Conformations of the Nine-Membered Ring in the *B*-Nor-5,10-secosteroids. X-Ray and NMR Analysis

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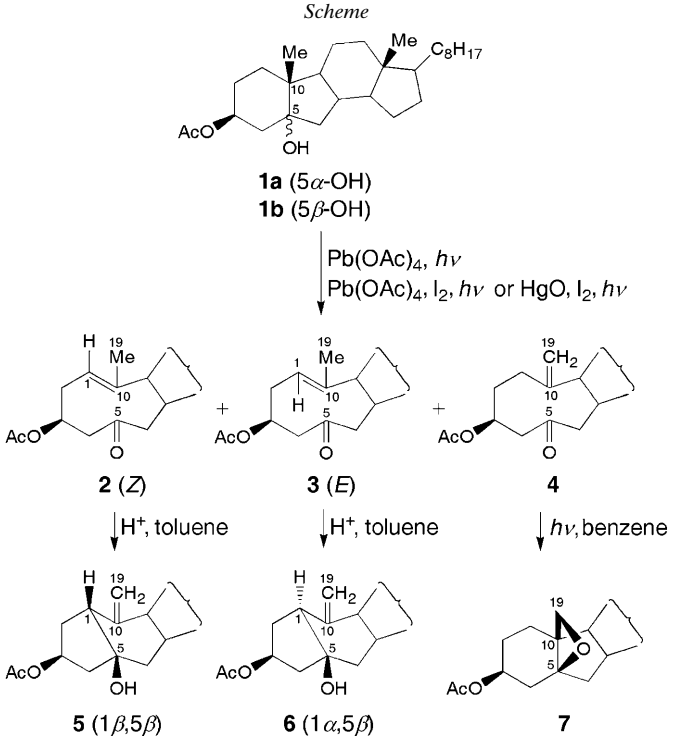
We dedicate this work to Professor *Ljubinka Lorenc*, with sentiments of gratitude and respect

The conformations of (*Z*)- and (*E*)-5-oxo-*B*-nor-5,10-secocholest-1(10)-en-3β-yl acetates (**2** and **3**, resp.) were examined by a combination of X-ray crystallographic analysis and NMR spectroscopy, with emphasis on the geometry of the cyclononenone moiety. The ^{1}H- and ^{13}C-NMR spectra showed that the unsaturated nine-membered ring of (*E*)-isomer **3** in C_6D_6 and (D_6)acetone solution exists in a sole conformation of type $\mathbf{B_1}$, which is similar to its solid-state conformation. The (*Z*)-isomer **2** in C_6D_6, $CDCl_3$, and (D_6)acetone solution, however, exists in two conformational forms of different families, with different orientation of the carbonyl group, the predominant form (85%) corresponding to the conformation of type $\mathbf{A_1}$ and the minor (15%) to the conformation $\mathbf{A_2}$ present also in the crystalline state. In this solid-state conformations of the nine-membered ring of both compounds, the 19-Me and 5-oxo groups are 'β'-oriented. The NMR analysis suggests that the nine-membered ring of **4** has a conformation of type $\mathbf{C_1}$ in $CDCl_3$ solution.

1. Introduction. – As recently reported [1], oxidative fragmentation of the C(5)–C(10) bond in 5α- or 5β-hydroxy-*B*-norcholestan-3β-yl acetates (**1a** and **1b**; *Scheme*) (by using $Pb(OAc)_4$ and/or the 'hypoiodite reaction') generated a new type of modified steroids containing a nine-membered ring instead of the fused A and B rings, *i.e.*, the (*Z*)- and (*E*)-5-oxo-*B*-nor-5,10-secocholest-1(10)-en-3β-yl acetates (**2** and **3**, resp.) as well as the 5-oxo-*B*-nor-5,10-secocholest-10(19)-en-3β-yl acetate (**4**). Our further investigations [2] have shown that the unsaturated *B*-nor-5,10-seco ketones **2**–**4** behave differently when treated by agents capable to participate in reactions involving bond formation across the nine-membered ring, resulting in the transannular cyclization to give the *A*-nor-1,5-cyclization products **5** (1β,5β) and **6** (1α,5β), and the (5β,10β)-oxetane derivative **7**, respectively (*Scheme*). This fact was explained by the different stereochemistry of these cyclononenones in solution. The conformational studies reported for various carbocyclic nine-membered rings were based mainly on X-ray crystal-structure analysis [3], NMR spectroscopy [4], and computational methods [5]. In the present paper, in an attempt to obtain more insight into the conformational aspects and the stereochemical course of different chemical transformations of the new nine-mem-

Scheme



bered ring steroids, X-ray crystal-structure analysis and detailed ^{1}H- and ^{13}C-NMR spectral analysis of the three *B*-nor-5,10-seco ketones **2**–**4** were performed.

