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Stereochemically Controlled Acetalizations in the Ten-Membered Ring of (Z)- and (E)-5,10-Seco-Steroidal Ketones*

Ljubinka Lorenc, Milan Dabović, Vladimir Pavlović, Ivan Juranić and Jože Foršek

Department of Chemistry, Faculty of Science, University of Belgrade, and Institute of Chemistry, Technology and Metallurgy, P. O. Box 550, 11001 Belgrade, Yugoslavia

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(Z)-3β-Acetoxy-5,10-seco-cholest-1(10)-en-5-one *2a* reacts with *m*-chloroperbenzoic acid to give the *cis*-(1*S*,10*R*)-epoxide 4, which, under acid-catalyzed conditions, undergoes stereospecific intramolecular cyclization to afford the (1*S*,5*S*,10*S*)-acetal 5. On the other hand, hydrolysis of the osmate ester of (*E*)-3β-acetoxy-5,10-seco-cholest-1(10)-en-5-one *3a* (with aqueous hydrochloric acid in methanol solution) produces two stereochemically different acetal derivatives, *i. e. the* (1*R*,5*R*,10*R*)-product 7 and (1*S*,5*S*,10*S*)-isomer 5, in ca. 49% and 28% yields, respectively. The stereochemical course of these transformations is discussed in terms of the most stable ground-state conformations of the starting (Z)- and (*E*)-seco-ketones (*2a* and *3a*) in solution.

For some time now we have been interested in 5,10-seco-steroids (compounds of type *2a—c* and *3a—c*, Scheme 1), obtained by oxidative β-fragmentation of the C(5)—C(10) bond in 5α- or 5β-hydroxy steroids such as *1a—c* (Scheme 1), under the conditions of the lead tetraacetate[1,2] and hypoiodite reaction.[3,4]

Due to the presence of several reactive functional groups incorporated into the ten-membered ring of the modified steroid molecules (i. e. the *Z* or *E* 1(10)-olefinic double bond, the transannular 5-keto-carbonyl group, and the homoallylic 3-acetate function) and the possibility of configurational and conformational isomerism, 5,10-secosteroids have proven to be very suitable substrates for the investigation of the structure-reactivity relationship in the ten-membered ring systems, particularly in reactions which might involve intramolecular and transannular processes.[5] The present study is concerned with the stereochemically controlled behaviour of the diastereomeric (Z)- and (*E*)-3β-acetoxy-5,10-seco-cholest-1(10)-en-5-ones (*2a* and *3a*, Scheme 1) in oxidations with *m*-chloroperbenzoic acid and osmium tetroxide, followed by acid-catalyzed processes.

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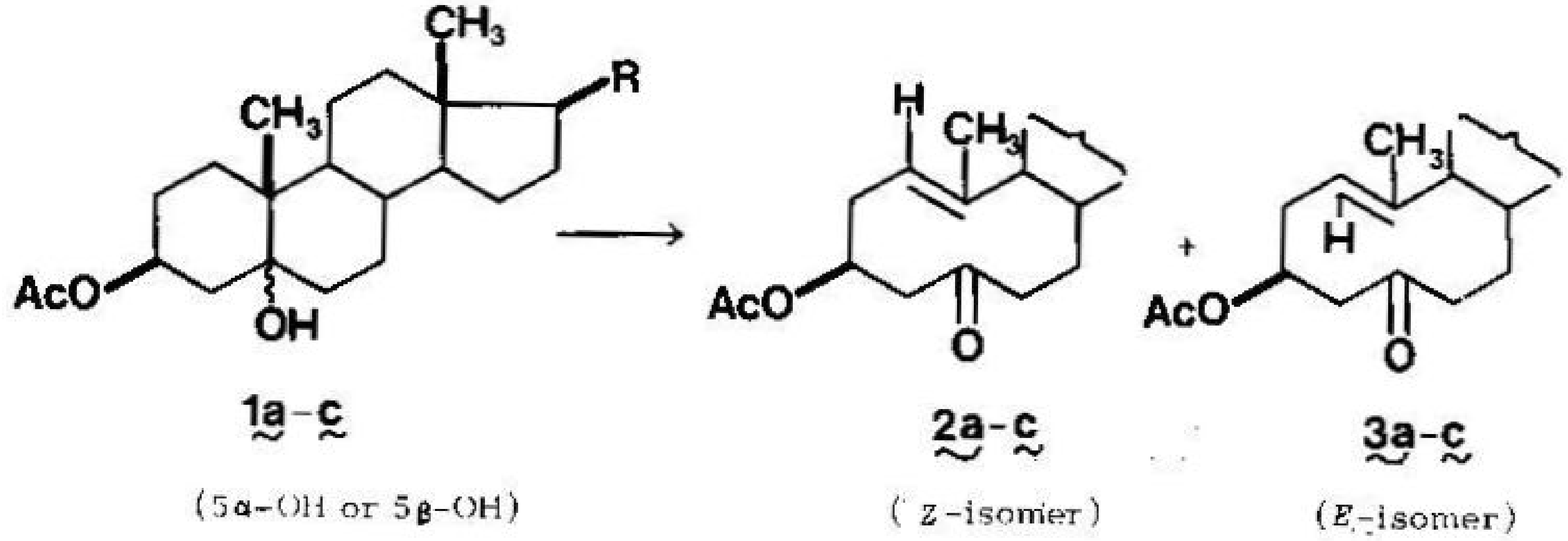
* Dedicated to Professor Mihailo Lj. Mihailović on the occasion of his 60th birthday.



a. $R = C_8H_{17}$

b. R = OAc

c. R = H, etc.

