72. Reactivity of 5,10:8,14-Disecosteroids: An Unusual Rearrangement of Cyclodecene-1,4-dione Systems to Five-Membered-Ring Spiro-γ-lactones

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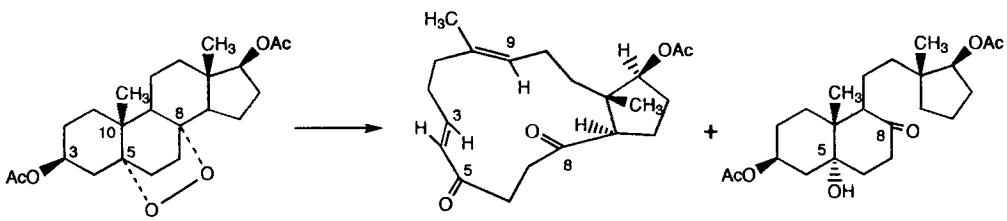
Upon heating in AcOH, the stereoisomeric (*Z*)- and (*R*)-6,9-dioxocyclodex-3-enyl derivatives, **5** and **6**, respectively, obtained by HgO/I_2 oxidation of 5-hydroxy-8-oxo-8,14-seco-5α-androstane-3β,17β-diyl diacetate (**3**), undergo an unusual intramolecular rearrangement to give the corresponding unsaturated (5*R*,9*R*)- and (5*R*,9*S*)-spiro-lactones **7** and **8**, respectively. Hydroxylation of the C=C bond in **7** and **8**, and subsequent glycol cleavage of the resulting diols **9** and **10** afforded the epimeric spiro-lactones (5*R*,9*S*)-**11** and (5*R*,9*R*)-**14**, respectively, and in both cases, the ring-D-containing fragments **12** and **13**.

Introduction. – We reported previously [1] [2] that thermal decomposition of 5,8α-peroxy-5α-androstane-3β,17β-diyl diacetate (**1**) in boiling AcOH afforded, in addition to the desired product formed by fragmentation of the ring junctions A/B and B/C, the (*E*,*E*)-5,8-dioxoandroklasta-3,9-dien-17β-yl acetate (**2**), a product of reductive monofragmentation, *i.e.*, 5-hydroxy-8-oxo-8,14-seco-5α-androstane-3β,17β-diyl diacetate (**3**, *Scheme 1*).

Scheme 1



Starting from the latter compound, we prepared, by oxidative cleavage of its C(5)–C(10) bond, a new type of modified 5,10:8,14-bisfragmentation, steroid derivatives containing an unsaturated ten-membered ring with incorporated γ-dioxo grouping, and we investigated their thermal reactivity in AcOH.

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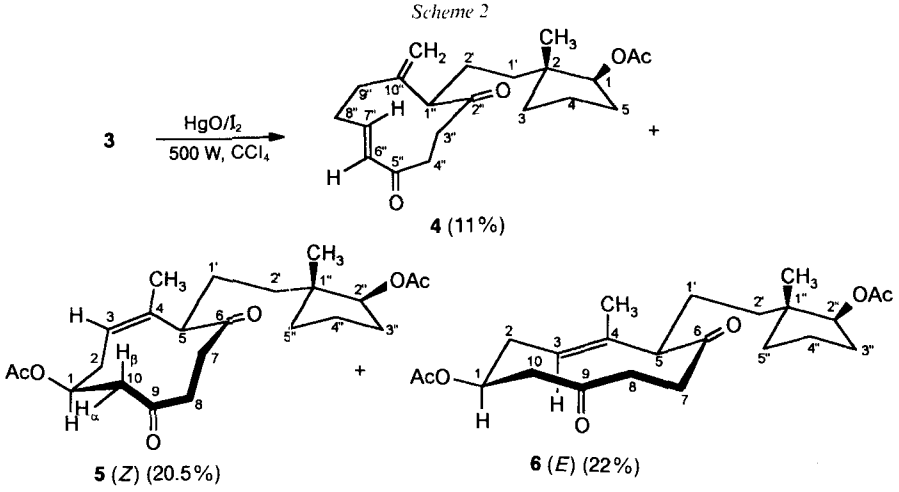
Results and Discussion. – *Oxidative Fragmentation of the C(5)–C(10) Bond in the 8,14-Seco-8-oxoandrostene Derivative* **3**. Oxidation of **3** was performed by methods which are known to effect cleavage of the C(5)–C(10) bond in non-modified 19-methyl-5-hydroxy steroids [3–5], *i.e.*, with $Pb(OAc)_4$ under thermal (14 h) or UV-photolytic conditions (3 h), and with the HgO/I_2 reagent (1.5 h). It was found that, in contrast to the non-modified 5-hydroxy steroids, procedures using $Pb(OAc)_4$ as oxidizing agent were inefficient to induce β-fragmentation in **3**, and in both cases only unchanged starting material was isolated in over 90% yield. However, in the reaction with HgO/I_2, **3** underwent (*Scheme 2*)[2]) β-fragmentation with participation of the C(5)–C(10) bond to give the methylidene derivative **4** (in 11% yield), the formation of which is accompanied by AcOH elimination, and both the expected (*Z*)- and (*E*)-stereoisomeric 6,9-dioxo derivatives **5** and **6**, respectively (in 20.5 and 22% yield)[3])[4]).

