71. Conformations of the Ten-membered Ring in 5,10- Secosteroids. III[1][2]): (*Z*)-3β- and (*Z*)-3α-Hydroxy-5,10-*seco*-1(10)-cholesten-5-one Esters and (*Z*)-5,10-*seco*-1(10)-Cholestene-3,5-dione

by **Hermann Fuhrer**[3]), **Ljubinka Lorenc**[4]), **Vladimir Pavlović**[4]), **Grety Rihs**[3]), **Günther Rist**[3]), **Jaroslav Kalvoda**[5]) and **Mihailo Lj. Mihailović**[4])

(16.II.81)

Summary

(*Z*)-3β-Acetoxy- and (*Z*)-3α-acetoxy-5,10-*seco*-1(10)-cholesten-5-one (**6a**) and (**7a**) were synthesized by fragmentation of 3β-acetoxy-5α-cholestan-5-ol (**1**) and 3α-acetoxy-5β-cholestan-5-ol (**2**), respectively, using in both cases the hypoiodite reaction (the lead tetraacetate/iodine version). The 3β-acetate **6a** was further transformed, *via* the 3β-alcohol **6d** to the corresponding (*Z*)-3β-*p*-bromobenzoate ester **6b** and to (*Z*)-5,10-*seco*-1(10)-cholestene-3,5-dione (**8**) (also obtainable from the 3α-acetate **7a**). The ^{1}H- and ^{13}C-NMR. spectra showed that the (*Z*)-unsaturated 10-membered ring in all three compounds (**6a**, **7a** and **8**) exists in toluene, in only one conformation of type $\mathbf{C}_1$, the same as that of the (*Z*)-3β-*p*-bromobenzoate **6b** in the solid state found by X-ray analysis. The unfavourable relative spatial factors (interdistance and mutual orientation) of the active centres in conformations of type $\mathbf{C}_1$ are responsible for the absence of intramolecular cyclizations in the (*Z*)-keto-esters **6** and **7** (**a** and **c**).

Introduction. – We have already reported [1] [2] the results of NMR. and X-ray studies concerning the ground-state conformations of the (*E*)-unsaturated 10-membered ring in the epimeric (*E*)-3β-acetoxy-(**3a**), (*E*)-3β-*p*-bromobenzoyloxy-(**3b**), and (*E*)-3α-acetoxy-5,10-*seco*-1(10)-cholesten-5-ones (**4a**), and in the corresponding (*E*)-3,5-diketone **5**. Detailed analysis of ^{1}H- and ^{13}C-NMR. spectra showed, that the major conformations *(Scheme 1)* in toluene were $\mathbf{A}_1^\beta$ for **3a** [1][6]), $\mathbf{A}_2^\alpha$ for **4a** [2] and $\mathbf{A}_1^\alpha$ for **5** [2], the first two also being the (only) conformations of **3**[7]) and **4a** in the solid state, as established by X-ray analysis, and that the minor

[1]) Part I: [1]; part II: [2].

[2]) Part XVIII in the series 'Synthesis, Structure and Reactions of Secosteroids Containing a Medium-sized Ring'. Part XVII: [3].

[3]) Central Function Research, *Ciba-Geigy* Ltd, 4002 Basle, Switzerland.

[4]) Department of Chemistry, Faculty of Science, University of Belgrade, and Institute of Chemistry, Technology and Metallurgy, Studentski trg 16, POB 550, YU-11001 Belgrade, Yugoslavia.

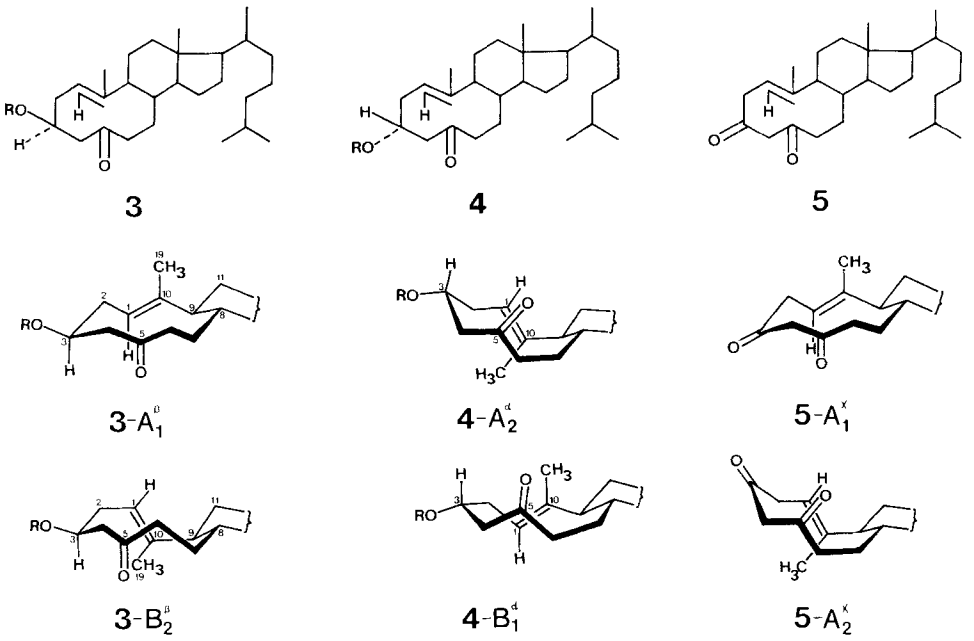
[5]) Research Laboratories, Pharmaceuticals Division, *Ciba-Geigy* Ltd, 4002 Basle, Switzerland.

[6]) For **3a**, the same major and minor conformations exist also in chloroform [1].

[7]) The (*E*)-3β-*p*-bromobenzoate **3b** was used for X-ray studies of the (*E*)-5,10-*seco*-system **3** [1].

0018-019X/81/3/0703-13$01.00/0

Scheme 1
(*E*)-Series



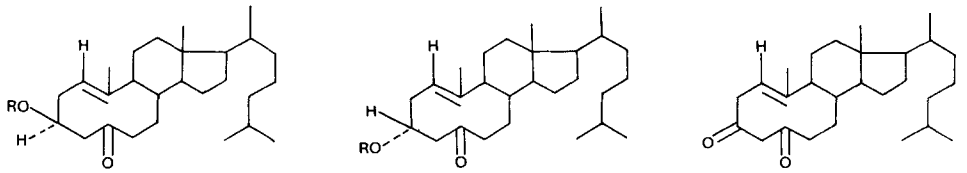
a R = CH_3CO; **b** R = *p*-Br–C_6H_4CO; **c** R = *p*-CH_3–$C_6H_4SO_2$; **d** R = H

conformations in toluene were $\mathbf{B}_2^{\beta 6}$), $\mathbf{B}_1^{\alpha}$ and $\mathbf{A}_2^{\chi}$ for **3a**, **4a** and **5**, respectively. Both the 3β-acetoxy- and 3α-acetoxyketones **3a** and **4a**, as well as the corresponding 3-tosylates **3c** and **4c**, undergo a variety of cyclizations involving intramolecular C(1)–C(5) and C(1)–C(3) bond formation, respectively, which can be accounted for by the favourable relative spatial arrangement of the reaction centres in the transition state conformations of the **A** and **B** type mentioned above *(Scheme 1)*, and in other similar reactive conformations of the (*E*)-cyclodecenone ring in these compounds [1–3].

