Efficient synthesis of novel A-ring-substituted 1,2,3-triazolylcholestane derivatives via catalytic azide-alkyne cycloaddition

Zalán Kádár,[a] Éva Frank,[a] Gyula Schneider,[a] Judit Molnár,[b] István Zupkó,[b] János Kóti,[c] Bruno Schönecker,[d] and János Wölfling[a,*]

[a]Department of Organic Chemistry, University of Szeged, Dóm tér 8, H-6720 Szeged, Hungary
[b]Department of Pharmacodynamics and Biopharmacy, University of Szeged, Eötvös u. 6, H-6720 Szeged, Hungary
[c]Spectroscopic Research Division, Gedeon Richter Ltd., Gyömrői út 19-21, H-1103 Budapest, Hungary
[d]Institute of Organic Chemistry and Macromolecular Chemistry, Friedrich Schiller University Jena, Humboldtstr. 10, D-07743 Jena, Germany
E-mail: wolfling@chem.u-szeged.hu

Dedicated to Professor Rainer Beckert on the occasion of his 60th birthday

DOI: http://dx.doi.org/10.3998/ark.5550190.0013.320

Abstract

A simple and convenient synthetic route is reported for the formation of novel 2α-triazolylcholestane derivatives. The scheme involves transformation of the starting cholestanone to the corresponding azido compound and efficient conversions of 2α-azido-5α-cholestan-3-one (**3**) with various terminal alkynes through use of the 'click' chemistry approach. Finally, the oxo group of these heterocyclic steroidal derivatives was reduced, and the resultant mixtures of epimeric triazolyl alcohols were separated. The antiproliferative activities of the synthesized 2-triazolyl-3-ketones against three human cancer cell lines were screened. Nevertheless, only a few of the tested compounds exerted moderate cell-growth inhibition.

Keywords: Click chemistry, steroid azides, triazoles, cholestanone, cycloaddition

Introduction

In the past few years, 'click' chemistry has become an increasingly attractive area in organic chemistry, as evidenced by a huge number of related publications. Click chemistry refers to a group of reactions that are fast, simple to use, versatile, regiospecific, and give high product

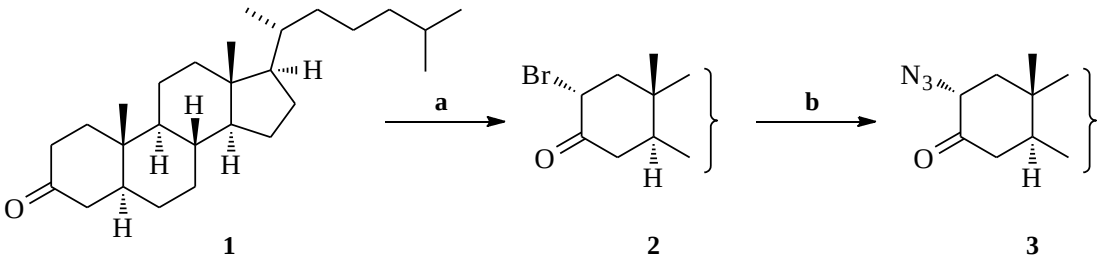
yields. While there are a number of reactions that fulfil the Sharpless criteria, the Cu-catalysed azide-alkyne 1,3-dipolar cycloaddition (CuAAC) is perhaps the best-known example of this group. The 1,2,3-triazole unit that results from the reaction has certain advantageous properties, such as high chemical stability, good hydrogen-bond-accepting ability, a strong dipole moment and an aromatic character.[1] Moreover, a number of compounds containing 1,2,3-triazoles have been reported to exert biological activity, including antibacterial,[2] antiallergic[3] and anti-HIV[4] effects.

Since the first reports,[5] several hundreds of articles exploring the synthetic possibilities of CuAAC have been published. Nevertheless, relatively few examples are to be found in the literature in which this reliable method is applied to steroid azides.[6] The syntheses of some 21-triazolyl derivatives of pregnenolone as potential anticancer agents were recently reported by Banday *et al*.[7]

In a continuation of our programme for the synthesis of steroidal heterocycles,[8] we have attempted to develop an effective route for the production of various 2-triazolyl derivatives of cholestanone, **4a**–**m**, and their reduced forms **5a**–**j** and **6a**–**j**. Since some steroid triazoles are known to exert antiproliferative activity,[7,9] it was decided to screen these compounds *in vitro* for their activities against a panel of three human cancer cell lines (HeLa, MCF7 and A431). Herein, we wish to describe the details of the synthesis of 2α-azido-5α-cholestan-3-one (**3**), followed by Huisgen 1,3-dipolar cycloaddition with different terminal alkynes and subsequent reduction of the resultant triazolyl ketones.

Results and Discussion

For the preparation of novel steroid derivatives via copper(I)-catalysed azide-alkyne cycloaddition (CuAAC), 2α-azido-5α-cholestan-3-one (**3**) was chosen as starting compound. The synthetic strategy for the preparation of the starting azide is illustrated in Scheme 1.



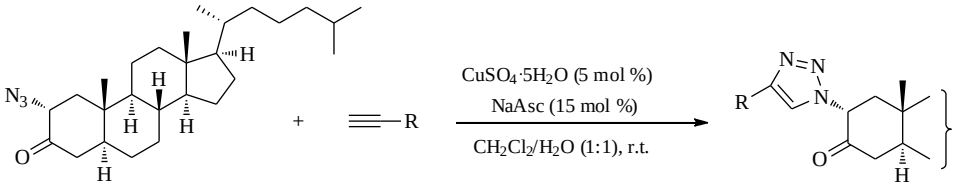
Scheme 1. Synthesis of 2α-azido-5α-cholestan-3-one. Reagents and conditions: (a) Br_2, HBr, AcOH; (b) NaN_3, DMF, 8 h.

2α-Bromo-5α-cholestan-3-one (**2**) was obtained via bromination from readily available cholestanone (**1**).[10] After purification of the α-bromo ketone, the compound was stirred for 8 h in

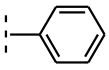
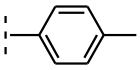
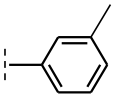
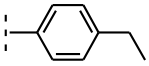
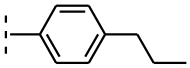
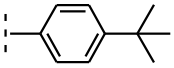
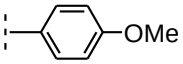
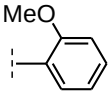
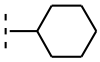
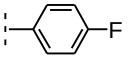
the presence of sodium azide to provide the desired 2α-azido ketone (**3**) in good yield. Substitutions α to carbonyl groups are known to follow an S_N2 mechanism, however in this particular case only 2α-azido ketone could be isolated. A base (NaN_3)-catalysed epimerization of the unisolated 2β-azido ketone can be assumed.[11]

Several A-ring-substituted 1,2,3-triazolylcholestan-3-ones (**4a**–**m**) were synthesized in very good yields by the reactions of **3** with various terminal alkynes (Table 1).

Table 1. 1,3-Dipolar cycloaddition with terminal alkynes



3 **4a-m**

Entry	R	Triazolyl ketone	Time (h)	Yield[a] (%)
1		**4a**	3	91
2		**4b**	3	92
3		**4c**	3	91
4		**4d**	2	88
5		**4e**	1.5	85
6		**4f**	1.5	92
7		**4g**	3	89
8		**4h**	4	90
9		**4i**	3	88
10		**4j**	3	84
11		**4k**	3	75
12		**4l**	6	86
13		**4m**	8	73

[a]Yields of purified isolated products.

Although there are a number of methods for generation of the active catalyst,[12] one of the most common techniques was chosen. The copper(I) species was generated *in situ* by the reduction of copper(II) sulfate with sodium ascorbate. Furthermore, an unusual solvent system (CH_2Cl_2 as a co-solvent with water) was used to eliminate the need for ligands and to simplify the reaction protocol.[13]

In all cases, total consumption of the starting compound was observed within 1.5–8 h at ambient temperature. The reactions were very selective, and the triazolyl ketones could generally be isolated in 84–92% yields; exceptions were **4k** and **4m** (75% and 73%, respectively). The trace quantities of copper and reagents remaining in the reaction mixtures were removed by flash chromatography.

