Synthesis of Cytostatic Tetradecacyclic Pyrazines and a Novel Reduction-Oxidation Sequence for Spiroketal Opening in Sapogenins

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Dedicated to Prof. *Albert Eschenmoser* on the occasion of his 75th birthday

Aiming towards spiroketal-modified artificial cephalostatin molecules, two orthogonal approaches were investigated. First, the introduction of 17-O-functionality into hecogenin derivatives with a closed spiroketal moiety was accomplished by different remote-oxidation procedures. These allowed the synthesis of tetradecacyclic artificial cephalostatin molecules with improved tumor-inhibiting properties. Second, a novel reduction-oxidation pathway for spiroketal opening in sapogenins was discovered, which should provide the basis for a broad access towards spiroketal-modified building blocks for cephalostatins.

Introduction. – The cephalostatins [1] and ritterazines [2], *e.g.*, cephalostatin 1 (**1**) and cephalostatin 7 (**2**), constitute a class of marine natural products consisting of 45 tridecacyclic pyrazines that exhibit extraordinarily high cytostatic activity [1–3]. Moreover, these tridecacyclic pyrazines operate *via* a novel mechanism that has not been elucidated so far [1c]. Despite their promising biological activity, the scarce availability from natural sources [1], which is typical for marine natural products [4], has limited investigations on the cephalostatins to date.

The scarcity and potency of cephalostatins, in combination with the new and interesting molecular architecture, has stimulated synthetic activities in various laboratories [5–7]. Among those, the *Fuchs* group has targeted and recently achieved the total synthesis of several members of the cephalostatin family, but due to the complex nature of the target structures, this was an enormous synthetic endeavor [7]. Differently, our approach aims at gaining fast access to cephalostatin analogs as tools to determine the pharmacologically active structural elements, and, if reaching significant activity, to eventually participate in *in vivo* studies [8].

In previous work, a short synthetic approach to the cytostatically active cephalostatin analog hydroxy ketone **3** (and to diketone **4**) starting from commercially available hecogenin acetate was established [8][9]. Hydroxy ketone **3** showed, in the *NCI*'s *in vitro* panel [10], an overall good tumor-inhibiting activity in the range of common anticancer drugs (*Table 1*, *Entries 3* and *7–9*)[1]). Furthermore, it exhibited the same activity pattern as the cephalostatins [1b], indicating that it deploys its activity in the general novel 'cephalostatin-like' mode [11].

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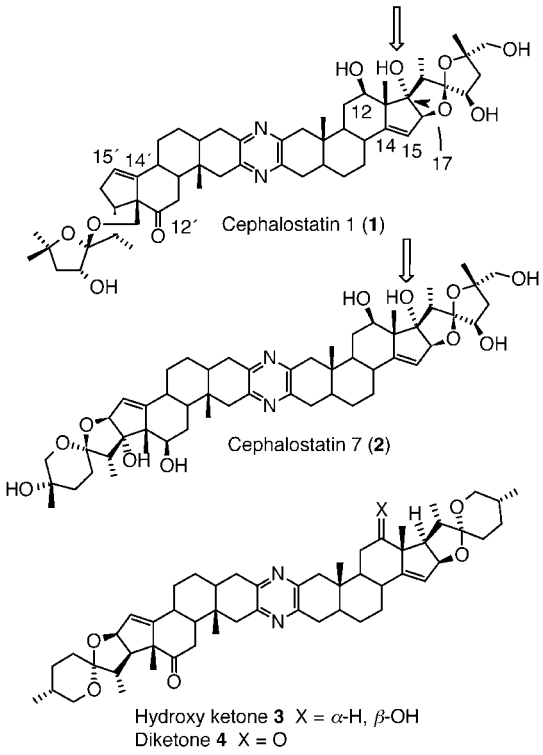
[1]) Detailed informations about the cytostatic activity of adriamycin (NSC-123127), cisplatin (NSC-119875), and 5-fluorouracil (NSC-19893) are available from the *National Cancer Institute* (*NCI*) *via* the internet [3].



The task was now to transform the spiroketal areas into a more cephalostatin-like appearance. Therefore, two orthogonal approaches were investigated. The first one consisted of selectively introducing additional functionality into the still closed spiroketal area – namely the introduction of 17-O-functionality (*vide infra*). The other approach called for a selective spiroketal opening to prepare the system for a wide variety of transformations without loss of any C-atoms or configurational information.

For a selective modification of the still closed spiroketal moiety, the introduction of a 17-O-functionality seemed worthwhile to investigate, because structure-activity relationships (SARs) available from the growing family of cephalostatins and ritterazines pointed to the importance of a 17-OH group for strong biological activity. Two pairs of ritterazine, for instance (ritterazine A/ritterazine T and ritterazine B/ritterazine Y; structures not shown) missing this particular functional group show a 25- to 330-fold drop of tumor-inhibiting activity [2][7b].

Results and Discussion. – To transform the unactivated H–C(17) into the corresponding tertiary alcohol, remote-oxidation approaches were investigated [12]. Aiming at the direct introduction of O-functionality to the 17-position, the $Pb(OAc)_4$ reaction [13] and an O-variation of the venerable *Barton* reaction [14] (*Oxygen-Barton* reaction) seemed suitable. Both processes require a six-membered chair-like transition state with an optimum distance between the O-radical and the C-atom of *ca.* 250–270 pm [13]. From the inspection of molecular models, we assumed that these

conditions could be fulfilled by temporarily adding an α-orientated CH_2OH group at the 12-position as a handle to functionalize the H–C(17) as depicted in *Fig. 1*.

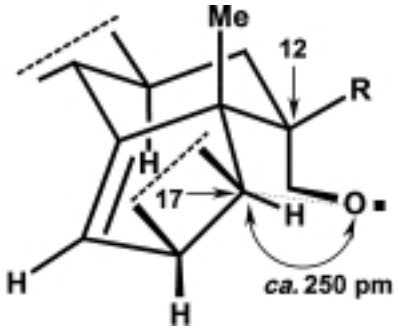
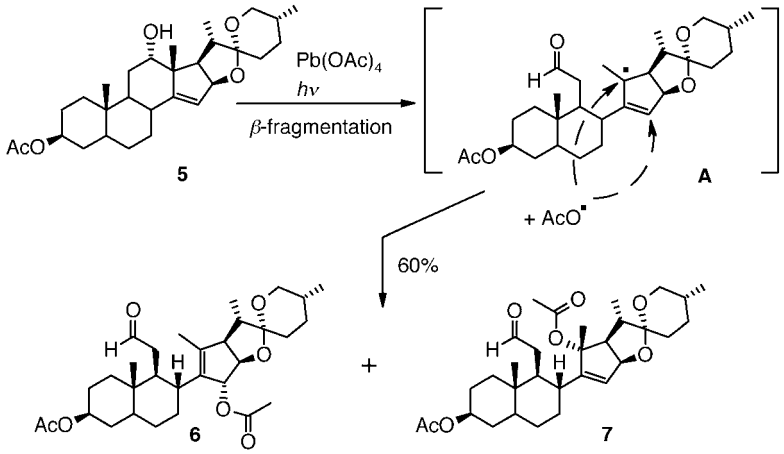


Fig. 1. *Stereochemical rationalization of a possible remote oxidation at C(17)*

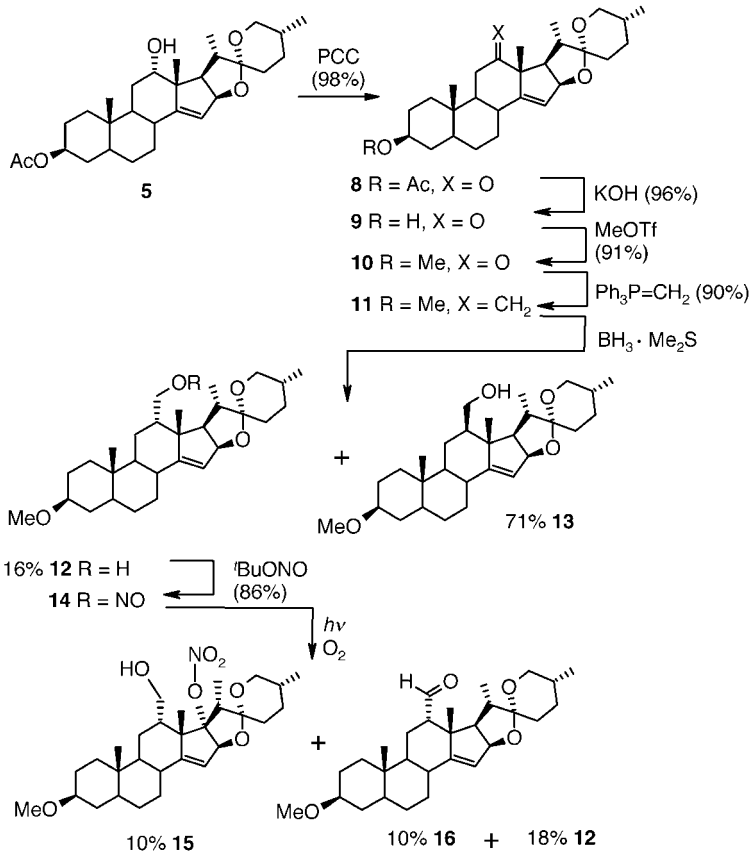
Parallel to these considerations, an orientating experiment was conducted to probe the straightforward access to the H–C(17) *via* the readily available 12α-OH group in homoallylic alcohol **5** [15][9b], since both these functions appeared to be in close proximity due to the concave shape of the steroidal region of rings C and D. Interestingly, when homoallylic alcohol **5** was directly subjected to the conditions of a photolytic $Pb(OAc)_4$ reaction, the regioisomeric allyl acetates **6** and **7** were formed by a β-fragmentation followed by recombination of the allyl radical with an acetate radical (*Scheme 1*) [16]. The observed diastereoselectivity – the acetate radical attacks only from the α-side – is caused by the concave shape of the rings D and E region and is in line with several other processes observed on hecogenin derived C-secosteroids [9b][15].

To attach the '12-handle', homoallylic alcohol **5** was first transformed into methoxy ketone **10** *via* **8** and **9** by a sequence of oxidation [17] and exchange of protecting groups [18] (*Scheme 2*). The sterically hindered C(12)=O group of **10** was then smoothly transformed by a *Wittig* reaction to the corresponding alkene **11**, which provided, after

Scheme 1. *C-Ring Cleavage in Homoallylic Alcohol* **5** via *Radical-Induced β-Fragmentation*



Scheme 2. *Successful* Oxygen-Barton *Reaction*

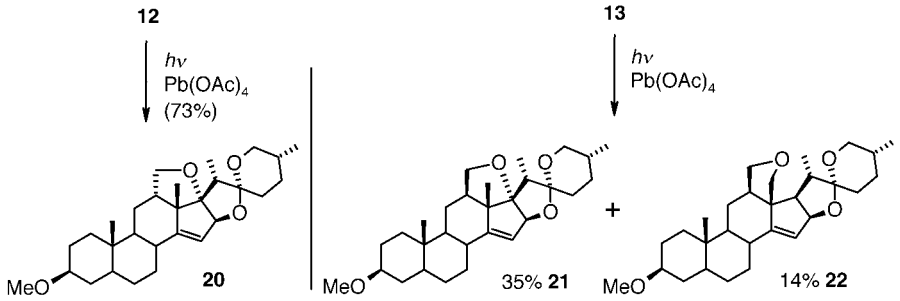


a chemoselective hydroboration-oxidation [19] and chromatographic separation, the two epimeric alcohols **12** and **13** ready for remote oxidation experiments (*Scheme 2*).

For the evaluation of the *Oxygen-Barton* reaction, the corresponding nitrites **14** and **17** (*Scheme 2*; nitrite **17** resulting from **13**, not shown) were prepared from alcohols **12** and **13**. On irradiation with UV light in an O_2-saturated benzene solution, α-nitrite **14** gave rise to the projected nitrate **15**, albeit in very low yield (10%; see *Scheme 2*). These conditions also afforded 10% of the aldehyde **16** and 18% of the free alcohol **12** [20]. The β-nitrite **17** behaved – to our surprise (*vide infra*) – similarly under identical reaction conditions, providing the corresponding nitrate **18** (9%), aldehyde **19** (19%), and alcohol **13** (22%; compounds not shown). The very low yield of the nitrates led to the termination of these particular investigations at this point. Nevertheless, the synthesis of nitrates **15** and **18** presents, to our knowledge, the first successful application of the *Oxygen-Barton* reaction on a tertiary center.

Fortunately, subjecting the α-alcohol **12** to the conditions of the photolytic $Pb(OAc)_4$ reaction delivered the projected α-ether **20** in good yield (*Scheme 3*) [21]. Interestingly, the β-alcohol **13** gave, under the same conditions, mainly rise to the 12,17-ether **21** and provided the expected 12,18-ether **22** only as a by-product (*Scheme 3*),

Scheme 3. *Lead Tetraacetate Reaction of Alcohols* **12** *and* **13**



though from the inspection of molecular models, β-alcohol **13** appeared to be an excellent candidate to furnish the 12,18-ether **22**.

Although the generation of **20** proved the feasibility of our plans, further transformations of this product, including the removal of the added CH_2 group, did not look very promising[2]). Therefore, an attempt was started to accomplish the 17-functionalization in a system that should permit the removal of this extra handle necessary for the remote oxidation. The synthesis of benzoate **26** was targeted (*Scheme 4*), which should then be transformed into the 12-keto-17-hydroxy compound *via* regioselective base-induced elimination followed by a chemoselective oxidative enol-ether cleavage (for examples, see [23]).

Addition of *in situ* generated [(4-methoxyphenoxy)methyl]lithium [24] to the hindered 12-keto function of methoxy ketone **10** proceeded smoothly with excellent yield and moderate diastereoselectivity (α/β 3.5 : 1) from the α-side to afford the 12α (4-methoxyphenoxy)methyl-substituted alcohol **23** (73%; absolute configuration 12β; *Scheme 4*) and its 12-epimer **23a** (23%; compound not shown). The protection of the sterically shielded tertiary alcohol function in **23** under vigorous conditions (deprotonation with BuLi followed by benzoyl-chloride treatment) furnished benzoate **24** and subsequent oxidative removal of the methoxyphenoxy group ($Ce(NH_4)_2(NO_3)_6$ in MeCN) provided the corresponding free primary alcohol **25** (*Scheme 4*)[3]). In contrast to alcohol **12**, benzoate **25**, when subjected to the $Pb(OAc)_4$ reaction, led only to slow decomposition of the starting material, and no **26** was formed.

Since the benzoyloxy group of **25** seemed to have a pivotal impact on the remote-oxidation procedure – possibly changing significantly the favorable orientation of the CH_2OH group and thereby 'hindering' the optimal conformation necessary for a successful remote reaction [13] – the synthesis of the free glycol **30** (*Scheme 4*) was targeted. A straightforward attempt to remove the methoxyphenoxy protecting group of alcohol **23** under standard oxidative conditions provided the unexpected quinone monoketal **27** (*Scheme 4*). Although this product represents a dead end in our efforts,

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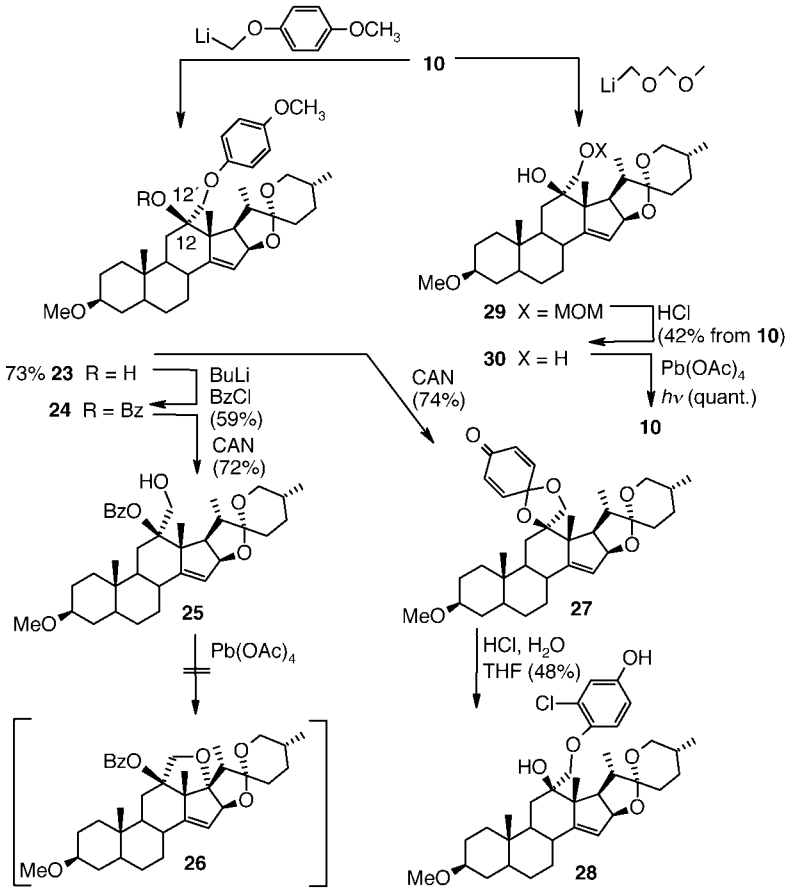
[2]) Few attempts to open the newly generated tetrahydrofuran system under *Lewis* acid catalyzed conditions [22a] or to oxidize it to the corresponding lactone [22b] were unsuccessful due to insufficient stability of the allyl-ether region and the spiroketal moiety under the required conditions.

[3]) The tertiary benzoate **25** showed modest stability to intramolecular transbenzoylation (on prolonged standing in polar solvents, *e.g.*, $CHCl_3$, the benzoyl shift proceeded slowly), and the existence of the tertiary benzoate in **25** was established by the coupling pattern of the CH_2OH protons (see *Exper. Part*).

Scheme 4. *Attempts towards Heptacycle* **26**. CAN = $Ce(NH_4)_2(NO_3)_6$, MOM = $MeOCH_2$



its easy formation merits a few comments. Several synthetic pathways to quinone monoketals – as important precursors for various types of natural products – exist, but none of them utilizes the versatile reagent $Ce(NH_4)_2(NO_3)_6$ [25–27]. Furthermore, the direct transformation of alkoxyanisoles into quinone monoketals had only so far been accomplished by electrochemical reactions [28]. Therefore – to our knowledge – the transformation **23** → **27** represents the first $Ce(NH_4)_2(NO_3)_6$-facilitated generation of a quinone monoketal.

Additionally, this quinone derivative **27** showed strong cytostatic activity (*Table 1*, *Entry 6*), but since all other monomeric steroids proved to be biologically inactive in our hands and also in the investigations from other groups [7], this unusual activity is most likely due to the strong *Michael*-acceptor system of the quinone monoketal moiety, therefore implying general toxic properties of this compound [29]. The attempt to hydrolyze the quinone monoketal **27** under acidic conditions (aq. HCl solution in THF) furnished the corresponding chlorohydroquinone **27** in a dienone-phenol-type rearrangement (*Scheme 4*) [30].

Table 1. *Selected Biological Data of Cephalostatins and Cephalostatin Analogs: Decadic Logarithms of Tumor-Inhibiting* in vitro *Concentrations against* NCI*'s Standard Screening Panel and Other Cell Lines* (n.t. = not tested)

Entry		MG-MID[a])	Ov-Mz-10[b])	Ov-Mz-17a[b])	Ov-Mz-1b[b])
Natural products:					
1	Cephalostatin 1 (**1**)	*– 8.9*	n.t.	n.t.	n.t.
2	Cephalostatin 7 (**2**)	*– 7.9*	n.t.	n.t.	n.t.
Artificial molecules:					
3	Hydroxy ketone **3**	*– 5.3*	– 5.2	> – 5.0	> – 5.0
4	α-Ether **36**	n.t.	– 5.5	> – 5.0	> – 5.0
5	β-Ether **37**	n.t.	– 6.3	> – 5.0	> – 5.0
6	Quinone monoketal **27**	n.t.	– 6.1	– 6.0	– 6.1
Anticancer drugs:					
7	Adriamycin [3]	*– 6.9*	– 7.2	– 7.2	– 7.0
8	Cisplatin [3]	*– 5.7*	– 5.1	> – 5.0	– 5.1
9	5-Fluorouracil [3]	*– 4.7*	n.t.	n.t.	n.t.

[a]) *NCI*'s standard *in vitro* screening panel (average value). [b]) Cell lines at university of Ulm.

A simple change in protecting-group strategy then allowed the synthesis of glycol **30** from methoxy ketone **10** and generated [(methoxymethoxy)methyl]lithium [31] ($\rightarrow$**29**) *in situ*, followed by deprotection (aq. HCl solution in THF) and separation of the 12-epimers (*Scheme 4*). Since the $Pb(OAc)_4$-triggered cleavage of glycols is reported to proceed with extremely varying reactions rates – depending on the nature of the substrate [32] – we dared to subject glycol **30** to the $Pb(OAc)_4$ oxidation, but glycol splitting delivered methoxy ketone **10** as the only product[4]).

The results regarding 17-O-functionalization were applied to hydroxy ketone **3**. It was TBS-protected ($\rightarrow$**31**) and then subjected to the *Wittig* reaction to deliver alkene **32**, which was consecutively hydroborated and oxidized to provide a mixture (α/β 2 : 1) of the epimeric primary alcohols **33** (*Scheme 5*). These alcohols were subjected to the conditions of a photolytic $Pb(OAc)_4$ reaction to furnish – after chromatographic separation – TBS ethers **34** and **35** as isolated products. Finally, deprotection afforded 12α-ether **36** and 12β-ether **37** in 10 and 19% overall yield, respectively, from hydroxy ketone **3**.

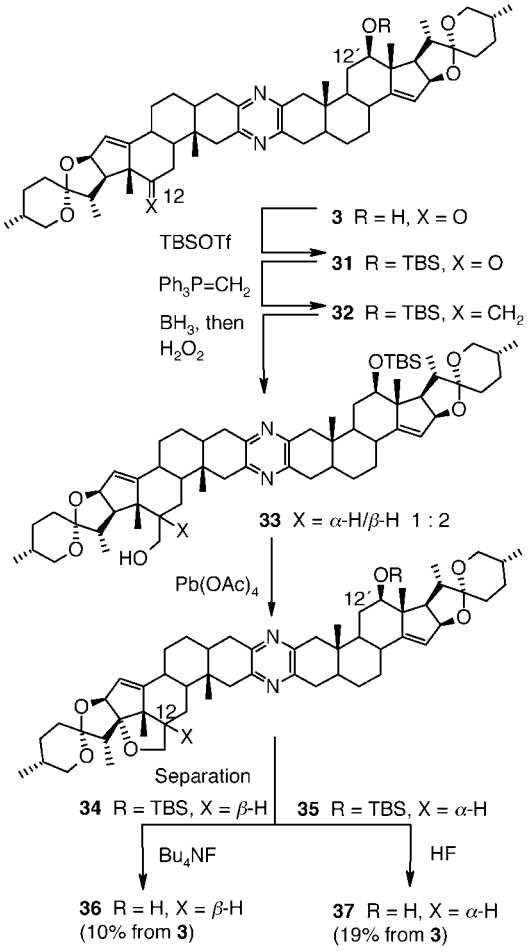
A first screen of these 17-O-functionalized artificial cephalostatin molecules against an *in vitro* cancer-cell-line assay provided evidence for an increased tumor-inhibiting activity (2 $\times$ and 13 $\times$) of these analogs compared to hydroxy ketone **3** (*Table 1*, *Entries 4* and *5*)[5]). Thus, the introduction of the 17-O-function did, indeed, improve tumor-inhibiting properties of these cephalostatin analogs and, therefore, justified our assumption from the SAR of the natural products (*vide supra*).