SCHEME 1

RESULTS AND DISCUSSION

Epoxidation of (*Z*)-3β-acetoxy-5,10-seco-cholest-1(10)-en-5-one *2a* with *m*-chloroperbenzoic acid (in dichloromethane solution at 0—5°) afforded stereoselectively the *cis*-(1*S*,10*R*)-epoxide *4* (Scheme 2) in ca. 90% yield.[*] When this compound was treated with perchloric acid (in tetrahydrofuran solution at 0°), it readily underwent transannular cyclization to give as the sole product the 3β-acetoxy-(1*S*,5*S*,10*S*)-acetal derivative *5*, in 87% yield.

On the other hand, when the (Z)-seco-ketone *2a* was treated with osmium tetroxide (in benzene-pyridine (1 : 1) solution at room temperature for 8 days), it remained mostly unchanged (over 90%),[**] while the part which had reacted consisted of a complex mixture from which no characterized product could be isolated.

When the diastereomeric (*E*)-3β-acetoxy-5,10-seco-cholest-1(10)-en-5-one *3a* was subjected to the same reactions under similar experimental conditions as those described above, it behaved differently. Thus, it also reacted stereoselectively with *m*-chloroperbenzoic acid to produce the *trans*-(1*R*,10*R*)-epoxide *6* (Scheme 3) in 85% yield; however, in contrast to the *cis*-epoxide *4*, this compound was stable when treated with perchloric acid. Also, contrary to the (*Z*)-isomer *2a*, the (*E*)-seco-ketone *3a* reacted quantitatively with osmium tetroxide. When the osmate ester thus obtained was hydrolyzed (with aqueous hydrochloric acid in methanol solution at room temperature), it afforded two stereochemically different acetal derivatives, i. e. the (1*R*,5*R*,10*R*)-product 7[+]

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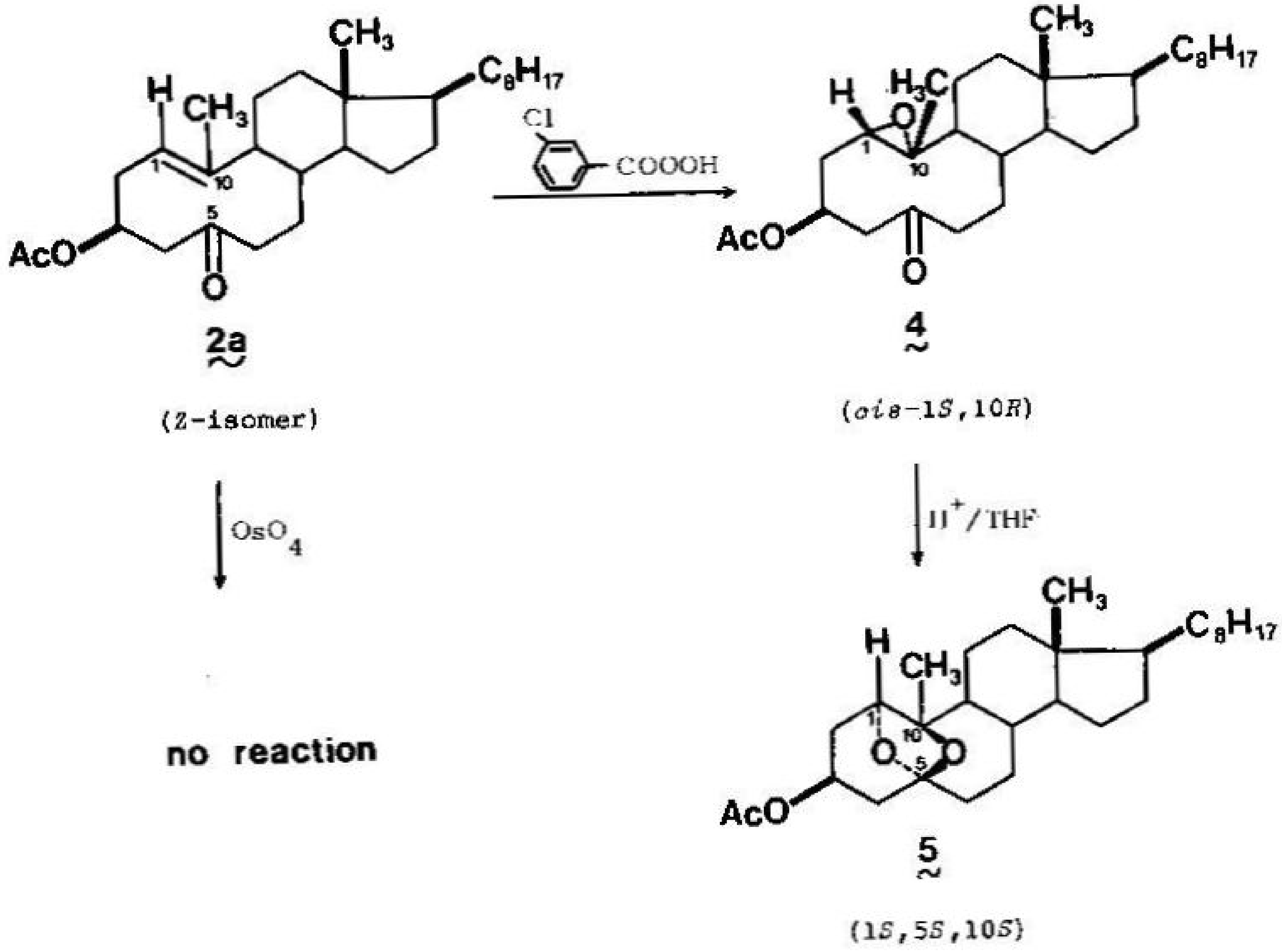
[*] All yields refer to recrystallized and analytically pure compounds.

