Reductive Amination of ω-Oxoecdysteroids in the Synthesis of Dimeric Ecdysteroids

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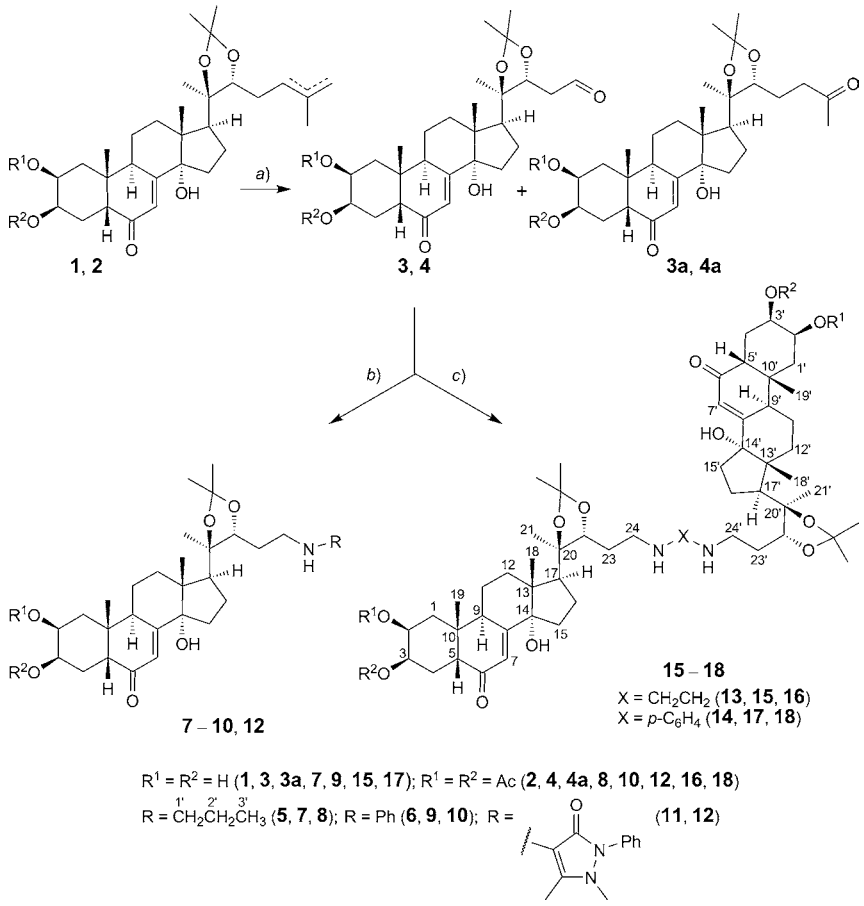
N-Alkyl- and *N*-arylaminoecdysteroids were synthesized for the first time by reductive amination of ω-oxoecdysteroids. By using aliphatic or aromatic diamines, dimeric ecdysteroids with an ethylenediamine or *p*-phenylenediamine bridge at the C(24), C(24′)-position of the monomeric moieties were obtained.

Introduction. – In recent years, dimeric steroids have attracted increasing attention of researchers owing to the cytotoxic, antimalarial, anticarcinogenic, and other valuable properties they possess [1–6]. According to the research data, the presence of OH groups in the dimer is important for biological activity [7], which increases with increasing number of OH groups in the molecule [8][9]. In view of this fact, one could expect high biological activity of ecdysteroid dimers, which refer to polyhydroxylated sterols [10]. Published data on the synthesis of dimeric ecdysteroids are virtually absent. It is only known that UV irradiation of an aqueous solution of *20-hydroxyecdysone*, *ponasterone A*, and *ajugasterone C* results in the formation of the 7,7′-dimers of $\Delta^{8(14)}$-ecdysteroids [11][12]. The reductive amination [13] of the corresponding ω-carbonyl derivatives involving α,ω-diaminoalkanes can become a promising method for the synthesis of dimeric ecdysteroids.

Within this context, we studied for the first time the reductive amination of ω-carbonyl derivatives of ecdysteroids using 2,3-dihydroxy- **3** and 2,3-diacetoxy-ω-aldehydes **4**. Each of the aldehydes **3** and **4** was prepared as a mixture (*ca.* 2 : 1) with the corresponding ketone **3a** and **4a** by ozonolysis of ω-anhydro derivatives **1** and **2**, respectively, followed by purification through column chromatography.