Scheme 2



The structures of dioxo derivatives **4**–**6** were deduced from their analytical and spectroscopic data (^{1}H-NMR, ^{13}C-NMR and IR). In the ^{1}H-NMR spectra of these compounds, the signal of the original CH_3(19) group is missing. Instead, in **4** a pair of *singlets* appears at 5.00 and 5.22 ppm, assignable to the protons of a CH_2=C(10″) group, while in **5** and **6** new *singlets* appear at 1.67 and 1.58 ppm, respectively, indicating that in these derivatives the former CH_3(19) group is added to the C(3)=C(4) bond. Differentiation between the (*Z*)- and (*E*)-configuration in the diastereoisomer pair **5** and **6** was accomplished on the basis of their ^{1}H-NMR spectral parameters which were correlated to those observed for the (*Z*)- and (*E*)-stereoisomers in the 5,10-secosteroidal 5-ketone series [3] [7–10][5]). In accordance with the (*Z*)-configuration, the signals for H_β–C(10) and H–C(3) in **5** (due to the

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[2]) For the mechanism of the oxidative β-fragmentation of 5-hydroxy steroids, see [4–6].

[3]) Yields in all *Schemes* refer to the pure samples obtained by chromatography on SiO_2 column.

[4]) In the 5,10:8,14-bisfragmentation products obtained, the steroid A-B-C ring skeleton is completely destroyed. Therefore, in the further text, these compounds, although derived from steroids, are considered as cyclodecenedione or cyclopentane derivatives, the nomenclature of which (naming and numbering of atoms) is accordingly applied.

[5]) The possibility that such a correlation is applicable for the present systems implies that conformations of the ten-membered ring in the (*Z*)- and (*E*)-diseco-dioxo derivatives **5** and **6** in solution (which are represented in *Scheme 2*) should be similar to those determined for the ten-membered rings in (*Z*)- and (*E*)-5-oxo-5,10-seco-cholest-1(10)-en-3β-yl acetates on the basis of their ^{1}H- and ^{13}C-NMR spectra (as described in [8–10]).

deshielding influence by the 9-oxo and 1β-OAc group, resp.) appear at lower fields, 2.97 ppm and 5.51 ppm, respectively, than the corresponding signals of **6**; for this stereoisomer the signal for H_β–C(10) is masked by overlapping with other resonances between 2.20 and 2.75 ppm, and H–C(3) appears at 5.15 ppm. (For additional spectroscopic characteristics supporting the proposed structures, see *Exper. Part.*)

Thermal Reactivity of the (Z)- and (E)-Dioxo Derivatives, **5** *and* **6**, *Respectively, in AcOH.* Compounds **5** and **6** were heated in boiling AcOH, until practically all starting material was consumed (*ca.* 4 h). Analysis of the resulting mixtures indicated that both substrates under these conditions underwent an unusual intramolecular rearrangement to give as the main (and only identifiable) reaction products (*Scheme 3*) the corresponding stereoisomeric spiro-γ-lactones **7** and **8**, respectively (in 66 and 60% yield, resp.).

Spectral data revealed that products **7** and **8** contain the original AcO groups (IR: 1729, 1244 (for **7**), and 1731, 1243 cm^{-1} (for **8**); ^{1}H-NMR: 2*s* at 2.01, 2.03 (for **7**) and 2 overlapped *s* at 2.05 (for **8**)); a five-membered spiro-lactone ring (IR: 1769 (for **7**) and 1771 cm^{-1} (for **8**); ^{13}C-NMR: 176.4 (*s*, C(2)), 94.8 (*s*, C(5)) (for **7**), and 176.0 (*s*, C(2)), 93.0 (*s*, C(5)) (for **8**)), 1 olefinic proton (^{1}H-NMR: *m* at 5.26 and 5.18 ppm, resp.), and 1 Me group at the C=C bond (^{1}H-NMR: *s* at 1.63 ppm (for **7**) and 1.64 ppm (for **8**)), while the (*E*)-configuration of the C=C bond in both **7** and **8** was ascertained on the basis of the measured long-range couplings of their corresponding CH_3–C(1′) signals in the ^{13}C-NMR spectra.

Chemical evidence for the proposed structures **7** and **8** was obtained by cleaving the C=C bond in these compounds (*Scheme 3*). Thus, spiro-lactones **7** and **8** were hydroxylated (OsO_4 method) to give the corresponding unresolvable mixtures of (1′*R*,2′*R*)- and (1′*S*,2′*S*)-dihydroxy derivatives **9** and **10**, respectively (in 71 and 78% yield, resp.), which, by subsequent glycol cleavage with $Pb(OAc)_4$ afforded two fragments each; namely, the corresponding configurationally different (5*R*,9*S*)- and (5*R*,9*R*)-7-acetylspiro-γ-lactones **11** and **14** (in 75% and 78% yield, resp.)[6]), and the steroid-ring-D-containing species, aldehyde **12** (R = H) and acid **13** (R = OH), which, irrespective of the diol mixture used (**9** or **10**), were identical.

The (5*R*,9*S*)-configuration for **11** and the (5*R*,9*R*)-configuration for **14** were deduced from ^{1}H-NMR NOE difference spectroscopy and ^{1}H-NMR spectral analysis (by correlating the spatial arrangement of the newly introduced asymmetric C(5) and C(9) centers with the configuration at C(7), corresponding to the known configuration at C(3) of the starting steroid molecule).

