

Manuscript Number: STEROIDS-D-19-00155R1

Title: Stereocontrolled Synthesis of the Four Possible 3-Methoxy and 3-Benzyloxy-16-Triazolyl-methyl-estra-17-ol Hybrids and their Antiproliferative Activities

Article Type: Regular Article

Keywords: 3-methoxy- and 3-benzyloxy-16-azidomethylestra-1,3,5(10)-triene-17-ols; 1,3-dipolar cycloaddition, 4'substituted-steroid triazoles; cytotoxic activity

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Abstract: The four possible isomers of each of 3-methoxy- and 3-benzyloxyestra-1,3,5(10)-triene-17-ols (5-8 and 9-12) were converted through 16-p-tosyloxymethyl- or 16-bromomethyl derivatives into their 3-methoxy- and 3-benzyloxy-16-azidomethylestra(1,3,5(10)-triene derivatives (13-16 and 17-20). The regioselective Cu(I)-catalyzed 1,3-dipolar cycloaddition of these compounds with different terminal alkynes afforded novel 1,4-disubstituted diastereomers (21a-f, 22a-f, 23a-f, 24a-f and 25a-f, 26a-f, 27a-f, 28a-f). The antiproliferative activities of the structurally related triazoles were determined in vitro with the microculture tetrazolium assay on four malignant human cell lines of gynecological origin (Hela, SiHa, MCF-7 and MDA-MB-231).

## Detailed Response to Reviewers

Response to Reviewer's comments:

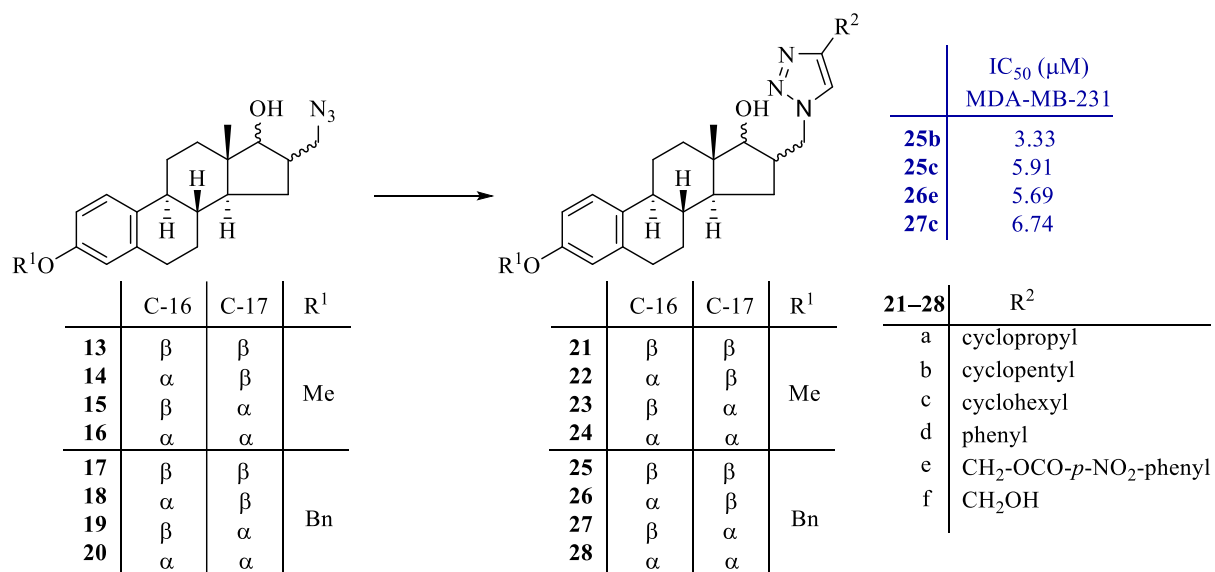
Reviewer 1:

1. Graphical abstract have been uploaded.
2. Absolute configuration of compounds **5** and **8** has been unambiguously discussed in Ref. 5 and 6, and in the Figure 1. of the present manuscript.
3. Corrected.
4. Corrected.

Reviewer 2:

1. Graphical abstract have been uploaded.
2. Corrected.
3. Copies of NMR spectra have been uploaded.
4. Corrected, and highlighted in yellow.

Thank you for your reviews.



Highlights

1. Synthesis of 3-methoxy- and 3-benzyloxy-16-azidomethylestra(1,3,5(10)-trienes.
2. CuAAC reaction of 16-azidomethyl steroidal compounds with different terminal alkynes.
3. Substantial antiproliferative activity for 3-benzyl-16-triazolylmethylene derivatives.

# Stereocontrolled Synthesis of the Four Possible 3-Methoxy and 3-Benzyloxy-16-Triazolyl-methyl-estra-17-ol Hybrids and their Antiproliferative Activities

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**ABSTRACT** The four possible isomers of each of 3-methoxy- and 3-benzyloxyestra-1,3,5(10)-trien-17-ols (**5–8** and **9–12**) were converted through 16-*p*-tosyloxymethyl- or 16-bromomethyl derivatives into their 3-methoxy- and 3-benzyloxy-16-azidomethylestra(1,3,5(10)-triene derivatives (**13–16** and **17–20**). The regioselective Cu(I)-catalyzed 1,3-dipolar cycloaddition of these compounds with different terminal alkynes afforded novel 1,4-disubstituted diastereomers (**21a–f**, **22a–f**, **23a–f**, **24a–f** and **25a–f**, **26a–f**, **27a–f**, **28a–f**). The antiproliferative activities of the structurally related triazoles were determined *in vitro* with the microculture tetrazolium assay on four malignant human cell lines of gynecological origin (Hela, SiHa, MCF-7 and MDA-MB-231).

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**Keywords:** 3-methoxy- and 3-benzyloxy-16-azidomethylestra-1,3,5(10)-triene-17-ols; 1,3-dipolar cycloaddition, 4 substituted-steroid triazoles; cytotoxic activity

## 1. Introduction

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4 Among the hybrid natural products, hybrids of steroid frameworks have attracted great attention  
5 due to significant biological properties and numerous therapeutic effects of the basic compound.  
6 Steroids have become ideal synthons for the development of diverse conjugates due to their rigid  
7 framework and potential for varying levels of functionalization, broad biological activity profile  
8 and their ability to penetrate the cell membranes and bind to specific hormonal receptors [1-3].  
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11 The place, length and orientation of the linkers between the two parts of the hybrids  
12 stems unequivocally from the method of their synthesis. The literature provides a large number of  
13 methods to introduce the linker onto the sterane skeleton. The effect of the length and character  
14 of the linker are very often discussed [4]. However, only limited information is available with  
15 respect to the steric effect of the linkers on biological properties. As concerns the 16-substituted  
16 estrogens, usually the 16 $\alpha$ -substituted-17 $\beta$ -hydroxy compounds have been studied. The  
17 biological activity has generally not been studied for the whole isomer series [5].  
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19 In the 16-substituted 17-hydroxysteroids, the two chiral centres permit four  
20 stereochemical modifications. Since availability of the complete series of isomers would permit a  
21 number of interesting comparative examinations.  
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23 We have previously reported the preparation and configurational assignment of the four  
24 possible isomers of the 3-methoxy- and 3-benzyloxy-16-hydroxymethyl-estra-1,3,5(10)-trien-17-  
25 ol derivatives (**5a-8a** and **9a-12a**) [6-8]. Treatment of 3-methoxy- and 3-benzyloxyestra-16-  
26 hydroxymethylidene-estra-1,3,5(10)-trien-17-ones (**2** and **4**). The C-16 formyl compounds were  
27 reduced with KBH<sub>4</sub> in methanol yielding a mixture of three (**5a-7a** and **9a-11a**) of the four  
28 possible isomers of each of the 3-methoxy- and 3-benzyloxy-16-hydroxymethylestra-1,3,5(10)-  
29 trien-17-ol isomers in a ratio of 50:45:5 in 94% yield [6,8]. The fourth isomers (**8a** and **12a**)  
30 were prepared from 16 $\alpha$ -acetoxymethyl-17 $\beta$ -toluenesulfonate mixed esters **6d** and **10d**,  
31 respectively, by neighbouring group participation during solvolysis in aqueous AcOH. The  
32 structures of the isomers were confirmed unambiguously by their IR, <sup>1</sup>H and <sup>13</sup>C NMR spectra  
33 (Scheme 1) [7,8].  
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### 53 (Scheme 1)

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55 The four 3-methoxy- and 3-benzyloxy-estra-1,3,5(10)-trien-17-ol isomers (**5a-8a** and **9a-12a**)  
56 are suitable starting materials to prepare 16-triazolyl-methyl derivatives. Triazoles are  
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4 attractive units because of their stability against metabolic degradation and their ability to form  
5 hydrogen bonds. The Cu(I)-catalysed azide–alkyne cycloaddition (CuAAC) is a facile method of  
6 wide applicability for the introduction of a triazole moiety into natural products [9]. In these  
7 compounds the triazole heterocycles and their substituted derivatives are connected through a  
8 methylene linker to the sterane skeleton. The 16-*p*-tolylsulfonyloxymethyl ester [5,6] and 16-  
9 bromomethyl derivatives [10] of the 16-hydroxymethyl starting materials were used for  
10 substitution reaction with NaN<sub>3</sub> in *N,N*-dimethylformamide to have the desired 3-methoxy- and  
11 3-benzyloxy-16-azidomethylestra-1,3,5(10)-trien-17-ols (**13–16** and **17–20**). From these azido  
12 compounds several D-ring-substituted estrane derivatives containing a 1,2,3-triazole ring were  
13 synthesized by the reaction of **13–16** and **17–20** with various terminal alkynes through the use of  
14 the “click” chemistry approach to deliver compounds **21a–e**, **22a–e**, **23a–e**, **24a–e**, **25a–e**, **26a–e**,  
15 **27a–e** and **28a–e**.  
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## 28 **2. Experimental**

### 29 *2.1. General*

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33 Melting points (Mp) were determined on a Kofler block and are uncorrected. Specific rotations  
34 were measured in CHCl<sub>3</sub> (*c* 1) at 20 °C with a POLAMAT-A (Zeiss-Jena) polarimeter and are  
35 given in units of 10<sup>-1</sup> deg cm<sup>2</sup> g<sup>-1</sup>. Elementary analysis data were determined with a Perkin-Elmer  
36 CHN analyzer model 2400. The reactions were monitored by TLC on Kieselgel-G (Merck Si 254  
37 F) layers (0.25 mm thick); solvent systems (ss): (A) diisopropyl ether, (B)  
38 acetone/toluene/hexane (30:35:35 v/v). The spots were detected by spraying with 5%  
39 phosphomolybdic acid in 50% aqueous phosphoric acid. The *R<sub>f</sub>* values were determined for the  
40 spots observed by illumination at 254 and 365 nm. Flash chromatography: silica gel 60, 40–63  
41 μm. All solvents were distilled prior to use. NMR spectra were recorded on a Bruker DRX 500  
42 and Bruker Ascend 500 instrument at 500 (<sup>1</sup>H NMR) or 125 MHz (<sup>13</sup>C NMR). Chemical shifts  
43 are reported in ppm (δ scale) and coupling constants (*J*) in Hertz. For the determination of  
44 multiplicities, the *J*-MOD pulse sequence was used.  
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### 57 *2.2. 3-Methoxy- and 3-benzyloxy-16-azidomethylestra-1,3,5(10)-trienes (13–16 and 17–20)*

#### 58 *General procedure*

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6 Compounds **5b–8b** [5,6] (4.70 g, 10 mmol) or **9c–12c** [] (4.55 g, 10 mmol) were dissolved in  
7 *N,N*-dimethylformamide (100 ml) and then NaN<sub>3</sub> (2.6 g) was added. The mixture was stirred for  
8 12 h at 80 °C, then poured into water (500 ml). The precipitate separating out was filtered off and  
9 subjected to chromatographic separation with CH<sub>2</sub>Cl<sub>2</sub>/hexane in different ratios.  
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### 15 2.2.1. 3-Methoxy-16β-azidomethyl-estra-1,3,5(10)-trien-17β-ol (**13**)

16 Compound **5b** (470 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
17 crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3 v/v) to yield pure **13**  
18 (318 mg, 93%). Mp 134–135 °C; *R*<sub>f</sub> = 0.65 (ss A); [α]<sub>D</sub><sup>20</sup> = + 80 (*c* 1 in CHCl<sub>3</sub>). (Found C, 70.23;  
19 H, 8.05. C<sub>20</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub> (341.45) requires C, 70.35; H, 7.97%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.82 (s,  
20 3H, 18-H<sub>3</sub>), 2.87 (m, 2H, 6-H<sub>2</sub>), 3.32 (dd, 1H, *J* = 12.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 3.61 (dd, 1H, *J* =  
21 12.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 3.78 (s, 3H, 3-OCH<sub>3</sub>), 3.87 (d, 1H, *J* = 10.0 Hz, 17-H), 6.64 (d, 1H,  
22 *J* = 2.5 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C  
23 NMR (δ, ppm, CDCl<sub>3</sub>): 12.2 (C-18), 26.3, 27.5, 29.7, 30.4, 37.7, 38.2, 40.2, 44.0, 44.3 (C-13),  
24 49.0, 53.4 (C-16a), 55.2 (3-OCH<sub>3</sub>), 81.5 (C-17), 111.6 (C-2), 113.9 (C-4), 126.2 (C-1), 132.5 (C-  
25 10), 137.9 (C-5), 157.7 (C-3).  
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### 37 2.2.2. 3-Methoxy-16α-azidomethylestra-1,3,5(10)-trien-17β-ol (**14**)

38 Compound **6b** (470 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
39 crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3 v/v) to yield pure **14**  
40 (287 mg, 84%). Mp 85–86 °C; *R*<sub>f</sub> = 0.62 (ss A); [α]<sub>D</sub><sup>20</sup> = + 48 (*c* 1 in CHCl<sub>3</sub>). (Found C, 70.42; H,  
41 7.65. C<sub>20</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub> (341.45) requires C, 70.35; H, 7.97%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.84 (s, 3H,  
42 18-H<sub>3</sub>), 2.86 (m, 2H, 6-H<sub>2</sub>), 3.43 (d, 1H, *J* = 7.5 Hz, 17-H), 3.48 (dd, 2H, *J* = 6.5 Hz, *J* = 3.5 Hz,  
43 16a-H<sub>2</sub>), 3.78 (s, 3H, 3-OCH<sub>3</sub>), 6.63 (s, 1H, 4-H), 6.72 (dd, 1H, *J* = 6.5 Hz, *J* = 2.0 Hz, 2-H), 7.20  
44 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 11.8 (C-18), 26.1, 27.2, 28.0, 29.7, 36.6,  
45 38.5, 43.6, 43.9, 44.2 (C-13), 48.5, 55.2 (3-OCH<sub>3</sub>), 55.6 (C-16a), 85.1 (C-17), 111.5 (C-2), 113.8  
46 (C-4), 126.3 (C-1), 132.4 (C-10), 137.8 (C-5), 157.5 (C-3).  
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### 58 2.2.3. 3-Methoxy-16β-azidomethylestra-1,3,5(10)-trien-17α-ol (**15**)

59 Compound **7b** (470 mg, 1 mmol) were used for the synthesis as described in Section 2.2. The  
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4 crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3 v/v) to yield pure **15**  
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6 (275 mg, 80%). Mp 96–98; °C; *R*<sub>f</sub> = 0.60 (ss A); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = + 68 (*c* 1 in CHCl<sub>3</sub>). (Found C, 70.26;  
7  
8 H, 8.15. C<sub>20</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub> (341.45) requires C, 70.35; H, 7.97%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.76 (s,  
9  
10 3H, 18-H<sub>3</sub>), 2.86 (m, 2H, 6-H<sub>2</sub>), 3.43 (dd, 2H, *J* = 7.5 Hz, *J* = 3.0 Hz, 16a-H<sub>2</sub>), 3.61 (s, 1H, 17-H),  
11  
12 3.78 (s, 3H, 3-OCH<sub>3</sub>), 6.64 (d, 1H, *J* = 2.5 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H),  
13  
14 7.22 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 17.7 (C-18), 25.9, 27.9, 29.8, 30.3,  
15  
16 31.9, 38.6, 43.3, 45.0 (C-13), 48.9, 55.2 (3-OCH<sub>3</sub>), 55.6 (C-16a), 83.0 (C-17), 111.5 (C-2), 113.8  
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18 (C-4), 126.3 (C-1), 132.4 (C-10), 137.9 (C-5), 157.5 (C-3).

#### 2.2.4. 3-Methoxy-16 $\alpha$ -azidomethylestra-1,3,5(10)-trien-17 $\alpha$ -ol (**16**)

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22 Compound **8b** (470 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
23  
24 crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3 v/v) to yield pure **16**  
25  
26 (283 mg, 86%). Mp 118–120 °C; *R*<sub>f</sub> = 0.65 (ss A); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = + 34 (*c* 1 in CHCl<sub>3</sub>). (Found C, 70.55;  
27  
28 H, 7.78. C<sub>20</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub> (341.45) requires C, 70.35; H, 7.97%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.80 (s,  
29  
30 3H, 18-H<sub>3</sub>), 2.87 (m, 2H, 6-H<sub>2</sub>), 3.35 (dd, 1H, *J* = 12.0 Hz, *J* = 6.0 Hz, 16a-H<sub>2</sub>), 3.53 (dd, 1H, *J* =  
31  
32 12.0 Hz, *J* = 9.5 Hz, 16a-H<sub>2</sub>), 3.78 (s, 3H, 3-OCH<sub>3</sub>), 3.84 (d, 1H, *J* = 6.0 Hz, 17-H), 6.63 (d, 1H, *J*  
33  
34 = 2.5 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR ( $\delta$ , ppm,  
35  
36 CDCl<sub>3</sub>): 17.3 (C-18), 26.1, 28.0, 29.2, 31.3, 39.1, 40.5, 43.6, 46.4 (C-13), 47.0, 52.4 (C-16a),  
37  
38 55.2 (3-OCH<sub>3</sub>), 79.9 (C-17), 111.6 (C-2), 114.0 (C-4), 126.3 (C-1), 132.7 (C-10), 137.9 (C-5),  
39  
40 157.6 (C-3).

#### 2.2.5. 3-Benzoyloxy-16 $\beta$ -azidomethylestra-1,3,5(10)-trien-17 $\beta$ -ol (**17**)

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44 Compound **9c** (455 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
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46 crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:1 v/v) to yield pure **17**  
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48 (250 mg, 59%). Mp 115–117 °C; *R*<sub>f</sub> = 0.45 (ss A). (Found C, 74.55; H, 7.64. C<sub>26</sub>H<sub>31</sub>N<sub>3</sub>O<sub>2</sub>  
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50 (417.54) requires C, 74.79; H, 7.48%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.82 (s, 3H, 18-H<sub>3</sub>), 2.86 (m,  
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52 2H, 6-H<sub>2</sub>), 3.33 (dd, 1H, *J* = 12.0 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 3.60 (dd, 1H, *J* = 12.5 Hz, *J* = 7.5 Hz,  
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54 16a-H<sub>2</sub>), 3.87 (d, 1H, *J* = 9.5 Hz, 17-H), 5.04 (s, 2H, Bn-H<sub>2</sub>), 6.73 (s, 1H, 4-H), 6.79 (d, 1H, *J* =  
55  
56 8.0 Hz, *J* = 2.0 Hz, 2-H), 7.21 (d, 1H, *J* = 8.0 Hz, 1-H), 7.32 (t, 1H, *J* = 7.5 Hz, 4'-H), 7.39 (t, 2H,  
57  
58 *J* = 7.5 Hz, 3'-H and 5'-H), 7.44 (d, 2H, *J* = 7.5 Hz, 2'-H and 6'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>):  
59  
60 12.2 (C-18), 26.2, 27.5, 29.7, 30.3, 37.6, 38.1, 40.1, 43.9, 44.2 (C-13), 48.8 (C-16), 53.3 (C-16a),  
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4 69.9 (Bn-CH<sub>2</sub>), 81.5 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.3 (C-2' and C-6'), 127.8  
5 (C-4'), 128.5 (C-3' and C-5'), 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.8 (C-3).  
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10 *2.2.6. 3-Benzoyloxy-16 $\alpha$ -azidomethylestra-1,3,5(10)-trien-17 $\beta$ -ol (18)*

11 Compound **10c** (455 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
12 crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (3:1 v/v) to yield pure **18**  
13 (254 mg, 61%). Mp 75–77 °C; *R<sub>f</sub>* = 0.40 (ss A). (Found C, 74.87; H, 7.32. C<sub>26</sub>H<sub>31</sub>N<sub>3</sub>O<sub>2</sub> (417.54)  
14 requires C, 74.79; H, 7.48%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.84 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>),  
15 3.44 (t, 1H, *J* = 8.0 Hz, 17-H), 3.48 (m, 2H, 16a-H<sub>2</sub>), 5.04 (s, 2H, Bn-H<sub>2</sub>), 6.73 (s, 1H, 4-H), 6.79  
16 (d, 1H, *J* = 8.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.39 (t, 2H,  
17 *J* = 7.0 Hz, 3'- and 5'-H), 7.44 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 11.8  
18 (C-18), 26.1, 27.2, 27.9, 29.7, 36.6, 38.5, 43.6, 43.9, 44.2 (C-13), 48.6 (C-16), 55.6 (C-16a), 69.9  
19 (Bn-CH<sub>2</sub>), 85.1 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'),  
20 128.5 (C-3' and -5'), 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.8 (C-3).  
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32 *2.2.7. 3-Benzoyloxy-16 $\beta$ -azidomethyl-estra-1,3,5(10)-trien-17 $\alpha$ -ol (19)*

33 Copound **11c** (455 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The crude  
34 product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (3:1 v/v) to yield pure **19** (23.  
35 mg, 40%). Mp. 134-136 °C. *R<sub>f</sub>* = 0.38 (ss A). (Found C, 74.92; H, 7.37. C<sub>26</sub>H<sub>31</sub>N<sub>3</sub>O<sub>2</sub> (417.54)  
36 requires C, 74.79; H, 7.48%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.84 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>),  
37 3.43 (d, 2H, *J* = 8.0 Hz, 17-H), 3.48 (t, 2H, *J* = 6.5 Hz, 16a-H<sub>2</sub>), 5.04 (s, 2H, Bn-H<sub>2</sub>), 6.73 (s, 1H,  
38 4-H), 6.79 (d, 1H, *J* = 8.0 Hz, 2-H), 7.22 (d, 1H, *J* = 8.0 Hz 1-H), 7.33 (d, 1H, *J* = 7.0 Hz, 4'-H),  
39 7.39 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.44 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H). <sup>13</sup>C NMR ( $\delta$ , ppm,  
40 CDCl<sub>3</sub>): 11.8 (C-18), 26.1, 27.2, 28.0, 29.7, 36.6, 38.4, 43.5, 43.9, 44.1 (C-13), 48.5 (C-16), 55.6  
41 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 85.1 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'),  
42 127.8 (C-4'), 128.5 (C-3' and -5'), 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.7 (C-3).  
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54 *2.2.8. 3-Benzoyloxy-16 $\alpha$ -azidomethyl-estra-1,3,5(10)-trien-17 $\alpha$ -ol (20)*

55 Compound **12c** (455 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
56 crude was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:1 v/v) to yield pure **20** (330 mg,  
57 79%). Mp 90–92 °C. *R<sub>f</sub>* = 0.45 (ss A). (Found C, 74.68; H, 7.55. C<sub>26</sub>H<sub>31</sub>N<sub>3</sub>O<sub>2</sub> (417.54) requires C,  
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4 74.79; H, 7.48%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.71 (m, 2H, 6-H<sub>2</sub>), 3.35 (dd,  
5 1H, *J* = 12.0 Hz, *J* = 6.5 Hz, 16a-H<sub>2</sub>), 3.52 (dd, 1H, *J* = 12.0 Hz, *J* = 6.5 Hz, 16a-H<sub>2</sub>), 3.84 (d, 1H,  
6 *J* = 5.0 Hz, 17-H), 5.04 (s, 2H, Bn-H<sub>2</sub>), 6.73 (s, 1H, 4-H), 6.79 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-  
7 H), 7.22 (d, 1H, *J* = 8.5 Hz, 1-H), 7.33 (t, 1H, *J* = 7.5 Hz, 4'-H), 7.39 (t, 2H, *J* = 7.5 Hz, 3'- and  
8 5'-H), 7.44 (d, 2H, *J* = 7.5 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.2 (C-18), 26.0, 27.9,  
9 29.0, 29.7, 31.2, 38.9, 40.4, 43.5, 46.3 (C-13), 46.8 (C-16), 52.2 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 79.7 (C-  
10 17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -  
11 5'), 132.8 (C-10), 137.3 (C-1'), 138.0 (C-5), 156.7 (C-3).  
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### 20 21 2.3. General procedure for the synthesis of triazoles (**21a–e**, **22a–e**, **23a–e**, **24a–e**, **25a–e**, **26a–e**, 22 **27a–e**, and **28a–e**)

23  
24 3-Methoxy-16-azidomethylestra-1,3,5(10)-trien-17-ol isomers (**13–16**) (342 mg, 1 mmol) or 3-  
25 benzyloxy-16-azidomethylestra-1,3,5(10)-trien-17-ol isomers (**17–20**) 418 mg, 1 mmol) were  
26 dissolved in CH<sub>2</sub>Cl<sub>2</sub> (20 ml), then CuI (19 mg, 0.10 mmol), Et<sub>3</sub>N (0.2 ml, 2 mmol) and the  
27 appropriate terminal alkynes (2 mmol) were added. The mixtures were stirred under reflux for 24  
28 h, then diluted with water (30 ml) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 30 ml). The combined organic  
29 phases were dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated *in vacuo*. The crude products were purified by  
30 flash chromatography using CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate in different ratios.  
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#### 39 2.3.1. 3-Methoxy-16β-(4'-cyclopropyl-1'-H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β- 40 ol (**21a**)

41  
42 Compound **13** (342 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
43 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
44 CH<sub>2</sub>Cl<sub>2</sub>/hexane (3:1 v/v) to yield pure **21a** (210 mg, 51%) as a white solid. Mp: 189–191 °C; *R*<sub>f</sub> =  
45 0.44 (ss B). (Found C, 73.84; H, 7.98. C<sub>25</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (407.55) requires C, 73.68; H, 8.16%). <sup>1</sup>H  
46 NMR (δ, ppm, CDCl<sub>3</sub>): 0.80 (s, 3H, 18-H<sub>3</sub>), 0.83 (s, 2H, cyclopropyl-H<sub>2</sub>), 0.94 (s, 2H,  
47 cyclopropyl-H<sub>2</sub>), 2.72 (d, 1H, *J* = 7.0 Hz, 1''-H), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 3.93  
48 (d, 1H, *J* = 9.5 Hz, 17-H), 4.21 (dd, 1H, *J* = 13.0 Hz, *J* = 6.0 Hz, 16a-H<sub>2</sub>), 4.62 (t, 1H, *J* = 8.0 Hz,  
49 16a-H<sub>2</sub>), 6.62 (s, 1H, 4-H), 6.71 (d, 1H, *J* = 8.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz, 1-H), 7.29 (s,  
50 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 6.7 (C-1''), 7.68 (C-2'' and -3''), 12.3 (C-18), 26.2, 27.4,  
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4 29.7, 30.8, 37.5, 38.0, 41.4, 43.8, 44.3 (C-16a), 48.7, 51.7 (C-13), 55.2 (3-OCH<sub>3</sub>), 80.7 (C-17),  
5  
6 111.5 (C-2), 113.8 (C-4), 126.3 (C-1), 132.4 (C-10), 137.8 (C-5), 157.5 (C-3).  
7  
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10 **2.3.2. 3-Methoxy-16 $\beta$ -(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17 $\beta$ -**  
11 **ol (21b)**

12  
13 Compound **13** (342 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
14  
15 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
16  
17 CH<sub>2</sub>Cl<sub>2</sub> to yield pure **21b** (370 mg, 85%) as a white solid. Mp: 191–192 °C; *R*<sub>f</sub>= 0.46 (ss B).  
18  
19 (Found C, 74.62; H, 8.42. C<sub>27</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (435.60) requires C, 74.45; H, 8.56%). <sup>1</sup>H NMR ( $\delta$ , ppm,  
20  
21 CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.19 (s, 1H, 1''-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 3.94  
22  
23 (d, 1H, *J* = 9.5 Hz, 17-H), 4.24 (d, 1H, *J* = 8.0 Hz, 16a-H<sub>2</sub>), 4.65 (s, 1H, 16a-H<sub>2</sub>), 6.62 (s, 1H, 4-  
24  
25 H), 6.71 (d, 1H, *J* = 8.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz, 1-H), 7.34 (s, 1H, 5'-H). <sup>13</sup>C NMR ( $\delta$ ,  
26  
27 ppm, CDCl<sub>3</sub>): 12.3 (C-18), 25.1 (C-3'' and -4''), 26.2, 27.4, 29.7 (C-2'' and 5''), 30.8, 33.2, 36.7,  
28  
29 37.5, 38.0, 42.4 (C-16a), 43.8, 44.3 (C-13), 48.7, 51.8, 55.2 (3-OCH<sub>3</sub>), 62.1 (C-16), 80.7 (C-17),  
30  
31 111.5 (C-2), 113.7 (C-4), 126.3 (C-1), 132.4 (C-10), 137.8 (C-5), 157.4 (C-3).  
32

33  
34 **2.3.3. 3-Methoxy-16 $\beta$ -(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17 $\beta$ -**  
35 **ol (21c)**

36  
37 Compound **13** (342 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
38  
39 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
40  
41 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **21c** (370 mg, 82%) as a white solid. Mp: 189–190  
42  
43 °C; *R*<sub>f</sub>= 0,40 (ss B). (Found C, 74.92; H, 8.55. C<sub>28</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (449.63) requires C, 74.80; H, 8.74%).  
44  
45 <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 3.94  
46  
47 (d, 1H, *J* = 9.5 Hz, 17-H), 4.24 (m, 1H, 16a-H<sub>2</sub>), 4.65 (m, 1H, 16a-H<sub>2</sub>), 6.62 (s, 1H, 4-H), 6.71 (d,  
48  
49 1H, *J* = 8.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32 (s, 1H, 5'-H). <sup>13</sup>C NMR ( $\delta$ , ppm,  
50  
51 CDCl<sub>3</sub>): 12.3 (C-18), 26.0, 26.1 (C-2'' and -6''), 26.2, 27.4, 29.7, 30.8, 33.0, 37.5, 38.0, 41.4 (C-  
52  
53 1''), 43.8, 44.3 (C-13), 48.3, 55.2 (3-OCH<sub>3</sub>), 62.1, 80.7 (C-17), 111.5 (C-2), 113.7 (C-4), 126.3  
54  
55 (C-1), 132.4 (C-10), 137.8 (C-5), 157.4 (C-3).  
56

57  
58 **2.3.4. 3-Methoxy-16 $\beta$ -(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17 $\beta$ -ol**  
59 **(21d)**

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4 Compound **13** (342 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
5  
6 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
7  
8 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **21d** (368 mg, 83%) as a white solid. Mp: 232–234  
9  
10 °C; *R*<sub>f</sub> = 0.35 (ss B). (Found C, 75.98; H, 7.36. C<sub>28</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (443.58) requires C, 75.81; H, 7.50%).  
11  
12 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.73 (m, 2H, 6-H<sub>2</sub>), 3.68 (s, 3H, 3-OCH<sub>3</sub>), 3.79  
13  
14 (d, 1H, *J* = 10.0 Hz, 17-H), 4.20 (t, 1H, *J* = 13.5 Hz, 16a-H<sub>2</sub>), 4.63 (dd, 1H, *J* = 13.5 Hz, *J* = 4.5  
15  
16 Hz, 16a-H<sub>2</sub>), 6.59 (s, 1H, 4-H), 6.67 (d, 1H, *J* = 8.5 Hz, 2-H), 7.16 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32  
17  
18 (t, 1H, *J* = 7.5 Hz, 4''-H), 7.44 (t, 2H, *J* = 7.5 Hz, 3''- and 5''-H), 7.85 (d, 2H, *J* = 7.5 Hz, 2''- and  
19  
20 6''-H), 8.60 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 12.4 (C-18), 25.8, 26.9, 29.1, 30.0, 36.9,  
21  
22 37.8, 40.4, 43.3, 43.7 (C-13), 47.8, 52.3 (C-16a), 54.8 (3-OCH<sub>3</sub>), 79.5 (C-17), 111.4 (C-2), 113.3  
23  
24 (C-4), 121.5 (C-5'), 124.5 (C-2'' and -6''), 126.0 (C-1), 127.6 (C-4''), 127.8 (C-3'' and -5''), 130.9  
25  
26 (C-1''), 132.0 (C-10), 137.3 (C-5), 146.0 (C-4'), 156.9 (C-3).

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28 2.3.5. *3-Methoxy-16β-(4'-nitro-benzoyloxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-*  
29  
30 *1,3,5(10)-trien-17β-ol (21e)*

31  
32 Compound **13** (342 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 410 mg) were used for  
33  
34 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
35  
36 with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **21e** (475 mg, 86%) as a yellow solid. Mp:  
37  
38 134–135.5 °C; *R*<sub>f</sub> = 30 (ss B). (Found C, 66.12; H, 6.08. C<sub>30</sub>H<sub>34</sub>N<sub>4</sub>O<sub>6</sub> (546.61) requires C, 65.92;  
39  
40 H, 6.27%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.73 (s, 3H, 18-H<sub>3</sub>), 2.70 (m, 2H, 6-H<sub>2</sub>), 3.66 (s, 3H, 3-  
41  
42 OCH<sub>3</sub>), 4.18 (dd, 1H, *J* = 13.5 Hz, *J* = 11.5 Hz, 16a-H<sub>2</sub>), 4.58 (dd, 1H, *J* = 13.5 Hz, *J* = 4.5 Hz,  
43  
44 16a-H<sub>2</sub>), 5.02 (d, 1H, *J* = 4.5 Hz, 17-H), 5.44 (s, 2H, 4'-H<sub>2</sub>), 6.55 (d, 1H, *J* = 1.5 Hz, 4-H), 6.63  
45  
46 (dd, 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.12 (d, 1H, *J* = 8.5 Hz, 1-H), 8.16 (d, 2H, *J* = 8.5 Hz, 3''-  
47  
48 and 5''-H), 8.31 (t, 3H, *J* = 8.5 Hz, 2''- and 6''-H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 12.3 (C-18),  
49  
50 25.8, 26.9, 29.1, 30.0, 36.9, 37.8, 40.4, 43.3, 43.7 (C-13), 47.8, 52.2 (C-16a), 54.7 (3-OCH<sub>3</sub>),  
51  
52 58.7 (4'-CH<sub>2</sub>), 79.5 (C-17), 111.3 (C-2), 113.3 (C-4), 123.8 (C-2'' and -6''), 125.1 (C-5'), 126.0  
53  
54 (C-1), 130.6 (C-3'' and -5''), 131.9 (C-10), 134.7 (C-1''), 137.2 (C-5), 141.0 (C-4''), 150.2 (C-4'),  
55  
56 156.9 (C-3), 163.9 (C=O).

