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Modification of A and B Rings in 20-Dihydroisoxazolyl Steroids and Their Derivatives with a Functionalized Side Chain

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Abstract—Steroidal 1,4,6-trien-3-ones which are precursors of 1α-hydroxylated vitamin D and its analogs were synthesized starting from 3β-hydroxy-Δ^5-20-dihydroisoxazolyl steroids and their open-chain derivatives.

In continuation of our studies on the use of steroid isoxazole derivatives in the synthesis of polyhydroxy steroids, in particular of vitamin D metabolites and their analogs [1–3], in the present study we examined the possibility of using the same compounds for preparation of 1α-hydroxylated vitamin D precursors. Most known procedures for introduction of a hydroxy group to C^1 of steroid molecules (which plays an important role in biological effect of steroid compounds) involve 1,4,6-trien-3-ones as key intermediates [4]. The corresponding Δ^5-1α,3β-diol can be obtained by treatment with hydrogen peroxide in alkaline medium, followed by reduction with lithium in liquid ammonia of the resulting 1α,2α-epoxy-4,6-dien-3-one [5].

In the present work we tried to develop methods for modification of **A** and **B** ring in 20-dihydroisoxazolyl steroids with the goal of obtaining 1,4,6-trien-3-ones as vitamin D precursors. As initial compound we used 5′-R-dihydroisoxazole derivative **I** which was synthesized from stigmasterol via a multistep procedure [6]. By heating of compound **I** with *p*-toluenesulfonic acid in boiling aqueous acetone and subsequent treatment of 3β-hydroxy-Δ^5 derivative **II** with 5,6-dichloro-2,3-dicyanobenzoquinone (DDQ) in dioxane [7] we obtained 28% of 1,4,6-trien-3-one **III** (Scheme 1), the conversion of the initial compound being 73%. We found that modification of the cyclic moiety was accompanied by dehydrogenation of dihydroisoxazole **III** to isoxazole **IV** (yield 6%). The yield of the latter increases on prolonged reaction.

The structure of the products was confirmed by spectral data which were consistent with those reported in [8]. The most characteristic are chemical shifts of protons at C^1, C^2, C^4, and C^6 (multiplet signals in the region δ 5.95–6.26 ppm) and a doublet signal from 7-H at δ 7.01 ppm in the ^{1}H NMR spectra. The corresponding carbon nuclei give doublet signals in the ^{13}C NMR spectra at δ_C 123.8, 127.7, 128.2, and 138.3 ppm for compound **III** and at δ_C 123.7, 127.6, 128.0, and 138.4 ppm for isoxazole **IV**. In the ^{1}H NMR spectrum of **IV** we also observed a singlet at δ 5.76 ppm, which belongs to proton in position *4* of the isoxazole ring [9]. The IR spectra of **III** and **IV** contained carbonyl absorption bands at 1650 and 1657 cm^{-1}, respectively, whose position is determined by conjugation with the double bonds.

Epoxidation of **III** with hydrogen peroxide in alkaline medium [5] gave 1α,2α-epoxydienone **V** in 48% yield. Compound **V** showed in the ^{1}H NMR spectrum a doublet at δ 3.57 ppm (J = 4 Hz) from 1-H and a doublet of doublets at δ 3.43 ppm (J_1 = 4 Hz, J_2 = 1.2 Hz) from 2-H. Its IR spectrum contained a band at 1668 cm^{-1} belonging to stretching vibrations of the conjugated carbonyl group and a band at 1617 cm^{-1} which was assigned to vibrations of the double bonds. The spectral parameters of epoxydienone **V** were in agreement with those given in [10].

The reduction of compound **V** with a large excess of lithium in the system liquid ammonia–tetrahydrofuran at –78°C [5] gave a complex mixture of products which we failed to identify. Obviously, this was the result of modification of both the cyclic fragment and the dihydroisoxazole moiety.

Taking into account that the above reactions take several pathways and that the yields of the target products are not high, we have developed another scheme which includes opening of the dihydroisoxazole ring, reduction of the β-hydroxy ketone thus formed to diol, and further functionalization of **A** and **B** rings in the steroid molecule (Scheme 2). By