2. Results and Discussion. – 2.1. *Determination of the Solid-State Conformations of the (*Z*)- and (*E*)-5-Oxo-*B*-nor-5,10-secocholest-1(10)-en-3β-yl Acetates* (**2** and **3**, resp.) *by X-Ray Analysis.* The results of X-ray structure analyses of compounds **2** and **3** are shown in *Figs. 1* and *2*, respectively. The 9-membered ring of the (*Z*)- and (*E*)-isomers **2** and **3** has the $\mathbf{A_2}$ (twist–chair–chair-like, *TCC*) and $\mathbf{B_1}$ (chair–chair, *CC*) conformation, respectively. C(19) and O(32) in both compounds assume pseudoaxial positions, while C(11), C(14), and O(28) are pseudoequatorially oriented. The olefinic Me(19) group and the 5-oxo group are above the average plane of the 9-membered ring ('β'-oriented). Similar shapes have been reported for the 9-membered ring of 13,14-secosteroids [6].

Ring C of both compounds adopts the normal chair conformation with an average bond angle of 111.4° for **2** and 110.6° for **3**, and an average torsion angle of 54.7° for **2** and 57.0° for **3**. The conformation of ring D is between a C(13) envelope and a C(16) half-chair, with the following *Romers* [7] geometrical (the maximum possible torsion angle) and conformational (the 'the phase angle') ring parameters: $\varphi_m = 45.9°$ and $\Delta = 13.9°$ for **2**, and $\varphi_m = 47.5°$ and $\Delta = 9.8°$ for **3**. The conformation of the side chain C(20) to C(27) is not unusual. Bond lengths and angles as well as torsion angles in

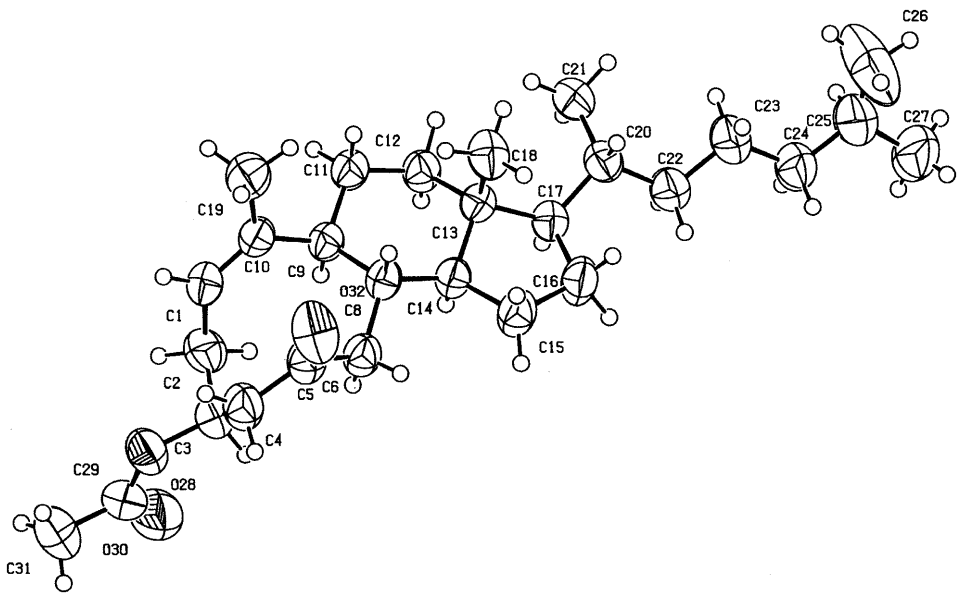


Fig. 1. *X-Ray crystal structure (*ORTEP plot*) of (*Z*)-B-norseco ketone* **2** [8]. Arbitrary numbering.

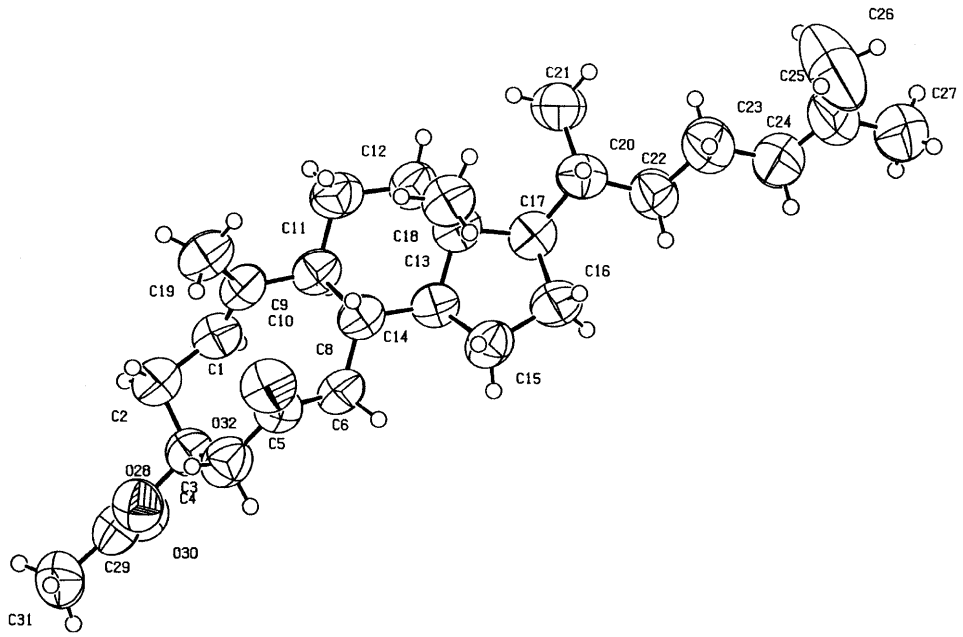


Fig. 2. *X-Ray crystal structure (*ORTEP plot*) of (*E*)-B-norseco ketone* **3** [8]. Arbitrary numbering.

this part of the molecules are unreliable reflecting the effect of either floppiness in the chain or disorder or both.