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58 2.3.6. *3-Methoxy-16β-(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
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60 *17β-ol (21f)*

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4 Compound **13** (274 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
5 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
6 and the precipitate separating out was filtered off and recrystallized from a mixture of ethyl  
7 acetate/hexane to afford **21f** (171 mg, 86%) as a white crystalline material. Mp: 194–195 °C; *R*<sub>f</sub>=  
8 0.25 (ss B). (Found C, 69.23; H, 8.04. C<sub>23</sub>H<sub>31</sub>N<sub>3</sub>O<sub>3</sub> (397.51) requires C, 69.49; H, 7.86%). <sup>1</sup>H  
9 NMR (δ, ppm, DMSO-d<sub>6</sub>): 0.76 (s, 3H, 18-H<sub>3</sub>), 2.71 (m, 2H, 6-H<sub>2</sub>), 3.68 (s, 3H, 3-OCH<sub>3</sub>), 3.76  
10 (d, 1H, *J* = 5.5 Hz, 17-H), 4.14 (t, 1H, *J* = 12.5 Hz, 16a-H<sub>2</sub>), 4.49 (m, 3H, 4'-H<sub>2</sub> and 16a-H<sub>2</sub>),  
11 5.03 (d, 1H, *J* = 3.5 Hz, 17-OH), 5.15 (brs, 1H, CH<sub>2</sub>-OH), 6.59 (s, 1H, 4-H), 6.66 (d, 1H, *J* = 8.5  
12 Hz, 2-H), 7.16 (d, 1H, *J* = 8.5 Hz, 1-H), 7.99 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, DMSO-d<sub>6</sub>): 12.4  
13 (C-18), 25.9, 26.9, 29.2, 30.0, 36.9, 37.9, 40.5, 43.4, 43.8 (C-13), 47.8, 52.0 (C-16a), 54.8 (3-  
14 OCH<sub>3</sub>), 55.0 (4'-CH<sub>2</sub>), 79.5 (C-17), 111.4 (C-2), 113.4 (C-4), 122.8 (C-5'), 126.1 (C-1), 132.0  
15 (C-10), 137.3 (C-5), 147.6 (C-4'), 157.0 (C-3).  
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### 28 2.3.7. 3-Methoxy-16a-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β- 29 ol (**22a**) 30

31 Compound **14** (342 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
32 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
33 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **22a** (261 mg, 64%) as a white solid. Mp: 67–69 °C;  
34 *R*<sub>f</sub>= 0.35 (ss B). (Found C, 73.55; H, 7.98. C<sub>25</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (407.55) requires C, 73.68; H, 8.16%). <sup>1</sup>H  
35 NMR (δ, ppm, CDCl<sub>3</sub>): 0.82 (m, 5H, 18-H<sub>3</sub> and cyclopropyl-H<sub>2</sub>), 0.95 (m, 2H, cyclopropyl-H<sub>2</sub>),  
36 2.83 (m, 2H, 6-H<sub>2</sub>), 3.53 (d, 1H, *J* = 7.5 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.35 (t, 1H, *J* = 7.5 Hz,  
37 16a-H<sub>2</sub>), 4.44 (dd, 1H, *J* = 13.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.0 Hz, 4-H), 6.70 (dd,  
38 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.18 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 6.7  
39 (C-1''), 7.7 (C-2'' and -3''), 11.8 (C-18), 26.1, 27.2, 28.2, 29.7, 36.6, 38.4, 43.9, 44.3, 44.3 (C-  
40 16a), 48.3, 54.5 (C-13), 62.1 (3-OCH<sub>3</sub>), 85.1 (C-17), 111.5 (C-2), 113.8 (C-4), 126.2 (C-1), 132.3  
41 (C-10), 137.8 (C-5), 157.4 (C-3).  
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### 54 2.3.8. 3-Methoxy-16a-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β- 55 ol (**22b**) 56

57 Compound **14** (342 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
58 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
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4 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **22b** (290 mg, 66%) as a white solid. Mp: 163–165  
5 °C; *R*<sub>f</sub> = 0.32 (ss B). (Found C, 74.63; H, 8.41. C<sub>27</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (435.60) requires C, 74.45; H, 8.56%).  
6 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.83 (s, 3H, 18-H<sub>3</sub>), 1.68 (s, 4H, 3''- and 4''-H<sub>2</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>),  
7 3.19 (m, 1H, 1''-H), 3.56 (d, 1H, *J* = 7.0 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.43 (m, 2H, 16a-H<sub>2</sub>),  
8 6.62 (s, 1H, 4-H), 6.70 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H), 7.35 (s, 1H, 5'-H).  
9 <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 11.9 (C-18), 25.1 (C-3'' and -4''), 26.1, 27.2, 28.3, 29.7 (C-2'' and -  
10 5''), 33.2, 36.6, 38.4, 43.9, 44.2, 44.3 (C-13), 48.4, 55.2 (3-OCH<sub>3</sub>), 62.1 (C-16a), 85.3 (C-17),  
11 111.5 (C-2), 113.8 (C-4), 126.3 (C-1), 132.3 (C-10), 137.8 (C-5), 157.5 (C-3).  
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21 **2.3.9. 3-Methoxy-16a-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β-**  
22 **ol (22c)**

23  
24 Compound **14** (342 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
25 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
26 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **22c** (345 mg, 76%) as a white solid. Mp: 80–82 °C;  
27 *R*<sub>f</sub> = 0.34 (ss B). (Found 74.96; H, 8.54. C<sub>28</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (449.63) requires C, 74.80; H, 8.74%). <sup>1</sup>H  
28 NMR (δ, ppm, CDCl<sub>3</sub>): 0.83 (s, 3H, 18-H<sub>3</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.55 (s, 1H, 17-H), 3.77 (s, 3H,  
29 3-OCH<sub>3</sub>), 4.46 (s, 2H, 16a-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.0 Hz, 4-H), 6.70 (dd, 1H, *J* = 8.5 Hz, *J* = 2.0  
30 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 11.9 (C-18), 26.0 and 26.1  
31 (C-2'' and -6'', C-3'' and -5''), 27.2, 28.3, 29.7, 36.6, 38.4, 43.9, 44.3 (C-13), 48.4, 55.2 (3-OCH<sub>3</sub>),  
32 62.1 (C-1''), 62.1 (C-16a), 85.2 (C-17), 111.5 (C-2), 113.8 (C-4), 126.2 (C-1), 132.3 (C-10),  
33 137.8 (C-5), 157.4 (C-3).  
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45 **2.3.10. 3-Methoxy-16a-(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β-**  
46 **ol (22d)**

47  
48 Compound **14** (342 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
49 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel ethyl  
50 acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **22d** (368 mg, 82%) as a white solid. Mp: 204–205 °C;  
51 *R*<sub>f</sub> = 0.38 (ss B). (Found C, 75.63; H, 7.72. C<sub>28</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (443.58) requires C, 75.81; H, 7.50%). <sup>1</sup>H  
52 NMR (δ, ppm, DMSO-*d*<sub>6</sub>): 0.73 (s, 3H, 18-H<sub>3</sub>), 2.73 (m, 2H, 6-H<sub>2</sub>), 3.67 (s, 3H, 3-OCH<sub>3</sub>), 4.36 (t,  
53 1H, *J* = 13.5 Hz, 16a-H<sub>2</sub>), 4.54 (dd, 1H, *J* = 13.5 Hz, *J* = 4.0 Hz, 16a-H<sub>2</sub>), 4.91 (d, 1H, *J* = 4.0 Hz,  
54 17-H), 6.58 (s, 1H, 4-H), 6.67 (d, 1H, *J* = 8.5 Hz, 2-H), 7.15 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32 (t, 1H,  
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4  $J = 7.0$  Hz, 4''-H), 7.44 (t, 2H,  $J = 7.0$  Hz, 3''- and 5''-H), 7.86 (d, 2H,  $J = 7.0$  Hz, 2''- and 6''-H),  
5  
6 8.61 (s, 1H, 5'-H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm, DMSO- $d_6$ ): 11.8 (C-18), 25.8, 26.7, 27.3, 29.1, 36.3, 38.1,  
7  
8 43.4, 43.5, 43.8, 47.5, 53.5 (C-13), 54.8 (3-OCH $_3$ ), 83.1 (C-17), 111.4 (C-2), 113.3 (C-4), 121.4  
9  
10 (C-5'), 125.0 (C-2'' and -6''), 126.0 (C-1), 127.6 (C-4''), 128.8 (C-3'' and -5''), 130.8 (C-1'),  
11  
12 132.0 (C-10), 137.3 (C-5), 146.1 (C-4'), 156.9 (C-3).

13  
14  
15 *2.3.11.3-Methoxy-16a-[4'(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-*  
16  
17 *1,3,5(10)-trien-17 $\beta$ -ol (22e)*

18  
19 Compound **14** (342 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 410 mg) were used for  
20  
21 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
22  
23 with ethyl acetate/CH $_2$ Cl $_2$  (5:95 v/v) to yield pure **22e** (445 mg, 81%) as a yellow solid. Mp:  
24  
25 86–88 °C;  $R_f = 0.28$  (ss B). (Found C, 66.08; H, 6.43. C $_{30}$ H $_{34}$ N $_4$ O $_6$  (546.61) requires C, 65.92; H,  
26  
27 6.27%).  $^1\text{H}$  NMR ( $\delta$ , ppm, DMSO- $d_6$ ): 0.69 (s, 3H, 18-H $_3$ ), 2.68 (m, 2H, 6-H $_2$ ), 3.57 (s, 3H, 3-  
28  
29 OCH $_3$ ), 4.38 (dd, 1H,  $J = 13.5$  Hz,  $J = 9.0$  Hz, 16a-H $_2$ ), 4.52 (dd, 1H,  $J = 13.5$  Hz,  $J = 4.5$  Hz,  
30  
31 16a-H $_2$ ), 4.86 (d, 1H,  $J = 4.5$  Hz, 17-H), 5.46 (s, 2H, 4'-H $_2$ ), 6.55 (d, 1H,  $J = 1.5$  Hz, 4-H), 6.63  
32  
33 (dd, 1H,  $J = 8.5$  Hz, 2-H), 7.10 (d, 1H,  $J = 8.5$  Hz, 1-H), 8.16 (d, 2H,  $J = 8.5$  Hz, 3''- and 5''-H),  
34  
35 8.28 (d, 2H,  $J = 8.5$  Hz, 2''- and 6''-H), 8.31 (s, 1H, 5'-H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm, DMSO- $d_6$ ): 11.7  
36  
37 (C-18), 25.7, 26.6, 27.1, 29.0, 36.4, 38.0, 43.3, 43.4 (C-13), 43.7, 47.7, 53.1 (C-16a), 54.7 (3-  
38  
39 OCH $_3$ ), 58.6 (4''-CH $_2$ ), 82.8 (C-17), 111.3 (C-2), 113.3 (C-4), 123.8 (C-2'' and -6''), 125.2 (C-5'),  
40  
41 125.9 (C-1), 130.6 (C-3'' and -5''), 131.8 (C-10), 134.7 (C-1'), 137.2 (C-5), 141.1 (C-4''), 150.2  
42  
43 (C-4'), 156.9 (C-3), 163.9 (C=O).

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45 *2.3.12. 3-Methoxy-16a-(4'-hydroxymethyl-1'H-1',2'3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
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47 *17 $\beta$ -ol (22f)*

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49  
50 Compound **22e** (274 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH $_3$  (14  
51  
52 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
53  
54 and the precipitate separating out was filtered off and recrystallized from a mixture of ethyl  
55  
56 acetate/hexane to afford **22f** (175 mg, 88%) as a white crystalline product. Mp: 98–100 °C;  $R_f =$   
57  
58 0.28 (ss B). (Found C, 69.74; H, 7.72. C $_{23}$ H $_{31}$ N $_3$ O $_3$  (397.51) requires C, 69.49; H, 7.86%).  $^1\text{H}$   
59  
60 NMR ( $\delta$ , ppm, CDCl $_3$ ): 0.81 (s, 3H, 18-H $_3$ ), 2.82 (m, 2H, 6-H $_2$ ), 3.50 (d, 1H,  $J = 7.0$  Hz, 17-H),  
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4 3.76 (s, 3H, 3-OCH<sub>3</sub>), 4.42 (d, 2H, *J* = 7.0 Hz, 16a-H<sub>2</sub>), 4.71 (s, 2H, 4'-H<sub>2</sub>), 6.61 (s, 1H, 4-H),  
5  
6 6.69 (d, 1H, *J* = 8.5 Hz, 2-H), 7.17 (d, 1H, *J* = 8.5 Hz, 1-H), 7.68 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ,  
7  
8 ppm, CDCl<sub>3</sub>): 11.9 (C-18), 26.1, 27.2, 28.2, 29.6, 36.5, 38.4, 43.8, 44.0, 44.4 (C-13), 48.2, 54.6  
9 (C-16a), 55.2 (3-OCH<sub>3</sub>), 56.0 (4'-CH<sub>2</sub>), 85.1 (C-17), 111.5 (C-2), 113.8 (C-4), 126.3 (C-1), 132.3  
10 (C-10), 137.8 (C-5), 157.4 (C-3).

15 2.3.13. *3-Methoxy-16α-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
16 *17β-ol (23a)*

17  
18 Compound **15** (342 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
19 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
20 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **23a** (261 mg, 64%) as a white solid. Mp: 67–69 °C;  
21 *R*<sub>f</sub> = 0.32 (ss B). (Found C, 73.85; H, 8.32. C<sub>25</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (407.55) requires C, 73.68; H, 8.16%). <sup>1</sup>H  
22 NMR (δ, ppm, CDCl<sub>3</sub>): 0.82 (m, 5H, 18-H<sub>3</sub> and cyclopropyl-H<sub>2</sub>), 0.95 (m, 2H, cyclopropyl-H<sub>2</sub>),  
23 2.83 (m, 2H, 6-H<sub>2</sub>), 3.53 (d, 1H, *J* = 7.5 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.35 (t, 1H, *J* = 7.5 Hz,  
24 16a-H<sub>2</sub>), 4.44 (dd, 1H, *J* = 13.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.0 Hz, 4-H), 6.70 (dd,  
25 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.18 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 6.7  
26 (C-1''), 7.7 (C-2'' and -3''), 11.8 (C-18), 26.1, 27.2, 28.2, 29.7, 36.6, 38.4, 43.9, 44.3, 44.3 (C-  
27 16a), 48.3, 54.5 (C-13), 62.1 (3-OCH<sub>3</sub>), 85.1 (C-17), 111.5 (C-2), 113.8 (C-4), 126.2 (C-1), 132.3  
28 (C-10), 137.8 (C-5), 157.4 (C-3).

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41 2.3.14. *3-Methoxy-16β-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17α-*  
42 *ol (23b)*

43  
44 Compound **15** (342 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
45 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
46 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **23b** (380 mg, 87%) as yellow crystalline material.  
47 Mp: 67–68 °C; *R*<sub>f</sub> = 0.36 (ss B). (Found C, 74.28; H, 8.47. C<sub>27</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (435.60) requires C,  
48 74.45; H, 8.56%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.68 (s,  
49 1H, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.44 (d, 2H, *J* = 15.0 Hz, 16a-H<sub>2</sub>), 6.62 (s, 1H, 4-H), 6.70 (d,  
50 1H, *J* = 8.5 Hz, 2-H), 7.20 (t, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.9 (C-18), 25.1  
51 (C-3'' and -4''), 25.9, 26.1, 27.2, 28.0, 29.7, 30.4, 31.8, 36.6 (C-16a), 38.5, 43.3, 43.8, 45.1 (C-  
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4 13), 48.9, 55.2 (3-OCH<sub>3</sub>), 62.1 (C-1''), 82.6 (C-17), 111.5 (C-2), 113.7 (C-4), 113.8 (C-5'), 126.2  
5 (C-1), 132.1 (C-10), 137.8 (C-5), 137.8 (C-4'), 157.4 (C-3).  
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10 **2.3.15. 3-Methoxy-16 $\beta$ -(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methyestra-1,3,5(10)-trien-17a-**  
11 **ol (23c)**

12  
13 Compound **15** (342, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
14 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
15 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **23c** (306 mg, 68%) as a white solid. Mp: 90-92 °C;  
16 *R*<sub>f</sub> = 0.37 (ss B). (Found C, 74.95; H, 8.83. C<sub>28</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (449.63) requires C, 74.80; H, 8.74%). <sup>1</sup>H  
17 NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.67 (d, 1H, *J* = 1.0 Hz, 17-H),  
18 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.43 (m, 1H, 16a-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.5 Hz, 4-H), 6.71 (dd, 1H, *J* = 8.5  
19 Hz, *J* = 2.5 Hz, 2-H), 7.20 (t, 1H, *J* = 8.5 Hz, 1-H), 7.35 (s, 1H, 5'-H). <sup>13</sup>C NMR ( $\delta$ , ppm,  
20 CDCl<sub>3</sub>): 17.9 (C-18), 25.9, 26.0, 26.1 (C-2'' and -6''), 28.0, 29.7, 30.4, 31.8, 33.0, 35.2 (C-1''),  
21 36.6, 38.5, 43.3, 45.1 (C-13), 48.9, 49.1, 54.3 (C-16a), 55.2 (3-OCH<sub>3</sub>), 82.6 (C-1), 132.4 (C-10),  
22 137.8 (C-5), 153.7 (C-4'), 157.7 (C-3).  
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33 **2.3.16. 3-Methoxy-16 $\beta$ -(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methy-estra-1,3,5(10)-trien-17a-ol**  
34 **(23d)**

35  
36 Compound **15** (342 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
37 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
38 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (2.5:97.5 v/v) to yield pure **23d** (299 mg, 67%) as white crystals. Mp:  
39 173–174 °C; *R*<sub>f</sub> = 0.34 (ss B). (Found C 75.98; H, 7.33. C<sub>28</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (443.58) requires C, 75.81;  
40 H, 7.50%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.71 (d, 1H, *J* =  
41 1.5 Hz, 17-H), 3.78 (s, 3H, 3-OCH<sub>3</sub>), 4.46 (dd, 1H, *J* = 13.5 Hz, *J* = 8.0 Hz, 16a-H<sub>2</sub>), 4.55 (dd,  
42 1H, *J* = 13.5 Hz, *J* = 8.0 Hz, 16a-H<sub>2</sub>), 6.63 (d, 1H, *J* = 2.0 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* =  
43 2.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.27 (t, 1H *J* = 7.5 Hz, 4''-H), 7.42 (t, 2H, *J* = 7.5 Hz,  
44 3''- and 5''-H), 7.83 (d, 2H, *J* = 7.5 Hz, 2''- and 6''-H), 7.87 (s, 1H, 5'-H). <sup>13</sup>C NMR ( $\delta$ , ppm,  
45 CDCl<sub>3</sub>): 17.9 (C-18), 25.9, 27.9, 29.7, 30.4, 31.8, 38.5, 43.3, 45.1, (C-13), 48.8, 49.1, 54.5 (C-  
46 16a), 55.2 (3-OCH<sub>3</sub>), 82.5 (C-17), 111.5 (C-2), 113.7 (C-4), 119.6 (C-5'), 125.7 (C-2'' and -6''),  
47 126.3 (C-1), 128.1 (C-4''), 128.8 (C-3'' and -5''), 130.5 (C-1''), 132.4 (C-10), 137.8 (C-5), 147.8  
48 (C-4'), 157.4 (C-3).  
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6 2.3.17.3-Methoxy-16 $\beta$ -[4'(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl)methylestra-  
7  
8 1,3,5(10)-trien-17a-ol (**23e**)  
9

10 Compound **15** (342, 1 mmol) and propargyl 4-nitro benzoate (2 mmol, 410 mg) were used for the  
11 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
12 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **23e** (370 mg, 67%) as a yellow crystalline material.  
13 Mp: 62–63 °C; *R*<sub>f</sub> = 0.38 (ss B). (Found C, 66.14; H, 6.42. C<sub>30</sub>H<sub>34</sub>N<sub>4</sub>O<sub>6</sub> (546.61) requires C,  
14 65.92; H, 6.27%). <sup>1</sup>H NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>): 0.65 (s, 3 H, 18-H<sub>3</sub>), 2.74 (m, 2H, 6-H<sub>2</sub>), 3.68 (s,  
15 3H, 3-OCH<sub>3</sub>), 4.41 (dd, 1H, *J* = 13.0 Hz, *J* = 8.5 Hz, 16a-H<sub>2</sub>), 4.56 (dd, 1H, *J* = 13.0 Hz, *J* = 8.5  
16 Hz, 16a-H<sub>2</sub>), 4.63 (d, 1H, *J* = 4.5 Hz, 17-H), 6.58 (s, 1H, 4-H), 6.66 (d, 1H, *J* = 8.5 Hz, 2-H), 7.16  
17 (d, 1H, *J* = 8.5 Hz, 1-H), 8.19 (d, 2H, *J* = 8.5 Hz, 3''- and 5''-H), 8.34 (d, 2H, *J* = 8.5 Hz, 2''- and  
18 6''-H). <sup>13</sup>C NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>): 17.5 (C-18), 25.6, 27.5, 29.6, 31.8, 38.2, 43.0, 44.5, 47.9  
19 (C-13), 48.2, 49.1, 53.6 (C-16a), 54.8 (3-OCH<sub>3</sub>), 58.7 (4'-CH<sub>2</sub>), 80.8 (C-17), 111.3 (C-2), 113.3  
20 (C-4), 123.8 (C-1), 126.1 (C-5'), 130.6 (C-2'' and -6''), 131.9 (C-3'' and -5''), 133.0 (C-10), 134.7  
21 (C-1''), 137.3 (C-5), 141.4 (C-4''), 150.2 (C-4'), 156.9 (C-3), 163.9 (C=O).  
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33 2.3.18. 3-Methoxy-16 $\beta$ -(4'-hydroxymethyl-1'H-1',2'3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
34 17a-ol (**23f**)  
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37 Compound **23e** (274 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
38 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
39 and the precipitate separating out was filtered off, dissolved in dichloromethane and washed with  
40 water. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated *in vacuo* to afford **23f** (183 mg,  
41 92%) as oil. *R*<sub>f</sub> = 0.26 (ss B). (Found C, 69.28; H, 7.95. C<sub>23</sub>H<sub>31</sub>N<sub>3</sub>O<sub>3</sub> (397.51) requires C, 69.49;  
42 H, 7.86%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.78 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.65 (s, 1H, 17-  
43 H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.46 (m, 2H, 16a-H<sub>2</sub>), 4.78 (s, 2H, 4'-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.0 Hz, 4-  
44 H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR ( $\delta$ , ppm,  
45 CDCl<sub>3</sub>): 17.9 (C-18), 25.9, 27.9, 29.7, 30.3, 31.8, 38.5, 43.3, 45.2 (C-13), 48.8, 49.2, 54.6 (C-  
46 16a), 55.2 (3-OCH<sub>3</sub>), 56.1 (4'-CH<sub>2</sub>), 82.1 (C-17), 111.5 (C-2), 113.7 (C-4), 123.5 (C-5'), 126.3  
47 (C-1), 132.4 (C-10), 137.8 (C-5), 157.4 (C-3).  
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4 2.3.19. 3-Methoxy-16a-(4'-cyclopropyl-1'-H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
5  
6 17a-ol (**24a**)

7 Compound **16** (342 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
8 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
9 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (2.5:97.5 v/v) to yield pure **24a** (310 mg, 76%) as a white solid. Mp:  
10 165–166 °C; *R*<sub>f</sub> = 0.40 (ss B). (Found C, 73.85; H, 8.34. C<sub>25</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (407.55) requires C, 73.68;  
11 H, 8.16%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.74 (s, 3H, 18-H<sub>3</sub>), 0.85 and 0.96 (2 x m, 4H, 2''- and 3''-  
12 H<sub>2</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.63 (d, 1H, *J* = 5.0 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.28 (dd, 1H, *J* =  
13 13.0 Hz, *J* = 5.0 Hz, 16a-H<sub>2</sub>), 4.59 (t, 1H, *J* = 12.0 Hz, 16a-H<sub>2</sub>), 6.63 (d, 1H, *J* = 2.0 Hz, 4-H),  
14 6.71 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.22 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm,  
15 CDCl<sub>3</sub>): 6.6 (C-1''), 7.7 and 7.8 (C-2'' and -3''), 17.1 (C-18), 26.0, 28.0, 28.9, 29.8, 31.2, 38.9,  
16 42.3, 46.3 (C-16a), 47.0, 50.5 (C-13), 55.2 (3-OCH<sub>3</sub>), 78.8 (C-17), 111.4 (C-2), 113.7 (C-4),  
17 120.6 (C-5'), 126.3 (C-1), 132.5 (C-10), 137.9 (C-5), 149.8 (C-4'), 157.4 (C-3).  
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30 2.3.20. 3-Methoxy-16a-(4'-cyclopentyl-1'-H-1',2',3'-triazol-1'-yl)methyl-estra-1,3,5(10)-trien-  
31  
32 17a-ol (**24b**)

33 Compound **16** (342 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
34 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
35 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **24b** (383 mg, 88%) as yellow crystalline product.  
36 Mp: 171–173 °C; *R*<sub>f</sub> = 0.42 (ss B). (Found C, 74.67; H, 8.72. C<sub>27</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (435.60) requires C,  
37 74.45; H, 8.56%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 1.25 (s, 8H, 2''-, 3''-, 4''- and  
38 5''-H<sub>2</sub>), 2.86 (m, 2H, 6-H<sub>2</sub>), 3.18 (m, 1H, 1''-H), 3.64 (d, 1H, *J* = 5.0 Hz, 17-H), 3.77 (s, 3H, 3-  
39 OCH<sub>3</sub>), 4.29 (dd, 1H, *J* = 13.5 Hz, *J* = 5.5 Hz, 16a-H<sub>2</sub>), 4.62 (dd, 1H, *J* = 13.5 Hz, *J* = 11.5 Hz,  
40 16a-H<sub>2</sub>), 6.63 (d, 1H, *J* = 2.0 Hz, 4-H), 6.71 (dd, 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.22 (d, 1H, *J* =  
41 8.5 Hz, 1-H), 7.36 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.2 (C-18), 25.1 (C-3'' and -4''),  
42 26.0, 28.0, 29.0, 29.7, 29.9, 31.2, 33.2, 36.7, 38.9, 42.4, 43.5, 46.3 (C-13), 47.0 (C-1''), 50.5 (C-  
43 16a), 55.2 (3-OCH<sub>3</sub>), 78.8 (C-17), 111.4 (C-2), 113.8 (C-4), 120.6 (C-5'), 126.3 (C-1), 132.6 (C-  
44 10), 137.9 (C-5), 152.3 (C-4'), 157.4 (C-3).  
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57 2.3.21. 3-Methoxy-16a-(4'-cyclohexyl-1'-H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17a-  
58  
59 ol (**24c**)  
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4 Compound **16** (342 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
5  
6 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
7  
8 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **24c** (162 mg, 36%) as yellow crystals. Mp: 208–210  
9  
10 °C; *R*<sub>f</sub> = 0.42 (ss B). (Found C, 74.97; H, 8.56. C<sub>28</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (449.63) requires C, 74.80; H, 8.74%).  
11  
12 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 1.26 (s, 8H, 2''-, 3''-, 5''- and 6''-H<sub>2</sub>), 2.88 (m, 2H,  
13  
14 6-H<sub>2</sub>), 2.90 (m, 2H, 4''-H<sub>2</sub>), 3.64 (d, 1H, *J* = 5.0 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.29 (dd, 1H, *J*  
15  
16 = 13.5 Hz, *J* = 5.0 Hz, 16a-H<sub>2</sub>), 4.62 (dd, 1H, *J* = 13.5 Hz, *J* = 11.0 Hz, 16a-H<sub>2</sub>), 6.63 (d, 1H, *J* =  
17  
18 2.0 Hz, 4-H), 6.71 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.22 (d, 1H, *J* = 8.5 Hz, 1-H), 7.34 (s,  
19  
20 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.2 (C-18), 26.0 and 26.1 (C-2'', -3'', -5'' and -6''), 28.0,  
21  
22 29.0, 29.7, 29.8, 31.2, 33.0, 25.2, 38.9, 42.4, 43.5, 46.3 (C-13), 47.0 (C-1''), 50.5 (C-16a), 55.0  
23  
24 (3-OCH<sub>3</sub>), 78.8 (C-17), 111.4 (C-2), 113.8 (C-4), 120.2 (C-5'), 126.3 (C-1), 132.6 (C-10), 137.9  
25  
26 (C-5), 153.3 (C-4'), 157.4 (C-3).

27  
28 2.3.22. *3-Methoxy-16a-(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17a-ol*  
29  
30 (**24d**)

31  
32 Compound **16** (342 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
33  
34 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
35  
36 CH<sub>2</sub>Cl<sub>2</sub> yield pure **24d** (394 mg, 89%) as white solid. Mp: 189.5–191 °C; *R*<sub>f</sub> = 0.46 (ss B). (Found  
37  
38 C, 75.65; H, 7.67. C<sub>28</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (443.58) requires C, 75.81; H, 7.50%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>):  
39  
40 0.75 (s, 3H, 18-H<sub>3</sub>), 2.86 (m, 2H, 6-H<sub>2</sub>), 3.68 (d, 1H, *J* = 5.0 Hz, 17-H), 3.78 (s, 3H, 3-OCH<sub>3</sub>),  
41  
42 4.41 (dd, 1H, *J* = 13.5 Hz, *J* = 6.0 Hz, 16a-H<sub>2</sub>), 4.69 (dd, 1H, *J* = 14.5 Hz, *J* = 10.5 Hz, 16a-H<sub>2</sub>),  
43  
44 6.64 (d, 1H, *J* = 2.0 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.22 (d, 1H, *J* = 8.5 Hz,  
45  
46 1-H), 7.34 (t, 1H, *J* = 7.5 Hz, 4''-H), 7.43 (t, 2H, *J* = 7.5 Hz, 3''- and 5''-H), 7.83 (d, 2H, *J* = 7.5  
47  
48 Hz, 2''- and 6''-H), 7.88 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.1 (C-18), 26.0, 28.0, 29.8,  
49  
50 31.2, 38.9, 42.3, 43.5, 46.4 (C-13), 47.0, 50.7, 55.2 (3-OCH<sub>3</sub>), 78.8 (C-17), 111.5 (C-2), 113.8  
51  
52 (C-4), 120.6 (C-5'), 125.6 (C-2'' and -6''), 126.3 (C-1), 128.1 (C-4''), 128.8 (C-3'' and -5''), 130.5  
53  
54 (C-1'), 132.5 (C-10), 137.9 (C-5), 147.3 (C-4'), 157.4 (C-3).

55  
56 2.3.23. *3-Methoxy-16a-[4'-(4'-nitrobenzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-*  
57  
58 *1,3,5(10)-trien-17a-ol* (**24e**)

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4 Compound **16** (342, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used for the  
5  
6 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
7  
8 CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3, v/v) to yield pure (344 mg, 63%) as yellow crystals. Mp: 64 °C; *R*<sub>f</sub> = 0.45 (ss  
9  
10 B). (Found, C, 66.14; H, 6.05. C<sub>30</sub>H<sub>34</sub>N<sub>4</sub>O<sub>6</sub> (546.61) requires C, 65.92; H, 6.27%). <sup>1</sup>H NMR (δ,  
11  
12 ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.66 (d, 1H, *J* = 4.5 Hz, 17-H), 3.77 (s,  
13  
14 3H, 3-OCH<sub>3</sub>), 4.40 (dd, 1H, *J* = 13.5 Hz, *J* = 5.5 Hz, 16a-H<sub>2</sub>), 4.66 (t, 1H, *J* = 13.5 Hz, 16a-H<sub>2</sub>),  
15  
16 5.53 (s, 2H, 4'-H<sub>2</sub>), 6.62 (t, 1H, *J* = 2.0 Hz, 4-H), 6.71 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.20  
17  
18 (d, 1H, *J* = 8.5 Hz, 1-H), 7.85 (s, 1H, 5'-H), 8.22 (d, 2H, *J* = 9.0 Hz, 3''- and 5''-H), 8.72 (d, 2H, *J*  
19  
20 = 9.0 Hz, 2''- and 6''-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.1 (C-18), 22.7, 25.9, 28.0, 29.0, 29.8,  
21  
22 31.2, 38.9, 42.0, 43.5, 46.4 (C-13), 47.0 (4'-CH<sub>2</sub>), 78.8 (C-17), 111.5 (C-2), 113.8 (C-4), 114.0  
23  
24 (C-1'), 123.5 (C-2'' and -6'') 126.3 (C-5'), 130.9 (C-3'' and -5''), 135.0 (C-10), 137.8 (C-5), 141.5  
25  
26 (C-4''), 150.6 (C-4'), 157.5 (C-3), 164.6 (C=O).

27  
28 *2.3.24. 3-Methoxy-16a-(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
29  
30 *17a-ol (24f)*

31  
32 Compound **24e** (274 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
33  
34 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
35  
36 and the precipitate separating out was filtered off and recrystallized from a mixture of  
37  
38 acetone/hexane to afford **24f** (187 mg, 94%) as a white crystalline product. Mp: 149–150 °C; *R*<sub>f</sub>  
39  
40 = 0.25 (ss B). (Found C, 69.55; H, 7.95. C<sub>23</sub>H<sub>31</sub>N<sub>3</sub>O<sub>3</sub> (397.51) requires C, 69.49; H, 7.86%). <sup>1</sup>H  
41  
42 NMR (δ, ppm, CDCl<sub>3</sub>): 0.74 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.62 (d, 1H, *J* = 4.0 Hz, 17-H),  
43  
44 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.39 (m, 1H, 16a-H<sub>2</sub>), 4.64 (m, 1H, 16a-H<sub>2</sub>), 6.63 (s, 1H, 4-H), 6.71 (d, 1H,  
45  
46 *J* = 8.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.77 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>):  
47  
48 11.9 (C-18), 26.0, 28.0, 28.9, 31.3, 31.9, 33.8 (C-13), 38.9, 41.9, 43.5, 46.4 (4'-CH<sub>2</sub>), 46.9, 51.0  
49  
50 (C-16a), 55.2 (3-OCH<sub>3</sub>), 78.6 (C-17), 111.5 (C-2), 113.8 (C-4), 123.4 (C-5'), 126.3 (C-1), 132.5  
51  
52 (C-10), 137.8 (C-5), 157.4 (C-3).

