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Original scientific paper

Lead tetraacetate oxidation of the Diels-Alder adduct of 7-dehydrocholestryl acetate with maleic anhydride

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The Diels-Alder adduct (**3**), obtained by cycloaddition of 7-dehydrocholesteryl acetate (**1**) and maleic anhydride (**2**), was heated at *ca.* 90 °C with a large excess of lead tetraacetate in pyridine solution for 5 h. Under these conditions, compound **3** underwent lactonization with the participation of the olefinic Δ^6-double bond to give two isomeric monolactone derivatives, **9** and **10** (in a total yield of *ca.* 6%), and the bislactone product **11** (in 11.5% yield). The starting material was recovered in 36% yield.

Keywords: Diels-Alder adduct, cholesteryl acetate, maleic anhydride, oxidative mono- and bis-lactonization.

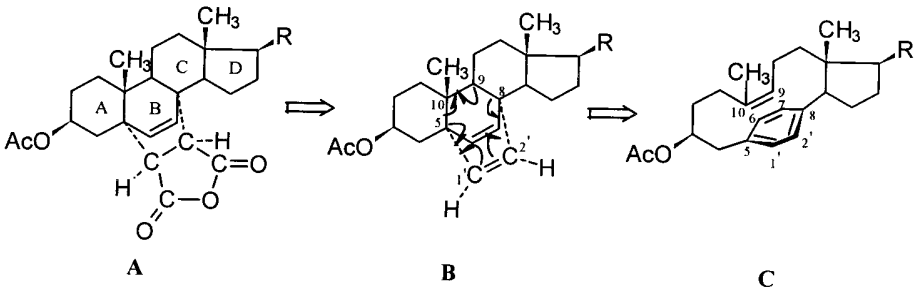
INTRODUCTION

In the course of work aimed at the preparation of modified steroids containing a 14-membered ring instead of the natural A-B-C-ring skeleton,[1-3] we considered also the possibility of using Diels-Alder adducts of type **A** (Scheme 1) as intermediates to these 5,10:8,9-diseco derivatives. The key step in the anticipated reaction scheme was the lead tetraacetate oxidative decarboxylation of the adduct **A** to the $\Delta^{6:1',2'}$-diene **B** (Scheme 1). The latter compound, by the known thermal cyclorеversion reaction [4,5] (involving the C(5)–C(10) and C(8)–C(9) σ-bonds, and the C(1')=C(2') π-bond, [6,7] was expected to be rearranged to the desired 14-membered ring compoud **C** with an incorporated aromatic ring ("ansa" steroid)**.

In the present paper the results obtained in the course of these investigations are presented.

* Serbian Chemical Society active member.

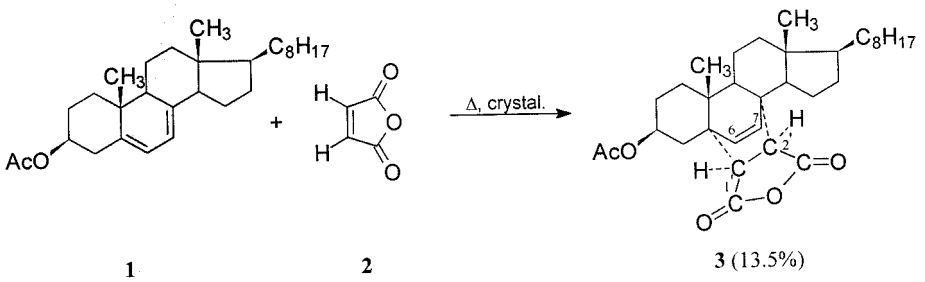
** In the original procedure for the preparation of "ansa" steroids the C(1')=C(2') double bond of the Diels-Alder adducts was formed in the course of the synthesis which consisted of the cycloaddition of steroidal 5,7-dienes with an acetylenic dienophile, *i.e.,* the propargylic aldehyde. [6,7] Since most other acetylenic dienophiles react with steroidal 5,7-dienes affording only the 7-"ene" derivatives, our approach, *i.e.*, the subsequent introduction of the C(1')=C(2') double bond into the primarily formed $\Delta^{1',2'}$-saturated Diels-Alder system, seemed to offer an opportunity for a more general synthetic application of the reaction.



Scheme 1.