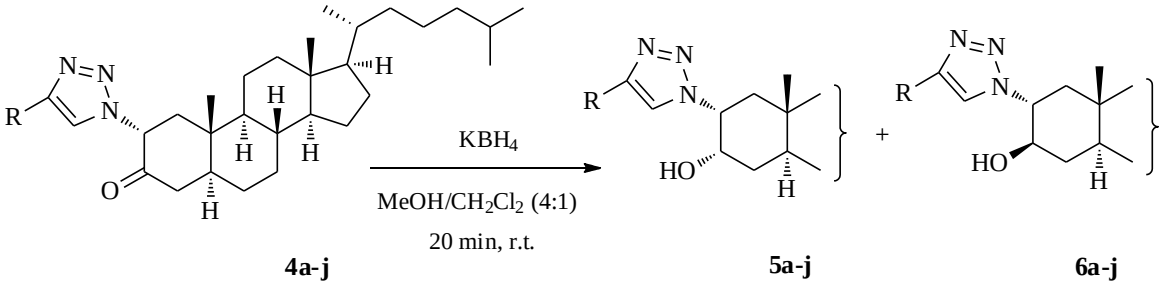
Treatment of **4a**–**j** with KBH_4 in MeOH/CH_2Cl_2 (4:1) resulted in two diastereomeric 3-hydroxy-2-triazolylcholestanes in an overall yield of ~ 95%. The mixture of epimers could be separated by flash chromatography to yield **5a**–**j** (3α-OH) and **6a**–**j** (3β-OH) in a ratio of ~ 1:2 (Table 2). A similar diastereomeric ratio was reported by Schönecker *et al* in the reduction of 2α-azidocholestan-3-one (**3**) with $LiBH_4$.[14]

The structures of all synthesized compounds were confirmed by ^{1}H and ^{13}C NMR measurements. The ^{1}H NMR spectra of **4a**–**h** and **4l**–**m** revealed the appearance of the new signals of the incorporated aryl groups at around 7–8 ppm as compared with the spectra of the starting material (**3**), while the 5'-H singlet was identified at around 7.7–8.1 ppm. Furthermore, in the spectra of **4i**–**k**, containing a cycloalkyl group, the aliphatic region was enriched by the signals of the appropriate CH_2 and CH protons, and the singlet of 5'-H appeared at around 7.2 ppm.

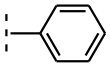
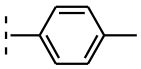
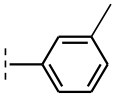
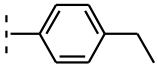
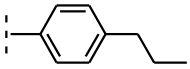
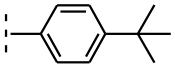
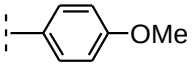
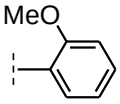
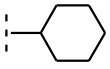
As far as the reduced epimers are concerned, significant differences were observed. For **5a**–**j** the broad 3-H singlet was identified at around 4.4 ppm, while the signal of 2-H appeared as a multiplet at around 4.7 ppm. Nevertheless, in the ^{1}H NMR spectra of **6a**–**j**, both peaks proved to be multiplets, with chemical shifts of ~ 4.1 ppm (3-H) and ~ 4.4 ppm (2-H).

The *exo*-heterocyclic steroidal ketones **4a**–**m** were tested *in vitro* on three malignant cell lines. None of the newly prepared compounds elicited greater than 50% inhibition of cancer cell proliferation, even at the higher applied concentration. Although there is no generally accepted threshold for efficacy, when the inhibition of cell growth is less than 25% at 30 μM, such a substance may be considered ineffective.[15] Compound **4a** exhibited a modest activity, which was eliminated by most of the substituents on the phenyl ring (**4b**–**4f**, **4h** and **4l**); only exception was the *p*-methoxy group (**4g**). Molecules containing a cycloalkyl group (**4j** and **4k**) or a heteroaromatic substituent (**4m**) exerted limited activity, and these structural elements might therefore be advantageous for the design of further analogues with more pronounced antiproliferative properties (Table 3). Treatment with all of the other tested compounds (**4b**–**4f**, **4h**–**i** and **4l**) resulted in an inhibition of cancer cell proliferation lower than 25% on every utilized cell line.

Table 2. Reduction of 2α-triazolyl-5α-cholestan-3-ones



4a-j **5a-j** **6a-j**

Entry	R	Triazolyl alcohols (**5** and **6**)	Yield[a] (%) of **5**	Yield[a] (%) of **6**
1		**a**	31	63
2		**b**	27	68
3		**c**	29	66
4		**d**	30	65
5		**e**	31	62
6		**f**	29	64
7		**g**	28	65
8		**h**	29	67
9		**i**	28	66
10		**j**	30	64

[a]Yields of purified isolated products.

Table 3. Antiproliferative effects of some selected triazolyl ketones

		Growth inhibition % (±SEM)		
Product	μM	HeLa	A431	MCF7
4a	10	16.5 (±2.7)	13.1 (±1.3)	9.0 (±2.4)
	30	32.1 (±1.6)	25.1 (±1.4)	28.6 (±2.2)
4g	10	25.0 (±2.6)	9.7 (±1.1)	14.2 (±2.2)
	30	40.9 (±1.4)	21.4 (±1.7)	33.2 (±1.2)
4j	10	10.9 (±2.4)	4.1 (±2.7)	14.6 (±2.1)
	30	32.3 (±1.5)	23.3 (±2.5)	26.0 (±2.4)
4k	10	3.7 (±2.6)	6.7 (±2.8)	3.6 (±2.2)
	30	29.7 (±2.3)	19.1 (±2.3)	25.7 (±2.4)
4m	10	16.8 (±2.6)	2.3 (±0.8)	1.2 (±1.6)
	30	43.5 (±2.3)	36.3 (±0.4)	29.5 (±1.6)
Cisplatin	10	42.6 (±2.3)	88.6 (±0.5)	53.0 (±2.3)
	30	99.9 (±0.3)	90.2 (±1.8)	86.9 (±1.3)

Conclusions

In conclusion, the efficient syntheses of several A-ring-substituted 1,2,3-triazolylcholestane derivatives were achieved by means of Huisgen 1,3-dipolar cycloaddition. The fast and reliable reactions were carried out under mild conditions that furnished the desired compounds in very good yields. An unusual, two-phase solvent system was applied to increase the solubility of the steroid and to eliminate the need for ligands. The cycloadducts were tested *in vitro* as concerns their antiproliferative activities, however just a few derivatives displayed limited cell growth inhibition. According to our observations different structural elements on the heteroring might have an impact on the cytostatic effects. Cycloalkyl group or a heteroaromatic substituent on the triazole moiety is generally favoured over substitution with aryl rings. The application of 'click chemistry' to further sterane skeletons is in progress and the promising results will be reported in due course.

Experimental Section

General. Melting points (mp) were determined on a Kofler block and are uncorrected. Specific rotations were measured in $CHCl_3$ (*c* 1) at 20 °C with a POLAMAT-A (Zeiss-Jena) polarimeter and are given in units of 10^{-1} deg cm^2 g^{-1}. The reactions were monitored by TLC on Kieselgel-G (Merck Si 254 F) layers (0.25 mm thick); solvent systems (ss): (A) CH_2Cl_2/EtOAc (95:5 v/v), (B) CH_2Cl_2/EtOAc (85:15 v/v).

The spots were detected by spraying with 5% phosphomolybdic acid in 50% aqueous phosphoric acid. The R_f values were determined for the spots observed by illumination at 254 and 365 nm. Flash chromatography: Merck silica gel 60, 40–63 μm. All solvents were distilled prior to use. Elementary analysis data were determined with a PerkinElmer CHN analyzer model 2400. IR spectra were recorded on a PerkinElmer FT-IR Spectrum 100. NMR spectra were recorded on a Bruker DRX 500 instrument at 500 MHz (^{1}H NMR) or 125 MHz (^{13}C NMR). Chemical shifts are reported in ppm (δ scale), and coupling constants (J) in Hz. For the determination of multiplicities, the *J*-MOD pulse sequence was used.

Synthesis of 2α-azido-5α-cholestan-3-one (3). To a solution of 2α-bromo-5α-cholestan-3-one **2** (931 mg, 2 mmol) in 20 mL DMF was added sodium azide (195 mg, 3 mmol). The reaction mixture was stirred at 40 ºC for 8 h and then poured into water. The precipitate that formed was filtered off and washed with water. Purification by column chromatography (CH_2Cl_2/hexane 1:1) afforded **3** as a white solid (720 mg, 84%), mp 146–148 ºC (lit.[16] mp 147–150 ºC). The spectroscopic data were consistent with those reported in the literature.

General procedure for the preparation of (4a–m)

Compound **3** (428 mg, 1 mmol) was dissolved in CH_2Cl_2 (10 mL), and a solution of $CuSO_4 \cdot 5H_2O$ (12.5 mg, 5 mol%) and sodium ascorbate (30 mg, 15 mol%) in water (10 mL) was poured into the organic phase. The appropriate terminal alkyne (1 mmol) was added to the reaction mixture, which was then stirred for 2-6 h at ambient temperature. After the consumption of the starting material (TLC monitoring), the two-phase solution was diluted with water (30 mL) and extracted with CH_2Cl_2 (2 x 30 mL). The combined organic layers were washed with water, dried over Na_2SO_4 and evaporated *in vacuo.* The resulting crude product was purified by flash chromatography with CH_2Cl_2/EtOAc (98:2) as eluent.

2α-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-5α-cholestan-3-one (4a). Alkyne: phenylacetylene (0.11 mL). After purification, **4a** was obtained as a white solid (482 mg, 91%), mp 171–173 ºC, R_f = 0.58 (ss A); $[\alpha]_D^{20}$ + 65 (*c* 1 in $CHCl_3$), IR (KBr): 2928, 1731, 1612, 1466, 1441, 1381, 1233, 1047, 765, 695 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.21 (s, 3H, 19-H_3), 2.34 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 5.53 (dd, 1H, *J* = 13.5 Hz and *J* = 5.5 Hz, 2-H), 7.32 (t, 1H, *J* = 7.5 Hz, 4”-H), 7.41 (t, 2H, *J* = 7.5 Hz, 3”- and 5”-H), 7.84-7.86 (overlapping multiplets, 3H, 5’-H, 2”- and 6”-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.6, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 28.0, 28.2, 28.5, 31.5, 34.9, 35.7, 36.1, 37.4, 39.5, 39.7, 42.6, 43.9, 47.0, 47.9, 53.7, 56.1, 56.2, 65.1 (C-2), 119.8 (C-5’), 125.7 (2C, C-2” and C-6”) 128.0 (C-4”), 128.7 (2C, C-3” and C-5”), 130.7 (C-1”), 147.6 (C-4’), 202.6 (C-3); Anal. Calcd for $C_{35}H_{51}N_3O$: C, 79.35; H, 9.70; N, 7.93. Found: C, 79.54; H, 9.63; N, 8.05.