[**] This reaction was previously tried under somewhat different experimental conditions.[1] It was reinvestigated in the present study for the purpose of comparison.

[+] Acetal 7 was earlier obtained as a minor product (in about 6.5% yield) when hydrolysis of the osmate ester was performed with hydrogen sulfide in acetone solution.[1]



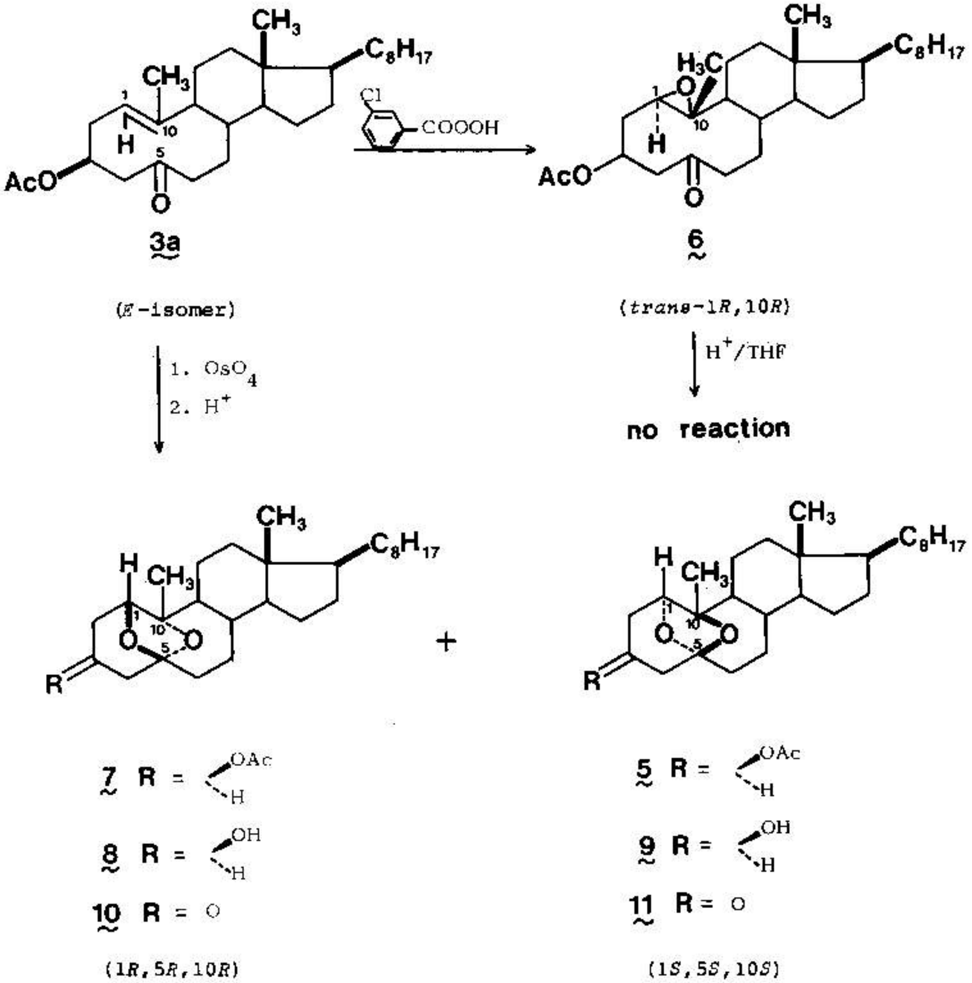
SCHEME 2

and the (1*S*,5*S*,10*S*)-isomer *5* (identical with the compound formed from the *cis*-epoxide *4* under acid-catalyzed conditions) (Scheme 3), in ca. 49% and 28% yields, respectively.[†]

Saponification of the 3β-acetoxy-acetal derivatives *7* and *5* (with 2.5% aqueous methanolic potassium hydroxide) gave the corresponding 3β-hydroxy-acetals *8* and *9*, which in turn were transformed (by oxidation with the Kiliani's chromic acid solution) to the corresponding ketone derivatives *10* and *11*, respectively (Scheme 3).[*] Also, separate experiments have shown that the acetal derivatives 5 and 7 are stable under the reaction conditions applied for their formation; therefore, the yields presented in Schemes 2 and 3 reflect the original amounts in which these compounds are produced in the respective transannular acetalization processes.

[†] Actually, in the course of the reaction the 3β-acetoxy group underwent partial hydrolysis. The resulting mixture, after isolation, was reacetylated and the 3β-acetoxy acetal derivatives 7 and 5 separated by column chromatography.

[*] The constitution and stereochemistry of all products given in Schemes 2 and 3 were established on the basis of elemental microanalysis and spectral data.



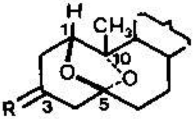
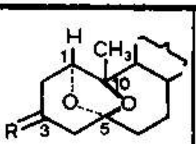
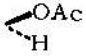
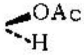
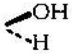
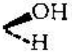
SCHEME 3

Configurational Assignments of the Acetal Grouping in Compounds 5 and 7

Since, due to steric reasons, intramolecular acetalization in the ten-membered ring of 5,10-secosteroidal ketones is feasible only when the hydroxy groups at C(1) and C(10) have the same (i. e. *R*,*R* or *S*,*S*) configuration, only the two stereoisomeric forms having the 1*R*,5*R*,10*R*- and 1*S*,5*S*,10*S*-configuration, should be considered as possible structures for the 3β-acetoxy acetals 5 and 7 (as well as for the derivatives *9* and *11*, and *8* and *10*, respectively). The distinction between these stereoisomeric pairs was made on the basis of physical data obtained for the compounds of both series.