In contrast to this behaviour of the (*E*)-ketones **3** and **4**, the corresponding (*Z*)-diastereomers **6** and **7** do not undergo internal ring closure under the same conditions [3–7]. These results suggest an unfavourable distance and/or relative steric orientation of the $\Delta^{1(10)}$-olefinic double bond with respect to the O=C(5) group in the (*Z*)-3-acetates **6a** and **7a**, and to the TsO–C(3) group in the (*Z*)-3-toluenesulfonate **6c** and **7c**, this being the case, for example, in conformations of type $\mathbf{C}_1$ *(Scheme 2)*.

We therefore examined (*Z*)-3β-acetoxy-5,10-*seco*-1(10)-cholesten-5-one (**6a**), (*Z*)-3α-acetoxy-5,10-*seco*-1(10)-cholesten-5-one (**7a**) and (*Z*)-5,10-*seco*-1(10)-cholestene-3,5-dione (**8**) by ^{1}H- and ^{13}C-NMR. spectroscopy and circular dichroism (CD.), and (*Z*)-3β-*p*-bromobenzoyloxy-5,10-*seco*-1(10)-cholesten-5-one (**6b**) by X-ray diffraction, in order to determine the ground-state conformation(s) in solution and in the solid state of their (*Z*)-unsaturated 10-membered ring.

Scheme 2
(*Z*)-Series



6 **7** **8**

6-C$_1^a$ (R^1 = OR, R^2 = H_α) **8-C$_1^x$**

7-C$_1^d$ (R^1 = H_β, R^2 = OR)

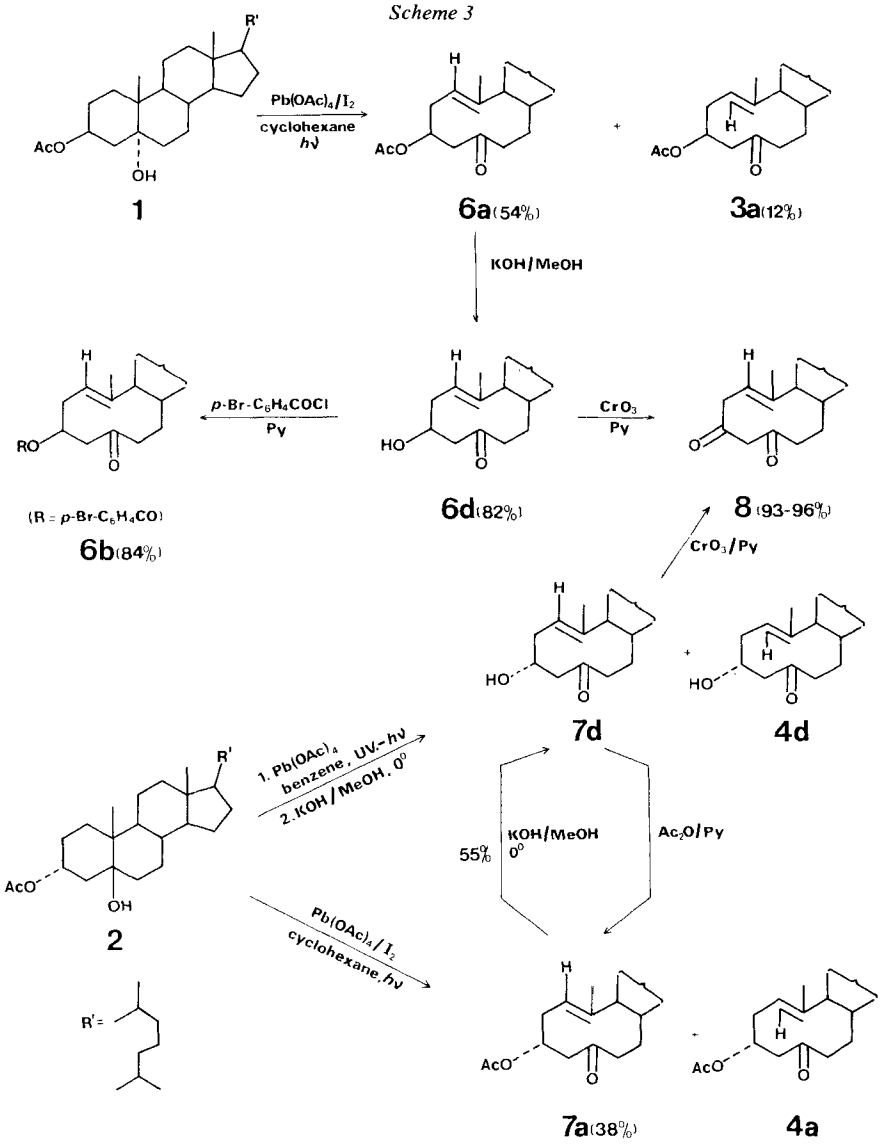
a R = CH_3CO; **b** R = *p*-Br–C_6H_4CO; **c** R = *p*-CH_3–$C_6H_4SO_2$; **d** R = H

1. Synthetic procedures. – The easily available 3β-acetoxy-5α-cholestan-5-ol (**1**) [8] was the starting material for the synthesis of the (*Z*)-5,10-*seco*-compounds **6a**, **6b** and **8** *(Scheme 3)*. The hypoiodite reaction of **1**, using lead tetraacetate/iodine in cyclohexane, afforded (*Z*)-3β-acetoxy-5,10-*seco*-1(10)-cholesten-5-one (**6a**) in considerably higher yield (*ca.* 54%) than the previously described lead tetraacetate oxidation of **1** [4], which gave only 15–17% of **6a** under thermolytic conditions [4] [9] and 27.5% under UV.-photolytic conditions [9]. The corresponding 3β-alcohol **6d** [4] was esterified to (*Z*)-3β-*p*-bromobenzoyloxy-5,10-*seco*-1(10)-cholesten-5-one (**6b**), required for X-ray analysis (*ca.* 69% yield from **6a**). The 3β-alcohol **6d** was also oxidized with chromic anhydride in pyridine to the (*Z*)-3,5-diketone **8**, in over 85% yield (from **6a**).

(*Z*)-3α-Acetoxy-5,10-*seco*-1(10)-cholesten-5-one (**7a**) was prepared from the readily obtainable 3α-acetoxy-5β-cholestan-5-ol (**2**) *(Scheme 3)*. The hypoiodite reaction (lead tetraacetate/iodine in cyclohexane) applied to **2** afforded about 38% of acetate **7a**. The lead tetraacetate oxidation of **2** under UV.-photolytic conditions [2], followed by careful saponification (0.5–1% methanolic KOH-solution, 0°, 3–4 h) of the reaction mixture to alcohols **7d** and **4d** and reacetylation of the separated (*Z*)-3α-alcohol **7d** to acetate **7a**, required more manipulations and more time, and was less efficient. The (*Z*)-3α-alcohol **7d**, upon oxidation with chromic anhydride in pyridine, could be also readily converted (as the (*Z*)-3β-alcohol **6d**) to the (*Z*)-3,5-diketone **8**.

2. Determination of the solid state conformation of (*Z*)-3β-*p*-bromobenzoyloxy-5,10-*seco*-1(10)-cholesten-5-one (6b) by X-ray analysis. – 2.1. *Crystal data.* Crystals

Scheme 3



are orthorhombic, space group P_{212121}, $a = 6.074$ (2), $b = 13.670$ (4), $c = 38.353$ (9) Å, $U = 3184$ Å^3.