Results and Discussion. – The reactions of aldehydes **3** and **4** with aliphatic (*n*-propylamine (**5**)) and aromatic (aniline (**6**)) amines, followed by reduction (without isolation of the intermediate imine) with $NaBH(OAc)_3$ [13] resulted in the synthesis of ecdysteroid *N*-alkyl-(**7** and **8**) and *N*-arylamines (**9** and **10**) in 68–74% yield. Aldehyde **4** was reacted with 4-aminoantipyrine (4-amino-2,3-dimethyl-1-phenylpyrazol-5-one, **11**), which possesses high analgesic, anti-inflammatory, antimicrobial, and antitumor activities [14], to give compound **12** (*Scheme*). Ketones **3a** and **4a** didn't undergo reductive amination; the reactions of mixtures comprising aldehyde **3** and **4**, and ketone **3a**, **4a** with amines **5** and **6** afforded only *N*-propyl (**7** and **8**) and *N*-phenylamines (**9** and **10**), while the ketones **3a** and **4a** were recovered unchanged (*Scheme*).

Scheme



a) O_3/CH_2Cl_2-Py. *b*) RNH_2 (**5**, **6**, **11**), then $NaBH(OAc)_3$. *c*) H_2N-X-NH_2 (**13**, **14**), then $NaBH(OAc)_3$.

The structures of the synthesized compounds **7**–**10**, and **12** were determined by homo- and heteronuclear 1D and 2D ^{1}H- and ^{13}C-NMR correlation methods. Out of the two CO groups of the starting compounds **3** and **4**, only the aldehyde group was involved in the reductive amination, whereas the 6-keto group was retained, as indicated by the signal at δ(C) 202–204 ppm correlated in the HMBC spectra of compounds **7**–**10** and **12** with the H–C(7) H-atom signal (δ(H) 5.8–5.9 ppm). The transformation of the aldehyde group into the aminomethylene group accounts for replacement of the ^{13}C-NMR signal for the aldehyde group (at δ(C) *ca.* 200 ppm) by a signal at *ca.* δ(C) 42–46 ppm corresponding to the CH_2 group attached to the secondary N-atom in the spectra of compounds **7**–**10** and **12** (*Tables 1* and *2*). The gross composition of the products **7**–**10** and **12** was confirmed by the molecular ions present in the MALDI-TOF-MS spectra.

Table 1. *^{1}H- and ^{13}C-NMR Data* (δ in ppm rel. to Me_4Si, *J* in Hz) *of Compounds* ***3****,* ***7****, and* ***8***[a]). Atom numbering as indicated in the *Scheme.*

Position	Compound **3**		Compound **7**		Compound **8**	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
1		36.36	1.59–1.68 (*m*)	31.75	1.54–1.58 (*m*), 1.84–1.91 (*m*)	34.02
2	3.78–3.91 (*m*)	67.73	3.83–3.94 (*m*)	67.43	5.04–5.15 (*m*)	67.82
3	3.98 (br. *s*)	67.37	4.04 (br. *s*)	67.23	5.37 (br. *s*)	67.06
4		30.93	1.94–1.99 (*m*)	30.93		30.90
5	2.29–2.41 (*m*)	50.03	2.37–2.42 (*m*)	50.43	2.39 (*dd*, *J* = 12.8, 4.4)	51.01
6		204.96		204.75		202.40
7	5.81 (*s*)	121.41	5.85 (*s*)	121.48	5.89 (*s*)	121.41
8		165.90		164.95		164.80
9	2.96–3.11 (*m*)	33.79	2.98–3.04 (*m*)	33.82	3.11–3.18 (*m*)	33.67
10		38.18		38.05		38.35
11		20.37		20.40		20.39
12		30.93		31.14		31.28
13		47.23		47.24		47.23
14		84.56		84.82		84.55
15		28.80		30.93		29.24
16		21.04		21.12		20.99
17	2.15–2.23 (*m*)	48.89	2.18–2.24 (*m*)	48.89	2.21–2.23 (*m*)	48.85
18	0.78 (*s*)	17.01	0.77 (*s*)	16.91	0.79 (*s*)	16.90
19	0.94 (*s*)	23.88	0.96 (*s*)	23.98	1.04 (*s*)	23.85
20		84.05		84.20		84.31
21	1.15 (*s*)	22.13	1.15 (*s*)	22.68	1.16 (*s*)	21.06
22	3.62–3.70 (*m*)	75.46	3.69–3.75 (*m*)	79.08	3.74–3.77 (*m*)	79.35
23		43.18		29.36	1.79–1.84 (*m*)	26.04
24	9.78 (br. *s*)	200.72	2.98–3.04 (*m*)	46.45	3.04–3.06 (*m*)	46.10
1′			2.83–2.89 (*m*)	50.12	2.82–2.90 (*m*)	49.53
2′			1.70–1.84 (*m*)	20.40	1.68–1.74 (*m*)	20.34
3′			0.99 (*t*, *J* = 7.3)	11.35	0.99 (*t*, *J* = 7.3)	11.26
2,3-OCO*CH$_3$*					2.08 (*s*), 2.12 (*s*)	22.01, 23.29
2,3-O*C*OCH$_3$						170.34, 173.22
20,22-*Me$_2$*C	1.34 (*s*), 1.40 (*s*)	26.90, 28.80	1.32 (*s*), 1.40 (*s*)	26.91, 29.69	1.33 (*s*), 1.41 (*s*)	26.93, 28.90
20,22-Me$_2$*C*		108.01		107.82		107.75