Thus, the resonance signals of the protons at C(1) and C(3) in the ^{1}H-NMR spectra of compounds *7*, *8* and *10* appear at considerably lower fields than the corresponding signals of the stereoisomeric analogues *5*, *9* and *11* (Table I). Inspection of Dreiding models reveals that in the compounds possessing the 1*R*,5*R*,10*R*-stereochemistry of the acetal grouping, the proton at C(1) is located in the deshielding zone of the C(9)—C(11) single bond, and the proton at C(3), likewise, in the deshielding zone of the C(5)—O—C(1) oxygen, implying that compounds *7*, *8* and *10* have the 1*R*,5*R*,10*R*-configuration, and compounds *5*, *9* and *11* the 1*S*,5*S*,10*S*-configuration.

Table 1. ^{1}H-NMR Chemical shifts of H-C(1) and H-C(3) in acetal derivatives (**5**,**7**-**11**)[a)]

 (1*R*,5*R*,10*R*)	H-C(1) (ppm)	H-C(3) (ppm)	 (1*S*,5*S*,10*S*)	H-C(1) (ppm)	H-C(3) (ppm)
R =  **7**	4.21	5.37	R =  **5**	3.82	5.11
R =  **8**	4.18	4.37	R =  **9**	3.86	3.98
R = oxo **10**	4.43		R = oxo **11**	4.11	

a) ^{1}H-NMR Spectra were recorded in $CDCl_3$ at 360 MHz for compounds **5** and **7**, and at 100 MHz for compounds **8**-**11**. For further NMR data see Experimental.

Also, the ^{13}C-NMR data observed for the stereoisomeric 3β-acetoxy acetals 5 and 7 (Table II) are consistent with the configurations deduced above (i. e. the upfield shifts of the C(1), C(9) and C(19) signals in compound 5, with respect to the same signals in compound 7, are to be expected on the basis of the greater steric shielding of these nuclei in the former acetal). However, a detailed ^{13}C-NMR analysis, which would consider other effects present in these polycyclic systems possessing two oxygens, requires additional spectral information.*

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* The investigations are in progress.

TABLE II

^{13}C-NMR Shifts of Selected Carbon Atoms in Compounds 5 *and* 7[a]

Carbon	5	7
C(1)	82.4	87.3
C(2)	30.1	27.9
C(3)	67.0	68.5
C(4)	39.6	40.4
C(5)	107.4	108.4
C(6)	33.7	34.1
C(7)	30.5	31.7
C(8)	39.5	40.2
C(9)	52.7	57.8
C(10)	84.6	76.0
C(11)	26.4	24.9
C(12)	39.4	39.2
C(13)	41.9	43.2
C(14)	56.3	56.6
C(18)	11.8	12.4
C(19)	17.1	20.0

[a] Spectra were measured at 25.15 MHz, in $CDCl_3$. Chemical shifts are given in δ p.p.m. values downfield from $SiMe_4$.

Additional support in favour of the proposed configurations was obtained from CD measurements (Table III) performed on the 3-oxo-acetals *10* and *11*.

TABLE III

CD Data for the 3-Oxo-acetate 10 and 11 (in Acetonitrile)[a]

Compound	λ_{max} ($\Delta\varepsilon$)
10	316(—0.056), 299sh(+0.17), 287sh(+0.37), 280(+0.418), 209(+0.36)
11	316(+0.057), 308(+0.017) 299sh(—0.15), 287sh(—0.29), 280(—0.33)

[a] λ given in nm

Namely, in analogy with structurally similar compounds from the anhydro-sugar series, it can be assumed that in the acetals *10* and *11* the heterocyclic system will determine the Cotton-effect.[6] According to the projections (Scheme 4), the CD of the ketone band at 280 nm should be positive for *10* and negative for *11*; and, actually, this was experimentally found (Table III).