2.2. *Intensity data, structure determination and refinement.* A *Picker* FACS-I automatic diffractometer was used for data collection with Mo*Ka* radiation and graphite monochromator. The intensities of 3508 independent reflections with $\theta \leq 27.5°$ were measured, of which 1348 were classified as observed with $I \geq 2\sigma(I)$.

The structure was solved by *Patterson* and *Fourier* techniques and refined by full-matrix least squares to a final R value of 0.091.

Table 1. *Fractional atomic coordinates for compound* **6b**

Atom	x/a	y/b	z/c
C(1)	0.421 (2)	0.526 (1)	0.8591 (3)
C(2)	0.625 (2)	0.584 (1)	0.8672 (2)
C(3)	0.593 (2)	0.684 (1)	0.8865 (3)
C(4)	0.382 (2)	0.743 (1)	0.8766 (3)
C(5)	0.405 (3)	0.781 (1)	0.8383 (3)
C(6)	0.205 (2)	0.795 (1)	0.8135 (3)
C(7)	0.075 (2)	0.696 (1)	0.8054 (3)
C(8)	0.188 (2)	0.629 (1)	0.7788 (2)
C(9)	0.384 (2)	0.572 (1)	0.7958 (3)
C(10)	0.303 (2)	0.517 (1)	0.8286 (3)
C(11)	0.492 (2)	0.497 (1)	0.7688 (3)
C(12)	0.544 (2)	0.546 (1)	0.7335 (2)
C(13)	0.353 (2)	0.604 (1)	0.7164 (2)
C(14)	0.283 (2)	0.679 (1)	0.7447 (3)
C(15)	0.121 (2)	0.749 (1)	0.7257 (2)
C(16)	0.238 (2)	0.751 (1)	0.6893 (2)
C(17)	0.428 (2)	0.674 (1)	0.6885 (3)
C(18)	0.162 (2)	0.531 (1)	0.7062 (2)
C(19)	0.115 (2)	0.447 (1)	0.8280 (2)
C(20)	0.463 (2)	0.631 (1)	0.6506 (2)
C(21)	0.641 (2)	0.546 (1)	0.6495 (2)
C(22)	0.539 (2)	0.727 (1)	0.6300 (3)
C(23)	0.554 (3)	0.696 (1)	0.5913 (3)
C(24)	0.582 (4)	0.788 (3)	0.5670 (4)
C(25)	0.821 (4)	0.819 (3)	0.5667 (4)
C(26)	0.910 (4)	0.728 (1)	0.5453 (3)
C(27)	0.839 (4)	0.905 (1)	0.5402 (3)
O(28)	0.596 (2)	0.803 (1)	0.8290 (2)
O(29)	0.548 (2)	0.661 (1)	0.9233 (2)
C(30)	0.687 (3)	0.632 (1)	0.9472 (4)
O(31)	0.880 (2)	0.633 (1)	0.9386 (2)
C(32)	0.583 (3)	0.620 (1)	0.9820 (3)
C(33)	0.373 (3)	0.640 (1)	0.9899 (3)
C(34)	0.315 (2)	0.624 (1)	1.0251 (4)
C(35)	0.476 (3)	0.580 (1)	1.0483 (3)
C(36)	0.686 (3)	0.554 (1)	1.0393 (4)
C(37)	0.752 (2)	0.570 (1)	1.0033 (3)
Br(38)	0.369 (1)	0.563 (0)	1.0957 (0)

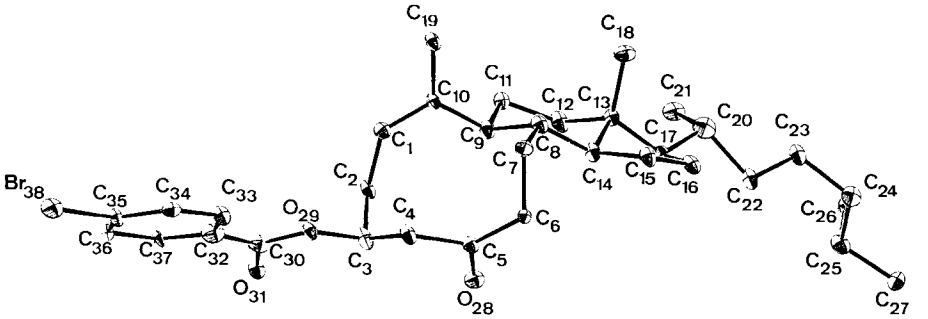


Fig. 1. *Perspective view of the molecule of* **6b**. The thermal ellipsoids are scaled to include 20% probability.

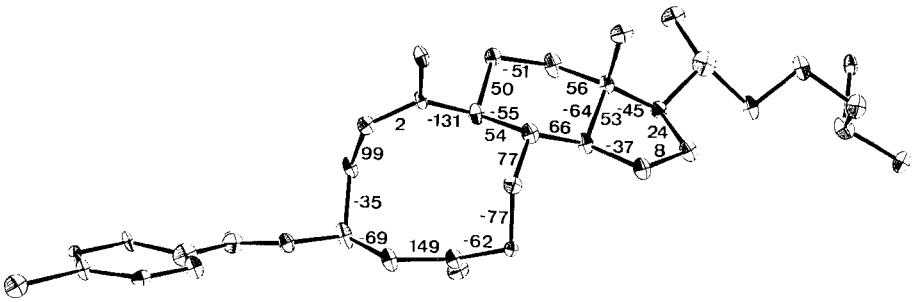


Fig. 2. *Selected torsion angles characterizing the secosteroid skeleton of* **6b**

2.3. *Results and discussion.* Final atomic coordinates with their standard deviations are given in *Table 1*. The molecular structure is illustrated in *Figures 1* and *2*. The bond lengths and selected transannular distances are listed in *Table 2*, whereby the estimated standard deviations from the least squares refinements lie between 0.008 Å (Br–C) and 0.02 Å (C–C). Bond angles are shown in *Table 3*, the standard angle deviations being about 1.5°. *Figure 2* shows the torsion angles (°) of the steroid skeleton.

The 10-membered ring in the (*Z*)-ester **6b** has the C_1 conformation (*Fig. 1* and *2*, *Scheme 2*). Ring C adopts the normal chair conformation with an average