2α-[4-(4-Tolyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestan-3-one (4b). Alkyne: 4-tolylacetylene (0.13 mL). After purification, **4b** was obtained as a white solid (500 mg, 92%), mp 177–179 ºC, R_f = 0.60 (ss A); $[\alpha]_D^{20}$ + 46 (*c* 1 in $CHCl_3$), IR (KBr): 2930, 1728, 1497, 1467, 1446, 1385, 1239,

1187, 1052, 835, 801 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.21 (s, 3H, 19-H_3), 2.33 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 2.37 (s, 3H, 4"-H_3), 5.53 (dd, 1H, *J* = 13.5 Hz and *J* = 5.5 Hz, 2-H), 7.22 (d, 2H, *J* = 8 Hz, 3"- and 5"-H), 7.73 (d, 2H, *J* = 8 Hz, 2"- and 6"-H), 7.78 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.3 (4"-CH_3), 21.5, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 28.0, 28.2, 28.4, 31.5, 34.9, 35.7, 36.1, 37.3, 39.5, 39.6, 42.5, 43.9, 47.0, 47.9, 53.6, 56.0, 56.1, 65.1 (C-2), 119.4 (C-5'), 125.7 (2C, C-2" and C-6"), 127.9 (C-1"), 129.4 (2C, C-3" and C-5"), 137.8 (C-4"), 147.7 (C-4'), 202.8 (C-3); Anal. Calcd for $C_{36}H_{53}N_3O$: C, 79.51; H, 9.82; N, 7.73. Found: C, 79.60; H, 9.61; N, 7.85.

2α-[4-(3-Tolyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestan-3-one (4c). Alkyne: 3-tolylacetylene (0.13 mL). After purification, **4c** was obtained as a white solid (495 mg, 91%), mp 172–174 °C, R_f = 0.62 (ss A); $[\alpha]_D^{20}$ + 54 (*c* 1 in $CHCl_3$), IR (KBr): 2946, 1732, 1612, 1591, 1469, 1445, 1383, 1228, 1054, 793 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.21 (s, 3H, 19-H_3), 2.34 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 2.39 (s, 3H, 3"-H_3), 5.53 (dd, 1H, *J* = 13.5 Hz and *J* = 6 Hz, 2-H), 7.13 (d, 1H, *J* = 7.5 Hz, 4"-H), 7.30 (t, 1H, *J* = 7.5 Hz, 5"-H), 7.61 (d, 1H, *J* = 7.5 Hz, 6"-H), 7.70 (s, 1H, 2"-H), 7.81 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.4 (3"-CH_3), 21.5, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 28.0, 28.2, 28.4, 31.5, 34.9, 35.7, 36.1, 37.3, 39.5, 39.6, 42.5, 43.9, 47.0, 47.9, 53.6, 56.0, 56.1, 65.1 (C-2), 119.7 (C-5'), (122.8, 126.4, 128.6, 128.8): (4C, C-2", C-4", C-5", C-6"), 130.5 (C-1"), 138.4 (C-3"), 147.7 (C-4'), 202.7 (C-3); Anal. Calcd for $C_{36}H_{53}N_3O$: C, 79.51; H, 9.82; N, 7.73. Found: C, 79.62; H, 9.95; N, 7.65.

2α-[4-(4-Ethylphenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestan-3-one (4d). Alkyne: 4-ethylphenylacetylene (0.14 mL). After purification, **4d** was obtained as a white solid (491 mg, 88%), mp 183–185 °C, R_f = 0.64 (ss A); $[\alpha]_D^{20}$ + 48 (*c* 1 in $CHCl_3$), IR (KBr): 2931, 1737, 1466, 1443, 1383, 1221, 1191, 1063, 835, 822 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.21 (s, 3H, 19-H_3), 1.26 (t, 3H, *J* = 7.5 Hz, Et-CH_3), 2.34 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 2.67 (q, 2H, *J* = 7.5 Hz, Et-CH_2), 5.53 (dd, 1H, *J* = 13.5 Hz and *J* = 5.5 Hz, 2-H), 7.25 (d, 2H, *J* = 8 Hz, 3"- and 5"-H), 7.76 (d, 2H, *J* = 8 Hz, 2"- and 6"-H), 7.79 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 15.5 (Et-CH_3), 18.6 (C-21), 21.5, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 28.0, 28.2, 28.4, 28.6 (Et-CH_2), 31.5, 34.9, 35.7, 36.1, 37.3, 39.4, 39.6, 42.5, 43.9, 47.0, 47.9, 53.6, 56.0, 56.1, 65.1 (C-2), 119.4 (C-5'), 125.7 (2C, C-2" and C-6"), 128.1 (C-1"), 128.2 (2C, C-3" and C-5"), 144.2 (C-4"), 147.7 (C-4'), 202.7 (C-3); Anal. Calcd for $C_{37}H_{55}N_3O$: C, 79.66; H, 9.94; N, 7.53. Found: C, 79.54; H, 10.02; N, 7.68.

2α-[4-(4-Propylphenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestan-3-one (4e). Alkyne: 4-propylphenylacetylene (0.16 mL). After purification, **4e** was obtained as a white solid (486 mg, 85%), mp 180–182 °C, R_f = 0.72 (ss A); $[\alpha]_D^{20}$ + 49 (*c* 1 in $CHCl_3$), IR (KBr): 2949, 1734, 1466, 1444, 1382, 1232, 1188, 1054, 798 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.95 (t, 3H, *J* = 7.5 Hz, Pr-

CH_3), 1.21 (s, 3H, 19-H_3), 2.34 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 2.61 (t, 2H, *J* = 7.5 Hz, CH_3-CH_2-$\underline{CH_2}$), 5.53 (dd, 1H, *J* = 13.5 Hz and *J* = 5.5 Hz, 2-H), 7.23 (d, 2H, *J* = 8 Hz, 3"- and 5"-H), 7.75 (d, 2H, *J* = 8 Hz, 2"- and 6"-H), 7.78 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 13.8 (Pr-CH_3), 18.6 (C-21), 21.5, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 24.4 (CH_3-$\underline{CH_2}$-CH_2), 28.0, 28.2, 28.4, 31.5, 34.9, 35.7, 36.1, 37.3, 37.8 (CH_3-CH_2-$\underline{CH_2}$), 39.4, 39.6, 42.5, 43.9, 47.0, 47.9, 53.6, 56.0, 56.1, 65.1 (C-2), 119.4 (C-5'), 125.6 (2C, C-2" and C-6") 128.1 (C-1"), 128.8 (2C, C-3" and C-5"), 142.6 (C-4"), 147.7 (C-4'), 202.7 (C-3); Anal. Calcd for $C_{38}H_{57}N_3O$: C, 79.81; H, 10.05; N, 7.35. Found: C, 79.95; H, 9.92; N, 7.58.

2α-[4-(4-Tert-butylphenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestan-3-one (4f). Alkyne: 4-*tert*-butylphenylacetylene (0.18 mL). After purification, **4f** was obtained as a white solid (539 mg, 92%), mp 188–190 ºC, R_f = 0.67 (ss A); $[\alpha]_D^{20}$ + 66 (*c* 1 in $CHCl_3$), IR (KBr): 2954, 1740, 1466, 1444, 1381, 1224, 1190, 1054, 824 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.21 (s, 3H, 19-H_3), 1.34 (s, 9H, 3 x *t*Bu-CH_3), 2.34 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 5.53 (dd, 1H, *J* = 13.5 Hz and *J* = 6 Hz, 2-H), 7.44 (d, 2H, *J* = 8.5 Hz, 3"- and 5"-H), 7.77 (d, 2H, *J* = 8.5 Hz, 2"- and 6"-H), 7.79 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.5, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 28.0, 28.2, 28.4, 31.3 (3C, 3 x *t*Bu-CH_3), 31.5, 34.6, 34.9, 35.7, 36.1, 37.3, 39.5, 39.6, 42.5, 43.9, 47.0, 47.9, 53.6, 56.0, 56.1, 65.1 (C-2), 119.5 (C-5'), 125.4 and 125.6 (4C, C-2",C-3",C-5",C-6"), 127.8 (C-1"), 147.6 (C-4'), 151.0 (C-4"), 202.7 (C-3); Anal. Calcd for $C_{39}H_{59}N_3O$: C, 79.95; H, 10.15; N, 7.17. Found: C, 80.12; H, 10.32; N, 7.35.

2α-[4-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestan-3-one (4g). Alkyne: 4-methoxyphenylacetylene (132 mg). After purification, **4g** was obtained as a white solid (498 mg, 89%), mp 179–181 ºC, R_f = 0.41 (ss A); $[\alpha]_D^{20}$ + 52 (*c* 1 in $CHCl_3$), IR (KBr): 2934, 1737, 1618, 1563, 1499, 1466, 1444, 1249, 1027, 834, 804 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.21 (s, 3H, 19-H_3), 2.34 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 3.83 (s, 3H, OCH_3) 5.52 (dd, 1H, *J* = 13.5 Hz and *J* = 5.5 Hz, 2-H), 6.95 (d, 2H, *J* = 8.5 Hz, 3"- and 5"-H), 7.73 (s, 1H, 5'-H), 7.76 (d, 2H, *J* = 8.5 Hz, 2"- and 6"-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.6, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 28.0, 28.2, 28.5, 31.5, 34.9, 35.7, 36.1, 37.4, 39.5, 39.7, 42.6, 43.9, 47.0, 47.9, 53.7, 55.3 (O-CH_3), 56.1, 56.2, 65.1 (C-2), 114.2 (2C, C-3" and C-5"), 118.9 (C-5'), 123.5 (C-1"), 127.0 (2C, C-2" and C-6"), 147.5 (C-4'), 159.5 (C-4"), 202.7 (C-3); Anal. Calcd for $C_{36}H_{53}N_3O_2$: C, 77.24; H, 9.54; N, 7.51. Found: C, 77.36; H, 9.68; N, 7.88.

2α-[4-(2-Methoxyphenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestan-3-one (4h). Alkyne: 2-methoxyphenylacetylene (0.13 mL). After purification, **4h** was obtained as a white solid (503 mg, 90%), mp 129–132 ºC, R_f = 0.57 (ss A); $[\alpha]_D^{20}$ + 51 (*c* 1 in $CHCl_3$), IR (KBr): 2943, 1735, 1606, 1584, 1551, 1491, 1466, 1445, 1244, 1070, 1049, 1019, 751 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.21 (s, 3H, 19-H_3), 2.36 and 2.56 (m, 2H, 4-H_2), 3.93 (s, 3H, OCH_3) 5.53 (dd, 1H, *J* = 13.5

Hz and *J* = 6 Hz, 2-H), 6.97 (d, 1H, *J* = 7.5 Hz, 3”-H), 7.07 (t, 1H, *J* = 7.5 Hz, 5”-H), 7.30 (td, 1H, *J* = 7.5 Hz and *J* = 1.5 Hz, 4”-H), 8.07 (s, 1H, 5’-H), 8.36 (dd, 1H, *J* = 7.5 Hz and *J* = 1.5 Hz, 6”-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.5 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 28.0, 28.2, 28.4, 31.5, 34.9, 35.7, 36.1, 37.3, 39.4, 39.6, 42.5, 43.9, 46.7, 47.7, 53.6, 55.3 (O-CH_3), 56.1, 56.2, 65.0 (C-2), 110.7, 119.5, 120.9, 123.0, 127.6, 128.7, 143.1 (C-4’), 155.6 (C-2”), 202.8 (C-3); Anal. Calcd for $C_{36}H_{53}N_3O_2$: C, 77.24; H, 9.54; N, 7.51. Found: C, 77.38; H, 9.42; N, 7.68.

2α-(4-Cyclopentyl-1*H*-1,2,3-triazol-1-yl)-5α-cholestan-3-one (4i). Alkyne: cyclopentyl acetylene (0.12 mL). After purification, **4i** was obtained as a white solid (459 mg, 88%), mp 162–164 ºC, R_f = 0.27 (ss A); $[\alpha]_D^{20}$ + 20 (*c* 1 in $CHCl_3$), IR (KBr): 2949, 1733, 1556, 1466, 1446, 1382, 1052, 828 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.84-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.20 (s, 3H, 19-H_3), 3.19 (m, 1H, 1”-H), 2.32 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 3.19 (m, 1H, 1”-H), 5.47 (dd, 1H, *J* = 13.5 Hz and *J* = 5.5 Hz, 2-H), 7.28 (s, 1H, 5’-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.6, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 25.2, 28.0, 28.2, 28.5, 31.6, 33.1, 33.2, 34.9, 35.7, 36.1, 36.9, 37.3, 39.5, 39.7, 42.6, 43.9, 47.0, 47.9, 53.7, 56.1, 56.2, 64.9 (C-2), 119.5 (C-5’), 152.5 (C-4’), 202.9 (C-3); Anal. Calcd for $C_{34}H_{55}N_3O$: C, 78.26; H, 10.62; N, 8.05. Found: C, 78.42; H, 10.76; N, 7.92.

2α-(4-Cyclohexyl-1*H*-1,2,3-triazol-1-yl)-5α-cholestan-3-one (4j). Alkyne: cyclohexylacetylene (0.13 mL). After purification, **4j** was obtained as a white solid (450 mg, 84%), mp 166–168 ºC, R_f = 0.27 (ss A); $[\alpha]_D^{20}$ + 20 (*c* 1 in $CHCl_3$), IR (KBr): 2932, 1742, 1552, 1467, 1447, 1380, 1219, 1056, 828 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.84-0.89 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.20 (s, 3H, 19-H_3), 2.32 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 2.76 (m, 1H, 1”-H), 5.46 (dd, 1H, *J* = 13.5 Hz and *J* = 5.5 Hz, 2-H), 7.26 (s, 1H, 5’-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.5, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 26.0, 26.1, 28.0, 28.2, 28.4, 31.5, 32.8, 32.9, 34.9, 35.3, 35.7, 36.1, 37.3, 39.5, 39.6, 42.5, 43.9, 47.0, 47.9, 53.7, 56.1, 56.2, 64.9 (C-2), 119.2 (C-5’), 153.5 (C-4’), 202.9 (C-3); Anal. Calcd for $C_{35}H_{57}N_3O$: C, 78.45; H, 10.72; N, 7.84. Found: C, 78.57; H, 10.88; N, 8.04.

2α-(4-Cyclopropyl-1*H*-1,2,3-triazol-1-yl)-5α-cholestan-3-one (4k). Alkyne: cyclopropyl-acetylene (0.085 mL). After purification, **4k** was obtained as a white solid (370 mg, 75%), mp 152–155 ºC, R_f = 0.28 (ss A); $[\alpha]_D^{20}$ + 22 (*c* 1 in $CHCl_3$), IR (KBr): 2944, 1732, 1568, 1468, 1445, 1233, 1058, 1035, 828 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.84-0.89 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.19 (s, 3H, 19-H_3), 2.32 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 5.45 (dd, 1H, *J* = 13.5 Hz and *J* = 5.5 Hz, 2-H), 7.26 (s, 1H, 5’-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 6.8 (C-1”), 7.6 (2C, C-2” and C-3”), 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.5, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 28.0, 28.2, 28.4, 31.5, 34.8, 35.7, 36.1, 37.3, 39.4, 39.6, 42.5, 43.9, 47.0, 47.9, 53.7, 56.1, 56.2, 64.9 (C-2), 119.7 (C-5’), 150.0 (C-4’), 202.9 (C-3); Anal. Calcd for $C_{32}H_{51}N_3O$: C, 77.84; H, 10.41; N, 8.51. Found: C, 77.65; H, 10.56; N, 8.72.

2α-[4-(4-Fluorophenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestan-3-one (4l). Alkyne: 4-fluorophenylacetylene (0.12 mL). After purification, **4l** was obtained as a white solid (471 mg, 86%), mp 185–188 ºC, R_f = 0.62 (ss A); $[\alpha]_D^{20}$ + 46 (*c* 1 in $CHCl_3$), IR (KBr): 2937, 1744, 1612, 1563, 1497, 1466, 1445, 1379, 1222, 1056, 840, 812 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.68 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.22 (s, 3H, 19-H_3), 2.35 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 5.53 (dd, 1H, *J* = 13.5 Hz and *J* = 6 Hz, 2-H), 7.10 (t, 2H, *J* = 9 Hz, 3"- and 5"-H), 7.78 (s, 1H, 5'-H), 7.81 (dd, 2H, *J* = 9 Hz and *J* = 5 Hz, 2"- and 6"-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.5 (C-19), 18.6 (C-21), 21.6, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 28.0, 28.2, 28.5, 31.5, 34.9, 35.7, 36.1, 37.4, 39.5, 39.7, 42.6, 43.9, 47.1, 48.0, 53.7, 56.1, 56.2, 65.2 (C-2), 115.7 (d, 2C, *J*= 21.5 Hz, C-3" and C-5"), 119.5 (C-5'), 126.9 (C-1"), 127.5 (d, 2C, *J* = 8 Hz, C-2" and C-6"), 146.8 (C-4'), 162.6 (d, *J* = 245 Hz, C-4") 202.6 (C-3); Anal. Calcd for $C_{35}H_{50}FN_3O$: C, 76.74; H, 9.20; N, 7.67. Found: C, 76.85; H, 9.37; N, 7.85.