[a]) Recorded in $CDCl_3$ at 500.17 (^{1}H) and 125.77 (^{13}C). All assignments are based on 1D and 2D recordings (HMBC, HSQC, COSY).

The amination of aldehydes with aliphatic or aromatic diamines opens up a route to dimeric ecdysteroids. Dimeric ecdysteroids **15**–**18** were synthesized by the reaction of aldehydes **3** and **4** with ethylenediamine **13**, and *p*-phenylenediamine **14** followed by treatment with $NaBH(OAc)_3$ (*Scheme*). The monomer moieties of the products are linked by a covalent bond between the C(24) and C(24′) atoms *via* an ethylenediamine or a *p*-phenylenediamine bridge.

Table 2. *^{1}H- and ^{13}C-NMR Data* (δ in ppm rel. to Me_4Si, *J* in Hz) *of Compounds* **9**, **12**[a]), *and* **10**[b]). Atom numbering as indicated in the *Scheme*.

Position	Compound **9**		Compound **10**		Compound **12**	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
1	1.39–1.41 (*m*), 1.84–1.86 (*m*)	36.51	1.55–1.59 (*m*), 1.89–1.93 (*m*)	33.97	1.49–1.51 (*m*), 1.86–1.89 (*m*)	34.02
2	3.84–3.92 (*m*)	67.71	5.01–5.11 (*m*)	68.70	5.02–5.09 (*m*)	68.77
3	3.99 (br. *s*)	67.39	5.34 (br. *s*)	67.05	5.29 (br. *s*)	67.16
4	1.63–1.65 (*m*), 1.72–1.75 (*m*)	31.33	1.78–1.86 (*m*)	30.82	1.73–1.77 (*m*), 2.07–2.11 (*m*)	30.92
5	2.38–2.43 (*m*)	50.08	2.38 (*dd*, *J* = 12.6, 3.8)	50.94	2.31–2.36 (*m*)	51.04
6		204.84		202.37		202.00
7	5.83 (*s*)	121.37	5.86 (*s*)	121.46	5.81 (*s*)	121.26
8		165.97		165.00		162.50
9	3.02–3.09 (*m*)	33.80	3.06–3.16 (*m*)	33.64	3.11–3.16 (*m*)	33.68
10		38.23		38.34		38.30
11	1.63–1.65 (*m*), 1.77–1.80 (*m*)	20.42	1.63–1.66 (*m*)	20.39	1.60–1.63 (*m*)	20.41
12	1.57–1.61 (*m*), 1.96–2.01 (*m*)	31.59	1.52–1.55 (*m*), 1.97–1.99 (*m*)	31.56	1.51–1.54 (*m*), 1.90–1.92 (*m*)	31.22
13		47.24		47.13		47.12
14		84.67		84.57		84.32
15	1.83–1.86 (*m*), 2.05–2.08 (*m*)	30.98	1.76–1.80 (*m*)	29.16		29.53
16	1.81–1.83 (*m*), 2.01–2.03 (*m*)	21.24	1.94–1.97 (*m*)	21.20		21.05
17	2.23–2.26 (*m*)	48.98	2.25–2.32 (*m*)	48.97	2.19–2.22 (*m*)	48.97
18	0.80 (*s*)	17.08	0.80 (*s*)	17.02	0.76 (*s*)	16.99
19	0.97 (*s*)	23.92	1.03 (*s*)	23.82	1.00 (*s*)	23.83
20		84.39		84.26		79.22
21	1.18 (*s*)	22.05	1.17 (*s*)	21.98	1.15 (*s*)	21.95
22	3.76–3.82 (*m*)	80.50	3.76–3.81 (*m*)	80.26	3.79–3.83 (*m*)	76.85
23	1.72–1.75 (*m*), 1.80–1.83 (*m*)	28.71	1.76–1.80 (*m*)	28.64		29.66
24	3.24–3.31 (*m*)	42.84	3.21–3.34 (*m*)	42.67	3.20–3.30 (*m*)	46.11
1′		148.32		148.39		
2′	6.65 (*d*, *J* = 8.0)	113.09	6.64 (*d*, *J* = 7.6)	112.94		
3′	7.19 (*t*, *J* = 7.8)	129.26	7.18 (*t*, *J* = 7.4)	129.22		140.86
4′	6.72 (*t*, *J* = 7.3)	117.49	6.70 (*t*, *J* = 7.4)	117.32		122.96
5′	7.19 (*t*, *J* = 7.8)	129.26	7.18 (*t*, *J* = 7.4)	129.22		165.09
6′	6.65 (*d*, *J* = 8.0)	113.09	6.64 (*d*, *J* = 7.6)	112.94		

Table 2 (cont.)

