TRANSFORMED STEROIDS.
184. PATHWAYS FOR THE USE OF 17α-PREGNA-4,9-DIEN-3-ON-17β-OL-20-YNE IN THE SYNTHESIS OF 9,11-DISUBSTITUTED PREGNANES

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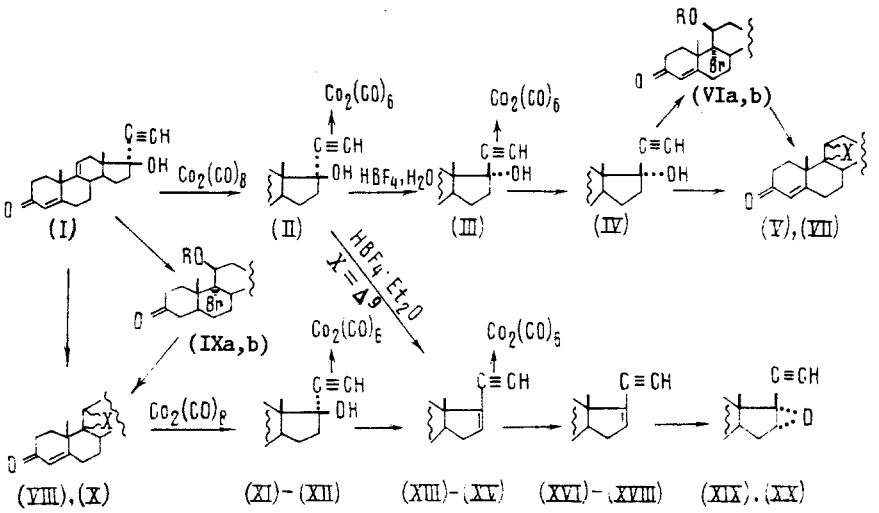
A study was carried out on pathways for the conversion of 17α-pregna-4,9-dien-3-on-17β-ol-20-yne to 9ξ,11ξ-epoxypregn-4-en-17α-ol-3-on-20-ynes and their Δ^{16}- and 16α,17α-epoxy derivatives, which are valuable intermediates in reported schemes for the synthesis of corticosteroids.

In the framework of our study of the preparation of 20-ketopregnanes with 17α-hydroxy-16α,17α-epoxy groups or a Δ^{16} bond starting from 17α-ethynylcarbinols [1,2], we investigated pathways for the functionalization of ring C and epimerization of the C^{17} site of presently available 17α-ethynylandrosta-4,9(11)-dien-17β-ol-3-one (I) [3,4]. A study was carried out on both possible reaction sequences, in which the functionalization of ring C is preceded by epimerization of the C^{17} site and vice versa.

Scheme 1



R = COH(VIa), (IXa); H(VIb), (IXb); X = Δ^9(XIII), (XVI); αO(V), (VIII), (XI), (XIV), (XVII), (XIX); βO(VII), (X), (XII), (XV), (XVIII), (XX).

A variant of dicobalt hexacarbonyl protection [1,2], permitting us to carry out the controlled conversion of 17α-ethynylcarbinol (I) to 17β-ethynylcarbinols (IV), (V), (VII), their Δ^{16} derivatives (XVI)-(XVIII), and 16α,17α-epoxy derivatives (XIX) and (XX) (see Scheme 1) suitable for conversion to 20-ketopregnanes by one of the reported methods [1], was used for the epimerization of 17α-ethynylcarbinols to 17β-ethynylcarbinols and dehydration of the 17β-hydroxyl group. 17α-Ethynylandrosta-4,9(11)-dien-17β-ol-3-one (I) under the conditions

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TABLE 1. PMR Spectra of Ethynylcarbinols (I)-(X) (C^{17} Epimers)

