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Nitrile Oxide Approach to the Synthesis of Δ^{23}-22-Oxo Steroids

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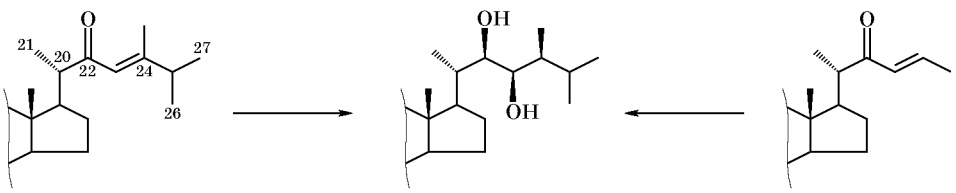
Abstract—Δ^{23}-22-Oxo steroids were synthesized via 1,3-dipolar cycloaddition of steroidal nitrile oxides to low-molecular dipolarophiles. Cycloaddition of 2-propynyl bromide to 20-carbonitrile oxide, followed by hydrogenation of the isoxazole derivative thus formed gave 22-enamino-24-keto steroid. The latter was then converted into the target enones via several pathways. Compounds with unnatural configuration of the C^{20} atom can also be obtained. Δ^{23}-22-Oxo steroids were also synthesized through isoxazole derivatives.

The isoxazole approach occupies an important place among modern methods for synthesizing complex natural molecules [1–4]. It involves 1,3-dipolar cycloaddition of nitrile oxides with formation of isoxazole or dihydroisoxazole derivatives which are then subjected to reductive cleavage of the heteroring. An advantage of this procedure is that it ensures simultaneous formation of a C–C bond and introduction of a number of functional groups under mild conditions, which is especially important for the synthesis of many natural steroids possessing polyfunctionalized side chains [5]. As a rule, cycloadditions of lower nitrile oxides to steroidal olefins were used [6–14], although in the recent years attempts were made to effect the reactions with steroidal nitrile oxides [15–17].

The goal of the present work was to study the potential of cycloaddition of steroidal 20-carbonitrile oxides to various dipolarophiles and further transformation of the adducts for preparation of Δ^{23}-22-keto steroids [18–21]. Such compounds, as well as Δ^{23}-22-hydroxy derivatives available via hydride reduction of 22-oxo steroids [22–24], are key intermediates in the synthesis of brassinolide (**II**). The brassinolide side chain can be built up both from enones **I** already containing a necessary side chain carbon skeleton and from enones **III** via introduction of the C^{25}–C^{27} isopropyl fragment (Scheme 1).

According to the first pathway, 20-carbonitrile oxide **IV** was brought into reaction with 2-propynyl bromide [15]. Reductive cleavage of the isoxazole ring in the adduct gave enaminoketone **V** which was converted into benzamide **VI** (Scheme 2). It should be noted that protection of the amino group in **V** through acetylation is ineffective. In this case the subsequent reaction with isopropylmagnesium chloride resulted in removal of the acetyl protection and regeneration of the initial enaminoketone instead of the addition at the ketone carbonyl. The necessity of synthesizing compound **VI** is explained as follows. First, organometallic reagent cannot add directly to enaminoketone **V** and, second, we intended to study in detail the stereochemistry of the C^{20} chiral center. Our further experiments showed the possibility for epimerization at that center. According to the X-ray diffraction data, the configuration of C^{20} does not change during the transformation of nitrile oxide **IV** into **VI** [14]. Dehydration of alcohol **VII** in aqueous dioxane by the

Scheme 1.



I **II** **III**

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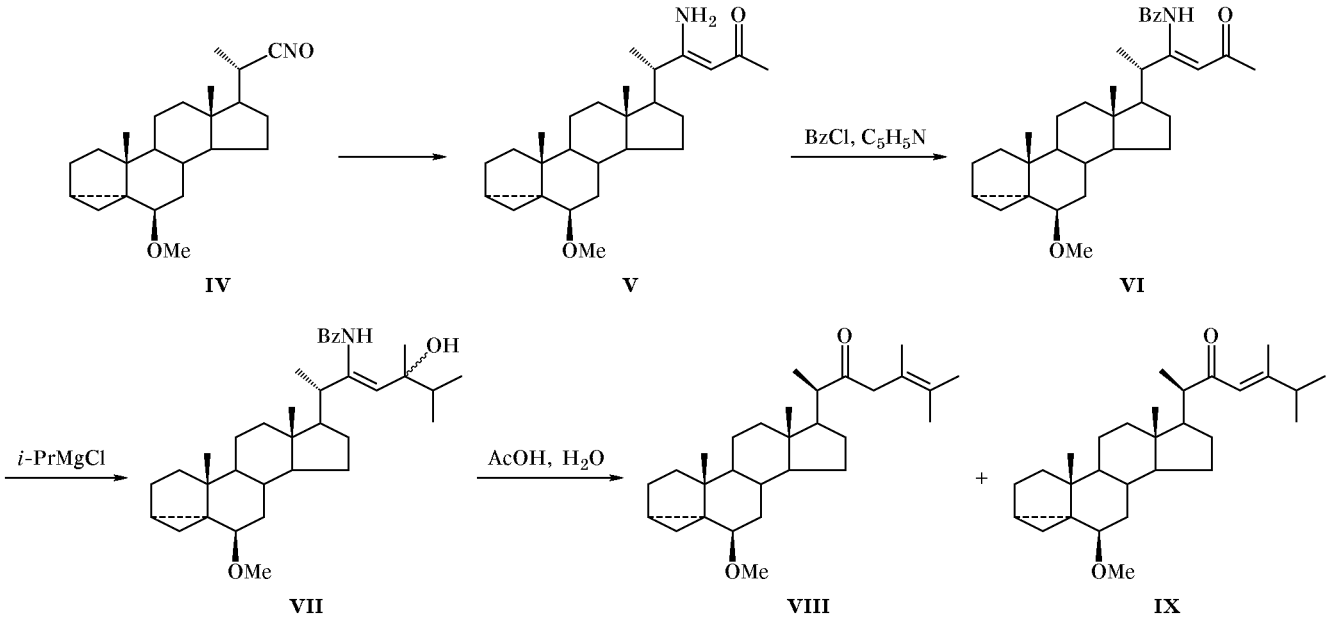
Scheme 2.