The second part of our investigations was directed towards a selective spiroketal opening (*vide supra*) as an ultimate requisite for a broad access to a multitude of

[4]) An alternative attempt to promote oxidation at C(17) *via* the *Baldwin* protocol [33] by reacting the 12-oxime (not shown; derived from methoxy ketone **10**) and PdH_2Cl_2 was also unsuccessful.

[5]) One must mention that two of the three cell lines used in this first assay system were insensitive towards the artificial cephalostatin molecules. That is not an unexpected effect since cephalostatins showed strongly pronounced selectivity against certain cell lines in the *NCI*'s *in vitro* panel – varying by a factor of 10000. Nevertheless, further biological evaluations would be useful to verify these results.

Scheme 5. *Synthesis of Tetradecacyclic Ethers* **36** *and* **37**. TBS = ^{t}BuMe$_2$Si.



spiroketal modifications as outlined in *Scheme 6*. This was a difficult task since spiroketal opening in steroids in the desired way (**A** → **B** in *Scheme 6*) are described to occur only in low yield and demand harsh acidic conditions [34][6]), and these were expected to be detrimental to the D-ring allyl ether system. Since from our own experiments [35], which were later confirmed by other results [7], it was evident that the establishment of the important C(14)=C(15) bond at a later stage of the synthesis would be problematic, directed spiroketal opening in the presence of this group was mandatory.

Indeed, first attempts to open the spiroketal moiety under acid-catalyzed conditions failed but provided a substantial variety of rearranged products, of which spiroketal dienes **39** and **40** (*Scheme 7*) are worth mentioning. Treatment of either the homoallylic

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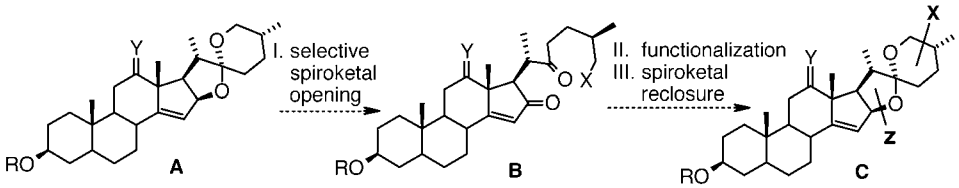
[6]) Orthogonal to these results, the versatile *Marker* degradation of the spiroketal moiety proceeds in high yield but *via* synthetic intermediates which were not suitable for our purposes.

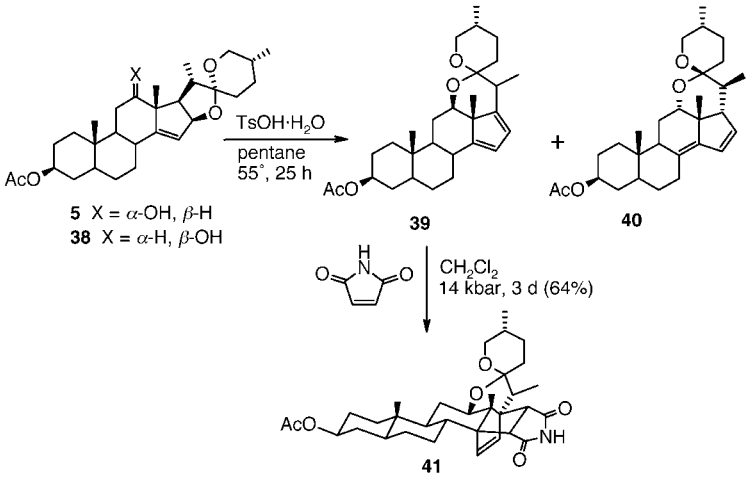
Scheme 6. *Potential Approach to a Flexible Spiroketal Functionalization*



alcohol **5** or its 12-epimer **38** [17b] with *p*-toluenesulfonic acid (TsOH) in pentane afforded the rearranged dienes **39** and **40** in modest yields. The structure of diene **40** was unambiguously established by X-ray analysis (*Fig. 2*), while – besides NMR, MS and IR studies – an important evidence for the structure of cyclopentadiene **39** was its readiness to form with maleimide the corresponding *Diels-Alder* adduct **41** – a reaction and a type of structure this laboratory is quite experienced with [36] (*Scheme 7*). A potential mechanism for these rearrangements is outlined in *Scheme 8*. The inversion of the configuration at C(12) (**5** → **39** and **38** → **40**) can be accounted for by an acid-catalyzed intramolecular nucleophilic substitution [37]. These results are consistent with related acid-catalyzed rearrangements of hecogenin derivatives reported recently by the *Fuchs* group [38].

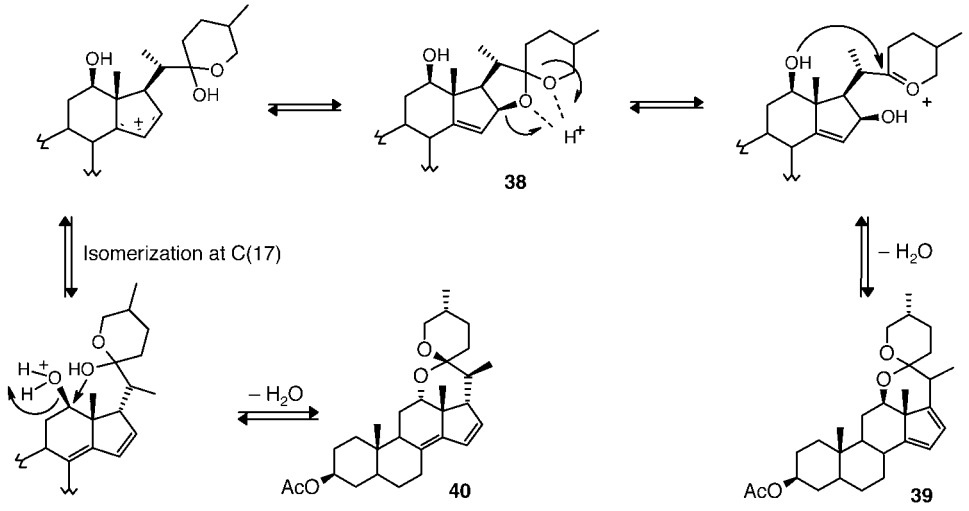
Further studies directed at alternative spiroketal opening procedures revealed that the reductive opening employing mild conditions ($NaCNBH_3$ in AcOH) [39] provided the tetrahydrofurans **44** (94% from **5**) and **45** (95% from **42**; *Scheme 9*). This comparatively mild ring-opening procedure[7]) proved to be of general nature in the sapogenin series since it was also applicable to the corresponding natural products

Scheme 7. *Acid-Catalyzed Rearrangements of Homoallylic Alcohols* **5** *and* **38**



7) Known vigorous reductive conditions for spiroketal opening in sapogenins are PtO_2/H_2 [40a] and $LiAlH_4/AlCl_3$ [40b].

Scheme 8. *Potential Mechanistic Pathways for the Formation of Dienes* **39** *and* **40**



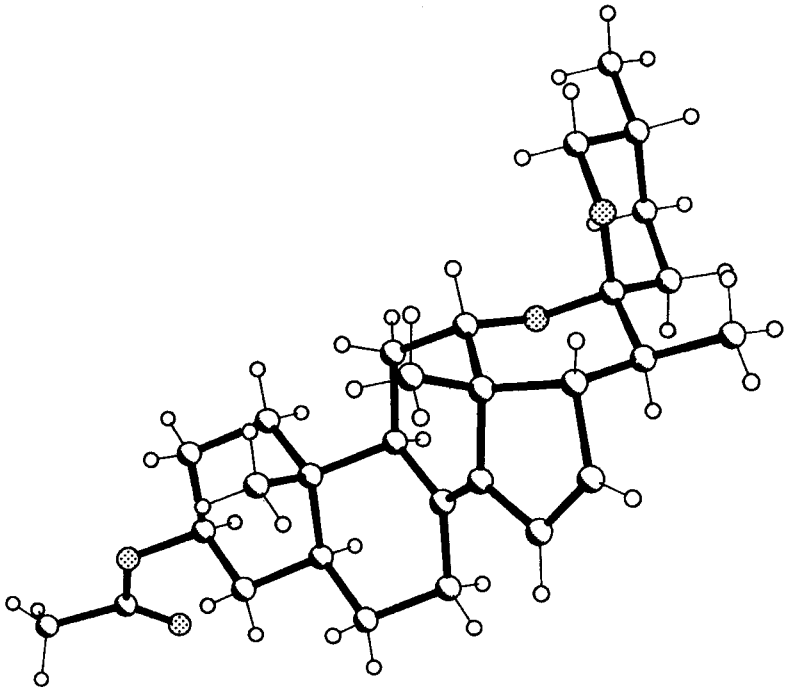
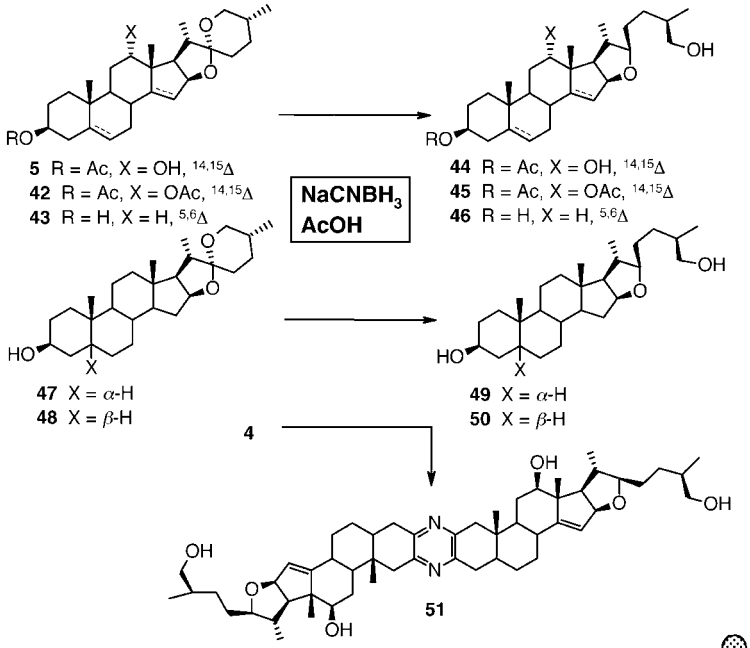


Fig. 2. *X-Ray structure of dienyl acetate* **40**

diosgenin **43** (→ 97% of **46**), tigogenin **47** (→ 55% of **49**), and smilagenin **48** (→ 76% of **50**) and also to the cephalostatin analog **4** (→ 96% of **51**) (*Scheme 9*). The structure of the furostane-type products was unambiguously established by X-ray analysis of the tigogenin derivative **49** (*Fig. 3*).

Scheme 9. *Novel Reductive Opening of Sapogenin Spiroketals*



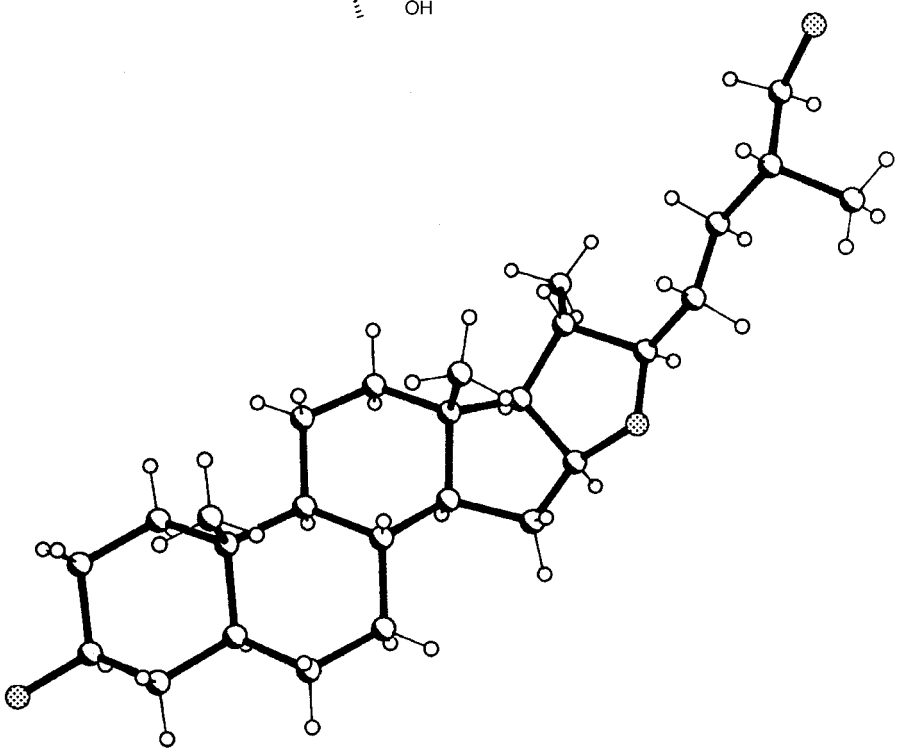
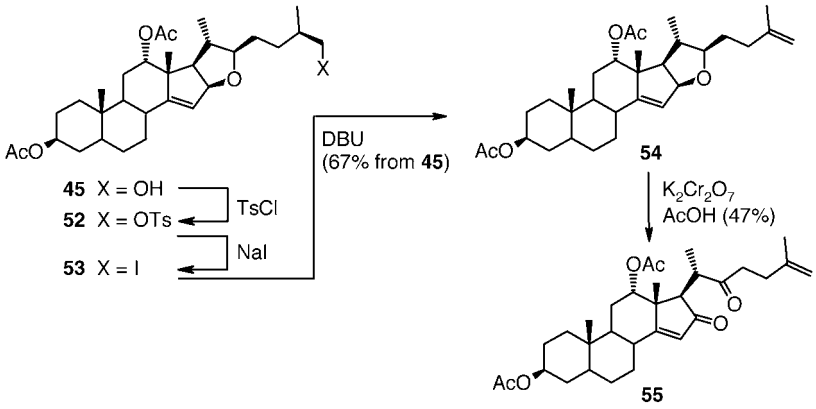


Fig. 3. *X-Ray structure of furostane-3,26-diol* **49**

Conversion of the primary alcohol function of **45** into the corresponding alkene **54** was then achieved smoothly according to standard protocols (*Scheme 10*) [41]. The following oxidative opening of the furan moiety of **54** required extensive optimization along known protocols [42], but finally, treatment of furostane **54** with potassium dichromate in AcOH at 70° for 3 h provided the desired dienedione **55** in acceptable yield. This diketone **55** offers numerous opportunities for introduction of functionality at all relevant C-atoms and for all possible types of cyclizations, thus giving access to the complete structural diversity in this field[8]).

Scheme 10. *Synthesis of Dienedione* **55**



Conclusion. – The synthesis of 17-O-functionalized tetradecacyclic cephalostatins with increased tumor-inhibiting potency is an additional piece of evidence for the importance of 17-O-functionality for biological activity – and a free 17-OH group is not a *sine qua non*. A novel way to access the important general intermediate dienedione **55** *via* a reduction-oxidation sequence was discovered, and this sequence should give general access to a variety of spiroketal-modified building blocks, which should pave the road for more exploratory research into the SAR of cephalostatins and related molecules.

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Experimental Part

General. Reactions were performed under dry conditions (dry solvents) under Ar, unless otherwise stated. Reagents were purchased from commercial sources (*Acros*, *Aldrich*, and *Fluka*) at highest quality available and were used as received unless otherwise stated.

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[8]) Since one of us (*E.W.*) will have to retire this fall, the activities at the Hannover laboratory will not continue. Colleagues interested in these results and in the further exploitation of this area are cordially invited to join the fun.

Irradiation experiments were performed in a quartz flask by a mercury high-pressure lamp (*Phillips-HPK* 125 W) with a *Pyrex* filter, the quartz flask being partly dipped into a 5°-cold water bath to maintain low temp. despite strong irradiation; the $Pb(OAc)_4$ was dried in a vacuum desiccator over P_2O_5 and KOH (contained in separate bowls!) and pulverized prior to use. TLC (reaction monitoring): silica gel $60F_{254}$ alu foils (*Merck*), detection by UV light at 254 nm and staining with cerium(IV) sulfate/phosphomolybdic acid and heat. Flash column chromatography (FC): *Baker* silica gel, particle size 0.03–0.06 mm, unless otherwise stated. M.p.: *Gallenkamp-MPD-350* apparatus; not corrected. UV Spectra: *Beckman* spectrometer, model *3600*, λ_{max} in nm, *s* = strong, *w* = weak, and sh = shoulder). IR Spectra: *Perkin-Elmer-580* and *FT-1710* spectrometers; in cm^{-1}. NMR Spectra: *Bruker-AM-400* instrument with Me_4Si or $CDCl_3$ as internal standards; δ in ppm, *J* in Hz; only Me protons and all protons downfield of 2.0 ppm are cited, other steroidal-proton signals between 0.7–2.0 ppm lacking analytical values; DEPT spectra are quoted as *q* (≡CH_3), *t* (≡CH_2), *d* (≡CH), and *s* (≡C), standard steroid numbering is used [43]. MS: *MAT-312* (*Finnigan*), ionization potential 70 eV; fast-atom-bombardment ionization (FAB) with a *VG Autospec* spectrometer in a 3-nitrobenzyl alcohol (NBA) matrix; high-resolution (HR) MS by the peak-matching method with a *VG-Autospec* spectrometer; HR-FAB-MS with a *MAT 95* (*Finnigan*) at the *Gesellschaft für Biotechnologische Forschung m.b.H.*, Brunswick. Elemental analysis were performed on a *CHN-Rapid* (*Heraeus*) and a *varioEL* (*elementar Analysensysteme GmbH*).

*(1*S*,2*R*,4a*S*,6*S*,8a*S*)-6-Acetoxy-2-[(2*R*,3*S*,3a*R*,4*R*,5′*R*,6a*S*)-6-acetoxy-3,3′,3a,4′,5′,6′,6,6′,6a-octahydro-3,4,5′-trimethylspiro[2*H*-cyclopenta[*b*]furan-2,2′-[2*H*]pyran]-5-yl]-octahydro-8a-methylnaphthalene-1-acetaldehyde* (**6**) *and (1*S*,2*R*,4a*S*,6*S*,8a*S*)-6-Acetoxy-2-[(2*R*,3*S*,3a*S*,4*R*,5′*R*,6a*S*)-4-acetoxy-3,3′,3a,4,4′,5′,6′,6a-octahydro-3,4,5′-trimethyl spiro[2*H*-cyclopenta[*b*]furan-2,2′-[2*H*]pyran]-5-yl]-octahydro-8a-methylnaphthalene-1-acetaldehyde* (**7**). A 10°-cold suspension of homoallyl alcohol **5** (200 mg, 0.423 mg, 1 equiv.), $Pb(OAc)_4$ (640 mg, 1.44 mmol, 3.3 equiv., dried prior to use, see *General*), and dry pyridine (0.15 ml, 1.89 mmol, 4.4 equiv.) in benzene (8 ml) was irradiated (see *General*) under vigorous stirring for 80 min. Then the solid material was removed by column filtration (silica gel, Et_2O), the combined org. layer washed with 5% H_2SO_4 soln., sat. $NaHCO_3$ soln., and brine, dried ($MgSO_4$), and evaporated. FC (petroleum ether/Et_2O 1:1) gave **6** (25 mg, 11%), **6**/**7** 1:1 (91 mg, 41%), and finally **7** (18 mg, 8%), all as white foams. Mixture **6**/**7**. Anal. calc. for $C_{31}H_{46}O_7$ (530.70): C 70.16, H 8.74; found: C 70.02, H 8.78.

Data of **6**: IR (KBr): 2928*s*, 2868*m*, 2720*w*, 1736*s*, 1452*m*, 1368*m*, 1240*s*. ^{1}H-NMR (400 MHz, $CDCl_3$; steroid numbering): 0.79 (*d*, *J* = 6, Me(27)); 0.84 (*s*, Me(19)); 1.06 (*d*, *J* = 7, Me(21)); 1.71 (*s*, Me(18)); 2.02 (*s*, AcO); 2.08 (*s*, AcO); 2.22 (br. *d*, *J* = 17.5, H–C(11)); 2.32 (br. *dd*, *J* = 17.5, 5.5, H–C(11)); 2.50 (br. *td*, *J* = 11.5, 3.5, H–C(8)); 2.84 (*dd*, *J* = 7, 6.5, H–C(17)); 3.38–3.49 (*m*, CH_2(26)); 4.16 (br. *d*, *J* = 7, H–C(16)); 4.69 (*tt*, *J* = 11, 5, H–C(3)); 5.77 (br. *s*, H–C(15)); 9.61 (br. *s*, H–C(12)). ^{13}C-NMR (100 MHz, $CDCl_3$; steroid numbering): 11.7, 13.3, 14.1, 17.1 (4*q*, C(18), C(19), C(21), C(27)); 21.4, 21.6 (2*q*, 2 *Me*CO); 27.2 (*t*); 28.2 (*t*), 28.5 (*t*); 30.3 (*d*); 30.7 (*t*); 31.0 (*t*); 33.9 (*t*); 36.77 (*d*); 36.82 (*s*, C(10)); 37.9 (*t*); 43.4 (*t*, C(11)); 44.1 (*d*); 46.9 (*d*); 47.8 (*d*); 58.7 (*s*, C(17)); 67.0 (*t*, C(26)); 73.0 (*d*, C(3)); 83.8, 84.7 (2*d*, C(15), C(16)); 107.1 (*s*, C(22)); 132.3, 145.4 (2*s*, C(13), C(14)); 170.3, 170.6 (2*s*, 2 Me*C*O); 202.9 (*d*, C(12)). MS (170°): 530 (1, M^+), 470 (8), 452 (8), 373 (19), 356 (33), 126 (100). HR-MS: 530.3250 ($C_{31}H_{46}O_7^+$; calc. 530.3244).

