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INVESTIGATION OF THE CONFORMATIONAL TRANSFORMATIONS IN SOME 7α-METHYL-6-OXA-14β-ANALOGS OF STEROIDAL ESTROGENS BY NMR SPECTROSCOPY*

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The stereochemical structure and conformational transformations of two 6-oxa-14β-estra-1,3,5(10),8(9)-tetraenes having an α-methyl group at position 7 were investigated. It was found that the substituent at the C-17 atom has an effect on the formation of the conformers in solution. In the analog containing a C-17 keto group in solution there are two conformers, whereas the 17α-acetoxy derivative has only one conformer.

Keywords: 6-oxa-14β-analogs of steroidal estrogens, conformational equilibria, NMR spectroscopy.

The introduction of an α-methyl group at position 7 of steroidal estrogens with "natural" ring fusion often leads to an increase in the affinity toward the corresponding nuclear receptors [1-5]. The same effect is observed in a steroid of the 14β series **1** [6]. The introduction of a double bond at position 8(9) of steroidal estrogens gives rise to an increase in the antioxidant activity [7]. This served as the basis of the synthesis and the investigation of stereochemical and conformational transformations in compounds **2** and **3**, which are among the analogs of the 14β series and have a double bond at position 8(9). The scheme for the synthesis of the model compounds is presented below.

Earlier the steroid **2** was obtained by the catalytic hydrogenation of 6-oxaestrapentaene **4** [8]. Reduction of the keto group of an analog of **2** with sodium borohydride followed by acetylation of the reaction product led to a new compound, to which the authors assigned the structure **5**. We repeated the sequence of reactions and showed that the authors of [8] had in fact synthesized the steroid **3**.

A necessary condition for conformational analysis of the model steroids is accurate identification of the signals of all the aliphatic protons. This task was solved by the combined use of some homo- and heteronuclear correlation procedures of NMR spectroscopy: DQF-COSY [9, 10], J-COSY [11, 12], NOESY [13-15], HSQC [16], and COLOC [17]. The results from full assignment of the signals are presented in the experimental section.

The unrestricted molecular MM^+ mechanics method, which can be used to determine the geometry of the 6-oxa analogs of estrogens [18, 19], was used to calculate the stereochemical structure of the model compounds.

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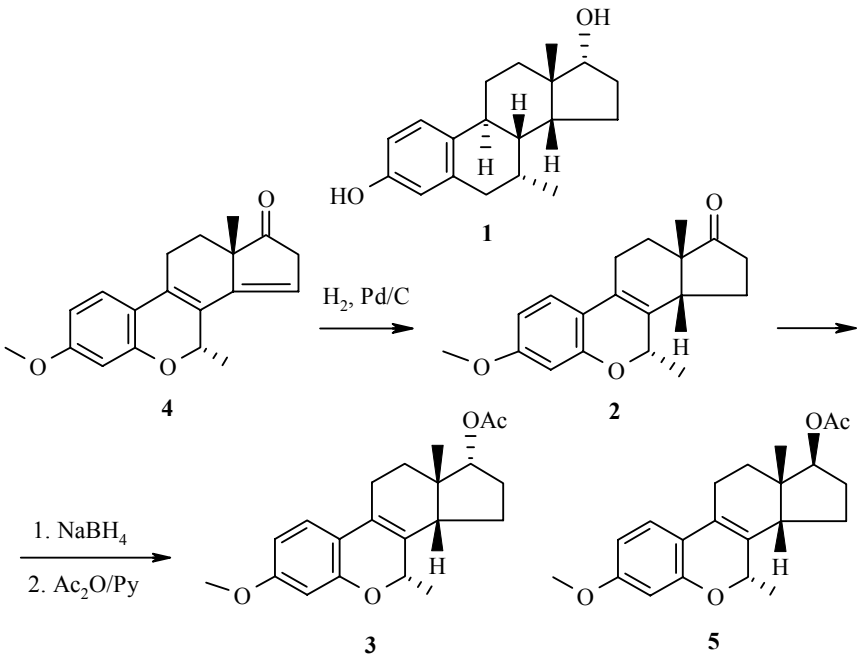

The distribution of the signals for the aliphatic protons of the estratetraenes **2** and **3** in the ^{1}H NMR spectrum reflect their structural and spectral features (Fig. 1).

Identification of the signals in the ^{1}H NMR spectra of the estratetraenes **2** and **3** (Fig. 1) shows that the least favorable arrangement of the signals of the aliphatic protons of rings C and D for conformational analysis is observed in the steroid **3**. In the ^{1}H NMR spectrum of this compound the signals for the H-12α, H-12β, H-15α, and H-16α protons in the region of 1.5-1.75, the H-14β and H-15β protons in the region of 1.85-2.05, and the H-11β and H-16βα protons in the region of 2.1-2.3 ppm partly or completely overlap. Only the signal for the H-11α proton at 2.55 ppm is suitable for conformational analysis. No less complicated was the arrangement of the signals for the protons in the spectrum of compound **2**; complete overlap is observed for the signals of the H-11β, H-14β, H-15β, and H-16β protons in the region of 2.2-2.4 and for the signals of the H-12α and H-15α in the region of 1.6-1.75 ppm. At the same time the multiplet structure of the signals for H-12β at 1.48 and H-11α at 2.56 ppm is clearly seen; its analysis makes it possible to conclude unambiguously that these protons in the dominant conformation of the estratetraenes **2** have a pseudoequatorial orientation. This is demonstrated by the vicinal constants: $^3J_{12\beta,11\alpha}$ = 2.55, $^3J_{12\beta,11\beta}$ = 5.96, and $^3J_{11\alpha,2\alpha}$ = 6.02 Hz, obtained at