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54 *2.3.25. 3-Benzoyloxy-16β-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
55  
56 *17β-ol (25a)*

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58 Compound **17** (420 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
59  
60 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
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4 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **25a** (394 mg, 84%) as a white solid. Mp: 278–280  
5 °C; *R*<sub>f</sub> = 0.35 (ss B). (Found C, 77.16; H, 7.62. C<sub>31</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (483.64) requires C, 76.98; H,  
6 7.71%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.80 (s, 3H, 18-H<sub>3</sub>), 0.86 and 0.97 (2 x m, 2 x 2H, 2''- and 3''-  
7 H), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.93 (d, *J* = 9.5 Hz, 1H, 17-H), 4.21 (m, 1H, 16a-H<sub>2</sub>), 4.64 (m, 1H, 16a-  
8 H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz,  
9 1-H), 7.31 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.38 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.43 (d, 2H, *J* = 7.0  
10 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 7.8 (C-2'' and -3''), 12.3 (C-18), 26.2, 27.4, 29.7,  
11 30.8, 37.5, 38.0, 41.4, 43.9, 44.3 (C-13), 48.7 (C-16), 67.8 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 80.7 (C-17),  
12 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and C-5'),  
13 132.7 (C-10), 137.3 (C-1'), 137.8 (C-5), 156.8 (C-3).  
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24 2.3.26. *3-Benzylxy-16β-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
25 *17β-ol (25b)*  
26

27 Compound **17** (420 mg, 1 mmol) and cyclopentylacetylene (2 mol, 0.22 ml) were used for the  
28 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
29 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **25b** (350 mg, 68%) as a white solid. Mp: 288–290  
30 °C; *R*<sub>f</sub> = 0.38 (ss B). Found C, 77.58; H, 7.92. C<sub>33</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (511.70) requires C, 77.46; H, 8.08%).  
31 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.75 (s, 1H, 1''-H), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.94 (d,  
32 1H, *J* = 9.5 Hz, 17-H), 4.24 (m, 1H, 16-H<sub>2</sub>), 4.67 (m, 1H, 16-H<sub>2</sub>), 5.03 (s., 2H, Bn-H<sub>2</sub>), 6.71 (s,  
33 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.5 Hz, 4'-  
34 H), 7.38 (t, 2H, *J* = 7.5 Hz, 3'- and 5'-H), 7.42 (d, 2H, *J* = 7.5 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ,  
35 ppm, CDCl<sub>3</sub>): 12.3 (C-18), 25.1 (C-3'' and -4''), 26.2, 27.5, 29.7, 30.8, 34.3 (C-2'' and -5''), 37.5,  
36 38.0, 41.4, 43.9, 44.3 (C-13), 48.7 (C-16), 62.1 (16a-CH<sub>2</sub>), 69.9 (Bn-CH<sub>2</sub>), 80.7 (C-17), 112.3 (C-  
37 2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.7 (C-  
38 10), 137.3 (C-1'), 137.8 (C-5), 156.8 (C-3).  
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52 2.3.27. *3-Benzylxy-16β-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
53 *17β-ol (25c)*  
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55 Compound **17** (420 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
56 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
57 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99, v/v) to yield pure **25c** (146 mg, 28%) as a white solid. Mp: 214–216  
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4 °C;  $R_f$  = 0.38 (ss B). (Found C, 77.43; H, 8.36.  $C_{34}H_{43}N_3O_2$  (525.72) requires C, 77.68; H, 8.24%).  
5  
6  $^1H$  NMR ( $\delta$ , ppm,  $CDCl_3$ ): 0.79 (s, 3H, 18- $H_3$ ), 2.79 (m, 4H, 3''- and 5''-H), 3.94 (d,  $J$  = 9.5 Hz,  
7 1H, 17-H), 4.25 (m, 1H, 16a- $H_2$ ), 4.67 (m, 1H, 16a- $H_2$ ), 5.03 (s, 2H, Bn- $H_2$ ), 6.71 (s, 1H, 4-H),  
8 6.78 (d, 1H,  $J$  = 8.5 Hz, 2-H), 7.19 (d, 1H,  $J$  = 8.5 Hz, 1-H), 7.32 (d, 1H,  $J$  = 7.0 Hz, 4'-H), 7.38  
9 (t, 2H,  $J$  = 7.0 Hz, 3'- and 5'-H), 7.42 (d, 2H,  $J$  = 7 Hz, 2'- and 6'-H).  $^{13}C$  NMR ( $\delta$ , ppm,  $CDCl_3$ ):  
10 12.3 (C-18), 26.0 (C-4''), 26.1 (C-3'' and -5''), 26.2, 27.5, 29.7, 30.8 (C-2'' and -6''), 33.0 (C-1''),  
11 37.5, 38.0, 41.4, 43.9, 44.3 (C-13), 48.7 (C-16), 62.1 (C-16a), 69.9 (Bn- $CH_2$ ), 80.7 (C-17), 112.3  
12 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.7  
13 (C-10), 137.3 (C-1'), 137.8 (C-5), 157.8 (C-3).  
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23 **2.3.28. 3-Benzoyloxy-16 $\beta$ -(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17 $\beta$ -ol**  
24 **(25d)**  
25

26 Compound **17** (420 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
27 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
28 ethyl acetate/ $CH_2Cl_2$  (5:95 v/v) to yield pure **25d** (391 mg, 75%) as a white solid. Mp: 202–204  
29 °C;  $R_f$  = 0.45 (ss B). (Found C, 78.73; H, 6.98.  $C_{34}H_{37}N_3O_2$  (519.68) requires C, 78.58; H, 7.18%).  
30  
31  $^1H$  NMR ( $\delta$ , ppm,  $C_6D_6$ ): 0.68 (s, 3H, 18- $H_3$ ), 2.69 (m, 2H, 6- $H_2$ ), 3.43 (dd,  $J$  = 9.5 Hz,  $J$  = 4 Hz,  
32 1H, 17-H), 3.77 (dd, 1H,  $J$  = 13.5 Hz,  $J$  = 7.0 Hz, 16a- $H_2$ ), 4.29 (dd, 1H,  $J$  = 13.5 Hz,  $J$  = 7.0 Hz,  
33 16a- $H_2$ ), 4.83 (s, 2H, Bn- $H_2$ ), 6.79 (s, 1H, 4-H), 6.87 (d, 1H,  $J$  = 8.0 Hz, 2-H), 7.02 (s, 1H, 1-H),  
34 7.08 (t, 1H,  $J$  = 7.5 Hz, 4'-H), 7.26 (t, 2H,  $J$  = 7.5 Hz, 3'- and 5'-H), 7.32 (d, 2H,  $J$  = 7.5 Hz, 2'-  
35 and 6'-H), 8.01 (d, 2H,  $J$  = 7.5 Hz, 2''- and 6''-H).  
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45 **2.3.29. 3-Benzoyloxy-16 $\beta$ -[4'-(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-**  
46 **1,3,5(10)-trien-17 $\beta$ -ol (25e)**  
47

48 Compound **17** (420 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used for  
49 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
50 ethyl acetate/ $CH_2Cl_2$  (5:95 v/v) to yield pure **25e** (480 mg, 77%) as a yellow solid. Mp: 187–189  
51 °C;  $R_f$  = 0.45 (ss B). (Found C, 69.32; H, 5.98.  $C_{36}H_{38}N_4O_6$  (622.71) requires C, 69.44; H, 6.15%).  
52  
53  $^1H$  NMR ( $\delta$ , ppm,  $CDCl_3$ ): 0.80 (s, 3H, 18- $H_3$ ), 2.82 (m, 2H, 6- $H_2$ ), 3.94 (d,  $J$  = 10.0 Hz, 1H, 17-  
54 H), 4.32 (dd, 1H,  $J$  = 13.0 Hz,  $J$  = 6.0 Hz, 16a- $H_2$ ), 4.72 (t, 1H,  $J$  = 6.0 Hz, 16a- $H_2$ ), 5.03 (s, 2H,  
55 Bn- $H_2$ ), 5.52 (s, 2H, triazol-H), 6.71 (s, 1H, 4-H), 6.78 (d, 1H,  $J$  = 8.5 Hz, 2-H), 7.19 (d, 1H,  $J$  =  
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4 8.5 Hz, 1-H), 7.32 (t, 1H,  $J = 7.0$  Hz, 4'-H), 7.38 (t,  $J = 7.5$  Hz, 2H, 3'- and 5'-H), 7.42 (d,  $J =$   
5 7.5 Hz, 2H, 2'- and 6'-H), 8.22 (d,  $J = 8$  Hz, 2H, 3''- and 5''-H), 8.27 (d,  $J = 8$  Hz, 2H, 2''- and  
6''-H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 12.3 (C-18), 26.2, 27.4, 29.7, 30.8, 37.4, 38.0, 41.2, 43.8, 44.4  
9 (C-13), 48.7 (C-16), 55.5 (C-16a), 58.7 (linker- $\text{CH}_2$ ), 69.9 (Bn- $\text{CH}_2$ ), 80.7 (C-17), 112.4 (C-2),  
11 114.8 (C-4), 123.5 (C-2' and -6'), 126.3 (C-1), 127.4 (C-2'' and -6''), 127.8 (C-4'), 128.5 (C-3''  
12 and -5''), 130.9 (C-3' and -5'), 132.5 (C-10), 135.1 (C-1''), 137.3 (C-1'), 137.8 (C-5), 150.7 (C-  
13 4''), 156.8 (C-3), 164.6 (C=O).

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19 **2.3.30.** *3-Benzoyloxy-16 $\beta$ -(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-*  
20 *trien-17 $\beta$ -ol (25f)*

21  
22 Compound **25e** (210 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing  $\text{NaOCH}_3$  (14  
23 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
24 and the precipitate separating out was filtered off and recrystallized from methanol to afford **25f**  
25 and the precipitate separating out was filtered off and recrystallized from methanol to afford **25f**  
26 (232 mg, 98%) as a white crystalline product. Mp: 283–285 °C;  $R_f = 0.25$  (ss B). (Found C,  
27 73.42; H, 7.35.  $\text{C}_{29}\text{H}_{35}\text{N}_3\text{O}_3$  (473.61) requires C, 73.54; H, 7.45%).  $^1\text{H}$  NMR ( $\delta$ , ppm,  $\text{DMSO-d}_6$ ):  
28 0.77 (s, 3H, 18- $\text{H}_3$ ), 3.77 (dd, 1H,  $J = 9.5$  Hz,  $J = 3.5$  Hz, 16a- $\text{H}_2$ ), 4.15 (t, 1H,  $J = 12.5$  Hz, 16a-  
29  $\text{H}_2$ ), 5.12 (d, 1H,  $J = 5.5$  Hz, 17-H), 6.68 (s, 1H, 4-H), 6.74 (d, 1H,  $J = 8.5$  Hz, 2-H), 7.16 (d,  $J =$   
30 8.5 Hz, 1H, 1-H), 7.31 (d, 1H,  $J = 7.0$  Hz, 4'-H), 7.37 (t, 2H,  $J = 7.0$  Hz, 3'- and 5'-H), 7.41 (d,  
31 2H,  $J = 7.0$  Hz., 2'- and 6'-H), 7.98 (s, 1H, triazol-H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm,  $\text{DMSO-d}_6$ ): 12.3 (C-  
32 18), 25.8, 26.9, 29.1, 30.0, 36.9, 37.8, 40.4, 43.4, 43.7 (C-13), 47.8 (C-16a), 55.0 (linker- $\text{CH}_2$ ),  
33 68.9 (Bn- $\text{CH}_2$ ), 79.5 (C-17), 112.1 (C-2), 114.4 (C-4), 122.7 (triazol-CH), 126.0 (C-1), 127.4 (C-  
34 2' and -6'), 127.6 (C-4'), 128.3 (C-3' and -5'), 132.3 (C-10), 137.3 (C-5), 147.6 (triazol-C), 156.0  
35 (C-3).  
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48 **2.3.31.** *3-Benzoyloxy-16a-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
49 *17 $\beta$ -ol (26a)*

50  
51 Compound **18** (420.0 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
52 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
53 ethyl acetate/ $\text{CH}_2\text{Cl}_2$  (1:99 v/v) to yield pure **26a** (310 mg, 64%) as a white solid. Mp: 191–193  
54 °C;  $R_f = 0.35$  (ss B). (Found C, 76.82; H, 7.94.  $\text{C}_{31}\text{H}_{37}\text{N}_3\text{O}_2$  (483.64) requires C, 76.98; H,  
55 7.71%).  $^1\text{H}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 0.83 (s, 3H, 18- $\text{H}_3$ ), 2.83 (m, 2H, 6- $\text{H}_2$ ), 3.54 (d,  $J = 7.5$  Hz,  
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4 1H, 17-H), 4.35 (dd, 1H,  $J = 13.0$  Hz,  $J = 7.5$  Hz, 16a-H<sub>2</sub>), 4.44 (dd, 1H,  $J = 13.0$  Hz,  $J = 7.5$  Hz,  
5 16a-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.77 (d, 1H,  $J = 8.5$  Hz, 2-H), 7.19 (d, 1H,  $J =$   
6 8.5 Hz, 1-H), 7.31 (t, 2H,  $J = 7.5$  Hz, 4'-H and triazol-H), 7.38 (t, 2H,  $J = 7.5$  Hz, 3'- and 5'-H),  
7 7.42 (d, 2H,  $J = 7.5$  Hz, 2'- and 6'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 6.6 (C-1''), 7.8 (C-2'' and -3''),  
8 11.8 (C-18), 26.1, 27.2, 28.2, 29.7, 36.6, 38.4, 43.9, 44.3, 44.3 (C-13), 48.3 (C-16), 54.5 (C-16a),  
9 69.9 (Bn-CH<sub>2</sub>), 85.2 (C-17), 112.3 (C-2), 114.8 (C-4), 120.0 (triazol-CH), 126.3 (C-1), 127.4 (C-  
10 2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.6 (C-10), 137.3 (C-1'), 137.8 (C-5), 150.2  
11 (triazol-C), 156.8 (C-3).  
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21 2.3.32. *3-Benzoyloxy-16a-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
22 *17 $\beta$ -ol (26b)*  
23

24 Compound **18** (420 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
25 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
26 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **26b** (442 mg, 86%) as a white solid. Mp: 268–270  
27 °C;  $R_f = 0.36$  (ss B). (Found C, 77.52; H, 7.93. C<sub>33</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (511.70) requires C, 77.46; H, 8.08%).  
28 <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.83 (s, 3H, 18-H<sub>3</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.19 (s, 1H, 1''-H), 3.46 (d,  
29 1H,  $J = 7.0$  Hz, 17-H), 4.42 (dd, 2H,  $J = 22.5$  Hz,  $J = 6.5$  Hz, 16-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71  
30 (s, 1H, 4-H), 6.76 (d, 1H,  $J = 8.5$  Hz, 2-H), 7.19 (d, 1H,  $J = 8.5$  Hz, 1-H), 7.31 (t, 1H,  $J = 7.5$  Hz,  
31 4'-H), 7.37 (t, 3H,  $J = 7.5$  Hz, 3'-, 5'-H and triazol-H), 7.42 (d, 2H,  $J = 7.5$  Hz, 2'- and 6'-H).  
32 <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 11.9 (C-18), 25.1 (C-3'' and -4''), 26.1, 27.2, 28.3, 29.7, 33.2 (C-2''  
33 and -5''), 36.6 (2C, C-1''), 36.7, 38.4, 43.9, 44.3 (C-13), 48.4 (C-16), 54.5 (C-16a), 69.9 (Bn-  
34 CH<sub>2</sub>), 85.2 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-3' and -5'), 127.8 (C-4'),  
35 128.5 (C-2' and -6'), 132.6 (C-10), 137.3 (C-1'), 137.8 (C-5), 156.7 (C-3).  
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48 2.3.33. *3-Benzoyloxy-16a-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
49 *17 $\beta$ -ol (26c)*  
50

51 Compound **18** (420 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
52 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
53 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (2.5:77.5 v/v) to yield pure **26c** (386 mg, 76%) as a white solid. Mp:  
54 261–263 °C;  $R_f = 0.34$  (ss B). (Found C, 77.93; H, 8.36. C<sub>34</sub>H<sub>43</sub>N<sub>3</sub>O<sub>2</sub> (525.72) requires C, 77.68;  
55 H, 8.24%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.83 (s, 3H, 18-H<sub>3</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.55 (d,  $J = 7.0$   
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4 Hz, 1H, 17-H), 4.43 (m, 2H, 16-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.77 (d, 1H, *J* = 8.5  
5  
6 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 2H, *J* = 7.0 Hz, 4'-H and triazol-H), 7.37 (t, 2H,  
7  
8 *J* = 7.0 Hz, 3'- and 5'-H), 7.42 (d, 2H, *J* = 7 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 11.9  
9  
10 (C-18), 25.9 (C-4''), 26.1 (C-3'' and -5''), 27.2, 28.3, 29.7 (C-2'' and -6''), 32.9, 33.0, 36.6, 38.4,  
11  
12 43.9, 44.2, 44.3 (C-13), 48.4 (C-16), 54.5 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 85.2 (C-17), 112.3 (C-2),  
13  
14 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.6 (C-10),  
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16 137.3 (C-1'), 137.8 (C-5), 156.7 (C-3).

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19 **2.3.34. 3-Benzoyloxy-16a-(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β-ol**  
20  
21 **(26d)**

22 Compound **18** (420 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
23  
24 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
25  
26 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> 5:95 v/v) to yield pure **26d** (372 mg, 71%) as a white solid. Mp: 132–134  
27  
28 °C; *R*<sub>f</sub> = 0.38 (ss B). (Found C, 78.63; H, 6.97. C<sub>34</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (519.68) requires C, 78.58; H, 7.18%).  
29  
30 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.84 (s, 3H, 18-H<sub>3</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.58 (d, 1H, *J* = 7.5 Hz, 17-  
31  
32 H), 4.46 (dd, 2H, *J* = 13.5 Hz, *J* = 8.0 Hz, 16a-H<sub>2</sub>), 4.55 (dd, 1H, *J* = 13.5 Hz, *J* = 8.0 Hz, 16a-  
33  
34 H<sub>2</sub>) 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz,  
35  
36 1-H), 7.30-7.86 (m, 11H, 2'-, 6'-, 3'-, 5'-, 4'-, 2''-, 6''-, 3''-, 5''-, 4''- and triazol-H). <sup>13</sup>C NMR (δ,  
37  
38 ppm, CDCl<sub>3</sub>): 11.8 (C-18), 26.1, 27.2, 28.2, 29.6, 36.5, 38.4, 43.9, 44.3, 48.3 (C-16), 54.6 (C-  
39  
40 16a), 62.1, 69.9 (Bn-CH<sub>2</sub>), 85.2 (C-17), 112.3 (C-2), 114.8 (C-4), 123.8 (triazol-CH), 125.7 (C-2'  
41  
42 and -6'), 126.3 (C-1'), 127.4 (C-2'' and -6''), 127.8 (C-4'), 128.2 (C-4), 128.5 (C-3'' and -5''),  
43  
44 128.8 (C-3' and -5'), 130.4 (C-10), 132.6 (C-1''), 137.3 (C-1'), 137.8 (C-5), 156.8 (C-3).

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47 **2.3.35. 3-Benzoyloxy-16a-[4'-(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-**  
48  
49 **1,3,5(10)-trien-17β-ol (26e)**

50 Compound **18** (420 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used for  
51  
52 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
53  
54 with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **26e** (484 mg, 77%) as a yellow solid. Mp:  
55  
56 94–96 °C; *R*<sub>f</sub> = 0.40 (ss B). (Found C, 69.73; H, 5.94. C<sub>36</sub>H<sub>38</sub>N<sub>4</sub>O<sub>6</sub> (622.71) requires C, 69.44; H,  
57  
58 6.15%). <sup>1</sup>H NMR (δ, ppm, DMSO-*d*<sub>6</sub>): 0.70 (s, 3H, 18-H<sub>3</sub>), 3.33 (m, 2H, 6-H<sub>2</sub>), 4.38 (dd, 1H, *J* =  
59  
60 13.5 Hz, *J* = 9.0 Hz, 16a-H<sub>2</sub>), 4.52 (dd, 1H, *J* = 13.5 Hz, *J* = 5.0 Hz, 16a-H<sub>2</sub>), 4.86 (d, 1H, *J* = 5  
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4 Hz, 17-H), 5.02 (s, 2H, Bn-H<sub>2</sub>), 5.47 (s, 2H, linker-H<sub>2</sub>), 6.64 (d, 1H, *J* = 2.0 Hz, 4-H), 6.72 (dd,  
5 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.10 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.0 Hz, 4'-H),  
6 7.37 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.42 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H), 8.16 (d, 2H, *J* = 9.0  
7 Hz, 3''- and 5''-H), 8.28 (d, 2H, *J* = 9.0 Hz, 2''- and 6''-H), 8.32 (s, 1H, triazol-H). <sup>13</sup>C NMR (δ,  
8 ppm, DMSO-d<sub>6</sub>): 11.7 (C-18), 25.7, 26.6, 27.1, 29.0, 30.6, 36.4, 37.9, 43.4, 43.4 (C-13), 43.7 (C-  
9 16), 53.1 (C-16a), 58.6 (linker-CH<sub>2</sub>), 68.9 (Bn-CH<sub>2</sub>), 82.8 (C-17), 112.1 (C-2), 114.3 (C-4), 123.7  
10 (C-2' and -6'), 125.1 (triazol-CH), 125.9 (C-1), 127.4 (C-2'' and -6''), 127.5 (C-4'), 128.3 (C-3''  
11 and -5''), 130.6 (C-3' and -5'), 132.1 (C-10), 134.7 (C-1''), 137.2 (C-1'), 137.3 (C-5), 141.1  
12 (triazol-C), 150.1 (C-4''), 155.9 (C-3), 163.9 (C=O).

23 2.3.36. *3-Benzoyloxy-16α-(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-*  
24 *trien-17β-ol (26f)*

25  
26 Compound **26e** (210 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
27 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
28 and the precipitate separating out was filtered off and recrystallized from a mixture of  
29 acetone/hexane to afford **26f** (190 mg, 89%) as a white crystalline product. Mp: 152–154 °C; *R*<sub>f</sub>=  
30 0.20 (ss B). (Found C, 73.72; H, 7.63. C<sub>29</sub>H<sub>35</sub>N<sub>3</sub>O<sub>3</sub> (473.61) requires C, 73.54; H, 7.45%). <sup>1</sup>H  
31 NMR (δ, ppm, DMSO-d<sub>6</sub>): 0.71 (s, 3H, 18-H<sub>3</sub>), 2.73 (m, 2H, 6H<sub>2</sub>), 3.29 (d, *J* = 8.0 Hz, 1H, 17-  
32 H), 4.28 (dd, 2H, *J* = 13.0 Hz, *J* = 10.0 Hz, 16a-H<sub>2</sub>), 4.47 (dd, 1H, *J* = 13.0 Hz, *J* = 4.5 Hz, 16a-  
33 H<sub>2</sub>), 4.51 (s, 2H, Bn-H<sub>2</sub>), 4.87 (s, 1H, linker-H<sub>2</sub>), 5.03 (s, 2H, triazol-H<sub>2</sub>), 5.15 (s, 1H, linker-H<sub>2</sub>),  
34 6.68 (s, 1H, 4-H), 6.74 (d, 1H, *J* = 8.5 Hz, 2-H), 7.15 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.0  
35 Hz, 4'-H), 7.37 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.41 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H), 7.97 (s,  
36 1H, triazol-H). <sup>13</sup>C NMR (δ, ppm, DMSO-d<sub>6</sub>): 11.8 (C-18), 25.8, 26.7, 27.3, 29.1, 36.4, 38.1,  
37 43.4, 43.5 (C-13), 43.9, 47.5 (C-16), 53.1 (C-16a), 54.9 (linker-CH<sub>2</sub>), 68.9 (Bn-CH<sub>2</sub>), 83.0 (C-  
38 17), 112.1 (C-2), 114.4 (C-4), 122.7 (triazol-CH), 126.0 (C-1), 127.4 (C-2' and -6'), 127.6 (C-4'),  
39 128.3 (C-3' and -5'), 132.3 (C-10), 137.3 (C-1'), 137.4 (C-5), 147.6 (triazol-C), 156.0 (C-3).  
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54 2.3.37. *3-Benzoyloxy-16β-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
55 *17a-ol (27a)*

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57 Compound **19** (420.0 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
58 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
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4 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **27a** (454 mg, 93%) as white crystals. Mp: 199–201  
5 °C; *R*<sub>f</sub> = 0.38 (ss B). (Found C, 77.15; H, 7.62. C<sub>31</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (483.64) requires C, 76.98; H,  
6 7.71%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.77 (s, 3H, 18-H<sub>3</sub>), 0.87 and 0.98 (2 x s, 2 x 2H, 2''- and 3''-  
7 H<sub>2</sub>), 2.05 (s, 1H, 1''-H), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.66 (s, 1H, 17-H), 4.42 (m, 2H, 16a-H<sub>2</sub>), 5.03 (s,  
8 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31  
9 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.38 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.43 (d, 2H, *J* = 7.0 Hz, 2'- and  
10 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 6.7 (C-1''), 7.7 (C-2'' and -3''), 17.9 (C-18), 25.9, 27.9, 29.7,  
11 30.4, 31.8, 38.5, 43.3, 45.1 (C-13), 48.9, 49.1 (C-16), 62.1 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 82.6 (C-17),  
12 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'),  
13 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.7 (C-3).  
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24 2.3.38. *3-Benzylxy-16β-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
25 *17a-ol (27b)*  
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27 Compound **19** (420 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
28 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
29 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **27b** (408 mg, 79%) as white crystalline. Mp:  
30 220–222 °C; *R*<sub>f</sub> = 0.40 (ss B). (Found C, 77.32; H, 7.93. C<sub>33</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (511.70) requires C, 77.46;  
31 H, 8.08%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.76 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.20 (s, 1H, 1''-  
32 H), 3.67 (s, 1H, 17-H), 4.43 (m, 2H, 16a-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.72 (s, 1H, 4-H), 6.78 (dd,  
33 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.0 Hz, 4'-H),  
34 7.38 (t, 3H, *J* = 7.0 Hz, 3'- and 5'-H, triazol-H), 7.43 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H). <sup>13</sup>C NMR  
35 (δ, ppm, CDCl<sub>3</sub>): 18.0 (C-18), 25.1 (C-3'' and -5''), 25.9, 28.0, 29.7, 30.4, 31.8 (C-2'' and -6''),  
36 33.2, 36.7, 38.5, 43.3, 45.1 (C-13), 48.9 (C-16), 49.1 (C-1''), 54.3 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 82.6  
37 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and  
38 -5'), 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.7 (C-3).  
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51 2.3.39. *3-Benzylxy-16β-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
52 *17a-ol (27c)*  
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54 Compound **19** (420 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
55 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
56 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **27c** (360 mg, 68%) as white crystalline product.  
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4 Mp: 243–245 °C;  $R_f$  = 0.38 (ss B). (Found C, 77.54; H, 8.38.  $C_{34}H_{43}N_3O_2$  (525.72) requires C,  
5 77.68; H, 8.24%).  $^1H$  NMR ( $\delta$ , ppm,  $CDCl_3$ ): 0.75 (s, 3H, 18- $H_3$ ), 2.84 (m, 2H, 6- $H_2$ ), 3.68 (s,  
6 1H, 17-H), 4.44 (m, 2H, 16a- $H_2$ ), 5.03 (s, 2H, Bn- $H_2$ ), 6.72 (s, 1H, 4-H), 6.78 (d, 1H,  $J$  = 8.5 Hz,  
7 2-H), 7.21 (d, 1H,  $J$  = 8.5 Hz, 1-H), 7.32 (t, 1H,  $J$  = 7.0 Hz, 4'-H), 7.38 (t, 3H,  $J$  = 7.0 Hz, 3'- and  
8 5'-H, triazol-H), 7.43 (d, 2H,  $J$  = 7.0 Hz, 2'- and 6'-H).  $^{13}C$  NMR ( $\delta$ , ppm,  $CDCl_3$ ): 17.9 (C-18),  
9 25.9 (C-4''), 26.0, 26.1 (C-3'' and -5''), 27.9, 29.7, 30.4, 31.8 (C-2'' and -6''), 32.1, 32.9 (C-1''),  
10 38.5, 43.3, 45.1 (C-13), 48.9, 49.1 (C-16), 62.1 (C-16a), 69.9 (Bn- $CH_2$ ), 82.5 (C-17), 112.3 (C-2),  
11 114.7 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.7 (C-10),  
12 137.2 (C-1'), 137.9 (C-5), 156.7 (C-3).  
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24 **2.3.40. 3-Benzoyloxy-16 $\beta$ -(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17a-ol**  
25 **(27d)**  
26

27 Compound **19** (420 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
28 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
29 ethyl acetate/ $CH_2Cl_2$  (10:90 v/v) to yield pure **27d** (487 mg, 93%) as white crystals. Mp:  
30 202–204 °C;  $R_f$  = 0.45 (ss B). (Found C, 78.68; H, 7.38.  $C_{34}H_{37}N_3O_2$  (519.68) requires C, 78.58;  
31 H, 7.18%).  $^1H$  NMR ( $\delta$ , ppm,  $CDCl_3$ ): 0.79 (s, 3H, 18- $H_3$ ), 2.84 (m, 2H, 6- $H_2$ ), 3.72 (s, 1H, 17-  
32 H), 4.48 (dd, 1H,  $J$  = 13.5 Hz,  $J$  = 7.5 Hz, 16a- $H_2$ ), 4.56 (t, 1H,  $J$  = 13.5 Hz, 16a- $H_2$ ), 5.03 (s, 2H,  
33 Bn- $H_2$ ), 6.72 (s, 1H, 4-H), 6.78 (d, 1H,  $J$  = 8.5 Hz, 2-H), 7.21 (d, 1H,  $J$  = 8.5 Hz, 1-H), 7.33 (t,  
34 1H,  $J$  = 7.5 Hz, 4'-H), 7.38 (t, 2H,  $J$  = 7.5 Hz, 3'- and 5'-H), 7.42 (d,  $J$  = 3.5 Hz, 4H, 2'- and 6'-  
35 H, 3''- and 5''-H), 7.84 (d, 2H,  $J$  = 7.5 Hz, 2''- and 6''-H), 7.88 (s, 1H, triazol-H).  $^{13}C$  NMR ( $\delta$ ,  
36 ppm,  $CDCl_3$ ): 17.9 (C-18), 25.9, 27.9, 29.7, 30.4, 31.8, 38.5, 43.3, 45.2 (C-13), 48.9, 49.1 (C-16),  
37 54.6 (C-16a), 69.9 (Bn- $CH_2$ ), 82.6 (C-17), 112.3 (C-2), 114.8 (C-4), 119.6 (triazol-CH), 125.7  
38 (C-2' and -6'), 126.3 (C-1'), 127.4 (C-2'' and -6''), 127.8 (C-4'), 128.2 (C-4''), 128.5 (C-3'' and -  
39 5''), 128.8 (C-3' and -5'), 130.5 (C-10), 132.64 (C-1''), 137.3 (C-1'), 137.9 (C-5), 147.7 (triazol-  
40 C); 156.8 (C-3).  
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56 **2.3.41. 3-Benzoyloxy-16 $\beta$ -[4'-(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-**  
57 **1,3,5(10)-trien-17a-ol (27e)**  
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4 Compound **19** (420.0 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used  
5  
6 for the synthesis as described in Section 2.3. The crude product was chromatographed on silica  
7  
8 gel with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (10:90 v/v) to yield pure **27e** (550 mg, 88%) as yellow crystals.  
9  
10 Mp: 177–179 °C; *R*<sub>f</sub> = 0.48 (ss B). (Found C, 69.55; H, 5.93. C<sub>36</sub>H<sub>38</sub>N<sub>4</sub>O<sub>6</sub> (622.71) requires: C,  
11  
12 69.44; H, 6.15%). <sup>1</sup>H NMR (δ, ppm, DMSO-d<sub>6</sub>): 0.65 (s, 3H, 18-H<sub>3</sub>), 2.73 (m, 2H, 6-H<sub>2</sub>), 4.40  
13  
14 (dd, 1H, *J* = 13.0 Hz, *J* = 8.5 Hz, 16a-H<sub>2</sub>), 4.56 (dd, 1H, *J* = 13.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 4.63  
15  
16 (d, 1H, *J* = 5.0 Hz, 17-H), 5.04 (s, 2H, Bn-H<sub>2</sub>), 5.47 (s, 2H, triazol-H<sub>2</sub>), 6.68 (s, 1H, 4-H), 6.74 (d,  
17  
18 1H, *J* = 8.5 Hz, 2-H), 7.16 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.37 (t, 2H, *J*  
19  
20 = 7.0 Hz, 3'- and 5'-H), 7.41 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H), 8.18 (d, 2H, *J* = 8.5 Hz, 3''- and  
21  
22 5''-H), 8.33 (d, 3H, *J* = 6 Hz, 2''- and 6''-H, triazol-H). <sup>13</sup>C NMR (δ, ppm, DMSO-d<sub>6</sub>): 17.5 (C-  
23  
24 18), 25.6, 27.5, 29.2, 29.6, 31.8, 38.2, 42.9, 44.5 (C-13), 48.2, 49.1 (C-16), 53.6 (C-16a), 58.7  
25  
26 (linker-CH<sub>2</sub>), 68.9 (Bn-CH<sub>2</sub>), 80.8 (C-17), 112.1 (C-2), 114.4 (C-4), 123.8 (C-2' and C-6'), 125.0  
27  
28 (triazol-CH), 126.1 (C-1), 127.4 (C-2'' and -6''), 127.6 (C-4'), 128.3 (C-3'' and -5''), 130.6 (C-3'  
29  
30 and -5'), 132.3 (C-10), 134.7 (C-1''), 137.3 (C-5 and C-1'), 141.1 (triazol-C), 150.2 (C-4''), 160.0  
31  
32 (C-3), 163.9 (C=O).

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34 **2.3.42. 3-Benzoyloxy-16β-(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-**  
35 **trien-17a-ol (27f)**

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37 Compound **27e** (210 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
38  
39 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
40  
41 and the precipitate separating out was filtered off and recrystallized from methanol to afford **27e**  
42  
43 (273 mg, 99%) as a white crystalline product. Mp: 172–174 °C; *R*<sub>f</sub> = 0.25 (ss B). (Found C,  
44  
45 73.68; H, 7.66. C<sub>29</sub>H<sub>35</sub>N<sub>3</sub>O<sub>3</sub> (473.61) requires C, 73.54; H, 7.45%). <sup>1</sup>H NMR (δ, ppm, DMSO-d<sub>6</sub>):  
46  
47 0.67 (s, 3H, 18-H<sub>3</sub>), 2.74 (m, 2H, 6-H<sub>2</sub>), 3.43 (s, 1H, 17-H), 4.34 (m, 1H, 16a-H<sub>2</sub>), 4.50 (m, 3H,  
48  
49 16a-H<sub>2</sub> and Bn-H<sub>2</sub>), 4.61 (brs, 1H, OH), 5.04 (s, 2H, triazol-H<sub>2</sub>), 5.16 (brs, 1H, OH), 6.69 (s, 1H,  
50  
51 4-H), 6.74 (d, 1H, *J* = 8.5 Hz, 2-H), 7.17 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (d, 1H, *J* = 7.0 Hz, 4'-H),  
52  
53 7.37 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.41 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H), 8.00 (s, 1H, triazol-  
54  
55 H). <sup>13</sup>C NMR (δ, ppm, DMSO-d<sub>6</sub>): 17.5 (C-18), 25.6, 27.5, 29.2, 29.6, 31.9, 38.2, 43.0, 44.5 (C-  
56  
57 13), 48.2, 49.1 (C-16), 53.5 (C-16a), 55.0 (linker-CH<sub>2</sub>), 61.6, 68.9 (Bn-CH<sub>2</sub>), 80.8 (C-17), 112.2  
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59 (C-2), 114.4 (C-4), 122.6 (triazol-CH), 126.6 (C-1), 127.4 (C-2' and -6'), 127.6 (C-4'), 128.3 (C-  
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61 3' and -5'), 132.4 (C-10), 137.3 (C-5 and C-1'), 147.6 (triazol-C), 156.0 (C-3).