Data of **7**. IR (KBr): 2928*s*, 2868*m*, 2720*w*, 1736*s*, 1452*m*, 1368*m*, 1244*s*. ^{1}H-NMR (400 MHz, $CDCl_3$; steroid numbering): 0.79 (*d*, *J* = 6, Me(27)); 0.84 (*s*, Me(19)); 1.15 (*d*, *J* = 7, Me(21)); 1.60 (*s*, Me(18)); 1.98 (*s*, AcO); 2.03 (*s*, AcO); 2.18 (*m*, H–C(8)); 2.23–2.38 (*m*, CH_2(11)); 2.92 (*dd*, *J* = 9.5, 7.5, H–C(17)); 3.38 (*t*, *J* = 11, 1 H–C(26)); 3.47 (br. *d*, *J* = 11, 1 H–C(26)); 4.72 (*tt*, *J* = 11, 5, H–C(3)); 4.89 (br. *d*, *J* = 7.5, H–C(16)); 5.79 (br. *s*, H–C(15)); 9.61 (br. *s*, H–C(12)). ^{13}C-NMR (100 MHz, $CDCl_3$; steroid numbering): 12.0, 13.3, 17.1, 19.3 (4*q*, C(18), C(19), C(21), C(27)); 21.4, 22.2 (2*q*, 2 *Me*CO); 27.1 (*t*); 28.5 (*t*); 28.6 (*t*); 30.3 (*d*); 31.1 (*t*); 33.85 (*t*); 33.89 (*t*); 36.86 (*d*); 36.91 (*t*); 36.93 (*s*, C(10)); 43.7 (*t*, C(11)); 43.9 (*d*); 45.2 (*d*); 47.2 (*d*); 56.1 (*s*, C(17)); 67.1 (*t*, C(26)); 73.1 (*d*, C(3)); 83.4 (*d*, C(16)); 93.9 (*s*, C(13)); 107.6 (*s*, C(22)); 130.8 (*d*, C(15)); 152.0 (*s*, C(14)); 170.1, 170.6 (2*s*, 2 Me*C*O); 202.1 (*d*, C(12)). MS (160°): 530 (1, M^+), 470 (10), 374 (16), 356 (34), 126 (100). HR-MS: 530.3246 ($C_{31}H_{46}O_7^+$; calc. 530.3244).

*(3β,5α,25*R*)-3-Hydroxyspirost-14-en-12-one* (**9**). A soln. of acetoxy ketone **8** (4.749 g, 10.08 mmol, 1 equiv.) and KOH (1.12 g, 20 mmol, 2 equiv.) in CH_2Cl_2/MeOH 1:1 (16 ml) was stirred at 50° for 2 h. The reaction was quenched by addition of H_2O (25 ml), the aq. layer extracted with CH_2Cl_2, the combined org. layer washed with sat. aq. NH_4Cl soln., dried (Na_2SO_4), and evaporated, and the residue recrystallized from CH_2Cl_2/MeOH: **9** (4.143 g, 96%). Colorless crystalline solid. M.p. 220° (from CH_2Cl_2/MeOH). IR (KBr): 3456*m* (br.), 2928*s*, 2860*s*, 1708*s*, 1644*w*, 1460*m*, 1376*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6.5, Me(27)); 0.93 (*s*, Me(19)); 1.04 (*d*, *J* = 7, Me(21)); 1.29 (*s*, Me(18)); 2.35 (*dd*, *J* = 14.5, 5, 1 H–C(11)); 2.43–2.48 (*m*, H–C(8)); 2.56 (*dd*, *J* = 14.5, 13.5, 1 H–C(11)); 3.33 (*t*, *J* = 8.5, H–C(17)); 3.41 (*t*, *J* = 11, 1 H–C(26)); 3.51 (br. *d*, *J* = 11, 1 H–C(26)); 3.59 (*tt*, *J* = 11, 4.5, H–C(3)); 4.76 (*dd*, *J* = 8.5, 2, H–C(16)); 5.43 (br. *s*, H–C(15)). ^{13}C-NMR

(100 MHz, $CDCl_3$): 11.8, 13.8, 17.1, 20.9 (4*q*, C(18), C(19), C(21), C(27)); 28.0 (*t*); 28.7 (*t*); 29.5 (*t*); 30.3 (*d*); 31.17 (*t*); 31.22 (*t*); 34.2 (*d*); 36.3 (*s*, C(10)); 36.5 (*t*); 37.4 (*t*); 37.8 (*t*); 44.1 (*d*); 44.2 (*d*); 49.7 (*d*); 53.7 (*d*); 62.3 (*s*, C(13)); 67.1 (*t*, C(26)); 70.8 (*d*, C(3)); 84.0 (*d*, C(16)); 107.1 (*s*, C(22)); 120.9 (*d*, C(15)); 154.9 (*s*, C(14)); 211.5 (*s*, C(12)). MS (140°): 428 (51, M^+), 411 (19), 356 (24), 313 (100), 299 (85), 148 (56), 126 (96). HR-MS: 428.2931 ($C_{27}H_{40}O_4^+$; calc. 428.2927). Anal. calc. for $C_{27}H_{40}O_4$ (428.61): C 75.66, H 9.41; found: C 75.62, H 9.39.

*(3β,5α,25*R*)-3-Methoxyspirost-14-en-12-one* (**10**). To a soln. of **9** (2.011 g, 4.70 mmol, 1 equiv.) and 2,6-di(*tert*-butyl)pyridine (1.28 ml, 6.11 mmol, 1.3 equiv.) in CH_2Cl_2 (10 ml), methyl triflate (0.67 ml, 6.11 mmol, 1.3 equiv.) was added dropwise. After 4 h, the reaction was quenched by addition of sat. NaOAc soln. (4 ml), the aq. layer extracted with CH_2Cl_2, the combined org. layer washed with H_2O, dried (Na_2SO_4), and evaporated and the residue submitted to FC (petroleum ether/Et_2O 7:1): **10** (1.881 g, 91%). White crystalline solid. M.p. 189° (from MeOH). IR (KBr): 2928*s*, 2860*s*, 1708*s*, 1644*w*, 1456*m*, 1372*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6, Me(27)); 0.92 (*s*, Me(19)); 1.04 (*d*, *J* = 7, Me(21)); 1.29 (*s*, Me(18)); 2.35 (*dd*, *J* = 14.5, 4.5, 1 H–C(11)); 2.45 (*m*, H–C(8)); 2.56 (*t*, *J* = 14.5, 1 H–C(11)); 3.12 (*tt*, *J* = 11, 5, H–C(3)); 3.33 (*t*, *J* = 8.5, H–C(17)); 3.34 (*s*, MeO); 3.41 (*t*, *J* = 11, 1 H–C(26)); 3.52 (br. *d*, *J* = 11, 1 H–C(26)); 4.76 (br. *d*, *J* = 8.5, H–C(16)); 5.43 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.8, 13.8, 17.1, 20.9 (4*q*, C(18), C(19), C(21), C(27)); 27.6 (*t*); 28.2 (*t*); 28.8 (*t*); 29.5 (*t*); 30.3 (*d*); 31.2 (*t*); 34.19 (*t*); 34.24 (*d*); 36.4 (*s*, C(10)); 37.4 (*t*); 44.2 (br., 2 *d*); 49.8 (*d*); 53.8 (*d*); 55.7 (*q*, MeO); 62.3 (*s*, C(13)); 67.1 (*t*, C(26)); 79.3 (*d*, C(3)); 84.0 (*d*, C(16)); 107.0 (*s*, C(22)); 120.8 (*d*, C(15)); 154.9 (*s*, C(14)); 211.5 (*s*, C(12)). MS (140°): 442 (73, M^+), 372 (33), 328 (100), 126 (93). HR-MS: 442.3078 ($C_{28}H_{42}O_4^+$; calc. 442.3083). Anal. calc. for $C_{28}H_{42}O_4$ (442.64): C 75.98, H 9.56; found: C 75.90, H 9.45.

*(3β,5α,25*R*)-3-Methoxy-12-methylenespirost-14-ene* (**11**). To a suspension of triphenyl(methyl)phosphonium bromide (6.432 g, 18.0 mmol, 7.1 equiv.) in THF (70 ml), 1.8M PhLi in cyclohexane/Et_2O 7:3 (8.8 ml, 15.84 mmol, 6.3 equiv.) was added under vigorous stirring. After 6 h, **10** (1.122 mg, 2.53 mmol, 1 equiv.) was added, and after further 2.5 h, the reaction was quenched by addition of Et_2O (50 ml) and brine (40 ml). The aq. layer was extracted with Et_2O, the combined org. layer washed with brine, dried (Na_2SO_4), and evaporated, and the residue subjected to FC (petroleum ether/AcOEt 15:1): **11** (1.076 g, 96%). White foam. M.p. 128° (after recrystallization from petroleum ether/Et_2O). IR (KBr): 2928*s*, 2860*m*, 1650*w*, 1632*m*, 1456*m*, 1372*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*d*, *J* = 6.5, Me(27)); 0.88 (*s*, Me(19)); 1.08 (*d*, *J* = 7, Me(21)); 1.18 (*s*, Me(18)); 2.21–2.34 (*m*, H–C(8), CH_2(11)); 2.93 (*t*, *J* = 8, H–C(17)); 3.12 (*tt*, *J* = 11, 5, H–C(3)); 3.35 (*s*, MeO); 3.45 (*t*, *J* = 11, 1 H–C(26)); 3.52 (br. *d*, *J* = 11, 1 H–C(26)); 4.67 (br. *s*, 1 H, CH_2=C(12)); 4.75 (br. *s*, 1 H, CH_2=C(12)); 4.82 (*dd*, *J* = 8, 2 H–C(16)); 5.30 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.9, 14.0, 17.2, 14.0 (4*q*, C(18), C(19), C(21), C(27)); 27.7 (*t*); 28.3 (*t*); 28.8 (*t*); 29.9 (*t*); 30.4 (*d*); 31.5 (*t*); 32.3 (*t*); 34.2 (*t*); 34.9 (*t*); 36.3 (*s*, C(10)); 36.7 (*t*); 44.1 (*d*); 44.3 (*d*); 53.4 (*s*, C(13)); 54.1 (*d*); 55.4 (*d*); 55.6 (*q*, MeO); 67.1 (*t*, C(26)); 79.6 (*d*, C(3)); 84.3 (*d*, C(16)); 105.8 (*t*, *C*H_2=C); 107.5 (*s*, C(22)); 117.5 (*d*, C(15)); 155.9, 159.5 (2*s*, C(12), C(14)). MS (110°): 440 (98, M^+), 425 (18), 353 (41), 326 (100), 297 (41), 169 (60), 127 (98). HR-MS: 440.3292 ($C_{29}H_{44}O_3^+$; calc. 440.3290). Anal. calc. for $C_{29}H_{44}O_3$ (440.66): C 79.04, H 10.06; found: C 78.96, H 9.97.

*(3β,5α,12α,25*R*)- and (3β,5α,12β,25*S*)-3-Methoxyspirost-14-ene-12-methanol* (**12** and **13**, resp.). To a 0°-cold soln. of **11** (410 mg, 0.930 mmol, 1 equiv.) in THF (4 ml), 10M $BH_3 \cdot SMe_2$ (0.28 ml, 2.8 mmol, 3 equiv.) was added dropwise. After 1.5 h, 6N aq. NaOH (1 ml) was slowly added, followed by EtOH (0.1 ml) and Et_2O (0.4 ml). After further 30 min, the mixture was warmed to r.t., 35% aq. H_2O_2 soln. (0.5 ml) was added and the mixture stirred for 2 h at 50°. Then the mixture was neutralized by addition of solid NH_4Cl, and the aq. layer was extracted with Et_2O. The combined org. layer was dried (Na_2SO_4) and evaporated and the residue recrystallized from Et_2O: **13** (289 mg, 0.630 mmol) as colorless crystals. The mother liquor was evaporated and provided, after FC (petroleum ether/AcOEt 2:1), **13** (15 mg, altogether 71%) and **12** (67 mg, 16%, 0.146 mmol), both as white, crystalline solids.

Data of **12**: M.p. 175° (from Et_2O). IR (KBr): 3452*m*, 2928*s*, 2860*s*, 1644*w*, 1456*m*, 1372*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6.5, Me(27)); 0.87 (*s*, Me(19)); 1.01 (*d*, *J* = 7, Me(21)); 1.21 (*s*, Me(18)); 2.14 (*m*, H–C(8)); 2.60 (*dd*, *J* = 9.5, 8, H–C(17)); 3.10 (*tt*, *J* = 11, 5, H–C(3)); 3.29 (br. *d*, *J* = 10, H_a of CH_2OH); 3.34 (*s*, MeO); 3.42 (*t*, *J* = 11, 1 H–C(26)); 3.49 (*m*, 1 H–C(26)); 3.68 (*dd*, *J* = 10, 4.5, H_b of CH_2OH); 4.78 (*dd*, *J* = 8, 1, H–C(16)); 5.32 (br. *s*, H–C(15)). NOE ($CDCl_3$): irr. at 3.68 (H_b of CH_2OH) → 4.78 (3.3%, H–C(16)); 3.29 (10.6%, H_a of CH_2OH); 2.60 (12.9%, H–C(17)); irr. at 2.60 (H–C(17)) → 4.78 (8.8%, H–C(16)); 3.68 (9.6%, H_b of CH_2OH); irr. at 1.21 (Me(18)) → 2.14 (4.8%, H–C(8)); 1.79 (7.4%, H–C(20) → *dq*, *J*(22,17) = 9.5, *J*(20,21) = 7), 1.66 (4.6%, H–C(11) → br. *d*, *J*(11b,9) = 14.5), 1.01 (2.0%, Me(21)); 0.87 (2.7%, Me(19)). NMR Data connectivity was established by C,H-COSY. ^{13}C-NMR (100 MHz, $CDCl_3$): 11.9 (*q*, Me(19)); 14.2 (*q*, Me(21)); 17.2 (*q*, Me(27)); 20.8 (*q*, Me(18)); 22.7 (*t*); 27.8 (*t*); 28.5 (*t*); 28.7 (*t*); 29.8 (*t*); 30.4 (*d*); 31.2 (*t*); 34.3 (*t*); 34.6 (*d*); 36.3 (*s*, C(10)); 36.8 (*t*); 44.8 (*d*); 45.0 (*d*); 48.9 (*d*); 49.3 (*s*, C(13)); 50.5 (*d*); 54.0 (*d*, C(17)); 55.6 (*q*, MeO); 61.9 (*t*, CH_2OH); 67.2 (*t*, C(26)); 79.7 (*d*, C(3)); 85.0 (*d*, C(16)); 106.5 (C, C(22));

118.7 (*d*, C(15)); 155.6 (*s*, C(14)). FAB-MS: 481 (16, $[M+Na]^+$), 459 (43, $[M+H]^+$), 315 (34), 154 (100). HR-MS: 458.3401 ($C_{29}H_{46}O_4^+$; calc. 458.3396). Anal. calc. for $C_{29}H_{46}O_4$ (458.68): C 75.94, H 10.11; found: C 75.58, H 10.04.

Data of **13**: M.p. 197° (from Et_2O). IR (KBr): 3464*m*, 2928*s*, 2872*s*, 1652*w*, 1456*m*, 1372*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*d*, *J* = 6, Me(27)); 0.86 (*s*, Me(19)); 0.87 (*s*, Me(18)); 1.03 (*d*, *J* = 7, Me(21)); 2.04–2.09 (*m*, H–C(8)); 2.45 (*t*, *J* = 8.5, H–C(17)); 3.12 (*tt*, *J* = 11, H–C(3)); 3.43–3.38 (*m*, MeO, H_a of CH_2OH); 3.43 (*t*, *J* = 11, 1 H–C(26)); 3.51 (br. *d*, *J* = 11, 1 H–C(26)); 3.75 (*dd*, *J* = 10.5, H_a of CH_2OH); 4.87 (*dd*, *J* = 8.5, 2, H–C(16)); 5.33 (br. *s*, H–C(15)). NOE ($CDCl_3$): irr. at 3.75 (H_b of CH_2OH) → 3.35 (23.6%, H_a of CH_2OH), 2.45 (5.9%, H–C(17)); irr. at 2.45 (H–C(17)) → 4.87 (11.2%, H–C(16)); 3.75 (4.8%, H_b of CH_2OH); 1.24 (6.6%, H–C(12) → br. *d*, *J*(12, H_a) = 10), 1.03 (3.6%, Me(21)); irr. at 0.86 (Me(18)) → 2.06 (4.6%, H–C(8)); 1.76 (5.0%, H–C(20) → *dq*, *J*(20,17) = 8.5, *J*(20,21) = 7), 1.35–1.28 and 1.25–1.19 (6.1%, two different protons, *m*). NMR Data connectivity was established by C,H-COSY. ^{13}C-NMR (100 MHz, $CDCl_3$): 12.2 (*q*, Me(19)); 14.1 (*q*, Me(21)); 15.6 (*q*, Me(18)); 17.1 (*q*, Me(27)); 24.9 (*t*); 27.7 (*t*); 28.4 (*t*); 28.7 (*t*); 29.9 (*t*); 30.4 (*d*); 31.1 (*t*); 34.3 (*t*); 34.9 (*d*); 36.4 (*s*, C(10)); 36.8 (*t*); 44.2 (*d*); 44.6 (*d*); 48.6 (*s*, C(13)); 52.2 (*d*); 54.8 (*d*); 55.6 (*q*, MeO); 56.8 (*d*, C(17)); 65.0 (*t*, CH_2OH); 67.1 (*t*, C(26)); 79.7 (*d*, C(3)); 84.7 (*d*, C(16)); 106.9 (*s*, C(22)); 116.8 (*d*, C(15)); 160.8 (*s*, C(14)). MS (180°): 458 (76, M^+), 440 (43, $[M-H_2O]^+$), 428 (75), 369 (77), 344 (83), 330 (77), 313 (100), 285 (73), 126 (87). HR-MS: 458.3400 ($C_{29}H_{46}O_4^+$; calc. 458.3396). Anal. calc. for $C_{29}H_{46}O_4$ (458.68): C 75.94, H 0.11; found: C 75.67, H 10.09.

*[(3β,5α,12α,25*R*)-3-Methoxyspirost-14-en-12-yl]methyl Nitrite* (**14**). A soln. of **12** (112 mg, 0.245 mmol, 1 equiv.) and *tert*-butyl nitrite (0.29 ml, 2.4 mmol, 10 equiv.) in $CHCl_3$ (1.6 ml; 0.15M) was stirred for 4 h. After addition of pyridine (3 ml), the solvent was rapidly evaporated. Basic-gradient FC (petroleum ether/Et_2O 5:1 + 2% Et_3N (→ **14**), then petroleum ether/AcOEt 2:1 (→ **12**)) gave **14** (103 mg, 86%) as a colorless foam and recovered **12** (9 mg, 0.020 mmol). **14**: UV (MeCN): 213. IR (KBr): 2948*s*, 1652*m* (ONO), 1616*s* (ONO), 1456*m*, 1360*m*, 1240*m*. ^{1}H-NMR (400 MHz, (D_5)pyridine): 0.73–0.75 (*m*, Me(19), Me(27)); 1.18 (*d*, *J* = 6.5, Me(21)); 1.28 (*s*, Me(18)); 1.98 (*dq*, *J* = 9.5, 6.5, H–C(20)); 2.09 (*m*, 1 H); 2.17 (br. *t*, *J* = 11, H–C(8)); 2.81 (*dd*, *J* = 9.5, 7.5, H–C(17)); 3.09 (*tt*, *J* = 11, 5, H–C(3)); 3.32 (*s*, MeO); 3.62–3.66 (*m*, 2 H–C(26)); 4.58 (br. *m*, H_a of CH_2ONO); 4.79 (br. *m*, H_b of CH_2ONO); 5.14 (br. *d*, *J* = 7.5, H–C(16)); 5.59 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, (D_5)pyridine): 8.0, 11.8, 14.5, 17.3 (4*q*, C(18), C(19), C(21), C(27)); 22.9 (*t*); 28.2 (*t*); 28.6 (*t*); 29.2 (*t*); 30.0 (*t*); 30.7 (*d*); 31.6 (*t*); 34.6 (*t*); 34.7 (*d*); 36.4 (*s*, C(10)); 36.7 (*t*); 44.6 (*d*); 45.6 (*d*); 46.0 (br. *d*, C(12)); 49.5 (*s*, C(13)); 50.4 (*d*); 54.9 (*d*); 55.3 (*q*, MeO); 67.3 (*t*, C(26)); 68.4 (br. *t*, CH_2ONO); 79.6 (*d*, C(3)); 85.3 (*d*, C(16)); 106.6. (*s*, C(22)); 120.5 (*d*, C(15)); 154.1 (*s*, C(14)). FAB-MS: 488 (22, $[M+H]^+$), 457 (26, $[M-NO]^+$), 307 (27, NBA matrix), 154 (100, NBA matrix). HR-MS: 487.3294 ($C_{29}H_{45}O_5N^+$; calc. 487.3298).

*(3β,5α,12α,25*R*)-3-Methoxy-17-(nitrooxy)spirost-14-ene-12-methanol* (**15**) *and (3β,5α,12α,25*S*)-3-Methoxyspirost-14-ene-12-carbaldehyde* (**16**). Through a vigorously stirred 4°-cold soln. of **14** (68 mg, 0.139 mmol) in benzene (10 ml) in a quartz flask, O_2 was bubbled for 20 min. Then the soln. was irradiated (see *General*) for 100 min under continuous O_2 bubbling and mild cooling (*T ca.* 10°). Then the soln. was evaporated and the residue subjected to gradient FC (petroleum ether/Et_2O 3:1 (→ **16**), then petroleum ether/Et_2O 1:1 (→ **15**), and finally petroleum ether/Et_2O 1:2 (→ **12**)): **16** (6.2 mg, 10%), **15** (7.3 mg, 10%), and **12** (11.7 mg, 18%), all as colorless, amorphous solids.