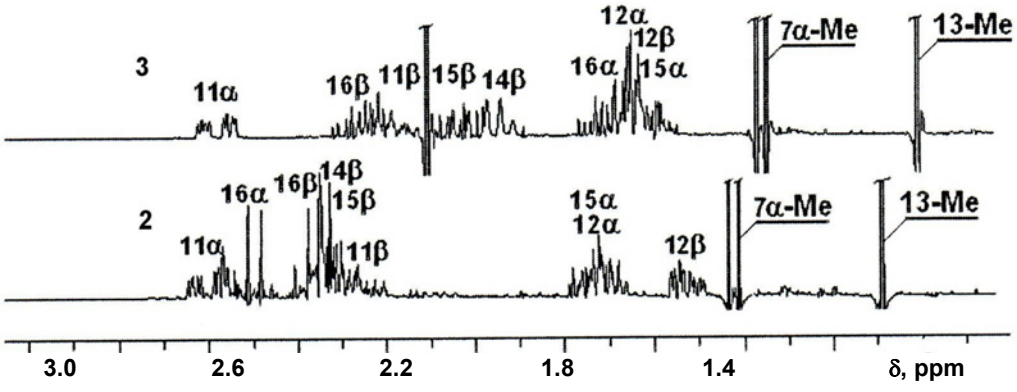

Fig. 1. Fragments of the aliphatic region in the ^{1}H NMR spectra of the estratetraenes **2** and **3**.

25°C with an accuracy not worse than ±0.02 Hz. Moreover, the multiplet structure of the signal for the H-12β proton contains one more doublet splitting with constant J = 1.04 Hz (Fig. 2a), corresponding to long-range ($^4J_{H,H}$) scalar coupling of this proton with the H-14β proton (2.31 ppm). This coupling was identified by means of an experiment with selective $^1H\{^1H\}$ double resonance, the result of which is shown in Fig. 2b. On account of the proximity of the chemical shifts of the H-14β (2.31 ppm) and H-11β (2.21 ppm) protons this experiment was conducted using a very low power radiofrequency field B_2, which was selected in such a way that the coupled transitions of the spins of the H-11β proton was not affected and selective irradiation did not affect its scalar coupling with the H-11β proton. Consequently, the presence of the $^4J_{12\beta,14\beta}$ constant demonstrates unambiguously that in the dominant conformation of analog **2** the H-12β and H-14β protons occupy the pseudoequatorial position and that scalar coupling of the W type between them is realized in this case.

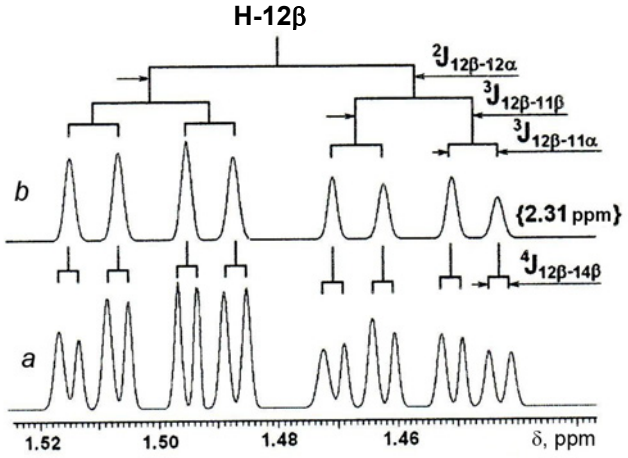

Fig. 2. The multiplet structure of the signal for the H-12β proton in the ^1H NMR spectrum of steroid **2**, obtained without decoupling (*a*) and with decoupling from the H-14β proton (*b*).

By means of an F1 section of the HSQCnd spectrum at 46.28 ppm a multiplet structure was obtained for the signal of the H-14β proton, and this made it possible to determine also the values of its vicinal couplings with the H-15α ($^3J_{14\beta,15\alpha}$ = 11.4) and H-15β ($^3J_{14\beta,15\beta}$ = 6.6 Hz) protons. These constants make it possible (on the basis of the Karplus relationship) to estimate the mutual spatial arrangement of the protons of the C(14)H–C(15)H_2 fragment, which corresponds to the energetically most favorable conformation *A* of the estratetraene **2** calculated by the MM^+ method and shown in Fig. 3b. The calculated values of the torsion angles H(14β)–C(14)–C(15)–H(15α) and H(14β)–C(14)–C(15)–H(15β) amount to 164.7 and 43.6° respectively, while the corresponding calculated values of the vicinal constants are $^3J_{14\beta,15\alpha}^{calc}$ = 12.1 and $^3J_{14\beta,15\beta}^{calc}$ = 6.1 Hz.

The isolated position of the spin system of protons in the C(7)H–CH_3 fragment does not make it possible to reach a conclusion about the spatial orientation of the methyl group at position 7. This problem can only be solved with the use of data from measurement of the direct proton interactions (NOE). Figure 3a shows fragments of the NOESY spectrum of estratetraene **2**, where the cross peaks most important for independent evidence of its preferred conformation are indicated. We note that this spectrum does not contain a cross peak between the H-7β proton and the protons of the methyl group at position 13, which should be present in the case of pseudoaxial orientation of this proton. Consequently, the α-methyl group in the dominant conformation of compound **2** occupies the pseudoaxial position, while the H-7β proton occupies the pseudoequatorial position (Fig. 3b). this conclusion is supported by the presence of a strong cross peak for 7α-Me/15α, the appearance of which is only possible in the case of the axial orientation of the methyl group at position 7α. (According to MM^+ calculations, in the equatorial arrangement of this methyl group the shortest distance $r_{7\alpha\text{-Me}-15\alpha}$ = 3.2, while in the axial arrangement it is 2.6 Å.)

Of no lesser importance as evidence for the stereochemical structure of the steroid **2** are the strong direct couplings between the protons of the methyl group at position 13β and the H-11β, H-12β, and H-14β protons and also between the H-1 proton and the H-11α and H-11β protons. In the last case the significantly higher intensity of the cross peak 1/11α, characteristic of the preferred conformation, compared with the cross peak 1/11β is observed (Fig. 3b). The ratio of their integral intensities amounts to 5.3:1 (Fig. 3a), but it is significantly smaller than the ratio 7.1:1 obtained from calculations (MM^+) of the distances $r_{1,11\alpha}^{A} = 2.12$ and $r_{1,11\beta}^{A} = 2.94$ Å for this conformer. Such a difference between the experimental and calculated data makes it possible to assume that the solution contains a fairly large amount of conformer *B*, characterized by the opposite relation between these interproton distances: $r_{1,11\alpha}^{B} = 2.68 > r_{1,11\beta}^{B} = 2.33$ Å. The experimental ratio of the intensities of the cross peaks 1/11α and 1/11β corresponds to the presence of 20.5% of conformer *B*, for which the calculated ratio of these intensities amounts to 0.43:1.

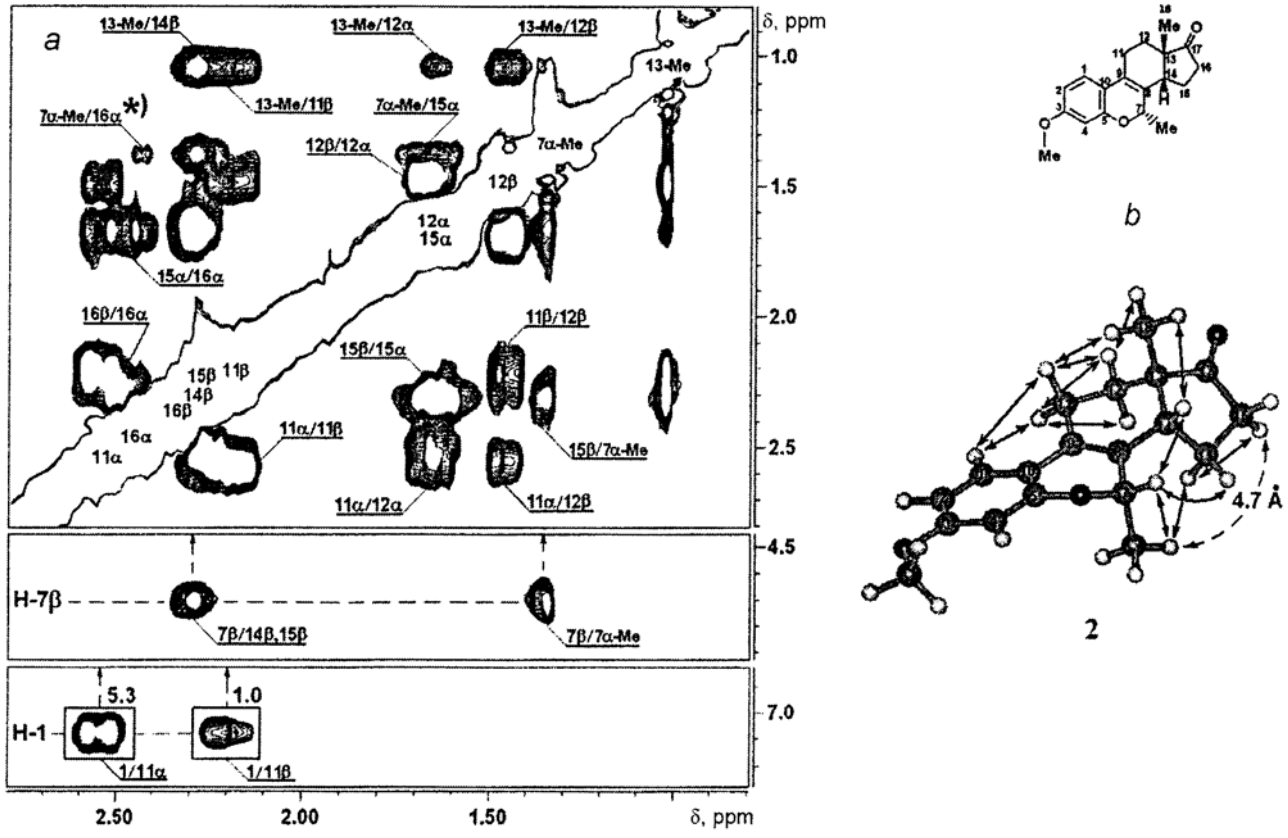

Fig. 3. *a* – A fragment of the NOESY spectrum (τ_m = 0.5 sec) of compound **2**. *b* – The stereochemical structure of its most stable conformer *A* (the double arrows represent the discovered direct interproton interactions, the dotted arrow the interaction of 7α-Me/16α, the corresponding cross peak for which in the spectrum is marked by an asterisk).

Independent evidence for the existence of conformer *B* of estratetraene **2** in the solution is provided by cross peaks in the NOESY spectrum for 13-Me/12α and 7α-Me/16α. They do not belong to conformation *A*, since the calculated distances $r_{13\text{-Me–}12\alpha}$ and $r_{7\alpha\text{-Me–}16\alpha}$ for the latter amount to 3.7 and 4.7Å respectively. Thus, the observed integral intensity of the cross peak for 7α-Me/16α (marked by an asterisk in Fig. 3a) is more than five times larger than its calculated value. Whereas in the case of the cross peak for 13-Me/12α its increased

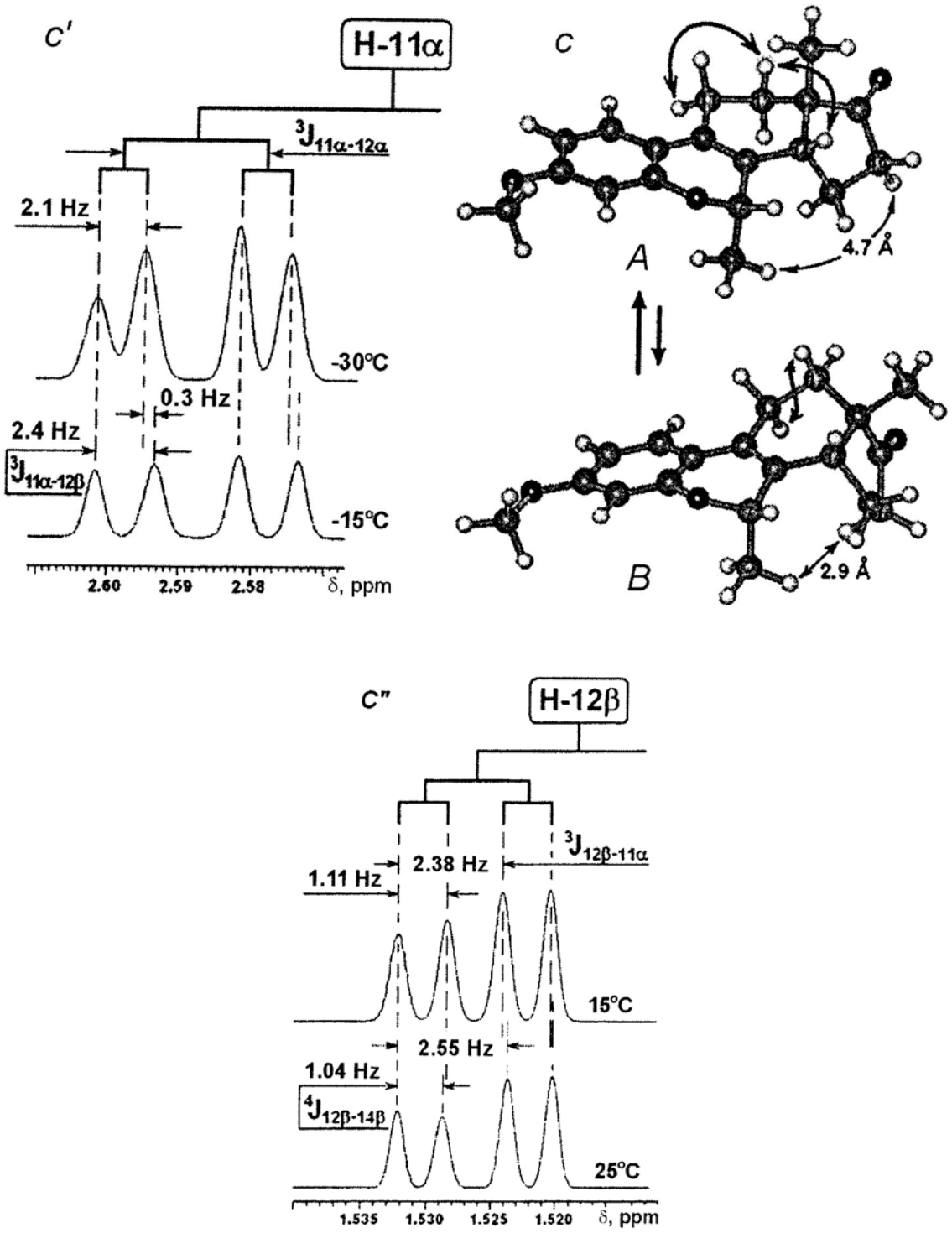

Fig. 3. *c* – The equilibrium between conformers *A* and *B* (the solid arrows represent the scalar interactions of 12β/11α and 12β/14β, the dotted arrows the direct interactions of 7α-Me/16α; the calculated values (MM^+) of the corresponding distances $r_{7α\text{-Me}–16α}^{(A)}$ and $r_{7α\text{-Me}–16α}^{(B)}$ are indicated).
c′, *c*″ – The high-frequency fragments of the multiplet signals for the H-11α and H-12β protons at various temperatures (the dotted lines represent the changes in the constants $^3J_{11α–12α}$, $^3J_{11α–12β}$, and $^3J_{12β–14β}$).

intensity can be explained at least partly by the effects of spin diffusion [9] according to the 13-Me → 12β → 12α mechanism and by the effects of the strong bonding [20] between the geminal protons H-12β and H-12α, these alternative explanations are impossible in the case of the cross peak for 7α-Me/16α. [According to data from the MM^+ method the strongest steric interaction of the proton of the methyl group at position 7α must occur with the H-15β proton ($r_{7\alpha\text{-Me}–15\beta}$ = 2,34 Å), which is at a distance of 2.77 Å from the H-16α proton, while the scalar constant $^3J_{15\beta,16\alpha}$ must not exceed 2-3 Hz, since the torsion angle is $\theta_{15\beta,16\alpha}^{(MM+)}$ = 86°.] Apart from this, it is necessary to take account of the fact that under the given conditions ($\omega_o\tau_s < 1$) the spin diffusion effects have a negative sign and must, consequently, lead to low values for the integral intensity of the cross peaks for 13-Me/12α and 7α-Me/16α. Thus, the observation of these cross peaks in the NOESY spectrum of steroid **2** provides further grounds for supposing the presence of a fast conformational equilibrium on the NMR time scale and the presence of a minor conformer *B*, characterized by the closeness between the protons of the C(7α)–Me and C(13β)–Me methyl groups and the H-16α and H-12α protons respectively. We demonstrated that the second conformer of steroid **2** has structure *B* (Fig. 3b), which may be formed from the main conformer *A* as a result of simultaneous inversion of rings C and D and for which the indicated steric interactions are observed: $r_{7\alpha\text{-Me}–16\alpha}$ = 2.9, $r_{13\text{-Me}–12\alpha}$ = 2.5 Å.

The temperature dependences of the scalar constants were used to confirm the existence of a fast conformational equilibrium $A \rightleftarrows B$ in a solution of the estratetraene **2**.

Figure 4 shows Newman projections of four fragments of this molecule and the changes in the spatial arrangement of the protons of rings C and D in the transition between conformations *A* and *B*.

By comparing the calculated (MM^+) torsion angles $\theta_{H,H}$ and the corresponding vicinal $^3J_{H,H}$ constants it is possible to predict the nature of the change in the observed values ($<^3J_{H,H}>$)* of this spectral parameter with increase of temperature, which under the conditions of fast conformational exchange must lead to an increase in the population of the minor conformer *B*.

In addition, this comparison makes it possible to reveal the most suitable vicinal constants for quantitative interpretation with the largest range of variation and, consequently, the highest sensitivity to displacement of the equilibrium toward increase in the fraction of conformer *B*. It is clear that in the ethane fragment $C(11)H_2–C(12)H_2$ the most sensitive to the position of the conformational equilibrium must be the constants $<^3J_{11\alpha,12\beta}>$ and $<^3J_{11\beta,12\alpha}>$ averaged by fast exchange, the values of which must increase and decrease respectively with increase of temperature. Here only a small decrease in their values must be observed for the constants $<^3J_{11\alpha,12\alpha}>$ and $<^3J_{11\beta,\,12\beta}>$. Figure 3c shows fragments of the signals of the H-11α and H-12β protons at −30, 15, and 25°C, the changes in structure of which must correspond fully to the calculated data (Fig. 4*a*). With increase of the temperature by 55°C the $<^3J_{11\alpha,12\beta}>$ constant increases by 0.45 Hz. If the calculated values of this constant in conformers *A* and *B* are used for the determination of the total range of its variation ($\Delta^3J_{11\alpha,12\beta}^{calc}$ = 11.45 Hz), this increase of the constant $<J_{11\alpha,12\beta}>$ reflects an increase of 3.9% in the fraction of the minor conformer *B*. Similarly, from the decrease in the constant $<^3J_{11\beta,12\alpha}>$ from 11.32 to 10.84 Hz, observed in the same temperature range on the signal of the H-11β proton (2.21 ppm), it is possible to estimate an increase of 4.6% in the fraction of conformer *B* ($\Delta^3J_{11\beta,12\alpha}^{calc}$ = 10.36 Hz).

It is clear that with such a small variation of the population P_B and an insignificant full range of variation of the constant between the H-11α and H-12α protons ($\Delta^3J_{11\alpha,12\alpha}^{calc}$ = 1.11 Hz) it is difficult to hope for accurate experimental determination of the corresponding decrease of this constant, which must amount to less than 0.05 Hz. In the ^{1}H NMR spectrum of the steroid **2** the signal of the H-12α proton (1.67 ppm) is fully overlapped by the multiplet signal of the H-15α proton, and the $<^3J_{11\alpha,12\alpha}>$ constant can only be measured for

* $<^3J_{H,H}>$ are the constants averaged by fast exchange.