Compound with 17α-ethynyl-17β-hydroxy group	PMR spectrum δ, ppm (J, Hz)	Compound with 17β-ethynyl-17α-hydroxy group	PMR spectrum δ, ppm (J, Hz)
(I)	0.87 s (18Me), 1.37 s (19Me), 2.6 s (H^{21}), 5.58 d (H^{11}, J=5,7), 5.77 d (H^4, J=1,5)	(IV)	0.87 s (18Me), 1.36 s (19Me), 2.53 s (H^{21}), 5.58 (H^{11}, J=5,75), 5.75 d (H^4, J=1,5)
(II)	1.04 s (18Me), 1.37 s (19Me), 6.11 s (H^{21}), 5.56 d (H^{11}, J=5,5), 5.76 s (H^4)	(III)	0.81 s(18Me), 1.36 s (19Me), 6.09 s (H^{21}), 5.55 t.t (H^{11}, J=5,75 and 2), 5.76 d (H^4, J=1,75)
(VIII)	0.94 d (18Me, J=1), 1.47 s (19Me), 2.63 s (H^{21}), 3.24 d (H^{11}, J=5,25), 5.84 d (H^4, J=2)	(V)	0.95 d (18Me, J=1,25), 1.46 s (19Me), 2.52 s (H^{21}), 3.24 d (H^{11}, J=5,25), 5.83 d (H^4, J=2)
(X)	1.05 s (18Me), 1.44 s (19Me), 2.64 s (H^{21}), 3.46 t (H^{11}, J=2), 5.8 t (H^4, J=1,5)	(VII)	1.07 s (18Me), 1.44 s (19Me) 2.51 s (H^{21}), 3.48 t (H^{11}, J=1,7), 5.79 t (H^4, J=2 and 1,3)
(IXa)	1.03 s (18Me), 1.67 br.s (19Me), 2.67 s (H^{21}), 5.73 t (H^{11}, J=3), 5.76 d (H^4, J=2), 8.06 s (COH)	(VIa)	1.03 s (18Me), 1.67 s (19Me) 2.49 s (H^{21}), 6.75 br.s (H^4 and H^{11}), 8.07 s (COH)
(IXb)	1.16 s (18Me), 1.77 d (19Me, J=0,5), 2.67 s (H^{21}), 4.68 q (H^{11}, J=5,75 and 3,5), 5.76 d (H^4, J=2,25)	(VIb)	1.15 s (18Me), 1.76 s (19Me) 2.5 s (H^{21}), 4.72 m (H^{11}, $\Delta W_{1/2}$=7,3 Hz), 5.76 d (H^4, J=2,25)

of the Nicholas reaction [1,2,5] gives β-epimer (IV) in 35% overall yield through a step involving cobalt complexes (II) and (III). Unfortunately, the yield of (IV) could not be enhanced due to competitive dehydration in the step involving epimerization of the cobalt complex (III) to form enyne (XIII). 17β-Ethynylcarbinol (IV) was obtained [6] in a patent procedure directly by the 17β-ethynylation of androsta-4,9-diene-3,17-dione in an amine solvent without indication of the physical indices or yield. However, repetition of this procedure at atmospheric pressure in ethylenediamine gave a 1:2 mixture of epimers (I) and (IV), which proved difficult to separate, in only about 35% yield. Hence, our method for the synthesis of (IV), in which the useful enyne (XVI) is the by-product (29% yield), may be seen as an alternative.

Enyne (XVI) was obtained in 54% yield in a planned synthesis by the dehydration of cobalt complex (II) upon its treatment with HBF_4Et_2O with subsequent decomplexation of cobalt complex (XIII).

While the reaction sequence, in which the epoxidation of ring C is preceded by transformation at the C^{17} site, is preferred in the synthesis of epoxides (V) and (VII), the reverse sequence proved the only possible procedure for the synthesis of epoxides (XVII)-(XVIII) to give diepoxides (XIX) and (XX). The 9α,11α-epoxidation of ethynylcarbinols (I) and (IV) to give (V) and (VIII) was carried out by standard treatment with meta-chloroperbenzoic acid [1] (60%). The α-monoepoxidation of enyne (XVI) could not be carried out by this method since α-diepoxide (XIX) was formed under these conditions. Diepoxide (XIX) was also produced by the 16α,17α-epoxidation of the epoxides (VIII, X), obtained from the monoepoxide (VIII) by the method described above with dicobalt hexacarbonyl protection.