Position	Compound **9**		Compound **10**		Compound **12**	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
C_6H_4-N(1′)					7.20–7.28 (*m*),7.38–7.49 (*m*)	123.14, 126.13, 129.04, 135.11
Me-C(3′)					2.23 (*s*)	10.92
Me-N(2′)					2.86 (*s*)	37.57
2,3-OCO*CH*$_3$			2.01 (*s*), 2.11 (*s*)	21.06, 21.11	1.99 (*s*), 2.09 (*s*)	21.12
2,3-O*C*OCH$_3$				170.28, 170.62		170.23, 170.33
20,22-*Me*$_2$C	1.35 (*s*), 1.46 (*s*)	27.03, 29.02	1.34 (*s*), 1.44 (*s*)	26.99, 28.99	1.33 (*s*), 1.41 (*s*)	26.95, 29.00
20,22-Me$_2$*C*		107.44		107.38		107.18

[a]) Recorded in $CDCl_3$ at 500.17 (^{1}H) and 125.77 (^{13}C). [b]) Recorded in $CDCl_3$ at 400.13 (^{1}H) and 100.62 (^{13}C). All assignments are based on 1D and 2D recordings (HMBC, HSQC, COSY).

In the ^{1}H- and ^{13}C-NMR spectra of the dimers **16** and **18**, the chemical shifts for the steroid core coincide in pairs and correspond to the core signals of the starting monomer **4**. In the ^{13}C-NMR spectrum of the dimer **16**, the presence of a single peak at δ(C) 46.69 ppm is diagnostic due to the C-atom of the ethylidene spacer. Dimer **18** with the 1,4-phenylidene spacer is identified by the presence of only two ^{13}C-NMR signals for aromatic C-atoms at δ(C) 116.69 and δ(C) 140.90 ppm (*Table 3*). The gross composition of the dimers **16** and **18** was confirmed by the molecular ions present in the MALDI-TOF-MS spectra. The synthesized compounds **15**–**18** are chiral, their optical rotations ($[\alpha]_D + 20.3$) being +38.6, +45.5, +20.3, and +58.3, respectively. The symmetry element existing in their structures is a two-fold axis (C_2) that is insufficient to identify dimers **15**–**18** with their mirror images [15].

Conclusions. – The earlier unknown *N*-alkyl-, *N*-arylamino-, and dimeric ecdysteroids were synthesized by an effective reductive amination of the side chain ω-oxoderivatives of 20-hydroxyecdysone.

Experimental Part

General. The starting monoamines and diamines were purchased from *Acros Organics*. Column chromatography (CC) and and thin layer chromatography (TLC): silica gel (SiO_2; < 0.06 mm) and precoated silica gel (*Silufol* plates), resp.; visualization by staining with 4-hydroxy-3-methoxybenzaldehyde in EtOH, acidified with H_2SO_4. M.p.: *Boetius* hot-stage microscope. Optical rotations: *Perkin–Elmer-341* polarimeter. 1D- (^{1}H and ^{13}C) and 2D- (COSY, HSQC, and HMBC) NMR spectra: *Bruker Avance 400* spectrometer at 400.13 (^{1}H) and 100.62 MHz (^{13}C), equipped with broadband observer probe and *Bruker Avance II 500 HD Ascend* spectrometer at 500.17 (^{1}H) and 125.77 MHz (^{13}C); δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MALDI-TOF-MS: *Bruker Autoflex III* spectrometer; in positive-ion mode; 3,5-dimethoxy-4-hydroxycinnamic (sinapic) acid and α-cyano-4-hydroxycinnamic acids were used as matrix; in *m*/*z*. Elemental analysis: *Carlo Erba EA-1108 CHNS-O* analyzer.

The stock compounds were synthesized from *20-hydroxyecdysone* ((M.p. 239–240°; $[\alpha]_D^{20} = +54.3$ ($c = 1.45$, MeOH). Literature: M.p. 241–242.5°; $[\alpha]_D^{20} = +61.8$ (MeOH) [16]; M.p. 246° (AcOEt/MeOH, 9:1); $[\alpha]_D^{17} = +65.3$ ($c = 1.0$, MeOH) [17]). *20-Hydroxyecdysone* was isolated from the juice of *Serratula coronata* L. [17]. ^{1}H- and ^{13}C-NMR data for *20-hydroxyecdysone* were identical with the NMR data in [17].