RESULTS AND DISCUSSION

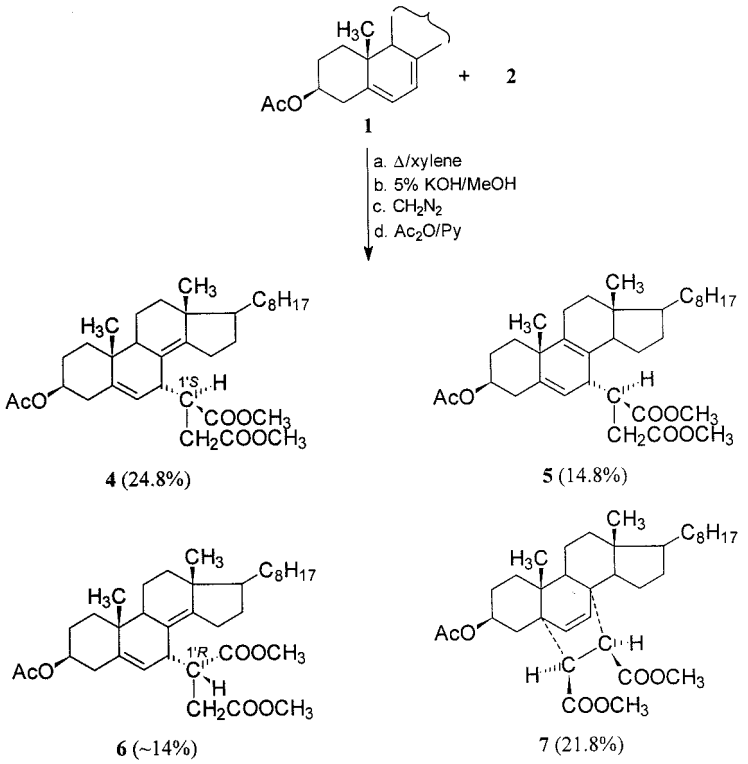
The Diels-Alder adduct used in the study was prepared by the condensation of 7-dehydrocholersteryl acetate (**1**) with maleic anydride **2***. The reaction was carried out under experimental conditions similar to those previously applied to the analogous ergosteryl system,[8,9] *i.e.*, 7-dehydrocholesteryl acetate (**1**) and maleic anhydride were heated under argon in xylene solution at reflux for 16 –18 h. The direct recrystallization (from acetone/methanol and methanol) of the isolated reaction mixture afforded pure crystals of the Diels-Alder adduct **3**, however, in a poor yield of only 13.5% (Scheme 2).



Scheme 2.

The structure **3** was deduced on the basis of the analytical ($C_{33}H_{48}O_5$) and spectral data of the above adduct. The IR spectrum of **3** contained absorption at 1848 and 1775 cm^{-1}, typical for a 5-membered ring anhydride. Its ^{1}H-NMR spectrum showed an AB pattern at δ = 2.90 and 3.51 ppm, J = 8.4 Hz (attributable to the C-1' and C-2' protons) and also a lower field AB system at δ = 5.85 and 6.27 ppm, J = 8.6 Hz (due to vinyl protons at the Δ^6-double bond). Besides, the number of primary, secondary, tertiary and H-free C-atoms detectable in the DEPT ^{13}C-NMR spectrum

* Although the reaction of ergosteryl acetate with maleic anhydride has been thoroughly investigated,[8,9] a similar study in which 7-dehydrocholesteryl acetate was used as the diene and maleic anhydride as the dienophile, has not yet been reported.



Scheme 3.

of **3** (6 CH_3, 10 CH_2, 10 CH (of which 2 olefinic) and 7 H-free C-atoms) is in complete agreement with the proposed structure.*

Since the yield of adduct **3** (given in Scheme 2) refered to the yield of crystallization, in order to establish the yield of its formation, and also to identify other products of the reaction, in a separate experiment the isolated mixture was sequentially treated with 5% methanolic potassium hydroxide, ethereal diazomethane, and acetic acid anhydride in pyridine. The acetoxy dimethyl esters thus formed (Scheme 3) were separated by column chromatography on silica gel to give the $\Delta^{8(14)}$-(1'*S*)-7a-ene derivative **4** (in 24.8% yield), the isomeric $\Delta^{8(9)}$-7a-ene derivate **5** (in 14.8% yield), a mixture containing as the main component $\Delta^{8(14)}$-(1'*R*)-7a-ene **6** (»14%), and the 5a, 8a-cycloadduect **7** (in 21.8% yield). Their structures were determined as follows.

The ^{1}H-NMR spectra of compounds **4**** and **5** showed a signal for one olefinic proton which appared at δ 5.13 ppm (*dd, J* = 3.4, 1.2 Hz), and δ 5.09 ppm (*br.d, J* =

* The stereochemistry of the cycloadduct **3** is as expected according to the known "rule of a-attack" upon steroids, and the preference of maleic anhydride to add dienophilically in an endo manner.[10]

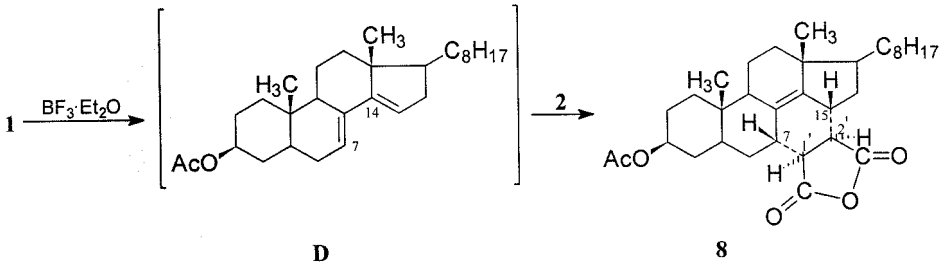
** The ^{1}H-NMR spectra of the $\Delta^{8(14)}$-(1'*S*)- and $\Delta^{8(14)}$ - (1'*R*)-enes **4** and **6** were almost identical, however, isomer **6**, due to insufficient purity, could not be fully characterized (see Experimental).