Stereoisomer **11** shows a NOE at H_α–C(6) and H_α–C(8) upon irradiation of the H_α–C(7), and a NOE at H_β–C(8) upon irradiation of H–C(9), indicating that the H–C(9) has the opposite β-orientation with respect to the H_α–C(7), and, consequently, that **11** has the (9*S*)-configuration. In the case of stereoisomer **14**, a NOE at H_α–C(6) and H_α–C(8), and a weak NOE at H–C(9) were observed upon irradiation at H_α–C(7), and also a NOE at H_α–C(8), and weak NOE's at H_α–C(7) and H_α–C(6) upon irradiation of H–C(9), confirming the α-orientation of the latter proton, and the (9*R*)-configuration of **14**. The (5*R*)-configuration for both stereoisomers was deduced from their ^{1}H-NMR characteristics; due to the deshielding influence by the lactone –O–CO– group, the signals of H_α–C(6) in **11** and **14** appear at considerably lower fields (2.60 ppm and 2.53 ppm, resp.) than the signals of the corresponding H_β–C(6) (1.96 ppm and

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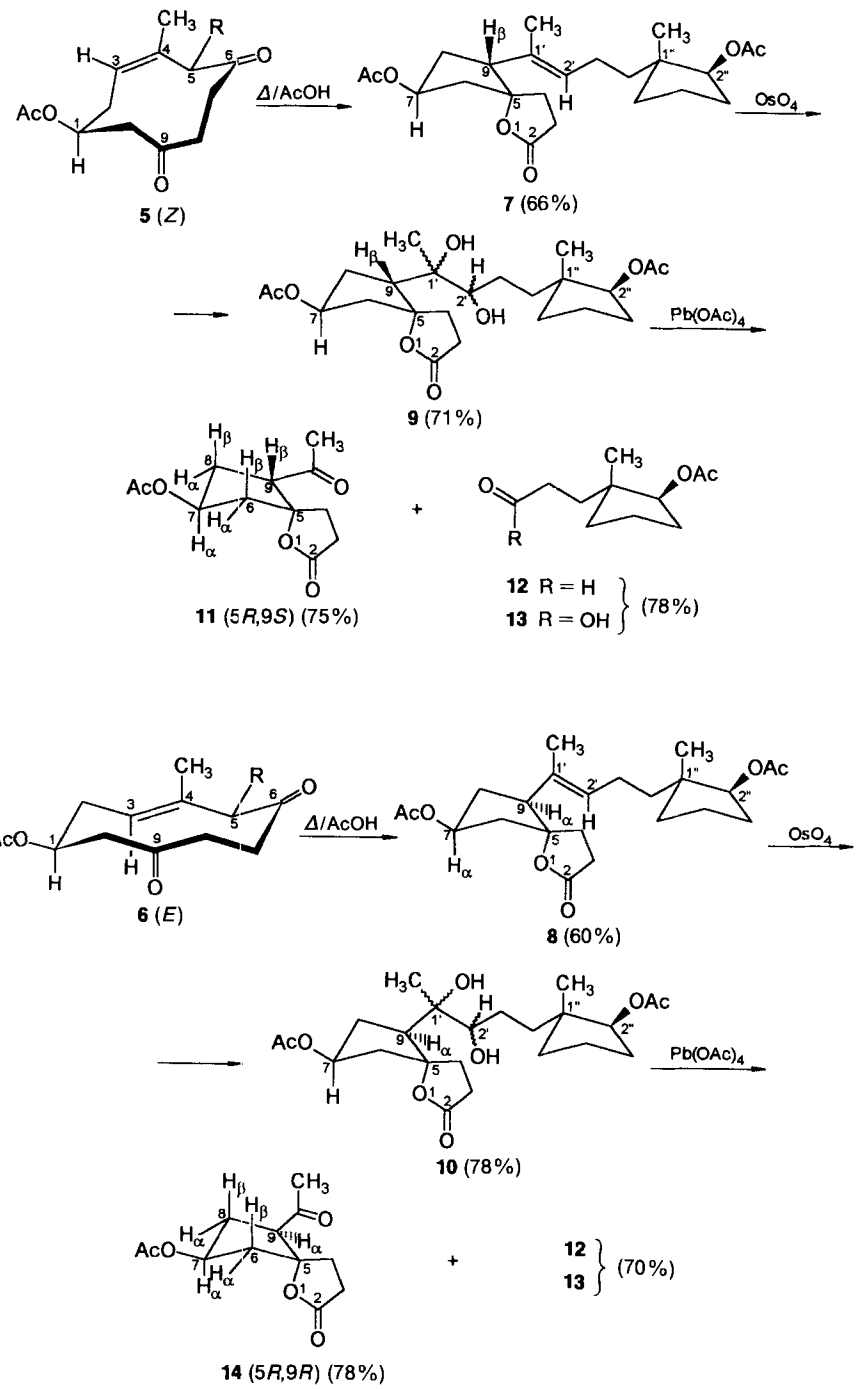
[6]) The apparent inversion of configuration at C(9) in **11** and **14** occurring in the course of oxidative fragmentation of the C(1′)=C(2′) bond in **7** and **8**, respectively, is due to different preferences of the respective C(9) substituents in these compounds.

Scheme 3


Δ/AcOH
OsO4
Pb(OAc)4
5 (Z)
7 (66%)
9 (71%)
11 (5R,9S) (75%)
12 R = H
13 R = OH
(78%)
6 (E)
8 (60%)
10 (78%)
14 (5R,9R) (78%)
(70%)

2.12 ppm, resp.). For the same reason, H_α–C(9) in isomer **14** appears at lower field (3.27 ppm) than the corresponding proton of isomer **11** (3.00 ppm).