The synthesis of 9β,11β-epoxyethynylcarbinols (VII) and (X) was accomplished through bromohydrins or bromoformates (VIa), (VIb), (IXa), and (IXb) with subsequent alkaline cyclization [7]. The 9β,11β-epoxides thereby obtained (VII) and (X) are valuable intermediates in the synthesis of 11β-hydroxysteroids. Thus, epoxide (VII) may be converted by reported methods into 9α-halocortisols, while it is preferable to use epoxide (X) in the synthesis of enyne (XVIII) and diepoxide (XX) in order to effect their further transformation into 16α,17α-disubstituted corticoids. For this purpose, 9β,11β-epoxide (X) was converted into enzyme (XVIII) in 60% yield using the indicated reaction sequence: (X) → (XII) → (XV) → (XVIII) and then epoxide (XX).

The structures of these compounds were demonstrated by physicochemical methods. Comparison of the PMR spectra of pairs of C^{17}-epimers for ethynylcarbinols (I)-(IV), (VIII)-(V), (X)-(VII), (IXa)-(VIa), and (IXb)-(VIb), which are summarized in Table 1, show the complete lack of difference in the chemical shifts of the C^{21}-acetylenic protons deshielded in 17α-ethynyl compounds (Δδ 0.07-0.18 ppm). Furthermore, the cobalt complexes of epimeric 17-ethynylcarbinols (II) and (III), in accord with our previous findings [2], differ primar-

ily and extremely significantly relative to the chemical shift of the 18-methyl group ($\Delta\delta$ 0.23 ppm). In accord with the data of Tori et al. [8], the signals for the C^{11} protons in 9ξ,11ξ-epoxy products (VIII)-(XII), (XIV), (XV), and (XVII)-(XX) are virtually always doublets for the 9α,11α-epoxy compounds (δ ~ 3.24 ppm, $J_{11\beta,12\beta}$ = 5.25-5.85 Hz) and triplets for the 9β,11β-epoxy compounds (δ ~ 3.41-3.48 ppm, $J_{11\alpha,12\alpha} = J_{11\alpha,12\beta}$ = 1.7-2.5 Hz). Two features of the PMR spectra of these compounds require comment. Firstly, we note the broadening of the signals of the protons of the angular methyl groups for many of these compounds and even the splitting of these signals. Thus, the resonance signals of the 18-methyl group of 9α,11α-epoxides (V) and (VIII) and the 19-methyl group in (IXa) are resolved into a doublet (J 0.5-1.2 Hz) due to long-range coupling through the system of four σ-bonds [9]. Secondly, the signal of the C^{18}-group protons in the cobalt complex of 17α-ethynylcarbinol (XII) with a 9β,11β-epoxide ring is strongly deshielded (δ 1.23 ppm) in comparison with the standard values (δ 1.02-1.06 ppm) [2] for similar analogs with trans-fusion of rings B and C.

EXPERIMENTAL

The melting points were obtained on a Koeffler block. The IR spectra were taken on Perkin-Elmer 577 and Specord M-80 spectrometers for KBr pellets. The PMR spectra were obtained on a Bruker WM-250 instrument relative to TMS. The mass spectra were taken on a Varian MAT CH-6 mass spectrometer with direct sample inlet into the ion source. Thin-layer chromatography was carried out on Silufol plates and developed with a solution of $CeSO_4$ in dilute sulfuric acid. Silpearl silica gel was used for preparative thin-layer chromatography.

Dicobalt Hexacarbonyl 17α-Pregna-4,9-dien-17β-ol-3-on-30-yne (II). A solution of 0.3 g (I) [3] and 0.34 g $Co_2(CO)_8$ in 10 ml CH_2Cl_2 was maintained for 2 h at 20°C and evaporated in vacuum. The residue was transferred to silica gel and eluted consecutively by hexane and chloroform. The chloroform solution yielded 0.52 g (II). IR spectrum (ν, cm^{-1}): 1618, 1660, 1996, 2008, 2016, 2028, 2050, 2092, 3067, 3108, 3375.