2.4 Hz), respectively, indicating the presence of the Δ^5-double bond*. In addition, the ^{13}C-NMR spectra of these compounds contained H-free C-atom peaks, at δ 147.6 and 143.4 ppm for **4**, and δ 140.0 and 136.3 ppm for **5**, corresponding to a tetrasubstituted ($\Delta^{8(14)}$ and $\Delta^{8(9)}$, respectively) olefinic double bond. That compounds **4** and **6** have the $\Delta^{8(14)}$- and compound **5** the $\Delta^{8(9)}$-structure was deduced from the ^{1}H-NMR chemical shifts of their angular methyl groups. In **4** and **6**, in common with other $\Delta^{8(14)}$-unsaturated steroids,[9,11] the C-18 and C-19 methyl group singlets coincided at δ 0.87 ppm, while in **5** (in agreement with the values observed in analogous systems [9,11]), these singlets appeared at δ 0.67 and 1.23 ppm.

On the other hand, the spectral evidence obtained for acetoxy dimethyl ester **7** (for details see Experimental) was consistent with the structure of the normal Diels-Alder adduct, thus showing that this compound arises from the cycloadduct **3**.

From the above results in follows that in the reaction of 7-dehydrocholesteryl acetate with maleic anhydride, cycloaddition is considerably suppressed by the competing "ene"-process which, in the steroidal 5,7-dienes, involves 14α- or 9α hydrogen abstraction by the dienophile and results in the formation of the corresponding $\Delta^{8(14)}$- and $\Delta^{8(9)}$-7α adduct.**

In an attempt to improve the yield of the Diels-Alder adduct **3**, the reaction was performed in the presence of borontrifluoride etherate. However, instead of the expected 5α, 8α-cycloadduct **3**, the rearranged 7α, 15α-isomer **8** was isolated as the sole reaction product. Obviously, in the presence of the Lewis catalyst, isomerization of the homoannular 5,7-diene to the more stable heteroannular 7,14-diene system **D**, preceded the Diels-Alder reaction (Scheme 4).



D 8

Scheme 4.

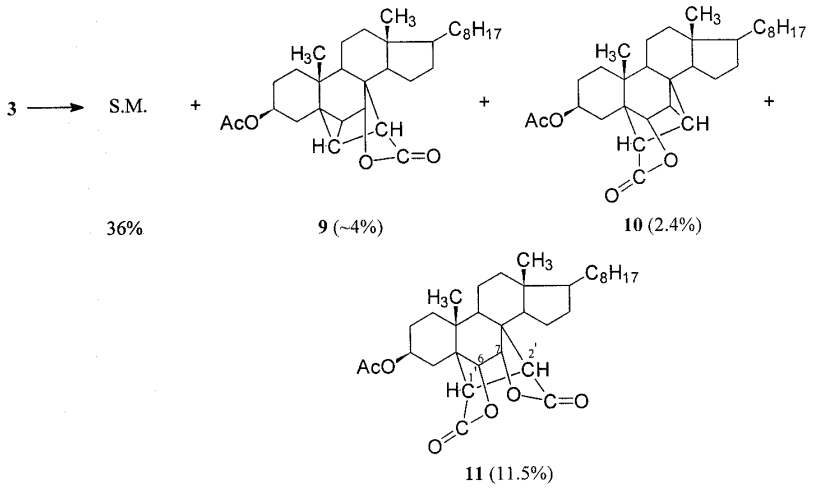
Structure **8** was assigned from the absence of any vinyl proton peaks in the ^{1}H-NMR spectrum, and the presence of two olefinic H-free C-atom peaks in the

* The olefinic C-6 proton in these compounds is coupled vicinally to the C-7 proton and allylically to the C-4 protons. The observed small vicinal coupling constant (»2-3 Hz) is in agreement with the dihedral angle (Dreiding models) of 55 ° between the C-6 and C-7 proton, thus confirming the expected 7α-orientation of the dimethoxycarbonyl ethano group in compounds **4** and **5**. [12]

** For the mechanism of the "ene" reaction see Refs. 9 and 13.

^{13}C-NMR spectrum of **8** (appearing at d 148.4 and 128.7 ppm). For additional spectral data confirming structure **8** see Experimental.

In order to introduce the 1,2-olefinic double bond into the 5a, 8a-adduct **3**, its oxidative bisdecarboxylation with lead tetraacetate was attempted under various experimental conditions. It was found that by standard procedures, [14] *i.e.,* upon heating compound **3** with a slight excess of lead tetraacetate in benzene or pyridine solution at 50-80 °C for 2 h, only unchanged starting material was recovered in almost quantitative yield (over 90%). A similar result was obtained when the reaction was carried out in the presence of $Cu(OAc)_2$ catalyst. However, under more vigorous conditions, when adduct **3** was heated with a large excess of lead tetraacetate in pyridine at *cca.* 90 °C for 5 h, it was partially attacked by the oxidant affording, in addition to the starting material (recovered in 36% yield), two isomeric ill-resolvable monolactones **9** and **10*** (in a total yield of *cca.* 6%), and a crystalline bislactone product **11** (in 11.5% yield) (Scheme 5).**



Sheme 5.