Data of **15**: IR ($CHCl_3$): 3618*w* (OH), 3392*w* (br., OH), 2932*s*, 2860*m*, 1636*s* (ONO_2), 1456*m*, 1384*m*, 1284*s* (ONO_2), 1244*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.79 (*d*, *J* = 6, Me(27)); 0.88 (*s*, Me(19)); 1.14 (*d*, *J* = 7, Me(21)); 1.45 (*s*, Me(18)); 2.02 (*m*, H–C(12)); 2.16–2.22 (*m*, H–C(8), H–C(20)); 3.11 (*tt*, *J* = 11, 5, H–C(3)); 3.34–3.37 (*m*, MeO, H_a of CH_2OH); 3.39 (*t*, *J* = 11, 1 H–C(26)); 3.48 (br. *d*, *J* = 11, 1 H–C(26)); 3.84 (*dd*, *J* = 10, 3, H_b of CH_2OH); 5.26 (br. *s*, H–C(16)); 5.33 (br. *s*, H–C(15)). ^{13}C-NMR (150 MHz, $CDCl_3$): 9.6, 11.9, 17.1, 19.9 (4*q*, C(18), C(19), C(21), C(27)); 22.2 (*t*); 27.9 (*t*); 28.5 (*t*); 28.7 (*t*); 29.4 (*t*); 30.0 (*d*); 32.6 (*t*); 34.3 (*d*); 34.5 (*t*); 36.4 (*s*, C(10)); 36.6 (*t*); 45.0 (*d*); 46.5 (*d*); 50.9 (*d*); 51.1 (*d*); 55.7 (*q*, MeO); 55.8 (*s*, C(13)); 61.5 (*t*, CH_2OH), 67.1 (*t*, C(26)); 79.7 (*d*, C(3)); 88.4 (*d*, C(16)); 106.2 (*s*, C(22)); 108.5 (*s*, C(17)); 118.9 (*d*, C(15)); 151.7 (*s*, C(14)). FAB-MS: 520 (27, $[M+H]^+$), 473 (40, $[M-NO_2]^+$), 154 (100, NBA matrix). HR-MS: 473.3264 ($[C_{29}H_{45}O_7N-NO_2]^+$; calc. 473.3267).

Data of **16**: IR ($CHCl_3$): 2932*s*, 2860*m*, 2717*w* (aldehyde CH), 1712*s* (C=O), 1456*m*, 1376*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6, Me(27)); 0.86 (*s*, Me(19)); 1.01 (*d*, *J* = 7, Me(21)); 1.21 (*s*, Me(18)); 2.25 (*m*, H–C(8)); 2.38 (br. *s*, H–C(12)); 2.52 (*dd*, *J* = 9, 8, H–C(17)); 3.11 (*tt*, *J* = 11, 5, H–C(3)); 3.34 (*s*, MeO); 3.40 (*t*, *J* = 11, 1 H–C(26)); 3.49 (br. *d*, *J* = 11, 1 H–C(26)); 4.85 (br. *d*, *J* = 8, H–C(16)); 5.48 (br. *s*, H–C(15)); 9.63 (*d*, *J* = 3, CHO). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.5, 14.2, 17.1, 20.2 (4*q*, C(18), C(19), C(21), C(27)); 24.2 (*t*); 27.7 (*t*); 28.3 (*t*); 28.7 (*t*); 29.7 (*t*); 30.4 (*d*); 31.0 (*t*); 34.2 (*t*); 34.6 (*d*); 36.5 (*s*, C(10)); 36.6 (*t*);

44.6 (*d*); 44.8 (*d*); 49.4 (*s*, C(13)); 51.6 (*d*); 55.6 (*q*, MeO); 55.8 (*d*); 58.2 (*d*, C(12)); 67.1 (*t*, C(26)); 79.5 (*d*, C(3)); 84.8 (*d*, C(16)); 106.6 (*s*, C(22)); 120.0 (*d*, C(15)); 156.1 (*s*, C(14)); 207.1 (*d*, CHO). MS (150°): 456 (32, M^+), 425 (7), 384 (6), 342 (13), 302 (18), 126 (100). HR-MS: 456.3240 ($C_{29}H_{44}O_4^+$; calc. 456.3240).

12β-Isomer **17** *of Nitrite* **14**. As described for **14**, from **13** (322 mg, 0.702 mmol, 1 equiv.): **17** (261 mg, 76%) and recovered **13** (58 mg, 0.126 mmol). **17**: UV (MeCN): 212. IR ($CHCl_3$): 2932*s*, 2860*m*, 1648*m* (ONO), 1608*m* (ONO), 1456*m*, 1376*m*, 1240*m*. ^{1}H-NMR (400 MHz, (D_5)pyridine): 0.74–0.76 (*m*, Me(19), Me(27)); 1.02 (*s*, Me(18)); 1.16 (*d*, *J* = 6.5, Me(21)); 2.07 (*m*, H–C(8)); 2.67 (*t*, *J* = 8.5, H–C(17)); 3.09 (*tt*, *J* = 11, 5, H–C(3)); 3.31 (*s*, MeO); 3.55–3.67 (*m*, CH_2(26)); 4.58 (br. *m*, H_a of CH_2ONO); 4.88 (br. *m*, H_b of CH_2ONO); 5.12 (*dd*, *J* = 8.5, 1.5, H–C(16)); 5.52 (br. *s*, H–C(15). ^{13}C-NMR (100 MHz, (D_5)pyridine): 12.0, 14.5, 15.8, 17.3 (4*q*, C(18), C(19), C(21), C(27)); 25.4 (*t*); 28.3 (*t*); 28.6 (*t*); 29.1 (*t*); 30.2 (*t*); 30.7 (*d*); 31.6 (*t*); 34.6 (*t*); 34.8 (*d*); 36.5 (*s*, C(10)); 36.8 (*t*); 44.4 (*d*); 44.8 (*d*); 48.9 (*s*, C(13)); 49.0 (br. *d*, C(12)); 54.7 (*d*); 55.3 (*q*, MeO); 57.3 (*d*); 67.2 (*t*, C(26)); 71.1 (br. *t*, CH_2ONO); 79.6 (*d*, C(3)); 85.0 (*d*, C(16)); 107.0 (*s*, C(22)); 118.4 (*d*, C(15)); 159.4 (*s*, C(14)). MS (160°): 487 (15, M^+), 457 (15, $[M-NO]^+$), 428 (29), 343 (68), 313 (81), 126 (100). HR-MS: 487.3310 ($C_{29}H_{45}O_5N^+$; calc. 487.3298).

12β-Isomer **18** *and 12β-Isomer* **19** of *Nitrooxy Derivative* **15** *and Aldehyde* **16**, *resp.* As described for **15** and **16**, from **17** (100 mg, 0.205 mmol); **19** (18 mg, 19%), **18** (10 mg, 9%), and **13** (21 mg, 22%), all as colorless, amorphous solids.

Nitrooxy Derivative **18**: IR ($CHCl_3$): 3620*w* (OH), 3400*w* (br., OH), 2932*s*, 2864*m*, 1628*s* (ONO_2), 1452*m*, 1380*m*, 1284*s* (ONO_2), 1244*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*d*, *J* = 6, Me(27)); 0.84 (*s*, Me(19)); 1.03 (*s*, Me(18)); 1.08 (*d*, *J* = 7.5, Me(21)); 2.05 (*m*, H–C(8), H–C(12)); 2.32 (*q*, *J* = 7, H–C(20)); 3.13 (*tt*, *J* = 11, 5, H–C(3)); 3.35–3.40 (*m*, MeO, H_a of CH_2OH); 3.46–3.55 (*m*, CH_2(26)); 3.82 (*dd*, *J* = 10.5, 3, H_b of CH_2OH); 5.43 (br. *s*, H–C(16)); 5.45 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 7.9, 12.1, 17.1, 20.3 (4*q*, C(18), C(19), C(21), C(27)); 25.9 (*t*); 27.7 (*t*); 28.25 (*t*); 28.31 (*t*); 29.6 (*t*); 29.9 (*d*); 31.1 (*t*); 34.3 (*t*); 35.4 (*d*); 36.2 (*s*, C(10)); 36.8 (*t*); 43.6 (*d*); 44.1 (*d*); 49.5 (*d*); 52.4 (*d*); 54.2 (*s*, C(13)); 55.6 (*q*, MeO); 65.7 (*t*); CH_2OH); 67.1 (*t*, C(26)); 79.7 (*d*, C(3)); 86.9 (*d*, C(16)); 106.8 (*s*, C(17)); 107.2 (*s*, C(22)); 115.6 (*d*, C(15)); 160.0 (*s*, C(14)). FAB-MS: 520 (15, $[M+H]^+$), 457 (10), 154 (100, NBA matrix). HR-MS: 473.3251 ($[C_{29}H_{45}O_7N-NO_2]^+$; calc. 473.3267).

Aldehyde **19**: IR ($CHCl_3$): 2932*s*, 2860*m*, 2728*w* (aldehyde CH), 1716*s* (C=O), 1628*w*, 1456*m*, 1376*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*d*, *J* = 6, Me(27)); 0.88 (*s*, Me(19)); 1.02 (*s*, Me(18)); 1.05 (*d*, *J* = 7, Me(21)); 2.07 (*m*, H–C(8)); 2.10 (br. *dd*, *J* = 12, 3, H–C(12)); 2.78 (*t*, *J* = 8.5, H–C(17)); 3.12 (*tt*, *J* = 11, 5, H–C(3)); 3.34 (*s*, MeO); 3.41–3.54 (*m*, CH_2(26)); 4.95 (br. *d*, *J* = 8.5, H–C(16)); 5.42 (br. *s*, H–C(16)); 9.78 (br. *s*, CHO). ^{13}C-NMR (100 MHz, $CDCl_3$): 12.1, 14.0, 16.7, 17.1 (4*q*, C(18), C(19), C(21), C(27)); 21.2 (*t*); 27.7 (*t*); 28.3 (*t*); 28.7 (*t*); 29.8 (*t*); 30.3 (*d*); 31.1 (*t*); 34.2 (*d*); 34.6 (*t*); 36.5 (*s*, C(10)); 36.7 (*t*); 44.4 (*d*); 44.6 (*d*); 48.3 (*s*, C(13)); 54.2 (*d*); 55.6 (*q*, MeO); 56.9 (*d*); 61.3 (*s*, C(12)); 67.2 (*t*, C(26)); 79.6 (*d*, C(3)); 84.6 (*d*, C(16)); 107.0 (*s*, C(22)); 118.2 (*d*, C(15)); 159.1 (*s*, C(14)); 204.3 (*d*, CHO). MS (170°): 456 (10, M^+), 427 (4), 384 (11), 342 (24), 314 (21), 126 (100). HR-MS: 456.3230 ($C_{29}H_{44}O_4^+$; calc. 456.3240).

*(3β,5α,12α,25*R*)-17,12-(Epoxymethano)-3-methoxyspirost-14-ene* (**20**). A vigorously stirred 10°-cold suspension of **12** (100 mg, 0.218 mmol, 1 equiv.), $Pb(OAc)_4$ (293 mg, 0.66 mmol, 3 equiv.; dried prior to use, see *General*), and pyridine (0.07 ml, 0.88 mmol, 4 equiv.) in benzene (4 ml) was irradiated (see *General*) for 2 h in a quartz flask. Then the solid particles were filtered off and washed with warm Et_2O. The combined org. layer was washed with 5% H_2SO_4 soln., 0.5M $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. FC (petroleum ether/Et_2O 2:1) of the crude product afforded **20** (73 mg, 73%). White crystalline solid. M.p. 167° (from Et_2O). IR ($CHCl_3$): 2932*s*, 2864*m*, 1640*w*, 1452*m*, 1372*m*, 1244*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6, Me(27)); 0.85 (*s*, Me(19)); 0.91 (*d*, *J* = 7.5, Me(21)); 1.12 (*s*, Me(18)); 2.08 (*m*, H–C(8)); 3.10 (*tt*, *J* = 11, 5, H–C(3)); 3.34–3.38 (*m*, MeO, H_a of CH_2O–C(17)); 3.43 (*t*, *J* = 11, 1 H–C(26)); 3.61 (br. *dd*, *J* = 11, 2.5, 1 H–C(26)); 3.78 (*t*, *J* = 7.5, H_b of CH_2O–C(17)); 4.45 (*d*, *J* = 2, H–C(16)); 5.52 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 8.4 (*q*); 12.1 (*q*); 17.2 (*q*); 20.7 (*t*); 21.8 (*q*); 27.8 (*t*); 28.1 (*t*); 28.4 (*t*); 29.2 (*t*); 30.0 (*d*); 31.8 (*t*); 34.3 (*t*); 35.7 (*d*); 36.3 (*s*, C(10)); 36.8 (*t*); 44.6 (*d*); 45.7 (*d*); 45.9 (*d*); 51.2 (*d*); 55.55 (*s*, C(13)); 55.59 (*q*, MeO); 67.1 (*t*, C(26)); 68.9 (*t*, CH_2O–C(17)); 79.6 (*d*, C(3)); 90.8 (*d*, C(16)); 98.5 (*s*, C(17)); 107.9 (*s*, C(22)); 117.8 (*d*, C(15)); 158.1 (*s*, C(14)). MS (170°): 456 (15, M^+), 358 (13), 342 (100), 330 (34), 315 (58), 148 (40), 133 (44). HR-MS: 456.3245 ($C_{29}H_{44}O_4^+$; calc. 456.3240). Anal. calc. for $C_{29}H_{44}O_4$ (456.66): C 76.27, H 9.71; found: C 76.54, H 9.72.

*(3β,5α,12β,25*R*)-17,12-(Epoxymethano)-3-methoxyspirost-4-ene* (**21**) *and (3β,5α,12β,25*R*)-18,12-(Epoxymethano)-3-methoxyspirost-4-ene* (**22**). As described for **20**, from **13** (100 mg, 0.218 mmol, 1 equiv.): **22** (14 mg, 14%) as a white foam and **21** (35 mg, 35%) as a white crystalline solid.

Data of **21**: M.p. 173° (from Et_2O). IR (KBr): 2928*s*, 2856*m*, 1632*w*, 1448*m*, 1372*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6, Me(27)); 0.93 (*s*, Me(18), Me(19)); 1.01 (*d*, *J* = 7, Me(21)); 2.38 (*m*, H–C(8));

3.14 (*tt*, *J* = 11, 5, H–C(3)); 3.35 (*s*, MeO); 3.44 (*t*, *J* = 11, 1 H–C(26)); 3.50 (*dd*, *J* = 12, 7.5, H_a of CH_2O–C(17)); 3.63 (*m*, 1 H–C(26)); 3.92 (*dd*, *J* = 7.5, 5.5, H_b of CH_2O–C(17)); 4.74 (*d*, *J* = 1.5, H–C(16)); 5.08 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 7.8 (*q*); 11.0 (*q*); 12.3 (*q*); 17.2 (*q*); 21.2 (*t*); 27.9 (*t*); 28.5 (*t*); 28.8 (*t*); 29.4 (*t*); 30.1 (*d*); 31.5 (*t*); 34.2 (*t*); 36.1 (*d*); 36.95 (*t*); 37.00 (*s*, C(10)); 45.2 (*d*); 47.3 (*d*); 55.6 (*q*, MeO); 56.9 (*s*, C(13)); 57.2 (*d*); 59.6 (*d*); 67.3 (*t*, C(26)); 71.2 (*t*, CH_2O); 79.6 (*d*, C(3)); 93.3 (*d*, C(16)); 99.3 (*s*, C(17)); 106.6 (*s*, C(22)); 112.8 (*d*, C(15)); 159.3 (*s*, C(14)). MS (160°): 456 (28, M^+), 441 (15), 342 (77), 331 (100), 314 (27), 274 (12), 126 (32). HR-MS: 456.3246 ($C_{29}H_{44}O_4^+$; calc. 456.3240). Anal. calc. for $C_{29}H_{44}O_4$ (456.66): C 76.27, H 9.71; found: C 76.15, H 9.58.

Data of **22**: IR ($CHCl_3$): 2932*s*, 2868*m*, 1640*w*, 1456*m*, 1372*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*d*, *J* = 6, Me(27)); 0.83 (*s*, Me(19)); 1.05 (*d*, *J* = 6.5, Me(21)); 2.09 (*m*, H–C(8)); 2.23 (*t*, *J* = 8.5, H–C(17)); 3.12 (*tt*, *J* = 11, 5, H–C(3)); 3.34 (*s*, MeO); 3.44 (*t*, *J* = 11, 1 H–C(26)); 3.52 (*m*, 1 H–C(26)); 3.65 (*d*, *J* = 8, 1 H–C(18)); 3.73 (br. *d*, *J* = 9.5, H_a of CH_2O–C(18)); 3.82–3.87 (*m*, 1 H–C(18), H_b of CH_2O–C(18)); 4.89 (*dd*, *J* = 8.5, 2, H–C(16)); 5.54 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 12.2 (*q*); 13.1 (*q*); 17.2 (*q*); 27.7 (*t*); 28.0 (*t*); 28.3 (*t*); 28.7 (*t*); 29.9 (*t*); 30.3 (*d*); 31.3 (*t*); 34.2 (*d*); 35.7 (*t*); 36.4 (*s*, C(10)); 36.9 (*t*); 44.5 (*d*); 45.4 (*d*); 51.4 (*d*); 55.0 (*d*); 55.6 (*q*, MeO); 57.9 (*d*); 58.1 (*s*, C(13)); 67.2 (*t*, C(26)); 68.7 (*t*, *C*H_2O–C(18)); 73.5 (*t*, C(18)); 79.6 (*d*, C(3)); 84.0 (*d*, C(16)); 107.3 (*s*, C(22)); 121.0 (*d*, C(15)); 153.9 (*s*, C(14)). MS (160°): 456 (19, M^+), 342 (40), 311 (26), 126 (100). HR-MS: 456.3237 ($C_{29}H_{44}O_4^+$; calc. 456.3240).

*(3β,5α,12β,25*R)- and (*3β,5α,12α,25*R)*-3-Methoxy-12-[(4-methoxyphenoxy)methyl]spirost-14-en-12-ol* (**23** and **23a** resp.). To a −78°-cold soln. of [(4-methoxyphenoxy)methyl]stannane [24] (1.44 g, 3.39 mmol, 5 equiv.) in THF (2.5 ml), 1.6M BuLi in hexane (1.9 ml, 3.05 mmol, 4 equiv.) was added slowly. After 30 min, **10** (300 mg, 0.677 mmol, 1 equiv.) was added (as a solid!), and the mixture was stirred for further 2 h. The reaction was quenched by addition of sat. NH_4Cl soln. (6 ml), the mixture warmed to r.t., the aq. layer extracted with Et_2O, the combined org. layer washed with brine, dried ($MgSO_4$), and evaporated, and the residue subjected to FC (petroleum ether/Et_2O 3:2): **23** (287 mg, 73%) and **23a** (89 mg, 23%), both as white foams.

Data of **23**: M.p. 114–115° (from petroleum ether/Et_2O). UV (MeOH): 225 (*s*), 288 (*w*). IR (KBr): 3456*m* (br.), 3056*w*, 2928*s*, 2856*m*, 1648*w* (C=C), 1508*s* (arom. C=C), 1464*m* (arom. C=C), 1372*m*, 1228*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*d*, *J* = 6, Me(27)); 0.88 (*s*, Me(19)); 1.05 (*d*, *J* = 6.5, Me(21)); 1.23 (*s*, Me(18)); 2.08 (*dd*, *J* = 13.5, 3.5, 1 H–C(11)); 2.16 (*m*, H–C(8)); 2.41 (*s*, exchange with D_2O, OH); 2.82 (*t*, *J* = 9, H–C(17)); 3.06 (*tt*, *J* = 11, 5, H–C(3)); 3.32 (*s*, MeO); 3.43 (*t*, *J* = 11, 1 H–C(26)); 3.52 (br. *d*, *J* = 11, 1 H–C(26)); 3.73 (*d*, *J* = 9, H_a of OCH_2–C(12)); 3.77 (*s*, *Me*OC_6H_4); 3.90 (*d*, *J* = 9, H_b of OCH_2–C(12)); 4.82 (br. *d*, *J* = 9, H–C(16)); 5.34 (br. *s*, H–C(15)); 6.84 (br. *s*, 4 arom. H). ^{1}H-NMR (400 MHz, C_6D_6): 0.66–0.68 (*m*, Me(19), Me(27)); 1.37 (*d*, *J* = 6.5, Me(21)); 1.40 (*s*, Me(18)); 2.01 (*dq*, *J* = 9.5, 6.5, Me(20)); 2.09 (*m*, H–C(8)); 2.12 (*dd*, *J* = 13.5, 4, 1 H–C(11)); 2.29 (*s*, OH); 2.87 (*tt*, *J* = 11, 5, H–C(3)); 3.18 (*s*, MeO); 3.23 (*dd*, *J* = 9.5, 8, H–C(17)); 3.31 (*s*, *Me*OC_6H_4); 3.66 (br. *J* = 11, 1 H–C(26)); 3.64 (*t*, *J* = 11, 1 H–C(26)); 3.84 (*d*, *J* = 9, H_a of OCH_2–C(12)); 4.01 (*d*, *J* = 9, H_b of OCH_2–C(12)); 5.23 (br. *d*, *J* = 8, H–C(16)); 5.51 (br. *s*, H–C(15)); 6.68–6.74 (*m*, 4 arom. H). NOE ($CDCl_3$): irr. at 4.82 (H–C(16)) → 5.34 (5.6%, H–C(15)); 3.90 (2.0%, H_b of OCH_2–C(12)); 2.82 (5.4%, H–C(17)); irr. at 3.90 (H_b of OCH_2–C(12)) → 4.82 (5.8%, H–C(16)); 3.73 (9.6%, H_a of OCH_2–C(12)); 2.82 (14.0%, H–C(17)); irr. at 3.73 (H_a of OCH_2–C(12)) → 3.90 (12.5%, H_b of OCH_2–C(12)); irr. at 2.82 (H–C(17)) → 4.82 (8.6%, H–C(16)); 3.90 (8.8%, H_b of OCH_2–C(12)); 2.41 (1.6%, OH–C(12)); 1.05 (6.9%, Me(21)); irr. at 1.23 (Me(18)) → 2.41 (0.8%, OH), 2.16 (2.0%, H–C(8)); 1.80 (5.0%, H–C(20)); 1.66 (3.5%, 1 H–C(11)); 1.05 (1.8%, Me(21)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.8 (*q*); 13.9 (*q*); 16.5 (*q*); 17.2 (*q*); 27.7 (*t*); 28.4 (*t*); 28.7 (*t*); 29.6 (*t*); 30.4 (*d*); 30.7 (*t*); 31.2 (*t*); 33.7 (*d*); 34.1 (*t*); 36.3 (*s*, C(10)); 36.5 (*t*); 44.5 (*d*); 44.9 (*d*); 51.2 (*d*); 51.6 (*d*); 54.4 (*s*, C(13)); 55.6 (*q*, MeO); 55.7 (*q*, MeO); 67.2 (*t*, C(26)); 70.7 (*t*, O*C*H_2–C(12)); 77.2 (*s*, C(12)); 79.6 (*d*, C(3)); 85.1 (*d*, C(16)); 106.6 (*s*, C(22)); 114.6 (*d*, 2 arom. C); 116.1 (*d*, 2 arom. C); 119.7 (*d*, C(15)); 152.9 (*s*, arom. C); 154.2 (*s*, arom. C); 155.8 (*s*, C(14)). MS (200°): 580 (14, M^+), 562 (6, $[M - H_2O]^+$), 443 (100), 329 (55), 316 (47), 138 (90), 124 (85). HR-MS: 580.3750 ($C_{36}H_{52}O_6^+$; calc. 580.3764).

