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NOVEL ECDYSTEROID ANALOGS WITH OXYGEN-CONTAINING HETEROCYCLES IN THE STEROID SKELETON

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The reaction of ecdysteroids (20-hydroxyecdysone and its acetonides) with lithium in liquid ammonia gave novel analogs with an oxetane 9α,14α-oxacycle in the steroid skeleton. In aqueous alcohol solution the 9,14-oxa analogs rearrange to the more stable 9α,13α–oxa analogs through a 1,2-migration of the 18-Me group from the C-13 to the C-14 atom.

Keywords: acetonides, 20-hydroxyecdysone, liquid ammonia, lithium, oxa analogs, ecdysteroids, synthesis.

Although widely used in the chemistry of steroids [1, 2] for the selective reduction of a double bond in conjugated enones, a reaction with alkali metals in liquid ammonia has been little studied amongst the series of ecdysteroids. It is only known that the reaction of 20-hydroxyecdysone diacetonide with lithium in liquid ammonia solution gives a 14α-hydroperoxy derivative rather than the corresponding 7,8-dihydro analog [3].

We have found that the action of a solution of lithium in liquid ammonia on the ecdysteroids 20-hydroxyecdysone (**1**), its 2,3:20,22 diacetonide (**2**), and the 20,22-acetonide (**3**) and 2,3-acetonide (**4**) and subsequent treatment of the reaction mixture with NH_4Cl gives the corresponding 14α-hydroperoxides **5-8** together with the previously unknown 9α,14α-oxa derivatives **9-12** which are analogs of ecdysteroids with an oxetane ring in the steroid skeleton (Scheme 1). In the case of compound **1** the corresponding oxetane **9** and 14α-hydroperoxide **5** are formed in approximately equimolar amounts while the acetonides **2** and **3** are primarily converted to the corresponding oxetanes **10** and **11**. For the 2,3-acetonide **4** the oxetane formed **12** is less stable than oxetanes **9-11** and elution of reaction products (SiO_2, MeOH/$CHCl_3$, 1:50) gave a mixture of the oxetane **12** and its isomerization product **19** as well as a mixture of the 14α-hydroperoxide **12** and starting material **4**. Repeated chromatography (SiO_2, MeOH/$CHCl_3$) of a mixture of compounds **12** and **19** gave the individual forms of the transformation products of oxetane **12**, i.e. compounds **15** and **19**.

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* Dedicated to Academician B. A. Trofimov in his 70th jubilee.

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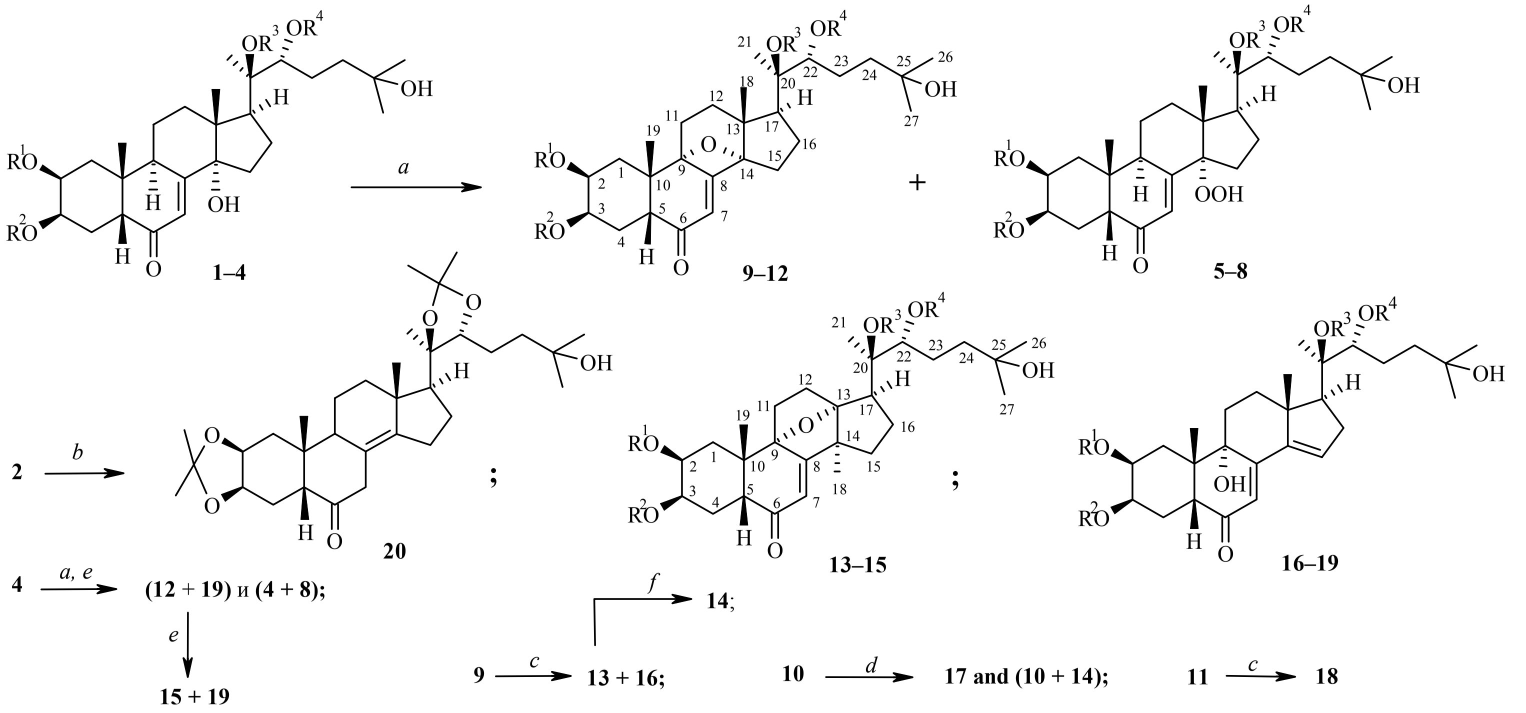

1, **5**, **9**, **13**, **16** $R^1 = R^2 = R^3 = R^4 = H$; **2**, **6**, **10**, **14**, **17** $R^1 + R^2 = R^3 + R^4 = CMe_2$; **3**, **7**, **11**, **18** $R^1 = R^2 = H$, $R^3 + R^4 = CMe_2$; **4**, **8**, **12**, **15**, **19** $R^1+R^2 = CMe_2$; $R^3 = R^4 = H$. *Reagents and conditions: a* (1) Li/ liquid NH_3, THF; (2) NH_4Cl; (3) NH_3 evaporation in air; *b* (1) Li/ liquid NH_3, THF, (2) NH_4Cl, (3) NH_3 evaporation in an argon stream; *c* $MeOH/H_2O$; *d* EtOH/THF; *e* $MeOH/SiO_2$; *f* Me_2CO/PMA

In methanol solution oxetane **9** undergoes a similar reaction to give a mixture of compounds **13** and **16** which were separated chromatographically. At the same time, oxetanes **10** and **11** isomerize in alcohol solution (MeOH or EtOH) to compounds **17** and **18** respectively (Scheme 1). In the case of the diacetonide **10**, along with compound **17**, a mixture of compound **14** and the starting oxetane **10** was produced which could not be separated. Compound **14** was obtained by acetonation of compound **13** under conditions given in [4].

The conversion of the ecdysteroids **1-4** to oxetanes **9-12** was supported by the shift to low field of the C-9 signal in the ^{13}C NMR spectra (Δδ ~ 59 ppm) and its transformation from a doublet to a singlet (*J*mod regime). A similar low field shift (Δδ ~ 22 ppm) is also observed for the C-14 signal (Tables 1 and 2). There are