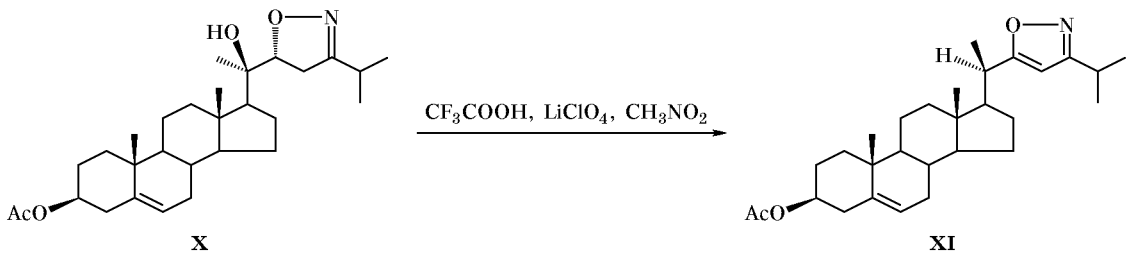


action of acetic acid was accompanied by hydrolysis of the amide group with formation of isomeric enones **VIII** and **IX** at a ratio of 1:2; their fractions were estimated on the basis of the $C^{28}H_3$ signal intensities in the ^1H NMR spectrum (δ 2.08 and 1.71 ppm). Pure compounds **VIII** and **IX** were isolated by column chromatography. Enone **IX** characteristically showed in the ^1H NMR spectrum a one-proton singlet from 23-H (δ 6.13 ppm) and a three-proton singlet from $C^{28}H_3$ (δ 2.08 ppm). The spectrum of enone **VIII** in which the carbonyl group and double bond are separated by the $C^{23}H_2$ methylene group contained a doublet from 23-H (δ 3.25 ppm) and a three-proton singlet from 28-H (δ 1.71 ppm). Moreover, the signals from 26-H and 27-H in the spectrum of enone **VIII** are displaced downfield (δ 1.66 ppm) relative to those of conjugated enone **IX** (δ 1.07 ppm).

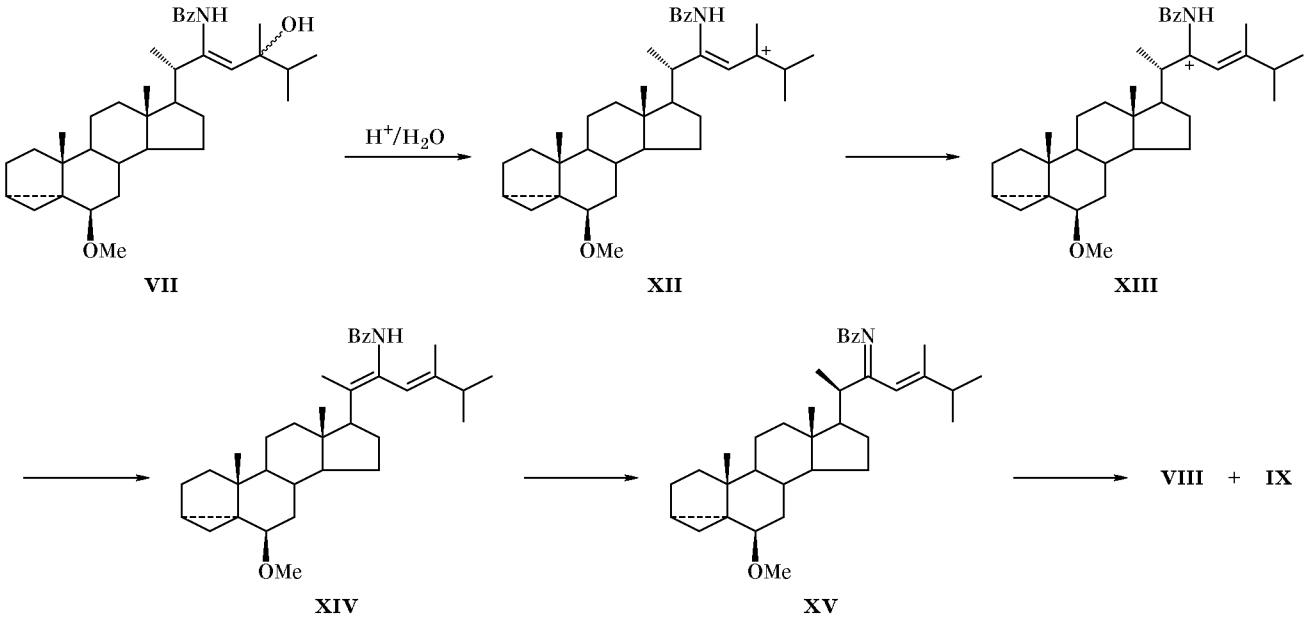
The chemical shifts of some protons in the ^1H NMR spectrum of (20*R*)-enone **IX** differ from those reported for its (20*S*)-isomer [7]. The vinyl proton signal of **IX** appears at δ 6.13 ppm, i.e., in a weaker field, as compared to the corresponding signal of the (20*S*)-isomer (δ 6.05 ppm); by contrast, the 18-H signal of **IX** is displaced upfield (δ 0.71 ppm) relative to the 18-H signal of the (20*S*)-isomer (δ 0.74 ppm). These findings indicate that the dehydration and hydrolysis of the amide group are accompanied by epimerization at C^{20}. A few examples of complete inversion of the C^{20} chiral center have been reported [25]. For example, treatment of 20-hydroxy isoxazolyl steroid **X** with trifluoroacetic acid and lithium perchlorate resulted in formation of the dehydration product, (20*R*)-isoxazole derivative **XI** (Scheme 3). No epimeric (20*S*)-isoxazole was formed; this means that the process is stereoselective.

