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SYNTHESIS OF *D*-PROVITAMINS CONTAINING A SIDE-CHAIN ISOXAZOLINE RING

R. P. Litvinovskaya, N. V. Koval', and V. A. Khripach

This is the first report of the synthesis of 20-isoxazoline steroids containing a 5,7-diene group by 1,3-dipolar cycloaddition of nitrile oxides to Δ^{22}-steroids, leading to 20-isoxazolin-5'-ylsteroids, or of steroidal 22-nitrile oxides to low-molecular-weight dipolarophiles, giving 20-isoxazolin-3'-ylsteroids.

We have already described steroid compounds containing an isoxazoline ring in the side-chain [1-3]. These compounds hold multiple interest. Firstly, we have shown that these compounds are convenient intermediates in the synthesis of brassinosteroids [4], ecdisones [5], and sapogenins of marine organisms [6]. Secondly, these compounds may hold independent interest in pharmacology and agriculture. In particular, several representatives of this steroid series have growth-regulation activity in plants [7].

In developing a new approach to the synthesis of metabolites of group D vitamins and their active analogs, we used intermediates of this type and obtained group D provitamins with a side-chain isoxazole ring [8]. The conditions for the introduction of heterocycle by the nitrile oxide method and its concealed functionalization, which may be realized in various forms, open broad possibilities for modification of both the major carbon skeleton and side-chain.

In the course of this investigation, we obtained examples of the synthesis of D group provitamins with a side-chain isoxazoline ring carried out by two methods. The first method involved use of a steroidal nitrile oxide and small olefins as the dipolarophiles (see Scheme 1). The second method entailed use of a Δ^{22}-steroid as the dipolarophile in the 1,3-dipolar cycloaddition with small nitrile oxides (see Scheme 2).

The reaction of steroidal nitrile oxide (II) generated from oxime (I) [8] with allyl alcohol leads to 20-isoxazolin-3'-ylsteroid (III). The PMR spectrum of III has characteristic signals for the methylene protons at $C_{(4')}$ and methine proton at $C_{(5')}$ as multiplets centered at 2.86 and 4.64 ppm, respectively, and a multiplet for the two hydroxymethylene group protons at 3.60-3.80 ppm. Acetylation of III gives diacetoxy derivative (IV). The PMR spectrum of IV has a second acetyl group signal at 2.10 ppm in comparison with the spectrum of the starting monoacetate. The IR spectrum of IV lacks the hydroxyl group stretching band, and the form of the C=O group bands is complicated.

PMR spectral data and the behavior of isoxazolinylsteroid III and its derivative IV upon thin-layer chromatography on silica gel indicate formation of a single regioisomer (only isoxazolin-3'-ylsteroid) but does not permit a conclusion concerning the epimeric composition at $C_{(5')}$ in III.

The chemical transformations of III indicated that the 1,3-dipolar cycloaddition of the steroidal nitrile oxide and allyl alcohol proceeds with formation of two epimers in approximately equal amounts. Thus, the removal of the protective group accomplished by heating adduct III at reflux with potassium carbonate in DMSO led to 5,7-dienic derivative (V), whose acetylation gave product (VI). The PMR spectrum of VI clearly shows differences of the epimeric compounds, which are especially characteristic for the 21-methyl group protons (doublets at 1.19 and 1.21 ppm, whose total intensity corresponds to three protons) and acetyl group protons (singlets at 2.10 and 2.12 ppm, also corresponding to three protons).

Realization of the above scheme for the preparation of 20-isoxazolin-3'-ylsteroids starting from oxime I using 2-methyl-3-buten-2-ol permits us to obtain isoxazoline (VII). The use of methyl vinyl ketone permits us to obtain isoxazoline (VIII). The ^{13}C NMR spectrum of adduct VII contains a double set of signals for $C_{(16)}$, $C_{(17)}$, $C_{(3')}$, $C_{(4')}$, and $C_{(5')}$, which