2β,3β,14α-Trihydroxy-20,22-isopropylidenedioxy-5β-cholesta-7,24(or25)dien-6-one (= *(2β,3β,5β,17β)-2,3,14-Trihydroxy-17-[(4*R,*5*R*)-2,2,4-trimethyl-5-(3-methylbut-2-en-1-yl)-1,3-dioxolan-4-yl]androst-7-en-6-one or (2β,3β,5β,17β)-2,3,14-Trihydroxy-17-[(4*R,*5*R*)-2,2,4-trimethyl-5-(3-methylbut-3-en-1-yl)-1,3-dioxolan-4-yl]androst-7-en-6-one*; **1**; (M.p. 135–137°; $[\alpha]_D^{23} = +56.2$ ($c = 3.07$, $CHCl_3$))) *and its 2,3-diacetates* **2** (M.p. 160–161°; $[\alpha]_D^{24} = +49.0$ ($c = 5.27$, $CHCl_3$) prepared as described in [18]).

4-C-*[(2β,3β,5β,17β)-2,3-Bis(acetyloxy)-14-hydroxy-6-oxoandrost-7-en-17-yl]-2,5-dideoxy-3,4*-O-*(1-methylethylidene)*-L-erythro-*pentose* (**4**) was prepared according to [19]). M.p. 165–166°. $[\alpha]_D^{20} = +53.3$ ($c = 0.62$, $CHCl_3$).

*(2β,3β,5β,17β)-14-Hydroxy-6-oxo-17-[(4*R,*5*R*)-2,2,4-trimethyl-5-(3-oxobutyl)-1,3-dioxolan-4-yl]androst-7-ene-2,3-diyl Diacetate* (**4a**) was prepared according to [18]. M.p. 143–144°. $[\alpha]_D^{21} = +52.4$ ($c = 5.30$, $CHCl_3$).

2,5-Dideoxy-3,4-O-*(1-methylethylidene)-4*-C-*[(2β,3β,5β,17β)-2,3,14-trihydroxy-6-oxoandrost-7-en-17-yl]*-L-erythro-*pentose* (**3**) *and (2β,3β,5β,17β)-2,3,14-Trihydroxy-17-[(4*R,*5*R*)-2,2,4-trimethyl-5-(3-oxobutyl)-1,3-dioxolan-4-yl]androst-7-en-6-one* (**3a**). The O_2/O_3 mixture (the ozonator productivity was 30 mmol O_3/h) was passed through a soln. of alkenes (**1**, 0.32 g, 0.64 mmol) in 5 ml of CH_2Cl_2/Py (5:1) at 0° with stirring over a period of 3 min (until 0.64 mmol of O_3 was absorbed). The mixture was

Table 3. *^{1}H- and ^{13}C-NMR Data* (δ in ppm rel. to Me_4Si, J in Hz) *of Compounds* **15**[a]), **16**[b]), **17**[c]), *and* **18**[d]). Atom numbering as indicated in the *Scheme*.