2.2. *NMR Analysis of the Conformations in Solution of the Nine-Membered Ring in the* B-*Nor-5,10-secosteroids* **2**–**4.** 2.2.1. *Preamble.* It is not an easy task to determine the conformations by NMR spectroscopy of molecules such as **2**–**4**. An NMR analysis similar to that described for conformations of the 10-membered ring in 5,10-secosteroids [9] was applied for the study of the conformational features of the 9-membered ring in *B*-nor-5,10-secosteroids **2**–**4**, supported by NMR experiments in different solvents (C_6D_6, $CDCl_3$, and (D_6)acetone) at room temperature. ^{1}H-NMR Spectra were carried out in C_6D_6 (**2**, **3**), $CDCl_3$ (**2**–**4**), and (D_6)acetone (**2**, **3**) and ^{13}C-NMR spectra in C_6D_6 (**2**, **3**) and $CDCl_3$ (**2**, **4**). Full assignment of all δ(H) and δ (C) of **2** was obtained by 2D-correlated spectroscopy (^{1}H,^{1}H-COSY and ^{1}H,^{13}C-COSY) in $CDCl_3$ solution.

The NMR parameters for the characterization of the possible conformations of compounds **2**–**4** were: *a*) the δ(H) of the olefinic proton H–C(1), *b*) the dihedral angles and the coupling constants between H–C(1) and CH_2(2) as well as between CH_2(4) and H–C(3), and *c*) the δ(C) of C(19) of **2** and **3** and of C(11) of **4**. The chemical shifts and coupling constants of selected protons (H–C(1), CH_2(2), H–C(3), CH_2(4), Me(19)) are collected in *Tables 1* and *2*. ^{13}C-NMR Data for all three compounds are listed and assigned in *Table 3*.

Table 1. *^{1}H-NMR Data of Selected Protons of* B-*Nor-5,10-seco ketones* **2**–**4**[a]). δ in ppm (rel. to $SiMe_4$), *J* in Hz.

	2		
	C_6D_6	$CDCl_3$	(D_6)Acetone
H–C(1)	5.35 (*dd*, *J* = 11.3, 6.0, main conf.)	5.33 (*dd*, *J* = 10.2, 6.9, main conf.)	5.26–5.40 (*m*, main conf.)[b])
	4.99 (*dd*, *J* = 12.0, 5.2, minor conf.)	5.01 (*dd*, *J* = 11.9, 7.0, minor conf.)	4.82–5.03 (*m*, minor conf.)[b])
H_β–C(2)	2.19 (*m*)	2.0–2.04 (*m*)[c])	*ca*. 2.0 (*m*)[c])
H_α–C(2)	2.78 (*m*)	2.79 (*m*)	2.50–2.80 (*m*)
H_α–C(3)	5.63 (*m*, main conf.)	5.48 (*m*, main conf.)	5.26–5.40 (*m*, main conf.)[b])
	5.35 (*dd*, minor conf.)	5.01 (*dd*, minor conf.)	4.82–5.03 (*m*, minor conf.)[b])
H_α–C(4)	2.58 (*dd*)	2.60 (*d*)	2.50–2.80 (*m*)
H_β–C(4)	2.52 (*dd*)	2.60 (*d*)	2.50–2.80 (*m*)
Me(19) or CH_2(19)	1.59 (*s*)	1.67 (*s*)	1.69 (*s*)

	3		**4**
	C_6D_6	(D_6)Acetone	$CDCl_3$
H–C(1)	5.00 (*dd*, *J* = 11.0, 4.7)	5.41 (*dd*, *J* = 10.3, 5.1)	–
H_β–C(2)	2.29–2.37 (*m*)[c])	2.74–2.95 (*m*)	–
H_α–C(2)	2.18 (*td*)	2.29–2.40 (*m*)	–
H_α–C(3)	5.14 (br. *quint.*)	5.13 (br. *quint.*)	5.21 (*m*)
H_α–C(4)	2.40 (*dd*)	2.74–2.95 (*m*)	2.44 (*dd*)
H_β–C(4)	2.57 (*dd*)	2.74–2.95 (*m*)	2.99 (*dd*)
Me(19) or CH_2(19)	1.44 (*s*)	1.32 (*s*)	4.93 (*s*), 4.96 (*s*)

[a]) ^{1}H-NMR Spectra were recorded at 400 MHz (in C_6D_6) or 250 MHz (in $CDCl_3$ and (D_6)acetone) for **2** and **3**, and at 200 MHz (in $CDCl_3$) for **4**, all at room temperature. [b]) Overlapping signals of the H–C(1) and H–C(3). [c]) Signal masked or ill-resolved due to overlap with other resonances.