Data of **23a**: UV (MeOH): 227 (*s*), 290 (*w*). IR (KBr): 3452*m* (br.), 3056*w*, 2928*s*, 2860*m*, 1652*w* (C=C), 1508*s* (arom. C=C), 1460*m* (arom. C=C), 1372*m*, 1228*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6, Me(27)); 0.86 (*s*, Me(19)); 1.02 (*d*, *J* = 7, Me(21)); 1.11 (*s*, Me(18)); 2.14 (*m*, H–C(8)); 2.26 (*s*, exchange with D_2O, OH); 2.98 (t, *J* = 9, H–C(17)); 3.13 (*tt*, *J* = 11, 5, H–C(3)); 3.35 (*s*, MeO); 3.44 (*t*, *J* = 10.5, 1 H–C(26)); 3.51 (br. *d*, *J* = 10.5, 1 H–C(26)); 3.77 (*s*, *Me*OC_6H_4); 3.79 (*d*, *J* = 9, H_a of OCH_2–C(12)); 3.88 (*d*, *J* = 9, H_b of OCH_2–C(12)); 4.91 (br. *d*, *J* = 9, H–C(16)); 5.51 (br. *s*, H–C(15)); 6.85 (*m*, 4 arom. H). NOE ($CDCl_3$): irr. at 4.91 (H–C(16)) → 5.51 (6.0%, H–C(15)); 2.98 (7.2%, H–C(17)); irr. at 3.88 (H_b of OCH_2–C(12)) → 2.98 (10.3%, H–C(17)); 3.79 (H_a of OCH_2–C(12)) and 1.11 (Me(18)) give no clear result; irr. at 3.79 (H_a of OCH_2–C(12)) → 6.85 (8.0%, arom. H), 3.88 (8.8%, H_b of OCH_2–C(12)); irr. at 2.98 (H–C(17)) → 4.91

(12.2%, H–C(16), 3.88 (1.5%, H_b of OCH_2–C(12)); 2.26 (4.0%, OH), 1.02 (5.3%, Me(21)); irr. at 1.11 (Me(18)) → 3.88 (1.4%, H_b of OCH_2–C(12)); 2.98 (1.0%, H–C(17)); 2.14 (3.9%, H–C(8)); 1.74 (5.2%, H–C(20)); 1.62 (1.7%, 1 H–C(11)). ^{13}C-NMR (100 MHz, $CDCl_3$): 12.1 (*q*); 14.3 (*q*); 17.1 (*q*); 18.4 (*q*); 27.7 (*t*); 28.4 (*t*); 28.7 (*t*); 29.6 (*t*); 30.4 (*d*); 30.9 (*t*); 31.1 (*t*); 34.2 (*t*); 34.3 (*d*); 36.1 (*s*, C(10)); 36.6 (*t*); 44.3 (*d*); 44.5 (*d*); 49.7 (*d*); 51.4 (*d*); 53.3 (*s*, C(13)); 55.6 (*q*, MeO); 55.7 (*q*, MeO); 67.1 (*t*, C(26)); 73.3 (*t*, O*C*H_2–C(12)); 76.2 (*s*, C(12)); 79.6 (*d*, C(3)); 85.4 (*d*, C(16)); 106.7 (*s*, C(22)); 114.6 (*d*, 2 arom. C); 115.8 (*d*, 2 arom. C); 119.9 (*d*, C(15)); 152.8 (*s*, arom. C); 154.2 (*s*, arom. C); 156.0 (*s*, C(14)). MS (200°): 580 (21, M^+), 457 (21), 443 (58), 329 (45), 138 (87), 124 (100). HR-MS: 580.3761 ($C_{36}H_{52}O_6^+$; calc. 580.3764).

*(3β,5α,12β,25*R*)-3-Methoxy-12-[(4-methoxyphenoxy)methyl]spirost-4-en-12-yl Benzoate* (**24**). To a −78°-cold soln. of **23** (50 mg, 0.086 mmol, 1 equiv.) in THF (0.5 ml), 1.6M BuLi in hexane (0.065 ml, 0.103 mmol, 1.2 equiv.) was added dropwise. After 30 min, benzoyl chloride (0.014 ml, 0.129 mmol, 1.5 equiv.) was added and after additional 45 min, the mixture was slowly warmed to r.t. within 3 h. The reaction was quenched by addition of 0.5M $NaHCO_3$ (0.5 ml) and Et_2O (15 ml), the org. layer washed with brine, dried ($MgSO_4$), and evaporated, and the residue submitted to gradient FC (petroleum ether/Et_2O 5 :2 (→ **24**) and 3 :2 (→ **23**)): **24** (35 mg, 59%, 82% based on recovered **23**) and recovered **23** (14 mg, 0.024 mmol), both as white foams. **24**: UV (MeOH): 229 (*s*), 280 (br. *m*). IR (KBr): 3060*w* (arom. CH), 2928*s*, 2860*m*, 1720*s* (C=O), 1648*w* (C=C), 1508s (arom. C=C), 1464*m*, 1450*m*, 1372*m*, 1276*s*, 1228*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.79 (*d*, *J* = 6, Me(27)); 0.88 (*s*, Me(19)); 1.13 (*d*, *J* = 7, Me(21)); 1.37 (*s*, Me(18)); 2.22 (*m*, H–C(8)); 2.94 (*dd*, *J* = 13, 3.5, 1 H–C(11)); 3.12 (*tt*, *J* = 11, 5, H–C(3)); 3.34 (*s*, MeO); 3.36 (*t*, *J* = 11, 1 H–C(26)); 3.48 (br. *d*, *J* = 11, 1 H–C(26)); 3.53 (*dd*, *J* = 9, 8, H–C(17)); 3.73 (*s*, arom. MeO); 4.27 (*d*, *J* = 10, H_a of OCH_2–C(12)); 4.32 (*d*, *J* = 10, H_b of OCH_2–C(12)); 4.76 (br. *d*, *J* = 8, H–C(16)); 5.48 (br. *s*, H–C(15)); 6.76 (br. *s*, 4 arom. H); 7.42 (*t*, *J* = 7.5, 2 arom. H); 7.54 (*t*, *J* = 7.5, 1 arom. H); 8.02 (*d*, *J* = 7.5, 2 arom. H). MS (200°): 684 (9, M^+), 562 (22), 547 (32), 439 (40), 105 (100). FAB-MS: 685 (17, $[M+H]^+$), 563 (30), 446 (75), 154 (100, NBA matrix). HR-MS: 684.4023 ($C_{43}H_{56}O_7^+$; calc. 684.4026).

*(3β,5α,12β,25*R*)-12-(Benzoyloxy)-3-methoxyspirost-14-ene-12-methanol* (**25**). A 0°-cold mixture of **24** (28 mg, 0.041 mmol, 1 equiv.) and cerium ammonium nitrate (32 mg, 0.095 mmol, 2.3 equiv.) in MeCN/H_2O 4 :1 (1 ml) was stirred vigorously for 30 min. Then the reaction was quenched by addition of sat. $NaHCO_3$ soln., the aq. layer extracted with CH_2Cl_2, the combined org. layer washed with brine, dried (Na_2SO_4), and evaporated, and the residue submitted to FC (petroleum ether/AcOEt 5 :1): **25** (17 mg, 72%). White foam. UV (MeOH): 232 (*s*), 274 (*m*). IR ($CHCl_3$): 3468*m* (br.), 3000*w* (arom. CH), 2932*s*, 2860*m*, 1692*s* (C=O), 1648*w* (C=C), 1600*m* (arom. C=C), 1452*m*, 1372*m*, 1292*s*, 1240*m*. ^{1}H-NMR (400 MHz, C_6D_6): 0.56 (*s*, Me(19)); 0.68 (*d*, *J*(27,25) = 6.5, Me(27)); 1.29 (*d*, *J*(21,20) = 6.5, Me(21)); 1.40 (*s*, Me(18)); 2.00 (*dq*, *J*(20,17) = 9, *J*(20,21) = 6.5, H–C(20)); 2.04 (br. *t*, *J*(8,7a and 9) = 10, H–C(8)); 2.80 (*dd*, *J*(17,20) = 9, *J*(17,16) = 8, H–C(17)); 2.89–2.97 (*m*, H–C(3), 1 H–C(11)); 3.20 (*s*, MeO); 3.59 (br. *d*, J_{gem} = 10.5, 1 H–C(26)); 3.64 (*t*, J_{gem} = *J*(26,25) = 10.5, 1 H–C(26)); 3.68 (*dd*, J_{gem} = 13.5, *J*(H_a,OH) = 12, H_a of CH_2OH); 3.87 (br. *d*, J_{gem} = 13.5, H_b of CH_2OH); 4.64 (*dd*, *J*(OH, H_a of CH_2OH) = 12, *J*(OH, H_b of CH_2OH) = 2, CH$_2$O*H*); 5.01 (br. *d*, *J*(16,17) = 8, H–C(16)); 5.49 (br. *s*, H–C(15)); 7.07 (*m*, 3 arom. H); 8.18 (*d*, *J* = 6.5, 2 arom. H). MS (180°): 578 (2, M^+), 560 (11, $[M-H_2O]^+$) 445 (25), 425 (22), 323 (43), 126 (92), 105 (100). HR-MS: 578.3608 ($C_{36}H_{50}O_6^+$; calc. 578.3607).

*(3″β,5″α,12″β,25″*R*)-3″-Methoxydispiro[cyclohexa-2,5-diene-1,2′-[1,3]dioxolane-4′,12″-spirost[14]en]-4-one* (**27**). As described for **25**, at −8° for 10 min, with **23** (118 mg, 0.203 mmol, 1 equiv.), cerium ammonium nitrate (263 mg, 0.480 mmol, 2.4 equiv.), and MeCN/H_2O 4 :1 (2.5 ml). FC (petroleum ether/Et_2O 3 :2) gave **27** (85 mg, 74%). White crystalline solid. M.p. 221° (from petroleum ether/Et_2O). UV (MeOH): 219 (*s*). IR (KBr): 2928*s*, 2860*s*, 1676*s* (conj. C=O), 1636*s* (conj. C=C), 1456*m*, 1384*m*, 1240*m*, 1176*s*, 1112*s*. ^{1}H-NMR (400 MHz, $CDCl_3$; steroid numbering): 0.82 (*d*, *J* = 6, Me(27)); 0.89 (*s*, Me(19)); 1.08 (*d*, *J* = 7, Me(21)); 1.19 (*s*, Me(18)); 2.08–2.17 (*m*, H–C(8), 1 H–C(11)); 2.76 (*t*, *J* = 8.5, H–C(17)); 3.13 (*tt*, *J* = 11, 5, H–C(3)); 3.35 (*s*, MeO); 3.41 (*t*, *J* = 11, 1 H–C(26)); 3.53 (br. *d*, *J* = 11, 1 H–C(26)); 3.77 (br. *s*, CH_2O); 4.89 (br. *d*, *J* = 8.5, H–C(16)); 5.42 (br. *s*, H–C(15)); 6.12 (*m*, COC*H*=CH); 6.21 (*m*, COC*H*=CH); 6.73–6.75 (*m*, 2 COH=C*H*). ^{13}C-NMR (100 MHz, $CDCl_3$; steroid numbering): 12.0, 14.3, 16.8, 17.2 (4*q*, C(18), C(19), C(21), C(27)); 27.7 (*t*); 28.2 (*t*); 28.7 (*t*); 29.5 (*t*); 30.4 (*d*); 31.0 (*t*); 33.6 (*d*); 34.0 (*t*); 35.1 (*t*); 36.2 (*s*, C(10)); 36.9 (*t*); 44.5 (*d*); 45.0 (*d*); 51.5 (*d*); 52.4 (*d*); 54.7 (*s*, C(13)); 55.6 (*q*, MeO); 67.2 (*t*, C(26)); 72.8 (*t*, CH_2O); 79.4 (*d*, C(3)); 84.9 (*d*, C(16)); 89.8 (*s*, C(12)); 99.2 (*s*, *C*(OR)$_2$); 106.4 (*s*, C(22)); 120.4 (*d*, C(15)); 127.6 (*d*, CO*C*H=CH); 130.0 (*d*, CO*C*H=CH); 143.3, 144.3 (2*d*, 2 COCH=*C*H); 156.7 (*s*, C(14)); 185.1 (*s*, *C*OCH=CH). FAB-MS: 587 (15, $[M+Na]^+$), 565 (100, $[M+H]^+$), 307 (35) 154 (82, NBA matrix). HR-MS: 564.3454 ($C_{35}H_{48}O_6^+$; calc. 564.3451).

*(3β,5α,12β,25*R*)-12-[(2-Chloro-4-hydroxyphenoxy)methyl]-3-methoxyspirost-4-en-12-ol* (**28**). A soln. of **27** (47 mg, 0.083 mmol) and conc. HCl soln. (0.1 ml) in THF (0.8 ml) and H_2O (0.2 ml) was stirred at 30° for 4 days. The reaction was quenched by addition of sat. K_2CO_3 soln. (2 ml), the aq. layer extracted with CH_2Cl_2, the

combined org. layer washed with brine, dried (Na_2SO_4), and evaporated, and the residue submitted to FC (petroleum ether/Et_2O 1:1): **28** (25 mg, 48%). White crystalline solid. M.p. 238° (dec.; from Et_2O). UV (MeOH): 223 (*s*), 293 (*w*). IR ($CHCl_3$): 3548*m* (OH); 3400*w* (br., OH); 3000*m*, 2932*s*, 2860*m*, 1496*s* (arom. C=C), 1464*m* (arom. C=C), 1372*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*d*, *J* = 6, Me(27)); 0.88 (*s*, Me(19)); 1.05 (*d*, *J* = 6.5, Me(21)); 1.23 (*s*, Me(18)); 2.04 (*dd*, *J* = 13.5, 3.5, 1 H–C(11)); 2.16 (*m*, H–C(8)); 2.27 (*s*, exchange with D_2O, OH–C(12)); 2.80 (*dd*, *J* = 9, 8, H–C(17)); 3.08 (*tt*, *J* = 11, 5, H–C(3)); 3.33 (*s*, MeO); 3.44 (*t*, *J* = 11, 1 H–C(26)); 3.53 (br. *d*, *J* = 11, 1 H–C(26)); 3.72 (*d*, *J* = 9, H_a of OCH_2–C(12)); 3.87 (*d*, *J* = 9, H_b of OCH_2–C(12)); 4.83 (br. *d*, *J* = 8, H–C(16)); 5.27 (*s*, exchange with D_2O, OH–C_6H_3); 5.36 (br. *s*, H–C(15)); 6.75 (*dd*, *J* = 9, 3, H_m); 6.88 (*d*, *J* = 3, H_m); 6.94 (*d*, *J* = 9, H_o); the position of the OH signals varied with the experiments. NOE ($CDCl_3$): irr. at 6.94 (H_o) → 6.75 (5.1%, H_m); irr. at 6.88 (H_m) → no effect; irr. at 6.75 (H_m) → 6.94 (14.1%, H_o); irr. at 2.30 (OH–C(12) → 6.94 (3.1%, H_o), 5.44 (–91.9%, OH–C_6H_3), 2.80 (1.5%, H–C(17)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.8, 13.9, 16.5, 17.2 (4*q*, C(18), C(19), C(21), C(27)); 27.7 (*t*); 28.4 (*t*); 28.7 (*t*); 29.6 (*t*); 30.4 (*d*); 30.7 (*t*); 31.2 (*t*); 33.7 (*d*); 34.1 (*t*); 36.3 (*s*, C(10)); 36.5 (*t*); 44.6 (*d*); 44.9 (*d*); 51.2 (*d*); 51.6 (*d*); 54.5 (*s*, C(13)); 55.6 (*q*, MeO); 67.3 (*t*, C(26)); 70.9 (*t*, CH_2O); 77.2 (*s*, C(12)); 79.6 (*d*, C(3)); 85.1 (*d*, C(16)); 106.7 (*s*, C(22)); 115.5, 115.6, 116.6 (3*d*, arom. C); 119.9 (br.; 1 *d* of C(15), 1 *s* of arom. C); 146.1, 152.7 (2*s*, arom. C); 155.7 (*s*, C(14)). MS (220°): 600 (2, $[M(^{35}Cl)]^+$), 582 (2, $[M - H_2O]^+$), 542 (3), 486 (5), 443 (100), 329 (55), 126 (22). HR-MS: 600.3192 ($C_{35}H_{49}O_6Cl^+$; calc. 600.3218).

*(3β,5α,12β,25*R*)- and (3β,5α,12α,25*R*)-3-Methoxy-12-[(methoxymethoxy)methyl]spirost-14-en-12-ol* (**29** and **29a**, resp.). As described for **23** and **23a**, with [(methoxymethoxy)methyl]stannane [31] (985 mg, 2.70 mmol, 4 equiv.), THF (2.5 ml), 1.6M BuLi in hexane (1.47 ml, 2.36 mmol, 3.5 equiv.), and **10** (300 mg, 0.677 mmol, 1 équiv.). Workup with sat. NH_4Cl soln. (4 ml) and Et_2O (40 ml). FC (petroleum ether/AcOEt 2:3): **29** (39 mg, 11%) and **29**/**29a** 3:2 (250 mg, 72%), both as white foams.

Data of **29**: IR ($CHCl_3$): 3560*w*, 3428*w* (br.), 3050*w*, 2932*s*, 2860*s*, 1648*w*, 1464*m*, 1372*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6, Me(27)); 0.87 (*s*, Me(19)); 1.03 (*d*, *J* = 7, Me(21)); 1.18 (*s*, Me(18)); 2.14 (*m*, H–C(8)); 2.73 (*s*, OH), 2.76 (*dd*, *J* = 9.5, 8, H–C(17)); 3.10 (*tt*, *J* = 11, 5, H–C(3)); 3.34 (*s*, MeO); 3.39 (*s*, MeO); 3.35–3.55 (*m*, 2 CH_2O); 4.63 (*d*, *J* = 6.5, H_a of OCH_2O); 4.67 (*d*, *J* = 6.5, H_b of OCH_2O); 4.79 (br. *d*, *J* = 8, H–C(16)); 5.32 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.8, 13.9, 16.5, 17.2, (4*q*, C(18), (C19), C(21), C(27)); 27.8 (*t*); 28.5 (*t*); 28.7 (*t*); 29.7 (*t*); 30.4 (*d*); 31.1 (br., 2*t*); 33.6 (*d*); 34.2 (*t*); 36.3 (*s*, C(10)); 36.7 (*t*); 44.7 (*d*); 44.8 (*d*); 51.1 (*d*); 51.4 (*d*); 54.3 (*s*, C(13)); 55.6, 55.7 (2*q*, MeO); 67.2 (*t*, C(26)); 70.6 (*t*, CH_2O); 76.7 (*s*, C(12)); 79.6 (*d*, C(3)); 85.2 (*d*, C(16)); 97.4 (*t*, OCH_2O); 106.5 (*s*, C(22)); 119.6 (*d*, C(15)); 155.7 (*s*, C(14)). MS (180°): 518 (1, M^+), 500 (8, $[M - H_2O]^+$), 487 (3), 443 (100), 426 (19), 387 (10), 329 (35), 317 (18), 126 (36). HR-MS: 518.3616 ($C_{31}H_{50}O_6^+$; calc. 518.3607).

Data of **29a**: Data from epimer mixture. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6, Me(27)); 0.85 (*s*, Me(19)); 1.01 (*d*, *J* = 6.5, Me(21)); 1.04 (*s*, Me(18)); 2.11 (*m*, H–C(8)); 2.33 (*s*, OH); 2.88 (*dd*, *J* = 9, 8, H–C(17)); 3.11 (*tt*, *J* = 11, 5, H–C(3)); 3.34 (*s*, MeO); 3.38 (*s*, MeO); 3.39–3.53 (*m*, 2 CH_2O); 4.67 (br. *s*, OCH_2O); 4.89 (br. *d*, *J* = 8, H–C(16)); 5.48 (br. *s*, H–C(15)).

*(3β,5α,12β,25*R*)- and (3β,5α,12α,25*R*)-12-Hydroxy-3-methoxyspirost-14-ene-12-methanol* (**30** *and* **30a**, resp.). A soln. of **29**/**29a** 1.6:1 (190 mg, 0.366 mmol) and 12N aq. HCl in THF (2 ml; not dry, no Ar) and H_2O (1 ml) was stirred for 5 h. Then the soln. was cooled to 0° and CH_2Cl_2 (25 ml) and sat. aq. K_2CO_3 soln. (2.5 ml) were added slowly. The org. layer was washed with brine, dried (Na_2SO_4) and evaporated and the residue submitted to FC (CH_2Cl_2/MeOH 30:1): **30a** (59 mg, 34%) as a crystalline solid and **30** (103 mg, 59%) as a white foam.

Data of **30**: IR (KBr): 3440*m* (br.), 2928*s*, 2860*m*, 1652*w*, 1456*m*, 1372*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6, Me(27)); 0.87 (*s*, Me(19)); 1.02 (*d*, *J* = 7, Me(21)); 1.18 (*s*, Me(18)); 2.13 (*m*, H–C(8)); 2.73 (*t*, *J* = 8.5, H–C(17)); 3.11 (*tt*, *J* = 11, 5, H–C(3)); 3.34 (*s*, MeO); 3.35–3.44 (*m*, 1 H–C(26), H_a of CH_2OH); 3.50 (br. *d*, *J* = 11, 1 H–C(26)); 3.58 (br. *d*, *J* = 11.5, H_b of CH_2OH); 4.79 (br. *d*, *J* = 8.5, H–C(16)); 5.32 (br. *s*, H–C(15)). ^{1}H-NMR (400 MHz, C_6D_6): 0.66 (*s*, Me(19)); 0.69 (*d*, *J* = 6, Me(27)); 1.25 (*s*, Me(18)); 1.30 (*d*, *J* = 7, Me(21)); 2.01 (*m*, H–C(8)); 2.96 (*tt*, *J* = 11, 5, H–C(3)); 2.99 (*dd*, *J* = 10, 8, H–C(17)); 3.20 (*d*, *J* = 10.5, H_a of CH_2OH); 3.21 (*s*, MeO); 3.28 (*d*, *J* = 10.5, H_b of CH_2OH); 3.65 (br. *d*, *J* = 11, 1 H–C(26)); 3.72 (*t*, *J* = 11, 1 H–C(26)); 5.02 (br. *d*, *J* = 8, H–C(16)); 5.41 (br. *s*, H–C(15)). NOE ($CDCl_3$): irr. at 4.79 (H–C(16)) → 5.32 (4.2%, H–C(15)); 3.58 (1.8%, H_b of CH_2OH); 2.73 (4.8%, H–C(17)); irr. at 3.58 (H_b of CH_2OH) → 4.79 (5.3%, H–C(16)); 3.36 (6.3%, H_a of CH_2OH); 2.73 (10.7%, H–C(17)); irr. at 2.73 (H–C(17)) → 4.79 (8.2%, H–C(16)); 3.58 (10.6%, H_b of CH_2OH); 1.02 (5.1%, Me(21)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.8, 13.9, 16.4, 17.1 (4*q*, C(18), C(19), C(21), C(27)); 27.7 (*t*); 28.5 (*t*); 28.7 (*t*); 29.7 (*t*); 30.2 (*t*); 30.4 (*d*); 31.1 (*t*); 33.6 (*d*); 34.2 (*t*); 36.3 (*s*, C(10)); 36.6 (*t*); 44.7 (*d*); 44.8 (*d*); 51.0 (*d*); 51.3 (*d*); 54.4 (*s*, C(13)); 55.6 (*q*, MeO); 63.4 (*t*, CH_2OH); 67.2 (*t*, C(26)); 77.6 (*s*, C(12)); 79.6 (*d*, C(3)); 85.2 (*d*, C(16)); 106.6 (*s*, C(22)); 119.6

(*d*, C(15)); 155.6 (*s*, C(14)). MS (180°): 474 (1, M^+), 456 (5, $[M-H_2O]^+$), 443 (53), 342 (49), 329 (43), 126 (100). HR-MS: 474.3352 ($C_{29}H_{46}O_5^+$; calc. 474.3345). Anal. calc. for $C_{29}H_{46}O_5$ (474.68): C 73.38, H 9.77; found: C 72.92, H 9.73.