Projection for **10**

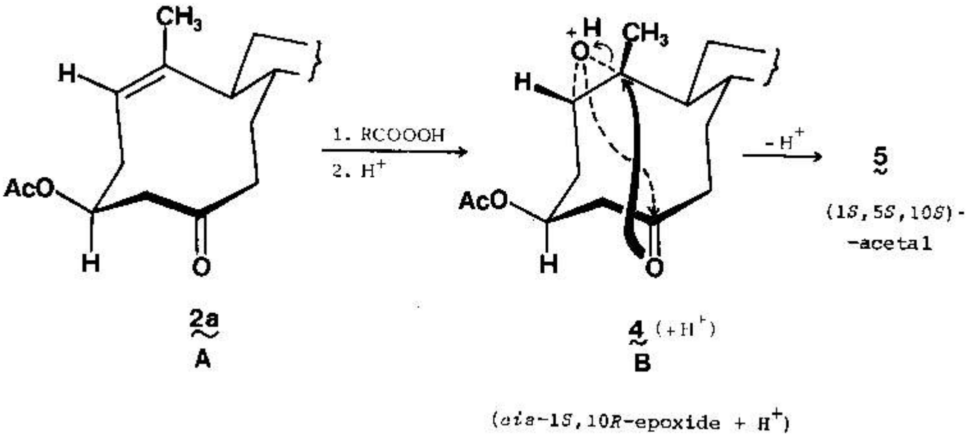
CD ⊕

Projection for **11**

CD ⊖

SCHEME 4

The results obtained in this study can be explained on the basis of mechanistic considerations, taking into account the most stable ground-state conformations of (Z)- and (E)-seco-ketones (*2a* and *3a*) in solution. The preferred conformations of these compounds in solution were deduced from ^{1}H- and ^{13}C-NMR spectral data.[7-9] They show that the 1(10)-cyclodecen-5-one ring in (Z)-seco-ketone (*2a*) is present in solution in only one conformation (A, Scheme 5)[7] in which approach of an external reagent to the olefinic double bond is sterically more favourable from the outside of the ring. Thus, reaction with *m*-chloroperbenzoic acid produces the *cis*-(1*S*,10*R*)-epoxide *4*. However, the stereochemical course of the subsequent transformation involving cleavage of epoxide ring and transannular acetalization is probably determined by the stability of the tertiary C(10) carbenium-ionic intermediate deriving from an oxonium-ion of type **B** (Scheme 5).



SCHEME 5

The ten-membered ring system of the (*E*)-stereoisomer 3a was found to exist in solution in two conformational forms (C, being the major and D the minor conformation, Scheme 6).[8,9] From the results presented in Scheme 3 it can be concluded that the (E)-seco-ketone *3a* reacts with *m*-chloroperbenzoic acid only in the major conformation C (producing the *trans*-(1*R*,10*R*)-epoxide *6*)* (Scheme 6), while in the reaction with osmium tetroxide both conformations (C and D) are involved, affording osmate esters with the 1*R*,10*R*- and 1*S*,10*S*-configuration *12* and *13*, respectively. The stereochemical course of the subsequent acid hydrolysis is determined by the stereochemistry of the starting osmate ester (*12* or *13*), the acetals produced being *7* (1*R*,5*R*,10*R*) and *5* (1*S*,5*S*,10*S*), respectively. According to molecular models, the final step in these transannular processes should be accompanied with extensive conformational changes in the respective intermediate(s).

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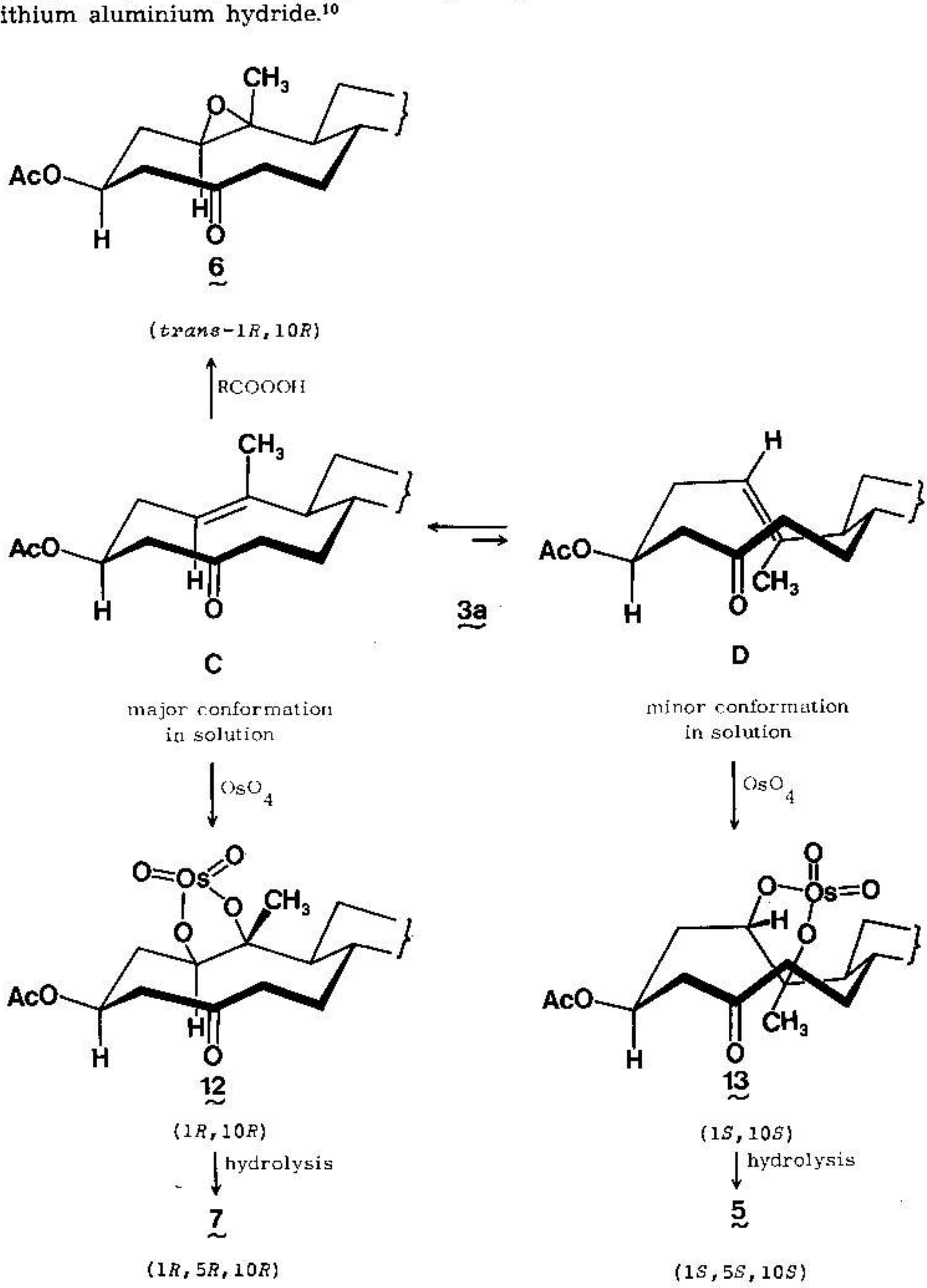
* For steric reasons protonation of the (1*R*,10*R*)-epoxide *6* cannot result in intramolecular acetalization.