Table 2. *Dihedral Angles*[a]) [°] *of the Preferred Conformers of Compounds* **2**–**4**, *Calculated and Experimental Coupling Constants* J [Hz] *of the H–C(1) and CH_2(4) Signals*

		Conformers					
		A_1	**A_2**	**B_1**	**B_2**	**C_1**	**C_2**
$\phi_{1,2\alpha}$		164	168	66	54	–	–
$\phi_{1,2\beta}$		48	49	173	173	–	–
$J_{1,2\alpha}$ (calc.)[b])		10.9	11.2	3.3	4.0	–	–
$J_{1,2\beta}$ (calc.)[b])		4.4	4.3	11.5	11.5	–	–
J(exper.)	(in C_6D_6)	11.3, 6.0	12.0, 5.2	4.7, 11.0		–	
	(in $CDCl_3$)	10.2, 6.9	–	5.1, 10.3			
$\phi_{4\beta,3\alpha}$		166	67	161	174	180	167
$\phi_{4\alpha,3\alpha}$		49	50	45	68	60	76
$J_{4\beta,3\alpha}$ (calc.)[b])		8.6	1.0	8.2	9.1	9.2	8.7
$J_{4\alpha,3\alpha}$ (calc.)[b])		3.3	3.2	4.0	0.9	1.8	0.2
J(exper.)		10.3, 6.4	–	7.9, 4.6		10.3, 3.0	

[a]) $\phi_{1,2\alpha} = \phi$(H–C(1)–C(2)–H_α), $\phi_{1,2\beta} = \phi$(H–C(1)–C(2)–H_β), $\phi_{4\beta,3\alpha} = \phi$($H_\beta$–C(4)–C(3)–$H_\alpha$), and $\phi_{4\alpha,3\alpha} = \phi$($H_\alpha$–C(4)–C(3)–$H_\alpha$). [b]) H,H-Coupling constants $J_{1,2\alpha}$ and $J_{1,2\beta}$ were calculated according to the *Garbish* [10] relation, whereas $J_{4\beta,3\alpha}$ and $J_{4\alpha,3\alpha}$ were obtained with the *Karplus* [11] equation.

Table 3. *^{13}C NMR Chemical Shifts of Compounds* **2** (main conformation), **3**, *and* **4**. δ in ppm.

	2[a])		**3**	**4**		**2**[a])		**3**	**4**
	C_6D_6	$CDCl_3$	C_6D_6	$CDCl_3$		C_6D_6	$CDCl_3$	C_6D_6	$CDCl_3$
C(1)	121.5 (*d*)	121.2 (*d*)	123.5 (*d*)	29.0 (*t*)	C(15)	25.2 (*t*)	25.0 (*t*)	25.7 (*t*)	24.8 (*t*)
	(121.0)	(120.1)			C(16)	28.1 (*t*)	27.7 (*t*)	28.3 (*t*)	28.6 (*t*)
C(2)	30.3 (*t*)	30.2 (*t*)	31.8 (*t*)	33.3 (*t*)	C(17)	56.7 (*d*)	56.3 (*d*)	56.9 (*d*)	56.3 (*d*)
C(3)	72.7 (*d*)	72.3 (*d*)	74.4 (*d*)	71.9 (*d*)	C(18)	11.8 (*q*)	11.7 (*q*)	12.2 (*q*)	12.1 (*q*)
	(73.2)	(73.1)				(12.7)	11.7 (12.7)		
C(4)	48.5 (*t*)	48.7 (*t*)	47.2 (*t*)	48.9 (*t*)	C(19)	19.3 (*q*)	19.3 (*q*)	13.6 (*q*)	116.9 (*t*)
	(51.0)	(51.1)			C(20)	36.1 (*d*)	35.7 (*d*)	36.1 (*d*)	35.7 (*d*)
C(5)	209.6 (*s*)	210.9 (*s*)	202.9 (*s*)	210.3 (*s*)	C(21)	18.9 (*q*)	18.7 (*q*)	18.9 (*q*)	18.6 (*q*)
	(205.0)	(207.4)			C(22)	36.5 (*t*)	36.0 (*t*)	36.5 (*t*)	36.0 (*t*)
C(6)	44.2 (*t*)	44.6 (*t*)	46.8 (*t*)	47.0 (*t*)	C(23)	24.3 (*t*)	23.8 (*t*)	24.3 (*t*)	23.7 (*t*)
C(8)	39.4 (*d*)	39.3 (*d*)	41.9 (*d*)	36.5 (*d*)	C(24)	39.9 (*t*)	39.5 (*t*)	39.9 (*t*)	39.4 (*t*)
C(9)	43.7 (*d*)	43.8 (*d*)	57.4 (*d*)	53.8 (*d*)	C(25)	28.3 (*d*)	28.0 (*d*)	28.3 (*d*)	27.9 (*d*)
C(10)	143.3 (*s*)	143.8 (*s*)	145.1 (*s*)	148.8 (*s*)	C(26)	22.7 (*q*)	22.6 (*q*)	22.7 (*q*)	22.5 (*q*)
	(142.2)	(142.4)			C(27)	23.0 (*q*)	22.8 (*q*)	22.9 (*q*)	22.7 (*q*)
C(11)	26.5 (*t*)	26.2 (*t*)	25.1 (*t*)	27.7 (*t*)	MeCOO	169.3 (*s*),	170.3 (*s*),	169.9 (*s*),	170.0 (*s*),
C(12)	39.5 (*t*)	39.5 (*t*)	39.7 (*t*)	39.5 (*t*)		20.7 (*q*)	21.3 (*q*)	20.9 (*q*)	21.3 (*q*)
C(13)	43.0 (*s*)	42.9 (*s*)	43.5 (*s*)	42.9 (*s*)					
C(14)	53.2 (*d*)	53.5 (*d*)	54.7 (*d*)	54.7 (*d*)					

