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Synthesis and Structure of Some 8α-Analogs of Steroid Estrogens

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Abstract—The distances between the protons of four 8α-analogues of steroid estrogens as determined by X-ray data are consistent with the calculated values obtained by ab initio, PM3 and MM+ methods, that can be used for docking of these stereochemical analogs onto α-estrogen receptors.

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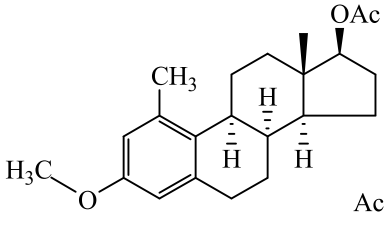
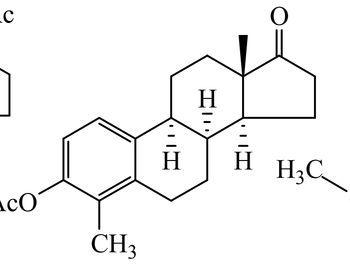
The broad clinical application of modified steroid estrogens [1–4] revealed the presence of a variety of significant side effects, so the search for new substances of this group of hormones with improved biological properties remains an actual task. Since the synthesis of new steroids is very laborious it is essencial to pre-evaluate potential biological properties of the model substances. To forecast the efficiency of ligand binding with different proteins (in particular, with nuclear estrogen receptors) computer simulation is used [5–13] by docking ligands to the appropriate site of a protein. Therefore the choice of method for calculating the conformations of model steroids of a certain stereochemical series is crucial. In the first stage of solving the problem the results of X-ray diffraction (XRD) of model compounds and computer simulation carried out using *ab initio* and semiempirical methods [14] are compared.

The aim of the current work was to study the structures of 8α-analogs of steroid estrogens, as this group of steroids may have better biological properties than the compounds with the natural ring junction [15–22].

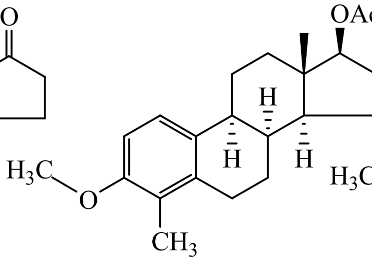
In selecting model compounds for the study we took into account that the 8α estrogen analogs with hydroxy groups at C^3 and C^{17} effectively bind with the α-estrogen receptors [16, 17]. Since in the crystals of such compounds conformers may appear, whose formation is caused by intermolecular hydrogen bonds, we chose as the model compounds 8α-analogs **I**–**IV** lacking hydroxy groups at C^3 and C^{17}. The choice of modifications in the carbon skeleton is connected with a noticeable influence of the substituents on the uterotropic action of the analogs [18–20].