Position	Compound **15**	Compound **16**		Compound **17**	Compound **18**	
	δ(H)	δ(H)	δ(C)	δ(H)	δ(H)	δ(C)
1(1′)		1.53–1.56 (*m*), 1.89–1.93 (*m*)	34.03		1.66–1.70 (*m*), 2.12–2.16 (*m*)	34.92
2(2′)	3.89–3.99 (*m*)	5.05–5.19 (*m*)	68.80	3.95–3.99 (*m*)	5.30–5.39 (*m*)	69.72
3(3′)	4.04 (br. *s*)	5.37 (br. *s*)	67.13	3.95–3.99 (*m*)	5.52 (br. *s*)	68.24
4(4′)		1.31–1.34 (*m*), 1.81–1.86 (*m*)	29.24		1.88–1.92 (*m*), 2.46–2.49 (*m*)	32.04
5(5′)	2.39–2.50 (*m*)	2.37–2.42 (*m*)	51.01	2.40 (*dd*, J = 12.2, 4.6)	2.63–2.67 (*m*)	52.05
6(6′)			202.61			201.84
7(7′)	5.84 (*s*), 5.86 (*s*)	5.89 (*s*), 5.91 (*s*)	121.40	5.83 (*s*)	6.25 (*s*)	121.99
8(8′)			164.95			166.41
9(9′)	3.02–3.10 (*m*)	3.12–3.22 (*m*)	33.66	3.10–3.13 (*m*)	3.52–3.63 (*m*)	34.76
10(10′)			38.37			38.99
11(11′)		1.63–1.66 (*m*), 1.77–1.80 (*m*)	20.38			21.31
12(12′)		1.60–1.63 (*m*), 1.98–2.03 (*m*)	31.15		1.70–1.73 (*m*), 1.84–1.89 (*m*)	32.04
13(13′)			47.21			48.20
14(14′)			84.48			85.44
15(15′)		1.81–1.86 (*m*), 2.11–2.15 (*m*)	30.99			29.86
16(16′)		1.87–1.90 (*m*), 1.96–1.99 (*m*)	21.13			21.31
17(17′)	2.19–2.27 (*m*)	2.22–2.27 (*m*)	48.98	2.29–2.33 (*m*)	2.67–2.71 (*m*)	50.28
18(18′)	0.80 (*s*)	0.80 (*s*)	16.93	0.84 (*s*)	1.02 (*s*)	17.70
19(19′)	0.98 (*s*)	1.04 (*s*)	23.84	0.98 (*s*)	1.07 (*s*)	24.47
20(20′)			84.29			84.47
21(21′)	1.17 (*s*)	1.17 (*s*)	22.00	1.18 (*s*)	1.24 (*s*)	22.48
22(22′)	3.66–3.78 (*m*)	3.80 (*dd*, J = 12.0, 6.0)	78.99	3.82–3.88 (*m*)	3.90–3.96 (*m*)	82.43
23(23′)			29.24		2.08–2.12 (*m*)	32.04
24(24′)	3.10–3.20 (*m*)	3.12–3.22 (*m*)	45.44	3.31–3.35 (*m*)	3.52–3.63 (*m*)	50.62
N-CH_2-CH_2-N	3.02–3.10 (*m*)	3.04 (*t*, J = 5.0)	46.69			
N-C_6H_4-N				6.61–6.65 (*m*)	6.88–6.97 (*m*)	116.59, 140.90

Table 3 (cont.)

Position	Compound **15**	Compound **16**		Compound **17**	Compound **18**	
	δ(H)	δ(H)	δ(C)	δ(H)	δ(H)	δ(C)
2,3-OCO*Me*, 2,3-OCO*Me′*		2.01 (*s*), 2.12 (*s*)	21.09, 21.13		2.04 (*s*), 2.07 (*s*)	21.41
2,3-O*CO*Me, 2,3-O*CO*Me′			170.25, 170.48			170.64
20,22-*Me*$_2$C, 20,22-*Me*$_2$C’	1.33 (*s*), 1.43 (*s*)	1.34 (*s*), 1.41 (*s*)	27.01, 28.96	1.34 (*s*), 1.45 (*s*)	1.48 (*s*), 1.56 (*s*)	27.62, 29.87
20,22-Me$_2$*C*, 20,22-Me$_2$*C*’			107.64			107.45

[a]) Recorded in $CDCl_3$ at 400.13 (^{1}H). [b]) Recorded in CD Cl_3 at 500.17 (^{1}H) and 125.77 (^{13}C). [c]) Recorded in CD_3OD at 400.13 (^{1}H). [d]) Recorded in C_5D_5N at 400.13 (^{1}H) and 100.62 (^{13}C). All assignments are based on 1D and 2D recordings (HMBC, HSQC, COSY).

purged with Ar and evaporated, the residue was subjected to CC (SiO_2, $CHCl_3$/MeOH, 10:1) to afford **3** and **3a**.

Analytical Data for **3**. 0.17 g, yield 56%. R_f 0.43 ($CHCl_3$/MeOH, 10:1). M.p. 137–139°. $[\alpha]_D^{16} = +47.9$ ($c = 0.87$, $CHCl_3$). ^{1}H- and ^{13}C-NMR: see *Table 1*. Anal. calc. for $C_{27}H_{40}O_7$: C 68.38, H 8.04; found: C 68.04, H 8.46.

Analytical Data for **3a**. 0.09 g, yield 28%. R_f 0.62 ($CHCl_3$/MeOH, 5:1). M.p. 158–160°. $[\alpha]_D^{16} = +49.8$ ($c = 0.54$, $CHCl_3$). ^{1}H- and ^{13}C-NMR spectra were identical to those given in [20]. MALDI-TOF-MS: 582.241 ($[M + 2\,K]^+$, $C_{29}H_{44}K_2O_7^+$; calc. 582.235).