Data of **30a**: M.p. 205° (from MeOH). IR (KBr): 3440*m* (br.), 2928*s*, 2872*m*, 1652*w*, 1456*m*, 1372*m*, 1420*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*d*, *J* = 6, Me(27)); 0.86 (*s*, Me(19)); 1.01 (*d*, *J* = 7, Me(21)); 1.03 (*s*, Me(18)); 2.13 (*m*, H–C(8)); 2.83 (*t*, *J* = 9, H–C(17)); 3.11 (*tt*, *J* = 11, 5, H–C(3)); 3.34 (*s*, MeO); 3.40–3.52 (*m*, CH_2(26), $H_a$of CH_2OH); 3.62 (br. *d*, *J* = 11, H_b of CH_2OH); 4.85 (br. *d*, *J* = 9, H–C(16)); 5.51 (br. *s*, H–C(15)). NOE ($CDCl_3$): irr. at 4.85 (H–C(16)) → 5.51 (4.0%, H–C(15)); 2.83 (6.1%, H–C(17)); irr. at 3.62 (H_b of CH_2OH) → 3.45 (9.5%, H_a of CH_2OH), 2.83 (8.2%, H–C(17)); irr. at 2.83 (H–C(17)) → 4.85 (10.0%, H–C(16)); 3.62 (4.7%, H_b of CH_2OH); 1.01 (2.9%, Me(21)). ^{13}C-NMR (100 MHz, $CDCl_3$): 12.2, 14.1, 17.1, 17.8 (4*q*, C(18), C(19), C(21), C(27)); 27.7 (*t*); 28.4 (*t*); 28.7 (*t*); 29.6 (*t*); 29.9 (*t*); 30.4 (*d*); 31.1 (*t*); 34.2 (*t*); 34.3 (*d*); 36.2 (*s*, C(10)); 36.7 (*t*); 44.3 (*d*); 44.6 (*d*); 50.3 (*d*); 51.2 (*d*); 53.5 (*s*, C(13)); 55.6 (*q*, MeO); 66.7 (*t*, CH_2OH); 67.1 (*t*, C(26)); 76.9 (*s*, C(12)); 79.6 (*d*, C(3)); 85.2 (*d*, C(16)); 106.8 (*s*, C(22)); 120.2 (*d*, C(15)); 156.2 (*s*, C(14)). MS (170°): 474 (3, M^+), 456 (5, $[M^+-H_2O]^+$), 442 (25), 342 (37), 328 (38), 126 (100). HR-MS: 474.3345 ($C_{29}H_{46}O_5^+$; calc. 474.3345). Anal. calc. for $C_{29}H_{46}O_5$ (474.68): C 73.38, H 9.77; found: C 73.41, H 9.70.

*(5α,5′α,12′β,25*R*,25′*R*)-12′-[[(*tert*-Butyl)dimethylsilyl]oxy}bisspirosta-2,14-dieno[2,3*-b:*2′,3′*-e*]pyrazin-12-one* (**31**) *and (5α,5′α,12′β,25*R*,25′*R*)-12′-[[(*tert*-Butyl)dimethylsilyl]oxy}-12-methylenebisspirosta-2,14-dieno[2,3*-b:*2′,3′*-e*]pyrazine* (**32**). To a −20°-cold soln. of **3** (600 mg, 0.708 mmol, 1 equiv.) and 2,6-dimethylpyridine (0.25 ml, 2.13 mmol, 3 equiv.) in CH_2Cl_2 (3 ml), (*tert*-butyl)dimethylsilyl triflat (0.38 ml, 1.633 mmol, 2.3 equiv.) was added drowpise. After 90 min, 0.5M $NaHCO_3$ (5 ml) and CH_2Cl_2 (10 ml) were added, and after warming to r.t., the aq. layer was extracted with CH_2Cl_2. The combined org. layer was washed with 0.3M HCl and brine, dried (Na_2SO_4), and evaporated: crude **31** (749 mg, 110%). Yellow foam. UV (MeOH): 208 (*s*), 288 (*s*), 304 (sh). IR (KBr): 3052*w* (alkene H), 2928*s*, 2876*s*, 1716*m* (C=O), 1648*w* (C=C), 1460*m*, 1396*s* (pyrazine), 1370*m*, 1252*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.08 (*s*, 1 MeSi); 0.09 (*s*, 1 MeSi); 0.81 (br. *d*, *J* = 6, Me(27), Me(27′)); 0.86 (*s*, Me(19′)); 0.91 (*s*, ^{t}BuSi); 0.92 (*s*, Me(19)); 1.01 (*s*, Me(18′)); 1.02 (*d*, *J* = 7, Me(21′)); 1.05 (*d*, *J* = 7, Me(21)); 1.33 (*s*, Me(18)); 2.02–2.10 (*m*, 2 H); 2.44–2.90 (*m*, CH_2(1), CH_2(1′), CH_2(4), CH_2(4′), CH_2(11), H–C(17′)); 3.22 (*dd*, *J* = 10.5, 5, H–C(12′)); 3.37 (*dd*, *J* = 9, 8, H–C(17)); 3.39–3.45 (*m*, 1 H–C(26), 1 H–C(26′)); 3.50–3.55 (*m*, 1 H–C(26), 1 H–C(26′)); 4.78 (*dd*, *J* = 8, 2, H–C(16)); 4.85 (*dd*, *J* = 8, 2, H–C(16′)); 5.43, 5.48 (2 br. *s*, H–C(15), H–C(15′)). FAB-MS (monoisotopic mass 960.64116): 962 (71, $[M+H]^+$), 847 (34, $[M+H-{}^t$BuMe$_2$Si$]^+$), 207 (32), 147 (100).

To a 0°-cold suspension of triphenyl(methyl)phosphonium bromide (2.0 g, 5.6 mmol) in THF (12 ml), 1.8M (PhLi in cyclohexane/Et_2O 7:3) (2.83 ml, 5.1 mmol) was added slowly. After 1 h, the vigorous stirring was stopped, and part of the soln. (6 ml) was decanted into a soln. of crude **31** (700 mg, max. 0.662 mmol) in THF (1 ml). After 5 h, the reaction was quenched by addition of half-sat. brine (5 ml) and CH_2Cl_2 (20 ml), the aq. layer extracted with CH_2Cl_2, the combined org. layer dried (Na_2SO_4) and evaporated, and the residue submitted to FC (petroleum ether/AcOEt 7:1): **32** (538 mg, 85% from **3**). White solid. M.p. 236° (from $CHCl_3$). UV (MeOH): 209 (*s*), 288 (*s*), 305 (sh). IR ($CHCl_3$): 2928*s*, 2876*s*, 1632*w*, 1460*m*, 1400*s* (pyrazine), 1376*m*, 1240*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.08 (*s*, 1 MeSi); 0.09 (*s*, 1 MeSi); 0.80 (*d*, *J* = 6, Me(27′)); 0.81 (*d*, *J* = 6, Me(27)); 0.86 (*s*, Me(19′)); 0.88 (*s*, Me(19)); 0.91 (*s*, ^{t}BuSi); 1.01 (*s*, Me(18′)); 1.02 (*d*, *J* = 7, Me(21′)); 1.09 (*d*, *J* = 7, Me(21)); 1.22 (*s*, Me(18)); 2.05 (*m*, H–C(8′)); 2.28 (*m*, H–C(8)); 2.37–2.67 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′), CH_2(11), H–C(17′)); 2.79–2.99 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′), H–C(17)); 3.22 (*dd*, *J* = 10.5, 4.5, H–C(12′)); 3.40–3.54 (*m*, CH_2(26), CH_2(26′)); 4.70 (br. *s*, 1 H, CH_2=C); 4.80 (*m*, 1 H, CH_2=C); 4.83–4.86 (*m*, H–C(16), H–C(16′)); 5.35 (br. *s*, H–C(15)); 5.43 (br. *s*, H–C(15′)). ^{13}C-NMR (100 MHz, $CDCl_3$): −4.2, −3.6 (2*q*, Me_2Si); 11.6, 11.8, 13.6, 14.0, 14.1, 17.2 (br.) (6*q*, C(18′), C(19), C(19′), C(21), C(21′), C(27), C(27′)); 18.0 (*s*, Me_3CSi); 23.7 (*q*, Me(18)); 26.0 (*q*, *Me*$_3$CSi); 27.9 (*t*); 28.2 (*t*); 28.79 (*t*); 28.82 (*t*); 29.2 (*t*); 29.4 (*t*); 30.38 (*d*); 30.45 (*d*); 30.7 (*t*); 31.2 (*t*); 31.5 (*t*); 32.3 (*t*); 33.8 (*d*); 34.6 (*d*); 35.3 (*t*); 35.4 (*t*); 36.0, 36.1 (2*s*, C(10), C(10′)); 41.3 (*d*); 41.5 (*d*); 44.2 (*d*); 44.8 (*d*); 45.55 (*t*); 45.61 (*t*); 52.0 (*d*); 53.3, 53.4 (2*s*, C(13), C(13′)); 54.0 (*d*); 54.8 (*d*); 55.5 (*d*); 67.09, 67.14 (2*t*, C(26), C(26′)); 79.7 (*d*, C(12′)); 84.3 (*d*, C(16)); 84.5 (*d*, C(16′)); 106.1 (*t*, CH_2=C); 106.5, 107.4 (2*s*, C(22), C(22′)); 117.8, 119.7 (2*d*, C(15), C(15′)); 148.3, 148.55, 148.64, 148.69 (4*s*, C(pyrazine)); 155.2, 157.2, (2*s*, C(14), C(14′)); 158.8 (*s*, C(12)). FAB-MS (monoisotopic mass 958.66189): 960 (100, $[M+H]^+$), 845 (32, $[M+H-{}^t$BuMe$_2$Si$]^+$), 126 (40). Anal. calc. for $C_{61}H_{90}N_2O_5Si$ (959.48): C 76.36, H 9.45, N 2.92; found: C 76.10, H 9.48, N 2.83.

*(5α,5′α,12α and 12β,12′β,25*R*,25′*R*)-12′-[[(*tert*-Butyl)dimethylsilyl]oxy}bisspirosta-2,14-dieno[2,3*-b:*2′,3′*-e*]pyrazin-12-methanol* (**33**). To a 0°-cold soln. of **32** (200 mg, 0.209 mmol, 1 equiv.) in THF (2 ml), 1M borane in THF (1.2 ml, 1.2 mmol, 5.8 equiv.) was added dropwise. After 6 h, 6N aq. NaOH (1.5 ml) was slowly added followed by EtOH (0.2 ml), H_2O (1 ml), and Et_2O (1 ml). After further 30 min, the mixture was warmed to r.t.

followed by addition of 35% aq. H_2O_2 soln. (0.4 ml). Then the mixture was stirred for 1 h. After neutralization by addition of solid NH_4Cl, the aq. layer was extracted with CH_2Cl_2, the combined org. layer dried (Na_2SO_4) and evaporated, and the residue submitted to FC (CH_2Cl_2/MeOH 30:1): inseparable mixture **33** (184 mg, 90%). White foam. UV (MeOH): 206 (*s*), 288 (*s*), 304 (sh). IR ($CHCl_3$): 3040*w*, 2956*s*, 2928*s*, 2876*s*, 2860*s*, 1648*w* (C=C), 1460*m*, 1400*s* (pyrazine), 1376*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.08 (*s*, 3 H, MeSi); 0.09 (*s*, 3 H, MeSi); 0.81 (br. *d*, *J* = 6, Me(27), Me(27′)); 0.86 (*s*, Me(19′)); 0.87 (*s*, 2 H, Me(19) (12*β*)); 0.88 (*s*, 1 H, Me(19) (12*α*)); 0.91 (*s*, ^{t}BuSi); 1.00 (*s*, Me(18′)); 1.02 (*d*, *J* = 7, 4 H, Me(21′), Me(21) (12*α*)); 1.04 (*d*, *J* = 7, 2 H, Me(21) (12*β*)); 1.25 (*s*, 1 H, Me(18) (12*α*)); 2.02–2.16 (*m*, H–C(8), H–C(8′)); 2.45–2.66 (*m*, 6 H, 4 H of CH_2(1,1′) and CH_2(4,4′), H–C(17), H–C(17′)); 2.78–3.00 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′)); 3.22 (*dd*, *J* = 10.5, 4.5, 1 H, H–C(12′)); 3.35–3.47 (*m*, 3 H, 1 H–C(26), 1 H–C(26′), H_a of CH_2OH); 3.47–3.54 (*m*, 2 H, H–C(26), H–C(26′)); 3.71–3.74 (*m*, 0.3 H, H_b of CH_2OH (12*α*)); 3.77 (*dd*, *J* = 10, 0.7 H, H_b of CH_2OH (12*β*)); 4.79 (*dd*, *J* = 8, 1.5, 0.3 H, H–C(16) (12*α*)); 4.85 (*dd*, *J* = 8, 2, 1 H, H–C(16′)); 4.87 (*dd*, *J* = 8, 1.5, 0.7 H, H–C(16) (12*β*)); 5.38, 5.43 (2 br. *s*, 2 H, H–C(15), H–C(15′)). FAB-MS (monoisotopic mass 976.67245): 978 (100, $[M+H]^+$), 136 (29).

*(5α,5′α,12α,12′β,25*R*,25′*R*)- and (5α,5′α,12β,12′β,25*R*,25′*R*)-12′-[[(*tert*-Butyl)dimethylsilyl]oxy]-17,12-(epoxymethano)bisspirosta-2,14-dieno[2,3*-b*:2′,3′*-e*]pyrazine* (**34** and **35**, resp.). A vigorously stirred 10°-cold suspension of mixture **33** (150 mg, 0.154 mmol, 1 equiv.), $Pb(OAc)_4$ (200 mg, 0.45 mmol, 3 equiv.; dried prior to use (see *General*)) and pyridine (0.05 ml, 0.60 mmol, 4 equiv.) in benzene (3 ml) was irradiated (see *General*) in a quartz flask for 2 h. Then the solid particles were removed by column filtration (silica gel, CH_2Cl_2/MeOH 5:1). The org. layer was evaporated and the residue submitted to 'gradient' FC (petroleum ether/AcOEt (→ **34**), 2:1 then CH_2Cl_2/MeOH 30:1) (→ **35**): **34** (20 mg, 14%) and **35** (50 mg, 34%), both as colorless, glass-like solids.

Data of **34**: UV (MeOH): 205 (*s*), 287 (*s*), 303 (sh). IR ($CHCl_3$): 3040*w*, 2956*s*, 2928*s*, 2872*s*, 2860*s*, 1644*w* (C=C), 1460*m*, 1400*s* (pyrazine), 1376*m*, 1244*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.08 (*s*, MeSi); 0.09 (*s*, MeSi); 0.80 (br. *d*, *J* = 6, Me(27), Me(27′)); 0.85, 0.86 (*s*, Me(19), Me(19′)); 0.91 (*s*, ^{t}BuSi); 0.93 (*d*, *J* = 7.5, Me(21)); 1.00 (*s*, Me(18′)); 1.02 (*d*, *J* = 7, Me(21′)); 1.15 (*s*, Me(18)); 2.00–2.14 (*m*); 2.41–2.67 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′)), H–C(17′)); 2.77–2.90 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′)); 3.22 (*dd*, *J* = 10.5, *J* = 5, H–C(12′)); 3.38–3.46 (*m*, 1 H–C(26), 1 H–C(26′), H_a of CH_2O–C(17)); 3.51 (br. *d*, *J* = 11, 1 H–C(26′)); 3.62 (br. *d*, *J* = 11, 1 H–C(26)); 3.81 (*dd*, *J* = 8, 7, H_b of CH_2O–C(17)); 4.47 (*d*, *J* = 2.5, H–C(16)); 4.85 (*dd*, *J* = 8, 2, H–C(16′)); 5.43 (br. *s*, H–C(15′)); 5.57 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): −4.2, −3.6 (2*q*, MeSi); 8.4, 11.6, 11.8, 13.6, 14.1, 17.2 (br.) (6*q*, C(18′), C(19), C(19′), C(21), C(21′), C(27), C(27′)); 18.0 (*s*, Me_3CSi); 20.7 (*t*); 21.7 (*q*, Me(18)); 26.0 (*q*, *Me*$_3$CSi); 27.7 (*t*); 28.2 (*t*); 28.4 (*t*); 28.77 (*t*); 28.83 (*t*); 29.2 (*t*); 30.0 (*d*); 30.5 (*d*); 30.7 (*t*); 31.2 (*t*); 31.8 (*t*); 33.8 (*d*); 35.3 (*t*); 35.38 (*t*); 35.41 (*d*); 36.05, 36.09 (2*s*, C(10), C(10′)); 41.5 (*d*); 41.6 (*d*); 44.8 (*d*); 45.53 (*t*); 45.55 (*d*); 45.7 (*t*); 45.9 (*d*); 50.4 (*d*); 52.0 (*d*); 53.3 (C, C(13′)); 55.5 (br., *d*, 1*s*, C(13)); 67.1, 67.2 (2*t*, C(26), C(26′)); 68.8 (*t*, CH_2O); 79.8 (*d*, C(12′)); 84.5 (*d*, C(16′)); 90.7 (*d*, C(16)); 98.4 (*s*, C(17)); 106.5, 107.9 (2*s*, C(22), C(22′)); 118.5, 119.7 (2*d*, C(15), C(15′)); 148.2, 148.5, 148.6, 148.7 (4*s*, C(pyrazine)); 157.2, 157.5 (*s*, C(14), C(14′)). FAB-MS (monoisotopic mass 974.6568): 976 (100, $[M+H]^+$), 861 (22, $[M+H^+ - {}^t\text{BuMe}_2\text{Si}]$), 136 (94).

Data of **35**: UV (MeOH): 207 (*s*), 288 (*s*), 304 (sh). IR ($CHCl_3$): 2956*s*, 2928*s*, 2876*s*, 2860*s*, 1645*w* (C=C), 1620*w* (C=C), 1460*m*, 1400*s* (pyrazine), 1384*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.08 (*s*, MeSi); 0.09 (*s*, MeSi); 0.81 (*d*, *J* = 6, Me(27), Me(27′)); 0.86 (*s*, Me(19′)); 0.91 (*s*, ^{t}BuSi); 0.93 (*s*, Me(19)); 0.97, 1.01 (*s*, Me(18), Me(18′)); 1.018, 1.022 (2*d*, *J* = 7, Me(21), Me(21′)); 2.05 (*m*, H–C(8′)); 2.40 (*m*, H–C(8)); 2.48–2.65 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′), H–C(17′)); 2.79–2.91 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′)); 3.22 (*dd*, *J* = 10.5, 4.5, H–C(12′)); 3.43 (*t*, *J* = 11, 1 H–C(26′)); 3.45 (*t*, *J* = 11, H–C(26)); 3.51 (br. *d*, *J* = 11, 1 H–C(26′)); 3.55 (*dd*, *J* = 12, 7.5, 1 H of CH_2O–C(17)); 3.64 (br. *d*, *J* = 11, 1 H–C(26)); 3.96 (*dd*, *J* = 7.5, 5.5, 1 H of CH_2O–C(17)); 4.76 (*d*, *J* = 2, H–C(16)); 4.85 (*dd*, *J* = 8, 2, H–C(16′)); 5.13 (br. *s*, H–C(15)); 5.43 (br. *s*, H–C(15′)). ^{13}C-NMR (100 MHz, $CDCl_3$): −4.2, −3.6 (2*q*, MeSi); 7.8, 11.0, 11.8, 12.2, 13.6, 14.1, 17.17, 17.19 (8*q*, C(18), C(18′), C(19), C(19′), C(21), C(21′), C(27), C(27′)); 18.0 (*s*, Me_3C*Si*); 21.2 (*t*); 26.0 (*q*, *Me*$_3$CSi); 28.1 (*t*); 28.46 (*t*); 28.52 (*t*); 28.8 (*t*); 29.0 (*t*); 29.2 (*t*); 30.1 (*d*); 30.4 (*d*); 30.7 (*t*); 31.2 (*t*); 31.6 (*t*); 33.8 (*d*); 35.4 (*t*); 36.0 (*d*); 36.1, 36.7 (2*s*, C(10), C(10′)); 41.5 (*d*); 42.2 (*d*); 44.8 (*d*); 45.6 (*t*); 45.9 (*t*); 47.3 (*d*); 52.0 (*d*); 53.3 (*s*, C(13′)); 55.5 (*d*); 56.8 (*s*, C(13)); 57.0 (*d*); 67.2, 67.4 (2*t*, C(26), C(26′)); 71.2 (*t*, CH_2O); 79.7 (*d*, C(12′)); 84.5 (*d*, C(16′)); 93.2 (*d*, C(16)); 99.3 (*s*, C(17)); 106.5, 106.7 (2*s*, C(22), C(22′)); 113.3 (*d*, C(15)); 119.7 (*d*, C(15′)); 148.3, 148.5, 148.6, 148.8 (4*s*, C(pyrazine)); 157.2, 158.7 (2*s*, C(14), C(14′)). FAB-MS (monoisotopic mass 974.6568): 976 (94, $[M+H]^+$), 103 (100).