Mechanistic and Stereochemical Considerations. Intramolecular rearrangement of the unsaturated (*Z*)- and (*E*)-6,9-dioxo derivatives **5** and **6** to the corresponding spiro-lactones **7** and **8** takes place by participation of three bonds which are incorporated into their dioxo-cyclodecene rings: *i*) the C(3)=C(4) bond; *ii*) the C(9)=O bond; and *iii*) the C(5)–C(6) bond. These bonds are cleaved, while three new bonds are formed, *i.e.*, *i*) a σ-bond between C(3) and C(9); *ii*) an ester bond between the C(9) carbonyl O-atom and the C(6) carbonyl C-atom; and *iii*) a π-bond between C(4) and C(5). Therefore, formally, the observed rearrangement could be considered as an 'ene-type' reaction. However, an acid-catalyzed process comprising the same reaction centers (initiated most probably by protonation of the C(9) carbonyl O-atom) would lead to identical products and, therefore, cannot be excluded on the basis of present evidence.

Introduction of two intramolecular bonds in the ten-membered rings of diseco-dioxo derivatives **5** and **6** results in the formation of two asymmetric centers in the resulting molecules, so that four configurationally different spiro-lactone moieties can be expected in the above transformation, *i.e.*, the stereoisomers with (5*R*,9*R*)-, (5*R*,9*S*)-, (5*S*,9*R*)-, and (5*S*,9*S*)-configuration. Besides, each of these spiro-lactone species may differ in configuration ((*Z*) or (*E*)) at the newly formed C(1′)=C(2′) bond, which leads to a total of eight stereoisomers.

Which of these configurationally different spiro-lactones will be formed in the course of intramolecular rearrangement depends on the configuration of the C(3)=C(4) bond in the starting molecules, as well as on the conformations of the ten-membered rings participating in this transformation.

From molecular models, it can be assumed that the configuration at C(9) of **7** and **8** is determined by the orientation of *H*–C(3) in the conformation of the ten-membered ring from which, by interaction of the C(3)=C(4) bond with C(9), the transannular C(5)–C(9) bond (in the final products **7** and **8**) is formed (conformations with the 'α-oriented' *H*–C(3) leading to the (9*S*)- and conformations with the 'β-oriented' *H*–C(3) to the (9*R*)-stereoisomer)[7][8]). On the other hand, the configuration at C(5) depends on the orientations of the C(6)=O and C(9)=O in the respective conformations, when approaching each other to form the lactone ring ('α-oriented' CO's will give the (5*R*)- and 'β-oriented' CO's the (5*S*)-stereoisomers)[9]). However, the mutual orientation of the *H*–C(5) (α in both unsaturated **5** and **6**) and the CH_3–C(4) (which, depending on the conformations of the ten-membered rings can be 'α-' or 'β-oriented') determines the stereochemistry ((*Z*) or (*E*)) of the newly introduced C(1′)=C(2′) bond.

The above stereochemical considerations and stereospecific formation of the (5*R*,9*R*)-spiro-lactone **7** from the (*Z*)-dioxo derivative **5**, and the (5*R*,9*S*)-spiro-lactone **8** from the (*E*)-isomer **6**, suggest that the reactive conformations of the ten-membered ring

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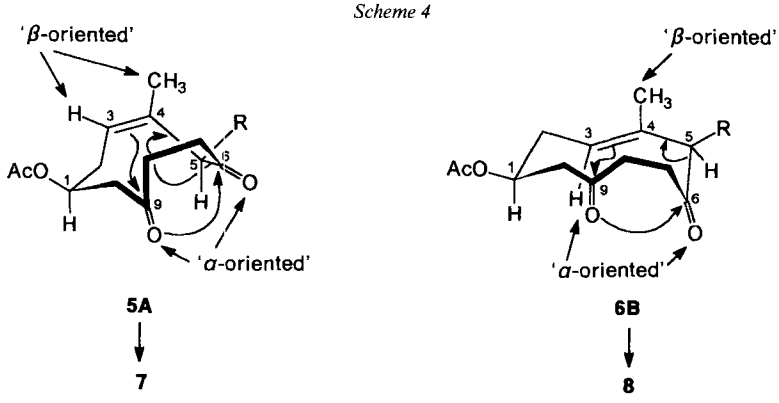
[7]) An atom or group is termed 'α-oriented', if it is directed below the general plane of the ten-membered ring, and 'β-oriented', if it is directed above this plane.

[8]) Due to the conformational flexibility of the ten-membered rings in the (*Z*)- and (*E*)-diseco-dioxo derivatives **5** and **6**, particularly to the mobility of their C=C bonds, the *H*–C(3) in both stereoisomers can be either 'α-' or 'β-oriented'.

[9]) For steric reasons, the C(6)=O and C(9)=O should be oriented in the same way in order to form the lactone ring.

Scheme 4



in the observed intramolecular transformation are of type **A** for the (*Z*)-isomer and of type **B** for the (*E*)-isomer (*Scheme 4*).

Conclusion. – Since all reactions in this study were carried out with optically pure compounds of known chirality (inherited from the starting natural steroid molecule **1**), the obtained spiro-lactones **11** and **14**, and the substituted cyclopentane derivatives **12** and **13** are also enantiomerically pure products. Therefore, they might be useful substrates for the preparation (starting from steroids) of other optically active products containing a spiro-γ-lactone ring or a substituted cyclopentane ring.

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Experimental Part

1. *General*[10]). Removal of solvents was carried out under reduced pressure. Column chromatography (CC): silica gel, 0.063–0.200 mm. TLC: control of reactions and separation of products on silica gel *G* (*Stahl*) with benzene/AcOEt 9:1, 7:3, or 1:1, detection with 50% aq. H_2SO_4 soln. M.p.: uncorrected. UV Spectrum: *Beckman DU-50* spectrophotometer, λ_{max} in nm (ε). IR Spectra: *Perkin-Elmer-337* spectrophotometer: $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Varian FT 80A* or *Bruker AH-360* (^1H at 80 or 360 MHz, ^{13}C at 90.55 MHz); $CDCl_3$ soln. at r.t.; TMS as internal standard; δ in ppm, J in Hz.