TABLE 1. ^{13}C NMR Spectra of Compounds **1-7**

C	Chemical shifts, δ, ppm							
	1	**2**	**3**	**4**	**5**		**6**	**7**
	CD_3OD (75 MHz) [6]	$CDCl_3$ (75 MHz) [4]	$CDCl_3$ (75 MHz) [4]	C_5D_5N (75 MHz)	CD_3OD (125 MHz) [8]	CD_3OD (75 MHz)	$CDCl_3$ (125 MHz)	$CDCl_3$ (75 MHz)
1	37.3	37.5	37.7	37.9	37.5	37.4	37.6	36.5
2	68.5	72.0	67.9	72.4	68.7	68.6	72.3	67.5
3	68.7	71.5	67.8	72.0	68.6	68.5	71.7	67.5
4	32.8	31.3	32.2	31.9	32.9	32.8	26.4	30.9
5	51.7	50.7	51.1	51.4	51.9	51.8	50.9	50.2
6	206.6	203.0	203.3	202.2	206.2	206.4	202.2	205.1
7	122.1	121.2	121.5	121.1	125.8	125.7	125.1	124.9
8	168.1	163.7	165.4	165.5	164.0	163.9	158.9	162.1
9	35.0	34.3	34.2	34.9	35.6	35.5	35.7	34.2
10	39.3	37.7	38.4	38.1	39.1	39.0	37.7	38.0
11	21.5	20.4	20.8	21.0	21.9	21.5	21.1	20.8
12	32.5	30.8	31.4	31.5	32.4	32.3	31.1	31.6
13	—*	47.2	47.6	48.3	50.2	—*	49.2	48.8
14	85.2	84.7	85.1	84.0	96.6	96.5	96.8	95.8
15	31.8	26.5	31.5	27.3	25.7	25.7	24.5	24.7
16	21.5	21.1	21.9	21.3	21.6	21.9	21.3	21.4
17	50.5	48.9	49.7	50.0	51.3	51.2	49.9	49.7
18	18.1	16.9	17.1	17.8	18.8	18.9	17.9	17.8
19	24.4	23.4	24.2	23.7	24.6	24.6	23.8	24.1
20	78.0	84.3	83.9	76.7	77.6	77.6	84.1	84.1
21	21.1	21.8	22.2	21.6	21.1	21.1	21.8	21.9
22	78.4	81.9	82.3	77.4	78.3	78.2	82.0	82.1
23	27.3	23.5	24.1	26.9	27.4	27.2	23.8	23.4
24	42.3	41.3	41.9	42.5	42.4	42.2	41.5	41.4
25	71.4	70.3	69.1	69.5	71.26	71.2	70.7	70.7
26	29.0	26.5	29.3	29.9	28.9	29.0	29.5	28.7
27	29.7	26.8	29.3	30.0	29.78	29.8	29.5	29.6
2,3-$\underline{C}(CH_3)_2$	—	108.2	—	108.0	—	—	108.6	–
2,3-$C(\underline{C}H_3)_2$	—	28.9 29.3	—	26.6 28.7	—	—	26.6 28.5	—
20,22-$\underline{C}(CH_3)_2$	–	106.9	106.7	—	—	—	107.5	107.0
20,22-$C(\underline{C}H_3)_2$	—	28.4 28.4	29.7 29.9	—	—	——	26.6 28.9	26.9 28.9

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* Signal obscured by the solvent signal (~ 49 ppm).

also marked changes in the ^{1}H NMR spectra of oxetanes **9-12** when compared with the corresponding spectra of the starting compounds [4-6]. Hence the H-9 signal is absent in the ^{1}H NMR spectra and the H-7 signal is shifted to low field (Δδ 0.1-0.2 ppm) and changed from a doublet to a singlet.

The structure of compound **10** is proved by a combination of 1D and 2D NMR procedures [7]. Proof for the 9,14 position of the oxetane ring follows from the ^{1}H–^{13}C correlation of protons 19-Me with C-9 (δ 92.7 ppm) and 18-Me with C-14 (δ 106.7 ppm) observed in the HMBC experiment.

TABLE 2. ^{13}C NMR Spectra of Compounds **8-14**

C	Chemical shifts, δ, ppm							
	8*	**9**	**10**	**11**	**12**	**13**		**14**
	$CDCl_3$ (100 MHz)	CD_3OD (75 MHz)	$CDCl_3$ (125 MHz)	$CDCl_3$ (75 MHz)	$CDCl_3$ (100 MHz)	$CDCl_3$ (125 MHz)	CD_3OD (100 MHz)	$CDCl_3$ (75 MHz)
1	37.5	35.2	29.2	33.4	35.3	33.8	36.0	29.9
2	72.3	69.1	70.9	67.7	72.9	68.7	70.1	73.0
3	71.7	69.8	72.7	68.5	71.1	67.7	69.1	71.3
4	29.1	27.3	24.2	24.6	26.2	24.8	25.5	29.2
5	50.8	52.8	50.4	51.5	50.7	50.5	51.9	49.8
6	203.2	199.7	196.7	198.0	196.6	—*2	201.7	198.5
7	124.8	112.4	110.8	111.1	111.1	115.4	116.2	115.4
8	160.3	171.1	168.3	169.6	168.2	178.2	181.2	177.8
9	35.3	94.4	92.7	92.6	92.7	89.4	90.8	89.5
10	37.8	41.5	40.6	40.2	40.6	36.8	38.1	37.0
11	20.5	28.5	26.4	23.0	26.7	26.6	27.6	23.9
12	31.1	35.4	33.9	33.8	34.2	29.5	30.6	29.3
13	49.3	52.2	50.6	50.7	50.6	99.5	101.1	99.4
14	95.9	108.4	106.7	106.6	106.7	57.5	58.8	56.8
15	26.2	29.2	28.0	27.2	28.3	34.9	35.9	35.3
16	21.6	23.3	22.9	23.0	22.4	28.7	29.8	24.5
17	49.8	54.2	52.7	52.7	53.0	48.9	50.7	47.9
18	18.3	18.6	17.5	17.7	18.2	19.2	20.1	19.7
19	23.8	22.8	21.5	22.2	21.6	22.1	22.8	22.2
20	77.0	77.1	82.9	83.3	76.0	75.8	76.1	82.8
21	20.7	20.4	21.1	21.2	20.1	21.2	21.4	21.7
22	76.8	79.5	81.7	81.8	76.7	76.4	77.9	81.7
23	24.5	25.5	23.5	23.5	24.5	26.5	27.3	27.0
24	40.8	42.2	41.3	41.3	40.7	40.3	42.2	41.0
25	71.0	71.3	70.8	70.3	70.7	71.2	71.3	70.4
26	29.4	29.0	28.8	28.9	29.4	29.0	29.0	29.1
27	29.6	29.8	29.6	28.9	29.9	30.1	29.9	29.6
2,3-$\underline{C}(CH_3)_2$	108.2	—	108.0	—	107.9	—	—	107.8
2,3-$C(\underline{C}H_3)_2$	26.5 28.6	—	25.9 28.4	—	25.7 28.5	—	—	26.1 28.6
20,22-$\underline{C}(CH_3)_2$	—	—	107.1	107.0	—	—	—	106.8
20,22-$C(\underline{C}H_3)_2$	—	—	26.3 28.7	26.6 29.5	—	—	—	27.0 29.6

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* ^{13}C NMR spectra of compounds **8** and **12** are given as differences from mixtures of compounds **8** and **4** and **12** and **19** respectively.

*2 Signals not determined due to the low solubility of compound **13** in $CDCl_3$.

TABLE 3. ^{13}C NMR Spectra of Compounds **15-20**

C	Chemical shifts, δ, ppm						
	15	**16**		**17**	**18**	**19**	**20**
	$CDCl_3$ (100 MHz)	$CDCl_3$ (125 MHz)	CD_3OD (75 MHz)	$CDCl_3$ (125 MHz)	$CDCl_3$ (75 MHz)	$CDCl_3$ (100 MHz)	$CDCl_3$ (75 MHz)
1	29.9	36.6	39.1	35.5	36.3	35.4	37.1
2	75.1	68.4	69.7	73.4	68.6	73.4	72.5
3	73.0	68.2	69.7	72.5	68.3	72.5	71.6
4	28.7	35.3	32.1	31.3	29.7	31.2	27.0
5	49.8	49.3	50.9	49.5	49.3	49.5	53.2
6	198.6	202.6	206.3	202.4	203.7	202.5	213.0
7	115.3	122.0	121.3	121.1	120.7	121.2	42.2
8	177.7	—*	157.2	152.3	154.0	152.5	121.6
9	89.5	74.7	75.1	74.0	74.3	73.9	37.4
10	36.9	41.6	42.8	41.1	41.6	40.6	43.9
11	24.5	28.6	29.4	28.4	28.3	28.3	20.2
12	29.1	35.7	36.4	35.2	31.9	35.3	37.3
13	99.5	47.7	—*[2]	47.4	47.4	47.5	38.2
14	57.2	147.2	149.6	147.1	147.6	147.1	145.4
15	35.0	131.6	132.1	131.1	131.0	131.5	25.1
16	26.3	31.2	37.0	32.0	35.1	31.1	22.6
17	48.9	57.7	58.9	57.8	57.5	57.8	55.6
18	19.6	19.0	20.0	18.8	18.9	19.0	19.8
19	21.7	28.5	29.0	28.3	28.9	25.8	23.7
20	77.0	76.1	77.2	83.3	83.2	76.1	84.0
21	21.3	20.1	20.4	21.1	21.2	20.0	22.0
22	76.5	76.5	78.5	81.7	81.8	76.6	81.8
23	26.7	25.9	27.2	23.8	23.6	25.9	24.0
24	40.7	40.3	42.2	41.3	41.1	40.9	41.5
25	71.2	71.2	71.3	70.4	70.6	70.9	70.5
26	29.0	29.5	29.6	29.5	29.9	29.4	29.3
27	30.3	29.5	29.9	29.5	30.9	30.0	29.8
2,3-$\underline{C}(CH_3)_2$	107.8	—	—	107.5	—	107.5	107.9
2,3-$C(\underline{C}H_3)_2$	26.1 28.6	—	—	25.8 28.0	—	28.1 28.4	26.0 29.1
20,22-$\underline{C}(CH_3)_2$	—	—	—	107.1	107.1	—	107.1
20,22-$C(\underline{C}H_3)_2$	—	—	—	26.7 28.8	26.8 29.9	—	26.9 28.2

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* Signals not determined due to the low solubility of compound **16** in $CDCl_3$.

*[2] Signal obscured by the solvent signal (~ 49 ppm).