[a]) Values of some signals of the minor conformation **A_2** are given in parentheses (due to signal overlapping, further NMR data cannot be given).

An inspection of molecular models indicated that the mobility of the 9-membered ring of *B*-nor compounds **2**–**4** in solution is strongly restricted by the presence of rings C and D and of the 3β-AcO group. Thus the number of stable conformers is limited to

the number of combinations of the directions of the olefinic Me(19) (for **2** and **3**) or exocyclic CH_2(19) group (for **4**) and the 5-oxo group. The Me(19) or CH_2(19) and 5-oxo groups can be either 'α'-oriented (below the average plane of the 9-membered ring) or 'β'-oriented (above the average plane of the ring). According to *Dreiding* molecular models and the ^{13}C-NMR data for Me(19) of **2** and **3** [9], it seems reasonable to consider only two preferred conformations of the 9-membered ring for *B*-nor compounds **2**, **3**, and **4** with respect to the orientation (α or β) of the Me(19) and 5-oxo group, *i.e.*, $\mathbf{A_1}$ (β,α) and $\mathbf{A_2}$ (β,β), $\mathbf{B_1}$ (β,β) and $\mathbf{B_2}$ (β,α), and $\mathbf{C_1}$ (β,β) and $\mathbf{C_2}$ (β,α), respectively (*Fig. 3*). The precise geometries of these preferred conformations were locally optimized by the molecular mechanics method (MM+) comprised in the HyperChem (Vs. 5.0) program package (applying *Polak-Ribiera* minimization algorithm), as depicted in *Fig. 3*.

2.2.2. *(Z)*-B-*Nor-5,10-secosteroid* **2**. According to the ^{1}H-NMR (C_6D_6, $CDCl_3$, and (D_6)acetone and ^{13}C-NMR (C_6D_6, $CDCl_3$) data of 5-oxo-*B*-nor-5,10-secosteroid **2**, the 1(10)-unsaturated 9-membered ring with (*Z*)-configuration adopts two different conformations (belonging to different conformational families) in solution at room temperature. (*Tables 1–3*). The δ(C) 19.3 (C_6D_6 and $CDCl_3$) as well as 43.7 (C_6D_6) and 43.8 ($CDCl_3$) of the main component assigned to Me(19) and C(9) (*Table 3*), respectively, are characteristic for the conformations where the Me group is located on the 'β'-side of the (*Z*)-5,10-secosteroid skeleton [9c]. A *γ-gauche* effect, due to the H_α–C(2) bond, is probably responsible for the upfield shift ($\Delta\delta = 13.7–13.8$) of the C(9) resonance (δ(C) 43.7–43.8) of the main conformation of **2** with a 'β'-positioned Me(19) group, as compared to that of (*E*)-*B*-nor-5,10-secosteroid **3** (δ(C) 57.4) as well as of possible conformations of **2** with an 'α'-positioned Me(19) group, where such an effect is absent. According to the results presented in *Table 3*, all the relevant δ(C) of both conformations of **2** in C_6D_6 and $CDCl_3$ solution are similar (within 1.4 ppm), besides the δ(C) of C(4) and C(5) which differ by 2.5 and 2.4 ppm, and by 4.6 and 3.5 ppm, respectively, indicating that in the nine-membered ring moiety, the environment of the 5-oxo group is different. The δ(C) of the relevant nuclei in the minor conformation are either masked owing to overlap with other resonances (C(9) and C(19)) or similar to the δ(C) of the main conformation (C(1), C(3), and C(10)). Also, the predicted minor conformation of **2** is confirmed by the δ(C) of the olefinic H–C(1).