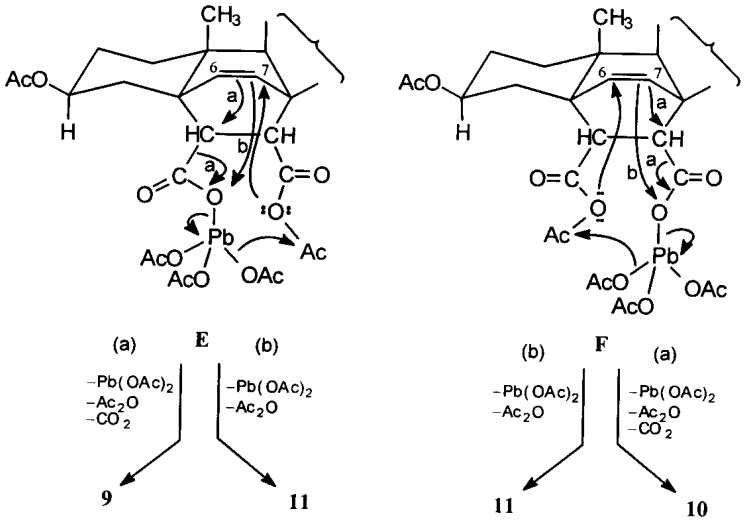
The IR spectra of derivatives **9** and **10** showed the characteristic absorption for a cyclopropane ring (n at 3030 and 3040 cm^{-1}, respectively) and for a 5-memered lactone ring (n at *cca.* 1790 cm^{-1}), while the spectral data of compound **11** revealed that it contained two 5-membered lactone rings (IR: strong absorption at n 1800 cm^{-1}; ^{1}H-NMR: two AB systems at d 2.41 and 3.10 ppm (for the H–C(1') and H–C(2')) and d 4.48 and 5.03 ppm (for the H–C(6) and H–C(7)); ^{13}C–NMR (H-decoupled): two singlets at d 176.7 and 175.4 ppm (for the two carbonyl groups of the lactone functions), and no signals for an olefinic double bond.

* The structures of monolactones **9** and **10** given in Scheme 5 are tentative and can be interchanged.

** Some unsaturated carboxylic acids are reported to react with lead tetraacetate to give cyclopopyl lactones [15] and bislactones. [16]

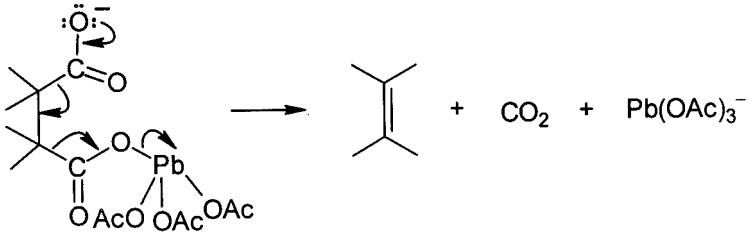
From the above it can be concluded that the lead tetraacetate oxidation of adduct **3** results in the mono- and bislactonization of its D^{6}-double bond (the former process being accompanied with closure of the cyclopropane ring), rather than in the expected bisdecarboxylation with formation of the $D^{1',2'}$-double bond.

Such a behaviour could be explained by the tentative mechanism shown in Scheme 6. It can be assumed that the reaction proceeds *via* the lead tetraacylate intermediates **E** and **F**, respectively.



Scheme 6.

Since similar lead tetraacylate species are also anticipated for the oxidative bisdecarboxylation of diacids[14] (Scheme 7), the obtained results suggest that, most probably, due to the close proximity of the D^{6}-double bond to the lead tetraacylate reacting center in **E** and **F**, the former process becomes more favourable, thus indicating that the $D^{1',2'}$-double bond cannot be subsequently introduced into Diels-Alder adducts of type **A** (Scheme 1).



Scheme 7.

EXPERIMENTAL

General. Removal of solvents was carried out under reduced pressure. Column chromatography (CC): silica gel, 0.063–0.200 mm. TLC: control of the reaction and the separation of products on silica gel G (Stahl) with benzene/AcOEt 9:1 and 7:3, detection with 50% aq. H_2SO_4 soln. M.p.: uncorrected. IR Spectra: Perkin-Elmer 337 spectrophotometer, ν in cm^{-1}. NMR-Spectra: Varian FT 80A or Varian Gemini 200 (^1H at 80 or 200 MHz, ^{13}C at 50 MHz); $CDCl_3$ soln at r.t., TMS as internal standard, δ in ppm, *J* in Hz.