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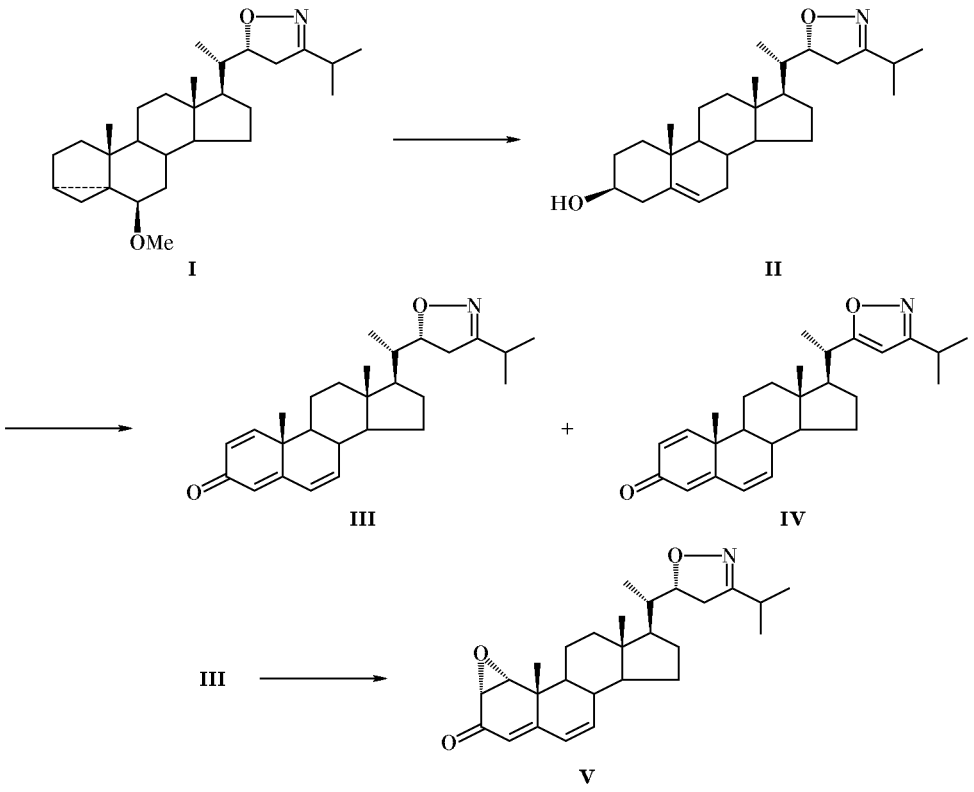
Scheme 1.



reduction of **II** over Raney nickel in the presence of $AlCl_3$ [11] we obtained β-hydroxy ketone **VI** as the sole product. When compound **II** was treated with hexacarbonylmolybdenum in aqueous acetonitrile [12], β-hydroxy ketone **VI** was formed in 57% yield, and the reaction was accompanied by dehydration of **VI** to Δ^{22}-24-ketone **VII** (8%).

In the ^{1}H NMR spectrum of **VI**, the signal from the $C^{22}H$ proton was observed in a stronger field (δ 4.07 ppm), as compared to initial compound **II**. The $C^{22}H$ signal of **VII** appears as a doublet of doublets at δ 6.73 ppm (J_1 = 15.6 Hz, J_2 = 9 Hz), and the $C^{23}H$ signal (δ 6.04 ppm) is a doublet with J = 15.6 Hz. These data indicate *trans* configuration of the Δ^{23}-double bond.