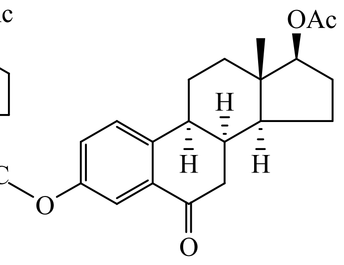
I



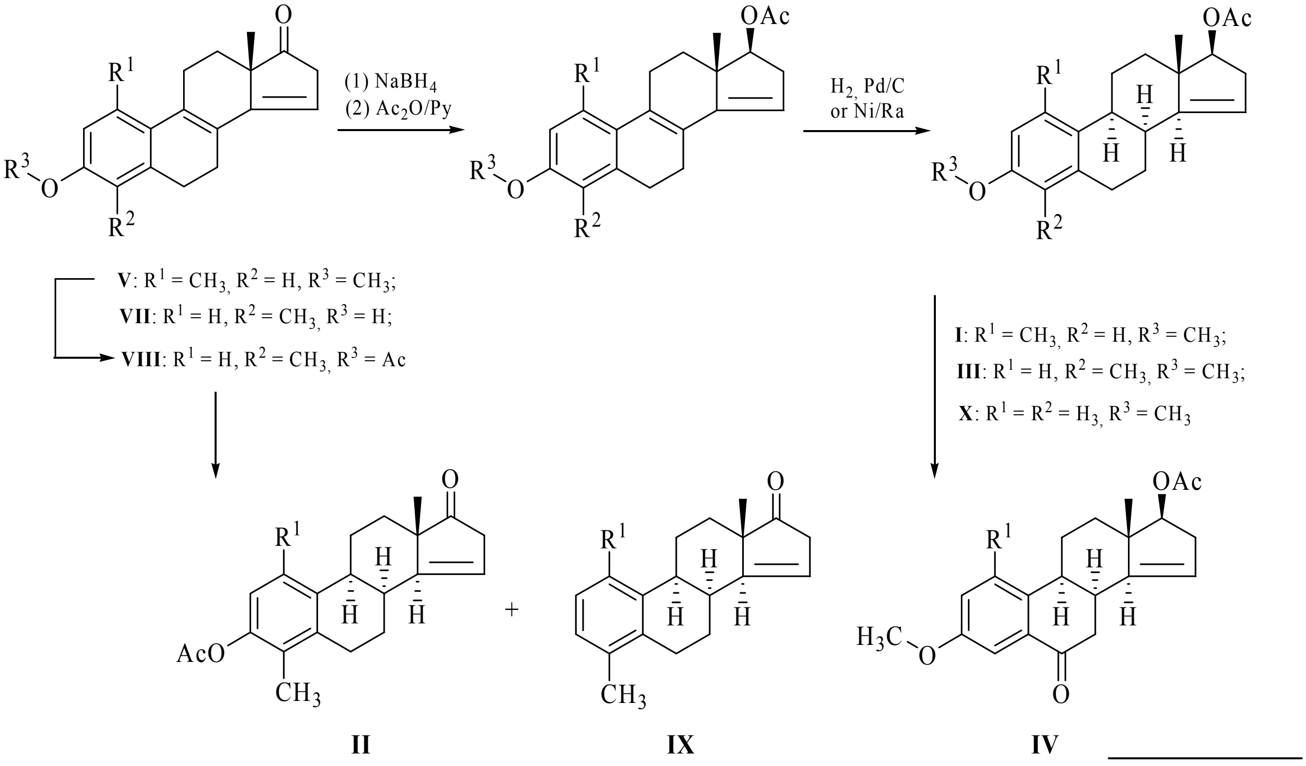
II



III



IV



Scheme of synthesis of model substances is given below. It is typical Torgov-Ananchenko [23, 24] scheme and needs no comment.

Full assignment of signals in the ^1H and ^{13}C NMR spectra of model steroids **I**–**IV** was performed using the homo- and heterocorrelation methods COSY-90 [25], COSY-DQF [26], J–COSY [27], COLOC [28], NOESY [29] and DEPT-135 [30]. The data presented in the experimental section of the work prove the structure of these substances. XRD data for the steroids **I** and **II** are given in [31] and [32], respectively.

Structures of steroids **III** and **IV** were solved by the direct method and optimized on F2 accounting for the anisotropy of thermal vibrations. The hydrogen atoms were placed in calculated positions. The extinction was not taken into account. Calculations were performed using the program packages CSD [33] and SHELXL 97 [34]. Distances between the protons in the molecules of **I**–**IV** (Table 5) were calculated using XRD data. Using *ab initio*, PM3 and MM+ [35] methods, we performed geometry optimization of these steroids and calculated distances between the same protons. In addition, the distances between O^1 and O^2 were determined. The data presented suggest a satisfactory agreement between the calculated and experimental values and, consequently, the possibility of using these calculation methods for docking new 8α-analogs of steroid estrogens in ligand binding sites of various macromolecules.

A detailed study of the structure of **I** in solution revealed a conformational equilibrium associated with the inversion in the ring B. The results of this work will be the subject of a special communication.

EXPERIMENTAL

All synthesized compounds are racemic. Their purity was checked by TLC on “Silufol” plates in the following solvent systems: petroleum ether–ethyl acetate (6:1) (4:1) and (3:1). Mass spectra were recorded on a MKh-1321 instrument (temperature in ionization chamber 200–210°C, energy of ionizing radiation 70 eV). NMR spectra were obtained at 295 K on a Bruker DPX-300 spectrometer with the operating frequencies 300.130 and 75.468 MHz for ^1H and ^{13}C nuclei, respectively. To record ^1H NMR spectra a solution of 5–7 mg of a substance in 0.6 ml of $CDCl_3$ was used and for ^{13}C NMR spectra, 30–50 mg in the same volume. Chemical shifts were measured relative to TMS by assigning a signal of the solvent ($CDCl_3$/$CHCl_3$ = 99.9/0.1) standard values 7.26 ppm (^1H) and 76.90 ppm (^{13}C) with an accuracy better than