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4 2.3.43. 3-Benzoyloxy-16a-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
5  
6 17a-ol (**28a**)

7 Compound **20** (420.0 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
8 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
9 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **28a** (305 mg, 63%) as white crystals. Mp: 143–144  
10 °C; *R*<sub>f</sub> = 0.40 (ss B). (Found C, 77.15; H, 7.53. C<sub>31</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (483.64) requires C, 76.98; H,  
11 7.71%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.74 (s, 3H, 18-H<sub>3</sub>), 0.87 and 0.97 (2 x s, 2 x 2H, 2''- and 3''-  
12 H<sub>2</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.63 (d, 1H, *J* = 5.0 Hz, 17-H), 4.26 (dd, 1H, *J* = 13.5 Hz, *J* = 5.5 Hz,  
13 16a-H<sub>2</sub>), 4.60 (t, 1H, *J* = 13.5 Hz, 16a-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.72 (d, 1H, *J* = 2.0 Hz, 4-H),  
14 6.78 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.22 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32 (t, 1H, *J* = 7.5 Hz,  
15 4'-H), 7.38 (t, 3H, *J* = 7.5 Hz, 3'- and 5'-H, triazol-H), 7.43 (d, 2H, *J* = 7.5 Hz, 2'- and 6'-H). <sup>13</sup>C  
16 NMR (δ, ppm, CDCl<sub>3</sub>): 6.5 (C-1''), 7.9 (2C, C-2'' and -3''), 17.1 (C-18), 26.0, 27.9, 28.9, 29.8,  
17 31.2, 38.9, 42.3, 43.5, 46.3 (C-16a), 47.0 (C-16), 50.7 (C-13), 69.9 (Bn-CH<sub>2</sub>), 78.7 (C-17), 112.2  
18 (C-2), 114.8 (C-4), 120.8 (triazol-CH), 126.3 (C-1), 127.4 (C-2' and -6'), 127.4 (C-4'), 128.5  
19 (C-3' and -5'), 132.5 (C-10), 137.2 (C-1'), 137.9 (C-5), 149.6 (triazol-C), 156.7 (C-3).  
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33 2.3.44. 3-Benzoyloxy-16a-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
34  
35 17a-ol (**28b**)

36 Compound **20** (420.0 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
37 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
38 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (2.5:97.5 v/v) to yield pure **28b** (417 mg, 82%) as white crystals. Mp:  
39 197–199 °C; *R*<sub>f</sub> = 0.42 (ss B). (Found: C, 77.62; H, 7.85. C<sub>33</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (511.70) requires C, 77.46;  
40 H, 8.08%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.76 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.20 (s, 1H, 1''-  
41 H), 3.66 (d, 1H, *J* = 5.0 Hz, 17-H), 4.29 (dd, 1H, *J* = 13.5 Hz, *J* = 5.5 Hz, 16a-H<sub>2</sub>), 4.62 (dd, 1H,  
42 *J* = 13.5 Hz, *J* = 9.5 Hz, 16a-H<sub>2</sub>), 5.04 (s, 2H, Bn-H<sub>2</sub>), 6.72 (s, 1H, 4-H), 6.78 (dd, 1H, *J* = 8.5 Hz,  
43 *J* = 2.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.37 (t, 2H, *J* = 7.0  
44 Hz, 3'- and 5'-H), 7.43 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.3 (C-  
45 18), 25.2 (2C), 26.1, 28.0, 29.1, 29.8 (2C), 31.3, 33.2, 36.8 (C-1''), 39.0, 42.4, 43.6, 46.4 (C-16a),  
46 47.2 (C-16), 50.6 (C-13), 70.1 (Bn-CH<sub>2</sub>), 79.0 (C-17), 112.4 (C-2), 115.0 (C-4), 126.3 (C-1),  
47 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 133.0 (C-10), 137.5 (C-1'), 137.9 (C-5),  
48 156.9 (C-3).  
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6 2.3.45. *3-Benzoyloxy-16a-(4-cyclohexyl-1H-1,2,3-triazol-1-yl)methyl-estra-1,3,5(10)-trien-17a-ol*  
7  
8 (**28c**)

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10 Compound **20** (420.0 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
11 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
12 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (2.5:97.5 v/v) to yield pure **28c** (200 mg, 76%) as a white solid. Mp:  
13 223–225 °C; *R*<sub>f</sub> = 0.44 (ss B). (Found C, 77.82; H, 8.35. C<sub>34</sub>H<sub>43</sub>N<sub>3</sub>O<sub>2</sub> (525.72) requires C, 77.68;  
14 H, 8.24%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 3H, 6-H<sub>2</sub>, 1''-H), 3.64 (s, 1H,  
15 17-H), 4.37 (m, 1H, 16a-H<sub>2</sub>), 4.69 (m, 1H, 16a-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.72 (d, 1H, *J* = 1.5 Hz,  
16 4-H), 6.78 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.22 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32 (t, 1H, *J* =  
17 7.0 Hz, 4'-H), 7.38 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.43 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H  
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26 2.3.46. *3-Benzoyloxy-16a-(4-phenyl-1H-1,2,3-triazol-1-yl)methyl-estra-1,3,5(10)-trien-17a-ol*  
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28 (**28d**)

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30 Compound **20** (420.0 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
31 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
32 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **28d** (337 mg, 64%) as a white solid. Mp: 205–206  
33 °C; *R*<sub>f</sub> = 0.46 (ss B). (Found C, 78.42; H, 7.32. C<sub>34</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (519.68) requires C, 78.58; H, 7.18%).  
34 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.76 (s, 3H, 18-H<sub>3</sub>), 2.87 (m, 2H, 6-H<sub>2</sub>), 3.68 (d, 1H, *J* = 5.0 Hz, 17-  
35 H), 4.41 (dd, 1H, *J* = 13.5 Hz, *J* = 5.5 Hz, 16a-H<sub>2</sub>), 4.69 (t, 1H, *J* = 13.5 Hz, 16a-H<sub>2</sub>), 5.04 (s, 2H,  
36 Bn-H<sub>2</sub>), 6.73 (s, 1H, 4-H), 6.79 (dd, 1H, *J* = 8.0 Hz, *J* = 2.0 Hz, 2-H), 7.22 (d, 1H, *J* = 8.0 Hz, 1-  
37 H), 7.38 (m, 8H, 2'-, 3'-, 4'-, 5'- and 6'-H, 3''-, 4''- and 5''-H), 7.84 (d, 2H, *J* = 7.5 Hz, 2''- and  
38 6''-H), 7.89 (s, 1H, triazol-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.1 (C-18), 26.0, 27.9, 29.8, 31.2,  
39 38.9, 42.2, 43.5, 46.4 (C-13), 47.0 (C-16), 50.8 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 78.8 (C-17), 112.3 (C-2),  
40 114.8 (C-4), 120.7 (triazol-CH), 125.7 (C-2' and -6'), 126.3 (C-1), 127.4 (C-2'' and -6''), 127.8  
41 (C-4'), 128.3 (C-4''), 128.5 (C-3'' and -5''), 128.9 (C-3' and -5'), 130.2 (C-10), 132.8 (C-1'),  
42 137.3 (C-1''), 137.9 (C-5), 147.1 (triazol-C), 156.7 (C-3).  
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56 2.3.47. *3-Benzoyloxy-16a-[4'-(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-*  
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58 *1,3,5(10)-trien-17a-ol* (**28e**)

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4 Compound **20** (420 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used for  
5 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
6 with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **28e** (610 mg, 98%) as a yellow solid. Mp:  
7 75–77 °C; *R*<sub>f</sub> = 0.45 (ss B). (Found C, 69.57; H, 61.32. C<sub>36</sub>H<sub>38</sub>N<sub>4</sub>O<sub>6</sub> (622.71) requires C, 69.44; H,  
8 6.15%). <sup>1</sup>H NMR (δ, ppm, DMSO-d<sub>6</sub>): 0.66 (s, 3H, 18-H<sub>3</sub>), 2.71 (m, 2H, 6-H<sub>2</sub>), 3.57 (s, 1H, 16-  
9 H), 4.29 (dd, 1H, *J* = 13.5 Hz, *J* = 8.5 Hz, 16a-H<sub>2</sub>), 4.47 (dd, 1H, *J* = 13.5 Hz, *J* = 8.5 Hz, 16a-  
10 H<sub>2</sub>), 4.85 (d, 1H, *J* = 5.0 Hz, 17-H), 5.44 (s, 2H, Bn-H<sub>2</sub>), 6.65 (s, 1H, 4-H), 6.72 (d, 1H, *J* = 8.5  
11 Hz, 2-H), 7.14 (d, 1H, *J* = 8.5 Hz, 1-H), 7.29 (t, 1H, *J* = 7.5 Hz, 4'-H), 7.35 (t, 2H, *J* = 7.5 Hz, 3'-  
12 and 5'-H), 7.40 (d, 2H, *J* = 7.5 Hz, 2'- and 6'-H), 8.17 (d, 2H, *J* = 8.5 Hz, 3''- and 5''-H), 8.28 (s,  
13 1H, triazol H), 8.31 (d, 2H, *J* = 8.5 Hz, 2''- and 6''-H). <sup>13</sup>C NMR (δ, ppm, DMSO-d<sub>6</sub>): 16.9 (C-  
14 18), 25.6, 27.5, 28.4, 29.2, 31.1, 38.5, 39.8, 39.9, 43.2, 45.9 (C-16a), 46.2 (C-16), 53.4 (C-13),  
15 58.7 (linker CH<sub>2</sub>), 68.9 (Bn-CH<sub>2</sub>), 78.0 (C-17), 112.1 (C-2), 114.4 (C-4), 123.8 (C-2'' and -6''),  
16 125.0 (triazol CH), 126.1 (C-1), 127.4 (C-2' and -6'), 127.5 (C-4'), 128.3 (C-3' and -5'), 130.6  
17 (C-3'' and -5''), 132.3 (C-10), 134.7 (C-1'), 137.3 (C-5), 141.0 (C-1''), 150.2 (triazol C), 156.0  
18 (C-3), 163.9 (C=O).

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34 **2.3.48. 3-Benzoyloxy-16a-(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-**  
35 **trien-17α-ol (28f)**

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37 Compound **28e** (220 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
38 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
39 and the precipitate separating out was filtered off and recrystallized from methanol to afford **28f**  
40 (126 mg, 53%) as a white crystalline product. Mp: 86–88 °C; *R*<sub>f</sub> = 0.25 (ss B). (Found C, 73.68;  
41 H, 7.63. C<sub>29</sub>H<sub>35</sub>N<sub>3</sub>O<sub>3</sub> (473.61) requires C, 73.54; H, 7.45%). <sup>1</sup>H NMR (δ, ppm, DMSO-d<sub>6</sub>): 0.68  
42 (s, 3H, 18-H<sub>3</sub>), 2.74 (m, 2H, 6-H<sub>2</sub>), 3.58 (brs, 1H, OH), 4.26 (t, 1H, *J* = 8.5 Hz, 16a-H<sub>2</sub>), 4.43 (dd,  
43 1H, *J* = 13.0 Hz, *J* = 7.0 Hz, 16a-H<sub>2</sub>), 4.51 (d, 2H, *J* = 5.0 Hz, linker H<sub>2</sub>), 4.85 (d, 1H, *J* = 4.0 Hz,  
44 17-H), 5.04 (s, 2H, Bn-H<sub>2</sub>), 5.13 (brs, 1H, OH), 6.68 (s, 1H, 4-H), 6.74 (d, 1H, *J* = 8.5 Hz, 2-H),  
45 7.17 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (d, 1H, *J* = 7.0 Hz, 4'-H), 7.37 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-  
46 H), 7.42 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H), 7.97 (s, 1H, triazol H). <sup>13</sup>C NMR (δ, ppm, DMSO-d<sub>6</sub>):  
47 16.9 (C-18), 25.6, 27.5, 28.5, 29.2, 31.1, 38.5, 40.7, 43.2, 45.9, 46.2 (C-16), 47.9 (C-13), 50.6 (C-  
48 16a), 55.0 (linker CH<sub>2</sub>), 68.9 (Bn-CH<sub>2</sub>), 78.0 (C-17), 112.1 (C-2), 114.4 (C-4), 122.7 (triazol  
49 H), 125.0 (triazol CH), 126.1 (C-1), 127.4 (C-2' and -6'), 127.5 (C-4'), 128.3 (C-3' and -5'), 130.6  
50 (C-3'' and -5''), 132.3 (C-10), 134.7 (C-1'), 137.3 (C-5), 141.0 (C-1''), 150.2 (triazol C), 156.0  
51 (C-3), 163.9 (C=O).

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4 CH), 126.1 (C-1), 127.4 (C-2' and -6'), 127.6 (C-4'), 128.3 (C-3' and -5'), 132.4 (C-10), 137.3  
5 (C-1'), 137.4 (C-5), 147.6 (triazol C), 156.0 (C-3).  
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#### 9 10 2.4. Determination of the antiproliferative activities

11 The growth-inhibitory effects of the compounds were tested *in vitro* by means of the MTT  
12 assay against a gynecological panel containing two breast cancer cell lines (MCF-7, MD-MB-  
13 231) and two cell lines isolated from cervical malignancies (HeLa, SiHa) [11]. All cell lines were  
14 obtained from the European Collection of Cell Cultures (Salisbury, UK). The cells were  
15 maintained in minimal essential medium supplemented with 10% fetal bovine serum (FBS), 1%  
16 non-essential amino acids and an antibiotic–antimycotic mixture (AAM). All chemicals, if  
17 otherwise not specified, were purchased from Sigma-Aldrich Ltd. (Budapest, Hungary). All cell  
18 lines were grown in a humidified atmosphere of 5% CO<sub>2</sub> at 37 °C. For pharmacological  
19 investigations, 10 mM stock solutions of the tested compounds were prepared with dimethyl  
20 sulfoxide (DMSO). The highest applied DMSO concentration of the medium (0.3%) did not have  
21 any substantial effect on the determined cellular functions. Cells were seeded into 96-well plates  
22 (5000 cells/well), allowed to stand overnight under cell culturing conditions, and the medium  
23 containing the tested compounds at two final concentrations (10 or 30 µM) was then added. After  
24 a 72-hour incubation viability was determined by the addition of 20 µl 3-(4,5-dimethylthiazol-2-  
25 yl)-2,5-diphenyltetrazolium bromide (MTT) solution (5 mg/ml). The formazan crystals  
26 precipitated in 4 h were solubilized in DMSO and the absorbance was determined at 545 nm with  
27 an ELISA plate reader utilizing untreated cells as controls. The most effective compounds  
28 eliciting at least 60% growth inhibition at 10 µM were tested again with a set of dilutions (0.3–30  
29 µM) in order to determine the IC<sub>50</sub> values by means of Graphpad Prism 4.0 (Graphpad Software;  
30 San Diego, CA, US). These promising compounds were additionally tested using nonmalignant  
31 murine fibroblasts (NIH-3T3) to obtain preliminary data concerning cancer selectivity of the  
32 tested molecules. Two independent experiments were performed with 5 parallel wells and  
33 cisplatin (Ebewe GmbH, Unterach, Austria), an agent administered clinically in the treatment of  
34 certain gynecological malignancies, was used as reference compound.  
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### 57 3. Results and discussion

#### 58 3.1. Synthetic studies 59 60 61 62 63 64 65

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To prepare novel steroid triazoles via 1,3-dipolar cycloaddition, we chose the 3-methoxy- and 3-benzyloxy-16-hydroxymethylestra-1,3,5(10)-trien-17-ol diastereomers (**5–8** and **9–12**). The synthesis strategy for the preparation of the starting diols (**21–28**) is illustrated in Scheme 1. The synthesis of steroidal 1,2,3-triazoles by CuAAC is outlined in Scheme 2.

Stereoselective tosylation of **5–8** and bromination of **9–12** gave **5b–8b** and **9c–12c**, respectively, which then underwent facile S<sub>N</sub>2 substitution with NaN<sub>3</sub> in *N,N*-dimethylformamide to furnish the corresponding 16-azidomethyl compounds (**13–16** and **17–20**).

The 16-azido compounds were subjected to the azide–alkyne CuAAC reaction with different alkyl- and aryl-acetylenes. The azide–alkyne reactions of these compounds were carried out with CuI as catalyst in the presence of Et<sub>3</sub>N in CH<sub>2</sub>Cl<sub>2</sub> under reflux conditions to obtain the required 3-methoxy- and 3-benzyloxyestra-1,3,5(10)-trien-16-(1',4'-substituted 1',2',3')-triazolyl derivatives (**21–24** and **25–28**).

### 3.2. Determination of the antiproliferative properties of the 16-triazolylmethyl diastereomers

We have published recently that introduction of a substituted triazole moiety onto different positions of the estrane skeleton might increase the antiproliferative properties of estrone derivatives [12]. It was also established that the presence of certain alkyl or aralkyl protecting groups at the phenolic OH function is advantageous. Concerning that 16-hydroxymethylene-17-hydroxy derivatives of estrone-3-methyl ether or 3-benzyl ether (**5a–12a**) displayed substantial cytostatic potential against different types of breast cancer cell lines, these compounds might be suitable for directed modifications with the aim of developing potentially more active antiproliferative steroidal derivatives [13]. In the light of the above-mentioned recent observations, here we aimed to combine the substituted triazole and the 16,17-disubstituted estrone 3-ether moieties. The present study included an evaluation of the direct antiproliferative capacities of the newly synthesized heterocyclic compounds (**21a–f**, **22a–f**, **23a–f**, **24a–f** and **25a–f**, **26a–f**, **27a–f**, **28a–f**). The antiproliferative activities were determined *in vitro* by means of MTT assays against human adherent cervical (SiHa, HeLa) and breast cancer (MCF-7 and MDA-MB-231) cell lines.

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4 The antiproliferative activities of the newly synthesized heterocyclic compounds  
5 depended on the nature of the protecting group at the 3-hydroxy function and on the orientation  
6 of the substituents at C-16 and C-17. In general, the 3-methyl ethers (**21–24**) exhibited weak  
7 antiproliferative action; none of them exerted any substantial effect at 10  $\mu$ M (Table 1). All  
8 diastereomers of the 3-benzyl ether series (**25–28**) proved to be more potent in comparison with  
9 their 3-methyl ether counterparts (Table 2). This is in agreement with our earlier results [14].  
10 Based on the substantial difference of the two groups, i.e. that of 3-methyl ethers and 3-benzyl  
11 ethers, it can be concluded that only the latter derivatives are promising from pharmacological  
12 point of view.  
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21 Concerning the orientation of the substituents at position C-16 and C-17, the 16 $\beta$ ,17 $\beta$ -  
22 derivatives (**25a–f**) displayed outstanding growth-inhibitory properties. Two derivatives bearing  
23 similar cycloalkyl groups at position C-4' displayed substantial selective antiproliferative action  
24 against the triple-negative breast cancer cell line MDA-MB-231 with IC<sub>50</sub> values in the low  
25 micromolar range. It should be underlined that **25b** and **25c** did not significantly influence the  
26 proliferation of other cell lines tested, including the non-cancerous fibroblast. Although both the  
27 4'-cyclohexyl (**25c**) and the 4'-phenyl derivative (**25d**) have six-membered substituents, their  
28 cytostatic behavior is completely different. This might be attributed to the different steric  
29 structure of the two rings (chair or planar) at C-4'. Compound **25d** exerted potent  
30 antiproliferative action against all tested cell lines without any selectivity. The *cis*-16 $\alpha$ ,17 $\alpha$ -3-  
31 benzyl ethers (**28a–f**) were less potent than their  $\beta,\beta$ -counterparts (**25a–f**), except for **28d**, which  
32 behaved similarly to its diastereomer **25d**. The *trans*-16 $\beta$ ,17 $\alpha$ -isomers (**27a–f**) exhibited activity  
33 exclusively on the breast cancer cell lines. Surprisingly, the tendency observed earlier (in the case  
34 of compounds **25a–f**) concerning the nature of C-4' substituent was not valid here. Only **26a** and  
35 **26e** inhibited cell growth markedly, but with no tumor selectivity. It's worth mentioning that  
36 *trans*-16 $\alpha$ ,17 $\beta$  isomer **26c** was the sole compound, which inhibited the proliferation of HPV 16+  
37 squamous cell carcinoma SiHa, showing an IC<sub>50</sub> value comparable with that of cisplatin.  
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52 In view of the cell lines, it should be noted that triple-negative breast cancer cell line MDA-MB-  
53 231 proved to be the most sensitive and all calculated IC<sub>50</sub> values were lower than that of the  
54 reference agent cisplatin (19.1  $\mu$ M).  
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56 Regarding the present and earlier results obtained for 16,17-disubstituted 3-benzyl ethers, it can  
57 be stated that introduction of a substituted triazolyl moiety onto the C-16 methylene group of the  
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4 *cis* isomers proved to be advantageous. In the case of compounds **25b** and **25c**, both the  
5 antiproliferative potential and the tumor selectivity were markedly improved.  
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## 10 **Acknowledgement**

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12  
13 The work of Anita Kiss was supported by a PhD Fellowship of the Talentum Fund of  
14 Richter Gedeon Plc. (Budapest). Financial support from the Economic Development and  
15 Innovation Operative Programme of Hungary (GINOP-2.3.2-15-2016-00038) and Ultrafast  
16 physical processes in atoms, molecules, nanostructures and biological systems (No: EFOP-3.6.2.-  
17 2017-00005) is gratefully acknowledged. This research was supported by the Hungarian  
18 Scientific Research Fund (OTKA K113150). Ministry of Human Capacities, Hungary grant  
19 20391-3/2018/FEKUSTRAT is acknowledged.  
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17 [14] Frank E, Molnar J, Zupko I, Kadar Z, Wölfling J. Synthesis of novel steroidal 17 $\alpha$ -triazolyl  
18 derivatives via Cu(I)-catalyzed azide-alkyne cycloaddition, and an evaluation of their cytotoxic  
19 activity in vitro. *Steroids* **2011**;76:1141–1148.  
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**Legends for Schemes and Tables**

**Scheme 1** Reagents and conditions: (i) NaOMe, HCOOEt, anhydrous toluene, 50 °C; (ii) KBH<sub>4</sub>, MeOH; (iii) KOAc, CH<sub>3</sub>COOH, NaOMe/MeOH.

**Scheme 2** Reagents and conditions: (i) appropriate alkyne, TEA, CuI, CH<sub>2</sub>Cl<sub>2</sub>, 40 °C, 24 h; (ii) NaOMe, MeOH, 24 h.

**Table 1** Antiproliferative activities of compounds **21a–f**, **22a–f**, **23a–f** and **24a–f**

**Table 2** Antiproliferative activities of compounds **25a–f**, **26a–f**, **27a–f** and **28a–f**

**Table 1**

Growth Inhibition, % $\pm$ SEM [calculated IC <sub>50</sub> ( $\mu$ M)]					
	Conc. ( $\mu$ M)	HeLa	SiHa	MCF-7	MDA-MB- 231
<b>21</b>					
<b>a</b>	10	<20	21.28 $\pm$ 1.88	<20	<20
	30	<20	28.71 $\pm$ 2.20	46.42 $\pm$ 1.47	<20
<b>b</b>	10	<20	<20	<20	<20
	30	39.86 $\pm$ .38	<20	57.42 $\pm$ 1.77	29.88 $\pm$ 1.57
<b>c</b>	10	<20	<20	<20	<20
	30	40.22 $\pm$ 1.02	<20	70.84 $\pm$ 1.55	37.96 $\pm$ 1.55
<b>d</b>	10	<20	<20	<20	<20
	30	44.16 $\pm$ 0.48	<20	54.93 $\pm$ 1.78	38.28 $\pm$ 1.84
<b>e</b>	10	<20	23.91 $\pm$ 1.61	34.23 $\pm$ 3.10	<20
	30	37.18 $\pm$ 1.65	54.72 $\pm$ 0.48	76.26 $\pm$ 0.72	35.93 $\pm$ 2.13
<b>f</b>	10	<20	28.06 $\pm$ 1.99	29.45 $\pm$ 1.67	<20
	30	41.03 $\pm$ 0.77	57.69 $\pm$ 1.12	70.23 $\pm$ 1.35	34.81 $\pm$ 2.88
<b>22</b>					
<b>a</b>	10	<20	25.55 $\pm$ 1.01	<20	<20
	30	<20	34.78 $\pm$ 2.47	57.43 $\pm$ 1.91	<20
<b>b</b>	10	<20	<20	<20	<20
	30	<20	26.57 $\pm$ 2.26	67.59 $\pm$ 1.65	<20
<b>c</b>	10	<20	<20	<20	<20
	30	<20	29.90 $\pm$ 2.59	69.68 $\pm$ 0.77	<20
<b>d</b>	10	<20	<20	<20	<20
	30	<20	29.96 $\pm$ 1.79	70.75 $\pm$ 1.05	14.54 $\pm$ 1.32
<b>e</b>	10	<20	<20	<20	<20
	30	<20	38.69 $\pm$ 2.09	63.12 $\pm$ 2.14	<20
<b>f</b>	10	<20	<20	22.02 $\pm$ 1.61	<20
	30	<20	37.79 $\pm$ 1.04	50.94 $\pm$ 1.55	<20
<b>23</b>					
<b>a</b>	10	<20	<20	<20	<20
	30	31.14 $\pm$ 1.28	<20	28.72 $\pm$ 0.93	25.08 $\pm$ 3.15
<b>b</b>	10	<20	<20	<20	<20
	30	58.25 $\pm$ 2.03	<20	48.01 $\pm$ 1.31	<20
<b>c</b>	10	<20	30.97 $\pm$ 2.69	<20	<20
	30	<20	33.89 $\pm$ 2.35	<20	<20
<b>d</b>	10	<20	<20	<20	<20
	30	26.90 $\pm$ 2.15	<20	63.27 $\pm$ 0.82	<20
<b>e</b>	10	<20	<20	<20	<20
	30	<20	37.53 $\pm$ 3.00	33.94 $\pm$ 0.75	28.19 $\pm$ 0.96
<b>f</b>	10	<20	29.13 $\pm$ 1.59	<20	<20
	30	26.61 $\pm$ 0.57	43.85 $\pm$ 3.32	38.45 $\pm$ 1.93	43.85 $\pm$ 3.32
<b>24</b>					
<b>a</b>	10	<20	<20	<20	<20
	30	89.01 $\pm$ 0.47	<20	78.65 $\pm$ 0.78	46.21 $\pm$ 1.54
<b>b</b>	10	<20	<20	<20	<20
	30	34.18 $\pm$ 0.81	<20	31.07 $\pm$ 2.36	<20
<b>c</b>	10	<20	<20	<20	<20
	30	49.11 $\pm$ 0.55	<20	43.22 $\pm$ 1.52	<20

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<b>d</b>	10	<20	<20	<20	<20
	30	42.13±1.66	<20	55.41±0.76	<20
<b>e</b>	10	<20	<20	<20	<20
	30	83.66±0.34	42.06±2.50	70.11±1.06	50.27±2.00
<b>f</b>	10	<20	<20	22.34±2.06	<20
	30	84.77±1.18	29.80±1.66	68.27±1.19	47.74±1.21
cisplatin	10	42.61±2.33	86.84±0.50	53.03±2.29	20.84±0.81
	30	99.93±0.26	90.18±1.78	86.90±1.24	74.47±1.20
		[12.43]	[7.84]	[5.78]	[19.13]

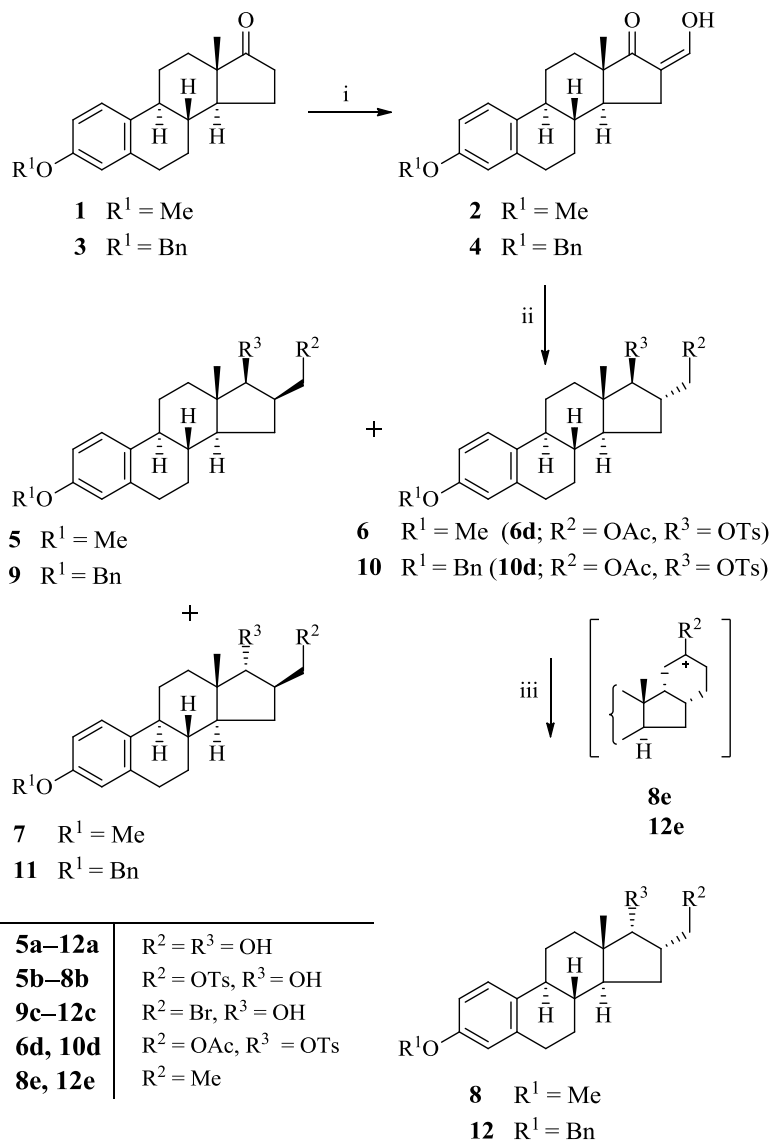
**Table 2**

Growth Inhibition, % ± SEM [calculated IC <sub>50</sub> (μM)]						
	Conc. (μM)	HeLa	SiHa	MCF-7	MDA-MB- 231	NIH-3T3
<b>25</b>						
<b>a</b>	10	44.94±1.04	21.17±2.05	41.71±0.64	47.32±1.15	44.91±1.36
	30	52.45±2.39	66.23±0.86	64.32±0.56	71.49±0.75	91.28±0.50
<b>b</b>	10	51.49±3.62	49.36±1.69	44.58±1.50	93.00±0.26	44.81±1.50
	30	62.58±2.21	73.94±2.04	50.52±3.26	93.71±0.09	59.09±0.73
<b>c</b>	10	54.70±1.88	49.58±2.11	44.04±3.32	77.13±1.07	
	30	53.66±2.56	61.83±2.77	59.33±2.99	88.81±0.55	[3.33]
<b>d</b>	10	64.14±0.86	70.88±1.03	73.41±1.22	95.04±0.16	95.60±0.25
	30	90.12±0.99	94.14±0.29	80.16±3.40	95.60±0.06	98.22±0.04
<b>e</b>	10	<20	<20	41.63±2.83	21.96±0.73	
	30	92.12±0.25	89.25±0.68	97.00±0.11	95.22±0.91	
<b>f</b>	10	45.08±0.72	41.26±1.25	55.41±1.26	55.57±1.50	
	30	39.39±0.49	52.60±1.31	62.52±0.67	88.92±0.99	
<b>26</b>						
<b>a</b>	10	37.98±2.68	<20	72.42±2.19	46.43±2.05	85.50±1.22
	30	96.56±0.11	96.71±0.17	98.72±0.09	97.96±0.17	97.63±0.12
<b>b</b>	10	38.55±1.32	<20	31.80±1.35	17.13±2.36	
	30	43.97±2.23	<20	84.44±0.71	37.72±2.28	
<b>c</b>	10	36.30±1.45	<20	24.95±2.15	<20	
	30	35.53±1.24	<20	74.73±1.00	<20	
<b>d</b>	10	<20	<20	47.25±1.78	45.55±2.63	
	30	22.15±1.29	<20	57.30±0.77	59.79±1.22	
<b>e</b>	10	<20	<20	68.51±0.71	89.24±0.70	31.41±2.21
	30	96.98±0.33	96.91±0.14	99.12±0.07	97.73±0.23	99.01±0.05
<b>f</b>	10	21.62±3.46	<20	29.14±2.06	40.46±2.98	10.00±1.01
	30	30.79±2.92	27.28±1.90	43.28±1.53	76.93±1.60	23.40±0.60
<b>27</b>						
<b>a</b>	10	24.26±2.63	34.00±1.43	58.38±3.20	56.24±0.98	25.56±2.21
	30	85.22±1.32	82.68±1.25	97.21±0.10	84.18±0.44	99.24±0.07
<b>b</b>	10	37.10±1.77	39.59±1.17	51.92±1.00	56.44±0.98	
	30	52.08±2.08	69.54±1.24	65.12±1.91	71.81±0.96	
<b>c</b>	10	38.89±2.60	64.05±1.24	49.68±1.66	72.37±1.27	13.99±1.79
	30	55.93±2.39	83.34±1.31	61.26±1.72	85.81±1.04	29.56±1.17
<b>d</b>	10	34.23±1.39	30.04±2.07	47.03±1.25	55.77±1.03	
	30	47.74±0.78	39.96±2.34	42.43±1.69	57.71±1.00	
<b>e</b>	10	<20	21.53±1.81	35.74±1.33	<20	
	30	99.06±0.09	96.91±0.06	98.50±0.93	99.01±0.52	
<b>f</b>	10	<20	24.65±1.46	25.50±2.93	24.79±2.20	
	30	98.72±0.13	96.04±0.25	98.41±0.15	98.79±0.16	
<b>28</b>						

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<b>a</b>	10	35.48±1.91	46.07±1.13	52.88±0.82	25.61±2.84	
	30	63.44±1.79	69.86±0.55	73.39±0.74	52.16±2.52	
<b>b</b>	10	39.75±2.45	<20	43.51±1.85	44.86±0.93	
	30	47.34±1.62	<20	42.28±1.44	43.73±2.25	
<b>c</b>	10	56.71±0.57	39.93±3.14	48.56±0.48	30.30±1.64	
	30	58.21±0.73	31.15±2.86	49.93±1.33	31.60±3.08	
<b>d</b>	10	74.18±1.15	76.88±0.49	75.97±0.89	86.12±0.33	70.18±1.15
	30	91.17±0.33	87.39±0.86	88.99±0.25	90.72±1.00	91.12±1.64
		[2.30]	[4.14]	[3.87]	[3.89]	[3.71]
<b>e</b>	10	27.42±2.16	<20	52.86±1.30	29.58±1.69	
	30	92.94±0.17	91.91±0.23	96.38±0.07	94.09±0.43	
<b>f</b>	10	30.97±1.02	39.85±1.24	50.60±0.65	31.89±2.92	
	30	91.88±0.26	90.94±0.18	95.12±0.10	92.56±0.34	
cisplatin	10	42.61±2.33	86.84±0.50	53.03±2.29	20.84±0.81	94.20±0.39
	30	99.93±0.26	90.18±1.78	86.90±1.24	74.47±1.20	96.44±0.17
		[12.43]	[7.84]	[5.78]	[19.13]	[3.23]

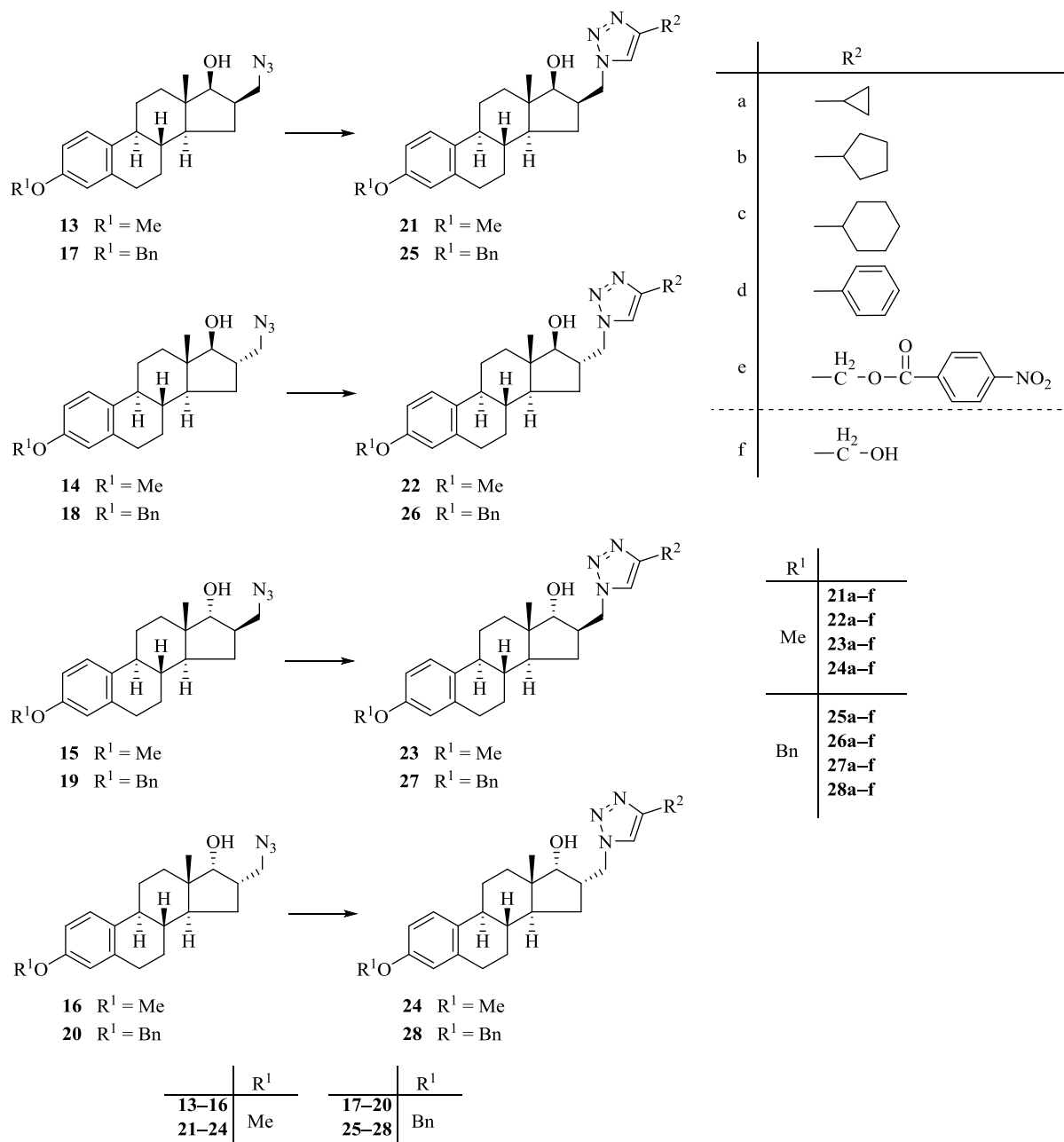
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**Scheme 1. Reagents and conditions:** (i) NaOMe, HCOOEt, anhydrous toluene, 50 °C; (ii)  $\text{KBH}_4$ , MeOH; (iii) KOAc,  $\text{CH}_3\text{COOH}$ , NaOMe/MeOH

**Scheme 1.**

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**Scheme 2.**

# Stereocontrolled Synthesis of the Four Possible 3-Methoxy and 3-Benzyloxy-16-Triazolyl-methyl-estra-17-ol Hybrids and their Antiproliferative Activities

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**ABSTRACT** The four possible isomers of each of 3-methoxy- and 3-benzyloxyestra-1,3,5(10)-trien-17-ols (**5–8** and **9–12**) were converted through 16-*p*-tosyloxymethyl- or 16-bromomethyl derivatives into their 3-methoxy- and 3-benzyloxy-16-azidomethylestra(1,3,5(10)-triene derivatives (**13–16** and **17–20**). The regioselective Cu(I)-catalyzed 1,3-dipolar cycloaddition of these compounds with different terminal alkynes afforded novel 1,4-disubstituted diastereomers (**21a–f**, **22a–f**, **23a–f**, **24a–f** and **25a–f**, **26a–f**, **27a–f**, **28a–f**). The antiproliferative activities of the structurally related triazoles were determined *in vitro* with the microculture tetrazolium assay on four malignant human cell lines of gynecological origin (Hela, SiHa, MCF-7 and MDA-MB-231).