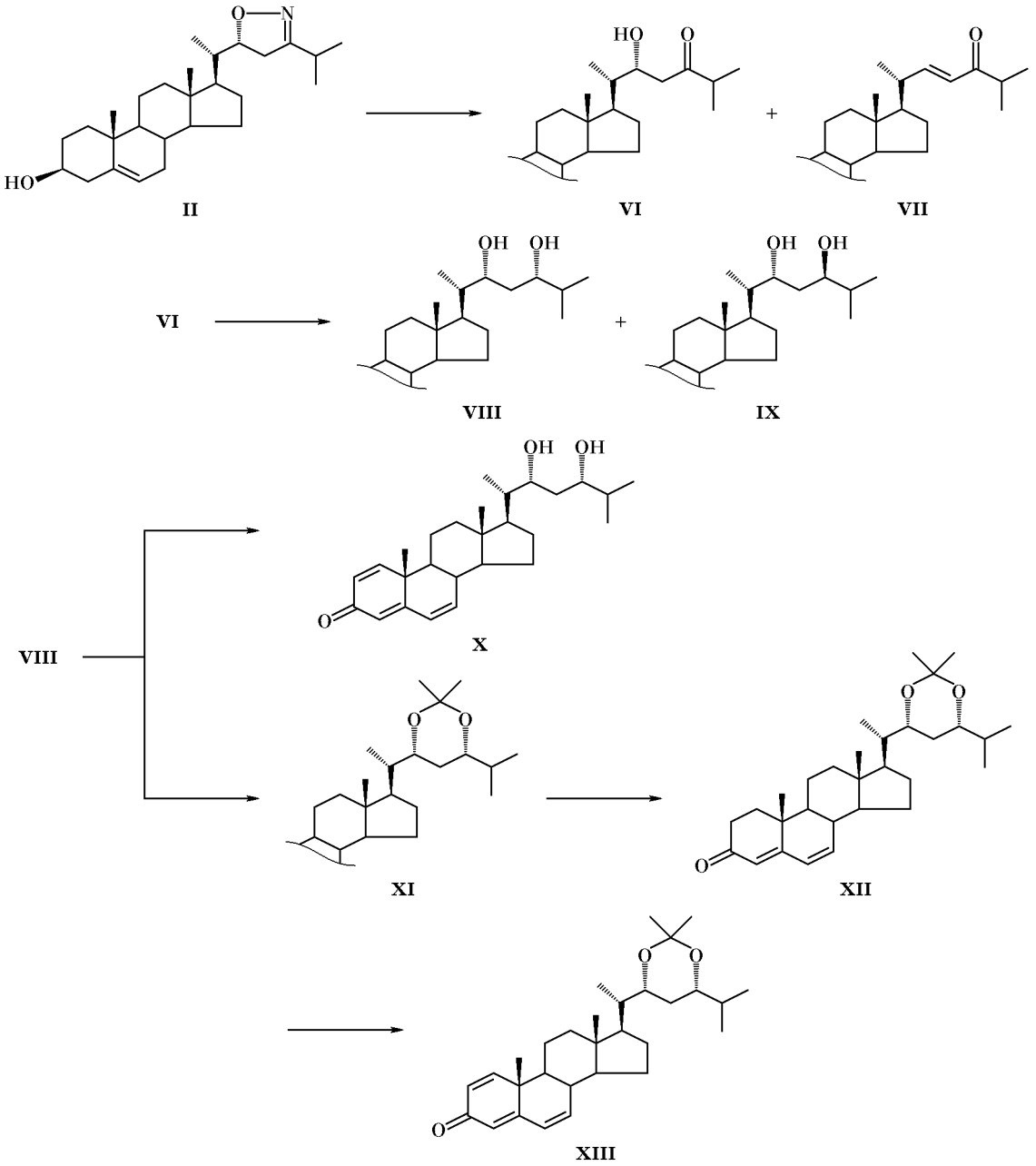
The β-hydroxy ketone moiety in **VI** was transformed into 22,24-diol fragment by the action of 1,3,2-benzodioxaborole which ensures a necessary substrate configuration and simultaneously acts as a proton donor, giving rise to *syn*-stereoselective reduction of the carbonyl group [13]. An obvious advantage of that reagent is its stability in aprotic solvents (such as benzene, toluene, chloroform, diethyl ether, or hexane) [14].

Treatment of β-hydroxy ketone **VI** with 1,3,2-benzodioxaborole at –10°C led to formation of a mixture of diastereoisomeric (with respect to C^{24}) 22,24-diols **VIII** and **IX** in an overall yield of 80% (*syn*–*anti* ratio 5:1). The major isomer **VIII** was isolated by crystallization. Compound **VIII** showed in the ^{1}H NMR spectrum multiplet signals from protons at C^{24} and C^{22} at δ 3.28 and 3.65 ppm, respectively. Its IR spectrum contained an absorption band at 3344 cm^{-1} due to stretching vibrations of the hydroxy group. It should be noted that treatment of structurally related 20,22-dihydroxy-24-oxo derivative with sodium tetrahydridoborate gives the corresponding *syn*- and *anti*-20,22,24-trihydroxy isomers at a ratio of 2:3 [15].

Diol **VIII** was oxidized with dichlorodicyanobenzoquinone under the conditions described in [16]. According to these data, secondary hydroxy groups should remain intact during the process. In boiling dioxane (8 h) the greatest yield of trienone **X** was 41%, the conversion of **VIII** being 75%. Presumably, the relatively low yield is the result of oxidation of one hydroxy group [7] and subsequent dehydration of the other on prolonged contact with the reagent. Therefore, we decided to preliminarily protect the 22,24-diol moiety.

For this purpose, compound **VIII** was treated with 2,2-dimethoxypropane in the presence of *d*-camphorsulfonic acid [17] to obtain *O*,*O*-isopropylidene

Scheme 2.



derivative **XI** in 85% yield. By reaction of stereoisomeric diols **VIII** and **IX** with 2,2-dimethoxypropane (reaction time 3 h) we obtained exclusively *syn* isomer **XI**. The ^{13}C NMR spectrum of the latter contained quartets from methyl carbon atoms at δ_C 19.4 and 30.3 ppm and a signal at δ_C 98.1 ppm from the quaternary carbon atom. These data reliably indicate the stereochemistry of *O,O*-isopropylidene derivatives of 1,3-diols [18].