The exclusive formation of (20*R*)-ketones **VIII** and **IX** may be rationalized as follows. Protonation of alcohol **VII** and subsequent elimination of water molecule yields carbocation **XII** which is converted into cation **XIII** via migration of the double bond. Cation **XIII** loses a proton to give diene **XIV** which undergoes isomerization with inversion of the C^{20}

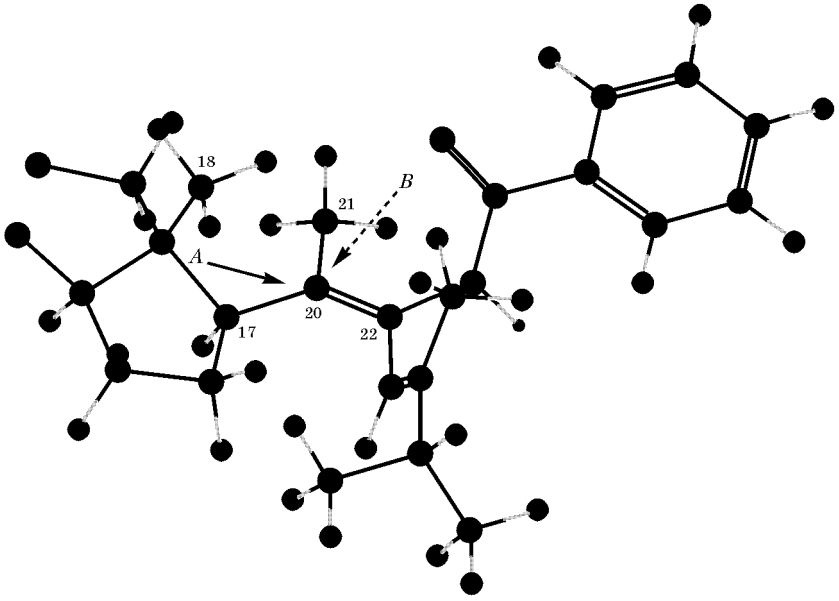
Scheme 3.



Scheme 4.



Scheme 5.

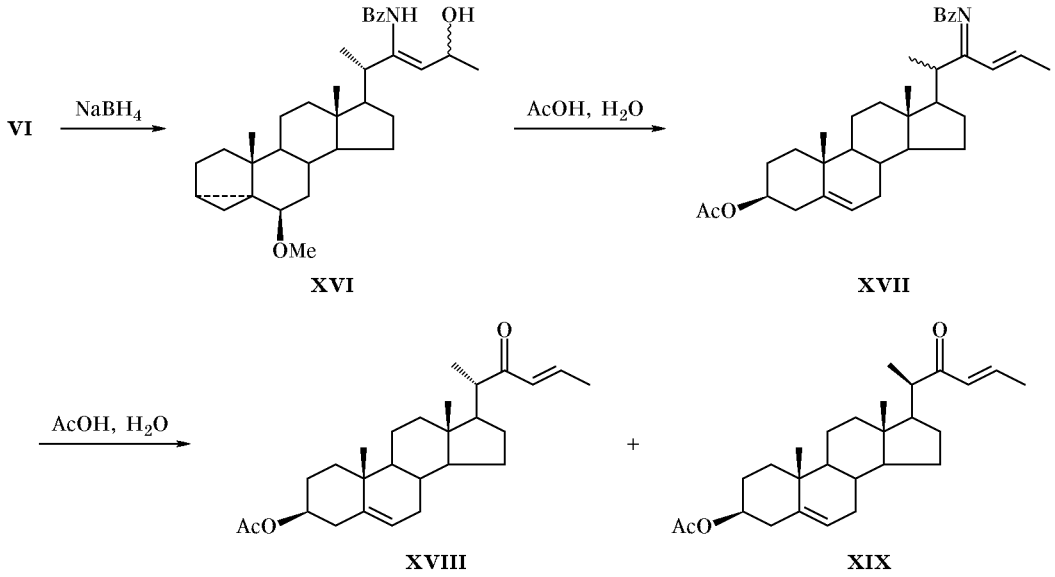


atom. Hydrolysis of benzoylimino derivative **XV** leads to the final products, enones **VIII** and **IX** (Scheme 4). Presumably, in the isomerization of **XIV** to **XV** the configuration of C^{20} is inversed due to preferential proton addition from the *B* side, as shown in Scheme 5 using Dreiding's model.