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**Keywords:** 3-methoxy- and 3-benzyloxy-16-azidomethylestra-1,3,5(10)-triene-17-ols; 1,3-dipolar cycloaddition, 4 substituted-steroid triazoles; cytotoxic activity

## 1. Introduction



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4 Among the hybrid natural products, hybrids of steroid frameworks have attracted great attention  
5 due to significant biological properties and numerous therapeutic effects of the basic compound.  
6 Steroids have become ideal synthons for the development of diverse conjugates due to their rigid  
7 framework and potential for varying levels of functionalization, broad biological activity profile  
8 and their ability to penetrate the cell membranes and bind to specific hormonal receptors [1-3].  
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13 The place, length and orientation of the linkers between the two parts of the hybrids  
14 stems unequivocally from the method of their synthesis. The literature provides a large number of  
15 methods to introduce the linker onto the sterane skeleton. The effect of the length and character  
16 of the linker are very often discussed [4]. However, only limited information is available with  
17 respect to the steric effect of the linkers on biological properties. As concerns the 16-substituted  
18 estrogens, usually the 16 $\alpha$ -substituted-17 $\beta$ -hydroxy compounds have been studied. The  
19 biological activity has generally not been studied for the whole isomer series [5].  
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26 In the 16-substituted 17-hydroxysteroids, the two chiral centres permit four  
27 stereochemical modifications. Since availability of the complete series of isomers would permit a  
28 number of interesting comparative examinations.  
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32 We have previously reported the preparation and configurational assignment of the four  
33 possible isomers of the 3-methoxy- and 3-benzyloxy-16-hydroxymethyl-estra-1,3,5(10)-trien-17-  
34 ol derivatives (**5a-8a** and **9a-12a**) [6-8]. Treatment of 3-methoxy- and 3-benzyloxyestra-16-  
35 hydroxymethylidene-estra-1,3,5(10)-trien-17-ones (**1** and **3**) with NaOMe and ethyl formate gave  
36 3-methoxy- and 3-benzyloxy-16-hydroxymethylidene-estra-1,3,5(10)-trien-17 ones (**2** and **4**).  
37 The C-16 formyl compounds were reduced with KBH<sub>4</sub> in methanol yielding a mixture of three  
38 (**5a-7a** and **9a-11a**) of the four possible isomers of each of the 3-methoxy- and 3-benzyloxy-16-  
39 hydroxymethylestra-1,3,5(10)-trien-17-ol isomers in a ratio of 50:45:5 in 94% yield [6,8 ]. The  
40 fourth isomers (**8a** and **12a**) were prepared from 16 $\alpha$ -acetoxymethyl-17 $\beta$ -toluenesulfonate mixed  
41 esters **6d** and **10d**, respectively, by neighbouring group participation during solvolysis in aqueous  
42 AcOH. The structures of the isomers were confirmed unambiguously by their IR, <sup>1</sup>H and <sup>13</sup>C  
43 NMR spectra (Scheme 1) [7,8].  
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(Scheme 1)

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4 The four 3-methoxy- and 3-benzyloxy-estra-1,3,5(10)-trien-17-ol isomers (**5a–8a** and **9a–**  
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6 **12a**) are suitable starting materials to prepare 16-triazolyl-methyl derivatives. Triazoles are  
7 attractive units because of their stability against metabolic degradation and their ability to form  
8 hydrogen bonds. The Cu(I)-catalysed azide–alkyne cycloaddition (CuAAC) is a facile method of  
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10 wide applicability for the introduction of a triazole moiety into natural products [9]. In these  
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12 compounds the triazole heterocycles and their substituted derivatives are connected through a  
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14 methylene linker to the sterane skeleton. The 16-*p*-tolylsulfonyloxymethyl ester [5,6] and 16-  
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16 bromomethyl derivatives [10] of the 16-hydroxymethyl starting materials were used for  
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18 substitution reaction with NaN<sub>3</sub> in *N,N*-dimethylformamide to have the desired 3-methoxy- and  
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20 3-benzyloxy-16-azidomethylestra-1,3,5(10)-trien-17-ols (**13–16** and **17–20**). From these azido  
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22 compounds several D-ring-substituted estrane derivatives containing a 1,2,3-triazole ring were  
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24 synthesized by the reaction of **13–16** and **17–20** with various terminal alkynes through the use of  
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26 the “click” chemistry approach to deliver compounds **21a–e**, **22a–e**, **23a–e**, **24a–e**, **25a–e**, **26a–e**,  
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28 **27a–e** and **28a–e**.

## 31 **2. Experimental**

### 32 *2.1. General*

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37 Melting points (Mp) were determined on a Kofler block and are uncorrected. Specific rotations  
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39 were measured in CHCl<sub>3</sub> (*c* 1) at 20 °C with a POLAMAT-A (Zeiss-Jena) polarimeter and are  
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41 given in units of 10<sup>-1</sup> deg cm<sup>2</sup> g<sup>-1</sup>. Elementary analysis data were determined with a Perkin-Elmer  
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43 CHN analyzer model 2400. The reactions were monitored by TLC on Kieselgel-G (Merck Si 254  
44  
45 F) layers (0.25 mm thick); solvent systems (ss): (A) diisopropyl ether, (B)  
46  
47 acetone/toluene/hexane (30:35:35 v/v). The spots were detected by spraying with 5%  
48  
49 phosphomolybdic acid in 50% aqueous phosphoric acid. The *R<sub>f</sub>* values were determined for the  
50  
51 spots observed by illumination at 254 and 365 nm. Flash chromatography: silica gel 60, 40–63  
52  
53 μm. All solvents were distilled prior to use. NMR spectra were recorded on a Bruker DRX 500  
54  
55 and Bruker Ascend 500 instrument at 500 (<sup>1</sup>H NMR) or 125 MHz (<sup>13</sup>C NMR). Chemical shifts  
56  
57 are reported in ppm (δ scale) and coupling constants (*J*) in Hertz. For the determination of  
58  
59 multiplicities, the *J*-MOD pulse sequence was used.  
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## 2.2. 3-Methoxy- and 3-benzyloxy-16-azidomethylestra-1,3,5(10)-trienes (**13–16** and **17–20**)

### General procedure

Compounds **5b–8b** [5,6] (470 mg, 1 mmol) or **9c–12c** [8] (455 mg, 1 mmol) were dissolved in *N,N*-dimethylformamide (25 ml) and then NaN<sub>3</sub> (260 mg) was added. The mixture was stirred for 6 h at 80 °C, then poured into water (50 ml). The precipitate separating out was filtered off and subjected to chromatographic separation with CH<sub>2</sub>Cl<sub>2</sub>/hexane in different ratios.

#### 2.2.1. 3-Methoxy-16 $\beta$ -azidomethyl-estra-1,3,5(10)-trien-17 $\beta$ -ol (**13**)

Compound **5b** (470 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3 v/v) to yield pure **13** (318 mg, 93%). Mp 134–135 °C; *R*<sub>f</sub> = 0.65 (ss A); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = + 80 (*c* 1 in CHCl<sub>3</sub>). (Found C, 70.23; H, 8.05. C<sub>20</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub> (341.45) requires C, 70.35; H, 7.97%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.82 (s, 3H, 18-H<sub>3</sub>), 2.87 (m, 2H, 6-H<sub>2</sub>), 3.32 (dd, 1H, *J* = 12.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 3.61 (dd, 1H, *J* = 12.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 3.78 (s, 3H, 3-OCH<sub>3</sub>), 3.87 (d, 1H, *J* = 10.0 Hz, 17-H), 6.64 (d, 1H, *J* = 2.5 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 12.2 (C-18), 26.3, 27.5, 29.7, 30.4, 37.7, 38.2, 40.2, 44.0, 44.3 (C-13), 49.0, 53.4 (C-16a), 55.2 (3-OCH<sub>3</sub>), 81.5 (C-17), 111.6 (C-2), 113.9 (C-4), 126.2 (C-1), 132.5 (C-10), 137.9 (C-5), 157.7 (C-3).

#### 2.2.2. 3-Methoxy-16 $\alpha$ -azidomethylestra-1,3,5(10)-trien-17 $\beta$ -ol (**14**)

Compound **6b** (470 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3 v/v) to yield pure **14** (287 mg, 84%). Mp 85–86 °C; *R*<sub>f</sub> = 0.62 (ss A); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = + 48 (*c* 1 in CHCl<sub>3</sub>). (Found C, 70.42; H, 7.65. C<sub>20</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub> (341.45) requires C, 70.35; H, 7.97%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.84 (s, 3H, 18-H<sub>3</sub>), 2.86 (m, 2H, 6-H<sub>2</sub>), 3.43 (d, 1H, *J* = 7.5 Hz, 17-H), 3.48 (dd, 2H, *J* = 6.5 Hz, *J* = 3.5 Hz, 16a-H<sub>2</sub>), 3.78 (s, 3H, 3-OCH<sub>3</sub>), 6.63 (s, 1H, 4-H), 6.72 (dd, 1H, *J* = 6.5 Hz, *J* = 2.0 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 11.8 (C-18), 26.1, 27.2, 28.0, 29.7, 36.6, 38.5, 43.6, 43.9, 44.2 (C-13), 48.5, 55.2 (3-OCH<sub>3</sub>), 55.6 (C-16a), 85.1 (C-17), 111.5 (C-2), 113.8 (C-4), 126.3 (C-1), 132.4 (C-10), 137.8 (C-5), 157.5 (C-3).

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4 2.2.3. 3-Methoxy-16 $\beta$ -azidomethylestra-1,3,5(10)-trien-17 $\alpha$ -ol (**15**)  
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6 Compound **7b** (470 mg, 1 mmol) were used for the synthesis as described in Section 2.2. The  
7 crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3 v/v) to yield pure **15**  
8 (275 mg, 80%). Mp 96–98; °C; *R<sub>f</sub>* = 0.60 (ss A); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = + 68 (*c* 1 in CHCl<sub>3</sub>). (Found C, 70.26;  
9 H, 8.15. C<sub>20</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub> (341.45) requires C, 70.35; H, 7.97%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.76 (s,  
10 3H, 18-H<sub>3</sub>), 2.86 (m, 2H, 6-H<sub>2</sub>), 3.43 (dd, 2H, *J* = 7.5 Hz, *J* = 3.0 Hz, 16a-H<sub>2</sub>), 3.61 (s, 1H, 17-H),  
11 3.78 (s, 3H, 3-OCH<sub>3</sub>), 6.64 (d, 1H, *J* = 2.5 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H),  
12 7.22 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 17.7 (C-18), 25.9, 27.9, 29.8, 30.3,  
13 31.9, 38.6, 43.3, 45.0 (C-13), 48.9, 55.2 (3-OCH<sub>3</sub>), 55.6 (C-16a), 83.0 (C-17), 111.5 (C-2), 113.8  
14 (C-4), 126.3 (C-1), 132.4 (C-10), 137.9 (C-5), 157.5 (C-3).  
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24 2.2.4. 3-Methoxy-16 $\alpha$ -azidomethylestra-1,3,5(10)-trien-17 $\alpha$ -ol (**16**)  
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26 Compound **8b** (470 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
27 crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3 v/v) to yield pure **16**  
28 (283 mg, 86%). Mp 118–120 °C; *R<sub>f</sub>* = 0.65 (ss A); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = + 34 (*c* 1 in CHCl<sub>3</sub>). (Found C, 70.55;  
29 H, 7.78. C<sub>20</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub> (341.45) requires C, 70.35; H, 7.97%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.80 (s,  
30 3H, 18-H<sub>3</sub>), 2.87 (m, 2H, 6-H<sub>2</sub>), 3.35 (dd, 1H, *J* = 12.0 Hz, *J* = 6.0 Hz, 16a-H<sub>2</sub>), 3.53 (dd, 1H, *J* =  
31 12.0 Hz, *J* = 9.5 Hz, 16a-H<sub>2</sub>), 3.78 (s, 3H, 3-OCH<sub>3</sub>), 3.84 (d, 1H, *J* = 6.0 Hz, 17-H), 6.63 (d, 1H, *J* =  
32 2.5 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR ( $\delta$ , ppm,  
33 CDCl<sub>3</sub>): 17.3 (C-18), 26.1, 28.0, 29.2, 31.3, 39.1, 40.5, 43.6, 46.4 (C-13), 47.0, 52.4 (C-16a),  
34 55.2 (3-OCH<sub>3</sub>), 79.9 (C-17), 111.6 (C-2), 114.0 (C-4), 126.3 (C-1), 132.7 (C-10), 137.9 (C-5),  
35 157.6 (C-3).  
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46 2.2.5. 3-Benzoyloxy-16 $\beta$ -azidomethylestra-1,3,5(10)-trien-17 $\beta$ -ol (**17**)  
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48 Compound **9c** (455 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
49 crude product was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:1 v/v) to yield pure **17**  
50 (250 mg, 59%). Mp 115–117 °C; *R<sub>f</sub>* = 0.45 (ss A). (Found C, 74.55; H, 7.64. C<sub>26</sub>H<sub>31</sub>N<sub>3</sub>O<sub>2</sub>  
51 (417.54) requires C, 74.79; H, 7.48%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.82 (s, 3H, 18-H<sub>3</sub>), 2.86 (m,  
52 2H, 6-H<sub>2</sub>), 3.33 (dd, 1H, *J* = 12.0 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 3.60 (dd, 1H, *J* = 12.5 Hz, *J* = 7.5 Hz,  
53 16a-H<sub>2</sub>), 3.87 (d, 1H, *J* = 9.5 Hz, 17-H), 5.04 (s, 2H, Bn-H<sub>2</sub>), 6.73 (s, 1H, 4-H), 6.79 (d, 1H, *J* =  
54 8.0 Hz, *J* = 2.0 Hz, 2-H), 7.21 (d, 1H, *J* = 8.0 Hz, 1-H), 7.32 (t, 1H, *J* = 7.5 Hz, 4'-H), 7.39 (t, 2H,  
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4  $J = 7.5$  Hz, 3'-H and 5'-H), 7.44 (d, 2H,  $J = 7.5$  Hz, 2'-H and 6'-H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ):  
5 12.2 (C-18), 26.2, 27.5, 29.7, 30.3, 37.6, 38.1, 40.1, 43.9, 44.2 (C-13), 48.8 (C-16), 53.3 (C-16a),  
6 69.9 (Bn- $\text{CH}_2$ ), 81.5 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.3 (C-2' and C-6'), 127.8  
7 (C-4'), 128.5 (C-3' and C-5'), 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.8 (C-3).  
8  
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#### 10 11 12 13 2.2.6. 3-Benzoyloxy-16 $\alpha$ -azidomethylestra-1,3,5(10)-trien-17 $\beta$ -ol (**18**)

14  
15 Compound **10c** (455 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
16 crude product was chromatographed on silica gel with  $\text{CH}_2\text{Cl}_2$ /hexane (3:1 v/v) to yield pure **18**  
17 (254 mg, 61%). Mp 75–77 °C;  $R_f = 0.40$  (ss A). (Found C, 74.87; H, 7.32.  $\text{C}_{26}\text{H}_{31}\text{N}_3\text{O}_2$  (417.54)  
18 requires C, 74.79; H, 7.48%).  $^1\text{H}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 0.84 (s, 3H, 18- $\text{H}_3$ ), 2.85 (m, 2H, 6- $\text{H}_2$ ),  
19 3.44 (t, 1H,  $J = 8.0$  Hz, 17-H), 3.48 (m, 2H, 16a- $\text{H}_2$ ), 5.04 (s, 2H, Bn- $\text{H}_2$ ), 6.73 (s, 1H, 4-H), 6.79  
20 (d, 1H,  $J = 8.5$  Hz, 2-H), 7.21 (d, 1H,  $J = 8.5$  Hz, 1-H), 7.32 (t, 1H,  $J = 7.0$  Hz, 4'-H), 7.39 (t, 2H,  
21  $J = 7.0$  Hz, 3'- and 5'-H), 7.44 (d, 2H,  $J = 7.0$  Hz, 2'- and 6'-H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 11.8  
22 (C-18), 26.1, 27.2, 27.9, 29.7, 36.6, 38.5, 43.6, 43.9, 44.2 (C-13), 48.6 (C-16), 55.6 (C-16a), 69.9  
23 (Bn- $\text{CH}_2$ ), 85.1 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'),  
24 128.5 (C-3' and -5'), 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.8 (C-3).  
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#### 35 2.2.7. 3-Benzoyloxy-16 $\beta$ -azidomethyl-estra-1,3,5(10)-trien-17 $\alpha$ -ol (**19**)

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37 Copound **11c** (455 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The crude  
38 product was chromatographed on silica gel with  $\text{CH}_2\text{Cl}_2$ /hexane (3:1 v/v) to yield pure **19** (23.  
39 mg, 40%). Mp. 134-136 °C.  $R_f = 0.38$  (ss A). (Found C, 74.92; H, 7.37.  $\text{C}_{26}\text{H}_{31}\text{N}_3\text{O}_2$  (417.54)  
40 requires C, 74.79; H, 7.48%).  $^1\text{H}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 0.84 (s, 3H, 18- $\text{H}_3$ ), 2.85 (m, 2H, 6- $\text{H}_2$ ),  
41 3.43 (d, 2H,  $J = 8.0$  Hz, 17-H), 3.48 (t, 2H,  $J = 6.5$  Hz, 16a- $\text{H}_2$ ), 5.04 (s, 2H, Bn- $\text{H}_2$ ), 6.73 (s, 1H,  
42 4-H), 6.79 (d, 1H,  $J = 8.0$  Hz, 2-H), 7.22 (d, 1H,  $J = 8.0$  Hz 1-H), 7.33 (d, 1H,  $J = 7.0$  Hz, 4'-H),  
43 7.39 (t, 2H,  $J = 7.0$  Hz, 3'- and 5'-H), 7.44 (d, 2H,  $J = 7.0$  Hz, 2'- and 6'-H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm,  
44  $\text{CDCl}_3$ ): 11.8 (C-18), 26.1, 27.2, 28.0, 29.7, 36.6, 38.4, 43.5, 43.9, 44.1 (C-13), 48.5 (C-16), 55.6  
45 (C-16a), 69.9 (Bn- $\text{CH}_2$ ), 85.1 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'),  
46 127.8 (C-4'), 128.5 (C-3' and -5'), 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.7 (C-3).  
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#### 57 2.2.8. 3-Benzoyloxy-16 $\alpha$ -azidomethyl-estra-1,3,5(10)-trien-17 $\alpha$ -ol (**20**)

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4 Compound **12c** (455 mg, 1 mmol) was used for the synthesis as described in Section 2.2. The  
5  
6 crude was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:1 v/v) to yield pure **20** (330 mg,  
7  
8 79%). Mp 90–92 °C. *R*<sub>f</sub> = 0.45 (ss A). (Found C, 74.68; H, 7.55. C<sub>26</sub>H<sub>31</sub>N<sub>3</sub>O<sub>2</sub> (417.54) requires C,  
9  
10 74.79; H, 7.48%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.71 (m, 2H, 6-H<sub>2</sub>), 3.35 (dd,  
11  
12 1H, *J* = 12.0 Hz, *J* = 6.5 Hz, 16a-H<sub>2</sub>), 3.52 (dd, 1H, *J* = 12.0 Hz, *J* = 6.5 Hz, 16a-H<sub>2</sub>), 3.84 (d, 1H,  
13  
14 *J* = 5.0 Hz, 17-H), 5.04 (s, 2H, Bn-H<sub>2</sub>), 6.73 (s, 1H, 4-H), 6.79 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-  
15  
16 H), 7.22 (d, 1H, *J* = 8.5 Hz, 1-H), 7.33 (t, 1H, *J* = 7.5 Hz, 4'-H), 7.39 (t, 2H, *J* = 7.5 Hz, 3'- and  
17  
18 5'-H), 7.44 (d, 2H, *J* = 7.5 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.2 (C-18), 26.0, 27.9,  
19  
20 29.0, 29.7, 31.2, 38.9, 40.4, 43.5, 46.3 (C-13), 46.8 (C-16), 52.2 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 79.7 (C-  
21  
22 17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -  
23  
24 5'), 132.8 (C-10), 137.3 (C-1'), 138.0 (C-5), 156.7 (C-3).

### 26 27 2.3. General procedure for the synthesis of triazoles (**21a–e**, **22a–e**, **23a–e**, **24a–e**, **25a–e**, **26a–e**, 28 29 **27a–e**, and **28a–e**)

30 3-Methoxy-16-azidomethylestra-1,3,5(10)-trien-17-ol isomers (**13–16**) (342 mg, 1 mmol) or 3-  
31  
32 benzyloxy-16-azidomethylestra-1,3,5(10)-trien-17-ol isomers (**17–20**) 418 mg, 1 mmol) were  
33  
34 dissolved in CH<sub>2</sub>Cl<sub>2</sub> (20 ml), then CuI (19 mg, 0.10 mmol), Et<sub>3</sub>N (0.2 ml, 2 mmol) and the  
35  
36 appropriate terminal alkynes (2 mmol) were added. The mixtures were stirred under reflux for 24  
37  
38 h, then diluted with water (30 ml) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 30 ml). The combined organic  
39  
40 phases were dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated *in vacuo*. The crude products were purified by  
41  
42 flash chromatography using CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate in different ratios.

#### 44 45 2.3.1. 3-Methoxy-16β-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β- 46 47 ol (**21a**)

48 Compound **13** (342 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
49  
50 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
51  
52 CH<sub>2</sub>Cl<sub>2</sub>/hexane (3:1 v/v) to yield pure **21a** (210 mg, 51%) as a white solid. Mp: 189–191 °C; *R*<sub>f</sub> =  
53  
54 0.44 (ss B). (Found C, 73.84; H, 7.98. C<sub>25</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (407.55) requires C, 73.68; H, 8.16%). <sup>1</sup>H  
55  
56 NMR (δ, ppm, CDCl<sub>3</sub>): 0.80 (s, 3H, 18-H<sub>3</sub>), 0.83 (s, 2H, cyclopropyl-H<sub>2</sub>), 0.94 (s, 2H,  
57  
58 cyclopropyl-H<sub>2</sub>), 2.72 (d, 1H, *J* = 7.0 Hz, 1''-H), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 3.93  
59  
60 (d, 1H, *J* = 9.5 Hz, 17-H), 4.21 (dd, 1H, *J* = 13.0 Hz, *J* = 6.0 Hz, 16a-H<sub>2</sub>), 4.62 (t, 1H, *J* = 8.0 Hz,  
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4 16a-H<sub>2</sub>), 6.62 (s, 1H, 4-H), 6.71 (d, 1H, *J* = 8.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz, 1-H), 7.29 (s,  
5 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 6.7 (C-1''), 7.68 (C-2'' and -3''), 12.3 (C-18), 26.2, 27.4,  
6 29.7, 30.8, 37.5, 38.0, 41.4, 43.8, 44.3 (C-16a), 48.7, 51.7 (C-13), 55.2 (3-OCH<sub>3</sub>), 80.7 (C-17),  
7 111.5 (C-2), 113.8 (C-4), 126.3 (C-1), 132.4 (C-10), 137.8 (C-5), 157.5 (C-3).  
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13 2.3.2. *3-Methoxy-16β-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β-*  
14 *ol (21b)*  
15

16 Compound **13** (342 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
17 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
18 CH<sub>2</sub>Cl<sub>2</sub> to yield pure **21b** (370 mg, 85%) as a white solid. Mp: 191–192 °C; *R*<sub>f</sub> = 0.46 (ss B).  
19 (Found C, 74.62; H, 8.42. C<sub>27</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (435.60) requires C, 74.45; H, 8.56%). <sup>1</sup>H NMR (δ, ppm,  
20 CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.19 (s, 1H, 1''-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 3.94  
21 (d, 1H, *J* = 9.5 Hz, 17-H), 4.24 (d, 1H, *J* = 8.0 Hz, 16a-H<sub>2</sub>), 4.65 (s, 1H, 16a-H<sub>2</sub>), 6.62 (s, 1H, 4-  
22 H), 6.71 (d, 1H, *J* = 8.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz, 1-H), 7.34 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ,  
23 ppm, CDCl<sub>3</sub>): 12.3 (C-18), 25.1 (C-3'' and -4''), 26.2, 27.4, 29.7 (C-2'' and 5''), 30.8, 33.2, 36.7,  
24 37.5, 38.0, 42.4 (C-16a), 43.8, 44.3 (C-13), 48.7, 51.8, 55.2 (3-OCH<sub>3</sub>), 62.1 (C-16), 80.7 (C-17),  
25 111.5 (C-2), 113.7 (C-4), 126.3 (C-1), 132.4 (C-10), 137.8 (C-5), 157.4 (C-3).  
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37 2.3.3. *3-Methoxy-16β-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β-*  
38 *ol (21c)*  
39

40 Compound **13** (342 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
41 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
42 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **21c** (370 mg, 82%) as a white solid. Mp: 189–190  
43 °C; *R*<sub>f</sub> = 0.40 (ss B). (Found C, 74.92; H, 8.55. C<sub>28</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (449.63) requires C, 74.80; H, 8.74%).  
44 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 3.94  
45 (d, 1H, *J* = 9.5 Hz, 17-H), 4.24 (m, 1H, 16a-H<sub>2</sub>), 4.65 (m, 1H, 16a-H<sub>2</sub>), 6.62 (s, 1H, 4-H), 6.71 (d,  
46 1H, *J* = 8.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm,  
47 CDCl<sub>3</sub>): 12.3 (C-18), 26.0, 26.1 (C-2'' and -6''), 26.2, 27.4, 29.7, 30.8, 33.0, 37.5, 38.0, 41.4 (C-  
48 1''), 43.8, 44.3 (C-13), 48.3, 55.2 (3-OCH<sub>3</sub>), 62.1, 80.7 (C-17), 111.5 (C-2), 113.7 (C-4), 126.3  
49 (C-1), 132.4 (C-10), 137.8 (C-5), 157.4 (C-3).  
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4 2.3.4. 3-Methoxy-16 $\beta$ -(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17 $\beta$ -ol  
5  
6 (21d)

7  
8 Compound **13** (342 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
9  
10 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
11 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **21d** (368 mg, 83%) as a white solid. Mp: 232–234  
12 °C; *R*<sub>f</sub> = 0.35 (ss B). (Found C, 75.98; H, 7.36. C<sub>28</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (443.58) requires C, 75.81; H, 7.50%).  
13 <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.73 (m, 2H, 6-H<sub>2</sub>), 3.68 (s, 3H, 3-OCH<sub>3</sub>), 3.79  
14 (d, 1H, *J* = 10.0 Hz, 17-H), 4.20 (t, 1H, *J* = 13.5 Hz, 16a-H<sub>2</sub>), 4.63 (dd, 1H, *J* = 13.5 Hz, *J* = 4.5  
15 Hz, 16a-H<sub>2</sub>), 6.59 (s, 1H, 4-H), 6.67 (d, 1H, *J* = 8.5 Hz, 2-H), 7.16 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32  
16 (t, 1H, *J* = 7.5 Hz, 4''-H), 7.44 (t, 2H, *J* = 7.5 Hz, 3''- and 5''-H), 7.85 (d, 2H, *J* = 7.5 Hz, 2''- and  
17 6''-H), 8.60 (s, 1H, 5'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 12.4 (C-18), 25.8, 26.9, 29.1, 30.0, 36.9,  
18 37.8, 40.4, 43.3, 43.7 (C-13), 47.8, 52.3 (C-16a), 54.8 (3-OCH<sub>3</sub>), 79.5 (C-17), 111.4 (C-2), 113.3  
19 (C-4), 121.5 (C-5'), 124.5 (C-2'' and -6''), 126.0 (C-1), 127.6 (C-4''), 127.8 (C-3'' and -5''), 130.9  
20 (C-1''), 132.0 (C-10), 137.3 (C-5), 146.0 (C-4'), 156.9 (C-3).  
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32 2.3.5. 3-Methoxy-16 $\beta$ -(4'-nitro-benzoyloxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-  
33  
34 1,3,5(10)-trien-17 $\beta$ -ol (21e)

35  
36 Compound **13** (342 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 410 mg) were used for  
37 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
38 with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **21e** (475 mg, 86%) as a yellow solid. Mp:  
39 134–135.5 °C; *R*<sub>f</sub> = 30 (ss B). (Found C, 66.12; H, 6.08. C<sub>30</sub>H<sub>34</sub>N<sub>4</sub>O<sub>6</sub> (546.61) requires C, 65.92;  
40 H, 6.27%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.73 (s, 3H, 18-H<sub>3</sub>), 2.70 (m, 2H, 6-H<sub>2</sub>), 3.66 (s, 3H, 3-  
41 OCH<sub>3</sub>), 4.18 (dd, 1H, *J* = 13.5 Hz, *J* = 11.5 Hz, 16a-H<sub>2</sub>), 4.58 (dd, 1H, *J* = 13.5 Hz, *J* = 4.5 Hz,  
42 16a-H<sub>2</sub>), 5.02 (d, 1H, *J* = 4.5 Hz, 17-H), 5.44 (s, 2H, 4'-H<sub>2</sub>), 6.55 (d, 1H, *J* = 1.5 Hz, 4-H), 6.63  
43 (dd, 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.12 (d, 1H, *J* = 8.5 Hz, 1-H), 8.16 (d, 2H, *J* = 8.5 Hz, 3''-  
44 and 5''-H), 8.31 (t, 3H, *J* = 8.5 Hz, 2''- and 6''-H, 5'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 12.3 (C-18),  
45 25.8, 26.9, 29.1, 30.0, 36.9, 37.8, 40.4, 43.3, 43.7 (C-13), 47.8, 52.2 (C-16a), 54.7 (3-OCH<sub>3</sub>),  
46 58.7 (4'-CH<sub>2</sub>), 79.5 (C-17), 111.3 (C-2), 113.3 (C-4), 123.8 (C-2'' and -6''), 125.1 (C-5'), 126.0  
47 (C-1), 130.6 (C-3'' and -5''), 131.9 (C-10), 134.7 (C-1''), 137.2 (C-5), 141.0 (C-4''), 150.2 (C-4'),  
48 156.9 (C-3), 163.9 (C=O).  
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4 2.3.6. 3-Methoxy-16 $\beta$ -(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
5  
6 17 $\beta$ -ol (**21f**)

7  
8 Compound **13** (274 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
9 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
10 and the precipitate separating out was filtered off and recrystallized from a mixture of ethyl  
11 acetate/hexane to afford **21f** (171 mg, 86%) as a white crystalline material. Mp: 194–195 °C; *R*<sub>f</sub>=  
12 0.25 (ss B). (Found C, 69.23; H, 8.04. C<sub>23</sub>H<sub>31</sub>N<sub>3</sub>O<sub>3</sub> (397.51) requires C, 69.49; H, 7.86%). <sup>1</sup>H  
13 NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>): 0.76 (s, 3H, 18-H<sub>3</sub>), 2.71 (m, 2H, 6-H<sub>2</sub>), 3.68 (s, 3H, 3-OCH<sub>3</sub>), 3.76  
14 (d, 1H, *J* = 5.5 Hz, 17-H), 4.14 (t, 1H, *J* = 12.5 Hz, 16a-H<sub>2</sub>), 4.49 (m, 3H, 4'-H<sub>2</sub> and 16a-H<sub>2</sub>),  
15 5.03 (d, 1H, *J* = 3.5 Hz, 17-OH), 5.15 (brs, 1H, CH<sub>2</sub>-OH), 6.59 (s, 1H, 4-H), 6.66 (d, 1H, *J* = 8.5  
16 Hz, 2-H), 7.16 (d, 1H, *J* = 8.5 Hz, 1-H), 7.99 (s, 1H, 5'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>): 12.4  
17 (C-18), 25.9, 26.9, 29.2, 30.0, 36.9, 37.9, 40.5, 43.4, 43.8 (C-13), 47.8, 52.0 (C-16a), 54.8 (3-  
18 OCH<sub>3</sub>), 55.0 (4'-CH<sub>2</sub>), 79.5 (C-17), 111.4 (C-2), 113.4 (C-4), 122.8 (C-5'), 126.1 (C-1), 132.0  
19 (C-10), 137.3 (C-5), 147.6 (C-4'), 157.0 (C-3).  
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32 2.3.7. 3-Methoxy-16a-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17 $\beta$ -  
33  
34 ol (**22a**)

35  
36 Compound **14** (342 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
37 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
38 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **22a** (261 mg, 64%) as a white solid. Mp: 67–69 °C;  
39 *R*<sub>f</sub>= 0.35 (ss B). (Found C, 73.55; H, 7.98. C<sub>25</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (407.55) requires C, 73.68; H, 8.16%). <sup>1</sup>H  
40 NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.82 (m, 5H, 18-H<sub>3</sub> and cyclopropyl-H<sub>2</sub>), 0.95 (m, 2H, cyclopropyl-H<sub>2</sub>),  
41 2.83 (m, 2H, 6-H<sub>2</sub>), 3.53 (d, 1H, *J* = 7.5 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.35 (t, 1H, *J* = 7.5 Hz,  
42 16a-H<sub>2</sub>), 4.44 (dd, 1H, *J* = 13.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.0 Hz, 4-H), 6.70 (dd,  
43 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.18 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 6.7  
44 (C-1''), 7.7 (C-2'' and -3''), 11.8 (C-18), 26.1, 27.2, 28.2, 29.7, 36.6, 38.4, 43.9, 44.3, 44.3 (C-  
45 16a), 48.3, 54.5 (C-13), 62.1 (3-OCH<sub>3</sub>), 85.1 (C-17), 111.5 (C-2), 113.8 (C-4), 126.2 (C-1), 132.3  
46 (C-10), 137.8 (C-5), 157.4 (C-3).  
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58 2.3.8. 3-Methoxy-16a-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17 $\beta$ -  
59  
60 ol (**22b**)  
61