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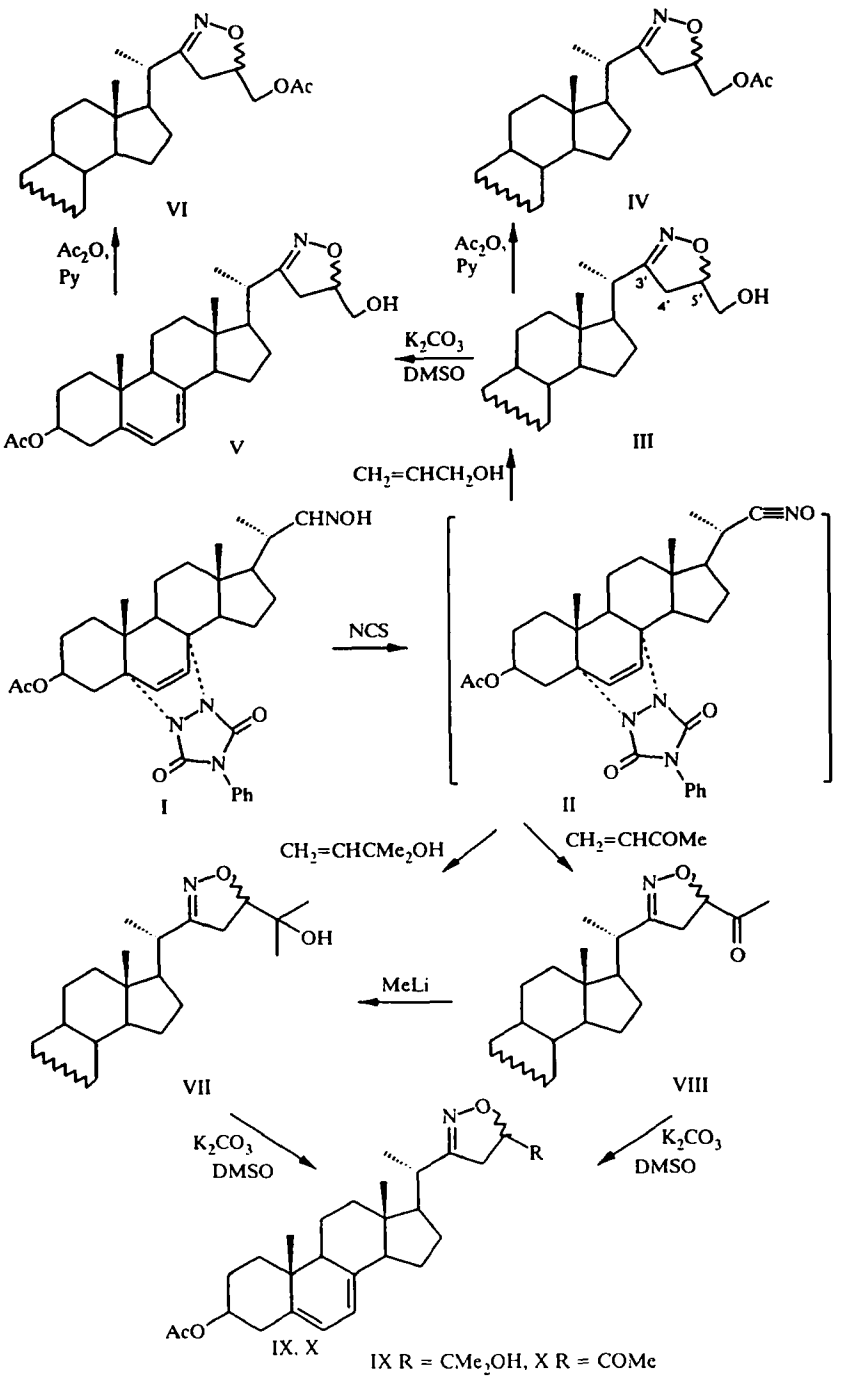
Scheme 1



suggests a mixture of two 3'-epimers. Thus, a method has been developed, which permits us to control the epimeric composition of the mixture. Pure epimers of VII were isolated by careful fractionation on a silica gel column and characterized. We should note that the ^{13}C NMR spectral data for 5,7-diene (IX) obtained after removal of the triazoline protective group in adduct VII, also permitted us to reveal the existence of two epimers: this spectrum has double signals for $C_{(16)}$, $C_{(17)}$, $C_{(4')}$, and $C_{(5')}$.

Special attention should be given to the synthesis of isoxazoline VIII, whose formation is accomplished using methyl vinyl ketone as the dipolarophile. Firstly, this cycloaddition proceeds much more rapidly than usual (the starting steroid is virtually absent after only 40-45 min), leading to a mixture of diastereomers. Secondly, the existence of the reactive 5'-acyl group in this product opens the possibility for the synthesis of many additional derivatives. We demonstrated this possibility

for the case of the addition of methyllithium and formation of alcohol VII, which was also obtained by the direct addition of an olefin to steroidal nitrile oxide II.

The removal of the triazoline protective group in VII and VIII (regeneration of the 5,7-diene group) was carried out as in the case of adduct III and led to a group of D provitamins modified by an isoxazoline ring in the side-chain, namely, IX and X.