The ratio of the conformers (*ca.* 85 : 15) was deduced from the ^{1}H-NMR spectra (C_6D_6 and $CDCl_3$) by the peak areas of the H–C(1) signals (*dd*) at δ(H) 5.35 and 5.33 of the major conformer and δ(H) 4.99 and 5.01 of the minor conformer, respectively (*Table 1*). In (D_6)acetone, an individual assignment of the overlapping signals of H–C(1) and H–C(3) at δ(H) 5.26–5.40 (major conformer) and 4.82–5.03 (minor conformer) was not possible. The coupling patterns of H–C(1) in C_6D_6 and $CDCl_3$ solution are similar for both conformers (*Table 1*). This could be interpreted by the similarity of dihedral angles between H–C(1) and CH_2(2) ($\Delta\phi_{1,2\alpha} = 4°$, $\Delta\phi_{1,2\beta} = 1°$), indicating that two conformational families exist. Calculated and experimental coupling constants for the two sets resonances of the two proposed conformations $\mathbf{A_1}$ and $\mathbf{A_2}$ are listed in *Table 2*. Another parameter important for the characterization of the possible conformations of **2** is the shielding influence of the 5-oxo group on the olefinic H–C(1). This influence causes a high-field shift of the H–C(1) signal of the minor conformer (δ 4.99, 5.01, 4.82–5.03) and no influence on the major conformer (δ 5.35, 5.33,

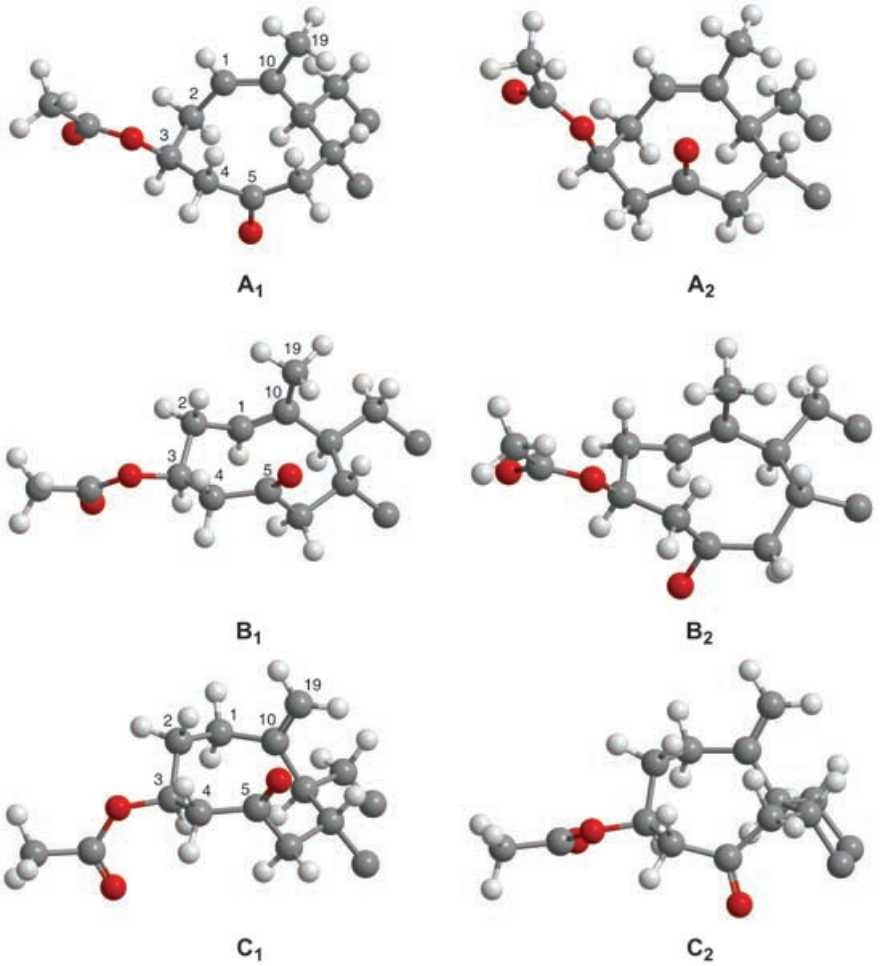


Fig. 3. *Preferred conformations of the 9-membered ring of compounds* **2**, **3**, *and* **4**: $\mathbf{A_1}$ *and* $\mathbf{A_2}$, $\mathbf{B_1}$ *and* $\mathbf{B_2}$, *and* $\mathbf{C_1}$ *and* $\mathbf{C_2}$, *respectively*

5.26–5.40), where the 5-oxo group and the olefinic proton are antiparallel to each other. The proposed conformations $\mathbf{A_1}$ (major) and $\mathbf{A_2}$ (minor) are in good agreement with the above observations (see *Fig. 3*).

The ^{1}H- and ^{13}C-NMR data of **2** in different solvents show that the spatial arrangement of H–C(1) and H–C(3) must be similar in both conformations (similar coupling pattern and constants). There is only a difference in the relative spatial orientation of the 5-oxo group ('α' in the main conformation and 'β' in the minor conformation).