General Procedure of the Reductive Amination of Aldehydes **3** *and* **4**. The amine (**5**, **6**, or **11**, 0.5 mmol) or the diamine (**13** or **14**, 0.25 mmol) was added to a stirring soln. of the aldehyde (**3** or **4**, 0.5 mmol) in 5 ml of CH_2Cl_2, and then was added a suspension of $NaBH(OAc)_3$ (1 mmol) in CH_2Cl_2. The mixture was stirred for 1 h (TLC) at 25° and then was filtered through a pad of SiO_2. The filtrate was evaporated, and the residue was subjected to CC (SiO_2; $CHCl_3 \rightarrow CHCl_3$/MeOH, 10:1) to afford **7**–**10**, **12**, or dimers **15**–**18**.

*1,4,5-Trideoxy-2,3-*O*-(1-methylethylidene)-5-(propylamino)-2-*C*-[(2β,3β,5β,17β)-2,3,14-trihydroxy-6-oxoandrost-7-en-17-yl]-*D-erythro-*pentitol* (**7**). Yield 72%. R_f 0.47 ($CHCl_3$/MeOH, 3:1). Solid. M.p. 139–141°. $[\alpha]_D^{19} = +51.1$ ($c = 0.87$, $CHCl_3$). ^{1}H- and ^{13}C-NMR: see *Table 1*. MALDI-TOF-MS: 518.337 ($[M - H]^+$, $C_{30}H_{48}NO_6^+$; calc. 518.288). Anal. calc. for $C_{30}H_{49}NO_6$ (519.36): C 69.33, H 9.50; found: C 69.08, H 9.04.

*2-*C*-[(2β,3β,5β,17β)-2,3-Bis(acetyloxy)-14-hydroxy-6-oxoandrost-7-en-17-yl]-1,4,5-trideoxy-2,3-*O*-(1-methylethylidene)-5-(propylamino)-*D-erythro-*pentitol* (**8**). Yield 68%. R_f 0.54 ($CHCl_3$/MeOH, 5:1). Solid. M.p. 146–148°. $[\alpha]_D^{22} = +43.2$ ($c = 0.75$, $CHCl_3$). ^{1}H- and ^{13}C-NMR: see *Table 1*. MALDI-TOF-MS: 604.365 ($[M + H]^+$; $C_{34}H_{54}NO_8^+$, calc. 604.384), 626.331 ($[M + Na]^+$, $C_{34}H_{53}NNaO_8^+$; calc. 626.366). Anal. calc. for $C_{34}H_{53}NO_8$ (603.38): C 67.63, H 8.85; found: C 66.98, H 8.24.

*1,4,5-Trideoxy-2,3-*O*-(1-methylethylidene)-5-(phenylamino)-2-*C*-[(2β,3β,5β,17β)-2,3,14-trihydroxy-6-oxoandrost-7-en-17-yl]-*D-erythro-*pentitol* (**9**). Yield 74%. R_f 0.45 ($CHCl_3$/MeOH, 10:1). Solid. M.p. 123–125°. $[\alpha]_D^{21} = +50.1$ ($c = 1.06$, $CHCl_3$). ^{1}H- and ^{13}C-NMR: see *Table 2*. MALDI-TOF-MS: 576.408 ($[M + Na]^+$, $C_{33}H_{47}NNaO_6^+$; calc. 576.330), 592.389 ($[M + K]^+$, $C_{33}H_{47}KNO_6^+$; calc. 592.304). Anal. calc. for $C_{33}H_{47}NO_6$ (553.34): C 71.58, H 8.56; found: C 71.64, H 8.24.

*2-*C*-[(2β,3β,5β,17β)-2,3-Bis(acetyloxy)-14-hydroxy-6-oxoandrost-7-en-17-yl]-1,4,5-trideoxy-2,3-*O*-(1-methylethylidene)-5-(phenylamino)-*D-erythro-*pentitol* (**10**). Yield 69%. R_f 0.62 ($CHCl_3$/MeOH, 10:1). Solid. M.p. 138–140°. $[\alpha]_D^{21} + 48.5$ ($c = 0.67$, $CHCl_3$). ^{1}H- and ^{13}C-NMR: see *Table 2*. Anal. calc. for $C_{37}H_{51}NO_8$ (637.36): C 69.68, H 8.06; found: C 69.04, H 8.32.

*2-*C*-[(2β,3β,5β,17β)-2,3-Bis(acetyloxy)-14-hydroxy-6-oxoandrost-7-en-17-yl]-1,4,5-trideoxy-5-[(2,3-dihydro-1,5-dimethyl-3-oxo-2-phenyl-1*H*-pyrazol-4-yl)amino]-2,3-*O*-(1-methylethylidene)-*D-erythro-*pentitol* (**12**). Yield 70%. R_f 0.59 ($CHCl_3$/MeOH, 10:1). Solid. M.p. 135–137°. $[\alpha]_D^{18} = +42.9$ ($c = 0.62$, $CHCl_3$). ^{1}H- and ^{13}C-NMR: see *Table 2*. MALDI-TOF-MS: 770.368 ($[M + Na]^+$, $C_{42}H_{57}N_3NaO_9^+$; calc. 770.399). Anal. calc. for $C_{42}H_{57}N_3O_9$ (747.41): C 67.45, H 7.68; found: C 67.08, H 7.29.