X-ray crystallographic analysis of compound **10** (Fig. 1) showed that inversion of the configuration of the chiral centers did not occur in the change from compound **2** to oxetane **10** and that compound **10** has the 9α,14α-epoxy-9-dehydro-14-desoxy-20-hydroxyecdysone 2,3:20,22 diacetonide structure. In the crystal the molecules of oxetane **10** form hydrogen bonded dimers (hydrogen bond O(25)–H···O(9,14) Å (symmetry code -x+1, y, -z+1), O···O distance 2.873(4) Å, O–H···O angle 165(5)°) (Fig. 2).

Since the ^1H and ^{13}C NMR spectra of compounds **9, 11, 12** are similar to the spectrum of compound **10** they are the 9α,14α-epoxy-9-dehydro-14-desoxy-20-hydroxyecdysone (**9**) and its 20,22- **11** and 2,3-acetonides **12**.

The ^{13}C NMR spectrum of compound **5** agrees with the spectrum of the previously obtained by photochromic transformation of the 20-hydroxyecdysone to 14α-hydroperoxy-20-hydroxyecdysone [8]. The ^{13}C NMR spectra of compounds **6-8** were similar to that of the 14α-hydroxyperoxide **5**. The shift of the C-14 signal to low field (Δδ ~ 11 ppm) is typical for the ^{13}C NMR spectra of hydroperoxides [3, 8].

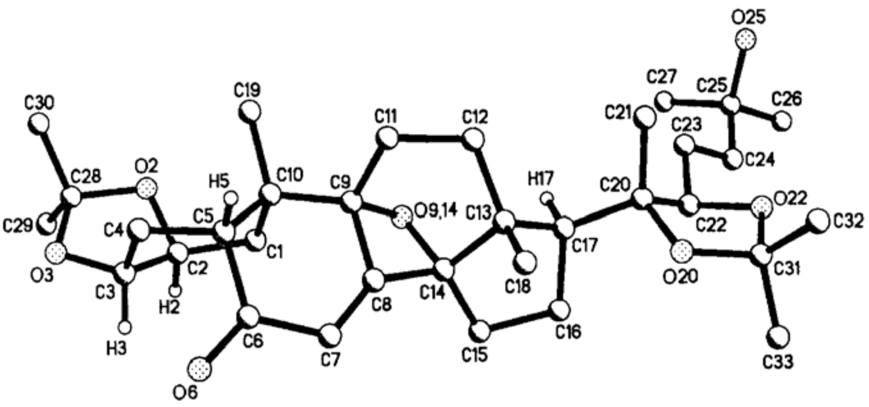


Fig. 1. Crystal structure of the compound **10** molecule.

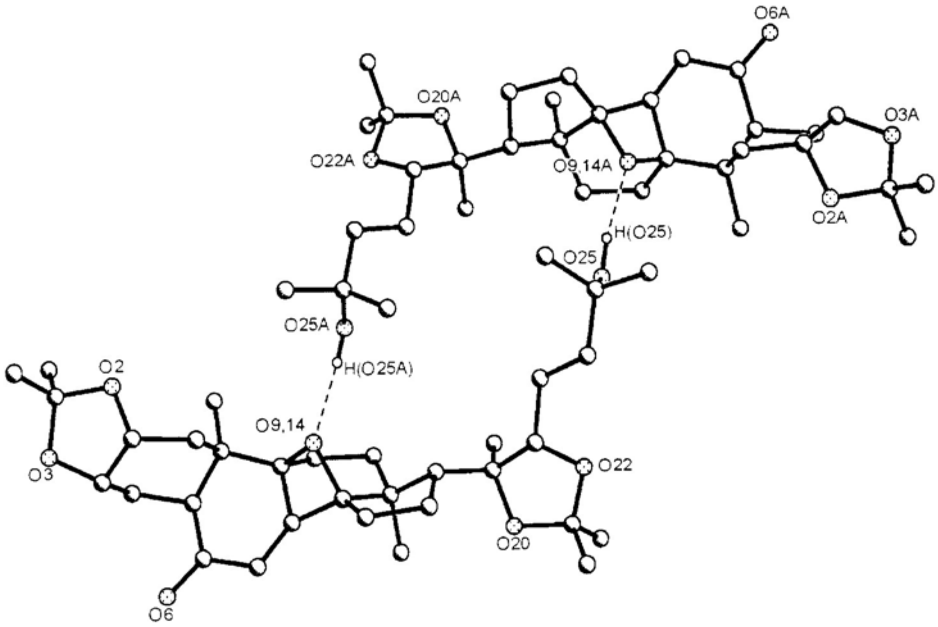


Fig. 2. H-Bonded dimer of oxetane **10** in the crystal.

The structure of compound **13** was proved from ^{1}H NMR and ^{13}C NMR spectroscopic data by a combination of 1D and 2D procedures. It was evident from the HMBC ^{1}H–^{13}C experiments that four of the five observed methyl signals are readily assigned as 26-Me, 27-Me (auto cross peak correlations present), 21-Me (correlated with the C-22 and C-17 signals), and 19-Me (correlated with the C-1 and C-5 signals), i.e. all of these methyl groups have typical chemical shifts. On the other hand a correlation of the signal for the 18-Me group (δ 19.2 ppm) with the C-17 signal is absent but a correlation is observed with the C-8 signal at 178.2 ppm and this points to a 1,2-migration of the 18-Me from C-13 to the C-14 atom. Such a change of the 18-Me positioning is also confirmed by the correlation of its signal with those of C-14, C-15, and C-13. The placing of the oxacycle between atoms C-9 and C-13 follows from the correlation of the 19-Me and H-7 signals with that at 89.4 ppm (C-9) and of the 18-Me and H-17 signals with that at 99.5 ppm (C-1).

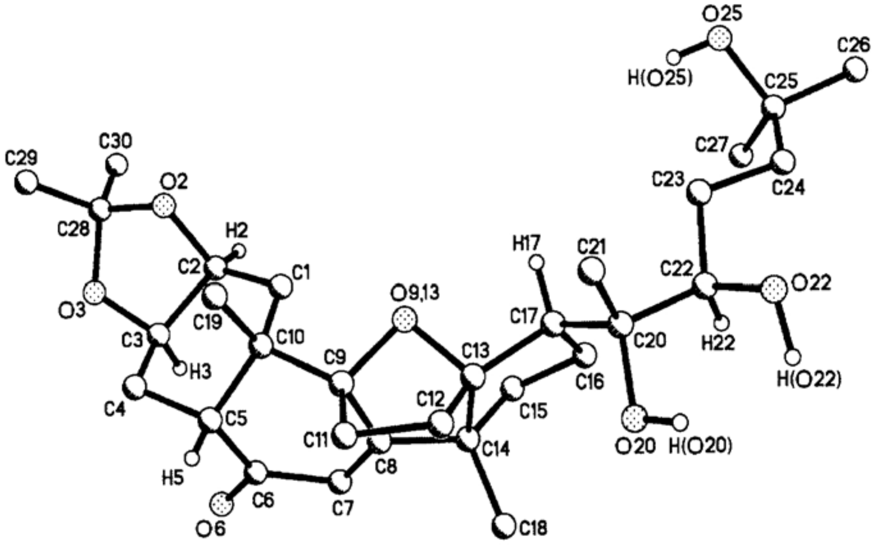


Figure 3. Crystal structure of the compound **15** molecule.

TABLE 4. Bond Lengths (*l*) in Compounds **10** and **15**

Bond	*l*, Å		Bond	*l*, Å	
	10	**15**		**10**	**15**
O(9,13)–C(9)	—	1.447(3)	C(8)–C(14)	1.493(5)	1.515(4)
O(9,13)–C(13)	—	1.467(3)	C(9)–C(10)	1.527(5)	1.534(4)
O(9,14)–C(9)	1.510(4)	—	C(9)–C(11)	1.534(5)	1.565(4)
O(9,14)–C(14)	1.506(4)	—	C(10)–C(19)	1.531(5)	1.531(5)
O(2)–C(2)	1.434(4)	1.442(4)	C(11)–C(12)	1.552(5)	1.565(4)
O(2)–C(28)	1.434(4)	1.430(3)	C(12)–C(13)	1.537(5)	1.541(4)
O(3)–C(3)	1.436(4)	1.434(4)	C(13)–C(14)	1.549(5)	1.568(4)
O(3)–C(28)	1.444(4)	1.465(4)	C(13)–C(17)	1.555(5)	1.549(4)
O(6)–C(6)	1.231(4)	1.221(4)	C(13)–C(18)	1.516(5)	—
O(20)–C(20)	1.448(4)	1.438(4)	C(14)–C(15)	1.503(5)	1.543(4)
O(20)–C(31)	1.459(4)	—	C(14)–C(18)	—	1.526(5)
O(22)–C(22)	1.430(4)	1.431(3)	C(15)–C(16)	1.542(5)	1.539(4)
O(22)–C(31)	1.423(4)	—	C(16)–C(17)	1.545(5)	1.554(4)
O(25)–C(25)	1.431(5)	1.462(4)	C(17)–C(20)	1.536(5)	1.542(4)
O(25)–H(O25)	0.92(5)	0.83(4)	C(20)–C(21)	1.517(5)	1.539(5)
C(1)–C(2)	1.516(5)	1.518(4)	C(20)–C(22)	1.540(5)	1.550(4)
C(1)–C(10)	1.544(5)	1.544(4)	C(22)–C(23)	1.512(5)	1.523(4)
C(2)–C(3)	1.523(5)	1.530(4)	C(23)–C(24)	1.528(5)	1.540(4)
C(3)–C(4)	1.517(5)	1.522(4)	C(24)–C(25)	1.535(5)	1.532(4)
C(4)–C(5)	1.536(5)	1.533(4)	C(25)–C(26)	1.511(5)	1.530(4)
C(5)–C(6)	1.535(5)	1.533(5)	C(25)–C(27)	1.518(6)	1.519(4)
C(5)–C(10)	1.569(5)	1.560(4)	C(28)–C(29)	1.505(6)	1.503(5)
C(6)–C(7)	1.467(5)	1.464(4)	C(28)–C(30)	1.513(5)	1.519(4)
C(7)–C(8)	1.320(5)	1.333(4)	C(31)–C(32)	1.513(6)	—
C(8)–C(9)	1.490(5)	1.505(5)	C(31)–C(33)	1.511(6)	—