All our attempts to obtain from alcohol **VII** conjugated enone with *S* configuration of the C^{20} chiral center were unsuccessful. Therefore, we examined possible ways of synthesizing Δ^{23}-22-ketones from enaminoketone **V**. The ketone carbonyl group in *N*-benzoyl derivative **VI** was reduced with sodium tetrahydridoborate, and the resulting alcohol **XVI** was subjected to dehydration and acid hydrolysis in acetic acid without isolation from the reaction mixture. Simultaneously, the 6β-methoxy-3α,5-cyclo fragment was converted into 3β-acetoxy-Δ^5 moiety to afford C^{20}-epimeric enones **XVIII** and **XIX** (Scheme 6).

We succeeded in minimizing cleavage of the cyclopropane ring in the hydrolysis of compounds **VII** and

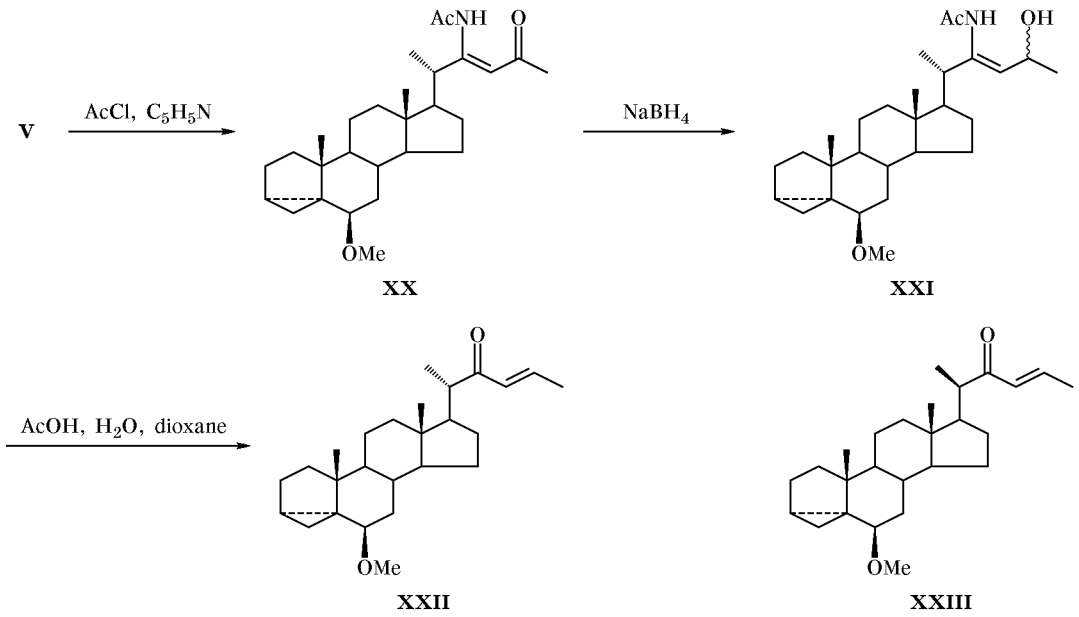
Scheme 6.