*Reaction of 7-dehydrocholesteryl acetate **1** wih maleic anhydride 2*

7-Dehydrocholesteryl acetate **1** (3.00 g) and maleic anhydride **2** (1.10 g) were heated at reflux under argon for 17 h. The resulting mixture was evaporated to dryness and the residue (3.7 g) was recrystallized twice from acetone-methanol and once from methanol to give pure 3β-acetoxy-5α,8α-etanoholest-6-ene-1',2'-dicarboxylic acid anhydride **3** (499 mg, 13.5%). M.p. 157-159 °C $[\alpha]_D^{20}$ = +0.20 (*c* = 1.00, $CHCl_3$). IR (KBr):1845, 1775, 1735, 1250, 1035. ^1H-NMR (200 MHz):0.73 (3H, *s*, Me(18)), 0.87 (6H, 2*d*, *J*=6.4 Hz, Me(26), Me(27)), 0.92 (3H, *d*, *J*=6.4 Hz, Me (21)), 0.96 (3H, *s*, Me(19)), 2.06 (3H, *s*, AcO), 2.47 (^1H, *m*, H_b-C(15)), 2.68 (1H, *dd*,*J*=10, 3.6 Hz, H_a-C(4), 2.90 and 3.51 (2H, *AB*, *J*=8.4 Hz, H-C(1'), H-C(2')), 5.17 (1H, *m*, H-C(3)), 5.85 and 6.27 (2H, *AB*, *J*=8.6 Hz, H-C(6), H-C(7)). ^{13}C-NMR (50 MHz): 171.3, 170.6 (two *s,* 2x anhydride C=O, 170.3 (*s*, CH_3CO), 136.0 (*d*, C(6)), 131.3 (*d,* C(7)), 69.0 (*d*, C(3)), 56.8 (*d*, C(17)), 55.0 (*d*, C(1'), 54.8 (*d*,C(2')), 52.6 (*d*, C(14)), 45.2 (*s*, C(8)), 44.6(*s*,C(5)), 43.6 (*d*, C(9)), 43.1 (*s*, C(13)), 40.4 (*s*, C(10)), 39.4 (*t*, C(24)), 38.7 (*t*, C(1)), 35.9 (*t*, C(22)), 35.2 (*d*, C(20)), 34.2 (*t*, C(12)), 30.8 (*t,* C(4)), 27.9 (*d*. C(25)), 27.6 (*t*, C(2)), 26.4 (*t*, C(16)), 23.7 (*t*, C(23)), 23.0 (*t,* C(15)), 22.7 (*q*, C(27)), 22.6 (*t*, C(11)), 22.5 (*q*, C(26)), 21.3 (*q*, *C*H_3CO), 18.9 (*q*, C(21)), 18.5 (*q*, C(19)), 12.2 (q, C(18)). Anal. calc. for $C_{33}H_{48}O_5$ (524.747): C 75.53, H 9.22; found: C 75.66, H 9.18.

*Formation of acetoxy dimethyl esters **4, 5, 6** and **7***

Asolution of cholest-5,7-dien-3β-yl acetate **1** (750 mg) in 30 ml dry xylene and maleic acid anhydride (280 mg) was heated at reflux under an argon atomosphere for 23 h, and then evaporated to dryness. The residue was disolved in metanol (30 ml) and 5% methanolic potassium hydroxide (10 ml), and boiled 2h. The mixture was cooled to 5 °, acidified with hydrochloric acid to pH 2, and extracted with diethyl ether. The ethereal extract was washed with water, dryed over anh. Na_2SO_4 and evaporated to dryness at 5 °C. The mixture was suspended in diethyl ether (20 ml), the ether cooled to –20 °C, treated with an ethereal solution of diazomethane until the persistance of a yellow colour and the mixture allowed to warm to room temperature. Evaporation of the diethyl ether gave an oil which was dissolved in pyridine (10 ml) and acetic acid anhydride (10 ml), and the solution left at room temperature overnight. The usual work up gave a mixture (978 mg, 97.5%) which was chromatographed on a silica gel column (30 g). Elution with benzene/Et_2O 96:4 afforded 3β-acetoxy-1',2'-dimetoxycarbonyl-7α-ethanocholesta-5.8(14)-diene (**4**) (249 mg, 24.8%). M.p. 65-66 °C (from methanol). $[\alpha]_D^{20}$ = – 109.82 (*c*=1.00, $CHCl_3$). IR (KBr): 1730, 1235, 1205, 1170, 1040. ^1H-NMR (200 MHz): 0.87 (6H, *s*, Me (18), Me(19)), 0.87 (6H, *d*, *J*=6.2 Hz, Me(26), Me(27)), 0.94 (3H, *d*, *J*=6.4 Hz, Me(21)), 2.04 (3H, *s*, AcO), 2.42 (1H, *dd*, *J*=16.8, 4.0 Hz,H-C(2')), 2.75 (1H, *dd*, *J*=16.8, 10.6 Hz, H-C(2')), »3.10 (1H, *m*, H-C(1')), 3.16 (1H, *m*, Hα-C(7)), 3.67, 3.69 (6H, two *s*, 2x MeOCO), 4.64 (1H, *m,* H-C(3)), 5.13 (1H, *dd*, *J*=3.4, 1.2 Hz, H-C(6)). ^{13}C-NMR (50 MHz):174.3 (*s*, CH_3OCO), 173.1 (*s*, CH_3OCO), 170.5 (*s*, *C*H_3CO), 147.6 (*s*, C(14)), 143.4 (*s*, C(5)), 124.8 (*s*, C(8)), 121.2 (*d*, C(6)), 73.2 (*d*, C(3)), 57.1 (*d*, C(17)), 51.8 (*q*, CH_3O), 51.7 (*q*, CH_3O), 45.3 (*d*, C(7)), 45.0 (*d*, C(1')), 43.2 (*s* C(13)), 39.4 (*t*, C(24)), 38.9 (*d,* C(9)), 38.5 (*s*, C(10)), 37.6 (*t*, C(1)), 36.9 (*t*, C(12)), 35.9 (*t*, C(4)), 35.9 (*t*, C(22)), 34.5 (*d*, C(20)), 32.8 (*t*, C(2')), 32.8 (*t*, C(2')), 27.9 (*d*, C(25)), 27.6 (*t*, C(2)), 26.7 (*t*, C(16)), 25.0 (*t*, C(15)), 23.8 (*t*, C(23)), 22.7 (*q*, C(27)), 22.5 (*q*, C(26)), 21.3 (*q*, *C*H_3CO),19.0 (*t*, C(11)), 19.0 (*q*, C(21)), 19.0 (*q*, C(19)), 17.4 (*q*, C(18)). Anal. calc. for $C_{35}H_{54}O_6$ (570.817): C 73.65, H 9.53; found C 73.63, H 9.60.