Table 1. Interatomic distances in steroids **I**–**IV**, Å

Distance between protons, Å	Compound															
	I				**II**				**III**				**IV**			
	XRD	*ab initio*	PM3	MM+	XRD	*ab initio*	PM3	MM+	XRD	*ab initio*	PM3	MM+	XRD	*ab initio*	PM3	MM+
1-9α	–	–	–	–	2.57	2.57	2.49	2.50	2.56	2.48	2.51	2.51	2.61	2.51	2.49	2.43
1-11α	–	–	–	–	2.34	2.45	2.38	2.36	2.36	2.40	2.34	2.38	2.45	2.59	2.43	2.57
1-11β	–	–	–	–	3.57	3.59	3.61	3.51	3.58	3.63	3.51	3.44	3.61	3.72	3.66	3.70
7α-15α	3.42	3.40	3.28	3.34	3.30	3.39	3.24	3.32	3.23	3.37	3.35	3.35	3.28	3.40	3.22	3.28
7α-15β	2.32	2.35	2.18	2.31	2.23	2.35	2.12	2.31	2.30	2.22	2.25	2.44	2.22	2.41	2.11	2.42
7β-11β	2.18	2.33	2.26	2.32	2.32	2.37	2.34	2.38	2.25	2.31	2.37	2.44	2.40	2.47	2.35	2.56
7β-15β	3.40	3.37	3.17	3.35	3.28	3.36	3.15	3.33	3.29	3.22	3.31	3.44	3.16	3.23	3.11	3.03
8α-9α	2.46	2.34	2.41	2.35	2.42	2.35	2.37	2.37	2.45	2.38	2.36	2.33	2.38	2.34	2.37	2.36
8α-14α	2.11	2.32	2.34	2.32	2.08	2.32	2.31	2.31	2.17	2.35	2.36	2.31	2.10	2.32	2.33	2.32
9α-12α	2.56	2.46	2.58	2.61	2.63	2.64	2.63	2.64	2.56	2.63	2.70	2.68	2.63	2.63	2.61	2.60
9α-14α	2.25	2.37	2.41	2.40	2.30	2.41	2.45	2.46	2.30	2.42	2.37	2.40	2.33	2.39	2.43	2.45
12α-14α	2.54	2.41	2.42	2.46	2.52	2.42	2.40	2.45	2.48	2.38	2.37	2.38	2.50	2.44	2.49	2.46
12α-17α	2.43	2.38	2.44	2.39	2.38	2.38	2.44	2.39	–	–	–	–	2.42	2.39	2.44	2.40
14α-17α	2.55	2.34	2.45	2.37	2.54	2.35	2.46	2.38	–	–	–	–	2.57	2.36	2.46	2.36
15α-16α	2.31	2.38	2.36	2.38	2.32	2.38	2.36	2.38	2,34	2.38	2.37	2.34	2.30	2.38	2.36	2.38
15α-16β	2.91	2.90	2.88	2.91	2.91	2.90	2.88	2.90	2.83	2.84	2.86	2.79	2.90	2.90	2.88	2.91
Distance between O^3–O^{17}, Å	10.96	10.91	10.82	10.89	10.97	10.90	10.78	10.85	10.72	10.78	10.71	10.79	10.79	10.94	10.81	10.86

±0.002 and ±0.01 ppm, respectively. Homonuclear coupling constants were measured with an accuracy ±0.02 Hz from ^{1}H NMR spectra obtained after additional processing of FIDs using Lorentz–Gauss transformation and procedures for direct linear prediction, as well as increasing the spectral digital resolution with zero filling. Pulse sequences and procedures for the processing of 2D spectra from Bruker BioSpin were used for the correlation spectra.

17β-Acetoxy-1-methyl-3-methoxy-8α-estra-1,3,5-(10)-triene (I). To a solution of 3.5 g of estrapentaene (**V**) [36] in 125 ml of a dioxane-water mixture (10:1) 1 g of sodium borohydride was added and the reaction mixture was stirred for 2 h at 25°C, then the excess of reducing agent was destroyed with acetic acid. After usual treatment [37] the reaction products were dissolved in 270 ml of benzene and 5 g of Raney nickel was added. The hydrogenation was carried out under conditions proposed in [37]. The reaction products were dissolved in a mixture of 20 ml of pyridine and 45 ml of acetic anhydride and left at room temperature for 24 h. After usual treatment the target compound **I** was obtained by crystallization from ethanol. Yield 3.06 g (75%), mp 126.5–128.5°C. Mass spectrum, *m/z* (I_{rel}, %): 342 (100), 282 (21), 267 (5), 253 (16.5), 213 (5.5), 200 (47), 187 (17), 174 (3), 159 (15). ^{1}H NMR spectrum, δ, ppm.: 6.48 (C^2–H), 6.48 (C^4–H), 2.86 (C^6–H_α), 2.68 (1H, C^6–H_β), 1.82 (C^7–H_α), 1.78 (C^7–H_β), 2.05 (C^8–H_α), 2.66 (C^9–H_α), 1.73 (C^{11}–H_α), 1.48 (C^{11}–H_β), 1.37 (C^{12}–H_α), 1.70 (C^{12}–H_β), 1.78 (C^{14}–H_α), 1.76 (C^{15}–H_α), 1.53 (C^{15}–H_β), 2.21 (C^{16}–H_α), 1.54 (C^{16}–H_β), 4.65 (C^{17}–H_α), 0.95 s (3H, C^{13}–CH_3), 2.29 (3H, C^1–CH_3), 2.05 (3H, CH_3CO), 3.75 (3H, CH_3O). Found, %: C 76.89, H 8.85. $C_{22}H_{30}O_3$. Calculated, %: C 77.27, H 8.03.