For compound **15** it proved possible to isolate crystals (from EtOA*c*/*n*-C_6H_{12}, 1:1) and X-ray structural analysis (Fig. 3) showed that the synthesized 9,13-oxa analog is the 2,3-acetonide of 9-dehydro-13-demethyl-14-desoxy-9α,13α-epoxy-20-hydroxy-14β-methylecdysone. The mutual similarity of the ^1H and ^{13}C NMR spectra of compounds **13-15** shows that they are all 9-dehydro-13-demethyl-14-desoxy-9α,13α-epoxy-20-hydroxy-14β-methylecdysone derivatives.

TABLE 5. Valence Angles (ω) in Compounds **10** and **15**

Angle	ω, deg		Angle	ω, deg	
	10	**15**		**10**	**15**
C(9)–O(9,13)–C(13)	—	98.2(2)	C(14)–C(13)–C(17)	99.5(3)	107.8(2)
C(9)–O(9,14)–C(14)	87.5(2)	—	O(9,13)–C(13)–C(12)	—	100.9(2)
C(2)–O(2)–C(28)	107.4(2)	105.6(2)	O(9,13)–C(13)–C(17)	—	107.9(2)
C(3)–O(3)–C(28)	108.6(2)	108.7(2)	O(9,13)–C(13)–C(14)	—	100.8(2)
C(20)-O(20)–C(31)	108.7(2)	—	C(8)–C(14)–C(15)	123.9(3)	114.4(2)
C(31)–O(22)–C(22)	106.5(2)	—	C(8)–C(14)–O(9,14)	86.0(2)	—
C(25)–O(25)–H(O25)	103(4)	106(3)	C(15)–C(14)–O(9,14)	114.6(3)	—
C(2)–C(1)–C(10)	114.7(3)	116.7(2)	C(8)–C(14)–C(13)	113.9(3)	100.6(3)
O(2)–C(2)–C(1)	111.4(3)	112.9(2)	C(15)–C(14)–C(13)	107.9(3)	101.1(2)
O(2)–C(2)–C(3)	101.4(3)	101.1(2)	O(9,14)–C(14)–C(13)	108.2(3)	—
C(1)–C(2)–C(3)	117.3(3)	116.9(2)	C(8)–C(14)–C(18)	—	112.6(3)
O(3)–C(3)–C(4)	111.6(3)	110.9(2)	C(18)–C(14)–C(15)	—	111.1(3)
O(3)–C(3)–C(2)	102.3(3)	102.8(2)	C(18)–C(14)–C(13)	—	116.2(2)
C(4)–C(3)–C(2)	113.4(3)	113.1(2)	C(14)–C(15)–C(16)	106.2(3)	102.2(2)
C(3)–C(4)–C(5)	112.8(3)	110.1(2)	C(15)–C(16)–C(17)	104.7(3)	105.1(2)
C(6)–C(5)–C(4)	110.4(3)	110.3(2)	C(20)–C(17)–C(16)	114.8(3)	113.8(2)
C(6)–C(5)–C(10)	114.2(3)	114.1(2)	C(20)–C(17)–C(13)	118.7(3)	118.1(2)
C(4)–C(5)–C(10)	109.6(3)	110.5(3)	C(16)–C(17)–C(13)	104.1(3)	103.8(2)
O(6)–C(6)–C(7)	120.9(3)	121.1(3)	O(20)–C(20)–C(21)	109.1(3)	110.1(2)
O(6)–C(6)–C(5)	120.9(3)	120.3(3)	O(20)–C(20)–C(17)	110.1(3)	105.8(2)
C(7)–C(6)–C(5)	118.2(3)	118.6(3)	C(21)–C(20)–C(17)	112.8(3)	111.9(3)
C(8)–C(7)–C(6)	117.2(3)	119.6(3)	O(20)–C(20)–C(22)	100.4(3)	108.0(2)
C(7)–C(8)–C(9)	127.2(3)	124.3(3)	C(21)–C(20)–C(22)	110.9(3)	109.7(2)
C(7)–C(8)–C(14)	141.8(3)	130.4(3)	C(17)–C(20)–C(22)	112.8(3)	111.2(2)
C(9)–C(8)–C(14)	88.7(3)	105.3(3)	O(22)–C(22)–C(23)	109.1(3)	107.6(2)
C(8)–C(9)–O(9,13)	—	101.5(2)	O(22)–C(22)–C(20)	101.7(3)	109.8(2)
C(8)–C(9)–O(9,14)	86.0(2)	—	C(23)–C(22)–C(20)	118.4(3)	115.0(2)
C(8)–C(9)–C(10)	115.1(3)	114.3(2)	C(22)–C(23)–C(24)	111.5(3)	111.8(2)
O(9,13)–C(9)–C(10)	—	112.7(2)	C(23)–C(24)–C(25)	114.5(3)	115.5(2)
O(9,14)–C(9)–C(10)	117.2(3)	—	O(25)–C(25)–C(26)	110.1(3)	106.1(3)
C(8)–C(9)–C(11)	109.1(3)	105.2(3)	O(25)–C(25)–C(27)	108.9(4)	109.0(2)
O(9,13)–C(9)–C(11)	—	102.3(2)	C(26)–C(25)–C(27)	110.4(4)	110.0(3)
O(9,14)–C(9)–C(11)	107.2(3)	—	O(25)–C(25)–C(24)	106.3(3)	109.8(3)
C(10)–C(9)–C(11)	117.8(3)	118.9(2)	C(26)–C(25)–C(24)	109.0(3)	109.5(2)
C(9)–C(10)–C(19)	111.2(3)	110.9(2)	C(27)–C(25)–C(24)	112.1(3)	112.3(3)
C(9)–C(10)–C(1)	110.2(3)	108.2(2)	O(2)–C(28)–O(3)	105.5(3)	104.8(2)
C(19)–C(10)–C(1)	110.6(3)	109.7(3)	O(2)–C(28)–C(29)	110.4(3)	109.1(2)
C(9)–C(10)–C(5)	104.9(3)	107.0(3)	O(3)–C(28)–C(29)	109.3(3)	110.0(2)
C(19)–C(10)–C(5)	111.1(3)	112.0(2)	O(2)–C(28)–C(30)	107.9(3)	111.6(2)
C(1)–C(10)–C(5)	108.7(3)	108.9(2)	O(3)–C(28)–C(30)	110.6(3)	108.4(2)
C(9)–C(11)–C(12)	109.9(3)	102.0(2)	C(29)–C(28)–C(30)	112.9(3)	112.7(3)
C(13)–C(12)–C(11)	113.4(3)	101.5(2)	O(22)–C(31)–O(20)	105.5(3)	—
C(18)–C(13)–C(12)	111.9(3)	—	O(22)–C(31)–C(33)	110.4(3)	—
C(18)–C(13)–C(14)	108.3(3)	—	O(20)–C(31)–C(33)	108.8(3)	—
C(12)–C(13)–C(14)	107.0(3)	110.2(3)	O(22)–C(31)–C(32)	108.5(3)	—
C(18)–C(13)–C(17)	113.8(3)	—	O(20)–C(31)–C(32)	110.0(3)	—
C(12)–C(13)–C(17)	115.1(3)	126.1(2)	C(33)–C(31)–C(32)	113.3(3)	—