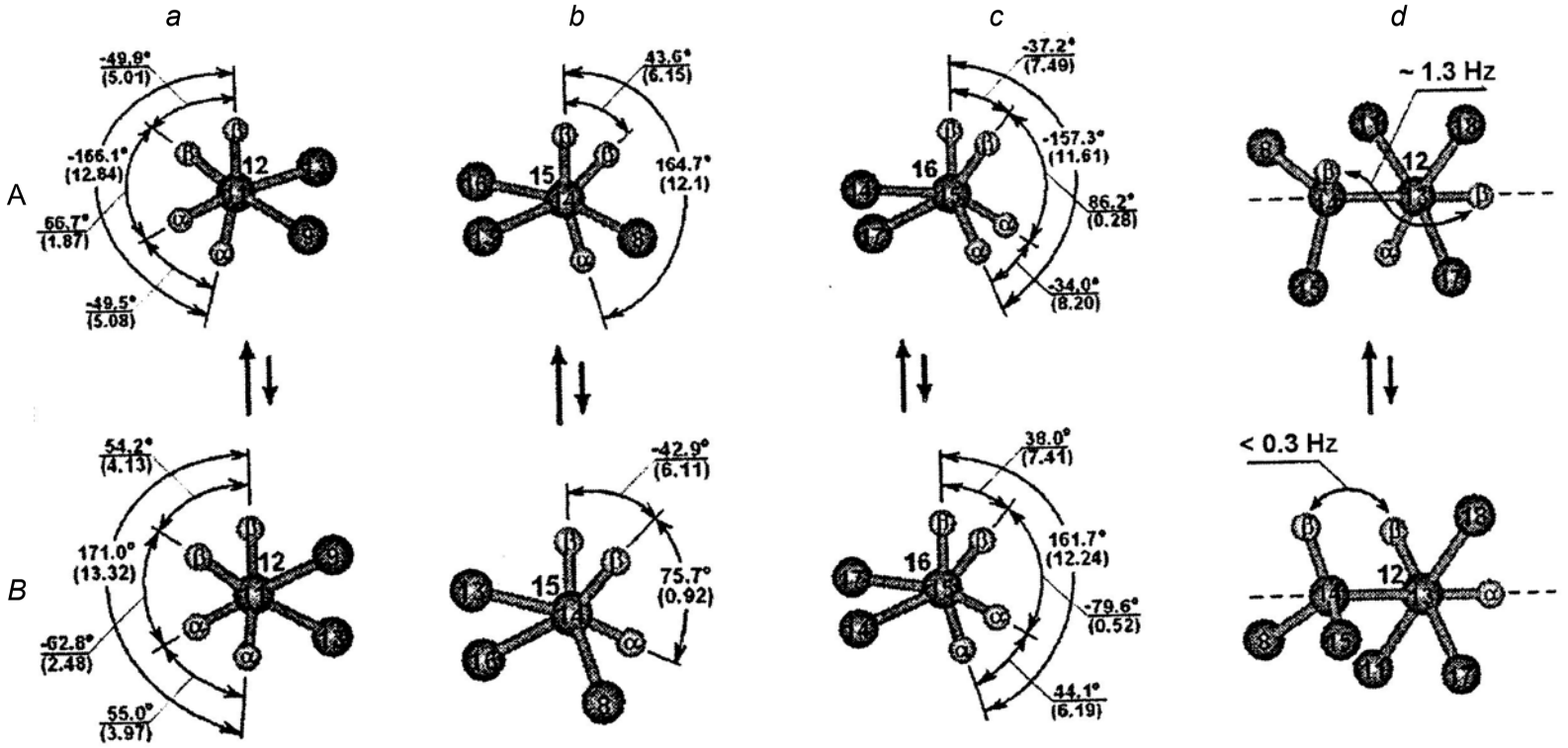

Fig. 4. Newman projections along the bonds for conformers *A* and *B* of the estratetraene **2**: *a* – C(11)–C(12); *b* – C(14)–C(15); *c* – C(15)–C(16); *d* – C(13)–C(12). On projections *a*–*c* the arrows represent the interproton torsion angles θ_{H-H} and their calculated values (MM^+), and the numbers in parentheses represent the corresponding values of the calculated constants $^3J_{H-H}$, Hz. On projection *d* the arrows represent the long-range (W-type) scalar couplings between the H-12β and H-14β protons and their typical $^4J_{H-H}$ values, the dotted line represents the C(14)–C(13)–C(12) plane.

the signal of the H-11α proton (2.56 ppm). The accuracy of this measurement is limited on account of the long-range scalar couplings of the proton, leading to additional broadening of the individual components of its signal. This is noticeable during comparison of the form of the lines in the signals of the H-11α and H-12β protons (Fig. 3c) with allowance for the different scale of their presentation. With increase of temperature from -30 to 15°C, therefore, the $^3J_{11\alpha,12\alpha}$ constant remains unchanged (within the limits of its measurement on the signal of the H-11α proton).

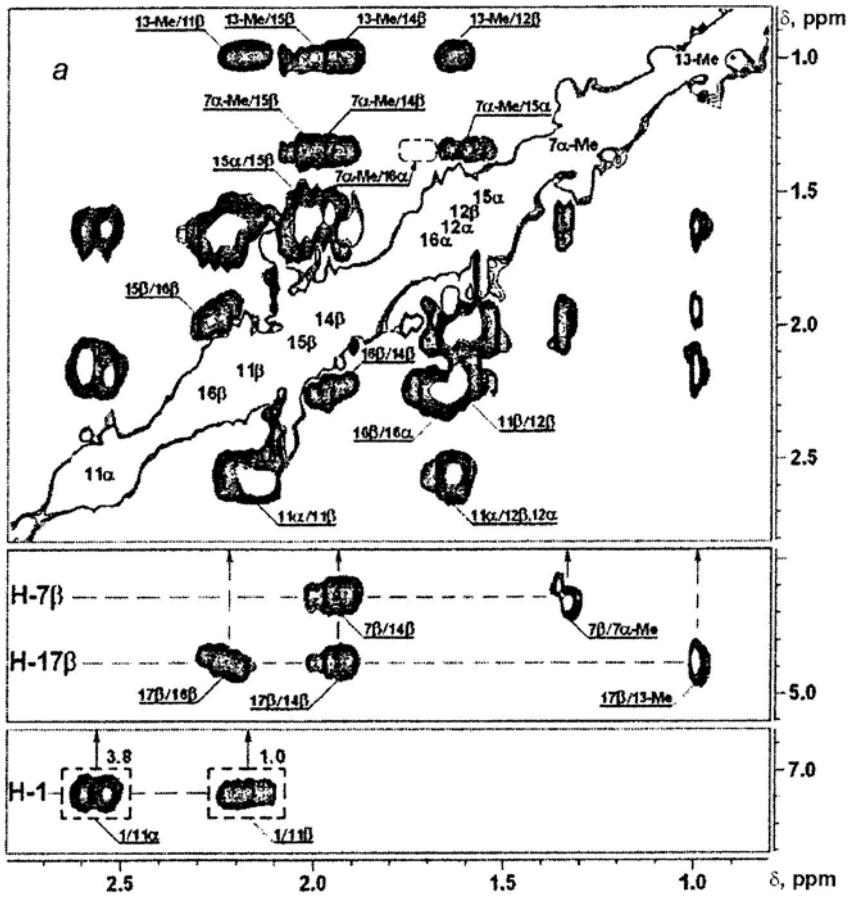

Fig. 5. *a* – Fragments of the NOESY spectrum (τ_m = 0.5 sec) of the steroid **3**. (The dotted rectangles represent the 1/11α and 1/11β cross peaks, the numbers are the relative integral intensities; the position of the cross peak corresponding to the 7α-Me/16α interaction in the minor conformer *B* is indicated by an oval dotted frame.)

Among the vicinal constants describing the stereochemical orientation of the protons of ring D in conformers *A* and *B* of steroid **2** $^3J_{14\beta,15\alpha}$, $^3J_{15\alpha,16\beta}$, and $^3J_{15\beta,16\alpha}$ must be most sensitive to conformational exchange (see their calculated values in Fig. 4b, c). However, under the conditions of overlap of the signals for the scalar couplings of protons H-14β, H-15β, and H-16β in the region of 2.2-2.4 ppm determination of the comparatively small changes (~0.4 Hz) of the constants in relation to temperature is impossible on account of the effects of the strong coupling between the protons of the C(14)H–C(15)H_2–C(16)H_2 fragment. For this reason the most convenient in this respect is the long-range constant $^4J_{14\beta,12\beta}$ (Fig. 4d), which can be measured

with high accuracy (±0.02 Hz) at the signal of the H-12β proton (see Figs. 2 and 3c). With increase of temperature from 15 to 60°C this constant decreases from 1.11 to 0.98 Hz, which corresponds qualitatively to the nature of the conformational changes in the region of the fusion of rings C and D in the analog **2**.