3-Hydroxy-4-methylestra-1,3,5(10),8,14-pentane-17-one acetate (VIII). To a solution of 1.50 g of compound **VII** [38] in 20 ml of pyridine 20 ml of acetic anhydride was added, the reaction mixture was stirred for 2 h at 80°C and then poured into ice water. After usual treatment the target compound was crystallized from methanol. Yield 1.34 g (78%). mp 118–119°C. ^{1}H NMR spectrum, δ, ppm: 1.12 s (3H, $C^{13}–CH_3$), 2.14 s (3H, $C^4–CH_3$), 2.34 s (3H, $C\mathit{H}_3CO$), 6.01 m (1H, C^{15}–H), 7.01 d (1H, J = 8.5Hz, C^2–H), 7.37 d (1H, J = 8.5 Hz, C^1–H). Found, %: C 77.90, H 6.81. $C_{21}H_{22}O_3$. Calculated, %: C 78.23, H 6.88.

4-Methyl-8α-estrone acetate (II). To a solution of 1 g of **VIII** in 80 ml of benzene 1 g of freshly prepared Raney nickel was added, the hydrogenation was carried out at 75–90°C and 90–150 at to absorb 30–40 fold excess of hydrogen compared with the amount required to reduce two double bonds and as keto group. The catalyst was filtered off, the solvent was removed on a rotary evaporator, the residue was dissolved in 30 ml of pyridine and oxidized with Sarette reagent. After the usual treatment the major reaction products were purified by TLC on silica gel, eluted with a mixture of hexane–ethyl acetate initially in the ratio 8:1, then 4:1. From the least polar fraction, after crystallization from hexane 0.08–0.12 g (9.6–14.4%) of compound **IX** was obtained, mp 108–109°C. Mass spectrum, m/z (I_{rel}, %): 268 (100), 250 (16), 235 (14), 226 (18), 224 (67), 207 (21), 205 (21), 197 (13), 183 (16), 170 (16), 156 (51). Found, %: C 84.76, H 9.02. $C_{21}H_{24}O$. Calculated, %: C 85.03, H 9.01.

Of the more polar fractions after double crystallization from methanol 0.36-0.41 g (36.5–41.5%) of **II** was obtained, mp 163–164°C. ^{1}H NMR spectrum, δ, ppm: 7.02 (C^1–H), 6.82 (C^2–H), 2.44 ($C^6–H_α$), 2.84 ($C^6–H_β$), 1.95 ($C^7–H_α$), 1.71 ($C^7–H_β$), 2.16 ($C^8–H_α$), 2.68 ($C^9–H_α$), 1.86 (1H, $C^{11}–H_α$), 1.74 ($C^{11}–H_β$), 1.45 ($C^{12}–H_α$), 1.80 ($C^{12}–H_β$), 1.84 ($C^{14}–H_α$), 1.84 ($C^{15}–H_α$), 2.00 ($C^{15}–H_β$), 2.18 ($C^{16}–H_α$), 1.47 ($C^{16}–H_β$), 1.00 ($C^{13}–CH_3$), 2.31 (3H, $C^4–CH_3$), 2.02 (3H, $C\mathit{H}_3CO$). ^{13}C NMR spectrum, δ, ppm: 127.5 (C^1), 119.0 (C^2), 146.7 (C^3), 127.8 (C^4), 136.5 (C^5), 28.5 (C^6), 21.2 (C^7), 37.6 (C^8), 41.9 (C^9), 138.7 (C^{10}), 28.1 (C^{11}), 32.2 (C^{12}), 47.0 (C^{13}), 48.3 (C^{14}), 21.3 (C^{15}), 35.6 (C^{16}), 220.4 (C^{17}), 16.5 (C^{18}), 20.7 and 169.6 (CH_3CO), 12.1 ($C^4–CH_3$). MS, m/z (I_{rel}, %): 326 (17), 284 (100), 227 (3), 199 (32), 186 (15), 171 (6), 160 (28). Found, %: C 77.35, H 8.14. $C_{21}H_{26}O_3$. Calculated, %: C 77.27, H 8.03.