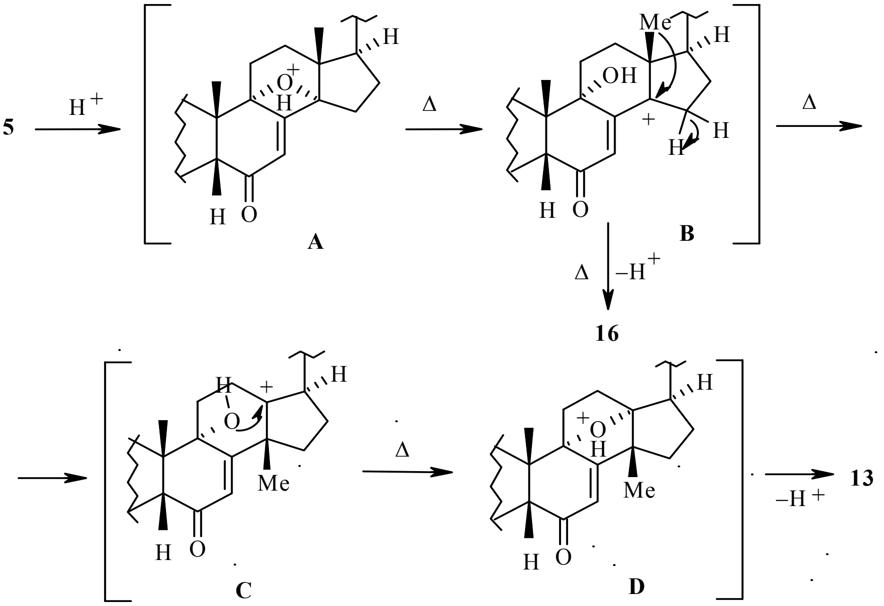
The ^{1}H and ^{13}C NMR spectra of compounds **16-19** are closely similar to the spectra of the previously reported [4] stachisterone B and its acetonides. The main difference in the spectra is due to the presence of a 9-hydroxy group in compounds **16-19** which causes a low field shift of the C-9 signal ($\Delta\delta \sim 35$ ppm) and its transformation from a doublet to a singlet (^{13}C NMR, *J*mod regime, Table 1). The H-9 signal is absent in the ^{1}H NMR spectra of compounds **16-19** and the H-7 signal becomes a singlet. Such a pattern is seen in the ^{1}H and ^{13}C NMR spectra recently reported for 9α,20-hydroxyecdysone separated from the plant species *Silene italica ssp. nemoralis* [9]. The close chemical shifts of the H-1 to H-5 protons in the ^{1}H NMR spectra of this ecdysteroid and compounds **16-19** points to an α-configuration for the 9-hydroxy group in the synthesized stachisterones.

Evidently the observed reaction of ecdysteroids needs the participation of oxygen which apparently occurs in the process of evaporation of ammonia from the reaction mixture in open air. In fact, if evaporation of ammonia after treatment of the reaction mixture with diacetonide **2** is carried out in an argon stream compound **20** (the $\Delta^{8(14)}$ analog of diacetonide **2)** can be separated. Its formation is due to the ready elimination of the 14α-hydroxyl group found in the γ-position of the Δ^{7}-6-keto group [3, 10]. It has been reported that a compound similar to compound **20** but with free hydroxyl groups, is formed upon photolysis of 20-hydroxyecdysone [3]. However, it was then shown that this stable in air compound was the dimer of the $\Delta^{8(14)}$ analog [8]. The structure of compound **20** was proved from the 1D and 2D ^{1}H and ^{13}C NMR spectra (HHCOSY, HSQC, HMBC, and NOESY). The tetrasubstituted double bond in the ^{13}C NMR spectrum of compound **20** corresponds to singlets (*J*mod regime) at 121.6 (C-8) and 145.4 (C-14), its $\Delta^{8(14)}$ position being confirmed in the HMBC experiment by cross peaks for the 7-CH$_2$ and 18-CH$_3$ protons with *sp*^{2}-atoms C-8 and C-14 respectively.

Compound **20** was progressively oxidized in air to give the 14α-hydroperoxide **10**. It can evidently be considered that the $\Delta^{8(14)}$ analog **20** is an intermediate compound at least for the 14α-hydroxperoxide **6**.

The reaction of oxetane **9** (and the remaining oxetanes **10-12**) in proton donor medium (ROH) is likely due to formation of the oxonium ion **A** which isomerizes to the C-14 carbenium ion **B**. Its stabilization occurs either as a result of fission of a proton from C-15 to form the 9-hydroxystachisterone **16** or through 1,2-migration of the 18-Me group to form carbenium ion **C** with subsequent formation of a 9,13 oxacycle and then compound **13** after deprotonation of oxonium ion **D** (Scheme 2).

Scheme 2



Hence, in place of a transformation to the corresponding saturated ketones typical of α,β-unsaturated ketones, ecdysteroids in litium solution in liquid ammonia undergo an unusual transformation to give 9,14-oxahetero analogs which can typically rearrange to the isomeric 9,13-oxahetero analogs occurring with 1,2-migration of the 18-Me group from position 13 to position 14.

EXPERIMENTAL

IR spectra were taken on a Specord IR-75 instrument for KBr tablets. UV spectra were recorded on a Specord M-40 spectrometer. ^1H and ^{13}C NMR spectra were obtained on Bruker AM-300 (300 and 75 MHz respectively), Bruker Avance-400 (400 and 100 MHz respectively), and Bruker Avance-500 (500 and 125 MHz respectively). Chemical shifts are reported relative to internal standard TMS. High resolution mass spectra were taken on VG ZAB-E and Finnigan MAT 8200 E instruments. Angles of rotation were measured on a Perkin-Elmer 141 polarimeter. Elemental analysis was performed on a Carlo Erba model 1106 analyzer. Melting points were determined on a Boetius hot stage apparatus. Column chromatography and TLC were carried out using silica gel (< 0.06 mm) and Silufol UV-254 plates respectively.

X-ray analysis of compounds **10** and **15** was carried out on a Bruker SMART APEX II diffractometer [11] (graphite monochromator, λ = 0.71073 Å, ω-scanning, 2θ = 52º). The structure was solved by a direct method and refined using F^2_{hkl} full matrix least squares analysis with anisotropic thermal parameters for all non-hydrogen atoms. The hydrogen atoms of the O(25)H groups were revealed in difference synthesis and refined in the isotropic approximation. The remaining hydrogen atoms were included in the geometrically calculated of position and refined in the "riding" model. The final difference factors were wR_2 = 0.0962 and GOOF = 1.016 for all of the independent reflections (R_1 = 0.0477 calculated for F_{hkl} for 2272 observed reflections with $I > 2\sigma(I)$). All calculations were carried out on a PC using the SHELXTL program package [12].

Crystals of compound **10** ($C_{33}H_{50}O_7$, M 558.73) grown in diethyl ether and **15** ($C_{30}H_{46}O_7$, M 518.67) are monoclinic, space group *C*2. For crystals of **10** at 100 K: a =25.754(4), b = 6.6209(11), c = 20.260(3) Å, β = 114.991(3)º, V = 3131.1(9) Å^3, Z = 4, ρ_{calc} =1.185 g/cm^3, μ(MoKα) = 0.82 cm^{-1}; for crystals of **15** at 120 K: a = 21.469(3), b = 8.9918(14), c = 15.286(2) Å, β = 109.933(2)º, V = 2774.1(7) Å^3, Z = 4, ρ_{calc} = 1.242 g/cm^3, μ(MoKα) = 0.87 cm^{-1}). Basic bond lengths and valence angles for crystals of compounds **10** and **15** are given in Tables 4 and 5 (atomic numbering corresponds with that in Figs. 1 and 3). The full tables of atomic coordinates, bond lengths, valence and torsional angles, and anisotropic thermal parameters have been placed in the Cambridge Crystallographic Data Center (No. CCDC 661563 for compound **10** and No. CCDC 688592 for compound **15**).

The ^{13}C NMR spectra of the compounds are given in Tables 1-3.

9-Dehydro-14-desoxy-9α,14α-epoxy-20-hydroxyecdysone or (20R,22R)-9α,14α-Epoxy-2β,3β,20,22,25-pentahydroxy-5β-cholest-7-en-6-one (9) and 14-Desoxy-14α-hydroperoxy-20-hydroxyecdysone or 2β,3β,20,22,25-Pentahydroxy-14α-hydroperoxy-5β-cholest-7-en-6-one (5). Compound **1** (2 g, 4.17 mmol) (prepared according to [6], mp 246ºC) in anhydrous THF (10 ml) was added to a solution of Li (0.35 g, 50 mmol) in ammonia (50 ml, distilled from Na). The mixture was stirred at -33ºC for 0.5 h, NH_4Cl (4.0 g) was added, and the reaction mixture was left for the ammonia to evaporate in air. The residue was extracted with ethyl acetate (3×50 ml) and the solvent was evaporated to give a solid residue which was chromatographed on a silica gel column (100 g SiO_2, eluent $CHCl_3$–MeOH, 10:1) to give compound **9** (1.02 g, 50%) with R_f 0.36 ($CHCl_3$–MeOH, 5:1) and compound **5** (0.9 g, 45%) with R_f 0.42 ($CHCl_3$–MeOH, 5: 1).

Compound 9. Mp 148–150°C, $[\alpha]_D^{20}$ +48.9° (*c* 0.92, MeOH). IR spectrum, ν, cm^{-1}: 3380, 2900, 1640. UV spectrum (MeOH), $\lambda_{\max}$, nm: 241. ^1H NMR spectrum (300 MHz, CD_3OD), δ, ppm (*J*, Hz): 1.07 (3H, s, 18-CH_3); 1.17 (3H, s, 21-CH_3); 1.19 (3H, s, 26-CH_3); 1.20 (3H, s, 27-CH_3); 1.38 (3H, s, 19-CH_3); 2.33 (1H, m, H-17); 2.54 (1H, m, H-5); 3.28 (1H, m, H-3); 3.32 (1H, m, H-22); 3.94 (1H, m, H-2); 5.70 (1H, s, H-7). Found: *m/z* 479.3006 $[M+H]^+$. $C_{27}H_{42}O_7$ + H. Calculated: [M + H] 479.3009.