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4 Compound **14** (342 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
5  
6 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
7  
8 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **22b** (290 mg, 66%) as a white solid. Mp: 163–165  
9  
10 °C; *R*<sub>f</sub> = 0.32 (ss B). (Found C, 74.63; H, 8.41. C<sub>27</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (435.60) requires C, 74.45; H, 8.56%).  
11  
12 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.83 (s, 3H, 18-H<sub>3</sub>), 1.68 (s, 4H, 3''- and 4''-H<sub>2</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>),  
13  
14 3.19 (m, 1H, 1''-H), 3.56 (d, 1H, *J* = 7.0 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.43 (m, 2H, 16a-H<sub>2</sub>),  
15  
16 6.62 (s, 1H, 4-H), 6.70 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H), 7.35 (s, 1H, 5'-H).  
17  
18 <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 11.9 (C-18), 25.1 (C-3'' and -4''), 26.1, 27.2, 28.3, 29.7 (C-2'' and -  
19  
20 5''), 33.2, 36.6, 38.4, 43.9, 44.2, 44.3 (C-13), 48.4, 55.2 (3-OCH<sub>3</sub>), 62.1 (C-16a), 85.3 (C-17),  
21  
22 111.5 (C-2), 113.8 (C-4), 126.3 (C-1), 132.3 (C-10), 137.8 (C-5), 157.5 (C-3).  
23

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25 2.3.9. *3-Methoxy-16a-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β-*  
26  
27 *ol (22c)*

28  
29 Compound **14** (342 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
30  
31 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
32  
33 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **22c** (345 mg, 76%) as a white solid. Mp: 80–82 °C;  
34  
35 *R*<sub>f</sub> = 0.34 (ss B). (Found 74.96; H, 8.54. C<sub>28</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (449.63) requires C, 74.80; H, 8.74%). <sup>1</sup>H  
36  
37 NMR (δ, ppm, CDCl<sub>3</sub>): 0.83 (s, 3H, 18-H<sub>3</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.55 (s, 1H, 17-H), 3.77 (s, 3H,  
38  
39 3-OCH<sub>3</sub>), 4.46 (s, 2H, 16a-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.0 Hz, 4-H), 6.70 (dd, 1H, *J* = 8.5 Hz, *J* = 2.0  
40  
41 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 11.9 (C-18), 26.0 and 26.1  
42  
43 (C-2'' and -6'', C-3'' and -5''), 27.2, 28.3, 29.7, 36.6, 38.4, 43.9, 44.3 (C-13), 48.4, 55.2 (3-OCH<sub>3</sub>),  
44  
45 62.1 (C-1''), 62.1 (C-16a), 85.2 (C-17), 111.5 (C-2), 113.8 (C-4), 126.2 (C-1), 132.3 (C-10),  
46  
47 137.8 (C-5), 157.4 (C-3).  
48

49  
50 2.3.10. *3-Methoxy-16a-(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β-*  
51  
52 *ol (22d)*

53  
54 Compound **14** (342 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
55  
56 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel ethyl  
57  
58 acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **22d** (368 mg, 82%) as a white solid. Mp: 204–205 °C;  
59  
60 *R*<sub>f</sub> = 0.38 (ss B). (Found C, 75.63; H, 7.72. C<sub>28</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (443.58) requires C, 75.81; H, 7.50%). <sup>1</sup>H  
61  
62 NMR (δ, ppm, DMSO-d<sub>6</sub>): 0.73 (s, 3H, 18-H<sub>3</sub>), 2.73 (m, 2H, 6-H<sub>2</sub>), 3.67 (s, 3H, 3-OCH<sub>3</sub>), 4.36 (t,  
63  
64  
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4 1H,  $J = 13.5$  Hz, 16a-H<sub>2</sub>), 4.54 (dd, 1H,  $J = 13.5$  Hz,  $J = 4.0$  Hz, 16a-H<sub>2</sub>), 4.91 (d, 1H,  $J = 4.0$  Hz,  
5 17-H), 6.58 (s, 1H, 4-H), 6.67 (d, 1H,  $J = 8.5$  Hz, 2-H), 7.15 (d, 1H,  $J = 8.5$  Hz, 1-H), 7.32 (t, 1H,  
6  $J = 7.0$  Hz, 4''-H), 7.44 (t, 2H,  $J = 7.0$  Hz, 3''- and 5''-H), 7.86 (d, 2H,  $J = 7.0$  Hz, 2''- and 6''-H),  
7  
8 8.61 (s, 1H, 5'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>): 11.8 (C-18), 25.8, 26.7, 27.3, 29.1, 36.3, 38.1,  
9 43.4, 43.5, 43.8, 47.5, 53.5 (C-13), 54.8 (3-OCH<sub>3</sub>), 83.1 (C-17), 111.4 (C-2), 113.3 (C-4), 121.4  
10 (C-5'), 125.0 (C-2'' and -6''), 126.0 (C-1), 127.6 (C-4''), 128.8 (C-3'' and -5''), 130.8 (C-1''),  
11 132.0 (C-10), 137.3 (C-5), 146.1 (C-4'), 156.9 (C-3).  
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19 *2.3.11.3-Methoxy-16a-[4'(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-*  
20 *1,3,5(10)-trien-17 $\beta$ -ol (22e)*  
21

22 Compound **14** (342 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 410 mg) were used for  
23 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
24 with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **22e** (445 mg, 81%) as a yellow solid. Mp:  
25 86–88 °C;  $R_f = 0.28$  (ss B). (Found C, 66.08; H, 6.43. C<sub>30</sub>H<sub>34</sub>N<sub>4</sub>O<sub>6</sub> (546.61) requires C, 65.92; H,  
26 6.27%). <sup>1</sup>H NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>): 0.69 (s, 3H, 18-H<sub>3</sub>), 2.68 (m, 2H, 6-H<sub>2</sub>), 3.57 (s, 3H, 3-  
27 OCH<sub>3</sub>), 4.38 (dd, 1H,  $J = 13.5$  Hz,  $J = 9.0$  Hz, 16a-H<sub>2</sub>), 4.52 (dd, 1H,  $J = 13.5$  Hz,  $J = 4.5$  Hz,  
28 16a-H<sub>2</sub>), 4.86 (d, 1H,  $J = 4.5$  Hz, 17-H), 5.46 (s, 2H, 4'-H<sub>2</sub>), 6.55 (d, 1H,  $J = 1.5$  Hz, 4-H), 6.63  
29 (dd, 1H,  $J = 8.5$  Hz, 2-H), 7.10 (d, 1H,  $J = 8.5$  Hz, 1-H), 8.16 (d, 2H,  $J = 8.5$  Hz, 3''- and 5''-H),  
30 8.28 (d, 2H,  $J = 8.5$  Hz, 2''- and 6''-H), 8.31 (s, 1H, 5'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>): 11.7  
31 (C-18), 25.7, 26.6, 27.1, 29.0, 36.4, 38.0, 43.3, 43.4 (C-13), 43.7, 47.7, 53.1 (C-16a), 54.7 (3-  
32 OCH<sub>3</sub>), 58.6 (4''-CH<sub>2</sub>), 82.8 (C-17), 111.3 (C-2), 113.3 (C-4), 123.8 (C-2'' and -6''), 125.2 (C-5'),  
33 125.9 (C-1), 130.6 (C-3'' and -5''), 131.8 (C-10), 134.7 (C-1'), 137.2 (C-5), 141.1 (C-4''), 150.2  
34 (C-4'), 156.9 (C-3), 163.9 (C=O).  
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48 *2.3.12. 3-Methoxy-16a-(4'-hydroxymethyl-1'H-1',2'3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
49 *17 $\beta$ -ol (22f)*  
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53 Compound **22e** (274 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
54 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
55 and the precipitate separating out was filtered off and recrystallized from a mixture of ethyl  
56 acetate/hexane to afford **22f** (175 mg, 88%) as a white crystalline product. Mp: 98–100 °C;  $R_f =$   
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4 0.28 (ss B). (Found C, 69.74; H, 7.72. C<sub>23</sub>H<sub>31</sub>N<sub>3</sub>O<sub>3</sub> (397.51) requires C, 69.49; H, 7.86%). <sup>1</sup>H  
5 NMR (δ, ppm, CDCl<sub>3</sub>): 0.81 (s, 3H, 18-H<sub>3</sub>), 2.82 (m, 2H, 6-H<sub>2</sub>), 3.50 (d, 1H, *J* = 7.0 Hz, 17-H),  
6 3.76 (s, 3H, 3-OCH<sub>3</sub>), 4.42 (d, 2H, *J* = 7.0 Hz, 16a-H<sub>2</sub>), 4.71 (s, 2H, 4'-H<sub>2</sub>), 6.61 (s, 1H, 4-H),  
7 6.69 (d, 1H, *J* = 8.5 Hz, 2-H), 7.17 (d, 1H, *J* = 8.5 Hz, 1-H), 7.68 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ,  
8 ppm, CDCl<sub>3</sub>): 11.9 (C-18), 26.1, 27.2, 28.2, 29.6, 36.5, 38.4, 43.8, 44.0, 44.4 (C-13), 48.2, 54.6  
9 (C-16a), 55.2 (3-OCH<sub>3</sub>), 56.0 (4'-CH<sub>2</sub>), 85.1 (C-17), 111.5 (C-2), 113.8 (C-4), 126.3 (C-1), 132.3  
10 (C-10), 137.8 (C-5), 157.4 (C-3).

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19 *2.3.13. 3-Methoxy-16a-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
20 *17β-ol (23a)*

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22 Compound **15** (342 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
23 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
24 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **23a** (261 mg, 64%) as a white solid. Mp: 67–69 °C;  
25 *R*<sub>f</sub> = 0.32 (ss B). (Found C, 73.85; H, 8.32. C<sub>25</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (407.55) requires C, 73.68; H, 8.16%). <sup>1</sup>H  
26 NMR (δ, ppm, CDCl<sub>3</sub>): 0.82 (m, 5H, 18-H<sub>3</sub> and cyclopropyl-H<sub>2</sub>), 0.95 (m, 2H, cyclopropyl-H<sub>2</sub>),  
27 2.83 (m, 2H, 6-H<sub>2</sub>), 3.53 (d, 1H, *J* = 7.5 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.35 (t, 1H, *J* = 7.5 Hz,  
28 16a-H<sub>2</sub>), 4.44 (dd, 1H, *J* = 13.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.0 Hz, 4-H), 6.70 (dd,  
29 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.18 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 6.7  
30 (C-1''), 7.7 (C-2'' and -3''), 11.8 (C-18), 26.1, 27.2, 28.2, 29.7, 36.6, 38.4, 43.9, 44.3, 44.3 (C-  
31 16a), 48.3, 54.5 (C-13), 62.1 (3-OCH<sub>3</sub>), 85.1 (C-17), 111.5 (C-2), 113.8 (C-4), 126.2 (C-1), 132.3  
32 (C-10), 137.8 (C-5), 157.4 (C-3).

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44 *2.3.14. 3-Methoxy-16β-(4'-cyclopentyl-1'H-1',2',3'-triazol-1-yl)methylestra-1,3,5(10)-trien-17a-*  
45 *ol (23b)*

46  
47 Compound **15** (342 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
48 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
49 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **23b** (380 mg, 87%) as yellow crystalline material.  
50 Mp: 67–68 °C; *R*<sub>f</sub> = 0.36 (ss B). (Found C, 74.28; H, 8.47. C<sub>27</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (435.60) requires C,  
51 74.45; H, 8.56%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.68 (s,  
52 1H, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.44 (d, 2H, *J* = 15.0 Hz, 16a-H<sub>2</sub>), 6.62 (s, 1H, 4-H), 6.70 (d,  
53 1H, *J* = 8.5 Hz, 2-H), 7.20 (t, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.9 (C-18), 25.1  
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(C-3'' and -4''), 25.9, 26.1, 27.2, 28.0, 29.7, 30.4, 31.8, 36.6 (C-16a), 38.5, 43.3, 43.8, 45.1 (C-13), 48.9, 55.2 (3-OCH<sub>3</sub>), 62.1 (C-1''), 82.6 (C-17), 111.5 (C-2), 113.7 (C-4), 113.8 (C-5'), 126.2 (C-1), 132.1 (C-10), 137.8 (C-5), 137.8 (C-4'), 157.4 (C-3).

2.3.15. *3-Methoxy-16β-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methyestra-1,3,5(10)-trien-17a-ol (23c)*

Compound **15** (342, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **23c** (306 mg, 68%) as a white solid. Mp: 90-92 °C; *R*<sub>f</sub> = 0.37 (ss B). (Found C, 74.95; H, 8.83. C<sub>28</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (449.63) requires C, 74.80; H, 8.74%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.67 (d, 1H, *J* = 1.0 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.43 (m, 1H, 16a-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.5 Hz, 4-H), 6.71 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.20 (t, 1H, *J* = 8.5 Hz, 1-H), 7.35 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.9 (C-18), 25.9, 26.0, 26.1 (C-2'' and -6''), 28.0, 29.7, 30.4, 31.8, 33.0, 35.2 (C-1''), 36.6, 38.5, 43.3, 45.1 (C-13), 48.9, 49.1, 54.3 (C-16a), 55.2 (3-OCH<sub>3</sub>), 82.6 (C-1), 132.4 (C-10), 137.8 (C-5), 153.7 (C-4'), 157.7 (C-3).

2.3.16. *3-Methoxy-16β-(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methy-estra-1,3,5(10)-trien-17a-ol (23d)*

Compound **15** (342 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (2.5:97.5 v/v) to yield pure **23d** (299 mg, 67%) as white crystals. Mp: 173–174 °C; *R*<sub>f</sub> = 0.34 (ss B). (Found C 75.98; H, 7.33. C<sub>28</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (443.58) requires C, 75.81; H, 7.50%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.71 (d, 1H, *J* = 1.5 Hz, 17-H), 3.78 (s, 3H, 3-OCH<sub>3</sub>), 4.46 (dd, 1H, *J* = 13.5 Hz, *J* = 8.0 Hz, 16a-H<sub>2</sub>), 4.55 (dd, 1H, *J* = 13.5 Hz, *J* = 8.0 Hz, 16a-H<sub>2</sub>), 6.63 (d, 1H, *J* = 2.0 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.27 (t, 1H, *J* = 7.5 Hz, 4''-H), 7.42 (t, 2H, *J* = 7.5 Hz, 3''- and 5''-H), 7.83 (d, 2H, *J* = 7.5 Hz, 2''- and 6''-H), 7.87 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.9 (C-18), 25.9, 27.9, 29.7, 30.4, 31.8, 38.5, 43.3, 45.1, (C-13), 48.8, 49.1, 54.5 (C-16a), 55.2 (3-OCH<sub>3</sub>), 82.5 (C-17), 111.5 (C-2), 113.7 (C-4), 119.6 (C-5'), 125.7 (C-2'' and -6''),

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4 126.3 (C-1), 128.1 (C-4''), 128.8 (C-3'' and -5''), 130.5 (C-1''), 132.4 (C-10), 137.8 (C-5), 147.8  
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6 (C-4'), 157.4 (C-3).

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10 *2.3.17.3-Methoxy-16β-[4'(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl)methylestra-*  
11 *1,3,5(10)-trien-17a-ol (23e)*

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13 Compound **15** (342, 1 mmol) and propargyl 4-nitro benzoate (2 mmol, 410 mg) were used for the  
14  
15 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
16  
17 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **23e** (370 mg, 67%) as a yellow crystalline material.  
18  
19 Mp: 62–63 °C; *R*<sub>f</sub> = 0.38 (ss B). (Found C, 66.14; H, 6.42. C<sub>30</sub>H<sub>34</sub>N<sub>4</sub>O<sub>6</sub> (546.61) requires C,  
20  
21 65.92; H, 6.27%). <sup>1</sup>H NMR (δ, ppm, DMSO-d<sub>6</sub>): 0.65 (s, 3 H, 18-H<sub>3</sub>), 2.74 (m, 2H, 6-H<sub>2</sub>), 3.68 (s,  
22  
23 3H, 3-OCH<sub>3</sub>), 4.41 (dd, 1H, *J* = 13.0 Hz, *J* = 8.5 Hz, 16a-H<sub>2</sub>), 4.56 (dd, 1H, *J* = 13.0 Hz, *J* = 8.5  
24  
25 Hz, 16a-H<sub>2</sub>), 4.63 (d, 1H, *J* = 4.5 Hz, 17-H), 6.58 (s, 1H, 4-H), 6.66 (d, 1H, *J* = 8.5 Hz, 2-H), 7.16  
26  
27 (d, 1H, *J* = 8.5 Hz, 1-H), 8.19 (d, 2H, *J* = 8.5 Hz, 3''- and 5''-H), 8.34 (d, 2H, *J* = 8.5 Hz, 2''- and  
28  
29 6''-H). <sup>13</sup>C NMR (δ, ppm, DMSO-d<sub>6</sub>): 17.5 (C-18), 25.6, 27.5, 29.6, 31.8, 38.2, 43.0, 44.5, 47.9  
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31 (C-13), 48.2, 49.1, 53.6 (C-16a), 54.8 (3-OCH<sub>3</sub>), 58.7 (4'-CH<sub>2</sub>), 80.8 (C-17), 111.3 (C-2), 113.3  
32  
33 (C-4), 123.8 (C-1), 126.1 (C-5'), 130.6 (C-2'' and -6''), 131.9 (C-3'' and -5''), 133.0 (C-10), 134.7  
34  
35 (C-1''), 137.3 (C-5), 141.4 (C-4''), 150.2 (C-4'), 156.9 (C-3), 163.9 (C=O).

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37 *2.3.18. 3-Methoxy-16β-(4'-hydroxymethyl-1'H-1',2'3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
38 *17a-ol (23f)*

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40 Compound **23e** (274 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
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42 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
43  
44 and the precipitate separating out was filtered off, dissolved in dichloromethane and washed with  
45  
46 water. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated *in vacuo* to afford **23f** (183 mg,  
47  
48 92%) as oil. *R*<sub>f</sub> = 0.26 (ss B). (Found C, 69.28; H, 7.95. C<sub>23</sub>H<sub>31</sub>N<sub>3</sub>O<sub>3</sub> (397.51) requires C, 69.49;  
49  
50 H, 7.86%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.78 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.65 (s, 1H, 17-  
51  
52 H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.46 (m, 2H, 16a-H<sub>2</sub>), 4.78 (s, 2H, 4'-H<sub>2</sub>), 6.62 (d, 1H, *J* = 2.0 Hz, 4-  
53  
54 H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm,  
55  
56 CDCl<sub>3</sub>): 17.9 (C-18), 25.9, 27.9, 29.7, 30.3, 31.8, 38.5, 43.3, 45.2 (C-13), 48.8, 49.2, 54.6 (C-  
57  
58 16a), 55.2 (3-OCH<sub>3</sub>), 56.1 (4'-CH<sub>2</sub>), 82.1 (C-17), 111.5 (C-2), 113.7 (C-4), 123.5 (C-5'), 126.3  
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60 (C-1), 132.4 (C-10), 137.8 (C-5), 157.4 (C-3).

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6 2.3.19. 3-Methoxy-16a-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
7 17a-ol (**24a**)  
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10 Compound **16** (342 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
11 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
12 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (2.5:97.5 v/v) to yield pure **24a** (310 mg, 76%) as a white solid. Mp:  
13 165–166 °C; *R*<sub>f</sub> = 0.40 (ss B). (Found C, 73.85; H, 8.34. C<sub>25</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (407.55) requires C, 73.68;  
14 H, 8.16%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.74 (s, 3H, 18-H<sub>3</sub>), 0.85 and 0.96 (2 x m, 4H, 2''- and 3''-  
15 H<sub>2</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.63 (d, 1H, *J* = 5.0 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.28 (dd, 1H, *J* =  
16 13.0 Hz, *J* = 5.0 Hz, 16a-H<sub>2</sub>), 4.59 (t, 1H, *J* = 12.0 Hz, 16a-H<sub>2</sub>), 6.63 (d, 1H, *J* = 2.0 Hz, 4-H),  
17 6.71 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.22 (d, 1H, *J* = 8.5 Hz, 1-H). <sup>13</sup>C NMR (δ, ppm,  
18 CDCl<sub>3</sub>): 6.6 (C-1''), 7.7 and 7.8 (C-2'' and -3''), 17.1 (C-18), 26.0, 28.0, 28.9, 29.8, 31.2, 38.9,  
19 42.3, 46.3 (C-16a), 47.0, 50.5 (C-13), 55.2 (3-OCH<sub>3</sub>), 78.8 (C-17), 111.4 (C-2), 113.7 (C-4),  
20 120.6 (C-5'), 126.3 (C-1), 132.5 (C-10), 137.9 (C-5), 149.8 (C-4'), 157.4 (C-3).  
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32 2.3.20. 3-Methoxy-16a-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methyl-estra-1,3,5(10)-trien-  
33 17a-ol (**24b**)  
34

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36 Compound **16** (342 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
37 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
38 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **24b** (383 mg, 88%) as yellow crystalline product.  
39 Mp: 171–173 °C; *R*<sub>f</sub> = 0.42 (ss B). (Found C, 74.67; H, 8.72. C<sub>27</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (435.60) requires C,  
40 74.45; H, 8.56%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 1.25 (s, 8H, 2''-, 3''-, 4''- and  
41 5''-H<sub>2</sub>), 2.86 (m, 2H, 6-H<sub>2</sub>), 3.18 (m, 1H, 1''-H), 3.64 (d, 1H, *J* = 5.0 Hz, 17-H), 3.77 (s, 3H, 3-  
42 OCH<sub>3</sub>), 4.29 (dd, 1H, *J* = 13.5 Hz, *J* = 5.5 Hz, 16a-H<sub>2</sub>), 4.62 (dd, 1H, *J* = 13.5 Hz, *J* = 11.5 Hz,  
43 16a-H<sub>2</sub>), 6.63 (d, 1H, *J* = 2.0 Hz, 4-H), 6.71 (dd, 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.22 (d, 1H, *J*  
44 = 8.5 Hz, 1-H), 7.36 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.2 (C-18), 25.1 (C-3'' and -4''),  
45 26.0, 28.0, 29.0, 29.7, 29.9, 31.2, 33.2, 36.7, 38.9, 42.4, 43.5, 46.3 (C-13), 47.0 (C-1''), 50.5 (C-  
46 16a), 55.2 (3-OCH<sub>3</sub>), 78.8 (C-17), 111.4 (C-2), 113.8 (C-4), 120.6 (C-5'), 126.3 (C-1), 132.6 (C-  
47 10), 137.9 (C-5), 152.3 (C-4'), 157.4 (C-3).  
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4 2.3.21. 3-Methoxy-16a-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17a-  
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6 ol (**24c**)

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8 Compound **16** (342 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
9  
10 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
11 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **24c** (162 mg, 36%) as yellow crystals. Mp: 208–210  
12 °C; *R*<sub>f</sub> = 0.42 (ss B). (Found C, 74.97; H, 8.56. C<sub>28</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (449.63) requires C, 74.80; H, 8.74%).  
13  
14 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 1.26 (s, 8H, 2''-, 3''-, 5''- and 6''-H<sub>2</sub>), 2.88 (m, 2H,  
15 6-H<sub>2</sub>), 2.90 (m, 2H, 4''-H<sub>2</sub>), 3.64 (d, 1H, *J* = 5.0 Hz, 17-H), 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.29 (dd, 1H, *J*  
16 = 13.5 Hz, *J* = 5.0 Hz, 16a-H<sub>2</sub>), 4.62 (dd, 1H, *J* = 13.5 Hz, *J* = 11.0 Hz, 16a-H<sub>2</sub>), 6.63 (d, 1H, *J* =  
17 2.0 Hz, 4-H), 6.71 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.22 (d, 1H, *J* = 8.5 Hz, 1-H), 7.34 (s,  
18 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.2 (C-18), 26.0 and 26.1 (C-2'', -3'', -5'' and -6''), 28.0,  
19 29.0, 29.7, 29.8, 31.2, 33.0, 25.2, 38.9, 42.4, 43.5, 46.3 (C-13), 47.0 (C-1''), 50.5 (C-16a), 55.0  
20 (3-OCH<sub>3</sub>), 78.8 (C-17), 111.4 (C-2), 113.8 (C-4), 120.2 (C-5'), 126.3 (C-1), 132.6 (C-10), 137.9  
21 (C-5), 153.3 (C-4'), 157.4 (C-3).  
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32 2.3.22. 3-Methoxy-16a-(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17a-ol  
33  
34 (**24d**)

35  
36 Compound **16** (342 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
37  
38 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
39 CH<sub>2</sub>Cl<sub>2</sub> yield pure **24d** (394 mg, 89%) as white solid. Mp: 189.5–191 °C; *R*<sub>f</sub> = 0.46 (ss B). (Found  
40 C, 75.65; H, 7.67. C<sub>28</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (443.58) requires C, 75.81; H, 7.50%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>):  
41 0.75 (s, 3H, 18-H<sub>3</sub>), 2.86 (m, 2H, 6-H<sub>2</sub>), 3.68 (d, 1H, *J* = 5.0 Hz, 17-H), 3.78 (s, 3H, 3-OCH<sub>3</sub>),  
42 4.41 (dd, 1H, *J* = 13.5 Hz, *J* = 6.0 Hz, 16a-H<sub>2</sub>), 4.69 (dd, 1H, *J* = 14.5 Hz, *J* = 10.5 Hz, 16a-H<sub>2</sub>),  
43 6.64 (d, 1H, *J* = 2.0 Hz, 4-H), 6.72 (dd, 1H, *J* = 8.5 Hz, *J* = 2.5 Hz, 2-H), 7.22 (d, 1H, *J* = 8.5 Hz,  
44 1-H), 7.34 (t, 1H, *J* = 7.5 Hz, 4''-H), 7.43 (t, 2H, *J* = 7.5 Hz, 3''- and 5''-H), 7.83 (d, 2H, *J* = 7.5  
45 Hz, 2''- and 6''-H), 7.88 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.1 (C-18), 26.0, 28.0, 29.8,  
46 31.2, 38.9, 42.3, 43.5, 46.4 (C-13), 47.0, 50.7, 55.2 (3-OCH<sub>3</sub>), 78.8 (C-17), 111.5 (C-2), 113.8  
47 (C-4), 120.6 (C-5'), 125.6 (C-2'' and -6''), 126.3 (C-1), 128.1 (C-4''), 128.8 (C-3'' and -5''), 130.5  
48 (C-1'), 132.5 (C-10), 137.9 (C-5), 147.3 (C-4'), 157.4 (C-3).  
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4 2.3.23. 3-Methoxy-16a-[4'-(4'-nitrobenzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-  
5  
6 1,3,5(10)-trien-17a-ol (**24e**)

7  
8 Compound **16** (342, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used for the  
9  
10 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
11  
12 CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:3, v/v) to yield pure (344 mg, 63%) as yellow crystals. Mp: 64 °C; R<sub>f</sub>= 0.45 (ss  
13  
14 B). (Found, C, 66.14; H, 6.05. C<sub>30</sub>H<sub>34</sub>N<sub>4</sub>O<sub>6</sub> (546.61) requires C, 65.92; H, 6.27%). <sup>1</sup>H NMR (δ,  
15  
16 ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.66 (d, 1H, J = 4.5 Hz, 17-H), 3.77 (s,  
17  
18 3H, 3-OCH<sub>3</sub>), 4.40 (dd, 1H, J = 13.5 Hz, J = 5.5 Hz, 16a-H<sub>2</sub>), 4.66 (t, 1H, J = 13.5 Hz, 16a-H<sub>2</sub>),  
19  
20 5.53 (s, 2H, 4'-H<sub>2</sub>), 6.62 (t, 1H, J = 2.0 Hz, 4-H), 6.71 (dd, 1H, J = 8.5 Hz, J = 2.5 Hz, 2-H), 7.20  
21  
22 (d, 1H, J = 8.5 Hz, 1-H), 7.85 (s, 1H, 5'-H), 8.22 (d, 2H, J = 9.0 Hz, 3''- and 5''-H), 8.72 (d, 2H, J  
23  
24 = 9.0 Hz, 2''- and 6''-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 17.1 (C-18), 22.7, 25.9, 28.0, 29.0, 29.8,  
25  
26 31.2, 38.9, 42.0, 43.5, 46.4 (C-13), 47.0 (4'-CH<sub>2</sub>), 78.8 (C-17), 111.5 (C-2), 113.8 (C-4), 114.0  
27  
28 (C-1'), 123.5 (C-2'' and -6'') 126.3 (C-5'), 130.9 (C-3'' and -5''), 135.0 (C-10), 137.8 (C-5), 141.5  
29  
30 (C-4''), 150.6 (C-4'), 157.5 (C-3), 164.6 (C=O).

31  
32 2.3.24. 3-Methoxy-16a-(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
33  
34 17a-ol (**24f**)

35  
36 Compound **24e** (274 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
37  
38 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
39  
40 and the precipitate separating out was filtered off and recrystallized from a mixture of  
41  
42 acetone/hexane to afford **24f** (187 mg, 94%) as a white crystalline product. Mp: 149–150 °C; R<sub>f</sub>  
43  
44 = 0.25 (ss B). (Found C, 69.55; H, 7.95. C<sub>23</sub>H<sub>31</sub>N<sub>3</sub>O<sub>3</sub> (397.51) requires C, 69.49; H, 7.86%). <sup>1</sup>H  
45  
46 NMR (δ, ppm, CDCl<sub>3</sub>): 0.74 (s, 3H, 18-H<sub>3</sub>), 2.85 (m, 2H, 6-H<sub>2</sub>), 3.62 (d, 1H, J = 4.0 Hz, 17-H),  
47  
48 3.77 (s, 3H, 3-OCH<sub>3</sub>), 4.39 (m, 1H, 16a-H<sub>2</sub>), 4.64 (m, 1H, 16a-H<sub>2</sub>), 6.63 (s, 1H, 4-H), 6.71 (d, 1H,  
49  
50 J = 8.5 Hz, 2-H), 7.21 (d, 1H, J = 8.5 Hz, 1-H), 7.77 (s, 1H, 5'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>):  
51  
52 11.9 (C-18), 26.0, 28.0, 28.9, 31.3, 31.9, 33.8 (C-13), 38.9, 41.9, 43.5, 46.4 (4'-CH<sub>2</sub>), 46.9, 51.0  
53  
54 (C-16a), 55.2 (3-OCH<sub>3</sub>), 78.6 (C-17), 111.5 (C-2), 113.8 (C-4), 123.4 (C-5'), 126.3 (C-1), 132.5  
55  
56 (C-10), 137.8 (C-5), 157.4 (C-3).

57  
58 2.3.25. 3-Benzoyloxy-16β-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
59  
60 17β-ol (**25a**)

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2  
3  
4 Compound **17** (420 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
5  
6 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
7  
8 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **25a** (394 mg, 84%) as a white solid. Mp: 278–280  
9  
10 °C; *R*<sub>f</sub>= 0.35 (ss B). (Found C, 77.16; H, 7.62. C<sub>31</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (483.64) requires C, 76.98; H,  
11  
12 7.71%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.80 (s, 3H, 18-H<sub>3</sub>), 0.86 and 0.97 (2 x m, 2 x 2H, 2''- and 3''-  
13  
14 H), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.93 (d, *J* = 9.5 Hz, 1H, 17-H), 4.21 (m, 1H, 16a-H<sub>2</sub>), 4.64 (m, 1H, 16a-  
15  
16 H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.20 (d, 1H, *J* = 8.5 Hz,  
17  
18 1-H), 7.31 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.38 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.43 (d, 2H, *J* = 7.0  
19  
20 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 7.8 (C-2'' and -3''), 12.3 (C-18), 26.2, 27.4, 29.7,  
21  
22 30.8, 37.5, 38.0, 41.4, 43.9, 44.3 (C-13), 48.7 (C-16), 67.8 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 80.7 (C-17),  
23  
24 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and C-5'),  
25  
26 132.7 (C-10), 137.3 (C-1'), 137.8 (C-5), 156.8 (C-3).

27  
28 2.3.26. *3-Benzoyloxy-16β-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
29  
30 *17β-ol (25b)*

31  
32 Compound **17** (420 mg, 1 mmol) and cyclopentylacetylene (2 mol, 0.22 ml) were used for the  
33  
34 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
35  
36 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **25b** (350 mg, 68%) as a white solid. Mp: 288–290  
37  
38 °C; *R*<sub>f</sub>= 0.38 (ss B). Found C, 77.58; H, 7.92. C<sub>33</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (511.70) requires C, 77.46; H, 8.08%).  
39  
40 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.75 (s, 1H, 1''-H), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.94 (d,  
41  
42 1H, *J* = 9.5 Hz, 17-H), 4.24 (m, 1H, 16-H<sub>2</sub>), 4.67 (m, 1H, 16-H<sub>2</sub>), 5.03 (s., 2H, Bn-H<sub>2</sub>), 6.71 (s,  
43  
44 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.5 Hz, 4'-  
45  
46 H), 7.38 (t, 2H, *J* = 7.5 Hz, 3'- and 5'-H), 7.42 (d, 2H, *J* = 7.5 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ,  
47  
48 ppm, CDCl<sub>3</sub>): 12.3 (C-18), 25.1 (C-3'' and -4''), 26.2, 27.5, 29.7, 30.8, 34.3 (C-2'' and -5''), 37.5,  
49  
50 38.0, 41.4, 43.9, 44.3 (C-13), 48.7 (C-16), 62.1 (16a-CH<sub>2</sub>), 69.9 (Bn-CH<sub>2</sub>), 80.7 (C-17), 112.3 (C-  
51  
52 2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.7 (C-  
53  
54 10), 137.3 (C-1'), 137.8 (C-5), 156.8 (C-3).

55  
56 2.3.27. *3-Benzoyloxy-16β-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
57  
58 *17β-ol (25c)*

1  
2  
3  
4 Compound **17** (420 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
5  
6 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
7  
8 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99, v/v) to yield pure **25c** (146 mg, 28%) as a white solid. Mp: 214–216  
9  
10 °C; *R*<sub>f</sub> = 0.38 (ss B). (Found C, 77.43; H, 8.36. C<sub>34</sub>H<sub>43</sub>N<sub>3</sub>O<sub>2</sub> (525.72) requires C, 77.68; H, 8.24%).  
11  
12 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.79 (m, 4H, 3''- and 5''-H), 3.94 (d, *J* = 9.5 Hz,  
13  
14 1H, 17-H), 4.25 (m, 1H, 16a-H<sub>2</sub>), 4.67 (m, 1H, 16a-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H),  
15  
16 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32 (d, 1H, *J* = 7.0 Hz, 4'-H), 7.38  
17  
18 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.42 (d, 2H, *J* = 7 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>):  
19  
20 12.3 (C-18), 26.0 (C-4''), 26.1 (C-3'' and -5''), 26.2, 27.5, 29.7, 30.8 (C-2'' and -6''), 33.0 (C-1''),  
21  
22 37.5, 38.0, 41.4, 43.9, 44.3 (C-13), 48.7 (C-16), 62.1 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 80.7 (C-17), 112.3  
23  
24 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.7  
25  
26 (C-10), 137.3 (C-1'), 137.8 (C-5), 157.8 (C-3).

27  
28 2.3.28. *3-Benzoyloxy-16β-(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β-ol*  
29  
30 (**25d**)

31  
32 Compound **17** (420 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
33  
34 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
35  
36 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **25d** (391 mg, 75%) as a white solid. Mp: 202–204  
37  
38 °C; *R*<sub>f</sub> = 0.45 (ss B). (Found C, 78.73; H, 6.98. C<sub>34</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (519.68) requires C, 78.58; H, 7.18%).  
39  
40 <sup>1</sup>H NMR (δ, ppm, C<sub>6</sub>D<sub>6</sub>): 0.68 (s, 3H, 18-H<sub>3</sub>), 2.69 (m, 2H, 6-H<sub>2</sub>), 3.43 (dd, *J* = 9.5 Hz, *J* = 4 Hz,  
41  
42 1H, 17-H), 3.77 (dd, 1H, *J* = 13.5 Hz, *J* = 7.0 Hz, 16a-H<sub>2</sub>), 4.29 (dd, 1H, *J* = 13.5 Hz, *J* = 7.0 Hz,  
43  
44 16a-H<sub>2</sub>), 4.83 (s, 2H, Bn-H<sub>2</sub>), 6.79 (s, 1H, 4-H), 6.87 (d, 1H, *J* = 8.0 Hz, 2-H), 7.02 (s, 1H, 1-H),  
45  
46 7.08 (t, 1H, *J* = 7.5 Hz, 4'-H), 7.26 (t, 2H, *J* = 7.5 Hz, 3'- and 5'-H), 7.32 (d, 2H, *J* = 7.5 Hz, 2'-  
47  
48 and 6'-H), 8.01 (d, 2H, *J* = 7.5 Hz, 2''- and 6''-H).