2.2.3. *(*E*)*-B-*Nor-5,10-secosteroid* **3**. The 1(10)-unsaturated 9-membered ring with (*E*)-configuration in *B*-nor-5,10-secosteroid **3** exhibits one set of NMR resonances and exists in only one conformation in C_6D_6 and (D_6)acetone solution. In C_6D_6 solution, the C(19) signal is situated upfield (δ(C) 13.6; *Table 3*) when compared to that of the

corresponding (*Z*)-diastereoisomer **2** (δ(C) 19.3), as a result of the additional shielding interaction of H_β–C(2) with the Me(19) group *(γ-cis* effect). This ^{13}C-NMR feature of **3** is in accordance with a spatial arrangement of the 9-membered ring in conformations $\mathbf{B_1}$ or $\mathbf{B_2}$ where the Me(19) group is also 'β'-oriented[1]).

The signal of the olefinic H–C(1) in C_6D_6 solution (δ(H) 5.00) is upfield-shifted compared to that in (D_6)acetone) solution (δ(H) 5.41). The corresponding relatively large chemical-shift difference ($\Delta\delta = 0.41$; *see Table 1*) is undoubtedly caused by considerable anisotropy originating in the benzene ring as the result of the coordination with the carbonyl group [12]. This solvent effect confirms the steric proximity of the 5-oxo group and olefinic proton which is only realized in the conformation $\mathbf{B_1}$ (*Fig. 3*). On the other hand, in conformation $\mathbf{B_1}$, the Me(19) group is in the shielding region of the 5-oxo group and should be shifted upfield, and H–C(1) is not influenced by the latter. The upfield shift of the Me(19) signal (δ(H) 1.44 in C_6D_6 and 1.32 in (D_6)acetone) points to conformation $\mathbf{B_1}$. The corresponding calculated coupling constants of H–C(1) with H_β– and H_α–C(2) in both proposed conformations $\mathbf{B_1}$ and $\mathbf{B_2}$ are compatible with observed values for **3** (*Table 2*). A comparison of the calculated coupling constants of CH_2(4) with H–C(3) ($J = 8.2, 4.0$ for $\mathbf{B_1}$; $J = 9.1, 0.9$ for $\mathbf{B_2}$) and the experimental ones ($J = 7.9, 4.6$) suggest again conformation $\mathbf{B_1}$. Finally, to distinguish between these two conformations, we compared the experimental δ(C) (202.9) of the carbonyl atom C(5) of **3** with that of the corresponding 3β-hydroxy derivative (δ(C) 212.0) [1], where an H-bond between O*H*–C(3) and C(5)=*O* causes a low-field shift of C(5), thus indicating a 'β'-orientation of C(5)=O and excluding the conformation $\mathbf{B_2}$.

2.2.4. *5-Oxo*-B-*nor-5,10-secocholest-10(19)-en-3β-yl Acetate* (**4**). The NMR parameters support only one conformation in $CDCl_3$ solution for the 9-membered ring of **4**. The δ(C) 27.7 (*Table 3*), assigned to C(11) of **4**, is characteristic for conformers with a 'β'-oriented exocyclic CH_2(19) group (see $\mathbf{C_1}$ and $\mathbf{C_2}$ in *Fig. 3*). Conformers with an 'α'-oriented exocyclic CH_2(19) group experience a γ-gauche effect (C(1)–C(10)–C(9)–C(11)) which should cause an upfield shift of the C(11) as well as C(1) signals relative to the value found for **4**, where this effect does not exist.

The CH_2(4) signals of **4** (*dd*) at δ(H) 2.99 and 2.44 were used to distinguish the conformers $\mathbf{C_1}$ and $\mathbf{C_2}$ (*Fig. 3*), these signals exhibiting coupling with H–C(3), *i.e.*, J(exper.) = 10.3 and 3 Hz, respectively. The corresponding vicinal coupling constants were calculated from the dihedral angles H_β–C(4)–C(3)–H_α and H_α–C(4)-C(3)–H_α ($J_{4\beta,3\alpha} = 9.2$ and $J_{4\alpha,3\alpha} = 1.8$ for $\mathbf{C_1}$; $J_{4\beta,3\alpha} = 8.7$ and $J_{4\alpha,3\alpha} = 0.2$ for $\mathbf{C_2}$), by using the three-dimensional structures of the two proposed conformers (*Table 2*). Only a conformation of type $\mathbf{C_1}$ has coupling constants compatible with the those observed for *B*-nor-seco ketone **4**.

Conclusions. – Our solvent-dependent NMR change studies showed that the nine-membered ring of both *B*-nor-5,10-seco ketones **3** and **4** exists in C_6D_6, $CDCl_3$, and (D_6)acetone solution in only one conformation, *i.e.*, $\mathbf{B_1}$ (corresponding to the solid-state conformation) and $\mathbf{C_1}$, respectively. The nine-membered ring of the (*Z*)-isomer **2** in C_6D_6, $CDCl_3$, and (D_6)acetone solution occurs, however, in two conformations

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[1]) The δ(C) of Me(19) in α-position of (*E*)-conformers is shifted downfield (δ(C) *ca.* 19) [9a].

each with a differently oriented 5-oxo group and belonging to different conformational families; the predominant form (*ca.* 85%) corresponds to a conformation of type $\mathbf{A_1}$, and the minor one resembles best the solid-state conformation $\mathbf{A_2}$.