Thus, the results from the investigation of compound **2** indicate the existence of a fast conformational equilibrium on the NMR time scale between forms *A* and *B* due to the inversion of rings C and D. Here the pseudoaxial orientation of the methyl group at position 7α remains unchanged (Fig. 3c). At room temperature the equilibrium is displaced toward conformer *A*, and the ratio of the populations of the conformers (P_A:P_A ~ 5:1) corresponds fairly well to the data from the MM^+ computational methods, which predict (ΔE = 0.78 kcal/mol) the presence of 21% of the minor conformer *B*. For the estratetraene **3** the computational methods

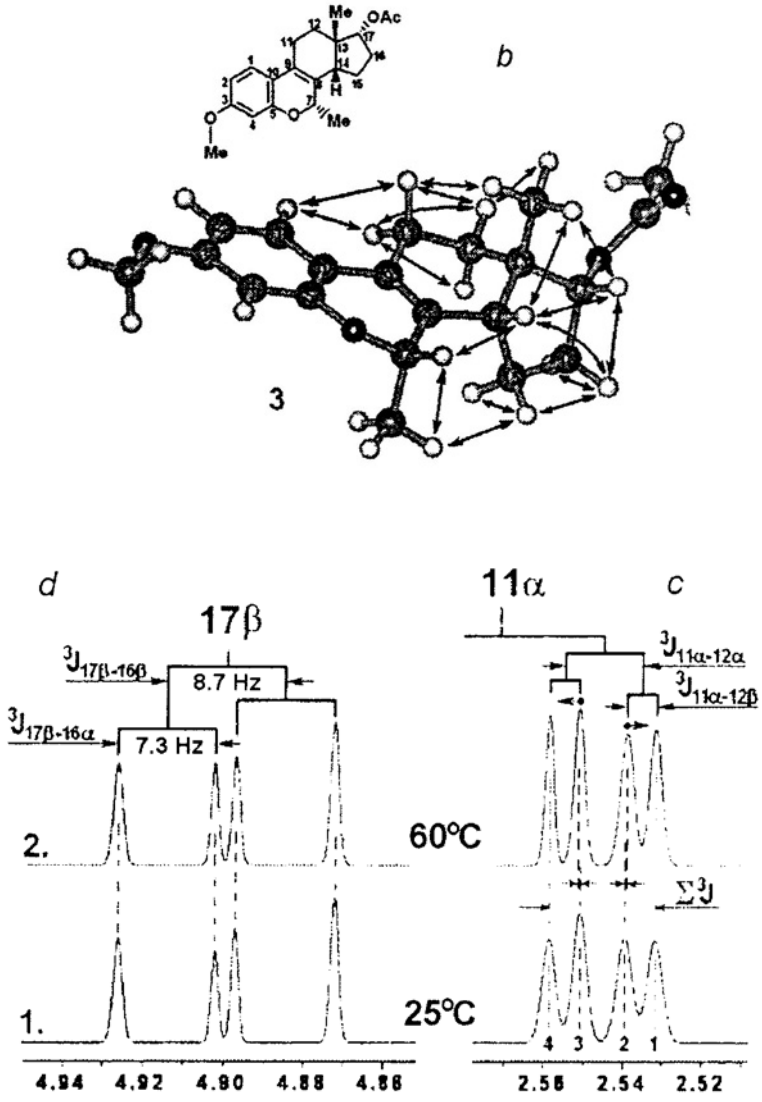

Fig. 5. *b* – The three-dimensional structure of the most energetically favorable conformer *A* (the double arrows indicate the discovered direct interproton couplings). *c* – H-11α (only the right (low-frequency) half of the signal is shown; the dotted lines and the arrows represent the relative changes in the position of the inner components (2 and 3) of the proton). *d* – H-17β.

predict (ΔE = 3.69 kcal/mol) a significant fraction of conformer *B* compared with steroid **2**: $P_B^{expt} < 1\%$. Consequently, the complete absence of conformer *B* from the solution can be expected for steroid **3** at room temperature: $P_B^{expt} < 1\%$. This suggestion is confirmed by the absence of the cross peaks for 7α-Me/16α in the NOESY spectrum of the analog **3** (Fig. 5a). (The position that it should occupy is shown by the dotted oval.) Unfortunately, it is not possible to determine the presence (or absence) of the 18/12α cross peak characteristic of conformer *B* on account of the overlap of the signals of H-12α and H-12β in the region of 1.5-1.7 ppm and the strong steric interaction of 18/12β in conformer *A*. In spite of this the ratio of the integral intensities of cross peaks 1/11α and 1/11β (3.8:1) indicates unambiguously almost complete absence of conformer *B*, since it coincides within the experimental error limits with their calculated (MM^+) ratio 3.75:1 for conformer *A*, in which $r_{1,11\alpha}$ = 2.15 and $r_{1,11\beta}$ = 2.68 Å. If the presence of even 2% of conformer *B* in the solution is assumed, then according to the data from the MM^+ method this should lead to a decrease in the relative intensity ratio of the cross peaks 1/11α and 1/11β to 3.7:1 ($r_{1,11\alpha}^B$ = 2.82 and $r_{1,11\beta}^B$ = 2.20 Å) and not to the increase observed experimentally.