2α-[4-(2-Pyridyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestan-3-one (4m). Alkyne: 2-ethynylpyridine (0.1 mL). After purification, **4m** was obtained as a white solid (387 mg, 73%), mp 214–216 ºC, R_f = 0.52 (ss B); $[\alpha]_D^{20}$ + 57 (*c* 1 in $CHCl_3$), IR (KBr): 2931, 1730, 1605, 1571, 1471, 1444, 1421, 1380, 1232, 1037, 792 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.67 (s, 3H, 18-H_3), 0.84-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 1.22 (s, 3H, 19-H_3), 2.34 (dd, 1H, *J* = 14 Hz and *J* = 3.5 Hz), 5.55 (dd, 1H, *J* = 13.5 Hz and *J* = 6 Hz, 2-H), 7.21 (dd, 1H, *J* = 6.5 Hz and *J* = 5 Hz, 5"-H), 7.76 (t, 1H, *J* = 6.5 Hz, 4"-H), 8.16 (d, 1H, 3"-H), 8.18 (s, 1H, 5'-H), 8.57 (d, 1H, *J* = 5 Hz, 6"-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.0 (C-18), 12.4 (C-19), 18.6 (C-21), 21.6, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 28.0, 28.2, 28.4, 31.5, 34.9, 35.7, 36.1, 37.3, 39.5, 39.6, 42.5, 43.8, 46.9, 47.9, 53.7, 56.0, 56.1, 65.2 (C-2), 120.2, 122.0, 122.7, 136.8, 148.3, 149.3, 150.3, 202.4 (C-3); Anal. Calcd for $C_{34}H_{50}N_4O$: C, 76.94; H, 9.49; N, 10.56. Found: C, 77.08; H, 9.36; N, 10.62.

General procedure for the preparation of (5a–j) and (6a–j)

Compound **4a**–**j** (1 mmol) was dissolved in a mixture of CH_2Cl_2 (10 mL) and MeOH (40 mL), cooled in an ice-bath to 15 ºC, and KBH_4 (430 mg, 8 mmol) was added in small portions. The mixture was allowed to stand for 20 min, then poured into water (100 mL), neutralized with diluted acetic acid and extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were washed with water, dried over Na_2SO_4 and evaporated *in vacuo*. The residue obtained was chromatographed on silica gel to afford **5a**–**j** and **6a**–**j**.

3α-Hydroxy-2α-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-5α-cholestane (5a) and 3β-hydroxy-2α-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-5α-cholestane (6a). Eluent: CH_2Cl_2/EtOAc (95:5), yielding **5a** as a white solid (165 mg, 31%), mp 264–266 ºC, R_f = 0.63 (ss B); IR (KBr): 3487, 3126, 2940, 1610, 1466, 1449, 1381, 1221, 1186, 1076, 975, 886, 822, 764, 693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.66 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 4.48 (br s, 1H, 3-H), 4.73 (m, 1H, 2-H), 7.25-7.30 (overlapping multiplets, 3H, 3"-, 4"- and 5"-H), 7.52 (d, 2H, *J* = 7.5 Hz, 2"- and 6"-H), 7.73 (s, 1H, 5'-H); ^{13}C

NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 18.7 (C-21), 20.9 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.8, 28.0, 28.2, 31.8, 35.0, 35.1, 35.8, 36.1, 37.1, 38.1, 38.4, 39.5, 39.8, 42.5, 54.0, 56.2, 56.4, 60.7 (C-2), 67.8 (C-3), 118.9 (C-5'), 125.2 (2C, C-2" and C-6"), 127.8 (C-4"), 128.7 (2C, C-3" and C-5"), 130.1 (C-1"), 146.5 (C-4'); Anal. Calcd for $C_{35}H_{53}N_3O$: C, 79.05; H, 10.05; N, 7.90. Found: C, 78.93; H, 10.24; N, 8.07.

Continued elution with CH_2Cl_2/EtOAc (90:10) resulted in **6a** as a white solid (335 mg, 63%), mp 278–279 ºC, R_f = 0.42 (ss B); IR (KBr): 3520, 3134, 2942, 1609, 1471, 1386, 1379, 1226, 1184, 1075, 1045, 764, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.66 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.98 (s, 3H, 19-H_3), 2.17 (dd, 1H, *J* = 13 Hz and *J* = 4 Hz), 4.11 (m, 1H, 3-H), 4.40 (m, 1H, 2-H), 7,31 (t, 1H, *J* = 7.5 Hz, 4"-H), 7.37 (t, 2H, *J* = 7.5 Hz, 3"- and 5"-H), 7.71 (d, 2H, *J* = 7.5 Hz, 2"- and 6"-H), 7.77 (s, 1H, 5'-H); Anal. Calcd for $C_{35}H_{53}N_3O$: C, 79.05; H, 10.05; N, 7.90. Found: C, 78.93; H, 10.22; N, 8.10.

3α-Hydroxy-2α-[4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestane (5b) and 3β-hydroxy-2α-[4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestane (6b). Eluent: CH_2Cl_2/EtOAc (95:5), yielding **5b** as a white solid (145 mg, 27%), mp 263–266 ºC, R_f = 0.65 (ss B); IR (KBr): 3304, 3158, 2930, 1444, 1383, 1234, 1072, 815 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.66 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 2.36 (s, 3H, 4"-CH_3), 4.45 (br s, 1H, 3-H), 4.71 (m, 1H, 2-H), 7.11 (d, 2H, *J*= 7.5 Hz, 3"- and 5"-H), 7.47 (d, 2H, *J* = 7.5 Hz, 2"- and 6"-H), 7.72 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 18.7 (C-21), 21.0 (C-11), 21.2 (4"-CH_3), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.8, 28.0, 28.2, 31.8, 35.0, 35.1, 35.8, 36.2, 37.1, 38.3, 38.4, 39.5, 39.8, 42.6, 54.1, 56.2, 56.4, 60.7 (C-2), 67.9 (C-3), 118.8 (C-5'), 125.2 (2C, C-2" and C-6"), 127.4 (C-1"), 129.3 (2C, C-3" and C-5"), 137.6 (C-4"), 146.7 (C-4'); Anal. Calcd for $C_{36}H_{55}N_3O$: C, 79.21; H, 10.16; N, 7.70. Found: C, 79.34; H, 10.25; N, 7.94.

Continued elution resulted in **6b** as a white solid (370 mg, 68%), mp 258–260 ºC, R_f = 0.46 (ss B); IR (KBr): 3512, 3144, 2934, 1497, 1466, 1443, 1387, 1227, 1183, 1108, 1073, 813 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.65 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 2.35 (s, 3H, 4"-CH_3), 4.10 (m, 1H, 3-H), 4.34 (m, 1H, 2-H), 7.11 (d, 2H, *J* = 8 Hz, 3"- and 5"-H), 7.46 (d, 2H, *J* = 8 Hz, 2"- and 6"-H), 7.68 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.9 (C-19), 18.7 (C-21), 21.3, 21.4, 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.9, 28.0, 28.2, 31.8, 35.0, 35.8, 36.2, 37.1, 39.5, 39.8, 42.6, 43.3, 44.4, 54.0, 56.2, 56.3, 64.8 (C-2), 72.8 (C-3), 119.9 (C-5'), 125.3 (2C, C-2" and C-6") 127.1 (C-1"), 129.3 (2C, C-3" and C-5"), 137.8, 146.3; Anal. Calcd for $C_{36}H_{55}N_3O$: C, 79.21; H, 10.16; N, 7.70. Found: C, 79.42; H, 10.25; N, 7.94.

3α-Hydroxy-2α-[4-(3-tolyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestane (5c) and 3β-hydroxy-2α-[4-(3-tolyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestane (6c). Eluent: CH_2Cl_2/EtOAc (95:5), yielding **5c** as a white solid (160 mg, 29%), mp 259–263 ºC, R_f = 0.66 (ss B); IR (KBr): 3252, 3157, 2931, 1614, 1590, 1444, 1382, 1236, 1078, 788 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.66 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 2.31 (s, 3H, 3"-CH_3), 4.46 (br s, 1H, 3-H), 4.72 (m, 1H, 2-H), 7.07 (d, 1H, *J* = 7.5 Hz, 4"-H), 7.23 (t,

1H, *J* = 7.5 Hz, 5”-H), 7.34 (s, 1H, 2”-H), 7.44 (d, 1H, *J* = 7.5 Hz, 6”-H), 7.75 (s, 1H, 5’-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 18.7 (C-21), 21.0 (C-11), 21.4 (3”-CH_3), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.8, 28.0, 28.2, 31.7, 35.0, 35.1, 35.8, 36.2, 37.1, 38.3, 38.4, 39.5, 39.8, 42.6, 54.1, 56.2, 56.4, 60.7 (C-2), 67.9 (C-3), 119.0 (C-5’), 122.4 (C-6”), 126.0 (C-2”), 128.6 and 128.7 (C-4” and C-5”), 130.1 (C-1”), 138.2 (C-3”), 146.7 (C-4’); Anal. Calcd for $C_{36}H_{55}N_3O$: C, 79.21; H, 10.16; N, 7.70. Found: C, 79.38; H, 10.35; N, 7.89.