*(5α,5′α,12α,12′β,25*R*,25′*R*)-17,12-(Epoxymethano)bisspirosta-2,14-dieno[2,3*-b*:2′,3′*-e*]pyrazin-12′-ol* (**36**). A soln. of **34** (11.5 mg, 0.012 mmol) and Bu_4NF (20 mg) in THF (1 ml) was stirred for 13 days in the dark. The reaction was quenched by addition of CH_2Cl_2 and H_2O, the aq. layer extracted with CH_2Cl_2, the combined org.

layer dried (Na_2SO_4) and evaporated, and the residue submitted to FC (CH_2Cl_2/MeOH 30:1): **36** (9.1 mg, 90%). White, crystalline solid. UV (MeCN): 289 (*s*), 306 (sh). IR ($CHCl_3$): 3605*w* (O–H), 3065*w* (alkene H), 2956*s*, 2928*s*, 2872*s*, 1456*m*, 1400*s* (pyrazine), 1376*m*, 1240*m*. ^{1}H-NMR (400 MHz, $CDCl_3$/CD_3OD 5:1): 0.818, 0.825 (*d*, *J* = 6, Me(27), Me(27′)); 0.876, 0.883 (*s*, Me(19), Me(19′)); 0.93 (*d*, *J* = 7, Me(21)); 1.03 (*s*, Me(18′)); 1.05 (*d*, *J* = 7, Me(21′)); 1.17 (*s*, Me(18)); 2.00–2.17 (*m*); 2.42–2.67 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′), H–C(17′)); 2.79–2.92 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′)); 3.21 (*dd*, *J* = 11, 4.5, H–C(12′)); 3.41 (*dd*, *J* = 11.5, 8.5, H_a of CH_2O–C(17)); 3.43 (*t*, *J* = 11, 1 H–C(26′)); 3.45 (*t*, *J* = 11, 1 H–C(26)); 3.52 (br. *d*, *J* = 11, H–C(26′)); 3.59 (br. *d*, *J* = 11, 1 H–C(26)); 3.83 (*dd*, *J* = 8.5, 7, H_b of CH_2O–C(17)); 4.46 (*d*, *J* = 2.5, H–C(16)); 4.88 (*dd*, *J* = 8, 1.5, H–C(16′)); 5.42 (br. *s*, H–C(15′)); 5.57 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$/CD_3OD 5:1): 8.4, 11.8, 12.0, 13.4, 13.6, 17.18, 17.19 (7*q*, C(18′), C(19), C(19′), C(21), C(21′), C(27), C(27′)); 20.8 (*t*); 21.8 (*q*, C(18)); 27.8 (*t*); 28.2 (*t*); 28.5 (*t*); 28.8 (*t*); 29.0 (*t*); 29.4 (*t*); 29.9 (*t*); 30.2 (*d*); 30.5 (*d*); 31.3 (*t*); 31.8 (*t*); 33.9 (*d*); 35.0 (*t*); 35.1 (*t*); 35.6 (*d*); 36.1, 36.2 (2*s*, C(10), C(10′)); 41.5 (*d*); 41.6 (*d*); 44.7 (*d*); 45.3 (*t*); 45.4 (*t*); 45.7 (*d*); 46.0 (*d*); 50.5 (*d*); 52.4 (*d*); 53.0 (*s*, C(13′)); 55.69 (*d*); 55.72 (*s*, C(13)); 67.2, 67.4 (2*t*, C(26), C(26′)); 69.0 (*t*, CH_2O); 78.7 (*d*, C(12′)); 85.0 (*d*, C(16′)); 90.9 (*d*, C(16)); 98.8 (*s*, C(17)); 107.2, 108.3 (2*s*, C(22)); 118.5, 119.6 (2*d*, C(15), C(15′)); 148.6, 148.91, 148.92, 149.1 (4*s*, C(pyrazine)); 157.8, 157.9 (2*s*, C(14), C(14′)). FAB (monoisotopic mass 860.57033): 862 (100, $[M^+H]^+$). HR-FAB-MS: 861.5811 ($[C_{55}H_{76}N_2O_6 + H]^+$; calc. 861.5782).

*(5α,5′α,12β,12′β,25*R*,25′*R*)-17,12-(Epoxymethano)bisspirosta-2,14-dieno[2,3-*b*:2′,3′-*e*]pyrazin-12′-ol* (**37**). To a soln. of **35** (20.4 mg, 0.021 mmol) in CH_2Cl_2 (0.5 ml) kept in a *Nalgene* vessel, MeCN (1.5 ml) and 48% aq. HF soln. (0.2 ml) were added. After 16 h stirring, the mixture was poured onto sat. $NaHCO_3$ soln. the aq. layer extracted with CH_2Cl_2, the combined org. layer washed with sat. $NaHCO_3$ soln., dried (Na_2SO_4), and evaporated, and the residue submitted to FC (CH_2Cl_2/MeOH 30:1): **37** (13.0 mg, 72%). White crystalline solid. UV (MeCN): 290 (*s*), 308 (sh). IR ($CHCl_3$): 3610*w* (O–H), 2956*s*, 2932*s*, 2872*s*, 1448*m*, 1400*s* (pyrazine), 1384*m*, 1224*s*. ^{1}H-NMR (400 MHz, $CDCl_3$/CD_3OD 5:1): 0.81, 0.82 (2*d*, *J* = 6, Me(27), Me(27′)); 0.88 (*s*, Me(19), Me(19′)); 0.99 (*s*, Me(18)); 1.02 (*d*, *J* = 6.5, Me(21)); 1.03 (*s*, Me(18′)); 1.05 (*d*, *J* = 7, Me(21′)); 2.08 (*m*, H–C(8′)); 2.40 (br. *t*, *J* = 10, H–C(8)); 2.49–2.66 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′), H–C(17′)); 2.80–2.93 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′)); 3.21 (*dd*, *J* = 11, 4.5, H–C(12′)); 3.43, 3.45 (2*t*, *J* = 11, 1 H–C(26), 1 H–C(26′)); 3.52 (br. *d*, *J* = 11, 1 H–C(26′)); 3.58 (*dd*, *J* = 12, 7.5, H_a of CH_2O–C(17)); 3.61 (br. *d*, *J* = 11, 1 H–C(26)); 3.96 (*dd*, *J* = 7.5, 5.5, H_b of CH_2O–C(17)); 4.75 (*d*, *J* = 2, H–C(16)); 4.88 (*dd*, *J* = 8, 1.5, H–C(16′)); 5.12 (br. *s*, H–C(15)); 5.42 (br. *s*, H–C(15′)). ^{13}C-NMR (100 MHz, $CDCl_3$/CD_3OD 5:1): 7.8, 11.1, 12.0, 12.4, 13.4, 13.6, 17.19, 17.22 (8*q*, C(18), C(18′), C(19), C(19′), C(21), C(21′), C(27), C(27′)); 21.4 (*t*); 28.2 (*t*); 28.54 (*t*); 28.57 (*t*); 28.8 (*t*); 29.2 (*t*); 29.4 (*t*); 29.9 (*t*); 30.2 (*d*); 30.5 (*d*); 31.3 (*t*); 31.5 (*t*); 33.9 (*d*); 35.0 (*t*); 36.1 (br., 1*d* and 1*s*, C(10′)); 36.9 (*s*, C(10)); 41.6 (*d*); 42.3 (*d*); 44.7 (*d*); 45.4 (*t*); 45.6 (*t*); 47.4 (*d*); 52.4 (*d*); 53.0 (*s*, C(13′)); 55.7 (*d*); 57.0 (*s*, C(13)); 57.2 (*d*); 58.7 (*d*); 67.4 br. (2*t*, C(26), C(26′)); 71.3 (*t*, CH_2O); 78.7 (*d*, C(12′)); 85.0 (*d*, C(16′)); 93.4 (*d*, C(16)); 99.8 (*s*, C(17)); 107.0, 107.2 (2*s*, C(22), C(22′)); 113.5 (*d*, C(15)); 119.6 (*d*, C(15′)); 148.8, 148.90, 148.95, 149.1 (4*s*, C(pyrazine)); 157.7, 158.9 (2*s*, C(14), C(14′)). FAB-MS (monoisotopic mass 860.57033): 862 (100, $[M+H]^+$. HR-FAB-MS: 861.5838 ($[C_{55}H_{76}N_2O_6 + H]^+$; calc. 861.5782).

(3β,5α,12β,20ξ,25ξ)-3-(Acetyloxy)-12,26-dihydroxycholesta-14,16-dien-22-one Inner Spirobicyclic Acetal (**39**). To a 0°-cold soln. of **5** (300 mg, 0.64 mmol, 1 equiv.) and Ph_3P (505 mg, 1.92 mmol, 3 equiv.) in CH_2Cl_2 (4 ml), a soln. of tetrabromomethane (637 mg, 1.92 mmol, 3 equiv.) in CH_2Cl_2 (4 ml) was added. The mixture was warmed to r.t. and turned greenish while a precipitate formed. After 20 h, the reaction was quenched by addition of Et_2O and brine. A yellow precipitate was removed by filtration, and the aq. layer was extracted with Et_2O. The combined org. layer was dried ($MgSO_4$) and evaporated and the residue submitted to FC (petroleum ether/AcOEt): **39** (115 mg, 40%). Yellow foam. UV (MeCN): 206, 255. IR (KBr): 3548*m*, 3476*s*, 3416*s*, 2932*s*, 2868*m*, 1732*s*, 1616*m*, 1244*s*, 1028*m*, 980*m*. ^{1}H-NMR (400 MHz, C_6D_6): 0.70 (*s*, 3 H); 1.01 (*s*, 3 H); 1.02 (*d*, *J* = 6, Me(27)); 1.39 (*d*, *J* = 7, Me(21)); 1.75 (*s*, AcO); 2.24–2.34 (*m*, 2 H); 2.54 (*m*, 1 H); 2.60 (*dd*, *J* = 11.5, 4.5, H–C(12)); 3.17 (*d*, *J* = 10.5, 1 H–C(26)); 3.78 (*dd*, *J* = 11, 3, 1 H–C(26)); 4.76 (*m*, H–C(3)); 6.04 (*m*, H–C(15)); 6.14 (*m*, H–C(16)). ^{13}C-NMR (100 MHz, C_6D_6): 12.0, 12.3, 12.8, 16.3 (4*q*, C(18), C(19), C(21), C(27)); 21.0 (*q*, *Me*CO); 25.5 (*t*); 26.3 (*t*); 27.2 (*t*); 27.4 (*t*); 27.8 (*t*); 28.6 (*t*); 29.4 (*t*); 34.3 (*t*); 35.1 (*d*); 36.2 (*s*, C(10)); 37.3 (*t*); 41.2 (*d*); 44.5 (*d*); 54.8 (*s*, C(13)); 56.6 (*d*); 65.0 (*t*, C(26)); 73.2 (*d*, C(3)); 78.3 (*d*, C(12)); 101.8 (*s*, C(22)); 121.0 (*d*, C(16)); 121.0 (*d*, C(15)); 155.6 (*s*, C(14)); 157.1 (*s*, C(17)); 169.6 (*s*, Me*C*O). FAB-MS: 455 (45, $[M^+H]^+$), 340 (100). HR-MS: 454.3087 ($C_{29}H_{42}O_4^+$; calc. 454.3083).

*(3β,5α,12α,17α,20*S*,25*R*)-3-(Acetyloxy)-12,26-dihydroxycholesta-8(14),15-dien-22-one Inner Spirobicyclic Acetal* (**40**). A soln. of **38** (50 mg, 0.106 mmol, 1 equiv.) and $TsOH \cdot H_2O$ (25 mg, 0.13 mmol, 1.2 equiv.) in pentane (3 ml) was refluxed for 2 h. Then the soln. was separated from the solid residue by filtration and evaporated and the residue submitted to FC (petroleum ether/AcOEt): **39** (11 mg, 23%) and **40** (9 mg, 18%). White foam. UV (MeCN): 257 (*s*). IR (KBr): 3552*m*, 3476*s*, 3416*s*, 2932*s*, 2864*m*, 1732*s*, 1616*m*, 1244*m*, 1052*m*,

1028*m*. ^{1}H-NMR (400 MHz, C_6D_6): 0.77 (*s*, 3 H), 0.81 (*d*, *J* = 7, 3 H); 1.19 (*d*, *J* = 6.5, 3 H); 1.54 (*s*, 3 H); 1.90 (*s*, AcO); 2.18 (*dd*, *J* = 11, 8, 1 H); 2.40 (*dd*, *J* = 10, 3, H–C(17)); 2.69 (*m*, 1 H); 3.42 (*t*, *J* = 11, H–C(26)); 3.71 (*m*, H–C(26)); 4.07 (br. *s*, H–C(12)); 4.91 (*m*, H–C(3)); 6.25 (*dd*, *J* = 5.8, 2.7, H–C(16)); 6.53 (*d*, *J* = 6, H–C(15)). ^{13}C-NMR (100 MHz, C_6D_6): 12.9, 14.5, 17.4, 21.0 (4*q*, C(18), C(19), C(21), C(27)); 25.4 (*t*); 27.1 (*t*); 27.2 (*q*, *Me*$_3$CO); 28.0 (*t*); 28.9 (*t*); 29.8 (*t*); 30.5 (*d*); 31.7 (*t*); 34.5 (*t*); 36.4 (*s*, C(10)); 37.0 (*t*); 42.0 (*s*, C(13)); 44.0 (*d*); 45.1 (*d*); 45.5 (*d*); 54.2 (*d*); 67.4 (*t*, C(26)); 68.3 (*d*, C(12)); 73.3 (*d*, C(3)); 96.6 (*s*, C(22)); 128.9 (*s*, C(8)); 129.3 (*d*, C(15)); 138.2 (*d*, C(16)); 139.9 (*s*, C(14)); 169.6 (*s*, Me*C*O). FAB: 455 (45, $[M^+H]^+$), 328 (100). HR-MS: 454.3084 ($C_{29}H_{42}O_4^+$; calc. 454.3083). Subjecting **5** to a similar procedure afforded **39** (7%) and **40** (19%) after 25 h.

*(3β,5α,12β,15β,16β,20ξ,25ξ)-3-(Acetyloxy)-15,16-dihydro-12,26-dihydroxy-14,17-etheno-1′*H*-cholest-15-eno-[15,16-*c*]pyrrole-2′,5′,22-trione Inner Spirocyclic Acetal* (**41**). A soln. of **39** (76 mg, 0.17 mmol, 1 equiv.) and maleic imide (20 mg, 0.2 mmol, 1.2 equiv.) in CH_2Cl_2 (2 ml) was kept for 3 days under a pressure of 14 kbar. Evaporation and FC (petroleum ether/AcOEt) gave **41** (50 mg, 64%). White foam. IR ($CHCl_3$): 2936*m*, 1768*m*, 1720*s*, 1360*m*, 1344*m*, 1252*s*, 1176*m*, 1028*m*, 992*m*, 964*m*. ^{1}H-NMR (400 MHz, C_6D_6): 0.49 (*s*, 3 H); 0.61 (*s*, 3 H); 1.00 (*d*, *J* = 7, 3 H); 1.63 (*d*, *J* = 4.5, 3 H); 1.76 (*s*, AcO); 1.93 (*m*, 1 H); 2.20 (*m*, 1 H); 2.52 (*d*, *J* = 6.5, 1 H); 2.65 (*m*, 1 H); 2.68 (*d*, *J* = 6.5, 1 H); 3.19 (*d*, *J* = 11, 1 H–C(26)); 3.80 (*dd*, *J* = 10.5, 2.5, 1 H–C(26)); 4.10 (*dd*, *J* = 12.5, 4.5, H–C(12)); 4.77 (*m*, H–C(3)); 5.84 (*d*, *J* = 6, C(14)C*H*=CHC(17)); 6.29 (*d*, *J* = 6, C(14)CH=C*H*C(17)); 7.93 (*s*, NH). ^{13}C-NMR (100 MHz, C_6D_6): 11.1, 12.0, 12.6, 16.3 (4*q*, C(18), C(19), C(21), C(27)); 21.0 (*q*, *Me*CO); 25.0 (*t*); 25.6 (*t*); 26.5 (*t*); 27.3 (*d*); 27.8 (*t*); 28.6 (*t*); 29.8 (*t*); 34.3 (*t*); 35.9 (*d*); 36.3 (*s*, C(10)); 37.1 (*t*); 40.9 (*d*); 44.3 (*d*); 51.9 (*d*); 53.8 (*d*); 55.5 (*d*); 60.5 (*d*); 61.6 (*s*); 62.9 (*d*); 64.7 (*t*, C(26)); 66.6 (*d*); 73.2 (*d*, C(3)); 100.7 (*s*, C(22)); 128.3 (*d*); 130.2 (*d*); 169.8 (*s*, Me*C*O); 176.7 (*s*, C=O); 176.8 (*s*, C=O). FAB: 552 (80, $[M^+H]^+$), 307 (100). HR-MS: 551.3236 ($C_{33}H_{45}NO_6^+$; calc. 551.3247).

*(3β,5α,12α,22β,25*R*)-Furost-14-ene-3,12,26-triol 3-Acetate* (**44**). $NaCNBH_3$ (excess) was added to a soln. of **5** (150 mg, 0.31 mmol) in AcOH (1 ml). After 90 min, the reaction was quenched by addition of CH_2Cl_2 and sat. Na_2CO_3 soln., the aq. layer extracted with Et_2O, the combined org. layer dried ($MgSO_4$) and evaporated, and the residue submitted to FC (AcOEt): **44** (140 mg, 94%). White foam. IR ($CHCl_3$): 2936*m*, 2872*w*, 1724*m*, 1456*w*, 1380*w*, 1264*s*, 1100*w*, 1028*m*, 960*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(19)); 0.89 (*d*, *J* = 6.5, Me(27)); 0.98 (*d*, *J* = 6.5, Me(21)); 1.12 (*s*, Me(18)); 2.01 (*s*, AcO); 2.12 (*m*, H–C(8)); 2.52 (*d*, *J* = 9, 1 H–C(17)); 3.30 (*d*, *J* = 8.5, Me(22)); 3.43 (*dd*, *J* = 10.5, 6, 1 H–C(26)); 3.49 (*dd*, *J* = 10.5, 6, 1 H–C(26)); 3.67 (br. *s*, H–C(12)); 4.66 (*m*, H–C(3)); 4.79 (*dd*, *J* = 8, 1.5, H–C(16)); 5.51 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.9, 16.6, 16.8, 18.9 (4*q*, C(18), C(19), C(21), C(27)); 21.4 (*q*, *Me*CO); 27.3 (*t*); 28.1 (*t*); 28.6 (*t*); 29.5 (*t*); 30.0 (*t*); 30.1 (*t*); 33.8 (*t*); 34.4 (*d*, C(25)); 35.8 (*s*, C(10)); 35.8 (*d*); 36.4 (*t*); 41.7 (*d*); 44.6 (*d*); 49.7 (*d*); 52.7 (*s*, C(13)); 55.8 (*d*, C(17)); 68.1 (*t*, C(26)); 73.3 (*d*, C(3)); 76.1 (*d*, C(12)); 86.1 (*d*, C(16)); 86.5 (*d*, C(22)); 121.5 (*d*, C(15)); 154.0 (*s*, C(14)); 170.6 (*s*, Me*C*O). FAB-MS: 475 (77, $[M+H]^+$), 359 (35), 154 (100, NBA matrix). HR-MS: 474.3347 ($C_{29}H_{46}O_5^+$; calc. 474.3345).

*(3β,5α,12α,22β,25*R*)-Furost-14-ene-3,12,26-triol 3,12-Diacetate* (**45**). $NaCNBH_3$ (917 mg, 14.6 mmol, 1.2 equiv.) was added to a soln. of **42** (6.26 g, 12.2 mmol, 1 equiv.) in AcOH (2 ml). After 150 min, CH_2Cl_2 was added and then sat. Na_2CO_3 soln. The aq. phase was extracted with CH_2Cl_2 and the combined org. layer dried ($MgSO_4$) and evaporated: 6.02 g (11.6 mmol, 95%) of **45**. IR ($CHCl_3$): 3452*w*, 3428*w*, 2940*m*, 2936*m*, 2872*w*, 1724*s*, 1648*w*, 1456*w*, 1376*m*, 1252*s*, 1176*w*, 1104*w*, 1028*s*, 960*w*, 960*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.85 (*s*, Me(19)); 0.88 (*d*, *J* = 6.6, Me(27)); 0.94 (*d*, *J* = 6.5, Me(21)); 1.13 (*s*, Me(18)); 2.00 (*s*, AcO); 2.02 (*s*, AcO); 2.09 (*t*, *J* = 8.5, H–C(17)); 2.12 (*m*, H–C(8)); 3.29 (*m*, H–C(22)); 3.42 (*dd*, *J* = 10.5, 6.0, 1 H–C(26)); 3.48 (*dd*, *J* = 10.5, 6.0, 1 H–C(26)); 4.65 (*m*, H–C(3)); 4.75 (*dd*, *J* = 8.5, 2, H–C(16)); 4.91 (br. *s*, H–C(12)); 5.42 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.8, 16.6, 16.8, 19.0 (4*q*, C(18), C(19), C(21), C(27)); 21.4 (*q*, *Me*CO); 21.4 (*q*, *Me*CO); 26.1 (*t*); 27.2 (*t*); 28.0 (*t*); 29.4 (*t*); 30.0 (*t*); 30.2 (*t*); 33.8 (*t*); 34.3 (*d*, C(25)); 35.6 (*s*, C(10)); 35.7 (*d*); 36.5 (*t*); 41.2 (*d*); 44.4 (*d*); 49.8 (*d*); 50.3 (*s*, C(13)); 55.6 (*d*, C(17)); 68.0 (*t*, C(26)); 73.3 (*d*, C(3)); 78.1 (*d*, C(12)); 86.3 (*d*, C(16)); 86.8 (*d*, C(22)); 120.8 (*d*, C(15)); 153.5 (*s*, C(14)); 170.6 (*s*, Me*C*O); 170.7 (*s*, Me*C*O). MS (170°): 516 ($[M+H]^+$, 7), 456 (26), 340 (100). HR-MS: 516.3450 ($C_{31}H_{48}O_6^+$; calc. 516.3450).

*(3β,22β,25*R*)-Furost-5-ene-3,26-diol* (**46**). As described for **45**, with diosgenin (**43**; 200 mg, 0.48 mmol): **46** (195 mg, 97%), after recrystallization of the crude product from MeOH/petroleum ether. IR ($CHCl_3$): 3612*w*, 3420*w*, 3000*m*, 2932*s*, 2904*s*, 2868*m*, 1452*w*, 1376*w*, 1240*s*, 1132*w*, 1096*m*, 1044*s*, 1016*m*, 964w. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*s*, 3 H); 0.90 (*d*, *J* = 6.5, 3 H); 0.98 (*d*, *J* = 7, Me(21)); 1.01 (*s*, 3 H); 1.94–2.04 (*m*, 2 H); 2.17–2.32 (*m*, 2 H); 3.32 (*td*, *J* = 8, 3, H–C(22)); 3.41–3.54 (*m*, CH_2(26), H–C(3)); 4.29 (*m*, H–C(17)); 5.33 (*m*, H–C(6)). ^{13}C-NMR (100MHz, $CDCl_3$): 16.4, 16.6, 18.9, 19.4 (4*q*, C(18), C(19), C(21), C(27)); 20.7 (*t*); 30.1 (*t*); 30.4 (*t*); 31.6 (*d*); 31.6 (*t*); 32.0 (*t*); 32.2 (*t*); 35.7 (*t*); 36.6 (*s*, C(10)); 37.2 (*t*); 37.9 (*d*); 39.4 (*t*); 40.7 (*s*, C(13));

42.3 (*d*); 50.1 (*d*); 57.0 (*d*); 65.1 (*d*); 68.0 (*t*); 71.7 (*d*); 83.2 (*d*); 90.3 (*d*); 121.4 (*d*); 140.8 (*s*). MS (120°): 417 (3, $[M^+H]^+$), 272 (100), 105 (73). HR-MS: 416.3291 ($C_{27}H_{44}O_7^+$; calc. 416.3290).