The overlap of the signals for the H-12α and H-12β protons complicates the interpretation of the temperature changes in the multiplet structure of the signal of the H-11α proton (2.25 ppm). If the temperature is raised from 25 to 60°C there is a decrease in the observed value of the constant $<^3J_{11\alpha,12\beta}>$ and a simultaneous increase in the constant $<^3J_{11\alpha,12\alpha}>$. The sum of the constants remains practically unchanged (Fig. 5c). It is perfectly clear that the differences in the vicinal constants are not due to change in the ratio of the populations of the conformers but are the result of the increase of the difference between the chemical shifts of the AB protons H-12α and H-12β in a spin system of the ABX type, reflected in the mutual position of the lines for the signal of the X proton H-11α. The absence of an increase in the sum of the constants ($\Sigma^3J = <^3J_{11\alpha,12\beta}> + <^3J_{11\alpha,12\alpha}>$) with increase of temperature, which would occur as a result of increase in the population of the thermodynamically less favorable conformer *B*, indicates the almost complete absence of the estratetraene **3** in the solution for the range of temperatures close to room temperature. This conclusion is confirmed by the absence of a temperature dependence of the $^3J_{16\alpha,17\beta}$ and $^3J_{16\beta,17\beta}$ constants, which can be measured with high accuracy on the signal of the H-17β proton (Fig. 5d).

The results from the investigations of the 6-oxa-14β analog **3** show that conformer *A* exists almost entirely in solution. The obtained data may prove important for predicting the biological characteristics of such compounds. We hope to present some results of biological trials on the steroids **2** and **3** in the near future.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were obtained at 298 K on a Bruker DPX-300 spectrometer (300 and 75 MHz respectively). The chemical shifts were measured with reference to TMS by assigning the standard values δ 7.26 (^1H) and 76.9 ppm (^{13}C) to the solvent signal ($CDCl_3/CHCl_3$) with an accuracy of not less than ±0.01 ppm. During the production of the two-dimensional spectra (DFQ-COSY, J-COSY, NOESY, GSQC, COLOC) standard pulse sequences and Bruker software were used to process the initial data. On account of fast conformational exchange on the NMR time scale the chemical shifts presented in the experimental section are averaged values.

All the investigated steroids were racemic.

3-Methoxy-7α-methyl-14β-estra-1,3,5(10),8(9)-tetraen-17-one (2). To a solution of compound **4** (500 mg) [22] in 14 ml of benzene we added 110 mg of 5% Pd/C. Hydrogen was conducted at 40°C until the initial compound had disappeared from the reaction mixture. The reaction was monitored by TLC on Silufol plates in the 2:1 petroleum ether–ethyl acetate solvent system. The catalyst was filtered off and washed on the filter with benzene. The benzene fractions were combined, the solvent was removed under vacuum, and the

residue was recrystallized from methanol. We obtained 327 g (65%) of compound **2**; mp 123-125°C (mp 119-121°C [8]). ^{1}H NMR spectrum, δ, ppm: 7.06 (1H, H-1); 6.48 (1H, H-2); 6.44 (1H, H-4); 4.69 (1H, H-7β); 2.56 (1H, H-11α); 2.21 (1H, H-11β); 1.67 (1H, H-12α); 1.48 (1H, H-12β); 2.31 (1H, H-14β); 1.67 (1H, H-15α); 2.30 (1H, H-15β); 2.49 (1H, H-16α); 2.29 (1H, H-16β); 1.04 (3H, H-18); 3.78 (3H, CH_30); 1.37 (3H, 7α-CH_3). ^{13}C NMR spectrum, δ, ppm: 123.37 (C-1); 106.54 (C-2); 160.11 (C-3); 102.11 (C-4); 152.70 (C-5); 74.99 (C-7); 128.24 (C-8); 123.13 (C-9); 116.12 (C-10); 20.13 (C-11); 25.23 (C-12); 46.43 (C-13); 46.28 (C-14); 27.19 (C-15); 36.72 (C-16); 221.94 (C-17); 18.79 (C-18); 55.16 (CH_3O); 20.20 (C-7α). Found, %: C 76.46; H 7.49. $C_{19}H_{22}0_3$. Calculated, %: C 76.48, H 7.43.

17α-Acetoxy-3-methoxy-7α-methyl-14β-estra-1,3,5(10),8(9)-tetraene (3). To a solution of the steroid **2** (100 mg) [21] in a mixture of THF and water (0.2 ml) we added $NaBH_4$ (20 mg). The reaction mixture was stirred at room temperature for 3 h, and the excess of the reducing agent was decomposed with acetic acid. The reaction mixture was treated and the reaction products were acetylated under the usual conditions [22]. The product **3** was isolated by crystallization from a 5:1 mixture of methanol and chloroform. The yield was 61 mg (53%); mp 134-136°C (mp 132-134°C [8]). ^{1}H NMR spectrum, δ, ppm: 7.07 (1H, H-1); 6.47 (1H, H-2); 6.42 (1H, H-4); 4.62 (1H, H-70); 2.55 (1H, H-11α); 2.15 (1H, H-11β); 1.64 (1H, H-12α); 1.61 (1H, H-12β); 1.91 (1H, H-14β); 1.58 (1H, H-15α); 2.00 (1H, H-15β); 1.68 (1H, H-16α); 2.21 (1H, H-16β); 4.87 (1H, H-17β); 0.98 (3H, H-18); 3.78 (3H, CH_30); 1.33 (3H, 7α-CH_3); 2.08 (3H, C$\underline{H}_3$CO). ^{13}C NMR spectrum, δ, ppm: 123.20 (C-1); 106.40 (C-2); 159.87 (C-3); 101.86 (C-4); 153.03 (C-5); 75.56 (C-7); 129.65 (C-8); 122.32 (C-9); 116.46 (C-10); 20.62 (C-11); 23.06 (C-12); 41.83 (C-13); 45.74 (C-14); 22.29 (C-15); 27.30 (C-16); 82.51 (C-17); 21.74 (C-18); 55.13 (CH_30); 20.60 (C-7α); 20.97 ($\underline{C}H_3CO$); 170.90 ($CH_3\underline{C}O$). Found, %: C 73.58; H 7.69. $C_{21}H_{26}0_4$. Calculated, %: C 73.66; H 7.65.

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