Table 2. *Interatomic distances* (Å) *in compound* **6b**

(a) Bond lengths			
C(1)–C(2)	1.51 (2)	C(14)–C(15)	1.55 (2)
C(1)–C(10)	1.38 (2)	C(15)–C(16)	1.57 (2)
C(2)–C(3)	1.57 (2)	C(16)–C(17)	1.59 (2)
C(3)–C(4)	1.56 (2)	C(17)–C(20)	1.58 (2)
C(3)–O(29)	1.47 (2)	C(20)–C(21)	1.56 (2)
C(4)–C(5)	1.56 (2)	C(20)–C(22)	1.60 (2)
C(5)–C(6)	1.55 (2)	C(22)–C(23)	1.54 (2)
C(5)–O(28)	1.25 (2)	C(23)–C(24)	1.57 (3)
C(6)–C(7)	1.59 (2)	C(24)–C(25)	1.51 (3)
C(7)–C(8)	1.53 (2)	C(25)–C(26)	1.58 (3)
C(8)–C(9)	1.56 (2)	C(25)–C(27)	1.56 (3)
C(8)–C(14)	1.58 (2)	O(29)–C(30)	1.31 (2)
C(9)–C(10)	1.55 (2)	C(30)–O(31)	1.22 (2)
C(9)–C(11)	1.60 (2)	C(32)–C(33)	1.34 (3)
C(10)–C(19)	1.49 (2)	C(32)–C(37)	1.48 (2)
C(11)–C(12)	1.55 (2)	C(33)–C(34)	1.41 (2)
C(12)–C(13)	1.55 (2)	C(34)–C(35)	1.45 (2)
C(13)–C(14)	1.56 (2)	C(35)–C(36)	1.37 (2)
C(13)–C(17)	1.51 (2)	C(35)–Br(38)	1.94 (1)
C(13)–C(18)	1.57 (2)	C(36)–C(37)	1.46 (2)
(b) Selected transannular distances			
C(1)···C(4)	3.04 (2)	C(5)···C(10)	3.67 (2)
C(1)···C(5)	3.58 (2)	C(6)···C(9)	3.30 (2)
C(1)···C(6)	4.28 (2)	C(6)···C(10)	3.88 (2)
C(2)···C(5)	3.20 (2)	C(7)···C(10)	2.95 (2)

Table 3. *Intramolecular bond angles* (deg.)

C(10)–C(1)–C(2)	131	C(12)–C(11)–C(9)	112	C(22)–C(23)–C(24)	111
C(1)–C(2)–C(3)	117	C(11)–C(12)–C(13)	116	C(25)–C(24)–C(23)	109
O(29)–C(3)–C(4)	101	C(17)–C(13)–C(12)	113	C(24)–C(25)–C(27)	106
O(29)–C(3)–C(2)	106	C(17)–C(13)–C(14)	99	C(24)–C(25)–C(26)	97
C(4)–C(3)–C(2)	116	C(17)–C(13)–C(18)	117	C(27)–C(25)–C(26)	103
C(5)–C(4)–C(3)	109	C(12)–C(13)–C(14)	104	C(30)–O(29)–C(3)	128
O(28)–C(5)–C(6)	121	C(12)–C(13)–C(18)	110	O(31)–C(30)–O(29)	115
O(28)–C(5)–C(4)	115	C(14)–C(13)–C(18)	113	O(31)–C(30)–C(32)	131
C(6)–C(5)–C(4)	123	C(15)–C(14)–C(13)	105	O(29)–C(30)–C(32)	113
C(5)–C(6)–C(7)	114	C(15)–C(14)–C(8)	115	C(33)–C(32)–C(37)	129
C(8)–C(7)–C(6)	114	C(13)–C(14)–C(8)	113	C(33)–C(32)–C(30)	126
C(7)–C(8)–C(9)	111	C(14)–C(15)–C(16)	98	C(37)–C(32)–C(30)	105
C(7)–C(8)–C(14)	117	C(17)–C(16)–C(15)	110	C(32)–C(33)–C(34)	115
C(9)–C(8)–C(14)	106	C(13)–C(17)–C(16)	101	C(33)–C(34)–C(35)	119
C(10)–C(9)–C(8)	110	C(13)–C(17)–C(20)	117	C(36)–C(35)–C(34)	125
C(10)–C(9)–C(11)	110	C(16)–C(17)–C(20)	112	C(36)–C(35)–Br(38)	121
C(8)–C(9)–C(11)	111	C(17)–C(20)–C(21)	113	C(34)–C(35)–Br(38)	114
C(1)–C(10)–C(19)	118	C(17)–C(20)–C(22)	101	C(35)–C(36)–C(37)	117
C(1)–C(10)–C(9)	119	C(21)–C(20)–C(22)	113	C(36)–C(37)–C(32)	113
C(19)–C(10)–C(9)	123	C(23)–C(22)–C(20)	106		

torsion angle of 57°. The conformation of ring D is between a C(13) envelope and a C(16) half-chair, with *Romers* [11] ring parameters $\varphi_m = 54°$ and $\Delta = 16°$. The side-chain is in a nearly extended conformation; all torsion angles lie within $180 \pm 11°$ or $60 \pm 12°$.

3. NMR. Studies of the conformations in solution of the 10-membered ring in the (*Z*)-secosteroids 6a, 7a and 8. – An NMR. analysis similar to that described [1] [2] was applied for the investigation of the (*Z*)-unsaturated 3-epimeric 3-acetoxy-5,10-*seco*-5-ketones **6a** and **7a**, and the corresponding 3,5-dione **8**. Whereas a rough estimate of the spatial arrangement of the 10-membered ring in these compounds could be deduced from ^{13}C-NMR. spectra, for finer details it was necessary to analyze ^{1}H-NMR. data. Chemical shifts and coupling parameters of protons

Table 4. *^{1}H-NMR. of selected 10-membered ring protons in compounds* **6a**, **7a** *and* **8**[a])

Proton	Chemical shifts (δ)[b]) and coupling patterns[c])		
	6a	**7a**	**8**
H–C(1)	5.29 (*d*×*d*)	~4.9[d])	4.98 (*d*×*d*)
H_β–C(2)	~2.14 (*d*×*d*×*d*)	2.25 (*d*×*d*)	2.58 (*d*×*d*)
H_α–C(2)	2.74 (~*t*×*d*)	2.81 (*qa*)	3.47 (*d*×*d*)
H_β–C(3)	–	~4.9[d])	–
H_α–C(3)	5.62 (*d*×*qa*)	–	–
H_β–C(4)	2.90 (*d*×*d*)	2.64 (*d*×*d*)	3.76 (*d*)
H_α–C(4)	~2.14 (*d*×*d*)	[d])	2.52 (*d*)

[a]) ^{1}H-NMR. spectra were recorded in (D_8) toluene at RT., at 360 MHz for compounds **6a** and **7a**, and at 100 MHz for compound **8** (no temperature dependence of the spectra could be detected).

[b]) In ppm/TMS.

[c]) Multiplicity: *d* doublet, *t* triplet, *qa* quadruplet.

[d]) Signal masked or ill-resolved due to overlap with other resonances.

H–C(1), H_2–C(2), H_2–C(3) and H_2–C(4) of **6a**, **7a** and **8** are listed in *Tables 4* and *5*, and ^{13}C-NMR. data for the 10-membered ring in *Table 6*. Since they exhibit only one set of temperature-independent NMR. resonances, each of the three (*Z*)-

Table 5. *Theoretical and experimental coupling constants J (in Hz) of selected 10-membered ring proton signals in compounds* **6a**, **7a** *and* **8**[a])

Protons[b]) (coupling type)[c])	Coupling constants *J*			
	Calculated[d])	Experimental[e])		
		6a	**7a**	**8**
1,19 (1,3-allyl)	< 1	< 1	[f])	< 1
1,2β (a,e)	3.6	4.7	4.7[g])	4.6
1,2α (a,a)	11.6	11.9	13[h])	11.5
2β,2α (*gem*)	15.0	14.5	14.5	14.5
2β,3β (e,e)	2.0	–	~ 0	–
2β,3α (e,a)	3.6	3.6	–	–
2α,3β (a,a)	12.0	–	13.0	–
2α,3α (e,a)	3.6	3.6	–	–
3β,4β (e,a)	3.6	–	3.6[i])	–
3β,4α (e,e)	2.0	–	[f])	–
3α,4β (a,a)	12.0	11.8	–	–
3α,4α (a,e)	3.6	3.6	–	–
4β,4α (*gem*)	15.0, 16.0 (**8**)	16.2	16.2[j])	18.0