Dicobalt Hexacarbonyl 17α-Pregna-4,9-dien-17α-ol-3-on-20-yne (III). A sample of 0.08 ml $HBF_4 \cdot Et_2O$ was added to a suspension of 0.06 g (II) and 0.16 g K_2CO_3 in 2 ml CH_2Cl_2 stirred at −70°C, maintained for 0.5 h, diluted with 0.3 ml H_2O, and stirred for an additional 1.5 h. The mixture was neutralized at −70°C by the addition of Et_3N and diluted with ether. The organic layer was washed with water and evaporated in vacuum. The residue was separated by thin-layer chromatography on silica gel with 20:1 benzene–ethyl acetate as the eluent to give 0.033 g (III) along with 4 mg (II) and 0.024 g (XIII) described below. IR spectrum for (III) (ν, cm^{-1}): 1618, 1668, 2000-2040, 2053, 2095, 3055, 3090, 3450.

Pregna-4,9-dien-17α-ol-3-on-20-yne (IV). a. Cobalt complex (III) obtained from 0.23 g (II) by the method described above was dissolved in 5 ml acetone and cooled to 0°C. A sample of 0.65 g $(NH_4)_2Ce(NO_3)_6$ was added in portions, stirred until colorless, and rapidly evaporated in vacuum. The residue was diluted with water. The precipitate was filtered and separated by thin-layer chromatography on silica gel using 10:1 benzene–ethyl acetate to give 0.05 g (IV), mp 213-221°C (from ethyl acetate–benzene) in addition to 0.04 g (XVI) described below. IR spectrum of (IV) (ν, cm^{-1}): 1615, 1646, 1672, 2115, 3052, 3263, 3310, 3455, 3532. Mass spectrum, m/z: 310 M^+, 292 $[M - H_2O]^+$, 277 $[M - H_2O - Me]^+$.

b. A suspension of 0.25 g androsta-4,9-diene-3,17-dione [3,4] in 5 ml ethylenediamine was added to a suspension of potassium acetylenide obtained by passing acetylene through 1.5 g $KOCMe_3$ in 5 ml abs. ethylenediamine at 20°C. The mixture was maintained for 2 h in an acetylene stream, cooled to 0°C, treated with 30% aq. NaH_2PO_4, and extracted with CH_2Cl_2. The extract was washed with water and evaporated. The residue was dissolved in 6 ml THF and 0.4 ml 3% hydrochloric acid was added. The mixture was stirred for 1.5 h at 20°C, neutralized by the addition of NH_4OH, and evaporated in vacuum. The crystalline precipitate was washed with water, dried, and purified by thin-layer chromatography on silica gel using 0.7:1 acetone–hexane as the eluent to give 0.06 g (IV) in addition to 0.03 g (I).

9α,11α-Epoxypregna-4-en-17α-ol-3-on-20-yne (V). A solution of 0.02 g (IV) in 2 ml CH_2Cl_2 and 0.027 g m-chloroperbenzoic acid was stirred for 4 h at 20°C, diluted with 30 ml CH_2Cl_2, washed with aq. Na_2SO_3 and $NaHCO_3$, dried over $MgSO_4$, and evaporated in vacuum. The dry residue was crystallized from ethyl acetate–hexane to give 0.014 g (V), mp 239-246°C. IR spectrum (ν, cm^{-1}): 1615, 1655, 3290, 3390. Mass spectrum, m/z 326 M^+, 311 $[M - Me]^+$, 308 $[M - H_2O]^+$, 293 $[M - H_2O - Me]^+$, 283 $[M - H_2O - C{=}CH]^+$.