Finally, it should be noted that the ketal grouping in compounds 5 and 7 is extremely stable, remaining unchanged upon treatment with acids, bases or lithium aluminium hydride.[10]



SCHEME 6

EXPERIMENTAL[*]

All m.ps are uncorrected. The CD spectra were recorded with an ISA-Jobin-Yvon dichrograph model Mark III at room temperature in acetonitrile, at concentrations of approximately 0.5 mg/ml. Optical rotations were measured in $CHCl_3$ solution. ^{1}H-NMR spectra were obtained at 100 MHz with a Varian HA-100 spectrometer and at 360 MHz with a Bruker HX-360 spectrometer; noise decoupled ^{13}C-NMR spectra were recorded at 25.15 MHz on a Varian XL-100 spectrometer equipped with a Fourier transform accessory; solvent — $CDCl_3$, internal standard — TMS, room temp.; chemical shifts are reported in ppm as δ values and coupling constants J in Hz; abbreviations: s singlet, d doublet, t triplet, q quartet, m multiplet. IR spectra were determined on a Perkin-Elmer instrument, Model 337; ν_{max} are given in cm^{-1} units. Silica gel (0.05—0.2 mm) was used for preparative column chromatography. Control of the reactions and separation of products were monitored by thin-layer chromatography on silica gel G (Stahl) with benzene-ethyl acetate (9 : 1 or 7 : 3), detection being effected with 50% aqueous sulfuric acid. Light petroleum refers to the fraction boiling at 40—60 °C.

Preparation of the (*Z*)- and (*E*)-5,10-seco-ketones *2a* and *3a* was reported previously.[1] *(Z)-3β-acetoxy-5,10-seco-cholest-1(10)-en-5-one 2a*, m. p. 138 °C, $[\alpha]_D^{23} = + 38.7°$; *(E)-3β-acetoxy-5,10-seco-cholest-1(10)-en-5-one 3a*, m. p. 136°C, $[\alpha]_D^{23} = + 4°$.[**]

Epoxidation of (Z)-3β-Acetoxy-5,10-seco-cholest-1(10)-en-5-one 2a

To a stirred solution of (*Z*)-seco-ketone *2a* (889 mg) in dichloromethane (10 ml) cooled at 0 °C, *m*-chloroperbenzoic acid (450 mg) in dichloromethane (5 ml) was added, and the mixture was kept at 0—5 °C with stirring for 4 hr. It was then diluted with ether, the organic layer washed with $NaHSO_3$ aq, water, sat $NaHCO_3$ aq and water, dried over Na_2SO_4 and evaporated in vacuo to dryness, to afford 3β-acetoxy-5,10-seco-(1*S*,10*R*)-epoxy-cholestan-5-one *4* (921 mg, 100%) which was recrystallized from acetone-methanol (826 mg, 89.7%), m. p. 157—8 °C; $[\alpha]_D^{20} = +20.1°$ ($c = 0.58\%$); IR (KBr): ν_{max} 1740, 1704, 1260, 1035 cm^{-1}; ^{1}H-NMR (360 MHz): δ 0.71 ($H_3C(18)$, s), 0.87 ($H_3C(26)$ and ($H_3C(27)$, d), 0.91 ($H_3C(21)$, d), 1.34 ($H_3C(19)$, s), 2.08 (AcO-3, s), 2.96 (H—C(1), dxd, J 12 Hz, J 3 Hz), 5.46 (H—C(3), m).

Anal. $C_{29}H_{48}O_4$ (460.70) calc'd.: C 75.61; H 10.50%.
found: C 75.76; H 10.48%.

Acid-catalyzed Acetalization of 3β-Acetoxy-5,10-seco-(1S,10R)-epoxy-cholestan-5-one 4

To a solution of *cis*-(1*S*,10*R*)-epoxide *4* (200 mg) in tetrahydrofurane (5 ml) cooled at 0°, 0.8 ml of perchloric acid was added and the mixture was kept at the same temperature for 1 hr. Then, it was diluted with ether, the organic layer washed with water, sat $NaHCO_3$ aq, water, dried over Na_2SO_4 and evaporated in vacuo to dryness to give 3β-acetoxy-(1*S*,5*S*,10*S*)-acetal *5* (200 mg, 100%), which after recrystallization from methanol had m. p. 124 °C (174 mg, 87.0%); $[\alpha]_D^{20} = -1°$ ($c = 0.30\%$); IR (KBr): ν_{max} 1725, 1262, 1190, 1075 cm^{-1}; ^{1}H-NMR (360 MHz): δ 0.67 ($H_3C(18)$, s), 0.86 ($H_3C(26)$ and $H_3C(27)$, d), 0.90 ($H_3C(21)$, d), 1.35 ($H_3C(19)$, s), 2.06 (AcO-3, s), 3.82 (H—C(1), d, J 5.5 Hz), 5.11 (H—C(3), t, J 7 Hz).

Anal. $C_{29}H_{48}O_4$ (460.70) calc'd.: C 75.61; H 10.50%.
found: C 75.42; H 10.34%.