[a]) *Table 4*, footnote a).
[b]) For the coupling patterns (and chemical shifts) of the protons discussed, see data in *Table 4*.
[c]) a,e = axial-equatorial; a,a = axial-axial; e,e = equatorial-equatorial; *gem* = geminal.
[d]) Calculated according to *Karplus* rule [12] for conformation $\mathbf{C_1}$ *(Scheme 2)*.
[e]) Most constants were obtained from signals of both protons involved in coupling (for exceptions see footnotes g), h), i) and j)).
[f]) These signals are masked (or ill-resolved) owing to overlap with other resonances.
[g]) Obtained only from the signal of H_β–**C**(2) at 2.25 ppm *(Table 4)*, and not from that of H–C(1)[f]).
[h]) Obtained only from the signal of H_α–C(2) at 2.81 ppm *(Table 4)*, and not from that of H–C(1)[f]).
[i]) Obtained only from the signal of H_β–C(4) at 2.64 ppm *(Table 4)*, and not from that of H_β–C(3)[f]).
[j]) Obtained only from the signal of H_β–C(4) at 2.64 ppm *(Table 4)*, and not from that of H_α–C(4)[f]).

Table 6. *^{13}C-NMR. chemical shift*[a]) *of selected carbon atoms in compounds* **6a**, **7a** *and* **8**[b])

Carbon	**6a**	**7a**	**8**
C(1)	120.4	121.7	119.6
C(2)	28.6	30.7	42.2
C(3)	70.6	70.7	201.5
C(4)	40.7	42.3	52.0
C(5)	210.5	209.2	207.7
C(6)	39.6	40.6	40.0
C(7)	27.5	27.5	27.2
C(8)	36.8	37.0	37.0
C(9)	41.7	41.1	41.7
C(10)	142.5	141.9	143.8
C(14)	50.3	50.9	50.5
C(18)	12.0	12.1	12.0
C(19)	18.8	18.9	18.8

[a]) In ppm/TMS.
[b]) Spectra measured in (D_8) toluene at RT. at 25.2 MHz.

seco-ketones (**6a**, **7a** and **8**) must exist in solution in only one (stable) ground-state conformation.

3.1. *(Z)-3β-Acetoxy-5,10-seco-5-ketone* **6a**. The NMR. parameters support conformation $\mathbf{C}_1$ in solution *(Scheme 2)*.

^{1}H-NMR. Spectrum. The 3β-acetoxy group is equatorial, since the proton at C(3) shows only one resolved major coupling (~12 Hz) with an adjacent proton H_β–C(4)), and three smaller vicinal couplings, with H_α–C(4), H_β–C(2) and H_α–C(2), of approximately the same magnitude (~3.5 Hz), and therefore must be axial.

The coupling parameters of the H–C(1) resonance suggest a dihedral angle of 180° between H–C(1) and H_α–C(2), and of 60° between H–C(1) and H_β–C(2). The signal of the vinyl proton in **6a** is shifted downfield, from 4.9 ppm in the (*Z*)-3α-acetoxy-5,10-*seco*-5-ketone **7a** (see below), to 5.3 ppm (in **6a**), probably owing to the deshielding influence of the 3β-acetoxy group on the proton at C(1) in **6a**.

^{13}C-NMR. Spectrum. The ^{13}C-data for **6a** are in accordance with a spatial arrangement of the 10-membered ring in which the C(1),C(2)- and C(6),C(7)-bonds are roughly parallel to the direction of the C(9)–H_α bond, since only in that relative steric relationship the two γ effects, due to the C(2)–H_α and C(6)–H_α bonds[8]) [13], can cause an overall upfield movement of the C(9) signal of about 13–14 ppm, *i.e.* from ~55 ppm in corresponding compounds where such or similar effects are absent (for example in the (*E*)-secosteroids **3a**, **4a** and **5** with conformations $\mathbf{A}_1^\beta$, $\mathbf{B}_1^\alpha$ and $\mathbf{A}_1^\kappa$ respectively, *Scheme 1*, [2][9])) to 41.7 ppm in **6a**. A marked double-shielding *γ-gauche* effect influences similarly the C(9) signal in 5β-steroids [13b] [16], the upfield shift of this resonance being usually in the range 12–14.5 ppm with respect to the same signal (at about 54–55 ppm) in the corresponding 5α-steroids [13b] [14–16]. A *γ-gauche* effect, due to the C(6)–H_α bond, is probably also responsible for the upfield shift of about 5–7 ppm exhibited by the resonance of C(14) (50.3 ppm) in **6a** (and also in **7a** and **8**, 50.9 and 50.5 ppm respectively), as compared to the value in the (*E*)-secoketones **3a**, **4a** and **5** (*ca.* 56.5 ppm), and in normal steroid compounds (55–57 ppm), where this effect is inexistent [14–16].

The ^{13}C(19) nucleus in **6a** resonates at about 19 ppm, and the same value is also observed for the C(19) signal of the other two (*Z*)-secosteroids **7a** and **8**. This signal is situated downfield when compared to the C(19) resonance (at 12.5–12.8 ppm) of the corresponding (*E*)-diastereoisomers **3a**, **4a** and **5** in conformations **3a**–$\mathbf{A}_1$, **4a**–$\mathbf{B}_1^\alpha$ and **5**-$\mathbf{A}_1^\kappa$ where the 19-methyl group is β-oriented *(Scheme 1)* [2]. Since in the conformation $\mathbf{C}_1$ *(Scheme 2)*, established for the (*Z*)-*seco*-ketones **6a**, **7a** and **8** (see below), the 19-methyl group is also located on the β-side of the steroid skeleton and suffers the same two *γ-gauche* effects from the steroid ring C, the observed difference in the C(19) chemical shift must be due to the *γ-cis* effect (*cis*-C(19)–C(10)=C(1)–C(2)) [13a] [13b], which is present only in the (*E*)-ketones mentioned above (**3a**–$\mathbf{A}_1^\beta$, **4a**–$\mathbf{B}_1^\alpha$ and **5**–$\mathbf{A}_1^\kappa$) and which, as the result of the shielding

[8]) One effect being of the *γ-cis* type, C(9)–C(10)=C(1)–C(2) [13a] [13b], and the other of the *γ-gauche* type, C(9)–C(8)–C(7)–C(6) [13b] [13c].

[9]) And also in normal 5α-steroid compounds [13b] [14] [15].

interaction of the C(2)–H_β bond with the CH_3(19) group, causes an upfield shift of the C(19) signal in the three (*E*)-compounds with the 19β-methyl group[10]).

3.2. (*Z*)-*3α-Acetoxy-5,10*-seco-*5-ketone* **7a**. The NMR. spectra of this compound closely resemble those of the (*Z*)-3β-epimer **6a** and also suggest conformation $\mathbf{C_1}$ in solution for the 10-membered ring *(Scheme 2)*.

^{1}H-NMR. Spectrum. Contrary to **6a**, in the epimer **7a** the 3α-acetoxy group is axial, since the signal of H–C(3) shows a large coupling (~13 Hz) with H_α–C(2) and must therefore be equatorial, with a dihedral angle of about 180° between H_β–C(3) and H_α–C(2). Unfortunately, the H_β–C(3) signal (at ~4.9 ppm) was not resolved owing to overlap with the resonance of the vinyl proton at C(1), so its fine structure could not be assessed even at 360 MHz. The H_β–C(4) signal appears at 2.64 ppm as a doublet of doublets (16.2 Hz and 3.6 Hz), indicating a dihedral angle of about 60° between H_β–C(4) and H_β–C(3). These and other features of the ^{1}H-NMR. spectrum of **7a** show that the spatial arrangement of C(1), C(2), C(3) and C(4) must be very similar to that in the 3β-epimer **6a**.