9α-Bromopregn-4-ene-11β,17α-diol-3-on-20-yne 11-Formate (VIa). A solution of 0.05 g (IV) and 0.04 g N-bromosuccinimide was stirred for 4 h at 35°C in 0.3 ml DMF containing 0.008

ml $HClO_4$. A sample of 0.1 g Na_2SO_3 in 0.2 ml water was added with stirring to the cooled mixture over 0.5 h and then 2 ml H_2O was added. The precipitate formed upon cooling was filtered off, washed with water, and purified by thin-layer chromatography on silica gel using 1:2 acetone–benzene as the eluent to give 0.06 g (VIa), mp 164-167°C (from acetone–hexane). IR spectrum (ν, cm^{-1}): 1148, 1615, 1655, 1722, 3290, 3440. Mass spectrum, m/z: 435 M^+, 389 $[M - HCO_2H]^+$, 372 $[M - HCO_2H - OH]^+$, 209 $[M - HCO_2H - Br]^+$.

9α-Bromopregn-4-ene-11β,17α-diol-3-on-20-yne (VIb). A sample of 0.025 g N-bromosuccinimide and 0.084 ml 10% $HClO_4$ was added to a solution of 0.04 g (IV) in 2 ml dioxane containing 0.4 ml water at 15°C and stirred for 4 h. The reaction mixture was treated with 10% aq. Na_2SO_3 and $NaHCO_3$ and diluted with ether. The ethereal solution was washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by thin-layer chromatography on silica gel using 1:2 acetone–hexane as the eluent to give 0.02 g (VIb), mp 163-165°C (from chloroform–hexane). IR spectrum (ν, cm^{-1}): 1615 sh, 1650, 3300, 3440.

9β,11β-Epoxypregn-4-ene-17α-ol-3-on-20-yne (VII). a. A sample of 1.2 ml 1 N MeONa was added to a mixture of 0.045 g (VIa) in 2.5 ml THF and 1.7 ml methanol, stirred for 75 min at 20°C, neutralized by the addition of acetic acid, evaporated in vacuum, and diluted with water. The precipitate formed was filtered off, washed with water, and purified by thin-layer chromatography on silica gel using 1:1 acetone–hexane as the eluent to give 0.02 g (VII), mp 194-201°C (from methanol–hexane). IR spectrum (ν, cm^{-1}): 1615, 1635, 2100, 3260, 3415. Mass spectrum, m/z: 326 M^+, 311 $[M - Me]^+$, 308 $[M - H_2O]^+$, 293 $[M - H_2O - Me]^+$, 283 $[M - H_2O - C{\equiv}CH]^+$.

b. A solution of 0.015 g (VIb) in 0.5 ml methanol containing 1 mg sodium was stirred for 15 min at 20°C, neutralized by the addition of acetic acid, and evaporated in vacuum. The precipitate was filtered and purified by thin-layer chromatography on silica gel using 1:2 acetone–hexane as the eluent to give 0.08 g (VII).

9α,11α-Epoxy-17α-pregn-4-en-17β-ol-3-on-20-yne (VIII). A solution of 0.1 g (I) and 0.17 g m-chloroperbenzoic acid in 10 ml CH_2Cl_2 was stirred for 4 h at 20°C, treated consecutively with aq. Na_2SO_3, aq. $NaHCO_3$, and water, and dried over $MgSO_4$. The solvent was removed in vacuum and the residue was crystallized from methanol–chloroform to give 0.05 g (VIII), mp 272-277°C (from methanol–chloroform). IR spectrum (ν, cm^{-1}): 1612, 1635 sh, 1655, 2100, 3260, 3390. Mass spectrum, m/z: 326 M^+, 311 $[M - Me]^+$, 308 $[M - H_2O]^+$, 293 $[M - H_2O - Me]^+$, 283 $[M - H_2O - C{\equiv}CH]^+$.

Separation of the mother liquor by thin-layer chromatography using acetone–hexane as the solvent gave an additional 0.01 g (VIII).