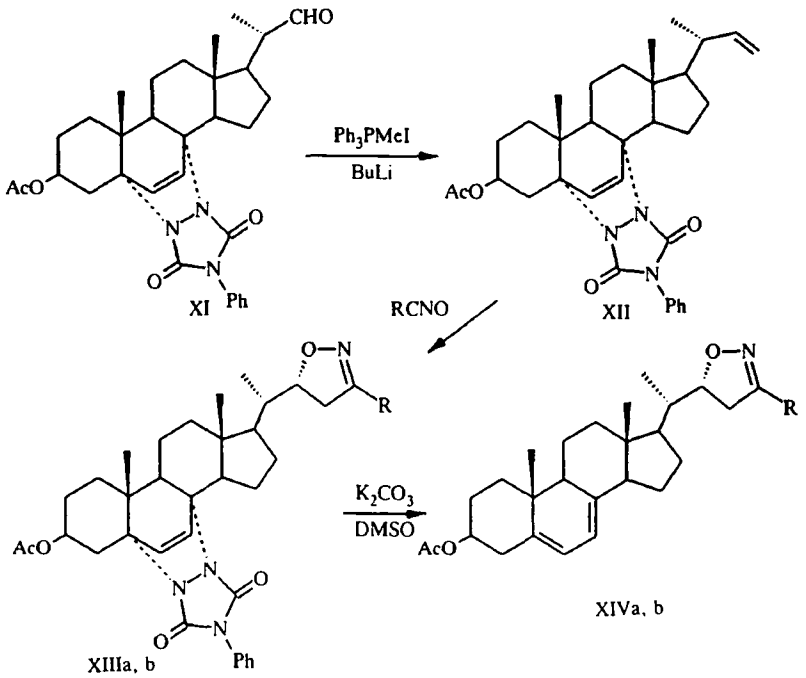
The method of synthesis of 5'-isoxazolinylsteroids [1] based on the addition of small nitrile oxides to steroidal olefins was used to obtain XII from aldehyde XI [9]. The 5,7-diene group in XII was protected by its conversion into a triazoline fragment. The reaction time and epimer composition in the latter case differed from those previously observed. Thus, the addition of acetonitrile oxide does not proceed completely: adduct (XIIIa) is formed in 42% yield, and 26% unreacted olefin remains. When isobutyronitrile oxide was used as the dipole, the addition proceeds slowly and required an additional amount of nitrile oxide. Isoxazolinylsteroid (XIIIb) was formed as a single epimer in 63% yield. This result is quite unexpected from the viewpoint of steric control since formation of two 5'-epimers is observed in the case of Δ^5-steroids unsubstituted in ring B [9].

This is the first report of such a course for the cycloaddition of nitrile oxides to steroidal olefins and may be attributed either to steric hindrance due to the bulky protective group or binding of this group with the nitrile oxide, leading to some decrease in the yield of products. Furthermore, the formation of only the 5'-(R)-epimer was noted in both cases, suggesting an available approach of the nitrile oxide to the steroidal olefin from only one side of the double bond plane.

Regeneration of the 5,7-diene group in the case of steroids XIIIa and XIIIb by heating in tetrahydrofuran at reflux in the presence of lithium aluminum hydride [10] leads to loss of the isoxazoline ring and other side reactions. Good results with yields up to 80% as for the 3'-isoxazolinylsteroids examined above are obtained by treating adducts XIIIa and XIIIb by anhydrous potassium carbonate in dimethylsulfoxide at 120°C, leading to dienes XIVa and XIVb.

Thus, a series of new group D provitamins was obtained. These compounds may prove to be convenient intermediates in the synthesis of reported metabolites and their analogs containing an isoxazoline ring in the side-chain or their transformation products.

Scheme 2



XIII, XIV a R = Me, b R = *i*-Pr

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer. The ^1H and ^{13}C NMR spectra were taken on a Bruker AC-200 spectrometerat 200 MHz for solutions in $CDCl_3$ with TMS as the internal standard. The UV spectra were taken on a Specord

M-400 spectrometer for solutions in methanol. The mass spectra were taken on a Shimadzu mass spectrometer with direct inlet and temperature programming from 30° to 350°C at 20°C/min. The ionizing emission energy was 70 eV. The course of the reactions was followed by thin-layer chromatography on Merck Kieselgel 60 F_{254} plates. Chemapol 40/100μ or Merck Kieselgel 40/60μ silica gel was used for preparative chromatography.

1,3-Dipolar Cycloaddition of Steroidal Nitrile Oxide II and Small Olefins. A solution of 0.178 mmole oxime I in 1 ml chloroform was added to a suspension of 0.536 mmole N-chlorosuccinimide in 1 ml chloroform and stirred for 20 min until a transparent solution formed. Then, 3.676 mmoles olefin was added. A solution of 0.539 mmole triethylamine in 7 ml chloroform was added dropwise. The reaction mixture was maintained for 24 h at room temperature and then washed with water. The organic layer was dried over anhydrous sodium sulfate and filtered. The solvent was evaporated off. The residue was subjected to chromatography on a silica gel column (eluent indicated below).