^{13}C-NMR. Spectrum. There are no significant differences in the ^{13}C-NMR. spectra of **6a** and **7a** *(Table 5)*, and the discussion above for **6a** is also valid for the 3α-epimer **7a**.

3.3. (*Z*)-*5,10*-seco-*5-diketone* **8**. The ^{1}H-NMR. and ^{13}C-NMR. parameters again suggest $\mathbf{C_1}$ as the sole conformation (in solution) of the (*Z*)-unsaturated 10-membered ring in the diketone **8** *(Scheme 2)*.

^{1}H-NMR. Spectrum. The H–C(1) resonance at 4.98 ppm shows the same coupling pattern as the corresponding signals in compounds **6a** and **7a**, and therefore the dihedral angles of H–C(1) with H_β–C(2) and H_α–C(2) must be very similar in all three (*Z*)-secocompounds, *i.e.* about 60° and 180°. Since the resonances assigned to H_β–C(4) and H_α–C(4) appear as an AB pattern at 3.76 and 2.52 ppm, respectively, it follows that the 4β-proton is in the deshielding and the 4α-proton in the shielding zone of the 5-carbonyl group.

^{13}C-NMR. Spectrum. The chemical shifts of the relevant ^{13}C nuclei C(9), C(14) and C(19) in **8** are very similar to the values observed for these carbon atoms in compounds **6a** and **7a**. This indicates that the spatial arrangement of the (*Z*)-unsaturated 10-membered ring is alike in all three (*Z*)-secosteroids, and, therefore, that in the diketone **8** the bonds C(1)–C(2) and C(6)–C(7) are again roughly parallel to the direction of the C(9)–H_α bond.

4. Discussion. – On the basis of this NMR. analysis we conclude that in toluene the three (*Z*)-unsaturated 5,10-*seco*-5-ketones **6a**, **7a** and **8** have one and the same conformation of the 10-membered ring, of type $\mathbf{C_1}$ *(Scheme 2)*, which corresponds to the solid state conformation, determined by X-ray analysis of the *p*-bromobenzoate ester **6b** (see Section 2). The (*Z*)-acetates **6a** and **7a** differ only in the relative spatial

[10]) In conformations $\mathbf{B}^{\beta}_{\frac{1}{2}}$, $\mathbf{A}^{\alpha}_{\frac{1}{2}}$ and $\mathbf{A}^{\alpha}_{\frac{1}{2}}$ of the (*E*)-compounds **3a**, **4a** and **5** *(Scheme 1)*, the 19-methyl group is α-oriented and (in contrast to the 19β-methyl group in the above discussed (*E*)-conformations **3a**–$\mathbf{A}^{\beta}_{\frac{1}{2}}$, **4a**–$\mathbf{B}^{\alpha}_{\frac{1}{2}}$ and **5**–$\mathbf{A}^{\alpha}_{\frac{1}{2}}$ *(Scheme 1)*, and the (*Z*)-conformation $\mathbf{C_1}$ of **6a**, **7a** and **8** *(Scheme 2)*) is not subjected to the *γ-gauche* effect of the C(8)–H_β and C(11)–H_β bonds or any other C–H bonds in ring C. Therefore, in spite of the still present *γ-cis* effect, the C(19) resonance in these (*E*)-conformations with the 19α-methyl group is deshielded and shifted downfield, appearing at 19–19.5 ppm [2].

orientation of the 3-acetoxy group, which is equatorial in the 3β-ester **6a** and axial in the 3α-epimer **7a**[11]). That the conformation of the (*Z*)-unsaturated 10-membered ring is very similar or the same in the 3-acetates **6a** and **7a**, and, hence, does not depend on the β- or α-configuration of the 3-acetoxy group (contrary to the corresponding compounds of the (*E*)-series *(Scheme 1)* [1] [2]), is also supported by the CD. measurements of **6a** and **7a**, both compounds exhibiting a positive *Cotton* effect. Conformation $\mathbf{C}_1$ of the (*Z*)-unsaturated 10-membered cyclodecenone ring in secocompounds **6** and **7** *(Scheme 2)*, which is of the same type as the conformation of (*Z*)-cyclodecene determined by X-ray analysis of its crystalline $AgNO_3$ adduct [17][12]), was postulated in our previous studies for the following reasons.

(i) The large distance between the keto-carbonyl C(5) and the $\Delta^{1(10)}$-olefinic double bond (over 3.5 Å; see *Table 2*) accounts for the non-formation of transannular C(5),C(1)- and/or C(5),C(10)-bonds in various reactions of the (*Z*)-3-acetoxy-5-ketones **6a** and **7a** [3–7][13]). The same reactions, however, in the case of the corresponding (*E*)-diastereoisomeric ketoacetates **3a** and **4a**, because of the suitable transannular C(5)···C(1) proximity *(Scheme 1)* [1] [2], do bring about internal ring closure (under acid-catalyzed [2] [4] [18], thermal [4] [18] and UV. [5] [20] conditions, and thermal conditions of oximes of **3a** and **4a** [6]).

(ii) The unfavourable stereoelectronic relationship between the orbital system at C(3) with its leaving tosyloxy group and the π-system of the $\Delta^{1(10)}$-double bond in conformation $\mathbf{C}_1$ *(Scheme 2)* should and does prevent intramolecular C(1)–C(3) bond formation in the solvolysis of the (*Z*)-3-toluene sulfonates **6c** and **7c** [3] [7][13]). In contrast, in the corresponding (*E*)-diastereoisomeric esters **3c** and **4c** the stereoelectronic situation[14]) is appropriate for solvolysis (departure of the 3-toluenesulfonate anion) with internal 1,3-cyclopropane ring closure [3] [7].

(iii) The fact that both the sodium borohydride and lithium aluminium hydride reductions of the (*Z*)-3β-acetoxy-5-ketone **6a** and the corresponding (*Z*)-3β-hydroxy-5-ketone **6d** afford mixtures of 5*S* (5α-OH)[15]) and 5*R* (5β-OH) 3-alcohols (*ca.* 4:1) [19], is consistent with the steric features of the (*Z*)-conformation $\mathbf{C}_1^{\beta}$. Inspection of molecular models reveals that this conformation *(Scheme 2)* allows approach of the reducing agent to the keto-carbonyl C(5) atom from both sides[15]), but that, because of the presence of rings C and D, attack from the β-side to give the alcohol with the 5*S* (5α-OH) configuration, should be preferred.

The authors from Yugoslavia are grateful to the *Serbian Academy of Sciences and Arts* and to the *Serbian Republic Research Fund* for financial support.

---

[11]) The situation is different in the corresponding (*E*)-*seco*esters **3a** and **4a**, where it was established that the 3-acetoxy group is always equatorial, regardless of its β- or α-configuration *(Scheme 1)* [1] [2].

[12]) Conformations of the $\mathbf{C}_1$ type are closely related to the stable conformation of cyclodecane [17].

[13]) Conceivable reactive (*Z*)-conformations in which such intramolecular cyclizations could be expected [4] [19], are associated with large steric (*I*) strain, and are therefore not attainable under the conditions of the reactions studied.