Elution with benzene/Et_2O 96.4 afforded 3β-acetoxy-1',2'-dimethoxycarbonyl-7α-ethano-cholesta-5,8(9)-diene (**5**) (149 mg, 14.8%). M.p. 152 °C (from methanol). $[\alpha]_D^{20}$= –63.2 (*c*=1.00,

$CHCl_3$). IR(KBr): 1739, 1242, 1204, 1171, 1038. ^{1}H-NMR (200 MHz): 0.67 (3H, *s*, Me(18)), 0.88 (6H, *d*, *J*=6.4 Hz, Me(26), Me(27)), 0.94 (3H, *d*, *J*=6.4 Hz, Me(21)), 1.23 (3H, *s*, Me(19)), 2.04 (3H, *s*, AcO), »2.40 (1H, *m* H-C(2')), 2.61 (1H, *dd*, *J*= 17.2, 10.6, H-C(2')), 3.21 (1H, *m*, H-C(1')), 3.24 (1H, *m*, Hα-C(7)), 3.67, 3.73 (6H, two *s*, 2x MeOCO), 4.61 (1H, *m*, H-C(3)), 5.09 (1H, br. *d*, *J*=2.4 Hz, H-C(6)). ^{13}C-NMR (50 MHz): 174.2, 173.5 (two *s*, 2 · CH_3OCO), 170.3 (*s*, CH_3CO), 140.0 (*s*, C(5)), 136.3 (*s*, C(9)), 126.2 (*s*, C(8)), 119.4 (*d*, C(6)), 73.8 (*d*, C(3)), 53.8 (*d*, C(17)), 51.9, 51.6 (two *q*, 2x CH_3O) 49.7 (*d*, C(7)), 42.7 (*d*, C(1')), 42.1 (*s*, C(13)), 39.4 (*t*, C(24)), 39.3 (*d*,C(14)), 38.0 (*s*,C(10), 37.9 (*t*, C(1)), 36.0 (*t*, C(12)), 36.0 (*t*, C(4)), 36.0 (*d*, C(20)), 35.6 (*t*, C(22)), 30.4 (*t*, C(2')), 28.6 (*t*, C(2)), 27.9 (*d*, C(25)), 27.7 (*t*, C(23)), 23.3 (*q*, CH_3CO), 22.8 (*t*, C(15)), 22.7 (*t*, C(11)), 22.7 (*q*, C(27)), 22.5 (*q*, C(26)), 21.3 (*q*, C(21)) 18.6 (*q*, C(19)), 11.4 (*q*, C(18)). Anal. calc. for $C_{35}H_{54}O_6$ (570.817): C 73.65, H 9.53; found: C 73.68, H 9.04.

Subsequent benzene/Et_2O (96:4) fractions eluted a mixture (202 mg) which was twice rechromatographed on a SiO_2 column (10 g each) to give 3β-acetoxy-1'(R),2'-dimethoxy-carbonyl-7α-ethanochlolesta-5,8(14)-diene (**6**), as the main component (140 mg, »14%). Oil. IR (CCl_4): 1738, 1240, 1208, 1165, 1032. ^{1}H-NMR (80 MHz) (main peaks): 0.87 (6H, *s*, Me(18), Me(19), 0.87 (6H, *d*, Me(26), Me(27)), 0.93 (3H, *d*, Me(21)), 2.04 (3H, *s*, AcO), »2.40–3.10 (3H, *m*, H-C(1'), $H_2C(2')$), »3.20 (1H, *m*, Hα-C(7)), 3.69 (6H, two *s*, 2x MeOCO), »4.60 (1H, *m*, H-C(3)), 5.20 (1H, *m*, H–C(6)).