The oxidation of compound **XI** with dichlorodicyanobenzoquinone in dioxane (8–10 h) both in the absence and in the presence of sodium carbonate led to formation of a complex mixture of products, among which we succeeded in identifying trienone **XIII** (yield 25%). Probably, this was the result of partial deprotection of the diol fragment and its subsequent oxidation (the oxidant is a fairly strong Lewis acid capable of promoting cleavage of acetals [19, 20]). When the reaction time was reduced to 2–3 h, up to 76% of partial oxidation product, dienone **XII**, was obtained. Compound **XII** is analogous to the Oppenauer oxidation products [21]. Therefore, it

seems unreasonable to perform preliminary oxidation according to Oppenauer, for difficulties are obviously encountered at the stage of oxidation of 4,6-dien-3-one **XII** to 2,4,6-trien-3-one **XIII**.

Thus, our results show that introduction of a 1,4,6-trien-3-one moiety into molecules of dihydroisoxazolyl steroids involves difficulties associated with insufficient stability of the heteroring under reaction conditions. Implementation of the latent functionality of isoxazole ring at the stage preceding introduction of the above fragment may be useful provided that the 1,3-diol moiety is reliably protected.

EXPERIMENTAL

The ^{1}H NMR spectra were obtained on a Bruker A-200 instrument (200 MHz) using chloroform-*d* as solvent and TMS as internal reference. The IR spectra were recorded on a UR-20 spectrometer from samples prepared as films or solutions in carbon tetrachloride. The mass spectra (70 eV) were run on a Hewlett Packard GC–MS system including HP-5890 gas chromatograph (linear oven temperature programming from 40 to 280°C at 10 deg/min). The UV spectra were obtained on a Specord M-400 spectrophotometer in methanol or ethanol. The melting points were determined on a Koeffler device. The progress of reactions was monitored by TLC on Silufol UV-254 and Kieselgel 60 F_{254} (Merck) plates. The reaction mixtures were separated on Kieselgel 60 (40/60 μm) silica gel (Merck).

(5′*R*,20*S*)-20-(3-Isopropyl-4,5-dihydroisoxazol-5-yl)pregn-5-en-3β-ol (II). *p*-Toluenesulfonic acid monohydrate, 0.133 g (0.7 mmol), was added to a solution of 0.9 g (2.1 mmol) of dihydroisoxazole derivative **I** in 50 ml of acetone and 30 ml of water. The mixture was refluxed for 30 min and cooled to room temperature, a saturated solution of sodium hydrogen carbonate was added, and the mixture was extracted with chloroform. The extract was washed with water, dried over anhydrous sodium sulfate, and evaporated. Yield of **II** 0.75 g (87%). mp 163–164°C (from MeOH). IR spectrum (CCl_4), cm^{-1}: 3384, 1466, 1381, 1213, 1055. ^{1}H NMR spectrum, δ, ppm: 0.69 s (3H, 18-Me), 0.84 d (3H, 21-Me, J = 6.6 Hz), 0.99 s (3H, 19-Me), 1.14 d (6H, 26-Me and 27-Me, J = 6.7 Hz), 2.65 d (2H, 4′-H, J = 10 Hz), 3.49 m (1H, 3-H), 4.61 t.d (1H, 5′-H, J_1 = 10 Hz, J_2 = 3.8 Hz), 5.33 d (1H, 6-H, J = 4.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.3 q, 11.5 q, 18.9 q, 19.6 d.q, 20.7 t, 24.0 t, 27.1 t, 27.7 d, 30.8 t, 31.5 t, 31.6 d, 33.2 t, 36.1 s, 36.9 t, 37.8 d, 39.3 t, 41.5 t, 42,4 s, 49.8 d, 52.6 d, 56.0 d, 70.9 d, 82.2 d, 121.0 d, 140.6 s, 163.5 s. Mass spectrum, *m*/*z*: 413 $[M]^+$, 395, 380, 275, 240.

Oxidation of ring A with 5,6-dichloro-2,3-dicyanobenzoquinone. *a*. 5,6-Dichloro-2,3-dicyano-1,4-benzoquinone, 1.32 mmol, was added to a solution of 0.165 g (0.4 mmol) of compound **II** in 8 ml of freshly distilled dioxane. The mixture was refluxed for 3 h under nitrogen (TLC monitoring) and cooled to room temperature, the precipitate was filtered off, and the filtrate was evaporated. The residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (2 : 1) as eluent. We isolated (in the order of elution) 0.009 g (6%) of trienone **IV**, 0.045 g (27%) of initial compound **II**, and 0.045 g (28%) of trienone **III**.