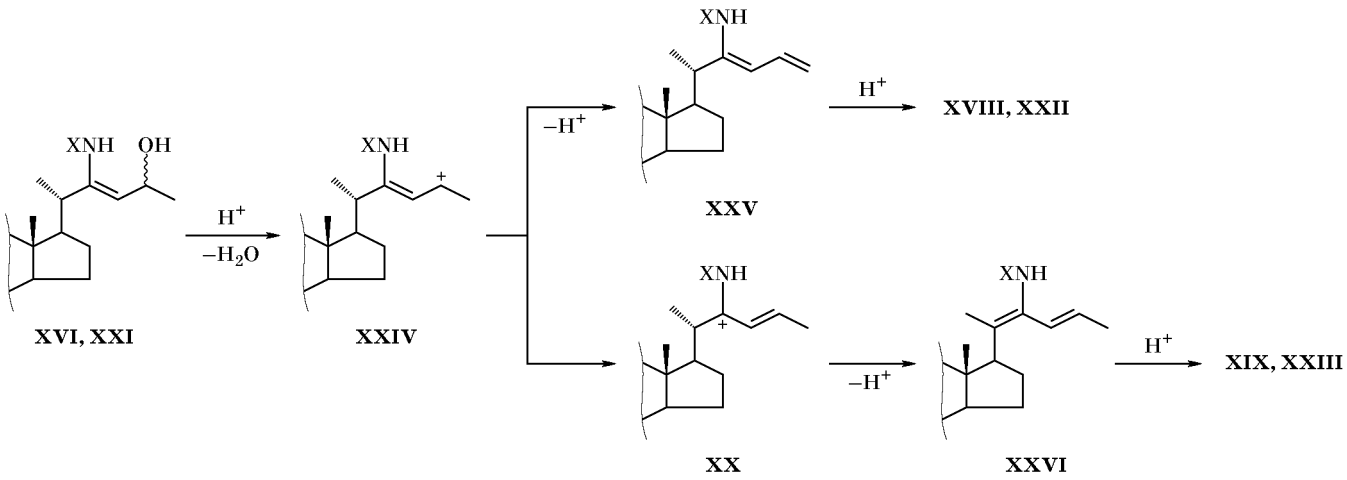
XXI by addition of dioxane. It should be emphasized that epimerization occurs at the stage of dehydration of alcohol **XVI** rather than of hydrolysis of amide **XVII**; the latter was isolated as a mixture of epimers at C^{20} at a ratio of 2:1 (the ratio was determined from the intensities of the $C^{18}H_3$ signals at δ 0.73 and 0.66 ppm). Similar results were obtained in the transformation of enone **V** into Δ^{23}-22-ketones **XXII** and **XXIII** through acetamide **XX** and alcohol **XXI** (Scheme 7). In this case it was interesting to compare the ^{1}H NMR spectra of compounds **XXII** and **XXIII**, specifically the positions of signals of the $C^{21}H_3$ group. It is known [26] that the $C^{21}H_3$ signal of compounds with the natural configuration of C^{20} always appears in a weaker field as compared to the corresponding unnatural isomer. An analogous pattern was observed in the spectra of enones **XXII** and **XXIII**, which contain doublets with J = 7 Hz at δ 1.11 ppm for ketone **XXII** (natural isomer) and δ 1.04 ppm for ketone **XXIII** (unnatural isomer).

The formation of two epimers from *N*-benzoyl and *N*-acetyl derivatives **VI** and **XX** may be explained

Scheme 7.



Scheme 8.



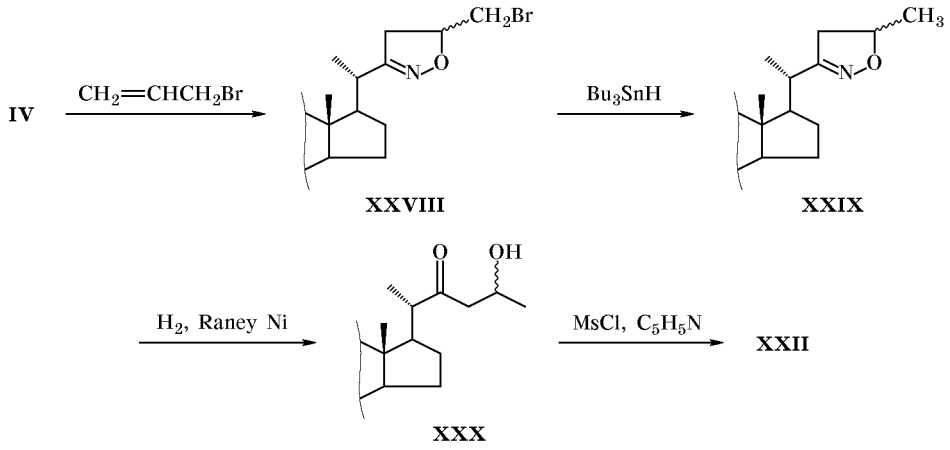
on the assumption that intermediate cation **XXIV** is less stable than its analog **XII** with a branched substituent at the double bond. Cation **XXIV** can be stabilized via elimination of proton from C^{25} to give diene **XXV**. Hydrolysis of the latter does not involve the C^{20} chiral center. Obviously, the transformation of **XXIV** through diene **XXVI** also occurs (Scheme 8).

The ^{1}H NMR spectra of **XXII** and **XXIII** contain a signal from the 23-H proton as a doublet of doublets at δ 6.17 and 6.20 ppm, respectively, and a multiplet signal from 24-H at δ 6.82–6.98 ppm. Signals from the other molecular fragments are also present. The $C^{18}H_3$ signal of enone **XXII** is observed in a weaker field (δ 0.76 ppm) than the corresponding signal of **XXIII** (δ 0.71 ppm). The coupling constant for 23-H and 24-H is equal to 16 Hz, indicating that the double bond in both isomers has *trans*-configuration.

An alternative approach to Δ^{23}-22-keto steroid **XXII** is based on cycloaddition of nitrile oxide **IV** to allyl bromide. The adduct, bromomethylisoxazolyl derivative **XXVIII** was obtained as a mixture of epimers at the C^{24} atom. According to the ^{1}H NMR data (intensities of the $C^{21}H_3$ signals, δ 1.15 and 1.17 ppm), the epimer ratio was 1:1. Hydrogenation of **XXVIII** over Raney nickel led to formation of pyrrolyl-substituted steroid [27]. In order to prevent participation of the neighboring group in the reductive cleavage of the dihydroisoxazole ring, compound **XXVIII** was subjected first to hydrodebromination by the action of tributylstannane. Subsequent hydrogenation of **XXIX** over Raney nickel gave β-hydroxy ketone **XXX** which was dehydrated by treatment with methanesulfonyl chloride in pyridine at room temperature (Scheme 9).

Thus, we have developed various versions of synthesis of Δ^{23}-22-keto steroids on the basis of 1,3-dipolar cycloaddition reactions of steroidal 20-carbonitrile oxides with low-molecular dipolarophiles.