(5'ξ)-20-(5'-Hydroxymethyl-3'-isoxazolinyl)-3β-acetoxy-5α,8α-(3",5"-dioxo-4"-phenyl-1",2",4"-triazolidine)-pregn-6-ene (III). The procedure described was used for the reaction of 0.1 g oxime I and 0.25 ml allyl alcohol (3:1 toluene–ethyl acetate as the eluent) to give 0.080 g (72.7%) isoxazoline III as an oil. PMR spectrum: 0.89 (3H, s, 18-Me), 1.01 (3H, s, 19-Me), 1.18 (3H, d, J = 7 Hz, 21-Me), 2.04 (3H, s, OAc), 2.86 (2H, m, 4'-H), 3.60 (2H, m, CH_2O), 4.65 (1H, m, 5'-H), 5.46 (1H, m, 3-H), 6.27 and 6.44 (2H, two d, J = 8.5 Hz, 6- and 7-H), 7.42 ppm (5H, m, Ph). IR spectrum (neat): 3420, 1745, 1710, 1250 cm^{-1}. Found: C, 68.70; H, 7.08; N, 9.00%. Calculated for $C_{35}H_{44}N_4O_6$: C, 68.15; H, 7.19; N, 9.08%.

(5'ξ)-3β-Acetoxy-20-(5'-acetyl-3'-isoxazolinyl)-5α,8α-(3",5"-dioxo-4"-phenyl-1",2",4"-triazolidine)pregn-6-ene (VIII). By analogy to the preparation of III, the reaction of 0.1 g oxime and 0.15 ml (1.802 mmole) methyl vinyl ketone using 6:1 toluene–ethyl acetate as eluent gave 0.1 g (89%) isoxazoline VIII as an oil. PMR spectrum: 0.78 (3H, s, 18-Me), 0.92 (3H, s, 19-Me), 1.10 (3H, d, J = 7 Hz, 21-Me), 1.98 (3H, s, 3-OAc), 2.18 and 2.22 (3H, two s, 5'-Ac), 3.06 (2H, m, 4'-H), 4.72 (1H, m, 5'-H), 5.38 (1H, m, 3-H), 6.17 and 6.33 (2H, two d, J = 8.5 Hz, 6- and 7-H), 7.42 ppm (5H, m, Ph). IR spectrum (neat): 1750, 1710, 1250 cm^{-1}. Found: C, 68.69; H, 7.09; N, 8.76%. Calculated for $C_{36}H_{44}N_4O_6$: C, 68.77; H, 7.05; N, 8.91%.

(5'ξ)-3β-Acetoxy-20-(5'-hydroxyisopropargyl-3'-isoxazolinyl)-5α,8α-(3",5"-dioxo-4"-phenyl-1",2",4"-triazolidine)pregn-6-ene (VII). A. Using the procedure for the preparation of III, the reaction of 0.5 g (0.892 mmole) oxime I and 1.87 ml (17.89 mmoles) 2-methyl-3-buten-2-ol gave 0.51 g (88.7%) isoxazoline VII as oily crystals.

B. A solution of 0.05 g (0.0795 mmole) ketone VIII in 15 ml THF was cooled in a nitrogen stream to −60°C and 0.2 ml (0.28 mmole) 1.4 M methyllithium in ether was added. The reaction mixture was stirred for 10 min. Saturated aqueous ammonium chloride was added and the mixture was extracted with ethyl acetate. The extract was dried over sodium sulfate and filtered. The solvent was evaporated and the residue was acetylated. Chromatography of the oily product on a silica gel column using 5:1 toluene–ethyl acetate as the eluent gave 0.02 g (39%) starting ketone VIII and 0.018 g (36%) isoxazoline VII as oily crystals. PMR spectrum of VII: 0.89 (3H, s, 18-Me), 1.02 (3H, s, 19-Me), 1.16-1.30 (9H, m, 21-Me and $C\underline{Me}_2OH$), 2.03 (3H, s, OAc), 2.84 (2H, m, 4'H), 4.36 (2H, m, 5'-H), 5.47 (1H, m, 3-H), 6.27 and 6.43 (2H, two d, J = 8.5 Hz, 6- and 7-H), 7.42 ppm (5H, m, Ph). IR spectrum (neat): 3430, 1755, 1745, 1705, 1250 cm^{-1}. UV spectrum, $\lambda_{max}(\varepsilon)$: 256 (3689). Found: C, 68.87; H, 7.54; N, 8.56%. Calculated for $C_{37}H_{48}N_4O_6$: C, 68.92; H, 7.50; N, 8.69%.

The mixture of isomers of isoxazoline VII was separated on a silica gel column using 3:1 toluene–ethyl acetate as the eluent and small amounts of the two pure epimers were isolated as oily crystals.

^{13}C NMR spectrum for the less polar epimer of VII: 13.1 ($C_{(18)}$), 17.5 ($C_{(19)}$), 18.3 and 18.5 ($C\underline{Me}_2OH$), 21.3 ($C_{(21)}$), 22.3 ($C_{(11)}$), 23.4 ($C_{(2)}$), 24.6 ($CO\underline{C}H_3$), 25.9 ($C_{(15)}$), 26.7 ($C_{(20)}$), 27.0 ($C_{(16)}$), 30.9 ($C_{(1)}$), 33.7 ($C_{(12)}$), 34.1 ($C_{(4')}$), 38.2 ($C_{(4)}$), 41.1 ($C_{(10)}$), 44.0 ($C_{(13)}$), 49.4 ($C_{(9)}$), 52.4 ($C_{(17)}$), 52.8 ($C_{(14)}$), 64.7 ($C_{(5)}$), 65.3 ($C_{(8)}$), 70.4 ($C_{(3)}$), 71.0 ($\underline{C}Me_2OH$), 86.1 ($C_{(5')}$), 126.2, 127.8, 128.8, 131.6 (Ph, $C_{(7)}$), 135.5 ($C_{(6)}$), 146.6 (NC=O), 149.0 (NC=O), 163.4 (C=N), 170.0 ppm ($\underline{C}OCH_3$).

^{13}C NMR spectrum for the more polar epimer of VII: 13.1 ($C_{(18)}$), 17.5 ($C_{(19)}$), 18.3 and 18.5 ($C\underline{Me}_2OH$), 21.3 ($C_{(21)}$), 22.3 ($C_{(11)}$), 23.4 ($C_{(2)}$), 24.6 ($CO\underline{C}H_3$), 25.9 ($C_{(15)}$), 26.4 ($C_{(20)}$), 26.9 ($C_{(16)}$), 30.9 ($C_{(1)}$), 33.7 ($C_{(12)}$), 34.3 ($C_{(4')}$),38.2 ($C_{(4)}$), 41.1 ($C_{(10)}$), 44.1 ($C_{(13)}$), 49.4 ($C_{(9)}$), 52.2 ($C_{(17)}$), 52.8 ($C_{(14)}$), 64.7 ($C_{(5)}$), 65.3 ($C_{(8)}$),70.4 ($C_{(3)}$), 71.0 ($\underline{C}Me_2OH$), 86.2 ($C_{(5')}$), 126.1, 127.8, 128.2, 128.8, 131.6 (Ph, $C_{(7)}$), 135.4 ($C_{(6)}$), 146.6 (NC=O), 149.0 (NC=O), 163.3 (C=N), 170.0 ppm ($\underline{C}OCH_3$).

1,3-Dipolar Cycloaddition of 22-Ene Steroid XII with Small Nitrile Oxides. (5'R)-3β-Acetoxy-20-(3'-methyl-5'-isoxazolinyl)-5α,8α-(3",5"-dioxo-4"-phenyl-1",2",4"-triazolidine)pregn-6-ene (XIIIa). A sample of 0.04 ml (0.657 mmole) acetaldoxime was added to a suspension of 0.084 g (0.644 mmole) N-chlorosuccinimide in 1 ml chloroform and 0.002 ml py-

ridine and stirred for 20 min until formation of a transparent solution. A solution of 0.07 g (0.129 mmole) olefin XII in 1 ml chloroform was then added and, after brief stirring, 0.09 ml (0.647 mmole) triethylamine in 6 ml chloroform was added dropwise with stirring. The reaction mixture was stirred for 2 h. Then, 0.026 g (0.195 mmole) N-chlorosuccinimide in 0.5 ml chloroform containing a drop of pyridine was added, followed by 0.012 ml (0.197 mmole) acetaldoxime, and finally, 0.03 ml (0.194 mmole) triethylamine in 3 ml chloroform was added dropwise over 3 h. The reaction mixture was maintained for 24 h at room temperature and then washed with water. The organic layer was dried over sodium sulfate and evaporated. Chromatography of the residue on a silica gel column using 5:1 toluene–ethyl acetate as the eluent gave 0.018 g (25.7%) starting olefin XII and 0.032 g (41.4%) adduct XIIIa. PMR spectrum of XIIIa: 0.84 (3H, s, 18-Me), 0.90 (3H, d, J = 7 Hz, 21-Me), 1.00 (3H, s, 19-Me), 1.97 (3H, s, 3'-Me), 2.02 (3H, s, Ac), 2.68 (2H, d, J = 10 Hz, 4'-H), 3.22 (1H, d.d, 9-H), 4.68 (1H, m, 3-H), 5.46 (1H, m, 5'-H), 6.27 and 6.42 (2H, two d, J = 8.5 Hz, 6- and 7-H), 7.44 ppm (5H, m, Ph). IR spectrum (neat): 1755, 1740, 1705, 1250 cm^{-1}. Found: C, 69.74; H, 7.60; N, 9.23%. Calculated for $C_{35}H_{44}N_4O_5$: C, 69.98; H, 7.38; N, 9.33%.

(5'R)-3β-Acetoxy-20-(3'-isopropyl-5'-isoxazolinyl)-5α,8α-(3",5"-dioxo-4"-phenyl-1",2",4"-triazolidine)-pregn-6-ene (XIIIb). The reaction of 0.135 g (1.011 mmole) olefin XII and 0.88 g (1.011 mmole) isobutyronitrile oxide was carried out according to the procedure for XIIIa to give 0.08 g (63%) isoxazoline XIIIb as an oil and 0.01 g (9%) starting olefin. PMR spectrum of XIIIb: 0.84 (3H, s, 18-Me), 0.88 (3H, d, J = 7 Hz, 21-Me), 1.01 (3H, s, 19-Me), 1.15 and 1.17 (6H, two d, CH<u>Me</u>$_2$), 2.02 (3H, s, Ac), 2.69 (2H, d.d, ^1J = 3, ^2J = 10 Hz, 4'-H), 3.22 (1H, d.d, 9-H), 4.65 (1H, m, 3-H), 5.46 (1H, m, 5'-H), 6.27 and 6.42 (2H, two d, J = 8.5 Hz, 6- and 7-H), 7.42 ppm (5H, m, Ph). IR spectrum (neat): 1755, 1740, 1710, 1250 cm^{-1}. Found: C, 70.45; H, 7.70, N, 8.80%. Calculated for $C_{37}H_{48}N_4O_5$: C, 70.67; H, 7.69; N, 8.91%.

Regeneration of 5,7-Diene Group. A sample of 0.072 mmole anhydrous potassium carbonate was added to a solution of 0.057 mmole triazoline derivative in 3.5 ml dimethylsulfoxide. The reaction mixture was maintained in a nitrogen stream at 120°C for 7 h, then cooled to room temperature, neutralized by adding 0.5% hydrochloric acid, and extracted with ethyl acetate. The extract was washed with water and dried over anhydrous sodium sulfate. The solvent was evaporated. Chromatography of the residue on a silica gel column (eluents given below) gave the corresponding 5,7-diene.

(5'ξ)-3β-Acetoxy-20-(5'-hydroxymethyl-3'-isoxazolinyl)pregna-5,7-diene (V). The above procedure was used to convert 0.035 g (0.057 mmole) III using 0.01 g potassium carbonate and 4:1 toluene–ethyl acetate as the eluent into 0.017 g (67.8%) 5,7-diene V as an oil. PMR spectrum: 0.69 (3H, s, 18-Me), 0.96 (3H, s, 19-Me), 1.19 (3H, d, J = 7 Hz, 21-Me), 2.04 (3H, s, Ac), 2.90 (2H, m, 4'-H), 3.55 and 3.78 (2H, two m, CH_2O), 4.67 (2H, m, 5'- and 3-H), 5.41 and 5.59 (2H, two d, J = 8.5 Hz, 6- and 7-H). IR spectrum (neat): 3400, 1740, 1665, 1255 cm^{-1}. Found: C, 67.10; H, 8.05; N, 11.46%. Calculated for $C_{27}H_{39}NO_4$: C, 67.05; H, 8.13; N, 11.58%.*

(5'ξ)-3β-Acetoxy-20-(5'-hydroxyisopropyl-3'-isoxazolinyl)pregna-5,7-diene (IX). The above procedure was used to convert 0.11 g (0.171 mmole) VII using 7:1 toluene–ethyl acetate as the eluent into 0.067 g (8.36%) IX as a mixture of two epimers. PMR spectrum: 0.68 (3H, s, 18-Me), 0.98 (3H, s, 19-Me), 1.16-1.36 (9H, m, 21-Me and C<u>Me</u>$_2$OH), 2.00 (3H, s, Ac), 2.90 (2H, m, 4'-H), 4.34 (2H, m, 5'-H), 4.70 (1H, m, 3-H), 5.40 and 5.57 ppm (2H, two d, J = 8.5 Hz, 6- and 7-H). ^{13}C NMR spectrum: 11.7 ($C_{(18)}$), 16.2 ($C_{(19)}$), 18.3 and 18.4 (C<u>Me</u>$_2$OH), 21.0 ($C_{(11)}$), 21.4 ($C_{(21)}$), 23.0 ($C_{(15)}$), 24.6 (CO<u>C</u>H$_3$), 27.6 and 27.7 ($C_{(16)}$), 28.0 ($C_{(2)}$), 34.4 and 34.6 ($C_{(4')}$), 35.8 ($C_{(20)}$), 36.6 ($C_{(4)}$), 37.1 ($C_{(10)}$), 37.9 ($C_{(1)}$), 39.1 ($C_{(12)}$), 43.1 ($C_{(13)}$), 45.9 ($C_{(9)}$), 52.8 and 52.9 ($C_{(17)}$), 54.4 ($C_{(14)}$), 71.0 and 71.1 (<u>C</u>Me$_2$OH), 72.7 ($C_{(3)}$), 85.97 and 86.02 ($C_{(5')}$), 116.8 ($C_{(7)}$), 120.1 ($C_{(6)}$), 138.8 and 138.9 ($C_{(5)}$), 140.5 ($C_{(8)}$), 163.7 (C=N), 170.5 ppm (<u>C</u>OCH$_3$). IR spectrum (KBr): 3485, 1730, 1710, 1640, 1255 cm^{-1}. UV spectrum, λ_{max} (ε): 270 (9317), 280 (9528), 292 (5296). Found: C, 74.10; H, 9.16; N, 2.87%. Calculated for $C_{29}H_{32}NO_4$: C, 74.16; H, 9.23; N, 2.98%.

(5'ξ)-3β-Acetoxy-20-(5'-acetyl-3'-isoxazolinyl)pregna-5,7-diene (X). The above procedure to convert 0.05 g (0.080 mmole)VIII using 24:1 toluene–ethyl acetate as the eluent into 0.01 g (27.7%) 5,7-diene X as an oil. PMR spectrum: 0.68 (3H, s, 18-Me), 0.91 (3H, m, 19-Me), 1.18 (3H, d, J = 7 Hz, 21-Me), 2.05 (3H, s, OAc), 2.32 (3H, d, Ac), 3.13 (2H, m, 4'-H), 4.78 (2H, m, 5'- and 3-H), 5.40 and 5.58 ppm (2H, two d, J = 8.5 Hz, 6- and 7-H). IR spectrum (neat): 1740, 1670, 1255 cm^{-1}. Found: C, 74.20; H, 8.59; N, 3.00%. Calculated for $C_{28}H_{39}NO_4$: C, 74.14; H, 8.67; N, 3.09%.

(5'R)-3β-Acetoxy-20-(3'-methyl-5'-isoxazolinyl)pregna-5,7-diene (XIVa). The above procedure was used to convert 0.04 g (0.067 mmole) triazolidine adduct XIIIa using 7:1 toluene–ethyl acetate as the eluent into 0.02 g (71%)

*As in Russian original — Translator.

5,7-diene XIVa. PMR spectrum: 0.66 (3H, s, 18-Me), 0.90 (3H, d, J = 7 Hz, 21-Me), 0.96 (3H, s, 19-Me), 1.97 (3H, s, 3'-Me), 2.04 (3H, s, Ac), 2.72 (2H, d, J = 10 Hz, 4'-H), 4.70 (2H, m, 5'- and 3-H), 5.41 and 5.59 (2H, two d, J = 8.5 Hz, 6- and 7-H). IR spectrum (neat): 1740, 1255 cm^{-1}. Found: C, 76.12; H, 9.70; N, 3.14%. Calculated for $C_{27}H_{39}NO_3$: C, 76.20; H, 9.24; N, 3.29%.

(5'R)-3β-Acetoxy-20-(3'-isopropylyl-5'-isoxazolinyl)pregna-5,7-diene (XIVb). The above procedure was used to convert 0.04 g (0.064 mmole) triazolidine adduct XIIIb using 7:1 toluene–ethyl acetate as the eluent into 0.023 g (80%) 5,7-diene XIVb. PMR spectrum: 0.65 (3H, s, 18-Me), 0.89 (3H, d, J = 7 Hz, 21-Me), 0.96 (3H, s, 19-Me), 1.18 (6H, d, J = 7 Hz, $CHMe_2$), 2.04 (3H, s, Ac), 2.72 (2H, d, J = 10 Hz, 4'-H), 4.70 (2H, m, 3'- and 3-H), 5.40 and 5.58 (2H, two d, J = 8.5 Hz, 6- and 7-H). IR spectrum (neat): 1740, 1255 cm^{-1}. Found: C, 76.49; H, 9.51; N, 3.13%. Calculated for $C_{29}H_{43}NO_3$: C, 76.78; H, 9.55; N, 3.09%.

Acetylation of Steroidal Alcohols. A sample of 0.5 ml acetic anhydride was added dropwise to a solution of 0.2 mmole steroidal alcohol in 1 ml pyridine. The reaction mixture was maintained at room temperature for 18-20 h, then treated with 10 ml water, and extracted with ether. The extract was washed with 5% hydrochloric acid until neutral and dried over anhydrous sodium sulfate. The solvent was evaporated. The residue was dissolved in a small amount of chloroform, purified by passing through a layer of silica gel, and subjected to chromatography (eluents given below) to give the acetoxy derivative.

(5'ξ)-3β-Acetoxy-5α,8α-(3",5"-dioxo-4"-phenyl-1",2",4"-triazolidin)-20-(5'-acetoxymethyl-3'-isoxazolinyl)pregn-6-ene (IV). The above acetylation procedure was used to convert 0.02 g (0.032 mmole) III with 1:1 hexane–ethyl acetate as the eluent into 0.015 g (70%) diacetate IV as an oil. PMR spectrum: 0.88 (3H, s, 18-Me), 1.01 (3H, s, 19-Me), 1.18 (3H, d, J = 7 Hz, 21-Me), 2.04 (3H, s, Ac), 2.10 (3H, s, Ac), 2.86 (2H, m, 4'-H), 4.09 (2H, m, CH_2O), 4.77 (1H, m, 5'-H), 5.46 (1H, m, 3-H), 6.26 and 6.42 (2H, two d, J = 8.5 Hz, 6- and 7-H), 7.42 ppm (5H, m, Ph). IR spectrum (neat): 1745, 1705, 1700, 1250 cm^{-1}. Found: C, 67.50; H, 7.10; N, 8.35%. Calculated for $C_{37}H_{46}N_4O_7$: C, 67.46; H, 7.04; N, 8.50%.

(5'ξ)-3β-Acetoxy-20-(5'-acetoxymethyl-3'-isoxazolinyl)pregna-5,7-diene (VI). Acetylation of 0.017 g V using the above procedure and 9:1 toluene–ethyl acetate as the eluent gave 0.012 g (64.5%) diacetate VI as an oil. PMR spectrum: 0.70 (3H, s, 18-Me), 0.97 (3H, s, 19-Me), 1.19 (1.5H, d, J = 7 Hz, 21-Me), 1.21 (1.5H, d, J = 7 Hz, 21-Me), 2.06 (3H, s, Ac), 2.10 and 2.12 (3H, two s, $CH_2O\underline{Ac}$), 2.78 (1H, m, 4'-H), 3.02 (1H, m, 4'-H), 4.10 (2H, m, CH_2O), 4.74 (2H, m, 5'- and 3-H), 5.42 and 5.60 ppm (2H, two d, J = 8.5 Hz, 6- and 7-H). IR spectrum (neat): 1745, 1740, 1255, 1250 cm^{-1}. Found: C, 72.20; H, 8.50; N, 2.86%. Calculated for $C_{29}H_{41}NO_4$: C, 72.02; H, 8.54; N, 2.90%.

3β-Acetoxy-5α,8α-(3',5'-dioxo-4'-phenyl-1',2',4'-triazolidine)-24-norcholane-6,23-diene (XII). A sample of 0.43 ml (1.29 mmole) 3 M butyllithium in hexane was added dropwise to a suspension of 0.593 g (1.467 mmole) methyltriphenylphosphonium iodide in 5 ml tetrahydrofuran cooled to 0°C and stirred for 30 min in an argon stream. The mixture turned lemon yellow. A solution of 0.2 g (0.366 mmole) aldehyde XI [8] in 2 ml tetrahydrofuran was added and stirred at room temperature for 30 min. Saturated aqueous ammonium chloride was added and the mixture was extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was acetylated as described above. The crude product was subjected to chromatography on a silica gel column using 12:1 toluene–ethyl acetate as the eluent to give 0.12 g (60%) enesteroid XII as an oil. PMR spectrum: 0.81 (3H, s, 18-Me), 0.98 (3H, s, 19-Me), 1.05 (3H, d, J = 7 Hz, 21-Me), 2.02 (3H, s, Ac); 3.22 (1H, d.d, 9-H), 4.90 (2H, m, 23-H), 5.46 (1H, m, 3-H), 5.64 (1H, m, 22-H), 6.24 and 6.42 (2H, two d, J = 8.5 Hz, 6- and 7-H), 7.44 ppm (5H, m, Ph). IR spectrum (neat): 1745, 1739, 1250 cm^{-1}. Found: C, 72.80; H, 7.68; N, 7.59%. Calculated for $C_{33}H_{41}N_3O_4$: C, 72.89; H, 7.61; N, 7.73%.

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