49  
50 2.3.29. *3-Benzoyloxy-16β-[4'-(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-*  
51  
52 *1,3,5(10)-trien-17β-ol* (**25e**)

53  
54 Compound **17** (420 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used for  
55  
56 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
57  
58 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **25e** (480 mg, 77%) as a yellow solid. Mp: 187–189  
59  
60 °C; *R*<sub>f</sub> = 0.45 (ss B). (Found C, 69.32; H, 5.98. C<sub>36</sub>H<sub>38</sub>N<sub>4</sub>O<sub>6</sub> (622.71) requires C, 69.44; H, 6.15%).  
61  
62  
63  
64  
65

1  
2  
3  
4 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.80 (s, 3H, 18-H<sub>3</sub>), 2.82 (m, 2H, 6-H<sub>2</sub>), 3.94 (d, *J* = 10.0 Hz, 1H, 17-  
5 H), 4.32 (dd, 1H, *J* = 13.0 Hz, *J* = 6.0 Hz, 16a-H<sub>2</sub>), 4.72 (t, 1H, *J* = 6.0 Hz, 16a-H<sub>2</sub>), 5.03 (s, 2H,  
6 Bn-H<sub>2</sub>), 5.52 (s, 2H, triazol-H), 6.71 (s, 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* =  
7 8.5 Hz, 1-H), 7.32 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.38 (t, *J* = 7.5 Hz, 2H, 3'- and 5'-H), 7.42 (d, *J* =  
8 7.5 Hz, 2H, 2'- and 6'-H), 8.22 (d, *J* = 8 Hz, 2H, 3''- and 5''-H), 8.27 (d, *J* = 8 Hz, 2H, 2''- and  
9 6''-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 12.3 (C-18), 26.2, 27.4, 29.7, 30.8, 37.4, 38.0, 41.2, 43.8, 44.4  
10 (C-13), 48.7 (C-16), 55.5 (C-16a), 58.7 (linker-CH<sub>2</sub>), 69.9 (Bn-CH<sub>2</sub>), 80.7 (C-17), 112.4 (C-2),  
11 114.8 (C-4), 123.5 (C-2' and -6'), 126.3 (C-1), 127.4 (C-2'' and -6''), 127.8 (C-4'), 128.5 (C-3''  
12 and -5''), 130.9 (C-3' and -5'), 132.5 (C-10), 135.1 (C-1''), 137.3 (C-1'), 137.8 (C-5), 150.7 (C-  
13 4''), 156.8 (C-3), 164.6 (C=O).

24 2.3.30. *3-Benzoyloxy-16β-(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-*  
25 *trien-17β-ol (25f)*

26  
27 Compound **25e** (210 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
28 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
29 and the precipitate separating out was filtered off and recrystallized from methanol to afford **25f**  
30 (232 mg, 98%) as a white crystalline product. Mp: 283–285 °C; *R*<sub>f</sub> = 0.25 (ss B). (Found C,  
31 73.42; H, 7.35. C<sub>29</sub>H<sub>35</sub>N<sub>3</sub>O<sub>3</sub> (473.61) requires C, 73.54; H, 7.45%). <sup>1</sup>H NMR (δ, ppm, DMSO-d<sub>6</sub>):  
32 0.77 (s, 3H, 18-H<sub>3</sub>), 3.77 (dd, 1H, *J* = 9.5 Hz, *J* = 3.5 Hz, 16a-H<sub>2</sub>), 4.15 (t, 1H, *J* = 12.5 Hz, 16a-  
33 H<sub>2</sub>), 5.12 (d, 1H, *J* = 5.5 Hz, 17-H), 6.68 (s, 1H, 4-H), 6.74 (d, 1H, *J* = 8.5 Hz, 2-H), 7.16 (d, *J* =  
34 8.5 Hz, 1H, 1-H), 7.31 (d, 1H, *J* = 7.0 Hz, 4'-H), 7.37 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.41 (d,  
35 2H, *J* = 7.0 Hz., 2'- and 6'-H), 7.98 (s, 1H, triazol-H). <sup>13</sup>C NMR (δ, ppm, DMSO-d<sub>6</sub>): 12.3 (C-  
36 18), 25.8, 26.9, 29.1, 30.0, 36.9, 37.8, 40.4, 43.4, 43.7 (C-13), 47.8 (C-16a), 55.0 (linker-CH<sub>2</sub>),  
37 68.9 (Bn-CH<sub>2</sub>), 79.5 (C-17), 112.1 (C-2), 114.4 (C-4), 122.7 (triazol-CH), 126.0 (C-1), 127.4 (C-  
38 2' and -6'), 127.6 (C-4'), 128.3 (C-3' and -5'), 132.3 (C-10), 137.3 (C-5), 147.6 (triazol-C), 156.0  
39 (C-3).

53 2.3.31. *3-Benzoyloxy-16a-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
54 *17β-ol (26a)*

55  
56  
57 Compound **18** (420.0 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
58 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
59  
60  
61

1  
2  
3  
4 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **26a** (310 mg, 64%) as a white solid. Mp: 191–193  
5 °C; *R*<sub>f</sub> = 0.35 (ss B). (Found C, 76.82; H, 7.94. C<sub>31</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (483.64) requires C, 76.98; H,  
6 7.71%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.83 (s, 3H, 18-H<sub>3</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.54 (d, *J* = 7.5 Hz,  
7 1H, 17-H), 4.35 (dd, 1H, *J* = 13.0 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 4.44 (dd, 1H, *J* = 13.0 Hz, *J* = 7.5 Hz,  
8 16a-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.77 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* =  
9 8.5 Hz, 1-H), 7.31 (t, 2H, *J* = 7.5 Hz, 4'-H and triazol-H), 7.38 (t, 2H, *J* = 7.5 Hz, 3'- and 5'-H),  
10 7.42 (d, 2H, *J* = 7.5 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 6.6 (C-1''), 7.8 (C-2'' and -3''),  
11 11.8 (C-18), 26.1, 27.2, 28.2, 29.7, 36.6, 38.4, 43.9, 44.3, 44.3 (C-13), 48.3 (C-16), 54.5 (C-16a),  
12 69.9 (Bn-CH<sub>2</sub>), 85.2 (C-17), 112.3 (C-2), 114.8 (C-4), 120.0 (triazol-CH), 126.3 (C-1), 127.4 (C-  
13 2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.6 (C-10), 137.3 (C-1'), 137.8 (C-5), 150.2  
14 (triazol-C), 156.8 (C-3).

25  
26 **2.3.32.** *3-Benzoyloxy-16a-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
27 *17β-ol (26b)*

28  
29 Compound **18** (420 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
30 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
31 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (1:99 v/v) to yield pure **26b** (442 mg, 86%) as a white solid. Mp: 268–270  
32 °C; *R*<sub>f</sub> = 0.36 (ss B). (Found C, 77.52; H, 7.93. C<sub>33</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (511.70) requires C, 77.46; H, 8.08%).  
33 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.83 (s, 3H, 18-H<sub>3</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.19 (s, 1H, 1''-H), 3.46 (d,  
34 1H, *J* = 7.0 Hz, 17-H), 4.42 (dd, 2H, *J* = 22.5 Hz, *J* = 6.5 Hz, 16-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71  
35 (s, 1H, 4-H), 6.76 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.5 Hz,  
36 4'-H), 7.37 (t, 3H, *J* = 7.5 Hz, 3'-, 5'-H and triazol-H), 7.42 (d, 2H, *J* = 7.5 Hz, 2'- and 6'-H).  
37 <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 11.9 (C-18), 25.1 (C-3'' and -4''), 26.1, 27.2, 28.3, 29.7, 33.2 (C-2''  
38 and -5''), 36.6 (2C, C-1''), 36.7, 38.4, 43.9, 44.3 (C-13), 48.4 (C-16), 54.5 (C-16a), 69.9 (Bn-  
39 CH<sub>2</sub>), 85.2 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-3' and -5'), 127.8 (C-4'),  
40 128.5 (C-2' and -6'), 132.6 (C-10), 137.3 (C-1'), 137.8 (C-5), 156.7 (C-3).

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53 **2.3.33.** *3-Benzoyloxy-16a-(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
54 *17β-ol (26c)*

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4 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (2.5:77.5 v/v) to yield pure **26c** (386 mg, 76%) as a white solid. Mp:  
5  
6 261–263 °C; *R*<sub>f</sub> = 0.34 (ss B). (Found C, 77.93; H, 8.36. C<sub>34</sub>H<sub>43</sub>N<sub>3</sub>O<sub>2</sub> (525.72) requires C, 77.68;  
7  
8 H, 8.24%). <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.83 (s, 3H, 18-H<sub>3</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.55 (d, *J* = 7.0  
9  
10 Hz, 1H, 17-H), 4.43 (m, 2H, 16-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.77 (d, 1H, *J* = 8.5  
11  
12 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 2H, *J* = 7.0 Hz, 4'-H and triazol-H), 7.37 (t, 2H,  
13  
14 *J* = 7.0 Hz, 3'- and 5'-H), 7.42 (d, 2H, *J* = 7 Hz, 2'- and 6'-H). <sup>13</sup>C NMR (δ, ppm, CDCl<sub>3</sub>): 11.9  
15  
16 (C-18), 25.9 (C-4''), 26.1 (C-3'' and -5''), 27.2, 28.3, 29.7 (C-2'' and -6''), 32.9, 33.0, 36.6, 38.4,  
17  
18 43.9, 44.2, 44.3 (C-13), 48.4 (C-16), 54.5 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 85.2 (C-17), 112.3 (C-2),  
19  
20 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.6 (C-10),  
21  
22 137.3 (C-1'), 137.8 (C-5), 156.7 (C-3).

23  
24  
25 **2.3.34. 3-Benzoyloxy-16a-(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17β-ol**  
26  
27 **(26d)**

28  
29 Compound **18** (420 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
30  
31 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
32  
33 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> 5:95 v/v) to yield pure **26d** (372 mg, 71%) as a white solid. Mp: 132–134  
34  
35 °C; *R*<sub>f</sub> = 0.38 (ss B). (Found C, 78.63; H, 6.97. C<sub>34</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (519.68) requires C, 78.58; H, 7.18%).  
36  
37 <sup>1</sup>H NMR (δ, ppm, CDCl<sub>3</sub>): 0.84 (s, 3H, 18-H<sub>3</sub>), 2.83 (m, 2H, 6-H<sub>2</sub>), 3.58 (d, 1H, *J* = 7.5 Hz, 17-  
38  
39 H), 4.46 (dd, 2H, *J* = 13.5 Hz, *J* = 8.0 Hz, 16a-H<sub>2</sub>), 4.55 (dd, 1H, *J* = 13.5 Hz, *J* = 8.0 Hz, 16a-  
40  
41 H<sub>2</sub>) 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.19 (d, 1H, *J* = 8.5 Hz,  
42  
43 1-H), 7.30-7.86 (m, 11H, 2'-, 6'-, 3'-, 5'-, 4'-, 2''-, 6''-, 3''-, 5''-, 4''- and triazol-H). <sup>13</sup>C NMR (δ,  
44  
45 ppm, CDCl<sub>3</sub>): 11.8 (C-18), 26.1, 27.2, 28.2, 29.6, 36.5, 38.4, 43.9, 44.3, 48.3 (C-16), 54.6 (C-  
46  
47 16a), 62.1, 69.9 (Bn-CH<sub>2</sub>), 85.2 (C-17), 112.3 (C-2), 114.8 (C-4), 123.8 (triazol-CH), 125.7 (C-2'  
48  
49 and -6'), 126.3 (C-1'), 127.4 (C-2'' and -6''), 127.8 (C-4'), 128.2 (C-4), 128.5 (C-3'' and -5''),  
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51 128.8 (C-3' and -5'), 130.4 (C-10), 132.6 (C-1''), 137.3 (C-1'), 137.8 (C-5), 156.8 (C-3).

52  
53 **2.3.35. 3-Benzoyloxy-16a-[4'-(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-**  
54  
55 **1,3,5(10)-trien-17β-ol (26e)**

56  
57 Compound **18** (420 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used for  
58  
59 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
60  
61 with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **26e** (484 mg, 77%) as a yellow solid. Mp:

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3  
4 94–96 °C;  $R_f = 0.40$  (ss B). (Found C, 69.73; H, 5.94.  $C_{36}H_{38}N_4O_6$  (622.71) requires C, 69.44; H,  
5 6.15%).  $^1H$  NMR ( $\delta$ , ppm, DMSO- $d_6$ ): 0.70 (s, 3H, 18- $H_3$ ), 3.33 (m, 2H, 6- $H_2$ ), 4.38 (dd, 1H,  $J =$   
6 13.5 Hz,  $J = 9.0$  Hz, 16a- $H_2$ ), 4.52 (dd, 1H,  $J = 13.5$  Hz,  $J = 5.0$  Hz, 16a- $H_2$ ), 4.86 (d, 1H,  $J = 5$   
7 Hz, 17-H), 5.02 (s, 2H, Bn- $H_2$ ), 5.47 (s, 2H, linker- $H_2$ ), 6.64 (d, 1H,  $J = 2.0$  Hz, 4-H), 6.72 (dd,  
8 1H,  $J = 8.5$  Hz,  $J = 2.0$  Hz, 2-H), 7.10 (d, 1H,  $J = 8.5$  Hz, 1-H), 7.31 (t, 1H,  $J = 7.0$  Hz, 4'-H),  
9 7.37 (t, 2H,  $J = 7.0$  Hz, 3'- and 5'-H), 7.42 (d, 2H,  $J = 7.0$  Hz, 2'- and 6'-H), 8.16 (d, 2H,  $J = 9.0$   
10 Hz, 3''- and 5''-H), 8.28 (d, 2H,  $J = 9.0$  Hz, 2''- and 6''-H), 8.32 (s, 1H, triazol-H).  $^{13}C$  NMR ( $\delta$ ,  
11 ppm, DMSO- $d_6$ ): 11.7 (C-18), 25.7, 26.6, 27.1, 29.0, 30.6, 36.4, 37.9, 43.4, 43.4 (C-13), 43.7 (C-  
12 16), 53.1 (C-16a), 58.6 (linker- $CH_2$ ), 68.9 (Bn- $CH_2$ ), 82.8 (C-17), 112.1 (C-2), 114.3 (C-4), 123.7  
13 (C-2' and -6'), 125.1 (triazol-CH), 125.9 (C-1), 127.4 (C-2'' and -6''), 127.5 (C-4'), 128.3 (C-3''  
14 and -5''), 130.6 (C-3' and -5'), 132.1 (C-10), 134.7 (C-1''), 137.2 (C-1'), 137.3 (C-5), 141.1  
15 (triazol-C), 150.1 (C-4''), 155.9 (C-3), 163.9 (C=O).

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27  
28 **2.3.36.** *3-Benzoyloxy-16a-(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-*  
29 *trien-17 $\beta$ -ol (26f)*

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32 Compound **26e** (210 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
33 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
34 and the precipitate separating out was filtered off and recrystallized from a mixture of  
35 acetone/hexane to afford **26f** (190 mg, 89%) as a white crystalline product. Mp: 152–154 °C;  $R_f =$   
36 0.20 (ss B). (Found C, 73.72; H, 7.63.  $C_{29}H_{35}N_3O_3$  (473.61) requires C, 73.54; H, 7.45%).  $^1H$   
37 NMR ( $\delta$ , ppm, DMSO- $d_6$ ): 0.71 (s, 3H, 18- $H_3$ ), 2.73 (m, 2H, 6 $H_2$ ), 3.29 (d,  $J = 8.0$  Hz, 1H, 17-  
38 H), 4.28 (dd, 2H,  $J = 13.0$  Hz,  $J = 10.0$  Hz, 16a- $H_2$ ), 4.47 (dd, 1H,  $J = 13.0$  Hz,  $J = 4.5$  Hz, 16a-  
39  $H_2$ ), 4.51 (s, 2H, Bn- $H_2$ ), 4.87 (s, 1H, linker- $H_2$ ), 5.03 (s, 2H, triazol- $H_2$ ), 5.15 (s, 1H, linker- $H_2$ ),  
40 6.68 (s, 1H, 4-H), 6.74 (d, 1H,  $J = 8.5$  Hz, 2-H), 7.15 (d, 1H,  $J = 8.5$  Hz, 1-H), 7.31 (t, 1H,  $J = 7.0$   
41 Hz, 4'-H), 7.37 (t, 2H,  $J = 7.0$  Hz, 3'- and 5'-H), 7.41 (d, 2H,  $J = 7.0$  Hz, 2'- and 6'-H), 7.97 (s,  
42 1H, triazol-H).  $^{13}C$  NMR ( $\delta$ , ppm, DMSO- $d_6$ ): 11.8 (C-18), 25.8, 26.7, 27.3, 29.1, 36.4, 38.1,  
43 43.4, 43.5 (C-13), 43.9, 47.5 (C-16), 53.1 (C-16a), 54.9 (linker- $CH_2$ ), 68.9 (Bn- $CH_2$ ), 83.0 (C-  
44 17), 112.1 (C-2), 114.4 (C-4), 122.7 (triazol-CH), 126.0 (C-1), 127.4 (C-2' and -6'), 127.6 (C-4'),  
45 128.3 (C-3' and -5'), 132.3 (C-10), 137.3 (C-1'), 137.4 (C-5), 147.6 (triazol-C), 156.0 (C-3).  
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4 2.3.37. 3-Benzoyloxy-16 $\beta$ -(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
5  
6 17a-ol (**27a**)

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8 Compound **19** (420.0 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
9  
10 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
11 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **27a** (454 mg, 93%) as white crystals. Mp: 199–201  
12 °C; *R*<sub>f</sub> = 0.38 (ss B). (Found C, 77.15; H, 7.62. C<sub>31</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (483.64) requires C, 76.98; H,  
13 7.71%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.77 (s, 3H, 18-H<sub>3</sub>), 0.87 and 0.98 (2 x s, 2 x 2H, 2''- and 3''-  
14 H<sub>2</sub>), 2.05 (s, 1H, 1''-H), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.66 (s, 1H, 17-H), 4.42 (m, 2H, 16a-H<sub>2</sub>), 5.03 (s,  
15 2H, Bn-H<sub>2</sub>), 6.71 (s, 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31  
16 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.38 (t, 2H, *J* = 7.0 Hz, 3'- and 5'-H), 7.43 (d, 2H, *J* = 7.0 Hz, 2'- and  
17 6'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 6.7 (C-1''), 7.7 (C-2'' and -3''), 17.9 (C-18), 25.9, 27.9, 29.7,  
18 30.4, 31.8, 38.5, 43.3, 45.1 (C-13), 48.9, 49.1 (C-16), 62.1 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 82.6 (C-17),  
19 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'),  
20 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.7 (C-3).  
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32 2.3.38. 3-Benzoyloxy-16 $\beta$ -(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
33  
34 17a-ol (**27b**)

35  
36 Compound **19** (420 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
37  
38 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
39 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **27b** (408 mg, 79%) as white crystalline. Mp:  
40 220–222 °C; *R*<sub>f</sub> = 0.40 (ss B). (Found C, 77.32; H, 7.93. C<sub>33</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub> (511.70) requires C, 77.46;  
41 H, 8.08%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.76 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.20 (s, 1H, 1''-  
42 H), 3.67 (s, 1H, 17-H), 4.43 (m, 2H, 16a-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.72 (s, 1H, 4-H), 6.78 (dd,  
43 1H, *J* = 8.5 Hz, *J* = 2.0 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.0 Hz, 4'-H),  
44 7.38 (t, 3H, *J* = 7.0 Hz, 3'- and 5'-H, triazol-H), 7.43 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H). <sup>13</sup>C NMR  
45 ( $\delta$ , ppm, CDCl<sub>3</sub>): 18.0 (C-18), 25.1 (C-3'' and -5''), 25.9, 28.0, 29.7, 30.4, 31.8 (C-2'' and -6''),  
46 33.2, 36.7, 38.5, 43.3, 45.1 (C-13), 48.9 (C-16), 49.1 (C-1''), 54.3 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 82.6  
47 (C-17), 112.3 (C-2), 114.8 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and  
48 -5'), 132.7 (C-10), 137.3 (C-1'), 137.9 (C-5), 156.7 (C-3).  
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4 2.3.39. 3-Benzoyloxy-16 $\beta$ -(4'-cyclohexyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-  
5  
6 17a-ol (**27c**)

7 Compound **19** (420 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
8 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
9 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **27c** (360 mg, 68%) as white crystalline product.  
10  
11 Mp: 243–245 °C; *R*<sub>f</sub> = 0.38 (ss B). (Found C, 77.54; H, 8.38. C<sub>34</sub>H<sub>43</sub>N<sub>3</sub>O<sub>2</sub> (525.72) requires C,  
12 77.68; H, 8.24%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.75 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.68 (s,  
13 1H, 17-H), 4.44 (m, 2H, 16a-H<sub>2</sub>), 5.03 (s, 2H, Bn-H<sub>2</sub>), 6.72 (s, 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz,  
14 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.32 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.38 (t, 3H, *J* = 7.0 Hz, 3'- and  
15 5'-H, triazol-H), 7.43 (d, 2H, *J* = 7.0 Hz, 2'- and 6'-H). <sup>13</sup>C NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 17.9 (C-18),  
16 25.9 (C-4''), 26.0, 26.1 (C-3'' and -5''), 27.9, 29.7, 30.4, 31.8 (C-2'' and -6''), 32.1, 32.9 (C-1''),  
17 38.5, 43.3, 45.1 (C-13), 48.9, 49.1 (C-16), 62.1 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 82.5 (C-17), 112.3 (C-2),  
18 114.7 (C-4), 126.3 (C-1), 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 132.7 (C-10),  
19 137.2 (C-1'), 137.9 (C-5), 156.7 (C-3).  
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33 2.3.40. 3-Benzoyloxy-16 $\beta$ -(4'-phenyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-17a-ol  
34 (**27d**)  
35

36 Compound **19** (420 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
37 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
38 ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (10:90 v/v) to yield pure **27d** (487 mg, 93%) as white crystals. Mp:  
39 202–204 °C; *R*<sub>f</sub> = 0.45 (ss B). (Found C, 78.68; H, 7.38. C<sub>34</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub> (519.68) requires C, 78.58;  
40 H, 7.18%). <sup>1</sup>H NMR ( $\delta$ , ppm, CDCl<sub>3</sub>): 0.79 (s, 3H, 18-H<sub>3</sub>), 2.84 (m, 2H, 6-H<sub>2</sub>), 3.72 (s, 1H, 17-  
41 H), 4.48 (dd, 1H, *J* = 13.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 4.56 (t, 1H, *J* = 13.5 Hz, 16a-H<sub>2</sub>), 5.03 (s, 2H,  
42 Bn-H<sub>2</sub>), 6.72 (s, 1H, 4-H), 6.78 (d, 1H, *J* = 8.5 Hz, 2-H), 7.21 (d, 1H, *J* = 8.5 Hz, 1-H), 7.33 (t,  
43 1H, *J* = 7.5 Hz, 4'-H), 7.38 (t, 2H, *J* = 7.5 Hz, 3'- and 5'-H), 7.42 (d, *J* = 3.5 Hz, 4H, 2'- and 6'-  
44 H, 3''- and 5''-H), 7.84 (d, 2H, *J* = 7.5 Hz, 2''- and 6''-H), 7.88 (s, 1H, triazol-H). <sup>13</sup>C NMR ( $\delta$ ,  
45 ppm, CDCl<sub>3</sub>): 17.9 (C-18), 25.9, 27.9, 29.7, 30.4, 31.8, 38.5, 43.3, 45.2 (C-13), 48.9, 49.1 (C-16),  
46 54.6 (C-16a), 69.9 (Bn-CH<sub>2</sub>), 82.6 (C-17), 112.3 (C-2), 114.8 (C-4), 119.6 (triazol-CH), 125.7  
47 (C-2' and -6'), 126.3 (C-1'), 127.4 (C-2'' and -6''), 127.8 (C-4'), 128.2 (C-4''), 128.5 (C-3'' and -  
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4 5''), 128.8 (C-3' and -5'), 130.5 (C-10), 132.64 (C-1''), 137.3 (C-1'), 137.9 (C-5), 147.7 (triazol-  
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6 C); 156.8 (C-3).

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10 2.3.41. 3-Benzoyloxy-16 $\beta$ -[4'-(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-  
11 1,3,5(10)-trien-17a-ol (**27e**)

12  
13 Compound **19** (420.0 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used  
14 for the synthesis as described in Section 2.3. The crude product was chromatographed on silica  
15 gel with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (10:90 v/v) to yield pure **27e** (550 mg, 88%) as yellow crystals.  
16  
17 Mp: 177–179 °C; *R*<sub>f</sub> = 0.48 (ss B). (Found C, 69.55; H, 5.93. C<sub>36</sub>H<sub>38</sub>N<sub>4</sub>O<sub>6</sub> (622.71) requires: C,  
18 69.44; H, 6.15%). <sup>1</sup>H NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>): 0.65 (s, 3H, 18-H<sub>3</sub>), 2.73 (m, 2H, 6-H<sub>2</sub>), 4.40  
19 (dd, 1H, *J* = 13.0 Hz, *J* = 8.5 Hz, 16a-H<sub>2</sub>), 4.56 (dd, 1H, *J* = 13.5 Hz, *J* = 7.5 Hz, 16a-H<sub>2</sub>), 4.63  
20 (d, 1H, *J* = 5.0 Hz, 17-H), 5.04 (s, 2H, Bn-H<sub>2</sub>), 5.47 (s, 2H, triazol-H<sub>2</sub>), 6.68 (s, 1H, 4-H), 6.74 (d,  
21 1H, *J* = 8.5 Hz, 2-H), 7.16 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (t, 1H, *J* = 7.0 Hz, 4'-H), 7.37 (t, 2H, *J*  
22 = 7.0 Hz, 3'- and 5'-H), 7.41 (d, 2H, *J* = 7.0 Hz, 2''- and 6''-H), 8.18 (d, 2H, *J* = 8.5 Hz, 3''- and  
23 5''-H), 8.33 (d, 3H, *J* = 6 Hz, 2''- and 6''-H, triazol-H). <sup>13</sup>C NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>): 17.5 (C-  
24 18), 25.6, 27.5, 29.2, 29.6, 31.8, 38.2, 42.9, 44.5 (C-13), 48.2, 49.1 (C-16), 53.6 (C-16a), 58.7  
25 (linker-CH<sub>2</sub>), 68.9 (Bn-CH<sub>2</sub>), 80.8 (C-17), 112.1 (C-2), 114.4 (C-4), 123.8 (C-2' and C-6'), 125.0  
26 (triazol-CH), 126.1 (C-1), 127.4 (C-2'' and -6''), 127.6 (C-4'), 128.3 (C-3'' and -5''), 130.6 (C-3'  
27 and -5'), 132.3 (C-10), 134.7 (C-1''), 137.3 (C-5 and C-1'), 141.1 (triazol-C), 150.2 (C-4''), 160.0  
28 (C-3), 163.9 (C=O).

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42 2.3.42. 3-Benzoyloxy-16 $\beta$ -(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-  
43 trien-17a-ol (**27f**)

44  
45 Compound **27e** (210 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
46 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
47 and the precipitate separating out was filtered off and recrystallized from methanol to afford **27e**  
48 (273 mg, 99%) as a white crystalline product. Mp: 172–174 °C; *R*<sub>f</sub> = 0.25 (ss B). (Found C,  
49 73.68; H, 7.66. C<sub>29</sub>H<sub>35</sub>N<sub>3</sub>O<sub>3</sub> (473.61) requires C, 73.54; H, 7.45%). <sup>1</sup>H NMR ( $\delta$ , ppm, DMSO-d<sub>6</sub>):  
50 0.67 (s, 3H, 18-H<sub>3</sub>), 2.74 (m, 2H, 6-H<sub>2</sub>), 3.43 (s, 1H, 17-H), 4.34 (m, 1H, 16a-H<sub>2</sub>), 4.50 (m, 3H,  
51 16a-H<sub>2</sub> and Bn-H<sub>2</sub>), 4.61 (brs, 1H, OH), 5.04 (s, 2H, triazol-H<sub>2</sub>), 5.16 (brs, 1H, OH), 6.69 (s, 1H,  
52 4-H), 6.74 (d, 1H, *J* = 8.5 Hz, 2-H), 7.17 (d, 1H, *J* = 8.5 Hz, 1-H), 7.31 (d, 1H, *J* = 7.0 Hz, 4'-H),  
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4 7.37 (t, 2H,  $J = 7.0$  Hz, 3'- and 5'-H), 7.41 (d, 2H,  $J = 7.0$  Hz, 2'- and 6'-H), 8.00 (s, 1H, triazol-  
5 H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm, DMSO- $d_6$ ): 17.5 (C-18), 25.6, 27.5, 29.2, 29.6, 31.9, 38.2, 43.0, 44.5 (C-  
6 13), 48.2, 49.1 (C-16), 53.5 (C-16a), 55.0 (linker- $\text{CH}_2$ ), 61.6, 68.9 (Bn- $\text{CH}_2$ ), 80.8 (C-17), 112.2  
7 (C-2), 114.4 (C-4), 122.6 (triazol-CH), 126.6 (C-1), 127.4 (C-2' and -6'), 127.6 (C-4'), 128.3 (C-  
8 3' and -5'), 132.4 (C-10), 137.3 (C-5 and C-1'), 147.6 (triazol-C), 156.0 (C-3).

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16 2.3.43. *3-Benzoyloxy-16a-(4'-cyclopropyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
17 *17a-ol (28a)*

18  
19 Compound **20** (420.0 mg, 1 mmol) and cyclopropylacetylene (2 mmol, 0.22 ml) were used for the  
20 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
21 ethyl acetate/ $\text{CH}_2\text{Cl}_2$  (1:99 v/v) to yield pure **28a** (305 mg, 63%) as white crystals. Mp: 143–144  
22 °C;  $R_f = 0.40$  (ss B). (Found C, 77.15; H, 7.53.  $\text{C}_{31}\text{H}_{37}\text{N}_3\text{O}_2$  (483.64) requires C, 76.98; H,  
23 7.71%).  $^1\text{H}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 0.74 (s, 3H, 18- $\text{H}_3$ ), 0.87 and 0.97 (2 x s, 2 x 2H, 2''- and 3''-  
24  $\text{H}_2$ ), 2.85 (m, 2H, 6- $\text{H}_2$ ), 3.63 (d, 1H,  $J = 5.0$  Hz, 17-H), 4.26 (dd, 1H,  $J = 13.5$  Hz,  $J = 5.5$  Hz,  
25 16a- $\text{H}_2$ ), 4.60 (t, 1H,  $J = 13.5$  Hz, 16a- $\text{H}_2$ ), 5.03 (s, 2H, Bn- $\text{H}_2$ ), 6.72 (d, 1H,  $J = 2.0$  Hz, 4-H),  
26 6.78 (dd, 1H,  $J = 8.5$  Hz,  $J = 2.5$  Hz, 2-H), 7.22 (d, 1H,  $J = 8.5$  Hz, 1-H), 7.32 (t, 1H,  $J = 7.5$  Hz,  
27 4'-H), 7.38 (t, 3H,  $J = 7.5$  Hz, 3'- and 5'-H, triazol-H), 7.43 (d, 2H,  $J = 7.5$  Hz, 2'- and 6'-H).  $^{13}\text{C}$   
28 NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 6.5 (C-1''), 7.9 (2C, C-2'' and -3''), 17.1 (C-18), 26.0, 27.9, 28.9, 29.8,  
29 31.2, 38.9, 42.3, 43.5, 46.3 (C-16a), 47.0 (C-16), 50.7 (C-13), 69.9 (Bn- $\text{CH}_2$ ), 78.7 (C-17), 112.2  
30 (C-2), 114.8 (C-4), 120.8 (triazol-CH), 126.3 (C-1), 127.4 (C-2' and -6'), 127.4 (C-4'), 128.5  
31 (C-3' and -5'), 132.5 (C-10), 137.2 (C-1'), 137.9 (C-5), 149.6 (triazol-C), 156.7 (C-3).

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45 2.3.44. *3-Benzoyloxy-16a-(4'-cyclopentyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-trien-*  
46 *17a-ol (28b)*

47  
48 Compound **20** (420.0 mg, 1 mmol) and cyclopentylacetylene (2 mmol, 0.22 ml) were used for the  
49 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
50 ethyl acetate/ $\text{CH}_2\text{Cl}_2$  (2.5:97.5 v/v) to yield pure **28b** (417 mg, 82%) as white crystals. Mp:  
51 197–199 °C;  $R_f = 0.42$  (ss B). (Found: C, 77.62; H, 7.85.  $\text{C}_{33}\text{H}_{41}\text{N}_3\text{O}_2$  (511.70) requires C, 77.46;  
52 H, 8.08%).  $^1\text{H}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 0.76 (s, 3H, 18- $\text{H}_3$ ), 2.85 (m, 2H, 6- $\text{H}_2$ ), 3.20 (s, 1H, 1''-  
53 H), 3.66 (d, 1H,  $J = 5.0$  Hz, 17-H), 4.29 (dd, 1H,  $J = 13.5$  Hz,  $J = 5.5$  Hz, 16a- $\text{H}_2$ ), 4.62 (dd, 1H,  
54  $J = 13.5$  Hz,  $J = 9.5$  Hz, 16a- $\text{H}_2$ ), 5.04 (s, 2H, Bn- $\text{H}_2$ ), 6.72 (s, 1H, 4-H), 6.78 (dd, 1H,  $J = 8.5$  Hz,  
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4  $J = 2.5$  Hz, 2-H), 7.21 (d, 1H,  $J = 8.5$  Hz, 1-H), 7.31 (t, 1H,  $J = 7.0$  Hz, 4'-H), 7.37 (t, 2H,  $J = 7.0$   
5 Hz, 3'- and 5'-H), 7.43 (d, 2H,  $J = 7.0$  Hz, 2'- and 6'-H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 17.3 (C-  
6 18), 25.2 (2C), 26.1, 28.0, 29.1, 29.8 (2C), 31.3, 33.2, 36.8 (C-1''), 39.0, 42.4, 43.6, 46.4 (C-16a),  
7 47.2 (C-16), 50.6 (C-13), 70.1 (Bn- $\text{CH}_2$ ), 79.0 (C-17), 112.4 (C-2), 115.0 (C-4), 126.3 (C-1),  
8 127.4 (C-2' and -6'), 127.8 (C-4'), 128.5 (C-3' and -5'), 133.0 (C-10), 137.5 (C-1'), 137.9 (C-5),  
9 156.9 (C-3).