Scheme 9.



EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200 spectrometer at 200 MHz for ^1H and 50 MHz for ^{13}C; chloroform-*d* was used as solvent, and tetramethylsilane, as internal reference. The IR spectra (700–3600 cm^{-1}) were measured on a UR-20 instrument from samples prepared as thin films or KBr pellets. The progress of reactions was monitored by TLC on Kieselgel 60 F_{254} plates (Merck).

(20*S*)-22-Benzoylamino-24-hydroxy-6β-methoxy-24-methyl-3α,5-cyclo-5α-cholest-22-ene (VII). To a solution of 1.26 g of *N*-benzoyl derivative **VI** in 50 ml of tetrahydrofuran we added at 0°C 6.25 ml of a 2.25 M solution of isopropylmagnesium chloride. When the reaction was complete, 1 g of ammonium chloride was added, and the mixture was diluted with water and extracted with ether. The extract was dried over sodium sulfate and evaporated, and the residue was applied to a column charged with silica gel. The column was eluted with cyclohexane–ethyl acetate mixtures (30 : 1, 20 : 1, and 10 : 1). We isolated 1.01 g (73%) of alcohol **VII**. ^1H NMR spectrum, δ, ppm: 0.80 s (3H, 18-Me), 0.96–1.00 m (9H, 21-Me, 26-Me, 27-Me), 1.04 s (3H, 19-Me), 2.78 m (1H, 6-H), 3.33 s (3H, OMe), 4.76 s and 4.80 s (1H, 23-H), 7.36–7.50 m (3H, H_{arom}), 7.86 d (2H, H_{arom}), 9.85 br.s (1H, NH). IR spectrum, ν, cm^{-1}: 3050–2800, 1705, 1675, 1600, 1540, 1460, 1385, 1320, 1295, 1190, 1105, 1075, 1020.

Dehydration and acid hydrolysis of compound VII). To a solution of 106 mg of compound **VII** in 26 ml of dioxane we added 17.5 ml of a 10 : 1 mixture of acetic acid and water, and the resulting mixture was left to stand for 36 h at room temperature. It was then neutralized with pyridine and evaporated, and the residue was washed with a saturated solution of sodium hydrogen carbonate, dried with sodium sulfate, and applied to a column charged with silica gel. The column was eluted with hexane–ethyl acetate (40 : 1) to isolate 75 mg (90%) of a mixture of enones **VIII** and **IX**. The product mixture was subjected to column chromatography on silica gel using hexane–ethyl acetate (80 : 1, 60 : 1, and 40 : 1) as eluent. Three fractions were collected.

The first fraction contained 32 mg (39%) of (20*R*)-6β-methoxy-24-methyl-3α,5-cyclo-5α-cholest-24-en-22-one (**VIII**). ^1H NMR spectrum, δ, ppm: 0.71 s (3H, 18-Me), 1.00 s (3H, 19-Me), 1.01 d (3H, 21-Me, J = 6.5 Hz), 1.66 s (6H, 26-Me, 27-Me), 1.71 s (3H, 28-Me), 2.77 m (1H, 6-H), 3.25 d (2H, 23-H, J = 4.5 Hz), 3.32 s (3H, OMe). ^{13}C NMR spectrum, δ_C, ppm: 13.2, 17.4, 19.3, 19.5, 20.7, 20.8, 21.5, 22.6, 23.7, 24.9, 26.4, 29.7, 30.6, 33.3, 35.1. 39.1, 42.4, 43.4, 48.0, 48.4, 52.3, 55.6, 56.6, 82.4, 121.1, 128.4, 213.0.

The second fraction was a mixture of enones **VIII** and **IX**, yield 18 mg (21%).

The third fraction contained 23 mg (28%) of (20*R*)-6β-methoxy-24-methyl-3α,5-cyclo-5α-cholest-23-en-22-one (**IX**). ^1H NMR spectrum, δ, ppm: 0.71 s (3H, 18-Me), 0.99 s (3H, 19-Me), 1.01 d (3H, 21-Me, J = 6.5 Hz), 1.07 d (6H, 26-Me, 27-Me, J = 7 Hz), 2.08 s (3H, 28-Me), 2.76 m (1H, 6-H), 3.32 s (3H, OMe), 6.13 s (1H, 23-H).

(20ξ)-22-Benzoylimino-6β-methoxy-3α,5-cyclo-26,27-bisnor-5α-cholest-23-ene (XVII). Sodium tetrahydridoborate, 78 mg, was added with stirring to a solution of 337 mg of compound **VI** in 34 ml of 1 : 1 ethyl acetate–methanol. When the reaction was complete, the mixture was neutralized with a saturated solution of ammonium chloride and extracted with ethyl acetate. The extract was dried over sodium sulfate and evaporated. The oily residue was dissolved in 15 ml of acetic acid, 3 ml of water was added, and the mixture was kept for 2 h at 65–70°C, neutralized with sodium hydrogen carbonate, and extracted with ethyl acetate. The extract was dried over sodium sulfate and evaporated, and the residue was applied to a column charged with silica gel. The column was eluted with cyclohexane–ethyl acetate mixtures (40 : 1, 30 : 1, and 20 : 1) to isolate 244 mg (77%) of product **XVII** as a 2 : 1 mixture of C^{20}-epimers. ^1H NMR spectrum, δ, ppm: 0.66 s and 0.73 s (3H, 18-Me), 1.01 s (3H, 19-Me), 1.13 d (3H, 21-Me, J = 7 Hz), 1.90 d (3H, 25-Me, J = 6.5 Hz), 3.46–3.66 m (1H, 3-H), 5.62 d (1H, 6-H, J = 6 Hz), 6.19 d.d and 6.23 d.d (1H, 23-H, J_1 = 16, 1.5 Hz), 6.84–7.02 m (1H, 24-H), 7.42–7.64 m and 8.06–8.14 m (5H, H_{arom}).