2. *HgO/I_2 Oxidation of 5-Hydroxy-8-oxo-8,14-seco-5α-androstane-3β,17β-diyl Diacetate* (**3**). A stirred suspension of **3** (3.043 g, 7.45 mmol), yellow HgO (12.91 g, 59.6 mmol), and I_2 (15.13 g, 59.6 mmol) in CCl_4 (500 ml) was irradiated for 75 min without heating with a 500-W tungsten lamp placed in a central water- and air-cooled jacket. The solid was removed by filtration and the filtrate washed successively with 10% aq. $Na_2S_2O_3$ soln., sat. aq. $NaHCO_3$ soln., H_2O, dried (Na_2SO_4), and evaporated. The resulting mixture (*ca.* 3 g) was separated by CC (SiO_2 (100 g)). Benzene/Et_2O 88:12 gave an oil (279 mg) which was not further investigated. Benzene/Et_2O 86:14 eluted first a mixture (388 mg) which, after chromatography on SiO_2 (30 g), afforded *(1S,2R)-2-methyl-2-{2'-[(1'',R,E)-10''-methylidene-2'',5''-dioxocyclodec-6''-enyl]ethyl}cyclopentyl acetate* (**4**; 283 mg, 11.0%). Oil. $[\alpha]_D^{20} = -66.6$ (c = 1.025, $CHCl_3$). UV (EtOH): 225 (5290). IR (neat): 3070*w*, 1735*s*, 1710*s*, 1670*s*, 1640*m*, 1250*s*. ^1H-NMR (360 MHz): 0.84 (*s*, Me–C(2)); 1.96 (*s*, AcO); 4.65 (*t*, J = 6, H–C(1)); 5.00, 5.22 (2*s*, CH_2=C(10'')); 5.67 (*d*, J = 16.5, H–C(6'')); 5.81 (*ddd*, J = 16.5, 9.5, 6, H–C(7'')). ^{13}C-NMR: 210.4 (*s*, C(2'')); 204.3 (*s*, C(5'')); 171.0 (*s*, Me*C*OO); 144.9 (*s*, C(10'')); 143.6 (*d*, C(7'')); 130.6 (*d*, C(6'')); 118.4 (*t*, *C*H_2=C(10'')); 81.7 (*d*, C(1)); 65.1 (*d*, C(1'')); 44.5 (*s*, C(2)); 38.0 (*t*, C(4'')); 37.5 (*t*, C(1')); 37.3 (*t*, C(3'')); 36.4 (*t*, C(3)); 33.8 (*t*, C(9'')); 30.4 (*t*, C(5)); 28.8 (*t*,

[10]) IR and ^1H-NMR (80 MHz) measurements and elemental analyses were carried out in the Laboratories for Instrumental Analysis of the Faculty of Chemistry, Belgrade. ^1H-NMR at 360 MHz and ^{13}C-NMR measurements were performed at *Ciba-Geigy Ltd.*, Basel, Switzerland.

C(8″)); 24.3 (*t*, C(4)); 21.4 (*q*, *Me*COO); 20.4 (*t*, C(2′)); 19.3 (*q*, *Me*–C(2)). Anal. calc. for $C_{21}H_{30}O_4$ (346.471): C 72.80, H 8.73; found: C 72.56, H 8.43.

Further benzene/Et_2O 86:14 fractions contained a mixture (713 mg) from which after chromatography on SiO_2 (40 g) was obtained *(1S,5R,Z)-5-{2′-[(1″R,2″S)-2″-(acetoxy)-1″-methylcyclopentyl]ethyl}-4-methyl-6,9-dioxocyclodec-3-enyl acetate* (**5**, 621 mg, 20.5%). Oil. $[\alpha]_D^{20} = -54.0$ (*c* = 1.29, $CHCl_3$). IR (neat): 1737*s*, 1708*s*, 1245*s*. ^{1}H-NMR (360 MHz): 0.92 (*s*, Me–C(1″)); 1.67 (*s*, Me–C(4)); 2.00, 2.05 (2*s*, 2 AcO); 2.97 (*dd*, *J* = 15.6, 10.8, H_β–C(10)); 3.15 (*dd*, *J* = 8.4, 6, H–C(5)); 4.71 (*dd*, *J* = 7.2, 6, H–C(2″)); 5.42 (*m*, H–C(1)); 5.51 (*dd*, *J* = 12, 6, H–C(3)). ^{13}C-NMR: 209.6 (*s*, C(6)); 209.0 (*s*, C(9)); 170.7, 169.9 (2*s*, 2 Me*C*OO); 136.7 (*s*, C(4)); 124.0 (*d*, C(3)); 81.7 (*d*, C(2″)); 70.8 (*d*, C(1)); 53.7 (*d*, C(5)); 44.4 (*s*, C(1″)); 43.6 (*t*, C(10)); 41.3 (*t*, C(7)); 39.2 (*t*, C(8)); 37.2 (*t*, C(2′)); 36.4 (*t*, C(5″)); 30.4 (*t*, C(3″)); 30.2 (*t*, C(2)); 23.5 (*t*, C(4″)); 21.2, 21.1 (3*q*, 2 *Me*COO, *Me*–C(4)); 20.3 (*t*, C(1′)); 19.2 (*q*, *Me*–C(1″)). Anal. calc. for $C_{23}H_{34}O_6$ (406.525): C 67.95, H 8.43; found: C 68.13, H 8.14.