9α-Bromo-17α-pregn-4-en-11β,17β-diol-3-on-20-yne 11-Formate (IXa). A sample of 0.05 g N-bromosuccinimide was added to a solution of 0.08 g (I) in 2.7 ml DMF containing 0.14 ml 57% $HClO_4$, stirred for 10 h at 30°C, treated with aq. Na_2SO_3, and diluted with 10 ml water. The precipitate formed was filtered off, washed with water, dried, and purified by thin-layer chromatography on silica gel using 1:2 acetone–hexane as the eluent to give 0.06 g (IXa), mp 179-180°C (dec.) (from acetone–hexane). IR spectrum (ν, cm^{-1}): 1144, 1620, 1648, 1656, 1715, 2105, 3290, 3390. Mass spectrum, m/z: 435 M^+, 389 $[M - HCO_2H]^+$, 372 $[M - HCO_2H - OH]^+$, 355 $[M - Br]^+$, 309 $[M - HCO_2H - Br]^+$, 291 $[M - HCO_2H - Br - H_2O]^+$.

9α-Bromo-17α-pregn-4-en-11β,17β-diol-3-on-20-yne (IXb). A sample of 0.053 g N-bromoacetamide was added in portions to a suspension of 0.1 g (I) in 6 ml 5:1 aqueous dioxane containing 0.21 ml 10% $HClO_4$ and stirred for 5.5 h at 20°C. The reaction mixture was diluted with 70 ml ether, washed consecutively with aq. Na_2SO_3, aq. $NaHCO_3$, and water, and dried over Na_2SO_4. The solvent was removed in vacuum and the residue was crystallized from acetone–hexane to give 0.09 g (IXb), mp 184-187°C (dec.). IR spectrum (ν, cm^{-1}): 1065, 1620, 1640 sh, 1655, 2100, 3255, 3370, 3590.

Separation of the mother liquor by thin-layer chromatography on silica gel using 1:1.5 acetone–hexane as the eluent gave an additional 0.02 g (IXb).

9β,11β-Epoxy-17α-pregn-4-en-17β-ol-3-on-20-yne (X). a. A solution of 0.04 g (IXa) in 2.3 ml THF and 1.7 ml methanol containing 1 ml 1 N MeONa was stirred for 1 h at 20°C, neutralized by the addition of acetic acid, and evaporated in vacuum. The residue was purified by thin-layer chromatography on silica gel using 1:2 acetone–hexane as the eluent to give 0.02 g (X), mp 219-222°C (from acetone–hexane). IR spectrum (ν, cm^{-1}): 1615, 1650, 3290, 3370. Mass spectrum, m/z: 326 M^+, 311 $[M - Me]^+$, 308 $[M - H_2O]^+$, 293 $[M - H_2O - Me]^+$, 283 $[M - H_2O - C{\equiv}CH]^+$.

b. A solution of 0.08 g (IXb) in 2 ml methanol containing 5 mg sodium was stirred for 0.5 h at 20°C, neutralized with acetic acid, and evaporated in vacuum. The residue was diluted with water. The precipitated was filtered off and purified by thin-layer chromatography on silica gel using 1:2 acetone–hexane as the eluent to give 0.06 g (X).

Dicobalt Hexacarbonyl (9α,11α-Epoxy-17α-pregn-4-en-17β-ol-3-on-20-yne) (XI). A solution of 0.025 g (VIII) and 0.028 g $Co_2(CO)_8$ was stirred for 3 h at 20°C. The solvent was removed in vacuum. The residue was transferred to silica gel and eluted consecutively with hexane and chloroform. The chloroform eluate gave 0.044 g (XI). IR spectrum (ν, cm^{-1}): 1622, 1671, 2020, 2050, 2093, 3060, 3440. PMR spectrum (δ, ppm): 1.09 s (18-Me), 1.47 s (19-Me), 3.24 d (H^{11}, J = 5.4 Hz), 3.48 d (OH, J = 5.4 Hz), 5.83 br.s (H^4), 6.15 s (H^{21}).