Hydrolysis of compound XVII. Water, 0.5 ml, was added to a solution of 221 mg of compound **XVII** in 5 ml of acetic acid. The mixture was refluxed for 4 h and evaporated, and the residue was applied to a column charged with silica gel. The column was eluted with cyclohexane–ethyl acetate mixtures (30 : 1, 20 : 1, and 10 : 1) to isolate 104 mg (54%) of a mixture of (20*S*)-3β-acetoxy-26,27-bisnorcholesta-5,23-dien-22-one (**XVIII**) and (20*R*)-3β-acetoxy-26,27-bisnorcholesta-5,23-dien-22-one (**XIX**). ^1H NMR spectrum, δ, ppm: 0.65 s and 0.73 s (3H, 18-Me), 1.03 s (3H, 19-Me), 1.08 d and 1.12 d (3H, 21-Me, J = 7 Hz), 1.90 d.d and 1.92 d.d (3H, 25-Me, J_1 = 7, J_2 = 1.5 Hz), 2.04 s (3H, Ac), 4.50–4.68 m (1H, 3-H), 5.38 d (1H, 6-H, J = 4.5 Hz), 6.18 d.d and 6.22 d.d (1H, 23-H, J_1 = 16, J_2 = 1.5 Hz), 6.80–7.00 m (1H,

24-H). IR spectrum, ν, cm^{-1}: 3030–2800, 1745, 1710, 1680, 1645, 1485, 1455, 1380, 1260, 1210, 1190, 1145, 1045, 990.

(20*S*)-22-Acetamino-6β-methoxy-3α,5-cyclo-26,27-bisnor-5α-cholest-22-en-24-one (XX). Acetyl chloride, 0.4 ml, was added with stirring to a solution of 94 mg of enaminoketone **V** in 20 ml of pyridine. After 3 h, the mixture was diluted with water and extracted with ether. The extract was dried over sodium sulfate, and evaporated, and the residue was applied to a column charged with silica gel. Elution with toluene–ethyl acetate mixtures (30 : 1, 20 : 1, and 10 : 1) gave 97 mg (93%) of acetamide **XX**. ^{1}H NMR spectrum, δ, ppm: 0.76 s (3H, 18-Me), 1.04 s (3H, 19-Me), 1.19 d (3H, 21-Me, J = 6.5 Hz), 2.06 s (3H, 25-Me), 2.78 m (1H, 6-H), 3.33 s (3H, OMe), 5.03 s (1H, 23-H), 4.98–5.18 br.s (1H, NH), 9.76–9.92 br.s (1H, NH). IR spectrum, ν, cm^{-1}: 3050–2800, 1720, 1650, 1605, 1370, 1245, 1105, 1025, 1005, 975.

Enones XXII and XXIII. *a.* Sodium tetrahydridoborate, 132 mg, was added at room temperature to a solution of 677 mg of compound **XX** in 20 ml of a 1 : 1 ethyl acetate–methanol mixture. When the reaction was complete, the mixture was neutralized with hydrochloric acid and extracted with ethyl acetate. The extract was dried over sodium sulfate and evaporated. The residue was dissolved in 40 ml of dioxane, 4 ml of acetic acid and 0.8 ml of water were added, and the mixture was kept for 8 h at 65–70°C. It was then evaporated, and the residue was applied to a column charged with silica gel. The column was eluted with hexane–ethyl acetate mixtures (60 : 1, 50 : 1, and 40 : 1). Two fractions were collected.

The first fraction contained 122 mg (20%) of (20*R*)-6β-methoxy-3α,5-cyclo-26,27-bisnor-5α-cholest-23-en-22-one (**XXIII**). ^{1}H NMR spectrum, δ, ppm: 0.71 s (3H, 18-Me), 1.00 s (3H, 19-Me), 1.04 d (3H, 21-Me, J = 7 Hz), 1.93 d (3H, 25-Me, J = 7 Hz), 2.76 m (1H, 6-H), 3.32 s (3H, OMe), 6.20 d.d (1H, 23-H, J_1 = 16, J_2 = 2 Hz), 6.82–6.98 m (1H, 24-H). IR spectrum, ν, cm^{-1}: 3070, 3050–2800, 1780, 1705, 1680, 1640, 1465, 1385, 1335, 1300, 1300, 1280, 1210, 1185, 1105, 1025, 1010, 980, 950, 935, 905, 870.