*(3β,5α,22β,25*R*)-Furostane-3,26-diol* (**49**). As described for **45**, with tigogenin (**47**, 300 mg, 0.72 mmol): **49** (165 mg, 55%). White foam after FC (petroleum ether/AcOEt). IR ($CHCl_3$): 3612*w*, 2996*m*, 2932*s*, 2848*s*, 1452*m*, 1380*w*, 1240*w*, 1096*w*, 1072*w*, 1032*s*, 960*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.77 (*s*, 3 H); 0.81 (*s*, 3 H); 0.90 (*d*, *J* = 7, 3 H); 0.98 (*d*, *J* = 7, 3 H); 1.99 (*m*, 1 H); 3.31 (*m*, H–C(22)); 3.45 (*m*, CH_2(26)); 3.57 (*m*, H–C(3)); 4.27 (*m*, H–C(16)). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.3, 16.6, 16.6, 18.9 (4*q*, C(18), C(19), C(21), C(27)); 20.9 (*t*); 28.6 (*t*); 30.0 (*t*); 30.3 (*t*); 31.5 (*t*); 32.1 (*t*); 32.2 (*t*); 35.3 (*d*); 36.5 (*s*, C(10)); 35.7 (*d*); 37.0 (*t*); 37.9 (*d*); 38.2 (*t*); 39.7 (*t*); 41.0 (*s*, C(13)); 44.8 (*d*); 54.4 (*d*); 56.7 (*d*); 65.2 (*d*); 68.0 (*t*); 71.2 (*d*); 83.2 (*d*); 90.3 (*d*). MS (160°): 418 (5, M^+), 331 (32), 274 (100). HR-MS: 418.3445 ($C_{27}H_{46}O_3^+$; calc. 418.3447).

*(3β,5β,22β,25*R*)-Furostane-3,26-diol* (**50**). As described for **45**, with smilagenin (**48**, 300 mg, 0.72 mmol): **50** (230 mg, 76%). White foam after FC (petroleum ether/AcOEt). IR ($CHCl_3$): 3404*m*, 2932*s*, 2864*m*, 1448*w*, 1376*w*, 1096*w*, 1032*m*, 1004*w*, 988*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.77 (*s*, 3 H); 0.90 (*d*, *J* = 6.5, 3 H); 0.97 (*s*, 3 H); 0.98 (*d*, *J* = 7, 3 H); 1.96 (*m*, 1 H); 3.31 (*td*, *J* = 8, 4, H–C(22)); 3.46 (*m*, CH_2(26)); 4.01 (*m*, H–C(3)); 4.28 (*dt*, *J* = 7.5, 5, H–C(16)). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.6, 16.6, 18.9, 23.9 (4*q*, C(18), C(19), C(21), C(27)); 20.7 (*t*); 26.4 (*t*); 26.5 (*t*); 27.8 (*t*); 29.9 (*t*); 30.1 (*t*); 30.3 (*t*); 32.2 (*t*); 33.5 (*t*); 35.2 (*s*, C(10)); 35.4 (*d*); 35.7 (*d*); 36.5 (*d*); 37.9 (*d*); 39.8 (*d*); 39.9 (*t*); 41.4 (*s*, C(13)); 56.9 (*d*); 65.3 (*d*); 67.0 (*d*); 68.0 (*t*); 83.3 (*d*); 90.3 (*d*). FAB-MS: 419 (97, $[M+H]^+$), 154 (100, NBA matrix). HR-MS: 418.3449 ($C_{27}H_{46}O_3^+$; calc. 418.3447).

*(5α,5′α,12β,12′β,22β,22′β,25*R*,25′*R*)-Difurosta-2,14-dieno[2,3-*b*:2′,3′-*e*]pyrazine-12,12′,26,26′-tetrol* (**51**). $NaCNBH_3$ (71 mg, 1.1 mmol, 5.5 equiv.) was added to a suspension of **4** (170 mg, 0.2 mmol, 1 equiv.) in AcOH (2 ml). After 60 min, the reaction was quenched by addition of CH_2Cl_2 and sat. Na_2CO_3 soln., the aq. phase extracted with CH_2Cl_2 and the combined org. layer dried ($MgSO_4$) and evaporated: **51** (164 mg, 96%). White foam. IR ($CHCl_3$): 3616*w* (OH), 2956*s*, 2932*s*, 2872*s*, 1648*w*, 1600*w*, 1460*m*, 1400*s* (pyrazine), 1328*w*, 1232*m*, 1252*w*, 1100*m*, 1032*m*, 964*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.85 (*s*, Me(19), Me(19′)); 0.89 (*d*, *J* = 7, Me(27), Me(27′)); 1.03 (*s*, Me(18), Me(18′)); 1.04 (*d*, *J* = 6.5, Me(21), Me(21′)); 2.31 (*t*, *J* = 8, H–C(17), H–C(17′)); 2.44–2.64 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′)); 2.76–2.93 (*m*, 4 H of CH_2(1,1′) and CH_2(4,4′)); 3.23 (*dd*, *J* = 10.5, 4.5, H–C(12), H–C(12′)); 3.31 (*td*, *J* = 8.5, 6, H–C(22), H–C(22′)); 3.42 (*dd*, *J* = 10.5, 6, CH_2(26)); 3.48 (*dd*, *J* = 10.5, 6, H–C(26), H–C(26′)); 4.76 (*dd*, *J* = 8.5, 2, H–C(16), H–C(16′)); 5.43 (br. *s*, H–C(15), H–C(15′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.8, 13.9, 16.6, 16.8 (4*q*, C(18), C(18′), C(19), C(19′), C(21), C(21′), C(27), C(27′)); 28.0 (*t*); 29.2 (*t*); 30.1 (*t*); 30.1 (*t*); 30.3 (*t*); 33.8 (*d*); 35.2 (*t*); 35.8 (*d*); 35.9 (*s*, C(10), C(10′)); 41.2 (*d*); 41.4 (*d*); 45.6 (*d*); 51.9 (*d*); 52.9 (*s*, C(13), C(13′)); 59.2 (*d*); 68.0 (*t*, C(26), C(26′)); 79.2 (*d*); 86.0 (*d*); 87.1 (*d*); 119.8 (*d*, C(15), C(15′)); 148.4, 148.5 (2*s*, C(pyrazine)); 157.6 (*s*, C(14), C(14′)). FAB: 853 (42, M^+), 154 (92, NBA matrix), 136 (100).

*(3β,5α,12α,22β,25*R*)-Furost-14-ene-3,12,26-triol 3,12-Diacetate 26-(4-Methylbenzenesulfonate)* (**52**). A soln. of **45** (21.8 g, 42.2 mmol, 1 equiv.), pyridine (7.2 ml, 84.3 mmol), TsCl (9.63 g, 50.6 mmol, 1.2 equiv.), and 4-(dimethylamino)pyridine (catalytic amount) in CH_2Cl_2 (300 ml) was stirred for 20 h. The reaction was quenched by addition of CH_2Cl_2 and 2M HCl, the org. layer washed with 2M HCl, sat. $NaHCO_3$ soln., and brine, dried ($MgSO_4$), and evaporated, and the residue submitted to FC (petroleum ether/AcOEt); **52** (27.2 g, 96%). White foam. IR ($CHCl_3$): 2932*m*, 2860*w*, 1724*s* (C=O), 1364*w*, 1252*s*, 1176*s*, 1096*w*, 1028*m*, 964*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.85 (*s*, Me(19)); 0.87 (*d*, *J* = 7, Me(27)); 0.92 (*d*, *J* = 6.5, Me(21)); 1.12 (*s*, Me(18)); 2.01 (*s*, AcO); 2.03 (*s*, AcO); 2.08 (*t*, *J* = 8.5, H–C(17)); 2.14 (*m*, H–C(8)); 2.44 (*s*, *Me*C_6H_4); 3.21 (*m*, H–C(22)); 3.80 (*dd*, *J* = 9.5, 6.5, 1 H–C(26)); 3.87 (*dd*, *J* = 9.5, 5.5, 1 H–C(26)); 4.65 (*m*, H–C(3)); 4.72 (*dd*, *J* = 8.5, 1 H–C(16)); 4.91 (br. *s*, H–C(12)); 5.41 (br. *s*, H–C(15)); 7.32 (*d*, *J* = 8.0, 2 arom. H); 7.76 (*d*, *J* = 8, 2 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.9, 16.4, 16.7, 19.1 (4*q*, C(18), C(19), C(21), C(27)); 21.4 (*q*); 21.4 (*q*); 21.6 (*q*); 26.1 (*t*); 27.2 (*t*); 28.1 (*t*); 29.4 (*t*); 29.7 (*t*); 30.3 (*t*); 33.0 (*d*); 33.8 (*t*); 34.3 (*d*); 35.5 (*s*, C(10)); 36.5 (*t*); 41.2 (*d*); 44.4 (*d*); 49.8 (*d*); 50.3 (*s*, C(13)); 55.9 (*d*, C(17)); 73.3 (*d*, C(3)); 75.0 (*t*, C(26)); 78.0 (*d*, C(12)); 86.3 (*d*, C(16)); 86.4 (*d*, C(22)); 120.8 (*d*, C(15)); 127.9 (*d*, arom. C); 129.8 (*d*, arom. C); 133.1 (*s*); 144.5 (*s*); 153.6 (*s*, C(14)); 170.6 (*s*, Me*C*O); 170.7 (*s*, Me*C*O). FAB-MS: 670 (45, M^+), 281 (60). HR-MS: 670.3536 ($C_{38}H_{54}O_8S^+$; calc. 670.3539).

*(3β,5α,12α,22β,25*R*)-26-Iodofurost-14-ene-3,12-diol Diacetate* (**53**). A 40°-warm soln. of **52** (5.2 g, 77.6 mmol, 1 equiv.) and NaI (11.68 g, 0.78 mol, 10 equiv.) in MeCN (35 ml) was stirred for 14 h. Then AcOEt was added, the org. layer washed with H_2O, sat. $NaHCO_3$ soln., and brine, dried ($MgSO_4$), and evaporated and the residue submitted to FC (petroleum ether/AcOEt): **53** (4.08 g, 84%). White foam. IR ($CHCl_3$): 2928*m*, 2860*w*, 1724*s* (C=O), 1456*w*, 1376*m*, 1264*s*, 1028*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.85 (*s*, Me(19)); 0.95–0.97 (*m*, Me(27), Me(21)); 1.14 (*s*, Me(18)); 2.01 (*s*, AcO); 2.03 (*s*, AcO); 2.10 (*t*, *J* = 8.5, H–C(17)); 2.12 (*m*, H–C(8)); 3.14 (*dd*, *J* = 9.5, 5.5, 1 H–C(26)); 3.24 (*dd*, *J* = 9.5, 4, 1 H–C(26)); 3.28 (*m*, H–C(22)); 4.65

(*m*, H–C(3)); 4.75 (*dd*, *J* = 8.0, 2, H–C(16)); 4.91 (br. *s*, H–C(12)); 5.43 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.9 (*q*); 16.9 (*q*); 17.7 (*t*, C(26)); 19.2 (*q*); 20.5 (*q*); 21.4 (*q*, *Me*CO); 21.4 (*q*, *Me*CO); 26.1 (*t*); 27.3 (*t*); 28.1 (*t*); 29.4 (*t*); 30.7 (*t*); 33.5 (*t*); 33.8 (*t*); 34.3 (*d*, C(25)); 34.9 (*d*); 35.6 (*s*, C(10)); 36.5 (*t*); 4.3 (*d*); 44.4 (*d*); 49.8 (*d*); 50.3 (*s*, C(13)); 56.0 (*d*, C(17)); 73.3 (*d*, C(3)); 78.0 (*d*, C(12)); 86.3 (*d*, C(16)); 86.6 (*d*, C(22)); 120.8 (*d*, C(15)); 153.6 (*s*, C(14)); 170.6 (*s*, Me*C*O); 170.7 (*s*, Me*C*O). MS (170°): 627 (12, $[M+H]^+$), 340 (100). HR-MS: 626.2469 ($C_{31}H_{47}IO_5^+$; calc. 626.2468).

(3β,5β,12α,22β)-Furosta-14,25-diene-3,12-diyl Diacetate (**54**). A soln. of **53** (4.07 g, 6.5 mmol, 1 equiv.) and DBU (1.9 ml, 12.8 mmol, 1.9 equiv.; freshly distilled) in MeCN (40 ml) was refluxed for 15 min. Then AcOEt was added, the org. layer washed with 2M HCl, sat. $NaHCO_3$ soln., and brine, dried ($MgSO_4$), and evaporated, and the residue submitted to FC (petroleum ether/AcOEt): **54** (2.68 g, 83%). White foam. IR ($CHCl_3$): 2936*m*, 2860*w*, 1724*s* (C=O), 1376*m*, 1252*s*, 1104*w*, 1024*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(19)); 0.96 (*d*, *J* = 6.5, Me(21)); 1.14 (*s*, Me(18)); 1.71 (*d*, Me(27)); 2.01 (*s*, AcO); 2.03 (*s*, AcO); 2.10 (*t*, *J* = 8.5, H–C(17)); 2.14 (*m*, 1 H); 2.25 (*m*, 1 H); 3.31 (*td*, *J* = 9, 2.5, H–C(22)); 4.65 (*m*, H–C(3)); 4.68 (br. *d*, CH_2(26)); 4.76 (*dd*, *J* = 8.5, 2, H–C(16)); 4.91 (br. *s*, H–C(12)); 5.44 (br. *s*, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.8, 16.8, 19.2, (3*q*, C(18), C(19), C(21)); 21.41 (*q*, MeCO); 21.44 (*q*, *Me*CO), 22.6 (*q*, C(27)); 26.1 (*t*); 27.3 (*t*); 28.1 (*t*); 29.4 (*t*); 31.2 (*t*); 33.8 (*t*); 34.3 (*d*); 34.6 (*t*); 35.6 (*s*, C(10)); 36.5 (*t*); 41.3 (*d*); 44.4 (*d*); 49.8 (*d*); 50.4 (*s*, C(13)); 56.1 (*d*, C(17)); 73.3 (*d*, C(3)); 78.1 (*d*, C(12)); 86.3 (*d*, C(16)); 86.3 (*d*, C(22)); 109.5 (*t*, C(26)); 120.9 (*d*, C(15)); 145.7 (*s*, C(25)); 153.5 (*s*, C(14)); 170.6 (*s*, Me*C*O); 170.7 (*s*, Me*C*O). MS (160°): 498 (44, M^+), 382 (100). HR-MS: 498.3348 ($C_{31}H_{46}O_5^+$; calc. 498.3345).

(3β,5α,12α)-3,12-Bis(acetyloxy)cholesta-14,25-diene-16,22-dione (**55**). A 70°-warm soln. of **54** (996 mg, 2 mmol, 1 equiv.) and potassium dichromate (2.47 g, 5 mmol, 2.5 equiv.) in glacial AcOH (25 ml) was stirred for 3 h. Then EtOH and H_2O were added. The aq. layer was extracted with CH_2Cl_2, the combined org. layer washed with sat. Na_2CO_3 soln., dried ($MgSO_4$), and evaporated, and the residue submitted to FC (Alox-N; petroleum ether/AcOEt): **55** (410 mg, 40%; 47% based on recovered **54**) and recovered **54** (160 mg, 0.23 mmol), both as white foams. **55**: IR ($CHCl_3$): 3688*w*, 2984*w*, 2932*w*, 1720*m* (C=O), 1700*m* (C=O), 1600*w*, 1372*w*, 1264*s*, 1028*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): (*s*, Me(19)); 1.04 (*d*, *J* = 7, Me(21)); 1.22 (Me(18)); 1.75 (*s*, Me(27)); 2.01 (*s*, AcO); 2.09 (*s*, AcO); 2.31–2.37 (*m*, 2 H); 2.45 (*m*, 1 H); 2.63–2.73 (*m*, 2 H); 2.83–2.91 (*m*, 1 H), 3.20 (*d*, *J* = 10.5, H–C(17)); 4.68 (*m*, H–C(3)); 4.71 (br. *d*, *J* = 9.5, CH_2(26)); 5.10 (br. *s*, H–C(12)); 5.76 (*d*, *J* = 2, H–C(15)). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.6, 15.9, 21.1 (3*q*, C(18), C(19), C(21)); 21.3 (*q*, *Me*CO); 21.5 (*q*, *Me*CO); 22.7 (*q*, C(27)); 25.5 (*t*); 26.9 (*t*); 27.2 (*t*); 27.6 (*t*); 29.1 (*t*); 33.7 (*t*); 35.5 (*s*, C(10)); 35.9 (*t*); 36.4 (*d*); 40.9 (*t*); 42.6 (*d*); 43.8 (*d*); 46.2 (*d*); 48.7 (*s*, C(13)); 55.9 (*d*); 73.0 (*d*); 74.5 (*d*); 109.7 (*t*, C(26)); 124.5 (*d*, C(15)); 145.0 (*s*, C(25)); 170.0 (*s*, Me*C*O); 170.5 (*s*, Me*C*O); 185.0 (*s*, C(14)); 206.7 (*s*, C(16)); 212.5 (*s*, C(22)). MS (160°): 512 (30, M^+), 356 (100). FAB-MS: 513 (100, $[M^+H]^+$), 136 (95). HR-MS: 512.3143 ($C_{31}H_{44}O_6^+$; calc. 512.3138).

X-Ray Structure Determinations for **40** *and* **49**. *Preparation and Crystal Growing*. Crystals were obtained by slow evaporation of a soln. of **40** in MeOH with some CH_2Cl_2 and a soln. of **49** in $CHCl_3$, resp., at r.t. A crystal of $0.6 \times 0.1 \times 0.1$ mm in the case of **40** and of $0.7 \times 0.3 \times 0.1$ mm in the case of **49** was selected and mounted on a glass fiber for data collection.

Data Collection. Data for both structures was collected on a *Bruker-AXS-P4* four-circle diffractometer with graphite-monochromated MoK_α (λ 0.71073 Å) at r.t. Intensities were obtained from ω scans with a maximum scan time of 1.5°/min for **40** and 2.5°/min for **49**; 4966 reflections (3961 unique) were measured to $2\theta_{max}$ of 50° for **40**, and 6931 reflections (3522 unique) to $2\theta_{max}$ of 46.5° for **49**. In both cases, *Friedel* opposites were not merged. Further details of data collection parameters are given in *Table 2*.

Structure Solution and Refinement. Compound **40** crystallizes in the orthorhombic space group $P2_12_12_1$ and **49** in the monoclinic space group $P2_1$, each with one molecule in the asymmetric unit. Both structures were solved by direct methods with the program SHELXS-86 [44]. Both structures were refined on F^2 (all data) with the program SHELXL-97 [45]. All H-atoms were added in idealized positions and refined with a 'riding' model. For **40**, the refinement converged to $R_1 = 0.0549$ for the 2346 $F_o > 4\alpha(F_o)$ and 0.1359 for all 3961 data. For **49**, restraints concerning the anisotropic displacement parameters were used for the whole molecule [46–48]. The refinement converged to $R_1 = 0.0913$ for the 2976 $F_o > 4\sigma(F_o)$ and 0.2700 for all 3522 data. The very bad quality of the crystal in the case of **49** explains the relatively high values of R_1 as well as ωR_2 and thus the relatively bad model. Nevertheless, the relative configuration could be determined for both structures. Further details of refinement parameters are listed in *Table 2*.

Crystallographic data (excluding structure factors) have been deposited in the *Cambridge Crystallographic Data Centre* as supplementary publication No. CCDC-141277 for **40** and No. CCDC-141276 for **49**. Copies of the data can be obtained free of charge, on application to the director, CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44 (0)1223 (336033; e-mail: teched@chemcrys.cam.ac.uk).

Table 2. *Crystal Data and Structure Refinement for* **40** *and* **49**

	40	**49**
Empirical formula	$C_{29}H_{42}O_4$	$C_{27}H_{46}O_3$
M_r	454.63	418.64
Temperature [K]	293	293
Wavelength [Å]	0.71073	0.71073
Crystal system	orthorhombic	monoclinic
Space group	$P2_12_12_1$	$P2_1$
Unit-cell dimensions [Å]	$a = 8.664(2)$	$a = 10.357(3)$
	$b = 10.507(2)$	$b = 7.274(2)$
	$c = 28.384(5)$	$c = 16.545(4)$
		$\beta = 91.75(1)$
V [Å^3]	2583.8(9)	1245.9(6)
Z	4	2
Density (calc.) [Mg/m^3]	1.169	1.116
Absorption coefficient [mm^3]	0.076	0.070
$F(000)$	992	464
Crystal size [mm]	$0.6 \times 0.1 \times 0.1$	$0.7 \times 0.3 \times 0.1$
2θ Range for data collection	4.14 to 50.00	3.94 to 46.52
Limiting indices	$-9 \geq h \leq 9$, $-11 \geq k \leq 1$, $-1 \geq 1 \leq 31$	$-11 \geq h \leq 11$, $-8 \geq k \leq 8$, $-18 \geq 1 \leq 18$
Reflections collected	4966	6931
Independent reflections	3961 ($R_{int} = 0.0380$)	3522 ($R_{int} = 0.0436$)
Refinement method	full-matrix least-squares on F^2	full-matrix least-squares on F^2
Data/restraints/parameter	3960/0/299	3522/293/274
Goodness-of-fit S[a])	1.076	1.028
Final R indices ($F > 4\sigma(F)$[b]))	$R_1 = 0.0549$, $wR_2 = 0.1114$	$R_1 = 0.0913$, $wR_2 = 0.2538$
R indices (all data)[c])	$R_1 = 0.1132$, $wR_2 = 0.1359$	$R_1 = 0.1064$, $wR_2 = 0.2700$
Absolute structure parameter	2.96(204)	−2(4)
Max. difference density [aÅ^3]	0.145	0.348
Min. difference density [aÅ^3]	−0.174	−0.221

[a]) $S = [\Sigma[w(F_o^2 - F_c^2)^2]/(n-p)]^{1/2}$. [b]) $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]\Sigma[w(F^2{}_o)^2]\}^{1/2}$; $w^{-1} = \sigma^2\ (F^2{}_o) + (g_1P)2 + g_2P$, where $P = (F_o^2 + 2\,F_c^2)/3$. [c]) $R_1 = \Sigma\,||F_o| - |F_c||/\Sigma\,|F_o|$

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