Continued elution resulted in **6c** as a white solid (360 mg, 66%), mp 251–254 ºC, R_f = 0.46 (ss B); IR (KBr): 3526, 3131, 2934, 1615, 1588, 1446, 1385, 1224, 1169, 1077, 792, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.65 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.95 (s, 3H, 19-H_3), 2.32 (s, 3H, 3”-CH_3), 4.11 (m, 1H, 3-H), 4.34 (m, 1H, 2-H), 7.08 (d, 1H, *J* = 7.5 Hz, 4”-H), 7.23 (t, 1H, *J* = 7.5 Hz, 5”-H), 7.36 (s, 1H, 2”-H), 7.44 (d, 1H, *J* = 7.5 Hz, 6”-H), 7.69 (s, 1H, 5’-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.9 (C-19), 18.6 (C-21), 21.3 (C-11), 21.4 (3”-CH_3), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.9, 28.0, 28.2, 31.8, 35.0, 35.8, 36.1, 36.2, 37.1, 39.5, 39.8, 42.5, 43.4, 44.4, 54.0, 56.2, 56.3, 64.7 (C-2), 72.9 (C-3), 120.0 (C-5’), 122.5 (C-6”), 126.1 (C-2”), 128.5 and 128.7 (2C, C-4” and C-5”), 130.0 (C-1”), 138.2 (C-3”), 146.6 (C-4’); Anal. Calcd for $C_{36}H_{55}N_3O$: C, 79.21; H, 10.16; N, 7.70. Found: C, 79.45; H, 10.38; N, 7.85.

2*α*-[4-(4-Ethylphenyl)-1*H*-1,2,3-triazol-1-yl]-3*α*-hydroxy-5*α*-cholestane (5d) and 2*α*-[4-(4-ethylphenyl)-1*H*-1,2,3-triazol-1-yl]-3β-hydroxy-5*α*-cholestane (6d). Eluent: CH_2Cl_2/EtOAc (95:5), yielding **5d** as a white solid (170 mg, 30%), mp 254–256 ºC, R_f = 0.71 (ss B); IR (KBr): 3267, 3156, 1446, 1367, 1216, 1078, 1041, 818 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.66 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 1.26 (t, 3H, *J* = 7.5 Hz, Et-CH_3), 2.65 (q, 2H, *J* = 7.5 Hz, Et-CH_2), 4.46 (br s, 1H, 3-H), 4.72 (m, 1H, 2-H), 7.11 (d, 2H, *J* = 8 Hz, 3”- and 5”-H), 7.47 (d, 2H, *J* = 8 Hz, 2”- and 6”-H), 7.74 (s, 1H, 5’-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 15.5 (Et-CH_3), 18.7 (C-21), 21.0 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.8, 28.0, 28.2, 28.6 (Et-CH_2), 31.7, 35.1, 35.2, 35.8, 36.2, 37.2, 38.3, 38.4, 39.5, 39.9, 42.6, 54.1, 56.2, 56.4, 60.8 (C-2), 67.8 (C-3), 118.9 (C-5’), 125.3 (2C, C-2” and C-6”) 127.3 (C-1”), 128.1 (2C, C-3” and C-5”), 144.1 (C-4”), 146.5 (C-4’); Anal. Calcd for $C_{37}H_{57}N_3O$: C, 79.38; H, 10.26; N, 7.51. Found: C, 79.54; H, 10.38; N, 7.65.

Continued elution resulted in **6d** as a white solid (365 mg, 65%), mp 249–252 ºC, R_f = 0.51 (ss B); IR (KBr): 3513, 3143, 2932, 1498, 1444, 1380, 1225, 1181, 1074, 1011, 822 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.65 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 1.24 (t, 3H, *J* = 7.5 Hz, Et-CH_3), 2.64 (q, 2H, *J* = 7.5 Hz, Et-CH_2), 4.06 (m, 1H, 3-H), 4.41 (m, 1H, 2-H), 7.15 (d, 2H, *J* = 8 Hz, 3”- and 5”-H), 7.54 (d, 2H, *J* = 8 Hz, 2”- and 6”-H), 7.82 (s, 1H, 5’-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.9 (C-19), 15.4 (Et-CH_3), 18.7 (C-21), 21.4 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.9, 28.0, 28.2, 28.7 (Et-CH_2), 31.8, 35.0, 35.8, 36.2, 36.3, 37.1, 39.5, 39.8, 42.6, 43.2, 44.4, 54.0, 56.2, 56.3, 65.2 (C-2), 72.8 (C-3), 120.6 (C-5’), 125.7 (2C, C-2” and C-6”) 126.1 (C-1”),

128.3 (2C, C-3" and C-5"), 144.8 (C-4"), 145.7 (C-4'); Anal. Calcd for $C_{37}H_{57}N_3O$: C, 79.38; H, 10.26; N, 7.51. Found: C, 79.53; H, 10.38; N, 7.85.

3α-Hydroxy-2α-[4-(4-propylphenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestane (5e) and 3β-hydroxy-2α-[4-(4-propylphenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestane (6e). Eluent: CH_2Cl_2/EtOAc (95:5), yielding **5e** as a white solid (180 mg, 31%), mp 262–265 ºC, R_f = 0.74 (ss B); IR (KBr): 3269, 3157, 2926, 1465, 1446, 1367, 1216, 1077, 1041, 811 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.66 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.93 (s, 3H, 19-H_3), 0.97 (t, 3H, *J* = 7.5 Hz, Pr-CH_3), 2.58 (t, 2H, *J* = 7.5 Hz, CH_3-CH_2-$\underline{CH_2}$), 4.47 (br s, 1H, 3-H), 4.71 (m, 1H, 2-H), 7.09 (d, 2H, *J* = 8 Hz, 3"- and 5"-H), 7.45 (d, 2H, *J* = 8 Hz, 2"- and 6"-H), 7.70 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 13.8 (Pr-CH_3), 18.7 (C-21), 21.0 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 24.5 (CH_3-$\underline{CH_2}$-CH_2), 27.8, 28.0, 28.2, 31.7, 35.0, 35.1, 35.8, 36.1, 37.1, 37.8 (CH_3-CH_2-$\underline{CH_2}$), 38.2, 38.4, 39.5, 39.8, 42.6, 54.0, 56.2, 56.4, 60.7 (C-2), 67.8 (C-3), 118.7 (C-5'), 125.1 (2C, C-2" and C-6") 127.6 (C-1"), 128.7 (2C, C-3" and C-5"), 142.4 (C-4"), 146.7 (C-4'); Anal. Calcd for $C_{38}H_{59}N_3O$: C, 79.53; H, 10.36; N, 7.32. Found: C, 79.82; H, 10.28; N, 7.45.

Continued elution resulted in **6e** as a white solid (355 mg, 62%), mp 218–220 ºC, R_f = 0.55 (ss B); IR (KBr): 3497, 3250, 2931, 1500, 1466, 1446, 1382, 1237, 1077, 1047, 797 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.65 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 0.96 (t, 3H, *J* = 7.5 Hz, Pr-CH_3), 2.58 (t, 2H, *J* = 7.5 Hz, CH_3-CH_2-$\underline{CH_2}$), 4.11 (m, 1H, 3-H), 4.34 (m, 1H, 2-H), 7.10 (d, 2H, *J* = 8 Hz, 3"- and 5"-H), 7.46 (d, 2H, *J* = 8 Hz, 2"- and 6"-H), 7.67 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.8 (C-19), 13.8 (Pr-CH_3), 18.6 (C-21), 21.3 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 24.4, 27.9, 28.0, 28.2, 31.8, 35.0, 35.8, 36.1, 36.2, 37.1, 37.8, 39.5, 39.8, 42.5, 43.3, 44.4, 54.0, 56.2, 56.3, 64.9 (C-2), 72.9 (C-3), 120.0 (C-5'), 125.3 (2C, C-2" and C-6") 127.2 (C-1"), 128.8 (2C, C-3" and C-5"), 142.7 (C-4"), 146.3 (C-4'); Anal. Calcd for $C_{38}H_{59}N_3O$: C, 79.53; H, 10.36; N, 7.32. Found: C, 79.81; H, 10.45; N, 7.48.

2α-[4-(4-Tert-butylphenyl)-1*H*-1,2,3-triazol-1-yl]-3α-hydroxy-5α-cholestane (5f) and 2α-[4-(4-tert-butylphenyl)-1*H*-1,2,3-triazol-1-yl]-3β-hydroxy-5α-cholestane (6f). Eluent: CH_2Cl_2/EtOAc (95:5), yielding **5f** as a white solid (170 mg, 29%), mp 282–285 ºC, R_f = 0.76 (ss B); IR (KBr): 3278, 3161, 1444, 1383, 1367, 1235, 1078, 985, 841, 819 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.66 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 1.34 (s, 9H, 3 x *t*Bu-CH_3), 4.47 (br s, 1H, 3-H), 4.72 (m, 1H, 2-H), 7.30 (d, 2H, *J* = 8,5 Hz, 3"- and 5"-H), 7.44 (d, 2H, *J* = 8,5 Hz, 2"- and 6"-H), 7.69 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 18.7 (C-21), 21.0 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.8, 28.0, 28.2, 31.3 (3C, 3 x *t*Bu-CH_3), 31.8, 34.6, 35.1, 35.2, 35.8, 36.2, 37.2, 38.2, 38.4, 39.5, 39.9, 42.6, 54.1, 56.2, 56.4, 60.7 (C-2), 67.8 (C-3), 118.7 (C-5'), 124.9 and 125.5 (4C, C-2", C-3", C-5", C-6"), 127.3 (C-1"), 146.5 (C-4'), 150.8 (C-4"); Anal. Calcd for $C_{39}H_{61}N_3O$: C, 79.67; H, 10.46; N, 7.15. Found: C, 79.85; H, 10.68; N, 7.34.