We can now try to correlate the preferred conformations with the stereochemical course of chemical transformations described for the *B*-nor compounds **2**–**4** [2]. The results obtained in the present work confirm that the proposed conformations of the nine-membered rings (see *Fig. 3*) are consistent with the structures of their transannular cyclization products **5**–**7** (*Scheme*). In the (*Z*)-isomer **2** a transannular interaction between the protonated carbonyl group and the C=C bond is, for steric reasons, possible only when the molecule assumes the minor conformation $\mathbf{A_2}$. The (*E*)-stereoisomer **3**, where the reacting centers (in conformation $\mathbf{B_1}$) are favorably oriented for cyclization, reacts much faster than the (*Z*)-isomer. The *B*-nor-5,10-seco ketone **4** which, according to the NMR analysis, exists in solution in one conformation ($\mathbf{C_1}$) only, undergoes a transannular *Paterno-Büchi* reaction, producing thus the (5β,10β)-oxetane derivative **7** as the sole transannular photoproduct.

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Table 4. *Crystal Data and Structure Refinement for* **2** *and* **3**

	2		**3**	
Crystallized from	MeOH		MeOH/hexane	
Crystal color, habit	colorless		colorless, very thin needle	
Empirical formula	$C_{28}H_{46}O_3$		$C_{28}H_{46}O_3$	
Formula weight	430.65		430.65	
Temperature	293(2) K		293(2) K	
Radiation and wavelength	MoK_α; 0.71069 Å		MoK_α; 0.71069 Å	
Crystal system, space group	monoclinic, *P*21		monoclinic, *P*21	
	$a=9.209(3)$ Å	$\alpha=90^\circ$	$a=9.047(3)$ Å	$\alpha=90^\circ$
	$b=5.945(2)$ Å	$\beta=95.66^\circ$	$b=5.927(2)$ Å	$\beta=97.23^\circ$
	$c=24.587(10)$ Å	$\gamma=90^\circ$	$c=24.959(8)$ Å	$\gamma=90^\circ$
Volume	1339.5(8) Å^3		1327.7(8) Å^3	
Z	2		2	
Calculated density	1.068 Mg/m^3		1.077 Mg/m^3	
Absorption coefficient	0.067 mm^{-1}		0.068 mm^{-1}	
F(000)	476		476	
Crystal size	0.50×0.20×0.10 mm		0.30×0.15×0.05 mm	
θ range for data collection	2.64–24.42°		2.27–21.45°	
Limiting indices	$-10\le h\le 10$, $-6\le k\le 6$, $-28\le l\le 28$		$0\le h\le 9$, $0\le k\le 6$, $-24\le l\le 25$	
Reflections collected, unique	10925, 4152 (R(int)=0.046)		3524, 1439 (R(int)=0.077)	
Completeness to	$\theta=24.42$ (96.0%)		$\theta=21.45$ (84.5%)	
Refinement method	full-matrix least-squares on F^2		full-matrix least-squares on F^2	
Data, restraints, parameters	4152, 1, 342		1439, 1, 282	
Goodness-of-fit on F^2	1.076		1.034	
Final *R* indices ($I>2\sigma(I)$)	$R_1=0.0558$, [3586], $wR_2=0.1555$		$R_1=0.0744$, [1145], $wR_2=0.1812$	
R indices (all data)	$R_1=0.0627$, $wR_2=0.1634$		$R_1=0.0880$, $wR_2=0.1971$	
Absolute structure parameter	−0.2(19) not reliable		−1(5) not reliable	
Extinction coefficient	0.157(17)		0.18(3)	
Largest diff. peak and hole	0.179 and −0.232 e·Å^{-3}		0.303 and −0.252 e·Å^{-3}	

Experimental Part

X-Ray Crystal-Structure Determination of **2** *and* **3** (*Table 4* and *Figs. 1* and *2*)[2]). Crystal data for both compounds are given in *Table 4*, together with refinement details. All measurements were performed with a *MAR345* image plate detector and graphite-monochromated MoK_α radiation (*RU200* rotating anode). For both compounds, the data were measured at r.t. These data are of relatively poor quality, specially for **3** with low $2\theta_{max}$ and low completeness. To get better data, we tried to recrystallize, but we did not obtain larger or better crystals. We also tried to collect the data at low temperature (100 K), but the resolution was unexpectedly lower for the crystals mounted in inert oil. The unit-cell parameters were refined by using all of the collected spots after the integration process. The data sets do not allow determining the absolute configuration reliably; it was known from the parent compound. Both structures were solved by direct methods with SHELXS-97 [13] and refined by full-matrix least squares on F^2 using SHELXL-97 [14]. All the H-atoms were calculated with AFIX and included in the refinement with a common isotropic temperature factor.

NMR Analysis. Varian Mercury-400, *Bruker AM-250* and *Varian Gemini-200* spectrometers; ^{1}H at 400, 250 and 200 MHz, and ^{13}C at 100, 62.9, and 50 MHz; chemical shifts δ in ppm rel. to $SiMe_4$ (=0 ppm) as internal standard and coupling constants J in Hz.

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[2]) CCDC-255960 and -255961 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif.