketone; at 21.40, 23.98-50.00, 56.84-81.42, 122.04 and 140.00 ppm for steroid moiety; at 50.66, 118.50 and 168.62-174.44 ppm for pyrrole ring; at 114.94, 127.10-128.10 and 156.44 ppm for phenyl group; at 174.44 and 209.23 ppm for ketone groups. In addition, the mass spectrum of **9** exhibited molecular ion peak at m/z 473.29.

Preparation of pyrrol-ethanediamine derivatives

The following stage was achieved by preparation of imino groups involved in the compounds **11** or **12**. It is important to mention, that there are several procedures for the synthesis of imines which are described in the literature^{15, 16}. For example, the synthesis of imine derivatives by the reaction of the compound 1-[(2-amino-ethylamino)phenyl-methyl]-naphthalen-2-ol with androsterone using as catalyst boric acid¹⁷. In this study the compounds **11** or **12** were synthesized by the reaction of **8** or **9** using boric acid as catalyst, because it is not an expensive reagent and no special conditions are required for use²¹. Reaction mechanism involves nucleophilic

addition of amino groups to the electron-deficient ketone central carbons resulting imino group. The ^1H NMR spectrum of **11** showed several signals at 1.22 ppm for methyl bound to steroid nucleus; at 1.22-1.90, 2.08-2.80, 6.68, 6.78 and 7.30 ppm for steroid nucleus; at 3.10, 3.16, 3.50 and 3.66 for methylene groups bound to both imino and amino groups; at 4.90 and 6.70 ppm for pyrrole ring; at 5.30 ppm for amino groups; at 6.74 and 7.24 ppm for phenyl group. The ^{13}C NMR spectrum exhibits the following signals at 15.80 ppm for methyl group; at 22.00-37.56, 41.44-43.32, 54.30, 114.26-114.51, 125.88, 134.14-140.80 and 154.80 ppm for steroid moiety; at 40.94, 41.00, 54.00 and 54.14 ppm for methylene groups bound to both imino and amino groups; at 59.52, 124.20 and 153.32-154.78 ppm for pyrrole ring; at 118.98, 129.10, 130.61 and 158.14 ppm for phenyl group; at 176.80 ppm for imino group. In addition, the mass spectrum of **11** exhibited molecular ion peak at m/z 511.33.

On the other hand, other results showed several signals of ^1H NMR spectrum for the compound **12** at 0.90 ppm for methyl group bound to steroid nucleus; at 0.90 and 1.00 ppm for methyl groups bound to steroid nucleus; at 1.80 ppm for methyl group bound to imino; 0.98, 1.22, 1.82-2.50, 4.18 and 5.44 ppm for steroid moiety; at 3.10, 3.16, 3.50 and 3.66 ppm for methylene groups bound to both imino and amino groups; 4.90 and 6.70 ppm for pyrrole ring; at 5.28 ppm for amino groups; at 6.78-7.14 ppm for phenyl group. The ^{13}C NMR spectrum exhibits the following signals at 13.30 and 19.40 ppm for methyl groups bound to steroid nucleus; at 16.70 ppm for methyl group bound to imino; at 21.22-40.00, 42.80, 42.82-50.40, 55.30, 63.10-81.40, 122.11 and 140.02; at 40.94-41.00 and 53.10-54.02 ppm for methylene groups bound to both imino and amino groups; at 59.52, 124.20, 153.32-154.78 ppm for pyrrole ring; at 116.26, 127.58-128.80 and 157.74 ppm for phenyl group; at 156.70 for imino group. Finally, the mass spectrum of **12** exhibited molecular ion peak at m/z 557.40.

Preparation of carboxy-propionylamino-steroid-succinamic acid

The following stage was achieved by formation of an amide involved in the chemical structure for compounds **14** or **15**. It is important

to mention that there are many procedures for the formation of amides which are known in the literature, for example the reaction of amine with trichloroisocyanuric acid¹⁸, NaH/DMF¹⁹, ZrOCl₂²⁰, tetrabutyl ammonium bromide²¹. Analyzing these data and other report which indicate the preparation of amide groups with some carbodiimides²²; therefore, in this study 11 or 12 were reacted with succinic acid in presence of a carbodiimide derivative to form the compounds 13 or 14. The ¹H NMR spectrum of 14 showed several signals at 1.00 ppm for methyl group; at 1.22-2.28, 2.60-2.80 and 6.68-6.78 ppm for steroid moiety; at 7.30 ppm for both amide and carboxyl groups; at 2.50-2.55 for methylene bound to both amide and carboxyl groups; at 3.32-3.70 ppm for methylene bound to both imino and amide groups; at 4.90-6.70 ppm for pyrrole ring; at 6.72-7.24 ppm for phenyl group. The ¹³C NMR spectrum exhibits the following signals at 15.80 ppm for methyl group; at 22.00-27.50, 29.76, 32.42, 31.56-43.32, 54.30, 114.26-114.51, 125.88, 134.14-140.80 and 154.78 ppm for steroid moiety; at 28.84-30.00 ppm for methylene groups bound to both amide and carboxyl groups; at 36.00-36.08 and 54.10-54.24 ppm for methylene groups bound to both imino and amide groups; at 59.52, 124.20 and 153.32-154.78 ppm for pyrrole ring; at 118.98, 129.10-130.61 and 158.14 ppm for phenyl group; at 166.80 ppm for amide groups; at 173.56 ppm for imino groups; at 176.88 ppm for carboxyl groups. In addition, the mass spectrum of 14 exhibited molecular ion peak at *m/z* 711.36.

The ¹H NMR spectrum of 15 showed several signals at 0.78 and 0.90 ppm for methyl group bound to steroid nucleus; at 1.68 ppm for methyl group bound to imino group; at 1.30-1.56, 1.70-2.42, 4.00, 5.40-5.60 ppm for steroid moiety; at 2.50-2.56 ppm for methylene group bound to both amide and carboxyl groups; at 3.46- 3.74 ppm for methylene groups bound to both imino and amide groups; at 4.88 and 6.70 ppm for pyrrole ring; at 6.80-7.12 ppm for phenyl groups; at 8.14 ppm for both amide and carboxyl groups. The ¹³C NMR spectrum exhibits the following signals at 14.64 and 16.36 ppm for methyl groups bound to steroid nucleus; at 22.58 ppm for methyl group bound to imino group; at 21.22, 26.20-28.90, 34.08-35.00, 37.46-53.00, 57.00, 82.66 and 129.48-130.80 ppm for steroid moiety; at 28.90-30.00 ppm for methylene groups bound to both amide

and carboxyl groups; at 35.70-36.00 and 54.10 ppm for methylene groups bound to both imino and amide groups; at 59.32, 124.21 and 153.32-154.78 ppm for pyrrole ring; at 116.00, 127.58-128.80 and 157.40 ppm for phenyl groups; at 162.70 ppm for nitrile group; at 166.80 ppm for amide group; at 173.64 ppm for carboxyl group. In addition, the mass spectrum of 15 exhibited molecular ion peak at *m/z* 743.42.

Preparation of pyrrolo-steroid-triazecin-oxobutanoic acids complex

Several triazecinone derivatives have been prepared using different reagents such as 1,2-diaminoethane, DMAP, tetrachloro-2-azabuta-1,3-dienes²³⁻²⁵ and others. In this study, the synthesis of steroid-pyrrolo-triazecin derivatives (16 or 17) was via cyclization of 14 or 15 using a carbodiimide derivative (method B) or boric acid (method A). It is important to mention with method A the yielding was higher in comparison with Method B, this phenomenon possibly is result of the reaction conditions that are involved in this study or to different structure chemical of catalyzers.

The ¹H NMR spectrum of 16 showed several signals at 1.02 ppm for methyl group; at 1.22-2.18, 2.25-2.28, 2.60-2.80, 6.68, 6.76 and 7.28 ppm for steroid moiety; at 2.22, 2.40, 3.52, 3.88 ppm for methylene groups involved in the triazecine-dione ring; at 2.52-2.56 ppm for methylene groups bound to both amide and carboxyl groups; at 3.32 and 3.55 ppm for methylene groups bound to both imino and amide groups; at 4.88-5.16 and 7.24 ppm for pyrrole ring; at 6.75 and 7.29 ppm for phenyl group; at 7.76 ppm for amide involved in the triazecine-dione ring; at 8.58 ppm for both amide and carboxyl groups involved in the arm bound to D-ring of steroid nucleus. The ¹³C NMR spectrum exhibits the following signals at 15.80 ppm for methyl group; at 22.00-27.50, 29.76, 32.42, 37.60, 41.44-43.32, 54.30, 114.26, 114.51, 125.88, 134.14-140.80 and 154.78 ppm for steroid moiety; at 28.84 and 30.00 for methylene groups bound to both amide and carboxyl group; at 31.60, 33.50, 37.79 and, 62.12 ppm for methylene groups involved in the triazecine-dione ring; 36.08 and 54.24 ppm for methylene groups bound to both amide and imino groups; at 58.92, 124.90 and 147.50-150.66 ppm for pyrrole ring; at 119.20, 129.10, 130.50 and 158.14 ppm for phenyl group; at 166.80-170.60 for amide groups; at 173.56 ppm for carboxyl group; at

176.88 ppm for imino group; at 180.94 ppm for ketone group. In addition, the mass spectrum of 16 exhibited molecular ion peak at m/z 693.35.

The ^1H NMR spectrum of **17** showed several signals at 0.98 and 1.00 ppm for methyl groups bound to steroid nucleus; at 1.28-1.56, 1.70-2.14, 2.30-2.40, 4.00 and 5.36-5.58 ppm for steroid moiety; at 2.20, 2.42, 3.58 and 3.96 ppm for methylene groups involved in the triazecine-dione ring; at 2.50-2.56 ppm for methylene groups bound to both amide and carboxyl groups; at 3.48 and 3.62 ppm for methylene groups bound to both imino and amide groups; at 3.80, 3.98 and 4.22 ppm for pyrrole ring; at 6.80-7.00 ppm for phenyl group; at 7.74 ppm for amide involved in the triazecine-dione ring; at 7.90 ppm for both amide and carboxyl groups involved in the arm bound to D-ring of steroid nucleus. The ^{13}C NMR spectrum exhibits the following signals at 14.60 and 16.30 ppm for methyl groups bound to steroid nucleus; at 22.60 ppm for methyl group bound to imino group; at 21.22, 26.20-26.25, 28.90, 34.08-35.00, 37.40-37.94, 43.60-51.00, 53.00, 57.00, 82.70 and 129.44-130.80

ppm for steroid moiety; at 28.98 and 30.00 ppm for methylene groups bound to both amide and carboxyl groups; at 35.70 and 53.32 ppm for methylene groups bound to both imino and amide groups; at 31.60-33.50, 37.98 and 62.16 ppm for methylene groups involved in the triazecine-dione ring; at 43.36-43.40, 51.70 and 156.30 ppm for pyrrole ring; at 114.54-128.74, and 156.08 ppm for phenyl group; at 162.66 ppm for imino group; at 166.80-170.60 ppm for amide groups; at 173.64 for carboxyl group; at 180.98 for ketone group. In addition, the mass spectrum of **17** exhibited molecular ion peak at m/z 693.35.

CONCLUSIONS

In this study is reported a straight forward route for synthesis of two steroid-pyrrolo-triazecine derivatives. The proposed methods offer some advantages such as simple procedure, low cost, and ease of workup. In addition, it is also important to mention that these compounds could be used as pharmacological tools to evaluate the biological activity from other type of steroid derivatives.

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