17β-Acetoxy-4-methyl-3-methoxy-8α-estra-1,3,5-(10)-triene (III). To a solution of 1 g of **VI** [39] in 100 ml of THF 500 mg of 10% Pd/C was added, and the hydrogenation was carried out until disappearance in UV spectrum of absorption bands characteristic of one or two double bonds conjugated with the aromatic ring. The catalyst was filtered off, the solvent was distilled off on a rotary evaporator, and the residue was crystallized from a mixture chloroform-methanol (1:4). 0.61 g (60%) of the target compound **III** was obtained, mp 178–180°C ([39], mp 178–180°C). Mass spectrum, m/z (I_{rel}, %): 342 (100, M^+), 282 (14.5), 267 (4), 253 (17.5), 241 (5.5), 225 (5.5), 213 (5.8), 200 (46), 187 (18.5), 174 (36), 159 (17). ^{1}H NMR spectrum, δ, ppm: 7.00 (C^1–H), 6.74 (C^2–H), 2.39 ($C^6–H_α$), 2.85 (1H, $C^6–H_β$), 1.92 ($C^7–H_α$), 1.68 ($C^7–H_β$), 2.01 ($C^8–H_α$), 2.64 ($C^9–H_α$), 1.74 ($C^{11}–H_α$), 1.69 ($C^{11}–H_β$), 1.36 ($C^{12}–H_α$), 1.77 ($C^{12}–H_β$), 1.71 ($C^{14}–H_α$), 1.53 ($C^{15}–H_α$), 1.82 ($C^{15}–H_β$), 2.23 ($C^{16}–H_α$), 1.52 ($C^{16}–H_β$), 4.64 ($C^{17}–H_α$), 0.93 (3H, $C^{13}–CH_3$), 2.12 ($C^4–CH_3$), 2.07 (3H, CH_3CO), 3.81 (3H, CH_3O). ^{13}C NMR spectrum, δ, ppm: 127.0 (C^1), 108.2 (C^2), 155.1 (C^3), 124.0 (C^4), 136.3 (C^5), 28.6(C^6), 20.7 (C^7), 36.9 (C^8), 41.8 (C^9), 133.8 (C^{10}), 28.7 (C^{11}), 37.5 (C^{12}), 41.6 (C^{13}), 47.2 (C^{14}), 22.2 (C^{15}), 26.9 (C^{16}), 82.5 (C^{17}), 13.4 (C^{18}), 21.1 and 170.1 (CH_3CO), 11.1($C^4–CH_3$). Found, %: C 76.96, H 8.99. $C_{22}H_{30}O_3$. Calculated, %: C 77.16, H 8.83.

Crystals of steroid **III** have been grown from hexane in the form of colorless flat pseudohexagonal plates. A three-dimensional set of 1618 independent nonzero reflections ($I \geq 4\sigma_I$), ($\sin\theta/\lambda \leq 0.70$) was obtained from a single crystal measuring 0.2×0.15×0.3 mm on the diffractometer $P2_1$ "Syntex" with a graphite monochromator ($MoK_α$ radiation) at room temperature. The crystals are triclinic, space group $P\bar{1}$, a = 7.338(2), b = 9.547(2), c = 14.620(3) Å, α = 73.31(1)°, β = 85.13(2)°, γ = 71.06(2)°, Z = 2, D_x = 1.226(3) g cm^{-3}, R_1 = 0.0489. The results of XRD are shown in Tables 1 and 2.

17β-Acetoxy-3-methoxy-8α-estra-1,3,5(10)-triene-6-one (IV). To a solution of 2 g of steroid **X** [37] in 18 ml of glacial acetic acid a solution of 3.4 g of sodium dichromate dihydrate in a mixture of 40 ml of acetic acid and 20 ml of acetic anhydride was added dropwise. The reaction mixture was heated for 5 h at 65°C, then cooled to room temperature and poured into 1 liter of water. The reaction products were extracted with ether, organic layer was washed with water to neutral reaction and dried over sodium sulfate. The solvent was removed on a rotary evaporator and the target compound was purified by flash chromatography on silica gel column (elution with a mixture of

Table 2. Coordinates (×10^4) and thermal parameters (Å×10^4) of basis atoms for compound **III**; U_{eq} equal to 1/3 of the sum of tensor U_{ij} projection on the orthogonal axes

Atom	*x*	*y*	*z*	U_{eq}
O^1	1810(3)	5622(3)	1530(2)	59(1)
O^2	4970(3)	–1439(2)	8942(2)	51(1)
O^3	6829(4)	–105(3)	9168(2)	75(1)
C^1	3730(4)	4495(4)	3960(2)	39(1)
C^2	3529(5)	5162(4)	2987(2)	43(1)
C^3	2129(5)	4995(4)	2498(2)	38(1)
C^{3A}	3240(6)	6212(5)	985(2)	75(1)
C^4	912(4)	4164(3)	2974(2)	38(1)
C^{4A}	–655(5)	4043(4)	2424(2)	62(1)
C^5	1173(4)	3462(3)	3959(2)	35(1)
C^6	–96(4)	2504(4)	4465(2)	43(1)
C^7	725(4)	1425(3)	5425(2)	38(1)
C^8	1244(4)	2318(3)	6022(2)	34(1)
C^9	2891(4)	2933(4)	5536(2)	36(1)
C^{10}	2585(4)	3628(3)	4467(2)	31(1)
C^{11}	4877(4)	1720(4)	5781(2)	41(1)
C^{12}	5264(4)	1001(4)	6854(2)	44(1)
C^{13}	3710(4)	289(3)	7327(2)	34(1)
C^{14}	1732(4)	1525(3)	7073(2)	35(1)
C^{15}	339(4)	797(4)	7724(2)	48(1)
C^{16}	1534(5)	–174(4)	8644(2)	58(1)
C^{17}	3560(4)	–39(4)	8412(2)	43(1)
C^{18}	3956(5)	–1194(4)	7047(2)	45(1)
C^{20}	6527(5)	–1297(5)	9287(2)	51(1)
C^{21}	7796(5)	–2836(4)	9847(3)	73(1)