Further elution with benzene/Et_2O 86:14 afforded an oil (740 mg) which was chromatographed on SiO_2 (40 g) to give *(1S,5R,E)-5-{2′-[(1″R,2″S)-2″-(acetoxy)-1″-methylcyclopentyl]ethyl}-4-methyl-6,9-dioxocyclodec-3-enyl acetate* (**6**, 677 mg, 22.4%). Oil. $[\alpha]_D^{20} = -166.4$ (*c* = 0.78, $CHCl_3$). IR (neat): 1735*s*, 1705*s*, 1240*s*. ^{1}H-NMR (360 MHz): 0.91 (*s*, Me–C(1″)); 1.58 (*s*, Me–C(4)); 2.00, 2.04 (2*s*, 2 AcO); 3.00 (*m*, H–C(5)); 4.73 (*dd*, *J* = 7.2, 6, H–C(2″)); 5.15 (*ddd*, *J* = 12, 7.8, 1.2, H–C(3)); 5.38 (*m*, H–C(1)). ^{13}C-NMR: 209.6 (*s*, C(6)); 205.5 (*s*, C(9)); 170.7, 169.9 (2*s*, 2 Me*C*OO); 81.7 (*d*, C(2″)); 71.5 (*d*, C(1)); 64.0 (*d*, C(5)); 47.9 (*t*, C(10)); 44.5 (*s*, C(1″)); 41.0 (*t*, C(2′)); 37.5 (*t*, C(8)); 37.4 (*t*, C(7)); 36.3 (*t*, C(5″)); 32.9 (*t*, C(2)); 30.3 (*t*, C(3″)); 23.5 (*t*, C(4″)); 21.3, 21.2 (2*q*, 2 *Me*COO); 20.3 (*t*, C(1′)); 19.2 (*q*, *Me*–C(1″)). Anal. calc. for $C_{23}H_{34}O_6$ (406.525): C 67.95, H 8.43; found: C 67.93, H 8.22.

Benzene/Et_2O 80:20 and 70:30 gave a complex mixture from which no defined product could be isolated.

Thermolysis of **5** *in AcOH*. A soln. of **5** (103 mg) in AcOH (30 ml) was refluxed with stirring for 4 h. The solvent was removed by distillation and the residue chromatographed on SiO_2 (12 g). Elution with benzene/Et_2O 88:12 afforded a mixture (14 mg) from which no defined product could be isolated. Benzene/Et_2O 84:16 eluted *(5R,7S,9R)-9-{(E)-4′-[(1″R,2″S)-2″-(acetoxy)-1″-methylcyclopentyl]-1′-methylbut-1′-enyl}-2-oxo-1-oxaspiro[4.4]non-7-yl acetate* (**7**, 68 mg, 66.0%). Oil. $[\alpha]_D^{20} = +62.6$ (*c* = 1.00, $CHCl_3$). IR (CH_2Cl_2): 1769*s*, 1729*s*, 1244*s*. ^{1}H-NMR (360 MHz): 0.94 (*s*, Me–C(1″)); 1.63 (*s*, Me–C(1′)); 2.01, 2.03 (2*s*, 2 AcO); 4.79 (*dd*, *J* = 7.2, 6, H–C(2″)); 5.26 (*m*, H–C(7)); 5.34 (*t*, *J* = 7, H–C(2′)). ^{13}C-NMR: 176.4 (*s*, C(2)); 171.0, 170.7 (2*s*, 2 *Me*COO); 131.5 (*d*, C(2′)); 131.0 (*s*, C(1′)); 94.8 (*s*, C(5)); 81.7 (*d*, C(2″)); 73.2 (*d*, C(7)); 55.7 (*d*, C(9)); 46.9 (*t*, C(6)); 44.6 (*s*, C(1″)); 39.6 (*t*, C(5″)); 36.5 (*t*, C(4)); 36.0 (*t*, C(4′)); 30.4 (*t*, C(3″)); 30.3 (*t*, C(3)); 29.4 (*t*, C(8)); 23.6 (*t*, C(4″)); 21.3 (2*q*, 2 *Me*COO); 20.3 (*t*, C(3′)); 19.3 (*q*, *Me*–C(1″)); 14.9 (*q*, *Me*–C(1′)). Anal. calc. for $C_{23}H_{34}O_6$ (406.525): C 67.95, H 8.43; found: C 68.13, H 8.28.

Thermolysis of **6** *in AcOH*. A soln. of **6** (91 mg) in AcOH (30 ml) was refluxed with stirring for 4 h. The mixture was worked up as described above, and the residue chromatographed on SiO_2 (12 g). Benzene/Et_2O 90:10 eluted *(5R,7S,9S)-9-{(E)-4′-[(1″R,2″S)-2″-(acetoxy)-1″-methylcyclopentyl]-1′-methylbut-1′-enyl}-2-oxo-1-oxaspiro[4.4]non-7-yl acetate* (**8**, 54 mg, 59.3%). Oil. $[\alpha]_D^{20} = +8.7$ (*c* = 1.77, $CHCl_3$). IR (CH_2Cl_2): 1771*s*, 1731*s*, 1243*s*. ^{1}H-NMR (360 MHz): 0.94 (*s*, Me–C(1″)); 1.64 (*s*, Me–C(1′)); 2.05 (*s*, 2 AcO); 4.80 (*dd*, *J* = 7.2, 6, H–C(2″)); 5.18 (*m*, H–C(7)); 5.27 (*t*, *J* = 7, H–C(2′)). ^{13}C-NMR: 176.0 (*s*, C(2)); 170.7, 170.3 (2*s*, 2 Me*C*OO); 131.5 (*s*, C(1′)); 129.5 (*d*, C(2′)); 93.0 (*s*, C(5)); 81.3 (*d*, C(2″)); 71.2 (*d*, C(7)); 53.5 (*d*, C(9)); 44.6 (*t*, C(6)); 44.4 (*s*, C(1″)); 39.5 (*t*, C(5″)); 36.3 (*t*, C(4′)); 34.4 (*t*, C(4)); 30.1 (*t*, C(3″)); 29.0 (*t*, C(3)); 28.8 (*t*, C(8)); 23.2 (*t*, C(4″)); 21.0, 20.9 (2*q*, 2 *Me*COO); 20.1 (*t*, C(3′)); 19.1 (*q*, *Me*–C(1″)); 15.9 (*q*, *Me*–C(1′)). Anal. calc. for $C_{23}H_{34}O_6$ (406.525): C 67.95, H 8.43; found: C 67.73, H 8.44.