Elution with benzene/Et_2O 95:5 afforded 3β-acetoxy-(1'β,2'β-dimethoxycarbonyl)-5α, 8α-ethanocholesta-6-ene (**7**) (219 mg, 21.8%). M.p. 120-121 °C (from methanol). $[\alpha]_D^{20}$ = –22.91 (*c*=1.00, $CHCl_3$). IR (KBr): 1762, 1735, 1245, 1180, 1155 cm^{-1}. ^{1}H-NMR (200 MHz): 0.75 (3H, *s*, Me(18)), 0.86 (6H, *d*, *J*=7.2, Me(26), Me(27)), 0.90 (3H, *d*, *J*=7.2, Me-21), 0.94 (3H, *s*, Me(19)), 2.01 (3H, *s*, AcO), 2.34 (1H, *dd*, *J*=13.8, 4.2 Hz, Hα-C(4)), 2.84, 3.54 (2H, *AB*, J=11.0 Hz, H-C(6), H-C(7)), 3.51, 3.57 (6H, two *s*, 2 · MeCO), 4.91 (1H, *m*, H-C(3)), 6.06, 6.22 (2H, *AB*, *J*=8.4 Hz, H-C(1'), H-C(2')). ^{13}C-NMR (50 MHz): 172.8, 171.9 (two *s*, 2 · O-C=O), 170.3 (*s*, CH_3CO), 136.1 (*d*, C(6)), 128.9 (*d*, C(7)), 69.6 (*d*, C(3)), 60.0 (*d*, C(17)), 55.4 (*d*, C(1')) 54.8 (*d*, C(2")), 53.0 (*d*, C(14)), 51.5, 51.4 (two *q*, 2 · CH_3O), 47.3 (*d*, C(9)), 44.5 (*s*, C(8)), 43.6 (*s*, C(5)), 43.2 (*s*, C(13)), 40.4 (*s*, C(10)), 39.4 (*t*, C(24)), 39.3 (*t*, C(1)), 35.9 (*t*, C(22)), 35.1 (*d*, C(20)), 34.3 (*t*, C(12)), 32.0 (*t*, C(4)), 27.9 (*d*, C(25)), 27.8 (*t*, C(2)), 26.4 (*t*, C(16)), 23.6 (*t*, C(23)), 23.3 (*t*, C(15)), 23.1 (*t*, C(11)), 22.7 (*q*, C(27)), 22.5 (*q*, C(26)), 21.3 (*q*, CH_3CO), 18.8 (*q*, C(21)), 18.8 (*q*, C(19)), 12.1 (*q*, C(18)). Anal. calc for $C_{35}H_{54}O_6$ (570.817): C 73.65, H 9.53; found C 73.41, H 9.67.

*Reaction of 7-dehydrocholesteryl acetate (**1**) with maleic anhydride (**2**) in the presence of borontrifluoride etherate*

To a solution of (**1**) (3.0g) and maleic anhydride (688 mg) in benzene (30 ml), borontrifluoride etherate (0.1 ml) was added and the mixture was boiled for 2 h. The reaction mixture was poured onto ice, and extracted with benzene several times (110 ml). The collected extract was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness. The oily resedue (3.603 g) was recrystallized from acetone to give 3β-acetoxy-7α, 15α-ethanocholest-8(14)-ene-1',2'-dicarboxylic acid anhydride (**8**) (771 mg, 20.9%). M.p. 204-205 °C (from acetone). $[\alpha]_D^{20}$= –26.33 (*c*=1.01, $CHCl_3$). IR (KBr: 1860, 1790, 1730, 1255. ^{1}H-NMR (200 MHz): 0.73 (3H, *s*, Me-18), 0.89 (9H, three *d*, *J*=7.8 Hz, Me(21), Me(26), Me(27), 0.90 (3H, *s*, Me(19)), 2.03 (3H, *s*, AcO), 3.27 (2H, two *m*, H-C(1'), H-C(2')), 4.73 (1H, *m*, H-C(3)). ^{13}C-NMR (50 Hz): 173.0, 172.1 (two *s*, 2x O-C=O), 170.4 (s, CH_3CO), 148.8 (*s*, C(14)), 128.7 (*s*, C(8)), 73.0 (*d*, C(3)), 55.5 (*d*, C(17)), 49.2 (*d*, C(2')), 47.3 (*d*, C(1'), 43.9 (*d*, C(15)), 42.1 (*s*, C(13)), 40.3 (*d*, C(7)), 39.4 (*t*, C(24)), 37.8 (*t*, C(1)), 35.6 (*t*, C(22)), 35.2 (*d*, C(20)), 35.0 (*t*, C(6)), 34.6 (*t*, C(12)), 34.4 (*d*, C(9)), 33.9 (*s*, C(10)), 31.2 (*d*, C(5)), 30.4 (*t*, C(4)), 29.0 (*t*, C(16)), 27.9 (*d*, C(25)), 27.5 (*t*, C(2)), 23.2 (*t*, C(23)), 22.7 (*q*, C(27)), 22.5 (*q*, C(26)), 21.3 (*q*, CH_3CO), 20.0 (*q*, C(21)), 19.6 (*t*, C(11)), 18.3 (*q*, C(19)), 12.2 (*q*, C(18)). Anal. calc. for $C_{33}H_{48}O_5$ (524.741): C 75.53, H 9.22; found: C 75.51, H 9.01.