Table 3. Torsion angles ω (deg) in compound **III**

Angle	ω	Angle	ω
$C^{10}C^1C^2C^3$	1.2(5)	$C^{10}C^9C^{11}C^{12}$	179.2(3)
$C^{3A}O^1C^3C^2$	12.6(5)	$C^8C^9C^{11}C^{12}$	–53.1(4)
$C^{3A}O^1C^3C^4$	–167.9(3)	$C^9C^{11}C^{12}C^{13}$	56.3(4)
$C^1C^2C^3O^1$	179.6(3)	$C^{11}C^{12}C^{13}C^{17}$	–162.5(3)
$C^1C^2C^3C^4$	0.2(5)	$C^{11}C^{12}C^{13}C^{18}$	72.4(3)
$O^1C^3C^4C^5$	178.7(3)	$C^{11}C^{12}C^{13}C^{14}$	–53.7(3)
$C^2C^3C^4C^5$	–1.8(5)	$C^7C^8C^{14}C^{15}$	–53.2(4)
$O^1C^3C^4C^{4A}$	–1.5(5)	$C^9C^8C^{14}C^{15}$	–179.6(3)
$C^2C^3C^4C^{4A}$	178.0(3)	$C^7C^8C^{14}C^{13}$	74.9(3)
$C^3C^4C^5C^{10}$	2.1(5)	$C^9C^8C^{14}C^{13}$	–51.5(4)
$C^{4A}C^4C^5C^{10}$	–177.7(3)	$C^{17}C^{13}C^{14}C^8$	175.9(3)
$C^3C^4C^5C^6$	–177.4(3)	$C^{18}C^{13}C^{14}C^8$	–68.7(4)
$C^{4A}C^4C^5C^6$	2.8(5)	$C^{12}C^{13}C^{14}C^8$	54.6(4)
$C^4C^5C^6C^7$	161.8(3)	$C^{17}C^{13}C^{14}C^{15}$	–48.5(3)
$C^{10}C^5C^6C^7$	–17.8(4)	$C^{18}C^{13}C^{14}C^{15}$	66.9(3)
$C^5C^6C^7C^8$	51.1(4)	$C^{12}C^{13}C^{14}C^{15}$	–169.8(3)
$C^6C^7C^8C^{14}$	168.6(2)	$C^8C^{14}C^{15}C^{16}$	167.8(3)
$C^6C^7C^8C^9$	–65.1(3)	$C^{13}C^{14}C^{15}C^{16}$	33.6(3)
$C^{14}C^8C^9C^{10}$	175.4(3)	$C^{14}C^{15}C^{16}C^{17}$	–4.9(4)
$C^7C^8C^9C^{10}$	44.2(3)	$C^{20}O^2C^{17}C^{13}$	99.6(3)
$C^{14}C^8C^9C^{11}$	48.0(3)	$C^{20}O^2C^{17}C^{16}$	–142.9(3)
$C^7C^8C^9C^{11}$	–83.2(3)	$C^{18}C^{13}C^{17}O^2$	45.6(3)
$C^2C^1C^{10}C^5$	–0.9(5)	$C^{12}C^{13}C^{17}O^2$	–79.9(4)
$C^2C^1C^{10}C^9$	–179.9(3)	$C^{14}C^{13}C^{17}O^2$	165.2(2)
$C^4C^5C^{10}C^1$	–0.8(4)	$C^{18}C^{13}C^{17}C^{16}$	–74.2(3)
$C^6C^5C^{10}C^1$	178.8(3)	$C^{12}C^{13}C^{17}C^{16}$	160.3(3)
$C^4C^5C^{10}C^9$	178.2(3)	$C^{14}C^{13}C^{17}C^{16}$	45.4(3)
$C^6C^5C^{10}C^9$	–2.3(5)	$C^{15}C^{16}C^{17}O^2$	–149.4(3)
$C^{11}C^9C^{10}C^1$	–64.9(4)	$C^{15}C^{16}C^{17}C^{13}$	–25.8(4)
$C^8C^9C^{10}C^1$	167.5(3)	$C^{17}O^2C^{20}O^3$	–1.5(5)
$C^{11}C^9C^{10}C^5$	116.1(3)	$C^{17}O^2C^{20}C^{21}$	177.8(3)
$C^8C^9C^{10}C^5$	–11.5(4)		