Continued elution resulted in **6f** as a white solid (375 mg, 64%), mp 262–265 ºC, R_f = 0.56 (ss B); IR (KBr): 3270, 2931, 1496, 1467, 1384, 1365, 1234, 1077, 1045, 845, 830, 799 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.65 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.96 (s, 3H, 19-H_3), 1.34 (s, 9H, 3x *t*Bu-CH_3), 4.15 (m, 1H, 3-H), 4.33 (m, 1H, 2-H), 7.31 (d, 2H, *J* = 8 Hz, 3"- and 5"-H), 7.46 (d, 2H, *J* = 8 Hz, 2"- and 6"-H), 7.65 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.9 (C-19), 18.7 (C-21), 21.4 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.9, 28.0, 28.2, 31.3 (3C, 3x *t*Bu-CH_3), 31.8, 34.6, 35.0, 35.8, 36.1, 36.2, 37.1, 39.5, 39.8, 42.6, 43.2, 44.4, 54.0, 56.2, 56.3, 64.7 (C-2), 72.9 (C-3), 119.8 (C-5'), 125.0 (2C), 125.5 (2C), 127.2, 146.4 (C-4"), 150.9 (C-4'); Anal. Calcd for $C_{39}H_{61}N_3O$: C, 79.67; H, 10.46; N, 7.15. Found: C, 79.81; H, 10.37; N, 7.34.

3α-Hydroxy-2α-[4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestane (5g) and 3β-hydroxy-2α-[4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl]-5α-cholestane (6g). Eluent: CH_2Cl_2/EtOAc (95:5), yielding **5g** as a white solid (155 mg, 28%), mp 266–269 ºC, R_f = 0.48 (ss B); IR (KBr): 3254, 3156, 2927, 1618, 1579, 1558, 1498, 1466, 1445, 1367, 1235, 1180, 1081, 1033, 834, 820 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.66 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.93 (s, 3H, 19-H_3), 3.82 (s, 3H, OCH_3), 4.46 (br s, 1H, 3-H), 4.70 (m, 1H, 2-H), 6.82 (d, 2H, *J* = 8.5 Hz, 3"- and 5"-H), 7.47 (d, 2H, *J* = 8.5 Hz, 2"- and 6"-H), 7.66 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 18.7 (C-21), 21.0 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.8, 28.0, 28.2, 31.7, 35.0, 35.1, 35.8, 36.1, 37.1, 38.2, 38.4, 39.5, 39.8, 42.6, 54.0, 55.3 (OCH_3), 56.2, 56.4, 60.7 (C-2), 67.8 (C-3), 114.1 (2C, C-3" and C-5"), 118.3 (C-5'), 123.0 (C-1"), 126.5 (2C, C-2" and C-6"), 146.4 (C-4'), 159.4 (C-4"); Anal. Calcd for $C_{36}H_{55}N_3O_2$: C, 76.96; H, 9.87; N, 7.48. Found: C, 77.12; H, 10.02; N, 7.32.

Continued elution with CH_2Cl_2/EtOAc (90:10) resulted in **6g** as a white solid (365 mg, 65%), mp 238–241 ºC, R_f = 0.30 (ss B); IR (KBr): 3521, 3135, 2940, 1618, 1563, 1498, 1467, 1387, 1248, 1185, 1074, 1039, 835, 814 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.65 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 3.82 (s, 3H, OCH_3), 4.11 (m, 1H, 3-H), 4.31 (m, 1H, 2-H), 6.84 (d, 2H, *J* = 8.5 Hz, 3"- and 5"-H), 7.47 (d, 2H, *J* = 8.5 Hz, 2"- and 6"-H), 7.59 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.8 (C-19), 18.6 (C-21), 21.3 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.9, 28.0, 28.2, 31.8, 35.0, 35.8, 36.1, 36.2, 37.1, 39.5, 39.8, 42.6, 43.3, 44.4, 53.9, 55.3 (OCH_3), 56.2, 56.3, 64.8 (C-2), 72.9 (C-3), 114.1 (2C, C-3" and C-5"), 119.4 (C-5'), 122.8 (C-1"), 126.7 (2C, C-2" and C-6"), 146.1 (C-4'), 159.4 (C-4"); Anal. Calcd for $C_{36}H_{55}N_3O_2$: C, 76.96; H, 9.87; N, 7.48. Found: C, 77.05; H, 9.92; N, 7.55.

3α-Hydroxy-2α-[4-(2-methoxyphenyl)-1H-1,2,3-triazol-1-yl]-5α-cholestane (5h) and 3β-hydroxy-2α-[4-(2-methoxyphenyl)-1H-1,2,3-triazol-1-yl]-5α-cholestane (6h). Eluent: CH_2Cl_2/EtOAc (95:5), yielding **5h** as a white solid (165 mg, 29%), mp 238–241 ºC, R_f = 0.65 (ss B); IR (KBr): 3250, 3191, 1607, 1586, 1547, 1492, 1467, 1441, 1245, 1072, 1027, 754 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.66 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.95 (s, 3H, 19-H_3), 3.82 (s, 3H, OCH_3), 4.45 (br s, 1H, 3-H), 4.72 (m, 1H,

2-H), 6.82 (d, 1H, *J* = 7.5 Hz, 3”-H), 7.02 (t, 1H, *J* = 7.5 Hz, 5”-H), 7.25 (t, 1H, *J* = 7.5 Hz, 4”-H), 8.06 (s, 1H, 5’-H), 8.17 (d, 1H, *J* = 7.5 Hz, 6”-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 18.7 (C-21), 21.0 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.8, 28.0, 28.2, 31.7, 35.0, 35.1, 35.8, 36.2, 37.2, 38.3, 38.4, 39.5, 39.9, 42.6, 54.0, 55.2 (OCH_3), 56.2, 56.4, 60.8 (C-2), 67.9 (C-3), 110.5 (C-3”), 118.6 (C-1”), 120.9 (C-5”), 122.7 (C-5’), 127.4 and 128.8 (C-4” and C-6”), 142.1 (C-4’), 155.5 (C-2”); Anal. Calcd for $C_{36}H_{55}N_3O_2$: C, 76.96; H, 9.87; N, 7.48. Found: C, 77.08; H, 10.04; N, 7.32.

Continued elution resulted in **6h** as a white solid (375 mg, 67%), mp 206–209 ºC, R_f = 0.40 (ss B); IR (KBr): 3511, 2931, 1607, 1582, 1551, 1490, 1465, 1440, 1247, 1070, 1029, 752 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.65 (s, 3H, 18-H_3), 0.85-0.9 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.97 (s, 3H, 19-H_3), 3.75 (s, 3H, OCH_3), 4.17 (m, 1H, 3-H), 4.38 (m, 1H, 2-H), 6.77 (d, 1H, *J* = 7.5 Hz, 3”-H), 7.00 (t, 1H, *J* = 7.5 Hz, 5”-H), 7.22 (t, 1H, *J* = 7.5 Hz, 4”-H), 8.03 (s, 1H, 5’-H), 8.10 (d, 1H, *J* = 7.5 Hz, 6”-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.9 (C-19), 18.6 (C-21), 21.3 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 27.9, 28.0, 28.2, 31.8, 35.1, 35.8, 36.1, 36.2, 37.1, 39.5, 39.8, 42.6, 43.3, 44.4, 54.0, 55.1 (OCH_3), 56.2, 56.3, 64.8 (C-2), 73.0 (C-3), 110.4 (C-3”), 118.2 (C-1”), 120.8 (C-5”), 123.9 (C-5’), 127.3 and 128.7 (2C, C-4” and C-6”), 141.5 (C-4’), 155.5 (C-2”); Anal. Calcd for $C_{36}H_{55}N_3O_2$: C, 76.96; H, 9.87; N, 7.48. Found: C, 77.03; H, 9.92; N, 7.67.

2*α*-(4-Cyclopentyl-1*H*-1,2,3-triazol-1-yl)-3*α*-hydroxy-5*α*-cholestane (5i) and 2*α*-(4-cyclopentyl-1*H*-1,2,3-triazol-1-yl)-3β-hydroxy-5*α*-cholestane (6i). Eluent: CH_2Cl_2/EtOAc (90:10), yielding **5i** as a white solid (145 mg, 28%), mp 192–195 ºC, R_f = 0.38 (ss B); IR (KBr): 3265, 3160, 2931, 1445, 1383, 1221, 1120, 1062, 890 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.64 (s, 3H, 18-H_3), 0.84-0.89 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.91 (s, 3H, 19-H_3), 3.08 (m, 1H, 1”-H), 4.35 (br s, 1H, 3-H), 4.61 (m, 1H, 2-H), 7.36 (s, 1H, 5’-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 18.6 (C-21), 20.9 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 25.1 (2C, C-3”, C-4”), 27.7, 28.0, 28.2, 31.7, 33.0 (2C, C-2”, C-5”), 35.0, 35.1, 35.7, 36.1, 36.6, 37.1, 38.2, 38.6, 39.5, 39.8, 42.5, 54.0, 56.1, 56.3, 60.4 (C-2), 67.8 (C-3), 119.4 (C-5’), 151.4 (C-4’); Anal. Calcd for $C_{34}H_{57}N_3O$: C, 77.96; H, 10.97; N, 8.02. Found: C, 77.85; H, 11.08; N, 8.19.