(5′*R*,20*S*)-20-(3-Isopropyl-4,5-dihydroisoxazol-5-yl)pregna-1,4,6-trien-3-one (III). Oily substance. IR spectrum (film), ν, cm^{-1}: 1650, 1601, 1464, 1381. ^{1}H NMR spectrum, δ, ppm: 0.74 s (3H, 18-Me), 0.79 d (3H, 21-Me, J = 6.8 Hz), 1.12 d (6H, 26-Me and 27-Me, J = 6.9 Hz), 1.16 s (3H, 19-Me), 2.65 d (2H, 4′-H, J = 9.8 Hz), 4.58 t.d (1H, 5′-H, J_1 = 9.8, J_2 = 3.9 Hz), 5.96–6.24 m (4H, 1-H, 2-H, 4-H, 6-H), 7.07 d (1H, 7-H, J = 10 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.7 q, 12.0 q, 20.1 q, 20.6 q, 21.8 t, 23.7 t, 27.3 t, 27.9 d, 33.6 t, 38.0 d, 38.1 s, 39.2 t, 41.2 s, 43.4 s, 48.3 d, 52.8 d, 53.2 d, 82.2 d, 123.7 d, 127.6 d, 128.0 d, 138.4 d, 153.1 d, 162.7 s, 186.4 s. UV spectrum: λ_{max} 299 nm (ε 13900).

(20*S*)-20-(3-Isopropylisoxazol-5-yl)pregna-1,4,6-trien-3-one (IV). Oily substance. IR spectrum (film), ν, cm^{-1}: 1657, 1652, 1603, 1463. ^{1}H NMR spectrum, δ, ppm: 0.83 s (3H, 18-Me), 1.18 s (3H, 19-Me), 1.24 d (3H, 21-Me, J = 6.9 Hz), 1.27 d (6H, 26-Me and 27-Me, J = 6.8 Hz), 5.76 s (1H, 4′-H), 5.95–6.26 m (4H, 1-H, 2-H, 4-H, 6-H), 7.04 d (1H, 7-H, J = 10 Hz). ^{13}C NMR spectrum, δ, ppm: 11.9 q, 19.5 q, 20.7 q, 21.8 q, 23.6 t, 26.5 d, 27.9 t, 29.7 s, 31.9 s, 35.5 d, 38.1 d, 39.2 t, 41.2 t, 43.2 s, 48.2 d, 53.4 d, 54.5 d, 97.5 d, 123.8 d, 127.7 d, 128.2 d, 138.3 d, 152.9 d, 162.6 s, 177.5 s, 186 s. UV spectrum: λ_{max} 299 nm (ε 13920).

Following the above procedure, by heating 0.1 mol of compound **VIII** with DDQ under reflux for 8 h and subsequent chromatographic separation we obtained (in the order of elution) 0.019 g (41%) of trienone **X** and 0.005 g (25%) of initial compound **VIII**.

(22*R*,24*S*)-3β,22,24-Trihydroxycholesta-1,4,6-trien-3-one (X). Oily substance. IR spectrum (film), ν, cm^{-1}: 3427, 1652, 1464. ^{1}H NMR spectrum, δ, ppm: 0.79 s (3H, 18-Me), 0.91 d (3H, 21-Me, J = 7 Hz), 0.94 d (6H, 26-Me and 27-Me, J = 7 Hz), 1.18 s (3H, 19-Me), 3.63 m (1H, 24-H), 3.90 m (1H, 22-H), 5.99–6.27 m (4H, 1-H, 2-H, 4-H, 6-H), 7.06 d (1H, 7-H, J = 10 Hz). UV spectrum: λ_{max} 299 nm (ε 13960).

By the same procedure (3 h under reflux), from 0.04 g (0.087 mmol) of compound **XI** we obtained 0.03 g (76%) of (22*R*,24*S*)-22,24-isopropylidenedioxycholesta-4,6-dien-3-one (XII). Oily substance. IR spectrum (film), ν, cm^{-1}: 1650, 1463. ^1H NMR spectrum, δ, ppm: 0.76 s (3H, 18-Me), 0.85 d (3H, 21-Me, *J* = 6.8 Hz), 0.90 d (6H, 26-Me and 27-Me, *J* = 6.9 Hz), 1.09 s (3H, 19-Me), 1.38 s (6H, CMe_2), 3.40 m (1H, 24-H), 3.85 m (1H, 22-H), 5.65 s (1H, 4-H), 6.10 s (2H, 6-H and 7-H).