Compound 5. Mp 150-152°C (mp 158°C [3]), $[\alpha]_D^{20}$ +49.3° (*c* 0.56, MeOH). IR spectrum, ν, cm^{-1}: 3400, 2900, 1700, 1450. UV spectrum (MeOH), λ_{max}, nm: 242. ^{1}H NMR spectrum (300 MHz, CD_3OD), δ, ppm (*J*, Hz): 1.11 (3H, s, 18-CH_3); 1.13 (3H, s, 19-CH_3); 1.32 (3H, s, 21-CH_3); 1.34 (3H, s, 26-CH_3); 1.36 (3H, s, 27-CH_3); 2.44 (1H, m, H-17); 2.55 (1H, dd, *J* = 12.5 and *J* = 3.5, H-5); 3.22 (1H, m, H-9); 3.46 (1H, m, H-22); 4.05 (1H, m, H-2); 4.11 (1H, m, H-3); 5.94 (1H, br. s, H-7). Found: *m/z* 481.3156 $[M+H–O]^+$. $C_{27}H_{44}O_8$+H–O. Calculated: [M+H–O] 481.3165.

9-Dehydro-14-desoxy-9α,14α-epoxy-20-hydroxyecdysone 2,3:20,22-Diacetonide or (20*R*,22*R*)-2β,3β:20,22-Bis[(dimethylmethylene)dioxy]-9α,14α-epoxy-25-hydroxy-5β-cholest-7-en-6-one (10) and 14-Desoxy-20-hydroxy-14α-hydroperoxyecdysone 2,3:20,22-diacetonide or 2β,3β:20,22-Bis[(dimethylmethylene)dioxy]-25-hydroxy-(20*R*,22*R*)-14α-hydroperoxy-5β-cholest-7-en-6-one (6). Compound **2** (2 g, 3.6 mmol) (prepared as in [4], mp 234-235ºC) was dissolved in anhydrous THF (10 ml) and added to a solution of Li (0.3 g, 43 mmol) in ammonia (50 ml, distilled from Na). The mixture was stirred for 0.5 h at -33°C, NH_4Cl (4 g) was added, and then worked up as reported in the previous preparation. The product was a solid residue which was chromatographed on a silica gel column (60 g, SiO_2, eluent $CHCl_3$–MeOH, 100:1) to give compound **10** (1.5 g, 75%) with R_f 0.60 ($CHCl_3$–MeOH, 8:1) and compound **6** (0.4 g, 19%) with R_f 0.49 ($CHCl_3$–MeOH, 8:1).

Compound 10. Mp 232-233°C, $[\alpha]_D^{18}$ +75° (*c* 1.0, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3400, 2900, 1650, 1450, 1370. UV spectrum (MeOH), λ_{max}, nm: 242. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.97 (3H, s, 18-CH_3); 1.16 (3H, s, 21-CH_3); 1.21 (3H, s, 26-CH_3); 1.22 (3H, s, 27-CH_3); 1.26 and 1.28 (6H, two s, 2,3-$C(CH_3)_2$); 1.33 (3H, s, 19-CH_3); 1.41 and 1.48 (6H, two s, 20,22-$C(CH_3)_2$); 1.46 and 1.55 (2H, two m, H-23); 1.52 and 1.69 (2H, two m, H-24); 1.56 (1H, m, H_a-4); 1.76 and 1.98 (2H, two m, H-16); 1.89 and 2.10 (2H, two m, H-15); 1.89 and 2.47 (2H, two m, H-11); 1.90 and 1.99 (2H, two m, H-12); 1.92 and 2.12 (2H, two m, H-1); 2.08 (1H, m, H-17); 2.19 (1H, m, H-5); 2.54 (1H, m, H_e-4); 3.71 (1H, d, *J* = 9.4, H-22); 4.01 (1H, m, $w_{1/2}$ = 25, H-3); 4.20 (1H, m, H-2); 5.61 (1H, s, H-7). Found: *m/z* 559.3641 $[M+H]^+$. $C_{33}H_{50}O_7$+H. Calculated: [M+H] 559.3635.

Compound 6. Mp 139-141°C (amorphous material [3]), $[\alpha]_D^{18}$ +17.2° (*c* 5.2, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3400, 2965, 1650. UV spectrum (CH_3OH), λ_{max}, nm: 242. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.85 (3H, s, 18-CH_3); 1.02 (3H, s, 19-CH_3); 1.12 (3H, s, 21-CH_3); 1.24 (3H, s, 26-CH_3); 1.25 (3H, s, 27-CH_3); 1.29 and 1.98 (2H, two m, H-1); 1.33 (6H, s, 2,3-$C(CH_3)_2$); 1.41 and 1.49 (6H, two s, 20,22-$C(CH_3)_2$); 1.48 and 1.59 (2H, two m, H-23); 1.58 and 1.72 (2H, two m, H-24); 1.64 and 1.76 (2H, two m, H-11); 1.77 and 1.94 (2H, two m, H-12); 1.78 and 2.05 (2H, two m, H-16); 1.81 and 2.06 (2H, two m, H-15); 1.99 (1H, m, H_a-4); 2.05 (1H, m, H_e-4); 2.12 (1H, m, H-17); 2.36 (1H, dd, *J* = 10.0 and *J* = 7.0, H-5); 2.73 (1H, m, $w_{1/2}$ = 23, H-9); 3.64 (1H, m, $w_{1/2}$ = 15, H-22); 4.25 (1H, m, $w_{1/2}$ = 21, H-2); 4.28 (1H, m, $w_{1/2}$ = 12, H-3); 5.83 (1H, d, *J* = 2.6, H-7). Found: *m/z* 561.3795 $[M+H–O]^+$. $C_{33}H_{52}O_8$+H–O. Calculated: [M+H–O] 561.3791.

9-Dehydro-14-desoxy-9α,14α-epoxy-20-hydroxyecdysone 20,22-Acetonide or 20,22-[(Dimethylmethylene)dioxy]-(20*R*,22*R*)-9α,14α-epoxy-2β,3β,25-trihydroxy-5β-cholest-7-en-6-one (11) and 14-Desoxy-20-hydroxy-14α-hydroperoxyecdysone 20,22-Acetonide or 20,22-[(Dimethylmethylene)dioxy]-2β,3β,25-trihydroxy-(20*R*,22*R*)-14α-hydroperoxy-5β-cholest-7-en-6-one (7). Compound **3** (1 g, 1.9 mmol) (prepared according to [4], mp 223-224ºC) was dissolved in anhydrous THF (5 ml) and added to a solution of Li (0.16 g, 23 mmol) in ammonia (30 ml, distilled from Na). The mixture was stirred for 20 min at -33ºC, NH_4Cl (2.0 g) was added, and the product was treated as above to give a solid residue. This was column chromatographed on silica gel (40 g SiO_2, eluent $CHCl_3$–MeOH, 20:1) to give compound **7** (0.6 g, 60%) with R_f 0.55 ($CHCl_3$–MeOH, 4:1) and compound **11** (0.15 g, 15%) with R_f 0.44 ($CHCl_3$–MeOH, 4:1).

Compound 11. Mp 134-136°C, $[\alpha]_D^{18}$ +61.1° (*c* 2.49, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3400, 2900, 1650, 1450, 1350. UV spectrum (CH_3OH), λ_{max}, nm: 242. ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.94 (3H, s, 18-CH_3); 1.14 (3H, s, 21-CH_3); 1.19 (3H, s, 26-CH_3); 1.19 (3H, s, 27-CH_3); 1.25 (3H, s, 19-CH_3); 1.36 and 1.39 (6H, two s, 20,22-$C(CH_3)_2$); 3.40 (1H, m, H-3); 3.96 (1H, d, *J* = 8.5, H-22); 3.99 (1H, m, H-2); 5.63 (1H, s, H-7). Found: *m/z* 518.3256 $[M]^+$. $C_{30}H_{46}O_7$. Calculated: M = 518.3243.

Compound 7. Mp 120-123°C, $[\alpha]_D^{20}$ +52.6° (*c* 4.27, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3400, 2950, 1660. UV spectrum (CH_3OH), λ_{max}, nm: 242. ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.83 (3H, s, 18-CH_3); 0.96 (3H, s, 19-CH_3); 1.12 (3H, s, 21-CH_3); 1.22 (3H, s, 26-CH_3); 1.25 (3H, s, 27-CH_3); 1.31 and 1.40 (6H, two s, 20,22-$C(CH_3)_2$); 2.14 (1H, m, H-17); 2.39 (1H, m, H-5); 2.93 (1H, m, H-9); 3.61 (1H, m, H-22); 3.88 (1H, m, H-2); 4.01 (1H, m, H-3); 5.85 (1H, br. s, H-7). Found, %: C 67.52; H 9.07. $C_{30}H_{48}O_8$. Calculated, %: C 67.14; H 9.01.