From the second fraction we isolated 216 mg (36%) of (20*S*)-6β-methoxy-3α,5-cyclo-26,27-bisnor-5α-cholest-23-en-22-one (**XXII**). ^{1}H NMR spectrum, δ, ppm: 0.76 s (3H, 18-Me), 1.01 s (3H, 19-Me), 1.11 d (3H, 21-Me, J = 7 Hz), 1.91 d (3H, 25-Me, J = 7 Hz), 2.76 m (1H, 6-H), 3.32 s (3H, OMe), 6.17 d.d (1H, 23-H, J_1 = 16, J_2 = 2 Hz), 6.82–6.98 m (1H, 24-H). IR spectrum, ν, cm^{-1}: 3070, 3050–2800, 1780, 1705, 1680, 1640, 1465, 1385, 1335, 1300, 1300, 1280, 1210, 1185, 1105, 1025, 1010, 980, 950, 935, 905, 870.

(20*S*)-6β-Methoxy-3α,5-cyclo-26,27-bisnor-5α-cholest-23-en-22-one (XXII). *b.* Methanesulfonyl chloride, 0.02 ml, was added to a solution of 47 mg of compound **XXX** in 4 ml of pyridine. The mixture was kept for 1.5 h at room temperature, diluted with water, and extracted with ether. The extract was dried over sodium sulfate and evaporated, and the residue was applied to a column charged with silica gel. Elution with toluene–ethyl acetate mixtures (60 : 1, 40 : 1, and 20 : 1) gave 43 mg (95%) of enone **XXII**.

(20*S*)-20-[5-(Bromomethyl)-4,5-dihydroisoxazol-3-yl]-6β-methoxy-3α,5-cyclo-5α-pregnane (XXVIII). Pyridine, 1 ml, and *N*-chlorosuccinimide, 200 mg, were added to a solution of 1.2 g of 6β-methoxy-3α,5-cyclo-24-nor-5α-cholan-23-al oxime [15] in 60 ml of chloroform, and the mixture was stirred until it became homogeneous. A mixture of 1 ml of triethylamine and 1 ml of chloroform was added over a period of 30 min, and 3 ml of allyl bromide was then added. When the reaction was complete, the mixture was evaporated, and the residue was applied to a column charged with silica gel. Elution with cyclohexane–ethyl acetate mixtures (40 : 1, 30 : 1, and 20 : 1) gave 1.07 g (67%) of bromomethylisoxazole **XXVIII**. ^{1}H NMR spectrum, δ, ppm: 0.78 s (3H, 18-Me), 1.03 s (3H, 19-Me), 1.15 d and 1.17 d (3H, 21-Me, J = 7 Hz), 2.78 m (1H, 6-H), 3.32 s (3H, OMe), 4.68–4.86 m (1H, 24-H). IR spectrum, ν, cm^{-1}: 3050–2800, 1470, 1390, 1340, 1305, 1280, 1220, 1110, 1025, 1010, 980, 900, 870.

(20*S*)-6β-Methoxy-20-[5-methyl-4,5-dihydroisoxazol-3-yl]-3α,5-cyclo-5α-pregnane (XXIX). Azobis(isobutyronitrile), 200 mg, and tributylstannane, 3 ml, were added to a solution of 1.4 g of bromomethyl derivative **XXVIII** in 25 ml of benzene. The mixture was refluxed for 2 h under argon and evaporated, and the residue was subjected to column chromatography on silica gel using cyclohexane–ethyl acetate mixtures (60 : 1, 40 : 1, and 20 : 1) as eluent. Yield of **XXIX** 1.1 g (94%). ^{1}H NMR spectrum, δ, ppm: 0.77 s (3H, 18-Me), 1.01 s (3H, 19-Me), 1.15 d (3H, 25-Me, J = 7 Hz), 1.27 d and 1.29 d (3H, 21-Me, J = 7 Hz), 2.38–2.54 m and 2.84–3.02 m (2H, 23-H), 2.78 m (1H, 6-H), 3.32 s (3H, OMe), 4.54–4.74 m (1H, 24-H). IR spectrum, ν, cm^{-1}: 3050–2800, 1465, 1390, 1335, 1305, 1280, 1210, 1190, 1105, 1025, 980, 870, 765.

(20*S*)-24-Hydroxy-6β-methoxy-3α,5-cyclo-26,27-bisnor-5α-cholestan-22-one (XXX). Boric acid,

300 mg, was added to a solution of 182 mg of compound **XXIX** in a mixture of 20 ml of ethanol and 2 ml of ethyl acetate. The mixture was hydrogenated over Raney nickel for 10 h and filtered through a layer of aluminum oxide which was washed with boiling ethanol. The filtrate was evaporated, and the residue was applied to a column charged with silica gel. Elution with toluene–ethyl acetate mixtures (20 : 1, 10 : 1, and 5 : 1) gave 163 mg (89%) of product **XXX**. ^{1}H NMR spectrum, δ, ppm: 0.75 s (3H, 18-Me), 1.02 s (3H, 19-Me), 1.11 d (3H, 25-Me, J = 7 Hz), 1.17 d and 1.25 d (3H, 21-Me, J = 7 Hz), 2.44–2.60 m (2H, 23-H), 2.76 m (1H, 6-H), 3.32 s (3H, OMe), 4.06–4.22 m (1H, 24-H). IR spectrum, ν, cm^{-1}: 3600–3300, 3050–2800, 1730, 1475, 1390, 1340, 1305, 1285, 1215, 1110, 1030, 1010, 980, 965, 795.

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