Elution with benzene/Et_2O 88:12 afforded a complex mixture (26 mg) from which no defined product could be isolated.

Hydroxylation of **7**. To a soln. of **7** (640 mg) in benzene (30 ml) containing pyridine (2.5 ml), OsO_4 (460 mg) was added and the mixture left at r.t. for 24 h. After dilution with AcOEt (100 ml), H_2S was bubbled through the soln. for 1 h and the separated solid removed by filtration through a *Celite* mat. The solvents were evaporated leaving an oil which was purified by CC (SiO_2 (40 g)). Elution with Et_2O afforded an unseparable mixture of the *(5R,7S,9R)-9-{(1′R,2′R)- and (1′S,2′S)-4′-[(1″R,2″S)-2″-(acetoxy)-1″-methylcyclopentyl]-1′,2′-dihydroxybutyl}-2-oxo-1-oxaspiro[4.4]non-7-yl acetate* (**9**, 492 mg, 70.9%), which was as such analyzed. Oil. $[\alpha]_D^{20} = +9.9$ (*c* = 1.00, $CHCl_3$). IR (neat): 3480*s*, 1770*s*, 1735*s*, 1250*s*, 930*m*, 755*m*. ^{1}H-NMR (80 MHz): 0.85 (*s*, Me–C(1″)); 1.12, 1.18 (parts of 2*s*, Me–C(1′)); 1.97 (*s*, 2 AcO); 3.10–3.40 (br. *m*, H–C(2′)); 4.75 (*m*, H–C(2″)); 5.15 (*m*, H–C(7)). Anal. calc. for $C_{23}H_{36}O_8$ (440.541): C 62.71, H 8.24; found: C 62.56, H 8.35.

Hydroxylation of **8**. To a soln. of **8** (159 mg) in benzene (10 ml) containing pyridine (1 ml) OsO_4 (115 mg) was added. The mixture was left at r.t. for 24 h and worked up as described above to give an oil which was chromatographed on SiO_2 (15 g). Elution with Et_2O afforded an unseparable mixture of the *(5R,7S,9S)-9-{(1′R,2′R)- and (1′S,2′S)-4′-[(1″R,2″S)-2″-(acetoxy)-1″-methylcyclopentyl]-1′,2′-dihydroxybutyl}-2-oxo-1-*

oxaspiro[4.4]non-7-yl acetate (**10**, 135 mg, 78.3%), which was as such analyzed. Oil. $[\alpha]_D^{20} = +18.5$ ($c = 1.00$, $CHCl_3$). IR (neat): 3490*s*, 1770*s*, 1732*s*, 1245*s*, 1025*m*, 755*m*. ^{1}H-NMR (80 MHz): 0.80, 0.83 (parts of 2*s*, Me–C(1″)); 1.00, 1.04 (parts of 2*s*, Me–C(1′)); 1.95 (*s*, 2 AcO); 3.00–3.45 (br. *m*, H–C(2′)); 4.75 (*m*, H–C(2″)); 5.05 (*m*, H–C(7)). Anal. calc. for $C_{23}H_{36}O_8$ (440.541): C 62.71, H 8.24; found: C 62.46, H 8.39.

Glycol Cleavage of **9**. $Pb(OAc)_4$ (280 mg) and **9** (240 mg) in dry benzene (27 ml) were stirred at r.t. for 30 min. The mixture was diluted with Et_2O, filtered through a *Celite* mat, and the insoluble precipitate washed with Et_2O and CH_2Cl_2. The org. soln. was thoroughly washed with H_2O, dried (Na_2SO_4), and evaporated to dryness leaving an oil mixture (211 mg) which was separated by CC (SiO_2 (10 g)). Elution with toluene/Et_2O 90:10 gave *(1S,2R)-2-methyl-2-(3′-oxopropyl)cyclopentyl acetate* (**12**, 59 mg, 62.1%). Oil. $[\alpha]_D^{20} = +22.1$ ($c = 1.24$, $CHCl_3$). IR (neat): 2722*w*, 1734*s*, 1250*s*. ^{1}H-NMR (360 MHz): 0.94 (*s*, Me–C(2)); 2.05 (*s*, AcO); 2.48 (*m*, 2 H–C(2′)); 4.78 (*t*, $J = 7$, H–C(1)); 9.80 (*s*, CHO). ^{13}C-NMR: 202.0 (*d*, C(3′)); 170.6 (*s*, Me*C*OO); 80.8 (*d*, C(1)); 43.7 (*s*, C(2)); 39.5 (*t*, C(2′)); 36.2 (*t*, C(3)); 31.2 (*t*, C(5)); 29.9 (*t*, C(1′)); 20.9 (*q*, *Me*COO); 19.9 (*t*, C(4)); 18.9 (*q*, *Me*–C(2)). Anal. calc. for $C_{11}H_{18}O_3$ (198.265): C 66.64, H 9.15; found: C 66.81, H 8.90.