[14]) In conformations **3c**–$\mathbf{B}_2$ and **4c**–$\mathbf{B}_1$ *(Scheme 1)*.

[15]) In general, the terms '*a*' and 'β' (denoting orientation of substituents or side of approach of a reagent) in the 10-membered ring of 5.10-secosteroids (*e.g.* in conformation $\mathbf{C}_1$) are formally defined with respect to the spatial position of the angular methyl C(18)-atom when the 10-membered ring has the hypothetical planar conformation, the side of the ring opposite to that in which CH_3(18) is located being called '*a*', and the same side 'β'.

Experimental Part[16])

Silica gel 0.05–0.20 was used for preparative column chromatography. The separation of products was controlled by TLC. on silica gel G *(Stahl)* using benzene/ethyl acetate 9:1, 7:3 or 1:1 for development and 50% aqueous sulfuric acid for detection.

Melting points (m.p.) are not corrected. Optical rotations were measured at 20° in $CHCl_3$. IR. spectra were determined on a *Perkin-Elmer* instrument, Model 337 ($\tilde{\nu}_{max}$ cm^{-1}). Noise decoupled ^{13}C-NMR. spectra were recorded at 25.2 MHz on a *Varian* XL-100 spectrometer equipped with a *Fourier* transform accessory. ^1H-NMR. spectra were measured at 100 MHz on the same apparatus and at 360 MHz on a *Bruker* HX-360 spectrometer. Deuterions of the deuteriated solvents ((D_8) toluene and $CDCl_3$) were used for a 15.4 MHz ^2H-lock during ^{13}C-work. Routine ^1H-NMR. spectra were recorded at 100 MHz on a *Varian* HD-100 spectrometer in $CDCl_3$ or at 60 MHz on a *Varian* A-60A spectrometer in CCl_4, at RT., using TMS as internal standard; chemical shifts are expressed in ppm (δ scale).

*(Z)-3β-Acetoxy-5,10-*seco*-1(10)-cholesten-5-one* (**6a**). A mixture of 3β-acetoxy-5α-cholestan-5-ol (**1**) [8] (2.23 g, 0.005 mol), dry lead tetraacetate (10.2 g, 0.023 mol) and I_2 (2.0 g, 0.008 mol) in dry cyclohexane (400 ml) was stirred and irradiated for 2 h without heating with a 500 W tungsten lamp placed in a central water- and air-cooled jacket. It was then filtered, washed with 10% aqueous $Na_2S_2O_3$-solution, aqueous $NaHCO_3$-solution and water, dried (Na_2SO_4) and evaporated *in vacuo*, to give a mixture which was chromatographed on silica gel (60 g). Benzene eluted 1.20 g (54%) of (*Z*)-3β-acetoxy-5,10-*seco*-1(10)-cholesten-5-one (**6a**), which was recrystallized from acetone/MeOH (976 mg, 44%), m.p. 138°. Further elution with benzene/ether 98–96:2–4 and then 90–80:10–20, afforded 266 mg (12%) of (*E*)-3β-acetoxy-5,10-*seco*-1(10)-cholesten-5-one (**3a**) [4], its 1,5-cyclization product (111 mg, 5%) [4] [18], and starting alcohol **1** (245 mg, 11%).

*(Z)-3β-*p*-Bromobenzoyloxy-5,10-*seco*-1(10)-cholesten-5-one* (**6b**). Saponification of **6a** (311 mg, 0.7 mmol) to (*Z*)-3β-hydroxy-5,10-*seco*-1(10)-cholesten-5-one (**6d**) (231 mg, 82%), m.p. 116–118° (from MeOH) [4], was effected with 5% methanolic KOH-solution [4]. A mixture of alcohol **6d** (201 mg, 0.5 mmol) and *p*-bromobenzoyl chloride (220 mg, 1 mmol) in dry pyridine (10 ml) was allowed to stand at RT. in the dark until complete consumption of the substrate **6** (about 48 h). It was then poured into ice-cold water (20 ml), acidified with diluted aqueous HCl-solution 1:1 and extracted with ether. The ethereal layer was washed with water, aqueous $NaHCO_3$-solution and water, dried (Na_2SO_4) and evaporated *in vacuo*. The solid residue was recrystallized from light petroleum (b.p. 40–60°) to give 246 mg (84%) of (*Z*)-3β-*p*-bromobenzoyloxy-5,10-*seco*-1(10)-cholesten-5-one (**6b**), m.p. 168°; $[\alpha]_D = +70°$ ($c = 1.0$). – IR. (KBr): 1720, 1692, 1584, 1270. – ^1H-NMR.: 0.71 (*s*, $H_3C(18)$); 0.89 (*d*, $H_3C(26)$, $H_3C(27)$, $H_3C(21)$); 1.75 (*s*, $H_3C(19)$)[17]); 5.10–5.80 (br. *m*, H–C(1), H–C(3)); 7.58 (*d*, $J = 9$ Hz, 2 aromatic H *ortho* to –COO); 7.90 (*d*, $J = 9$ Hz, 2 aromatic H *ortho* to –Br).

$C_{34}H_{49}BrO_3$ (585.64) Calc. C 69.72 H 8.31% Found C 69.48 H 8.24%

*(Z)-3α-Acetoxy-5,10-*seco*-1(10)-cholesten-5-one* (**7a**) *and (Z)-3α-hydroxy-5,10-*seco*-1(10)-cholesten-5-one* (**7d**). A mixture of 3α-acetoxy-5β-cholestan-5-ol (**2**) [10] (2.0 g, 0.0045 mol), dry lead tetraacetate (8.0 g, 0.018 mol) and I_2 (1.5 g, 0.006 mol) in dry cyclohexane (400 ml) was stirred and irradiated for 2 h (without heating) with a 500 W tungsten lamp contained in a central water- and air-cooled jacket. The precipitate was removed by filtration, and the filtrate washed with aqueous $Na_2S_2O_3$-solution, aqueous $NaHCO_3$-solution and water, dried ($MgSO_4$) and evaporated *in vacuo*, to give a mixture which was chromatographed on silica gel (60 g). Elution with benzene/ether 99:1 afforded a mixture (1.45 g, 72.4%) of the diastereoisomeric (*Z*)- and (*E*)-3α-acetoxy-*seco*-ketones **7a** and **4a**, from which, after several recrystallizations from acetone/MeOH, 760 mg (38%) of pure **7a** [3] was obtained, m.p. 129–130°; $[\alpha]_D = +17°$ ($c = 1.0$). – IR. (KBr): 1728, 1705, 1265. – ^1H-NMR.: 0.68 (*s*, $H_3C(18)$); 0.87 (*d*, $H_3C(26)$, $H_3C(27)$); 0.91 (*d*, $H_3C(21)$); 1.64 (*s*, $H_3C(19)$)[17]); 2.06 (*s*, AcO); 4.8–5.2 (*m*, H–C(1), H–C(3)).

$C_{29}H_{48}O_3$ (444.67) Calc. C 78.32 H 10.88% Found C 78.18 H 10.81%

A solution of **7a** (200 mg, 0.45 mmol) in 0.5% methanolic KOH-solution (30 ml) was stirred 2.5 h at 0°; then diluted with water and extracted with ether. The organic layer was washed with water until

---

[16]) IR. and routine ^1H-NMR. (at 60 MHz) spectral measurements were performed in the Laboratories for Instrumental Analysis (directed by Prof. *D. Jeremić*), and elemental microanalyses in the Microanalytical Laboratory (Dr. *R. Tasovac*) of the Department of Chemistry, Faculty of Science, Belgrade.