Likewise, from 0.03 g (0.066 mmol) of dienone **XII** (10 h under reflux) we obtained 0.01 g (33%) of (22*R*,24*S*)-22,24-isopropylidenedioxycholest-1,4,6-trien-3-one (**XIII**). Oily substance. IR spectrum (film), ν, cm^{-1}: 1655, 1461, 1376, 1254. ^1H NMR spectrum, δ, ppm: 0.79 s (3H, 18-Me), 0.85 d (3H, 21-Me, *J* = 6.8 Hz), 0.89 d (6H, 26-Me and 27-Me, *J* = 6.9 Hz), 0.96 s (3H, 19-Me), 1.38 s (6H, CMe_2), 3.39 m (1H, 24-H), 3.85 m (1H, 22-H), 5.92–6.26 m (4H, 1-H, 2-H, 4-H, 6-H), 7.05 d (1H, 7-H, *J* = 10 Hz). UV spectrum: λ_{max} 299 nm (ε 13900).

b. Dichlorodicyanobenzoquinone, 0.33 mmol, and sodium carbonate, 0.1 mmol, were added to a solution of 0.045 g (0.098 mmol) of compound **XI** in 2 ml of freshly distilled dioxane. The mixture was refluxed for 8 h under nitrogen (TLC monitoring) and cooled to room temperature, the precipitate was filtered off, the filtrate was evaporated, and the residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (2:1) as eluent to isolate 0.011 g (25%) of trienone **XIII**.

Cleavage of the heteroring in 20-dihydroisoxazolyl steroids. *a*. To a solution of 0.04 mmol of 20-dihydroisoxazolyl steroid in 5 ml of acetonitrile and 0.05 ml of water we added 0.044 mmol of hexacarbonylmolybdenum. The mixture was refluxed for 30 min, silica gel was added, the mixture was evaporated, and the residue was applied to a column charged with silica gel, which was then eluted with toluene–ethyl acetate. From 0.2 g (0.48 mmol) of compound **II** we isolated (in the order of elution) 0.015 g (8%) of ketone **VII** and 0.115 g (57%) of 22-hydroxy-24-ketone **VI**.

(22*R*)-3β,22-Dihydroxycholest-5-en-24-one (VI). mp 165–166°C (from CHCl3–MeOH). IR spectrum (CCl_4), ν, cm^{-1}: 3405, 1698, 1466, 1380. ^1H NMR spectrum, δ, ppm: 0.67 s (3H, 18-Me), 0.91 d (3H, 21-Me, *J* = 6.7 Hz), 0.98 s (3H, 19-Me), 1.08 d (6H, 26-Me and 27-Me, *J* = 6.9 Hz), 3.47 m (1H, 3-H), 4.07 d.t (1H, 22-H, J_1 = 9.6, J_2 = 2.9 Hz), 5.31 d (1H, 6-H, *J* = 5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.8 q, 12.7 q, 18.1 q, 19.3 q, 21.0 t, 24.3 t, 27.4 t, 29.7 t, 31.5 t, 31.8 d, 36.4 s, 37.2 t, 39.7 t, 39.9 t, 40.4 d, 41.6 t, 42.2 t, 42.6 s, 50.1 d, 53.0 d, 56.4 d, 69.0.d, 71.7 d, 121.5 d, 140.8 s, 217.0 s. Mass spectrum, *m*/*z*: 416 $[M]^+$, 398 $[M-H_2O]$, 330, 302, 284.

(22*E*)-3β-Hydroxycholesta-5,22-dien-24-on (VII). Oily substance. IR spectrum (film), ν, cm^{-1}: 1695, 1669, 1623, 1464, 1381. ^1H NMR spectrum, δ, ppm: 0.69 s (3H, 18-Me), 0.98 s (3H, 19-Me), 1.06 d (3H, 21-Me, *J* = 6.9 Hz), 1.07 d (6H, 26-Me and 27-Me, *J* = 6.8 Hz), 3.48 m (1H, 3-H), 5.35 d (1H, 6-H, *J* = 5 Hz), 6.04 d (1H, 23-H, *J* = 15.6 Hz), 6.73 d.d (1H, 22-H, J_1 = 15.6, J_2 = 9 Hz). ^{13}C NMR spectrum, δ, ppm: 12.1 q, 18.4 q, 18.6 q, 19.3 q, 21.0 t, 24.2 t, 28.1 t, 31.5 t, 31.8 d, 36.4 s, 37.2 t, 38.2 d, 39.6 t, 40.0 d, 42.2 t, 42.6 s, 50.0 d, 54.9 d, 56.5 d, 71.6 d, 121.4 d, 126.1 d, 140.8 s, 152.6 d, 204.7 s.

b. To a solution of 1 mmol of 20-dihydroisoxazolyl steroid in 6 ml of methanol–water (5:1) we added 3.6 g of Raney nickel and 9 mmol of aluminum chloride. The mixture was stirred for 3 h, diluted with water, and extracted with ether, and the extract was dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was purified by column chromatography on silica gel using toluene–ethyl acetate as eluent. Following this procedure, from 0.22 g (0.51 mmol) of compound **II** we obtained 0.1 g (47%) of 22-hydroxy-24-ketone **VI**.

Epoxidation of trienone III. (5′*R*,20*S*)-20-(3-Isopropyl-4,5-dihydroisoxazol-5-yl)-1α,2α-epoxypregna-4,6-dien-3-one (V). To a solution of 0.06 g (0.15 mmol) of trienone **III** in 2 ml of methanol we added 0.085 ml of a 30% solution of hydrogen peroxide and 0.015 ml of a 10% solution of sodium hydroxide in methanol. The mixture was stirred for 2 h at room temperature, a saturated solution of ammonium chloride was added, and the mixture was extracted with ethyl acetate. The extract was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (3:1) as eluent to isolate 0.03 g (48%) of epoxydienone **V**. mp 148–150°C (from EtOH). IR spectrum (CCl_4), ν, cm^{-1}: 1668, 1617. ^1H NMR spectrum, δ, ppm: 0.78 s (3H, 18-Me), 0.85 d (3H, 21-Me, *J* = 6.6 Hz), 1.13 d (6H, 26-Me and 27-Me, *J* = 6.9 Hz), 1.16 s (3H, 19-Me), 2.67 d (2H, 4′-H, *J* = 10 Hz), 3.43 d.d (1H, 2-H, J_1 = 4, J_2 = 1.2 Hz), 3.57 d (1H, 1-H, *J* = 4 Hz), 4.60 t.d (1H, 5′-H, *J*1 = 10 Hz, J_2 = 4 Hz), 5.62 d (1H, 4-H, *J* = 1.2 Hz), 6.05 s (2H, 6-H and 7-H).

(22*R*,22*S*)-Cholest-5-ene-3β,22,24-triol (VIII). To a solution of 0.09 g (0.22 mmol) of β-hydroxy ketone **VI** in 9 ml of tetrahydrofuran, cooled to –10°C, we added 1.1 ml of a 1 M solution of

1,3,2-benzodioxaborole in tetrahydrofuran. The mixture was stirred for 1 h, treated with a 2 M solution of sodium hydroxide, and washed with water. The product was extracted into ethyl acetate, and the extract was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated to obtain 0.073 g (80%) of a mixture of *syn*-diol **VIII** and its *anti* isomer **IX** at a ratio of 5:1 (according to the ^{1}H NMR spectrum of the mixture). By crystallization from petroleum ether–ethyl acetate we isolated 0.06 g (66%) of diol **VIII**. mp 208–209°C (from petroleum ether–ethyl acetate). IR spectrum (CCl_4): ν 3344 cm^{-1}. ^{1}H NMR spectrum ($CDCl_3$–CD_3OD), δ, ppm: 0.48 s (3H, 18-Me), 0.70 m (9H, 21-Me, 26-Me and 27-Me), 0.78 s (3H, 19-Me), 2.01 m (2H, 23-H), 3.28 m (2H, 3-H and 24-H), 3.65 m (1H, 22-H), 5.11 d (1H, 6-H, J = 4.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.3 q, 12.0 q, 16.9 q, 17.9 q, 18.9 q, 20.7 t, 24.0 t, 27.0 t, 30.7 t, 30.9 t, 31.5 t, 31.6 d, 33.7 d, 36.1 s, 36.9 t, 39.3 t, 41.4 d+t, 42.2 s, 49.8 d, 52.7 d, 55.9 d, 70.8 d, 74.3 d, 121.0 d, 140.5 s. Mass spectrum, *m*/*z*: 418 $[M]^+$, 302, 285, 284, 269.