*(2*S*,3*R*,5*R*,9*R*,10*R*,13*R*,14*S*,17*S*,2′S,3′R,5′R,9′R,10′R,13′R,14′S,17′S)-17,17′-(Ethane-1,2-diylbis{iminoethane-2,1-diyl[(4*R*,5*R*)-2,2,4-trimethyl-1,3-dioxolane-5,4-diyl]})bis(1,2,3,4,5,9,10,11,12,13,14,15,16,17-tetradecahydro-2,3,14-trihydroxy-10,13-dimethyl-6*H*-cyclopenta[a]phenanthren-6-one)* (**15**). Yield 40%. R_f 0.44 (AcOEt/MeOH, 4:1). Solid. M.p. 180–182°. $[\alpha]_D^{22} = +38.6$ ($c = 0.62$, $CHCl_3$). ^{1}H-NMR: see *Table 3*. Anal. calc. for $C_{56}H_{88}N_2O_{12}$ (980.63): C 68.54, H 9.04; found: C 68.99, H 9.10.

*Ethane-1,2-diylbis{iminoethane-2,1-diyl[(4*R*,5*R*)-2,2,4-trimethyl-1,3-dioxolane-5,4-diyl](2*S*,3*R*,5*R*,9*R*,10*R*,13*R*,14*S*,17*S*)-14-hydroxy-10,13-dimethyl-6-oxo-2,3,4,5,6,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[a]phenanthrene-17,2,3-triyl} Tetraacetate* (**16**). Yield 52%. R_f 0.46 ($CHCl_3$/MeOH, 4:1). Solid. M.p. 206–208°. $[\alpha]_D^{22} = +45.5$ ($c = 0.71$, $CHCl_3$). ^{1}H- and ^{13}C-NMR: see *Table 3*. MALDI-TOF-MS: 1172.003 ($[M + Na]^+$, $C_{64}H_{96}N_2NaO_{16}^+$; calc. 1171.665). Anal. calc. for $C_{64}H_{96}N_2O_{16}$ (1134.66): C 66.87, H 8.42; found: C 67.08, H 8.09.

*(2*S*,3*R*,5*R*,9*R*,10*R*,13*R*,14*S*,17*S*,2′S,3′R,5′R,9′R,10′R,13′R,14′S,17′S)-17,17′-(Benzene-1,4-diylbis-{iminoethane-2,1-diyl[(4*R*,5*R*)-2,2,4-trimethyl-1,3-dioxolane-5,4-diyl]})bis(2,3,14-trihydroxy-10,13-dimethyl-1,2,3,4,5,9,10,11,12,13,14,15,16,17-tetradecahydro-6*H*-cyclopenta[a]phenanthren-6-one)* (**17**).

Yield 46%. R_f 0.56 ($CHCl_3$/MeOH, 5:1). Solid. M.p. 189–191°. $[\alpha]_D^{18} = +20.3$ ($c = 0.10$, MeOH). ^{1}H-NMR: see *Table 3*. Anal. calc. for $C_{60}H_{88}N_2O_{12}$ (1028.63): C 70.01, H 8.62; found: C 69.89, H 8.90.

*Benzene-1,4-diylbis{iminoethane-2,1-diyl[(4*R*,5*R*)-2,2,4-trimethyl-1,3-dioxolane-5,4-diyl](2*S*,3*R*,5*R*,9*R*,10*R*,13*R*,14*S*,17*S*)-2,3,4,5,6,9,10,11,12,13,14,15,16,17-tetradecahydro-14-hydroxy-10,13-dimethyl-6-oxo-1*H*-cyclopenta[a]phenanthrene-17,2,3-triyl} Tetraacetate* (**18**). Yield 54%. R_f 0.43 ($CHCl_3$/MeOH, 10:1). Solid. M.p. 198–200°. $[\alpha]_D^{18} = +58.3$ ($c = 0.24$, $CHCl_3$). ^{1}H- and ^{13}C-NMR: see *Table 3*. MALDI-TOF-MS: 1219.593 ($[M + Na]^+$, $C_{68}H_{96}N_2NaO_{16}^+$; calc. 1219.665). Anal. calc. for $C_{68}H_{96}N_2O_{16}$ (1196.68): C 68.20; H 8.08; found: C 68.72, H 8.61.

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