ethyl acetate–petroleum ether 1:10). After crystallization from methanol 315 mg (15%) of steroid **IV** was obtained, mp 185–186°C. Synthesis of **V** was reported previously [40, 41], but with no data on its mp and spectral characteristics. ^{1}H NMR spectrum, δ, ppm: 7.18 (C^1–H), 7.07 (C^2–H), 7.45 (C^4–H), 2.65 (C^7–H_α), 2.72 (C^7–H□), 2.52 (C^8–H_α), 2.78 (C^9–H_α), 1.78 (C^{11}–H_α), 1.73 (C^{11}–H_β), 1.40 (C^{12}–H_α), 1.83 (C^{12}–H_β), 1.69 (C^{14}–H_α), 1.71 (C^{15}–H_α), 1.52 (C^{15}–H_β), 2.20 (C^{16}–H_α), 1.54 (C^{16}–H_β), 4.65 (C^{17}–H_α), 0.98 (C^{13}–CH_3), 3.84 (CH_3O), 2.07 (CH_3CO). ^{13}C NMR spectrum, δ, ppm: 130.1 (C^1), 108.3 (C^2), 158.1 (C^3), 121.9 (C^4), 147.5 (C^5), 197.9 (C^6), 36.5 (C^7), 35.5 (C^8), 41.2 (C^9), 132.3 (C^{10}), 26.9 (C^{11}), 36.7 (C^{12}), 41.6 (C^{13}), 46.8 (C^{14}), 21.5 (C^{15}), 25.5 (C^{16}), 81.7 (C^{17}), 13.2 (C^{18}), 20.8 and 170.6 (CH_3CO), 55.1 (CH_3O). Mass spectrum, *m/z* ($I_{rel,}$ %): 342 (100), 300 (12.4), 282 (9), 272 (4.5), 256 (13), 241 (26.5), 200 (13), 187 (45), 174 (34), 161 (9). Found, %: C 73.60, H 7.75. $C_{21}H_{26}O_4$. Calculated, %: C 73.66, H 7.65.

Crystals of the steroid **III** have been grown from hexane in the form of colorless flat pseudohexagonal plates. A three-dimensional set of 1545 independent nonzero reflections ($I \geq 4\sigma_I$), ($\sin\theta/\lambda \leq 0.73$) was obtained from a single crystal measuring 0.2×0.15×

Table 4. Coordinates ($\times 10^4$) and thermal parameters (Å$\times 10^4$) of basis atoms for compound **IV**; U_{eq} equal to 1/3 of the sum of tensor U_{ij} projection on the orthogonal axes

Atom	*x*	*y*	*z*	U_{eq}
O^1	−1713(2)	−201(3)	−9265(2)	58(1)
O^2	2500(3)	−8048(3)	−5346(2)	61(1)
O^3	2283(6)	−10735(4)	−5843(3)	122(1)
O^4	3385(3)	−2156(3)	−8918(2)	78(1)
C^1	−2152(3)	−3992(4)	−8589(3)	48(1)
C^2	−2602(3)	−2729(4)	−8847(3)	48(1)
C^3	−1406(3)	−1521(3)	−9018(2)	41(1)
C^{3A}	−3231(4)	204(5)	−9095(3)	65(1)
C^4	200(3)	−1655(4)	−8953(2)	44(1)
C^5	646(3)	−2918(3)	−8664(2)	38(1)
C^6	2404(3)	−2931(4)	−8532(3)	47(1)
C^7	2869(4)	−3919(4)	−7883(3)	48(1)
C^8	1694(3)	−5606(3)	−8234(2)	42(1)
C^9	−80(3)	−5457(3)	−8090(2)	39(1)
C^{10}	−527(3)	−4109(3)	−8453(2)	39(1)
C^{11}	−438(4)	−5242(4)	−6934(3)	51(1)
C^{12}	15(4)	−6564(4)	−6509(3)	50(1)
C^{13}	1804(4)	−6588(3)	−6565(2)	43(1)
C^{14}	2128(4)	−6840(4)	−7732(2)	45(1)
C^{15}	3817(4)	−7228(5)	−7761(3)	63(1)
C^{16}	3897(5)	−8169(4)	−6964(3)	65(1)
C^{17}	2305(4)	−8116(4)	−6456(3)	54(1)
C^{18}	2902(4)	−5050(4)	−5729(3)	55(1)
C^{20}	2446(5)	−9451(5)	−5149(3)	72(1)
C^{21}	2683(7)	−9190(6)	−3986(4)	104(2)

0.2 mm on the diffractometer $P2_1$ "Syntex" with a graphite monochromator (MoK_α radiation) at room temperature. The crystals are triclinic, space group $P\bar{1}$, $a = 8.421(5)$, $b = 8.810(5)$, $c = 13.252(5)$ Å, $\alpha = 107.67(5)^\circ$, $\beta = 93.65(5)^\circ$, $\gamma = 101.28(5)^\circ$, $Z = 2$, $D_x = 1.249(3)$ g cm^{-3}, $R_1 = 0.0413$. The results of XRD are shown in Tables 3 and 4.