[17]) This signal of H_3C–C(19) which is attached to the olefinic C(10) is actually a singlet-like multiplet *(d)*, because of small vinyl and allyl couplings ($J \sim 0.5$–1 Hz) with H–C(1) and 2 H–C(2) [4].

neutral, dried ($MgSO_4$) and evaporated *in vacuo*. The residue was chromatographed on silica gel (8 g). Elution with benzene/ether 80:20 afforded **7d** [3] (152 mg, 84%), m.p. 116° after several crystallizations from acetone (100 mg, 55%); $[\alpha]_D = -14°$ ($c = 0.8$). – IR. (KBr): 3498, 3440, 1680. – ^{1}H-NMR.: 0.71 (*s*, $H_3C(18)$); 0.88 (*d*, $H_3C(26)$, $H_3C(27)$); 0.93 (*d*, $H_3C(21)$); 1.64 (*s*, $H_3C(19)$)[17]), ~3.7 (br. *m*, H–C(3)); ~5.1 (*m*, H–C(1)).

$C_{27}H_{46}O_2$ (402.64) Calc. C 80.54 H 11.52% Found C 80.63 H 11.61%

(*Z*)-*5,10*-seco-*1(10)-Cholesten-3,5-dione* (**8**). A solution of (*Z*)-3β-hydroxy-5,10-*seco*-1(10)-cholesten-5-one (**6d**) [4] (201 mg, 0.5 mol) or its 3α-epimer **7d** (see above) in dry pyridine (2.5 ml) was added to a slurry of CrO_3 (200 mg, 2 mmol) in dry pyridine (2 ml). The mixture was allowed to stand 24 h at RT., and was then diluted with ether and filtered. The filtrate was washed with water, dilute acetic acid, aqueous $NaHCO_3$-solution and water, and dried ($MgSO_4$). Removal of the solvent *in vacuo* afforded 193 mg (96%) of **8** [3], m.p. 128° (from acetone); $[\alpha]_D = +320°$ ($c = 1.0$). – IR. (KBr): 1735, 1720, 1705. – ^{1}H-NMR.: 0.73 (*s*, $H_3C(18)$); 0.87 (*d*, $H_3C(26)$, $H_3C(27)$); 0.90 (*d*, $H_3C(21)$); 1.74 (*s*, $H_3C(19)$)[17]); 5.20 (*m*, H–C(1)).

$C_{27}H_{44}O_2$ (400.62) Calc. C 80.94 H 11.07% Found C 80.88 H 11.20%

REFERENCES

[1] *H.-C. Mez, G. Rist, O. Ermer, Lj. Lorenc, J. Kalvoda & M. Lj. Mihailović*, Helv. Chim. Acta *59*, 1273 (1976).

[2] *H. Fuhrer, Lj. Lorenc, V. Pavlović, G. Rihs, G. Rist, J. Kalvoda & M. Lj. Mihailović*, Helv. Chim. Acta *62*, 1770 (1979).

[3] *Lj. Lorenc, M.J. Gašić, I. Juranić, M. Dabović & M. Lj. Mihailović*, J. Chem. Soc. Perkin II *1980*, 1356.

[4] *M. Lj. Mihailović, Lj. Lorenc, M. Gašić, M. Rogić, A. Melera & M. Stefanović*, Tetrahedron *22*, 2345 (1966).

[5] *M. Lj. Mihailović, Lj. Lorenc, N. Popov & J. Kalvoda*, Helv. Chim. Acta *54*, 2281 (1971).

[6] *M. Lj. Mihailović, Lj. Lorenc, Z. Maksimović & J. Kalvoda*, Tetrahedron *29*, 2683 (1973).

[7] *Lj. Lorenc, M.J. Gašić, I. Juranić, M. Dabović & M. Lj. Mihailović*, Tetrahedron Lett. *1974*, 395.

[8] *Pl. A. Plattner, Th. Petrzilka & W. Lang*, Helv. Chim. Acta *31*, 1833 (1948); ibid. *27*, 513 (1944); *M. Lj. Mihailović, Lj. Lorenc, V. Pavlović & J. Kalvoda*, Tetrahedron *33*, 441 (1977).

[9] *Lj. Lorenc, Z. Maksimović, R. Božinov, J. Kalvoda & M. Lj. Mihailović*, unpublished results.

[10] *Pl. A. Plattner, H. Heusser & A.B. Kulkarni*, Helv. Chim. Acta *31*, 1822, 1885 (1948); ibid. *32*, 265 (1949).

[11] *C. Altona, H.J. Geise & C. Romers*, Tetrahedron *24*, 13 (1968).

[12] See, for example, *E.W. Garbisch*, J. Am. Chem. Soc. *86*, 5561 (1964); *E. Becker*, 'High Resolution NMR', Academic Press, New York, N.Y. 1969, p. 104.

[13] a) *P.A. Couperus, A.D.H. Clague & J.P.C.M. van Dongen*, Org. Magn. Reson. *8*, 426 (1976); b) *N.K. Wilson & J.B. Stothers*, in 'Topics in Stereochemistry', Vol. 8, Eds. E.L. Eliel & N.L. Allinger, Wiley-Interscience, New York–London 1974, pp. 25–54, and ref. therein; c) *F.W. Wehrli & T. Wirthlin*, 'Interpretation of Carbon-13 NMR Spectra', Heyden & Son, London–New York 1976, pp. 22–45, and ref. therein.

[14] *H.J. Reich, M. Jautelat, M.T. Messe, F.J. Weigert & J.D. Roberts*, J. Am. Chem. Soc. *91*, 7445 (1969); *H. Eggert, C.L. VanAntwerp, N.S. Bhacca & C. Djerassi*, J. Org. Chem. *41*, 71 (1976).

[15] *J.W. Blunt & J.B. Stothers*, Org. Magn. Reson. *9*, 439 (1977), and ref. therein; *W.B. Smith*, in 'Annual Reports on NMR. Spectroscopy', Vol. 8, Ed. G.A. Webb, Academic Press, New York, N.Y. 1978, pp. 199–226, and ref. therein.

[16] *J.L. Gough, J.P. Guthrie & J.B. Stothers*, Chem. Commun. *1972*, 979; *D. Leibfritz & J.D. Roberts*, J. Am. Chem. Soc. *95*, 4996 (1973).

[17] *J.D. Dunitz*, in 'Perspectives in Structural Chemistry', Vol. 2, Eds. J.D. Dunitz & J.A. Ibers, Wiley, New York–London 1968, pp. 54–62; *O. Ermer*, Ph. D. Thesis (No. 4465), ETH, Zürich 1970; *J.D. Dunitz*, Pure Appl. Chem. *25*, 495 (1971).

[18] *M. Lj. Mihailović, Lj. Lorenc, J. Foršek, H. Nešović, G. Snatzke & P. Trška*, Tetrahedron *26*, 557 (1970).

[19] *M. Lj. Mihailović, M.J. Gašić, I. Juranić & Lj. Lorenc*, Bull. Soc. Chim. Beograd *36*, 401 (1971).

[20] *M. Lj. Mihailović, Lj. Lorenc, V. Pavlović & J. Kalvoda*, Tetrahedron *33*, 441 (1977).