Continued elution with CH_2Cl_2/EtOAc (85:15) resulted in **6i** as a white solid (345 mg, 66%), mp 207–209 ºC, R_f = 0.26 (ss B); IR (KBr): 3521, 3140, 2939, 1550, 1466, 1451, 1380, 1216, 1076, 1050 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.64 (s, 3H, 18-H_3), 0.84-0.89 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.93 (s, 3H, 19-H_3), 3.04 (m, 1H, 1”-H), 4.06 (m, 1H, 3-H), 4.30 (m, 1H, 2-H), 7.29 (s, 1H, 5’-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.9 (C-19), 18.6 (C-21), 21.3 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 25.1 (2C, C-3” and C-4”), 27.9, 28.0, 28.2, 31.8, 33.0 (2C, C-2” and C-5”), 35.0, 35.7, 36.0, 36.1, 36.6, 37.0, 39.5, 39.8, 42.5, 43.5, 44.4, 54.0, 56.1, 56.3, 64.1 (C-2), 72.7 (C-3), 119.7 (C-5’), 151.3 (C-4’); Anal. Calcd for $C_{34}H_{57}N_3O$: C, 77.96; H, 10.97; N, 8.02. Found: C, 77.83; H, 11.06; N, 8.14.

2*α*-(4-Cyclohexyl-1*H*-1,2,3-triazol-1-yl)-3*α*-hydroxy-5*α*-cholestane (5j) and 2*α*-(4-cyclohexyl-1*H*-1,2,3-triazol-1-yl)-3β-hydroxy-5*α*-cholestane (6j). Eluent: CH_2Cl_2/EtOAc

(90:10), yielding **5j** as a white solid (160 mg, 30%), mp 225–228 ºC, R_f = 0.40 (ss B); IR (KBr): 3522, 3127, 2930, 1466, 1447, 1382, 1210, 1054, 887 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.65 (s, 3H, 18-H_3), 0.85-0.90 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.91 (s, 3H, 19-H_3), 2.68 (m, 1H, 1''-H), 4.35 (br s, 1H, 3-H), 4.61 (m, 1H, 2-H), 7.35 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.2 (C-19), 18.6 (C-21), 20.9 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.1, 26.0, 26.1, 27.7, 28.0, 28.2, 31.7, 32.8, 32.9, 35.0, 35.1, 35.2, 35.8, 36.1, 37.1, 38.2, 38.7, 39.5, 39.8, 42.6, 54.0, 56.2, 56.4, 60.4 (C-2), 67.9 (C-3), 119.1 (C-5'), 152.5 (C-4'); Anal. Calcd for $C_{35}H_{59}N_3O$: C, 78.16; H, 11.06; N, 7.81. Found: C, 78.32; H, 9.98; N, 7.93.

Continued elution with CH_2Cl_2/EtOAc (85:15) resulted in **6j** as a white solid (345 mg, 64%), mp 232–233 ºC, R_f = 0.25 (ss B); IR (KBr): 3520, 3137, 2933, 1544, 1466, 1446, 1380, 1213, 1076, 1049 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$); δ [ppm] = 0.65 (s, 3H, 18-H_3), 0.84-0.89 (overlapping multiplets, 9H, 21-, 26- and 27-H_3), 0.94 (s, 3H, 19-H_3), 2.67 (m, 1H, 1''-H), 4.04 (m, 1H, 3-H), 4.32 (m, 1H, 2-H), 7.29 (s, 1H, 5'-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ [ppm] = 12.1 (C-18), 12.9 (C-19), 18.6 (C-21), 21.4 (C-11), 22.5 and 22.8 (C-26 and C-27), 23.8, 24.2, 26.0, 26.1, 27.9, 28.0, 28.2, 31.8, 32.8, 32.9, 33.0, 35.0, 35.1, 35.8, 36.0, 36.1, 37.1, 39.5, 39.8, 42.5, 43.5, 44.4, 54.0, 56.2, 56.3, 64.0 (C-2), 72.8 (C-3), 119.3 (C-5'), 152.5 (C-4'); Anal. Calcd for $C_{35}H_{59}N_3O$: C, 78.16; H, 11.06; N, 7.81. Found: C, 78.34; H, 11.23, N, 7.67.

Determination of antiproliferative effects

Human cancer cell lines were purchased from ECACC (Salisbury, UK). HeLa (cervix adenocarcinoma), A431 (skin epidermoid carcinoma) and MCF7 (breast adenocarcinoma) cells were cultivated in minimal essential medium supplemented with 10% foetal bovine serum, 1% non-essential amino acids and an antibiotic-antimycotic mixture.

Near-confluent cancer cells were seeded onto a 96-well microplate (5000/well) and attached to the bottom of the well overnight. On the second day, 200 µL of new medium containing the tested compound (at 10 or 30 µM) was added. After incubation for 72 h at 37 ºC in humidified air with 5% CO_2, the living cells were assayed by the addition of 20 µL of 5 mg/mL MTT solution. MTT was converted by intact mitochondrial reductase and precipitated as blue crystals during a 4 h contact period. The medium was then removed and the precipitated crystals were dissolved in 100 µL DMSO during a 60 min period of shaking at 25 ºC. Finally, the reduced MTT was assayed at 545 nm, using a microplate reader; wells with untreated cells were utilized as controls (Mosmann, 1983).[17] All *in vitro* experiments were carried out on two microplates with at least five parallel wells. Cisplatin was used as positive control. Stock solutions of the tested substances (10 mM) were prepared with DMSO. The DMSO content of the medium (0.1% or 0.3%) did not have any significant effect on the cell proliferation.

Acknowledgements

This work was supported by the New Hungary Development Plan (TÁMOP 4.2.1/B-09/1/KONV) and the Hungarian Scientific Research Fund (OTKA K101659).

References

1. Wu, P.; Fokin, V. V. *Aldrichim. Acta* **2007**, *40*, 7.
2. Genin, M. J.; Allwine, D. A.; Anderson, D. J.; Barbachyn, M. R.; Emmert, D. E.; Garmon, S. A.; Graber, D. R.; Grega, K. C.; Hester, J. B.; Hutchinson, D. K.; Morris, J.; Reischer, R. D.; Stper, D.; Yagi, B. H. *J. Med. Chem.* **2000**, *43*, 953.
3. Buckle, D. R.; Rockell, C. J. M.; Smith, H.; Spicer, B. A. *J. Med. Chem.* **1986**, *29*, 2262.
4. Alvarez, R.; Velazquez, S.; San-Felix, A.; Aquaro, S.; De Clercq, E.; Perno, C. F.; Karlsson, A.; Balzarini, J.; Camarasa, M. J. *J. Med. Chem.* **1994**, *37*, 4185.
5. (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596. (b) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.
6. (a) Pore, V. S.; Aher, N. G.; Kumar, M.; Shukla, P. K. *Tetrahedron* **2006**, *62*, 11178. (b) Aher, N. G.; Pore, V. S.; Patil, S. P. *Tetrahedron* **2007**, *63*, 12927. (c) Aher, N. G.; Pore, V. S. *Synlett* **2005**, *14*, 2155. (d) Zhang, Z.; Ju, Y.; Zhao, Y. *Chem. Lett.* **2007**, *36*, 1450.
7. Banday, A. H.; Shameem, A. S.; Gupta, B. D.; Sampath Kumar, H. M. *Steroids* **2010**, *75*, 801.
8. (a) Frank, É.; Molnár, J.; Zupkó, I.; Kádár, Z.; Wölfling, J. *Steroids* **2011**, *76*, 1141. (b) Ondré, D.; Wölfling, J.; Tóth, I.; Szécsi, M.; Julesz, J.; Schneider, Gy. *Steroids* **2009**, *74*, 1025. (c) Ondré, D.; Wölfling, J.; Iványi, Z.; Schneider, Gy.; Tóth, I.; Szécsi, M.; Julesz, J. *Steroids* **2008**, *73*, 1375. (d) Frank, É.; Mucsi, Z.; Zupkó, I.; Réthy, B.; Falkay, G.; Schneider, Gy.; Wölfling, J. *J. Am. Chem. Soc.* **2009**, *131*, 3894.
9. Kádár, Z.; Kovács, D.; Frank, É.; Schneider, Gy.; Huber, J.; Zupkó, I.; Bartók, T.; Wölfling, J. *Molecules* **2011**, *16*, 4786.
10. (a) Butenandt, A.; Wolff, A. *Ber. Dtsch. Chem. Ges.* **1935**, *68*, 2091. (b) Fieser, L. F.; Dominguez X. A. *J. Am. Chem. Soc.* **1953**, *75*, 1704.
11. Salunke, D. B.; Hazra, B. G.; Gonnade, R. G.; Bhadbhade, M. M.; Pore, V. S. *Tetrahedron* **2005**, *61*, 3605.
12. Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952.
13. Lee, B. Y.; Park, S. R.; Jeon, H. B.; Kim, K. S. *Tetrahedron Lett.* **2006**, *47*, 5105.
14. Gonschior, M.; Kötteritzsch, M.; Rost, M.; Schönecker, B.; Wyrwa, R. *Tetrahedron Asymmetry* **2000**, *11*, 2159.
15. Kamuhabwa, A.; Nshimo, C.; de Witte, P. *J. Ethnopharmacol.* **2000**, *70*, 143.
16. Schönecker, B.; Ponsold, K. *J. prakt. Chem.* **1971**, *313*, 817.
17. Mosmann, T. *J. Immunol. Methods* **1983**, *65*, 55.