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17 2.3.45. *3-Benzylxy-16a-(4-cyclohexyl-1H-1,2,3-triazol-1-yl)methyl-estra-1,3,5(10)-trien-17a-ol*  
18 (**28c**)

19  
20 Compound **20** (420.0 mg, 1 mmol) and cyclohexylacetylene (2 mmol, 0.22 ml) were used for the  
21 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
22 ethyl acetate/ $\text{CH}_2\text{Cl}_2$  (2.5:97.5 v/v) to yield pure **28c** (200 mg, 76%) as a white solid. Mp:  
23 223–225 °C;  $R_f = 0.44$  (ss B). (Found C, 77.82; H, 8.35.  $\text{C}_{34}\text{H}_{43}\text{N}_3\text{O}_2$  (525.72) requires C, 77.68;  
24 H, 8.24%).  $^1\text{H}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 0.75 (s, 3H, 18- $\text{H}_3$ ), 2.84 (m, 3H, 6- $\text{H}_2$ , 1''-H), 3.64 (s, 1H,  
25 17-H), 4.37 (m, 1H, 16a- $\text{H}_2$ ), 4.69 (m, 1H, 16a- $\text{H}_2$ ), 5.03 (s, 2H, Bn- $\text{H}_2$ ), 6.72 (d, 1H,  $J = 1.5$  Hz,  
26 4-H), 6.78 (dd, 1H,  $J = 8.5$  Hz,  $J = 2.5$  Hz, 2-H), 7.22 (d, 1H,  $J = 8.5$  Hz, 1-H), 7.32 (t, 1H,  $J =$   
27 7.0 Hz, 4'-H), 7.38 (t, 2H,  $J = 7.0$  Hz, 3'- and 5'-H), 7.43 (d, 2H,  $J = 7.0$  Hz, 2'- and 6'-H  
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37 2.3.46. *3-Benzylxy-16a-(4-phenyl-1H-1,2,3-triazol-1-yl)methyl-estra-1,3,5(10)-trien-17a-ol*  
38 (**28d**)

39  
40 Compound **20** (420.0 mg, 1 mmol) and phenylacetylene (2 mmol, 0.22 ml) were used for the  
41 synthesis as described in Section 2.3. The crude product was chromatographed on silica gel with  
42 ethyl acetate/ $\text{CH}_2\text{Cl}_2$  (5:95 v/v) to yield pure **28d** (337 mg, 64%) as a white solid. Mp: 205–206  
43 °C;  $R_f = 0.46$  (ss B). (Found C, 78.42; H, 7.32.  $\text{C}_{34}\text{H}_{37}\text{N}_3\text{O}_2$  (519.68) requires C, 78.58; H, 7.18%).  
44  $^1\text{H}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 0.76 (s, 3H, 18- $\text{H}_3$ ), 2.87 (m, 2H, 6- $\text{H}_2$ ), 3.68 (d, 1H,  $J = 5.0$  Hz, 17-  
45 H), 4.41 (dd, 1H,  $J = 13.5$  Hz,  $J = 5.5$  Hz, 16a- $\text{H}_2$ ), 4.69 (t, 1H,  $J = 13.5$  Hz, 16a- $\text{H}_2$ ), 5.04 (s, 2H,  
46 Bn- $\text{H}_2$ ), 6.73 (s, 1H, 4-H), 6.79 (dd, 1H,  $J = 8.0$  Hz,  $J = 2.0$  Hz, 2-H), 7.22 (d, 1H,  $J = 8.0$  Hz, 1-  
47 H), 7.38 (m, 8H, 2'-, 3'-, 4'-, 5'- and 6'-H, 3''-, 4''- and 5''-H), 7.84 (d, 2H,  $J = 7.5$  Hz, 2''- and  
48 6''-H), 7.89 (s, 1H, triazol-H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm,  $\text{CDCl}_3$ ): 17.1 (C-18), 26.0, 27.9, 29.8, 31.2,  
49 38.9, 42.2, 43.5, 46.4 (C-13), 47.0 (C-16), 50.8 (C-16a), 69.9 (Bn- $\text{CH}_2$ ), 78.8 (C-17), 112.3 (C-2),  
50 114.8 (C-4), 120.7 (triazol-CH), 125.7 (C-2' and -6'), 126.3 (C-1), 127.4 (C-2'' and -6''), 127.8  
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4 (C-4'), 128.3 (C-4''), 128.5 (C-3''' and -5'''), 128.9 (C-3' and -5'), 130.2 (C-10), 132.8 (C-1'),  
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6 137.3 (C-1''), 137.9 (C-5), 147.1 (triazol-C), 156.7 (C-3).  
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10 **2.3.47. 3-Benzoyloxy-16a-[4'-(4''-nitro-benzoyloxymethyl)-1'H-1',2',3'-triazol-1'-yl]methylestra-**  
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12 **1,3,5(10)-trien-17a-ol (28e)**

13 Compound **20** (420 mg, 1 mmol) and propargyl 4-nitrobenzoate (2 mmol, 210 mg) were used for  
14 the synthesis as described in Section 2.3. The crude product was chromatographed on silica gel  
15 with ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> (5:95 v/v) to yield pure **28e** (610 mg, 98%) as a yellow solid. Mp:  
16 75–77 °C; *R*<sub>f</sub> = 0.45 (ss B). (Found C, 69.57; H, 61.32. C<sub>36</sub>H<sub>38</sub>N<sub>4</sub>O<sub>6</sub> (622.71) requires C, 69.44; H,  
17 6.15%). <sup>1</sup>H NMR (δ, ppm, DMSO-d<sub>6</sub>): 0.66 (s, 3H, 18-H<sub>3</sub>), 2.71 (m, 2H, 6-H<sub>2</sub>), 3.57 (s, 1H, 16-  
18 H), 4.29 (dd, 1H, *J* = 13.5 Hz, *J* = 8.5 Hz, 16a-H<sub>2</sub>), 4.47 (dd, 1H, *J* = 13.5 Hz, *J* = 8.5 Hz, 16a-  
19 H<sub>2</sub>), 4.85 (d, 1H, *J* = 5.0 Hz, 17-H), 5.44 (s, 2H, Bn-H<sub>2</sub>), 6.65 (s, 1H, 4-H), 6.72 (d, 1H, *J* = 8.5  
20 Hz, 2-H), 7.14 (d, 1H, *J* = 8.5 Hz, 1-H), 7.29 (t, 1H, *J* = 7.5 Hz, 4'-H), 7.35 (t, 2H, *J* = 7.5 Hz, 3'-  
21 and 5'-H), 7.40 (d, 2H, *J* = 7.5 Hz, 2''- and 6''-H), 8.17 (d, 2H, *J* = 8.5 Hz, 3'''- and 5'''-H), 8.28 (s,  
22 1H, triazol H), 8.31 (d, 2H, *J* = 8.5 Hz, 2'''- and 6'''-H). <sup>13</sup>C NMR (δ, ppm, DMSO-d<sub>6</sub>): 16.9 (C-  
23 18), 25.6, 27.5, 28.4, 29.2, 31.1, 38.5, 39.8, 39.9, 43.2, 45.9 (C-16a), 46.2 (C-16), 53.4 (C-13),  
24 58.7 (linker CH<sub>2</sub>), 68.9 (Bn-CH<sub>2</sub>), 78.0 (C-17), 112.1 (C-2), 114.4 (C-4), 123.8 (C-2'' and -6''),  
25 125.0 (triazol CH), 126.1 (C-1), 127.4 (C-2' and -6'), 127.5 (C-4'), 128.3 (C-3' and -5'), 130.6  
26 (C-3'' and -5'''), 132.3 (C-10), 134.7 (C-1'), 137.3 (C-5), 141.0 (C-1''), 150.2 (triazol C), 156.0  
27 (C-3), 163.9 (C=O).  
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43 **2.3.48. 3-Benzoyloxy-16a-(4'-hydroxymethyl-1'H-1',2',3'-triazol-1'-yl)methylestra-1,3,5(10)-**  
44 **trien-17α-ol (28f)**

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46 Compound **28e** (220 mg, 0.5 mmol) was dissolved in methanol (10 ml) containing NaOCH<sub>3</sub> (14  
47 mg, 0.25 mmol), and the solution was allowed to stand for 24 h. It was then diluted with water,  
48 and the precipitate separating out was filtered off and recrystallized from methanol to afford **28f**  
49 (126 mg, 53%) as a white crystalline product. Mp: 86–88 °C; *R*<sub>f</sub> = 0.25 (ss B). (Found C, 73.68;  
50 H, 7.63. C<sub>29</sub>H<sub>35</sub>N<sub>3</sub>O<sub>3</sub> (473.61) requires C, 73.54; H, 7.45%). <sup>1</sup>H NMR (δ, ppm, DMSO-d<sub>6</sub>): 0.68  
51 (s, 3H, 18-H<sub>3</sub>), 2.74 (m, 2H, 6-H<sub>2</sub>), 3.58 (brs, 1H, OH), 4.26 (t, 1H, *J* = 8.5 Hz, 16a-H<sub>2</sub>), 4.43 (dd,  
52 1H, *J* = 13.0 Hz, *J* = 7.0 Hz, 16a-H<sub>2</sub>), 4.51 (d, 2H, *J* = 5.0 Hz, linker H<sub>2</sub>), 4.85 (d, 1H, *J* = 4.0 Hz,  
53 17-H), 5.04 (s, 2H, Bn-H<sub>2</sub>), 5.13 (brs, 1H, OH), 6.68 (s, 1H, 4-H), 6.74 (d, 1H, *J* = 8.5 Hz, 2-H),  
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4 7.17 (d, 1H,  $J = 8.5$  Hz, 1-H), 7.31 (d, 1H,  $J = 7.0$  Hz, 4'-H), 7.37 (t, 2H,  $J = 7.0$  Hz, 3'- and 5'-  
5 H), 7.42 (d, 2H,  $J = 7.0$  Hz, 2'- and 6'-H), 7.97 (s, 1H, triazol H).  $^{13}\text{C}$  NMR ( $\delta$ , ppm, DMSO- $d_6$ ):  
6 16.9 (C-18), 25.6, 27.5, 28.5, 29.2, 31.1, 38.5, 40.7, 43.2, 45.9, 46.2 (C-16), 47.9 (C-13), 50.6 (C-  
7 16a), 55.0 (linker  $\text{CH}_2$ ), 68.9 (Bn- $\text{CH}_2$ ), 78.0 (C-17), 112.1 (C-2), 114.4 (C-4), 122.7 (triazol  
8 CH), 126.1 (C-1), 127.4 (C-2' and -6'), 127.6 (C-4'), 128.3 (C-3' and -5'), 132.4 (C-10), 137.3  
9 (C-1'), 137.4 (C-5), 147.6 (triazol C), 156.0 (C-3).  
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#### 17 2.4. Determination of the antiproliferative activities

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19 The growth-inhibitory effects of the compounds were tested *in vitro* by means of the MTT  
20 assay against a gynecological panel containing two breast cancer cell lines (MCF-7, MD-MB-  
21 231) and two cell lines isolated from cervical malignancies (HeLa, SiHa) [11]. All cell lines were  
22 obtained from the European Collection of Cell Cultures (Salisbury, UK). The cells were  
23 maintained in minimal essential medium supplemented with 10% fetal bovine serum (FBS), 1%  
24 non-essential amino acids and an antibiotic-antimycotic mixture (AAM). All chemicals, if  
25 otherwise not specified, were purchased from Sigma-Aldrich Ltd. (Budapest, Hungary). All cell  
26 lines were grown in a humidified atmosphere of 5%  $\text{CO}_2$  at 37 °C. For pharmacological  
27 investigations, 10 mM stock solutions of the tested compounds were prepared with dimethyl  
28 sulfoxide (DMSO). The highest applied DMSO concentration of the medium (0.3%) did not have  
29 any substantial effect on the determined cellular functions. Cells were seeded into 96-well plates  
30 (5000 cells/well), allowed to stand overnight under cell culturing conditions, and the medium  
31 containing the tested compounds at two final concentrations (10 or 30  $\mu\text{M}$ ) was then added. After  
32 a 72-hour incubation viability was determined by the addition of 20  $\mu\text{l}$  3-(4,5-dimethylthiazol-2-  
33 yl)-2,5-diphenyltetrazolium bromide (MTT) solution (5 mg/ml). The formazan crystals  
34 precipitated in 4 h were solubilized in DMSO and the absorbance was determined at 545 nm with  
35 an ELISA plate reader utilizing untreated cells as controls. The most effective compounds  
36 eliciting at least 60% growth inhibition at 10  $\mu\text{M}$  were tested again with a set of dilutions (0.3–30  
37  $\mu\text{M}$ ) in order to determine the  $\text{IC}_{50}$  values by means of Graphpad Prism 4.0 (Graphpad Software;  
38 San Diego, CA, US). These promising compounds were additionally tested using nonmalignant  
39 murine fibroblasts (NIH-3T3) to obtain preliminary data concerning cancer selectivity of the  
40 tested molecules. Two independent experiments were performed with 5 parallel wells and  
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4 cisplatin (Ebewe GmbH, Unterach, Austria), an agent administered clinically in the treatment of  
5 certain gynecological malignancies, was used as reference compound.  
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### 9 **3. Results and discussion**

#### 10 *3.1. Synthetic studies*

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14 To prepare novel steroid triazoles via 1,3-dipolar cycloaddition, we chose the 3-methoxy- and 3-  
15 benzyloxy-16-hydroxymethylestra-1,3,5(10)-trien-17-ol diastereomers (**5–8** and **9–12**). The  
16 synthesis strategy for the preparation of the starting diols (**21–28**) is illustrated in Scheme 1. The  
17 synthesis of steroidal 1,2,3-triazoles by CuAAC is outlined in Scheme 2.  
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21 Stereoselective tosylation of **5–8** and bromination of **9–12** gave **5b–8b** and **9c–12c**,  
22 respectively, which then underwent facile S<sub>N</sub>2 substitution with NaN<sub>3</sub> in *N,N*-dimethylformamide  
23 to furnish the corresponding 16-azidomethyl compounds (**13–16** and **17–20**).  
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27 The 16-azido compounds were subjected to the azide–alkyne CuAAC reaction with different  
28 alkyl- and aryl-acetylenes. The azide–alkyne reactions of these compounds were carried out with  
29 CuI as catalyst in the presence of Et<sub>3</sub>N in CH<sub>2</sub>Cl<sub>2</sub> under reflux conditions to obtain the required 3-  
30 methoxy- and 3-benzyloxyestra-1,3,5(10)-trien-16-(1',4'-substituted 1',2',3')-triazolyl  
31 derivatives (**21–24** and **25–28**).  
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#### 39 *3.2. Determination of the antiproliferative properties of the 16-triazolylmethyl diastereomers*

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42 We have published recently that introduction of a substituted triazole moiety onto  
43 different positions of the estrane skeleton might increase the antiproliferative properties of  
44 estrone derivatives [12]. It was also established that the presence of certain alkyl or aralkyl  
45 protecting groups at the phenolic OH function is advantageous. Concerning that 16-  
46 hydroxymethylene-17-hydroxy derivatives of estrone-3-methyl ether or 3-benzyl ether (**5a–12a**)  
47 displayed substantial cytostatic potential against different types of breast cancer cell lines, these  
48 compounds might be suitable for directed modifications with the aim of developing potentially  
49 more active antiproliferative steroidal derivatives [13]. In the light of the above-mentioned recent  
50 observations, here we aimed to combine the substituted triazole and the 16,17-disubstituted  
51 estrone 3-ether moieties. The present study included an evaluation of the direct antiproliferative  
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4 capacities of the newly synthesized heterocyclic compounds (**21a–f**, **22a–f**, **23a–f**, **24a–f** and  
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6 **25a–f**, **26a–f**, **27a–f**, **28a–f**). The antiproliferative activities were determined *in vitro* by means  
7  
8 of MTT assays against human adherent cervical (SiHa, HeLa) and breast cancer (MCF-7 and  
9  
10 MDA-MB-231) cell lines.

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12 The antiproliferative activities of the newly synthesized heterocyclic compounds  
13  
14 depended on the nature of the protecting group at the 3-hydroxy function and on the orientation  
15  
16 of the substituents at C-16 and C-17. In general, the 3-methyl ethers (**21–24**) exhibited weak  
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18 antiproliferative action; none of them exerted any substantial effect at 10  $\mu$ M (Table 1). All  
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20 diastereomers of the 3-benzyl ether series (**25–28**) proved to be more potent in comparison with  
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22 their 3-methyl ether counterparts (Table 2). This is in agreement with our earlier results [14].  
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24 Based on the substantial difference of the two groups, i.e. that of 3-methyl ethers and 3-benzyl  
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26 ethers, it can be concluded that only the latter derivatives are promising from pharmacological  
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28 point of view.

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30 Concerning the orientation of the substituents at position C-16 and C-17, the 16 $\beta$ ,17 $\beta$ -  
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32 derivatives (**25a–f**) displayed outstanding growth-inhibitory properties. Two derivatives bearing  
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34 similar cycloalkyl groups at position C-4' displayed substantial selective antiproliferative action  
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36 against the triple-negative breast cancer cell line MDA-MB-231 with IC<sub>50</sub> values in the low  
37  
38 micromolar range. It should be underlined that **25b** and **25c** did not significantly influence the  
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40 proliferation of other cell lines tested, including the non-cancerous fibroblast. Although both the  
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42 4'-cyclohexyl (**25c**) and the 4'-phenyl derivative (**25d**) have six-membered substituents, their  
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44 cytostatic behavior is completely different. This might be attributed to the different steric  
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46 structure of the two rings (chair or planar) at C-4'. Compound **25d** exerted potent  
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48 antiproliferative action against all tested cell lines without any selectivity. The *cis*-16 $\alpha$ ,17 $\alpha$ -3-  
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50 benzyl ethers (**28a–f**) were less potent than their  $\beta,\beta$ -counterparts (**25a–f**), except for **28d**, which  
51  
52 behaved similarly to its diastereomer **25d**. The *trans*-16 $\beta$ ,17 $\alpha$ -isomers (**27a–f**) exhibited activity  
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54 exclusively on the breast cancer cell lines. Surprisingly, the tendency observed earlier (in the case  
55  
56 of compounds **25a–f**) concerning the nature of C-4' substituent was not valid here. Only **26a** and  
57  
58 **26e** inhibited cell growth markedly, but with no tumor selectivity. It's worth mentioning that  
59  
60 *trans*-16 $\alpha$ ,17 $\beta$  isomer **26c** was the sole compound, which inhibited the proliferation of HPV 16+  
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62 squamous cell carcinoma SiHa, showing an IC<sub>50</sub> value comparable with that of cisplatin.  
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4 In view of the cell lines, it should be noted that triple-negative breast cancer cell line MDA-MB-  
5 231 proved to be the most sensitive and all calculated IC<sub>50</sub> values were lower than that of the  
6 reference agent cisplatin (19.1 μM).  
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9  
10 Regarding the present and earlier results obtained for 16,17-disubstituted 3-benzyl ethers, it can  
11 be stated that introduction of a substituted triazolyl moiety onto the C-16 methylene group of the  
12 *cis* isomers proved to be advantageous. In the case of compounds **25b** and **25c**, both the  
13 antiproliferative potential and the tumor selectivity were markedly improved.  
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## 21 **Acknowledgement**

22  
23 The work of Anita Kiss was supported by a PhD Fellowship of the Talentum Fund of  
24 Richter Gedeon Plc. (Budapest). Financial support from the Economic Development and  
25 Innovation Operative Programme of Hungary (GINOP-2.3.2-15-2016-00038) and Ultrafast  
26 physical processes in atoms, molecules, nanostructures and biological systems (No: EFOP-3.6.2.-  
27 2017-00005) is gratefully acknowledged. This research was supported by the Hungarian  
28 Scientific Research Fund (OTKA K113150). Ministry of Human Capacities, Hungary grant  
29 20391-3/2018/FEKUSTRAT is acknowledged.  
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**Legends for Schemes and Tables**

**Scheme 1** Reagents and conditions: (i) NaOMe, HCOOEt, anhydrous toluene, 50 °C; (ii) KBH<sub>4</sub>, MeOH; (iii) KOAc, CH<sub>3</sub>COOH, NaOMe/MeOH.

**Scheme 2** Reagents and conditions: (i) appropriate alkyne, TEA, CuI, CH<sub>2</sub>Cl<sub>2</sub>, 40 °C, 24 h; (ii) NaOMe, MeOH, 24 h.

**Table 1** Antiproliferative activities of compounds **21a–f**, **22a–f**, **23a–f** and **24a–f**

**Table 2** Antiproliferative activities of compounds **25a–f**, **26a–f**, **27a–f** and **28a–f**

**Table 1**

Growth Inhibition, % $\pm$ SEM [calculated IC <sub>50</sub> ( $\mu$ M)]					
	Conc. ( $\mu$ M)	HeLa	SiHa	MCF-7	MDA-MB- 231
<b>21</b>					
<b>a</b>	10	<20	21.28 $\pm$ 1.88	<20	<20
	30	<20	28.71 $\pm$ 2.20	46.42 $\pm$ 1.47	<20
<b>b</b>	10	<20	<20	<20	<20
	30	39.86 $\pm$ .38	<20	57.42 $\pm$ 1.77	29.88 $\pm$ 1.57
<b>c</b>	10	<20	<20	<20	<20
	30	40.22 $\pm$ 1.02	<20	70.84 $\pm$ 1.55	37.96 $\pm$ 1.55
<b>d</b>	10	<20	<20	<20	<20
	30	44.16 $\pm$ 0.48	<20	54.93 $\pm$ 1.78	38.28 $\pm$ 1.84
<b>e</b>	10	<20	23.91 $\pm$ 1.61	34.23 $\pm$ 3.10	<20
	30	37.18 $\pm$ 1.65	54.72 $\pm$ 0.48	76.26 $\pm$ 0.72	35.93 $\pm$ 2.13
<b>f</b>	10	<20	28.06 $\pm$ 1.99	29.45 $\pm$ 1.67	<20
	30	41.03 $\pm$ 0.77	57.69 $\pm$ 1.12	70.23 $\pm$ 1.35	34.81 $\pm$ 2.88
<b>22</b>					
<b>a</b>	10	<20	25.55 $\pm$ 1.01	<20	<20
	30	<20	34.78 $\pm$ 2.47	57.43 $\pm$ 1.91	<20
<b>b</b>	10	<20	<20	<20	<20
	30	<20	26.57 $\pm$ 2.26	67.59 $\pm$ 1.65	<20
<b>c</b>	10	<20	<20	<20	<20
	30	<20	29.90 $\pm$ 2.59	69.68 $\pm$ 0.77	<20
<b>d</b>	10	<20	<20	<20	<20
	30	<20	29.96 $\pm$ 1.79	70.75 $\pm$ 1.05	14.54 $\pm$ 1.32
<b>e</b>	10	<20	<20	<20	<20
	30	<20	38.69 $\pm$ 2.09	63.12 $\pm$ 2.14	<20
<b>f</b>	10	<20	<20	22.02 $\pm$ 1.61	<20
	30	<20	37.79 $\pm$ 1.04	50.94 $\pm$ 1.55	<20
<b>23</b>					
<b>a</b>	10	<20	<20	<20	<20
	30	31.14 $\pm$ 1.28	<20	28.72 $\pm$ 0.93	25.08 $\pm$ 3.15
<b>b</b>	10	<20	<20	<20	<20
	30	58.25 $\pm$ 2.03	<20	48.01 $\pm$ 1.31	<20
<b>c</b>	10	<20	30.97 $\pm$ 2.69	<20	<20
	30	<20	33.89 $\pm$ 2.35	<20	<20
<b>d</b>	10	<20	<20	<20	<20
	30	26.90 $\pm$ 2.15	<20	63.27 $\pm$ 0.82	<20
<b>e</b>	10	<20	<20	<20	<20
	30	<20	37.53 $\pm$ 3.00	33.94 $\pm$ 0.75	28.19 $\pm$ 0.96
<b>f</b>	10	<20	29.13 $\pm$ 1.59	<20	<20
	30	26.61 $\pm$ 0.57	43.85 $\pm$ 3.32	38.45 $\pm$ 1.93	43.85 $\pm$ 3.32
<b>24</b>					
<b>a</b>	10	<20	<20	<20	<20
	30	89.01 $\pm$ 0.47	<20	78.65 $\pm$ 0.78	46.21 $\pm$ 1.54
<b>b</b>	10	<20	<20	<20	<20
	30	34.18 $\pm$ 0.81	<20	31.07 $\pm$ 2.36	<20
<b>c</b>	10	<20	<20	<20	<20
	30	49.11 $\pm$ 0.55	<20	43.22 $\pm$ 1.52	<20

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<b>d</b>	10	<20	<20	<20	<20
	30	42.13±1.66	<20	55.41±0.76	<20
<b>e</b>	10	<20	<20	<20	<20
	30	83.66±0.34	42.06±2.50	70.11±1.06	50.27±2.00
<b>f</b>	10	<20	<20	22.34±2.06	<20
	30	84.77±1.18	29.80±1.66	68.27±1.19	47.74±1.21
cisplatin	10	42.61±2.33	86.84±0.50	53.03±2.29	20.84±0.81
	30	99.93±0.26	90.18±1.78	86.90±1.24	74.47±1.20
		[12.43]	[7.84]	[5.78]	[19.13]

**Table 2**

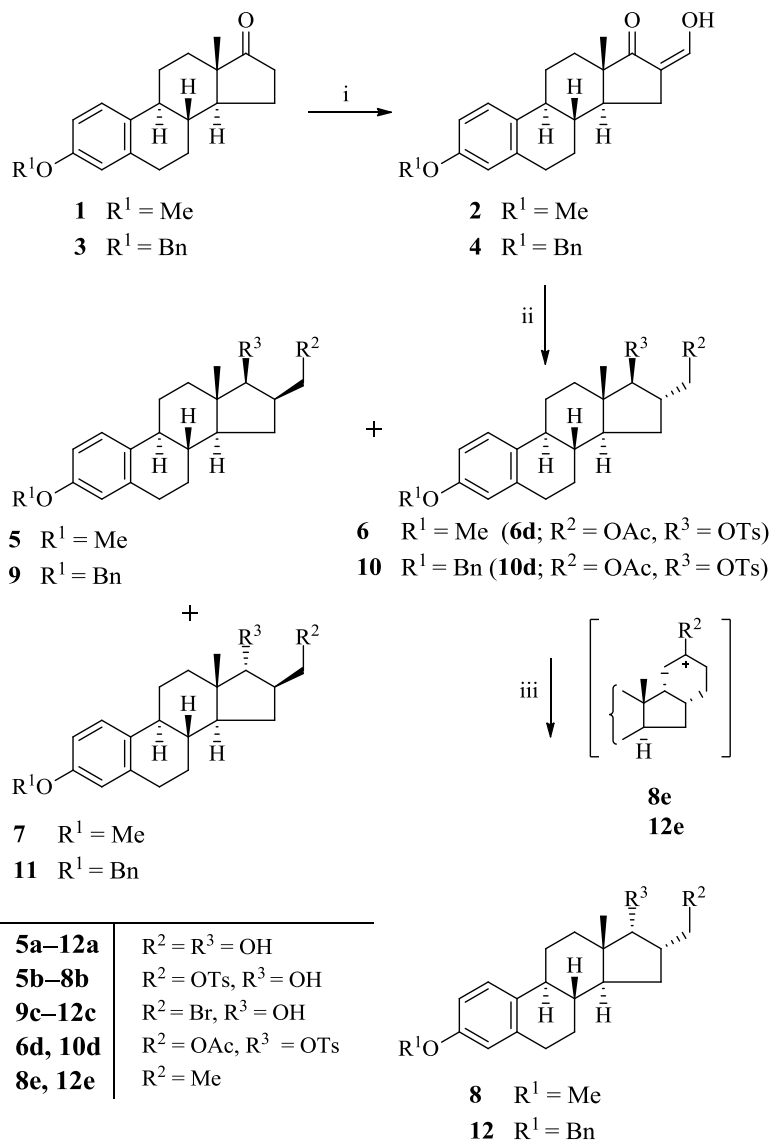
Growth Inhibition, % ± SEM [calculated IC <sub>50</sub> (μM)]						
	Conc. (μM)	HeLa	SiHa	MCF-7	MDA-MB- 231	NIH-3T3
<b>25</b>						
<b>a</b>	10	44.94±1.04	21.17±2.05	41.71±0.64	47.32±1.15	44.91±1.36
	30	52.45±2.39	66.23±0.86	64.32±0.56	71.49±0.75	91.28±0.50
<b>b</b>	10	51.49±3.62	49.36±1.69	44.58±1.50	93.00±0.26	44.81±1.50
	30	62.58±2.21	73.94±2.04	50.52±3.26	93.71±0.09	59.09±0.73
<b>c</b>	10	54.70±1.88	49.58±2.11	44.04±3.32	77.13±1.07	
	30	53.66±2.56	61.83±2.77	59.33±2.99	88.81±0.55	[3.33]
<b>d</b>	10	64.14±0.86	70.88±1.03	73.41±1.22	95.04±0.16	95.60±0.25
	30	90.12±0.99	94.14±0.29	80.16±3.40	95.60±0.06	98.22±0.04
<b>e</b>	10	<20	<20	41.63±2.83	21.96±0.73	
	30	92.12±0.25	89.25±0.68	97.00±0.11	95.22±0.91	
<b>f</b>	10	45.08±0.72	41.26±1.25	55.41±1.26	55.57±1.50	
	30	39.39±0.49	52.60±1.31	62.52±0.67	88.92±0.99	
<b>26</b>						
<b>a</b>	10	37.98±2.68	<20	72.42±2.19	46.43±2.05	85.50±1.22
	30	96.56±0.11	96.71±0.17	98.72±0.09	97.96±0.17	97.63±0.12
<b>b</b>	10	38.55±1.32	<20	31.80±1.35	17.13±2.36	
	30	43.97±2.23	<20	84.44±0.71	37.72±2.28	
<b>c</b>	10	36.30±1.45	<20	24.95±2.15	<20	
	30	35.53±1.24	<20	74.73±1.00	<20	
<b>d</b>	10	<20	<20	47.25±1.78	45.55±2.63	
	30	22.15±1.29	<20	57.30±0.77	59.79±1.22	
<b>e</b>	10	<20	<20	68.51±0.71	89.24±0.70	31.41±2.21
	30	96.98±0.33	96.91±0.14	99.12±0.07	97.73±0.23	99.01±0.05
<b>f</b>	10	21.62±3.46	<20	29.14±2.06	40.46±2.98	10.00±1.01
	30	30.79±2.92	27.28±1.90	43.28±1.53	76.93±1.60	23.40±0.60
<b>27</b>						
<b>a</b>	10	24.26±2.63	34.00±1.43	58.38±3.20	56.24±0.98	25.56±2.21
	30	85.22±1.32	82.68±1.25	97.21±0.10	84.18±0.44	99.24±0.07
<b>b</b>	10	37.10±1.77	39.59±1.17	51.92±1.00	56.44±0.98	
	30	52.08±2.08	69.54±1.24	65.12±1.91	71.81±0.96	
<b>c</b>	10	38.89±2.60	64.05±1.24	49.68±1.66	72.37±1.27	13.99±1.79
	30	55.93±2.39	83.34±1.31	61.26±1.72	85.81±1.04	29.56±1.17
<b>d</b>	10	34.23±1.39	30.04±2.07	47.03±1.25	55.77±1.03	
	30	47.74±0.78	39.96±2.34	42.43±1.69	57.71±1.00	
<b>e</b>	10	<20	21.53±1.81	35.74±1.33	<20	
	30	99.06±0.09	96.91±0.06	98.50±0.93	99.01±0.52	
<b>f</b>	10	<20	24.65±1.46	25.50±2.93	24.79±2.20	
	30	98.72±0.13	96.04±0.25	98.41±0.15	98.79±0.16	
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<b>a</b>	10	35.48±1.91	46.07±1.13	52.88±0.82	25.61±2.84	
	30	63.44±1.79	69.86±0.55	73.39±0.74	52.16±2.52	
<b>b</b>	10	39.75±2.45	<20	43.51±1.85	44.86±0.93	
	30	47.34±1.62	<20	42.28±1.44	43.73±2.25	
<b>c</b>	10	56.71±0.57	39.93±3.14	48.56±0.48	30.30±1.64	
	30	58.21±0.73	31.15±2.86	49.93±1.33	31.60±3.08	
<b>d</b>	10	74.18±1.15	76.88±0.49	75.97±0.89	86.12±0.33	70.18±1.15
	30	91.17±0.33	87.39±0.86	88.99±0.25	90.72±1.00	91.12±1.64
		[2.30]	[4.14]	[3.87]	[3.89]	[3.71]
<b>e</b>	10	27.42±2.16	<20	52.86±1.30	29.58±1.69	
	30	92.94±0.17	91.91±0.23	96.38±0.07	94.09±0.43	
<b>f</b>	10	30.97±1.02	39.85±1.24	50.60±0.65	31.89±2.92	
	30	91.88±0.26	90.94±0.18	95.12±0.10	92.56±0.34	
cisplatin	10	42.61±2.33	86.84±0.50	53.03±2.29	20.84±0.81	94.20±0.39
	30	99.93±0.26	90.18±1.78	86.90±1.24	74.47±1.20	96.44±0.17
		[12.43]	[7.84]	[5.78]	[19.13]	[3.23]



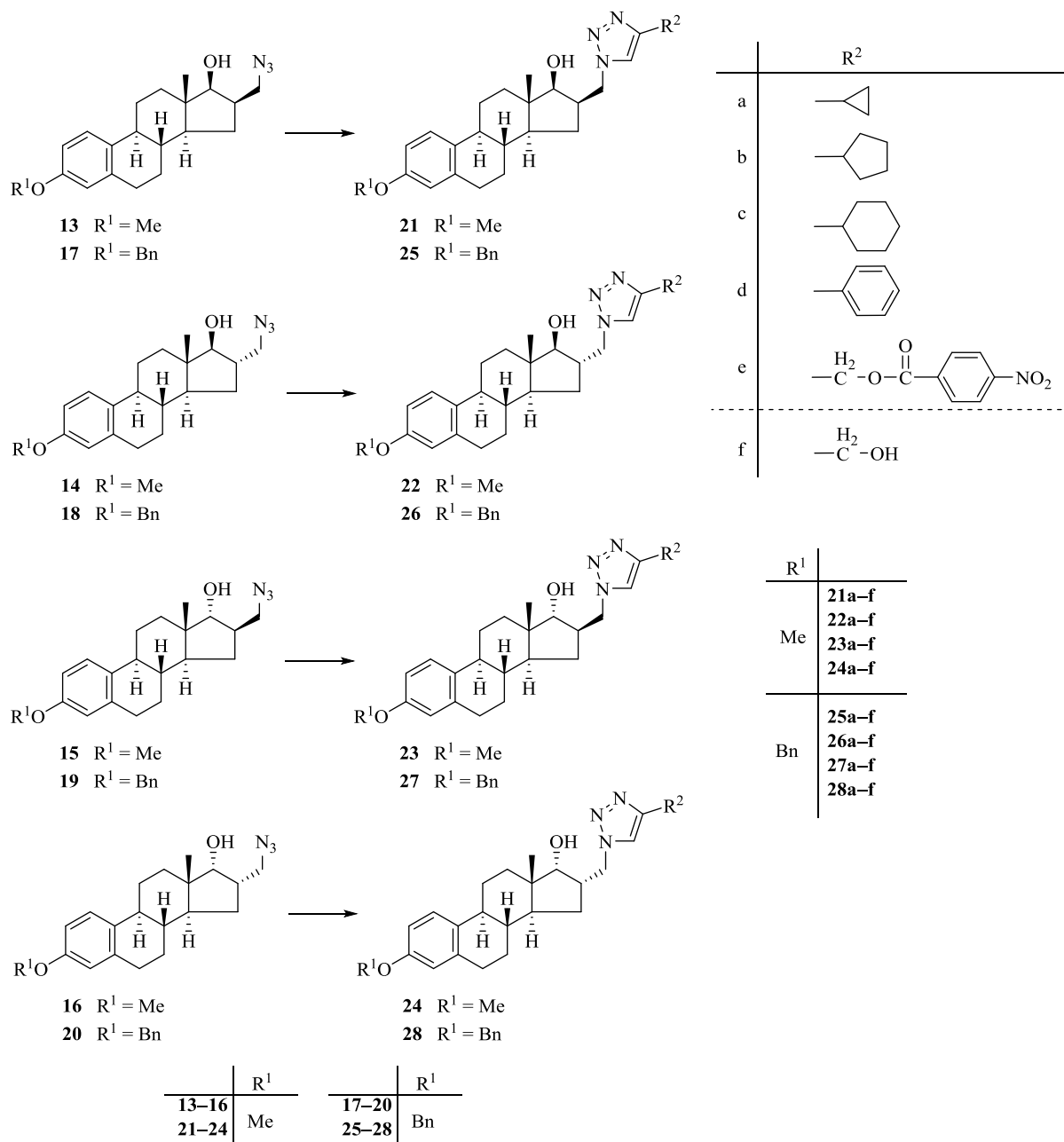
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**Scheme 1. Reagents and conditions:** (i) NaOMe, HCOOEt, anhydrous toluene, 50 °C; (ii)  $\text{KBH}_4$ , MeOH; (iii) KOAc,  $\text{CH}_3\text{COOH}$ , NaOMe/MeOH

**Scheme 1.**

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**Scheme 2.**

**Supplementary Material**

[Click here to download Supplementary Material: SCH\\_supporting\\_info\\_16-triazolylmethyl.pdf](#)