Elution with toluene/Et_2O 70:30 afforded *(5R,7S,9S)-9-acetyl-2-oxo-1-oxaspiro[4.4]non-7-yl acetate* (**11**, 86 mg, 74.7%). M.p. 55–57° (from Et_2O). $[\alpha]_D^{20} = +4.4$ ($c = 0.39$, $CHCl_3$). IR (KBr): 1775*s*, 1736*s*, 1713*s*, 1246*s*. ^{1}H-NMR (360 MHz): 1.96 (*dd*, $J = 15.6, 4.8$, H_β–C(6)); 2.05 (*s*, AcO); 2.20 (*s*, MeCO); 2.18, 2.28 (2*m*, 2 H–C(4)); *ca.* 2.55 (3*m*, 2 H–C(8), H–C(3)); 2.60 (*dd*, $J = 15.6, 7.5$, H_α–C(6)); 2.76 (*m*, H–C(3)); 3.00 (*dd*, $J = 12, 7.5$, H–C(9)); 5.30 (*m*, H–C(7)). ^{13}C-NMR: 205.9 (*s*, Me*C*O); 175.3 (*s*, C(2)); 169.8 (*s*, Me*C*OO); 91.6 (*s*, C(5)); 72.0 (*d*, C(7)); 57.8 (*d*, C(9)); 46.2 (*t*, C(6)); 34.2 (*t*, C(8)); 30.9 (*t*, C(4)); 29.8 (*q*, *Me*CO); 28.3 (*t*, C(3)); 20.5 (*q*, *Me*COO). Anal. calc. for $C_{12}H_{16}O_5$ (240.260): C 59.99, H 6.71; found: C 60.05, H 6.80.

Toluene/Et_2O 60:40 and 50:50 eluted *3-[(1′R,2′S)-2′-(acetoxy)-1′-methylcyclopentyl]propionic acid* (**13**, 16 mg, 15.6%). Oil. $[\alpha]_D^{20} = +3.5$ ($c = 0.29$, $CHCl_3$). IR (neat): 3700–2500*w*, 1736*s*, 1713*s*, 1374*m*, 1249*s*. ^{1}H-NMR (80 MHz): 0.86 (*s*, Me–C(1′)); 1.98 (*s*, AcO); 4.75 (*t*, $J = 7$, H–C(2′)); 8.5–9.2 (br., COO*H*). Anal. calc. for $C_{11}H_{18}O_4$ (214.265): C 61.66, H 8.47; found: C 61.85, H 8.27.

Glycol Cleavage of **10**. $Pb(OAc)_4$ (240 mg) and **10** (178 mg) in dry benzene (20 ml) were stirred at 60° for 30 min. The mixture was diluted with Et_2O, filtered through a *Celite* mat, and the insoluble precipitate washed with Et_2O and CH_2Cl_2. The combined org. soln. was washed with sat. aq. $NaHCO_3$ soln. and H_2O, dried (Na_2SO_4), and evaporated to dryness. The resulting mixture was separated by CC (SiO_2 (12 g)). Toluene/Et_2O 90:10 eluted **12** (15 mg, 18.7%). Spectral data are identical to those reported for **12** obtained from **9**.

Elution with toluene/Et_2O 70:30 and 60:40 afforded *(5R,7S,9R)-9-acetyl-2-oxo-1-oxaspiro[4.4]non-7-yl acetate* (**14**, 76 mg, 78.2%). M.p. 100–101°. $[\alpha]_D^{20} = -48.0$ ($c = 0.90$, $CHCl_3$). IR (KBr): 1761*s*, 1730*s*, 1708*s*, 1273*s*, 1243*s*, 1220*s*. ^{1}H-NMR (360 MHz): 2.00 (*m*, 1 H); 2.03 (*s*, AcO); 2.12 (*dd*, $J = 16.2, 4.8$, H_β–C(6)); 2.24 (*s*, MeCO); 2.30 (2*m*, 2 H); 2.53 (*dd*, $J = 16.2, 7.2$, H_α–C(6)); 2.60 (2*m*, 2 H); 2.65 (*dt*, $J = 16.2, 9$, H_α–C(8)); 3.27 (*t*, $J = 8.4$, H–C(9)); 5.23 (*m*, H–C(7)). ^{13}C-NMR: 207.3 (*s*, Me*C*O); 175.7 (*s*, C(2)); 170.6 (*s*, Me*C*OO); 92.7 (*s*, C(5)); 72.2 (*d*, C(7)); 58.2 (*d*, C(9)); 44.7 (*t*, C(6)); 34.2 (*t*, C(8)); 31.0 (*q*, *Me*CO); 29.2 (*t*, C(4)); 29.1 (*t*, C(3)); 21.2 (*q*, *Me*COO). Anal. calc. for $C_{12}H_{16}O_5$ (240.260): C 59.99, H 6.71; found: C 60.05, H 6.80.

Aq. $NaHCO_3$ soln. was acidified with 6M HCl and extracted with CH_2Cl_2 (3 × 60 ml). The combined CH_2Cl_2 extract was dried (Na_2SO_4) and evaporated to dryness affording **13** (44 mg, 50.8%) which was identical (TLC, IR, ^{1}H-NMR) to the acid **13** obtained from **9**.

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