9-Dehydro-13-demethyl-14-desoxy-9α,13α-epoxy-20-hydroxy-14β-methylecdysone or (20*R*,22*R*)-13-Demethyl-9α,13α-epoxy-2β,3β,20,22,25-pentahydroxy-14β-methyl-5β-cholest-7-en-6-one (13) and 9α-Hydroxystachisterone B or (20*R*,22*R*)-2β,3β,9α,29,22,25-Hexahydroxy-5β-cholest-7,14-dien-6-one (16). Compound **9** (0.1 g, 0.21 mmol) was dissolved in MeOH (10 ml) and water (1 ml) and stirred for 24 h at room temperature. The reaction product was evaporated to give a solid residue which was column chromatographed on silica gel (10 g SiO_2, eluent $CHCl_3$–MeOH, 9:1) to give compound **13** (0.04 g, 40%) with R_f 0.37 and compound **16** (0.05 g, 50%) with R_f 0.27 ($CHCl_3$–MeOH, 5:1).

Compound 13. Mp 122-124°C, $[\alpha]_D^{21}$ +40.3° (*c* 1.1, CH_3OH). IR spectrum, ν, cm^{-1}: 3400, 2900, 1650, 1450, 1370. UV spectrum (MeOH), λ_{max}, nm: 242. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 1.20 (3H, s, 18-CH_3); 1.25 (3H, s, 26-CH_3); 1.26 (3H, s, 27-CH_3); 1.31 (3H, s, 21-CH_3); 1.39 and 1.71 (2H, two m, H-15); 1.41 and 1.65 (2H, two m, H-23); 1.45 and 2.17 (2H, two m, H-12); 1.49 (3H, s, 19-CH_3); 1.58 and 1.70 (2H, two m, H-24); 1.69 and 1.95 (2H, two m, H-1); 1.85 and 2.08 (2H, two m, H-16); 1.92 (1H, m, H_a-4); 2.10 (2H, m, H-11); 2.22 (1H, m, H-5); 2.39 (1H, m, H_e-4); 2.45 (1H, m, H-17); 3.49 (1H, m, H-3); 3.52 (1H, m, H-22); 3.98 (1H, m, H-2); 5.63 (1H, s, H-7). ^{1}H NMR spectrum (400 MHz, CD_3OD), δ, ppm: 1.18 (3H, s, 26-CH_3); 1.20 (3H, s, 27-CH_3); 1.24 (3H, s, 18-CH_3); 1.28 (3H, s, 21-CH_3); 1.38 and 1.60 (2H, two m, H-23); 1.42 and 1.81 (2H, two m, H-24); 1.43 and 1.73 (2H, two m, H-15); 1.46 and 2.18 (2H, two m, H-12); 1.49 (3H, s, 19-CH_3); 1.73 and 1.87 (2H, m, H-1); 1.87 and 2.11 (2H, two m, H-16); 1.94 (1H, m, H_a-4); 2.16 (2H, m, H-11); 2.29 (1H, m, H-5); 2.37 (1H, m, H_e-4); 2.52 (1H, m, H-17); 3.43 (1H, m, H-22); 3.94 (1H, m, H-2); 3.94 (1H, m, H-3); 5.67 (1H, s, H-7). Found: *m/z* 479.3002 $[M+H]^+$. $C_{27}H_{42}O_7$+H. Calculated: [M+H] 479.3009.

Compound 16. Mp 147-148°C, $[\alpha]_D^{21}$ -166° (*c* 1.0, CH_3OH). IR spectrum, ν, cm^{-1}: 3400, 2900, 1650, 1450, 1360. UV spectrum (CH_3OH), λ_{max}, nm: 298. ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.07 (3H, s, 19-CH_3); 1.14 (3H, s, 18-CH_3); 1.27 (6H, two s, 26-CH_3, 27-CH_3); 1.28 (3H, s, 21-CH_3); 1.43 and 1.61 (2H, two m, H-23); 1.44 and 2.12 (2H, two m, H-1); 1.62 and 1.75 (2H, two m, H-24); 1.75 and 2.12 (2H, two m, H-12); 1.94 (1H, m, H_a-4); 1.98 and 2.05 (2H, m, H-11); 2.16 (1H, m, H-17); 2.23 (1H, m, H_e-4); 2.26 (1H, ddd, *J* = 17.0, *J* = 7.8 and *J* = 3.8, H_a-16); 2.63 (1H, dd, *J* = 13.6 and *J* = 4.7, H-5); 2.65 (1H, ddd, *J* = 17.0, *J* = 11.0 and *J* = 2.2, H_e-16); 3.07 (1H, m, $w_{1/2}$ = 8.9, H-3); 3.47 (1H, d, *J* = 9.6, H-22); 4.42 (1H, m, $w_{1/2}$ = 22.0, H-2); 6.03 (1H, s, H-7); 6.12 (1H, dd, *J* = 3.4 and *J* = 2.2, H-15). ^{1}H NMR spectrum (300 MHz, CD_3OD) δ, ppm (*J*, Hz): 1.02 (3H, s, 19-CH_3); 1.12 (3H, s, 18-CH_3); 1.18 (3H, s, 26-CH_3); 1.20 (3H, s, 27-CH_3); 1.24 (3H, s, 21-CH_3); 3.32 (1H, m, H-22); 3.95 (1H, m, $w_{1/2}$ = 7, H-3); 4.38 (1H, m, $w_{1/2}$ = 20, H-2); 5.99 (1H, s, H-7); 6.14 (1H, br. s, H-15). Found: *m/z* 479.3006 $[M+H]^+$. $C_{27}H_{42}O_7$+H. Calculated: [M+H] 479.3009.

9-Dehydro-13-demethyl-14-desoxy-9α,13α-epoxy-20-hydroxy-14β-methylecdysone 2,3:20,22-Diacetonide or 13-Demethyl-14β-methyl-2β,3β:20:22,bis[(dimethylmethylene)dioxy]-(20*R*,22*R*)-9α,13α-epoxy-25-hydroxy-5β-cholest-7-en-6-one (14). Phosphomolybdic acid (40 mg, 0.02 mmol) was added to a solution of compound **13** (0.12 g, 0.25 mmol) in acetone (7 ml). The mixture was stirred for 15 min at room temperature (monitoring by TLC), the reaction product was evaporated, and water (3 ml) and saturated $NaHCO_3$ solution (3 ml) were added. The mixture was extracted with ethyl acetate (3×100 ml), solvent was evaporated, and the solid residue was column chromatographed in silica gel (10 g SiO_2, eluent $CHCl_3$–MeOH, 5:1) to give compound **14** (0.073 g, 52%) with R_f 0.76 ($CHCl_3$–MeOH, 5:1). Mp 192-194 °C, $[\alpha]_D^{20}$ +110° (*c* 1.0, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3400, 2900, 1650, 1450, 1380. UV spectrum (CH_3OH), λ_{max}, nm: 242. ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.19 (3H, s, 18-CH_3); 1.25 (6H, s, 26-CH_3 and 27-CH_3); 1.29 (3H, s, 21-CH_3);

1.31 and 1.42 (6H, two s, 20,22-$C(CH_3)_2$); 1.35 and 1.46 (6H, two s, 2,3-$C(CH_3)_2$); 1.52 (3H, s, 19-CH_3); 2.26 (1H, m, H-5); 2.38 (1H, m, H-17); 3.38 (1H, dd, *J* = 8.6 and *J* = 2.7, H-22); 4.06 (1H, m, H-2); 4.17 (1H, m, H-3); 5.63 (1H, s, H-7). Found, %: C 70.54; H 9.09. $C_{33}H_{50}O_7$. Calculated, %: C 70.94; H 9.02.

9-Dehydro-13-demethyl-14-desoxy-9α,13α-epoxy-20-hydroxy-14β-methylecdysone 2,3-Acetonide or 13-demethyl-(20*R*,22*R*)- 2β,3β-[(dimethylmethylene)dioxy]-9α,13α-epoxy-20,22,25-trihydroxy-14β-methyl-5β-cholest-7-en-6-one (15) and 9α-Hydroxystachisterone B 2,3-Acetonide or (20*R*,22*R*)-2,3-[(Dimethylmethylene)dioxy]-20,22,9α,25-tetrahydroxy-5β-cholest-7,14-dien-6-one (19). Compound **4** (1 g, 1.9 mmol) (prepared according to [13]) was dissolved in anhydrous THF (5 ml) and added to a solution of Li (0.16 g, 23 mmol) in ammonia (30 ml, distilled from Na). The mixture was stirred for 20 min at -33°C, NH_4Cl (2.0 g) was added, and the product was worked up as described in the experiment with the diacetonide **2**. The solid residue was column chromatographed on silica gel (40 g SiO_2, eluent $CHCl_3$–MeOH, 40:1) to give a mixture of compounds **12** and **19** (0.3 g, ^1H and ^{13}C NMR data) with R_f 0.42 ($CHCl_3$–MeOH, 7:1) in the ratio of about 2.4:1 from the relative intensities of the H-7 singlets at δ 5.62 and 6.05 ppm respectively) and a mixture of compounds **4** and **8** (0.41 g) with R_f 0.40 ($CHCl_3$–MeOH, 7:1) (^1H and ^{13}C NMR data). Repeated chromatography of the mixture of **12** and **19** (10 g, SiO_2, $CHCl_3$–MeOH, 40:1) gave compound **15** (0.12 g, 12%) with R_f 0.55 ($CHCl_3$–MeOH, 7:1) and compound **19** (0.13 g, 13%) with R_f 0.42 ($CHCl_3$–MeOH, 7: 1).