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[*] We thank Prof. G. Snatzke (Lehrstuhl für Strukturchemie, Ruhruniversität Bochum, West Germany) for the CD measurements and Dr. R. Tasovac (Faculty of Science, Belgrade) for carrying out elemental microanalyses. NMR spectral determinations were performed at Ciba-Geigy Ltd., Basle, Switzerland (direction Dr. H. Fuhrer), while IR and routine NMR spectra were recorded in the Laboratories for Instrumental Analysis, Faculty of Science, Belgrade (direction Prof. D. Jeremić).

[**] For additional physical data see Ref. 1.

Epoxidation of (E)-3β-Acetoxy-5,10-seco-cholest-1(10)-en-5-one 3a

Compound *3a* (889 mg) in dichloromethane (10 ml) was treated with *m*-chloroperbenzoic acid (450 mg) in dichloromethane (5 ml) as above. The crystalline solid (910 mg, 98.8%) obtained after the usual work up procedure was recrystallized from acetone-methanol to afford 3β-acetoxy-5,10-seco-(1*R*,10*R*)-epoxy-cholestan-5-one *6* (782 mg, 84.9%), m. p. 156—7 °C; $[\alpha]_D^{20} = +16.2°$ (c = 0.42%); IR (KBr): ν_{max} 1760, 1704, 1242, 1030 cm^{-1}; ^{1}H-NMR (360 MHz): δ 0.71 ($H_3C(18)$, s), 0.86 ($H_3C(26)$ and $H_3C(27)$, d), 0.90 ($H_3C(21)$, d), 1.34 ($H_3C(19)$, s), 2.05 (AcO-3, s), 2.70 (H—C(1) and H—C(4), m), 5.39 (H—C(3), m).

Anal. $C_{29}H_{48}O_4$ (460.70) calc'd.: C 75.61; H 10.50%.
found: C 75.80; H 10.66%.

*Treatment of 3β-Acetoxy-5,10-seco-(1*R*,10*R*)-epoxy-cholestan-5-one 6 with Perchloric Acid*

Compound *6* (100 mg) in tetrahydrofurane (2.5 ml) was treated with perchloric acid as above. The mixture was worked up in the usual way to give 86 mg of the unchanged starting material, m. p. 156—7 °C (from acetone-methanol).

Reaction of (E)-3β-Acetoxy-5,10-seco-cholest-1(10)-en-5-one 3a *with Osmium Tetroxide and Hydrolysis of the Resulting Osmate Ester with Hydrochloric Acid*

To a solution of (*E*)-seco-ketone *3a* (1.00 g) in benzene (35 ml) and pyridine (15 ml), osmium tetroxide (800 mg) was added and the mixture was left at room temperature for 8 days. It was then evaporated to dryness under reduced pressure, the residue dissolved in methanol (100 ml) and the solution treated with hydrochloric acid (7 ml 37% HCl + 3 ml H_2O)[11] at room temperature. The mixture was stirred overnight, diluted with ether, filtered through a Calit mat and the inorganic salts thoroughly washed with ether. The combined organic filtrates were washed with water, sat $NaHCO_3$ aq and water, dried over Na_2SO_4 and evoparated in vacuo to dryness. The residue was reacetylated with acetic anhydride (5 ml) and pyridine (5 ml) at room temperature for 18 hr. The mixture (1.1 g) obtained after the usual work up was chromatographed on silica gel (40 g). First, benzene fractions eluted a complex mixture (41 mg) which was not further investigated. Further elution with benzene gave 3β-acetoxy-(1*R*,5*R*,10*R*)-acetal *7* (579 mg, 55.9%), which was recrystallized from acetone-methanol (502 mg, 48.5%), m. p. 124 °C; $[\alpha]_D^{20} = +84.0°$ (c = 0.48%); IR (KBr): ν_{max} 1750, 1248, 1108, 1080, 1055 cm^{-1}; ^{1}H-NMR (360 MHz): δ 0.69 ($H_3C(18)$, s), 0.86 ($H_3C(26)$ and ($H_3C(27)$, d), 0.90 ($H_3C(21)$, d), 1.32 ($H_3C(19)$, s), 2.03 (AcO-3, s), 4.21 (H—C(1), d, *J* 5 Hz), 5.37 (H—C(3), m).

Anal. $C_{29}H_{48}O_4$ (460.70) calc'd.: C 75.61; H 10.50%.
found: C 75.84; H 10.25%.

Benzene-ether (99 : 1) fractions afforded 349 mg (33.7%) of 3β-acetoxy-(1*S*,5*S*,10*S*)-acetal 5, which after recrystallization from methanol (291 mg, 28.1%) had m. p. 124 °C (undepressed by admixture with the sample obtained from the cis-(1*S*,10*R*)-epoxy-seco-ketone 4 under acid-catalyzed conditions).

*Saponification of 3β-Acetoxy-(1*R*,5*R*,10*R*)-acetal* 7

To a solution of 3β-acetoxy-(1*R*,5*R*,10*R*)-acetal *7* (200 mg) in methanol (10 ml), 5% methanolic potassium hydroxide (10 ml) was added and the mixture was left overnight at room temperature. It was then diluted with water, extracted with ether, the organic layer washed with water, dried over Na_2SO_4 and evaporated in vacuo to dryness. The residue (182 mg, 100%) was dissolved in benzene, passed through a SiO_2 column and the filtrate evaporated under reduced pressure to give 3β-hydroxy-(1*R*,5*R*,10*R*)-acetal *8* (172 mg, 94.6%), which was recrystallized from acetone (154 mg, 84.7%), m. p. 103 °C; $[\alpha]_D^{20} = +78.7°$ (c = 1.00); IR (KBr): ν_{max} 3470, 3320, 1100, 1070, 1045 cm^{-1}; ^{1}H-NMR (100 MHz): δ 0.68 ($H_3C(18)$, s), 0.85 ($H_3C(26)$, and $H_3C(27)$, d), 0.90 ($H_3C(21)$, d), 1.25 ($H_3C(19)$, s), 4.18 (H—C(1), d, *J* 4 Hz), 4.37 (H—C(3), m).