(22*R*,24*S*)-22,24-Isopropylidenedioxycholest-5-en-3β-ol (XI). To a solution of 0.013 g (0.031 mmol) of diol **VIII** in 2 ml of acetone we added 0.08 ml (0.65 mmol) of 2,2-dimethoxypropane and a catalytic amount of D-camphorsulfonic acid. The mixture was stirred for 3 h at room temperature, treated with 0.01 ml of triethylamine, and evaporated. The product was extracted into diethyl ether, and the extract was washed with water, dried over anhydrous sodium sulfate, and evaporated. The residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (3:1). Yield of **XI** 0.012 g (85%). Oily substance. IR spectrum (film), ν, cm^{-1}: 3365, 1462, 1378, 1256. ^{1}H NMR spectrum, δ, ppm: 0.68 s (3H, 18-Me), 0.84 d (3H, 21-Me, J = 6.8 Hz), 0.89 d (6H, 26-Me and 27-Me, J = 6.8 Hz), 0.97 s (3H, 19-Me), 1.37 s (6H, CMe_2), 3.43 m (2H, 3-H and 24-H), 3.83 m (1H, 22-H), 5.32 d (1H, 6-H, J = 4.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.8 q, 13.2 q, 17.9 q, 18.6 q, 19.4 q, 20.0 q, 21.1 t, 24.4 t, 26.4 t, 27.5 t, 30.3 q, 31.6 t, 31.9 t+d, 33.2 d, 36.5 s, 37.2 t, 39.7 t, 40.0 d, 42.3 t, 42.7 s, 50.1 d, 52.2 d, 56.4 d, 70.7 d, 71.8 d, 74.2 d, 98.1 s, 121.6 d, 140.9 s.

REFERENCES

1. Litvinovskaya, R.P., Koval', N.V., and Khripach, V.A., *Russ. J. Org. Chem.*, 1997, vol. 33, no. 10, pp. 1442–1446.
2. Litvinovskaya, R.P., Koval', N.V., and Khripach, V.A., *Khim. Geterotsikl. Soedin.*, 1998, no. 2, pp. 267–273.
3. Litvinovskaya, R.P., Koval', N.V., and Khripach, V.A., *Khim. Geterotsikl. Soedin.*, 2000, no. 2, pp. 230–236.
4. Zhu, G.-D. and Okamura, W.H., *Chem. Rev.*, 1995, vol. 95, no. 6, pp. 1847–1952.
5. Barton, D.H.R., Hesse, R.H., Pechet, M.M., and Kizzardo, E.A., *J. Am. Chem. Soc.*, 1973, vol. 95, no. 8, pp. 2748–2749.
6. Khripach, V.A., Litvinovskaya, R.P., Baranovskii, A.V., and Akhrem, A.A., *Dokl. Akad. Nauk SSSR*, 1991, vol. 318, no. 3, pp. 597–600.
7. Turner, A.B., *J. Chem. Soc. C.*, 1968, pp. 2568–2569.
8. Dolle, F., Kappler, Ch., and Hetru, Ch., *Tetrahedron*, 1990, vol. 46, no. 15, pp. 5305–5316.
9. Akhrem, A.A., Lakhvich, F.A., and Khripach, V.A., *Dokl. Akad. Nauk SSSR*, 1987, vol. 297, no. 2, pp. 364–367.
10. Sai, H., Takatsuto, S., and Ikekawa, N., *Chem. Pharm. Bull.*, 1984, vol. 32, no. 10, pp. 1866–1872.
11. Kozikowski, A.P. and Adamczyk, M., *Tetrahedron Lett.*, 1982, vol. 23, pp. 3123–3126.
12. Baradi, P.G., Barco, A., and Benetti, S., *Synthesis*, 1987, no. 3, pp. 276–278.
13. Evans, D.A. and Hoveyda, A.H., *J. Org. Chem.*, 1990, vol. 55, pp. 5190–5192.
14. Kabalka, G.W., Baker, J.D., and Neal, G.W., *J. Org. Chem.*, 1977, vol. 42, no. 3, pp. 512–517.
15. Khripach, V.A., Litvinovskaya, R.P., and Baranovsky, A.V., *Mendeleev Commun.*, 1992, no. 3, pp. 117–118.
16. Iwamura, J. and Mirao, W., *Tetrahedron. Lett.*, 1973, no. 27, pp. 2447–2450.
17. Evans, D.A., Dow, R.L., and Shin, T.L., *J. Am. Chem. Soc.*, 1990, vol. 112, no. 13, pp. 5290–5313.
18. Rychnovsky, S.D., Rogers, B., and Yang, G., *J. Org. Chem.*, 1993, vol. 58, pp. 3511–3515.
19. Tanemura, K., Suzuki, T., and Horaguchi, T., *J. Chem. Soc., Chem. Commun.*, 1992, no. 14, pp. 979–980.
20. Oku, A., Kinugasa, M., and Kamada, T., *Chem. Lett.*, 1993, pp. 165–168.
21. Ochi, K., Matsunaga, I., Shindo, M., and Kaneko, C., *Chem. Pharm. Bull.*, 1978, vol. 26, no. 8, pp. 2386–2390.