Table 5. Torsion angles ω (deg) in compound **IV**

Angle	ω	Angle	ω
$C^{10}C^{1}C^{2}C^{3}$	2.0(5)	$C^{10}C^{9}C^{11}C^{12}$	−179.2(3)
$C^{3A}O^{1}C^{3}C^{4}$	−165.2(3)	$C^{8}C^{9}C^{11}C^{12}$	−52.6(3)
$C^{3A}O^{1}C^{3}C^{2}$	15.8(5)	$C^{9}C^{11}C^{12}C^{13}$	57.3(4)
$C^{1}C^{2}C^{3}O^{1}$	−179.1(3)	$C^{11}C^{12}C^{13}C^{17}$	−164.2(3)
$C^{1}C^{2}C^{3}C^{4}$	1.9(5)	$C^{11}C^{12}C^{13}C^{14}$	−56.2(3)
$O^{1}C^{3}C^{4}C^{5}$	177.4(3)	$C^{11}C^{12}C^{13}C^{18}$	70.7(3)
$C^{2}C^{3}C^{4}C^{5}$	−3.5(4)	$C^{7}C^{8}C^{14}C^{15}$	−52.7(4)
$C^{3}C^{4}C^{5}C^{10}$	1.4(5)	$C^{9}C^{8}C^{14}C^{15}$	179.9(3)
$C^{3}C^{4}C^{5}C^{6}$	−175.7(3)	$C^{7}C^{8}C^{14}C^{13}$	75.7(3)
$C^{4}C^{5}C^{6}O^{4}$	−19.0(5)	$C^{9}C^{8}C^{14}C^{13}$	−51.8(3)
$C^{10}C^{5}C^{6}O^{4}$	164.0(3)	$C^{12}C^{13}C^{14}C^{8}$	56.3(3)
$C^{4}C^{5}C^{6}C^{7}$	159.8(3)	$C^{17}C^{13}C^{14}C^{8}$	176.6(3)
$C^{10}C^{5}C^{6}C^{7}$	−17.3(4)	$C^{18}C^{13}C^{14}C^{8}$	−67.9(3)
$O^{4}C^{6}C^{7}C^{8}$	−134.3(3)	$C^{12}C^{13}C^{14}C^{15}$	−167.7(3)
$C^{5}C^{6}C^{7}C^{8}$	47.0(4)	$C^{17}C^{13}C^{14}C^{15}$	−47.5(3)
$C^{6}C^{7}C^{8}C^{14}$	173.0(2)	$C^{18}C^{13}C^{14}C^{15}$	68.0(3)
$C^{6}C^{7}C^{8}C^{9}$	−60.3(3)	$C^{8}C^{14}C^{15}C^{16}$	167.0(3)
$C^{14}C^{8}C^{9}C^{10}$	173.2(2)	$C^{13}C^{14}C^{15}C^{16}$	33.3(3)
$C^{7}C^{8}C^{9}C^{10}$	43.0(3)	$C^{14}C^{15}C^{16}C^{17}$	−5.1(4)
$C^{14}C^{8}C^{9}C^{11}$	47.8(3)	$C^{20}O^{2}C^{17}C^{13}$	160.3(3)
$C^{7}C^{8}C^{9}C^{11}$	−82.5(3)	$C^{20}O^{2}C^{17}C^{16}$	−81.7(4)
$C^{2}C^{1}C^{10}C^{5}$	−4.1(4)	$C^{12}C^{13}C^{17}O^{2}$	−79.0(3)
$C^{2}C^{1}C^{10}C^{9}$	175.5(3)	$C^{14}C^{13}C^{17}O^{2}$	166.7(2)
$C^{4}C^{5}C^{10}C^{1}$	2.4(4)	$C^{18}C^{13}C^{17}O^{2}$	46.7(4)
$C^{6}C^{5}C^{10}C^{1}$	179.4(3)	$C^{12}C^{13}C^{17}C^{16}$	158.4(3)
$C^{4}C^{5}C^{10}C^{9}$	−177.2(3)	$C^{14}C^{13}C^{17}C^{16}$	44.1(3)
$C^{6}C^{5}C^{10}C^{9}$	−0.2(4)	$C^{18}C^{13}C^{17}C^{16}$	−75.9(3)
$C^{11}C^{9}C^{10}C^{1}$	−66.4(4)	$C^{15}C^{16}C^{17}O^{2}$	−146.5(3)
$C^{8}C^{9}C^{10}C^{1}$	167.1(3)	$C^{15}C^{16}C^{17}C^{13}$	−25.2(4)
$C^{11}C^{9}C^{10}C^{5}$	113.1(3)	$C^{17}O^{2}C^{20}O^{3}$	1.8(6)
$C^{8}C^{9}C^{10}C^{5}$	−13.4(4)	$C^{17}O^{2}C^{20}C^{21}$	179.3(3)

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