Compound 15. Mp 198-200°C, $[\alpha]_D^{20}$+72.1° (*c* 0.24, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3400, 2900, 1650, 1450, 1380. UV spectrum (CH_3OH), λ_{max}, nm: 242. ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 1.22 (3H, s, 18-CH_3); 1.26 (3H, s, 26-CH_3); 1.27 (3H, s, 27-CH_3); 1.29 (3H, s, 21-CH_3); 1.33 and 1.45 (6H, two s, 2,3-$C(CH_3)_2$); 1.52 (3H, s, 19-CH_3); 2.26 (1H, m, H-5); 2.45 (1H, m, H-17); 3.52 (1H, m, H-22); 4.05 (1H, m, H-2); 4.16 (1H, m, H-3); 5.62 (1H, s, H-7). Found, %: C 69.56; H 8.87. $C_{30}H_{46}O_7$. Calculated, %: C 69.47; H 8.94.

Compound 19. Mp 116-118°C, $[\alpha]_D^{25}$-179.5° (*c* 1.77, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3400, 2900, 1650, 1450, 1370. UV spectrum (CH_3OH), λ_{max}, nm: 298. ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.12 (3H, s, 18-CH_3); 1.14 (3H, s, 19-CH_3); 1.27 (9H, s, 21-CH_3, 26-CH_3, 27-CH_3); 1.34 and 1.58 (6H, two s, 2,3-$C(CH_3)_2$); 2.52 (1H, dd, *J* = 13.2 and *J* = 4.4, H-5); 3.46 (1H, m, H-22); 4.30 (1H, m, H-3); 4.54 (1H, dd, *J* = 12.8 and *J* = 6.4, H-2); 6.06 (1H, s, H-7); 6.14 (1H, br. s, H-15). Found, %: C 69.63; H 8.77. $C_{30}H_{46}O_7$. Calculated, %: C 69.47; H 8.94.

9α-Hydroxystachisterone B 2,3:20,22-Diacetonide or (20*R*,22*R*)-2β,3β:20,22-Bis[(dimethylmethylene)dioxy]-9α,25-dihydroxy-5β-cholest-7,14-dien-6-one (17). Compound **10** (0.3 g, 0.54 mmol) was dissolved in EtOH (15 ml) and THF (15 ml) and stirred for 240 h at room temperature. The reaction mixture was evaporated. The solid residue was chromatographed on a silica gel column (10 g SiO_2, eluent $CHCl_3$–MeOH, 30:1) to give a mixture of compounds **10** and **14** (0.1 g) (^1H and ^{13}C NMR data) with R_f 0.60 ($CHCl_3$–MeOH, 8:1) and compound **17** (0.2 g) (yield 67%) with R_f 0.40 ($CHCl_3$–MeOH, 8:1).

Compound 17. Mp 228-230°C, $[\alpha]_D^{18}$ -222° (*c* 1.0, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3400, 2900, 1650, 1450, 1370. UV spectrum (CH_3OH), λ_{max}, nm: 298. ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.07 (3H, s, 18-CH_3); 1.11 (3H, s, 19-CH_3); 1.22 (3H, s, 21-CH_3); 1.24 (3H, s, 26-CH_3); 1.25 (3H, s, 27-CH_3); 1.31 and 1.33 (6H, two s, 2,3-$C(CH_3)_2$); 1.39 and 2.24 (2H, two m, 1-CH_2); 1.43 and 1.50 (6H, two s, 20,22-$C(CH_3)_2$); 1.48 and 1.64 (2H, two m, H-23); 1.57 and 1.73 (2H, two m, H-24); 1.68 and 2.04 (2H, two m, H-12); 1.80 and 2.02 (2H, two m, H-11); 2.03 (1H, m, H-17); 2.09 (1H, m, H_a-4); 2.21 (1H, m, H_e-4); 2.37 (1H, ddd, *J* = 16.8, *J* = 7.6 and *J* = 3.8, H_a-16); 2.52 (1H, dd, *J* = 13.3 and *J* = 4.6, H-5); 2.67 (1H, ddd, *J* = 16.6, *J* = 10.8 and *J* = 1.7, H_e-16); 3.73 (1H, dd, *J* = 9.5 and *J* = 2.3, H-22); 4.30 (1H, m, $w_{1/2}$ = 12.0, H-3); 4.52 (1H, m, $w_{1/2}$ = 21.0, H-2); 6.04 (1H, s, H-7); 6.12 (1H, dd, *J* = 3.4 and *J* = 2.3, H-15). Found, %: C 71.07; H 8.91. $C_{33}H_{50}O_7$. Calculated, %: C 70.94; H 9.02.

9α-Hydroxystachisterone B 20,22-Acetonide or (20*R*,22*R*)-[(Dimethylmethylene)dioxy]-2β,3β,9α,25-tetrahydroxy-5β-cholest-7,14-dien-6-one (18). Compound **11** (0.29 g, 0.6 mmol) was dissolved in a mixture of MeOH (15 ml) and water (1 ml) and stirred for 120 h at room temperature. The reaction mixture was evaporated and the solid residue was column chromatographed on silica gel (10 g SiO_2, $CHCl_3$–MeOH, 15:1) to give the starting compound **11** (0.5 g, 15%) with R_f 0.32 ($CHCl_3$–MeOH, 8:1) and compound **18** (0.23 g, 80%) with R_f 0.21 ($CHCl_3$–MeOH, 8:1).

Compound 18. Mp 113-115°C, $[\alpha]_D^{24}$ -133.5° (*c* 2.4, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3400, 2900, 1650, 1450, 1370. UV spectrum (CH_3OH), λ_{max}, nm: 298. ^1H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.03 (3H, s, 19-CH_3); 1.05 (3H, s, 18-CH_3); 1.22 (3H, s, 26-CH_3); 1.25 (3H, s, 21-CH_3); 1.25 (3H, s, 27-CH_3); 1.31 and 1.43 (6H, two s, 20,22-$C(CH_3)_2$); 2.25-2.69 (1H, m, H-17); 2.25-2.69 (1H, m, H-5); 3.72 (1H, m, H-22); 4.01 (1H, m, $w_{1/2}$ = 12.0, H-3); 4.37 (1H, m, $w_{1/2}$ = 23.0, H-2); 6.00 (1H, s, H-7); 6.08 (1H, br. s, H-15). Found, %: C 69.55; H 8.85. $C_{30}H_{46}O_7$. Calculated, %: C 69.47; H 8.94.

$\Delta^{8(14)}$ Analog of 20-Hydroxyecdysone Diacetonide or (20*R*,22*R*)-2,3:20,22-Bis[(dimethylmethylene)-dioxy]-25-hydroxy-5β-cholest-8(14)-en-6-one (20). Compound **2** (1.5 g, 2.7 mmol) was dissolved in anhydrous THF (10 ml) and added to a solution of Li (0.22 g, 31 mmol) in ammonia (50 ml, distilled from Na). The mixture was stirred for 0.5 h at -33ºC, NH_4Cl (3.0 g) was added, and the ammonia was evaporated in a stream or argon. After extraction of the residue with ether (3×50 ml), solvent was evaporated off, and the solid residue was column chromatographed on silica gel (40 g SiO_2, eluent $CHCl_3$–MeOH, 100:1) to give compound **20** (0.85 g, 58%) with R_f 0.38 ($CHCl_3$–MeOH, 6:1) and compound **10** (0.6 g, 38.5%) with R_f 0.3 ($CHCl_3$–MeOH, 6:1).

Compound 20. Mp 107-110°C, $[\alpha]_D^{20}$ +0.7° (*c* 1.6, $CHCl_3$). ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.77 (3H, s, 19-CH_3); 0.93 (3H, s, 18-CH_3); 1.12 (3H, s, 21-CH_3); 1.18 (6H, s, 26,27-CH_3); 1.23 and 1.75 (2H, two m, H-12); 1.24 and 1.27 (6H, two s, 2,3-$C(CH_3)_2$); 1.29 (1H, m, H_a-1); 1.36 and 1.43 (6H, two s, 20,22-$C(CH_3)_2$); 1.37 and 1.55 (2H, two m, H-23); 1.38 (1H, m, H-17); 1.49 and 1.66 (2H, two m, H-24); 1.59 (2H, m, H-11); 1.65 and 1.98 (2H, two m, H-16); 1.78 (1H, m, H_e-1); 1.99 (1H, m, H_e-4); 2.02 and 2.23 (2H, two m, H-15); 2.09 (1H, m, H_a-4); 2.25 (1H, m, H-9); 2.35 (1H, dd, *J* = 12.4 and *J* = 4.4, H-5); 2.91 and 2.93 (2H, two d, ^2J = 14.0, H-7); 3.71 (1H, m, H-22); 4.19 (1H, m, H-2); 4.22 (1H, m, H-3). Found, %: C 72.18; H 9.47. $C_{33}H_{52}O_6$. Calculated, %: C 72.76; H 9.62.

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