*Reaction of 3*b*-acetoxy-5*a*,8*a*-ethanocholest-6-ene-1',2'-dicarboxylic acid anhydride (**3**) with $Pb(OAc)_4$ in pyridine solution*

Anhydride **3** (800 mg, 0.0015 mol) was dissolved in dry pyridine (50 ml). To this solution warmed at *cca.* 90 °C (under argon), lead tetraacetate (12.5 g, 0.0225 mol) was gradually added during 5 h. The cooled reaction mixture was diluted with diethyl ether and the pyridine was neutralized with 6 *M* HCl[11]. The separated solid was filtered off, and the etheral solution washed with H_2O, dried over Ha_2SO_4, and evaporated to dryness. The residue (625 mg) was chromatographed on silica gel column (25 g). Elution with benzene/Et_2O 98:2 afforded the starting product (**3**) (288 mg, 36.0%) identified by m.p., IR and ^{1}H-NMR spectra.

Elution with benzene/Et_2O 97:3 and 96:4 afforded lactone **9** (30 mg, 3.9%). Oil. IR (CCl_4): 3030, 1795, 1742, 1240. Benzene/Et_2O (94:6) eluted first a » 1:1 mixture of lactones **9** and **10** (about 10 mg) and then lactone **10** (18 mg, 2.4%). Oil. IR (CCl_4): 3040, 1790, 1740, 1240.

Benzene/Et_2O (90:10, 88:12 and 86:14) eluted the bislactone derivate **11** (95 mg, 11.5%). M.p. 197-200 °C (decomp.). $[a]_D^{20} = -20.1$ (*c*= 1.00, $CHCl_3$). IR (CCl_4): 1800, 1780, 1740, 1240. ^{1}H-NMR (200 MHz): 0.84 (3H, *s*, Me (18)), 0.86 (6H, *d*, *J*=6.0 Hz, Me(26), Me(27)), 0.91 (3H, *d*, *J*=8.6 Hz, Me(21)), 1.09 (3H, *s*, Me(19)), 2.01 (3H, *s*, AcO), 2.41 (1H, *dd*, *J*=10.0, 2.6 Hz, H-C(1')), 3.10 (1H, *dd*, *J*=10.0, 2.4 Hz, H-C(2')), 4.48 (1H, *dd*, *J*=6.4, 2.2 z, H-C(7)), 4.72 (1H, *m*, H-C(3)), 5.03 (1H, *dd*, *J*=6.4, 2.6 Hz, H-C(6)). ^{13}C-NMR (50 MHz): 176.7, 175.4 (two *s*, 2 · O–C=O), 170.1 (*s*, CH_3CO), 79.1 (d, C(6)), 76.6 (*d*, C(7)), 69.2 (*d*, C(3)), 56.4 (*d*, C(1')), 55.4 (*d*, C(2')) 49.9 (*d*, C(17)), 49.2 (*s*, C(8)), 49.1 (*s*, C(5)), 45.0 (*d*, C(14)), 44.2 (*d*, C(9)), 43.6 (*s*, C(13)), 39.3 (*t*, C(24)), 39.1 (*t*, C(1)), 36.6 (*t*, C(4)), 35.6 (*t*, C(22)), 35.4 *(d*, C(20)), 34.2 (*t*, C(12)), 31.9 (*s*, C(10)), 27.9 (*d*, C(25)), 27.2 (*t*, C(2)), 26.2 (*t*, C(16)), 24.5 (*t*, C(15)), 23.7 (*t*, C(23)), 22.7 (*q*, C(27)), 22.4 (*q* C(26)), 22.1 (*t*, C(11)), 21.1 (*q*, CH_3CO), 18.7 (*q*, C(21)), 18.2 *(q*, C(19)), 12.4 (*q*, C(18)). Anal. calc. for $C_{33}H_{48}O_6$ (540.747): C 73.30, H 8.95; found C 73.08, H 8.69.

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ИЗВОД

ОЛОВОТЕТРААЦЕТАТНА ОКСИДАЦИЈА ДИЛС-АЛДЕРОВОГ АДУКТА 7-ДЕХИДРОХОЛЕСТЕРИЛ-АЦЕТАТА СА АНХИДРИДОМ МАЛЕИНСКЕ КИСЕЛИНЕ

ЛИДИЈА Г. БОНДАРЕНКО-ГЕОРГИЈУ, ЉУБИНКА Б. ЛОРЕНЦ и МИХАИЛО Љ. МИХАИЛОВИЋ

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Дилс-Алдеров адукт **3**, добивен циклоадицијом 7-дехидрохолестерил-ацетата **1** и анхидрида малеинске киселине **2**, оксидован је великим вишком оловотетраацетата у пиридинском раствору на око 90 °C у току 5h. Под наведеним условима извршена је оксидативна лактонизација једињења **3** са партиципацијом олефинске D^6-двогубе везе при чему су добивена два изомерна монолактонска деривата **9** и **10** (у укупнм приносу од око 6%) и бислактонски производ **11** (у приносу од око 11,5%); при томе је непромењен полазни адукт изолован у приносу од »36%.

(Примљено 12. септембар 1999.)

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