Anal. $C_{27}H_{46}O_3$ (418.66) calc'd.: C 77.46; H 11.08%.
found: C 77.39; H 10.97%.

*Saponification of 3β-Acetoxy-(1*S*,5*S*,10*S*)-acetal* 5

Compound *5* (200 mg) in methanol (10 ml) was saponified with 5% methanolic potassium hydroxide (10 ml) as above to give 3*β*-hydroxy-(1*S*,5*S*,10*S*)-acetal *9* (164 mg, 90.2%), which after recrystallization from acetone had m. p. 102 °C (151 mg, 83.1%); $[\alpha]_D^{20} = -25.6°$ (c = 1.03%); IR (KBr): ν_{max} 3520, 3460, 1095, 1060, 1023 cm^{-1}; ^{1}H-NMR (100 MHz): δ 0.68 ($H_3C(18)$, s), 0.86 ($H_3C(26)$ and $H_3C(27)$, d), 0.91 ($H_3C(21)$, d), 1.39 ($H_3C(19)$, s), 3.86 (H—C(1), t, *J* 3.5 Hz), 3.98 (H—C(3), m).

Anal. $C_{27}H_{46}O_3$ (418.66) calc'd.: C 77.46; H 11.08%.
found: C 77.63; H 11.15%.

*Oxidation of 3β-Hydroxy-(1*R*,5*R*,10*R*)-acetal* 8

To a cooled (0 °C) solution of 3*β*-hydroxy-(1*R*,5*R*,10*R*)-acetal *8* (135 mg) in 10 ml of acetone (distilled over $KMnO_4$) Kiliani's chromic acid solution[13] (0.22 ml of 8 N) was added (in 1 min) with swirling. After 10 min at 0°C, water was added and the reaction mixture extracted with ether. The organic layer was washed with water, sat $NaHCO_3$ aq, water, dried over Na_2SO_4 and evaporated in vacuo to dryness. Crystallization of the solid residue (124 mg, 92.4%) from acetone afforded 105 mg (78.2%) of 3-oxo-(1*R*,5*R*,10*R*)-acetal derivative *10*, m. p. 95 °C; $[\alpha]_D^{20} = +78.4°$ (c = 0.51%); IR (KBr): ν_{max} 1708, 1294, 1060, 890 cm^{-1}; ^{1}H-NMR (100 MHz): δ 0.71 ($H_3C(18)$, s), 0.86 ($H_3C(26)$, and $H_3C(27)$, d), 0.90 ($H_3C(21)$, d), 1.26 ($H_3C(19)$, s), 4.43 (H—C(1), t, *J* 3.5 Hz).

Anal. $C_{27}H_{44}O_3$ (416.65) calc'd.: C 77.83; H 10.65%.
found: C 77.61; H 10.56%.

*Oxidation of 3β-Hydroxy-(1*S*,5*S*,10*S*)-acetal* 9

Compound *9* (120 mg) in acetone (10 ml) was oxidized with Kiliani's chromic acid solution (0.2 ml of 8 M) as above to give 118 mg (98.8%) of 3-oxo-(1*S*,5*S*,10*S*)-acetal *11*, which was recrystallized from acetone (98 mg, 82.1%), m. p. 148°; $[\alpha]_D^{20} = -17.3°$ (c = 0.55%); IR (KBr): ν_{max} 1704, 1204, 1020, 950 cm^{-1}; ^{1}H-NMR (100 MHz): δ 0.67 ($H_3C(18)$, s), 0.86, ($H_3C(26)$ and $H_3C(27)$, d), 0.90 ($H_3C(21)$, d), 1.17 ($H_3C(19)$, s), 4.11 (H—C(1), dxd, *J* 4 Hz, *J* 1.5 Hz).

Anal. $C_{27}H_{44}O_3$ (416.65) calc'd.: C 77.83; H 10.65%.
found: C 77.67; H 10.77%.

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IZVOD

Stereohemijski kontrolisane acetalizacije u desetočlanom prstenu (Z)- i (E)-5,10-seko-steroidnih ketona

Ljubinka Lorenc, Milan Dabović, Vladimir Pavlović, Ivan Juranić i Jože Foršek

(Z)-3β-Acetoksi-5,10-seko-holest-1(10)-en-5-on *2a* reaguje sa *m*-hloroperbenzoevom kiselinom i daje *cis*-(1*S*,10*R*)-epoksid, koji se pod kiselo-katalizovanim uslovima pretvara u (1*S*,5*S*,10*S*)-acetal *5*. Sa druge strane, kiselom hidrolizom osmatnog estra (*E*)-3β-acetoksi-5,10-seko-holest-1(10)-en-5-ona postaju dva stereohemijski različita acetala, to jest (1*R*,5*R*,10*R*)-proizvod *7* i (1*S*,5*S*,10*S*)-izomer *5*, u prinosu od oko 49%, odnosno 28%. U radu je razmatran stereohemijski tok ovih transformacija, uzimajući u obzir najstabilnije konformacije osnovnih stanja polaznih (Z)- i (*E*)-seko-ketona (*2a* i *3a*) u rastvoru.