Dicobalt Hexacarbonyl (9β,11β-Epoxy-17α-pregn-4-en-17β-ol-3-on-20-yne) (XII). Using the above procedure, 0.07 g (X) gave 0.12 g (XII). IR spectrum (ν, cm^{-1}): 1612, 1642, 1655, 1995, 2013, 2024, 2036, 2050, 2090, 2095, 3100, 3360, 3450. PMR spectrum (δ, ppm): 1.23 s (18-Me), 1.43 s (19-Me), 3.43 br.s (H^{11}, $\Delta W_{\frac{1}{2}}$ = 5.8 Hz), 5.79 s (H^4), 6.17 s (H^{21}).

Dicobalt Hexacarbonyl (Pregna-4,19,16-trien-3-on-20-yne) (XIII). A sample of 0.12 ml $HBF_4 \cdot Et_2O$ was added to a solution of 0.3 g (II) in 5 ml CH_2Cl_2 at −70°C, stirred for 15 min, neutralized at −10°C by the addition of Et_3N, and evaporated in vacuum. The residue was diluted with water. The precipitate was filtered off, dried, and eluted through an alumina column with ether to give 0.28 g (XIII). IR spectrum (ν, cm^{-1}): 1618, 1678, 1998, 2013, 2020, 2027, 2063, 2092, 3055, 3100. PMR spectrum (δ, ppm): 0.9 s (18-Me), 1.39 s (19-Me), 5.57 m (H^{11}, $\Delta W_{\frac{1}{2}}$ = 10.5 Hz), 5.77 d (H^4, J = 1.3 Hz), 6.17 s (H^{21}), 6.19 t (H^{16}), J = 2.8 Hz).

Dicobalt Hexacarbonyl (9α,11α-Epoxypregna-4,16-dien-3-on-20-yne) (XIV). A sample of 0.06 ml $BF_3 \cdot Et_2O$ was added to a solution of 0.04 g (XI) in 2 ml CH_2Cl_2 at −70°C, stirred for 10 min at −70°C and 5 min at −5°C, and neutralized with triethylamine at −30°C. The reaction mixture was diluted with CH_2Cl_2 and washed with water. The solvent was removed in vacuum and the residue was purified by thin-layer chromatography on silica gel using 1:2 acetone–hexane as the eluent to give 0.02 g (XIV). PMR spectrum (δ, ppm): 0.97 s (18-Me), 1.49 s (19-Me), 3.24 d (H^{11}, $J_{11\beta,12\beta}$ = 5.3 Hz), 5.84 s (H^4), 6.13 br.s (H^{16}, H^{21}).

Dicobalt Hexacarbonyl (9β,11β-Epoxypregna-4,16-dien-3-on-20-yne) (XV). A sample of 0.15 ml $BF_3 \cdot Et_2O$ was added to a solution of 0.1 g (XII) in 6 ml CH_2Cl_2 at −20°C and stirred for 15 min at from −15 to −20°C. The cold solution was rapidly eluted through an alumina column containing $NaHCO_3$ and evaporated in vacuum to give 0.09 g (XV). IR spectrum (ν, cm^{-1}): 1614, 1665, 2016, 2025 sh, 2050, 2090, 3070. PMR spectrum (δ, ppm): 1.09 s (18-Me), 1.48 s (19-Me), 3.42 br.s (H^{11}, $\Delta W_{\frac{1}{2}}$ = 6.5 Hz), 5.8 s (H^4), 6.12 and 6.19 s (H^{16}, H^{21}).

Pregna-4,9,16-trien-3-on-20-yne (XVI). A sample of 0.68 g $(NH_4)_2Ce(NO_3)_6$ was added to a solution of 0.24 g (XIII) in 3 ml acetone at −10°C, stirred until the color disappeared (10 min), and evaporated in vacuum. The residue was diluted with water. The precipitate formed was filtered and purified by thin-layer chromatography on silica gel using 1:2 acetone–hexane as the eluent to give 0.08 g (XVI), mp 160-169°C (from acetone–hexane). IR spectrum (ν, cm^{-1}): 1616, 1632, 1660, 3025, 3058, 3260, 3280. PMR spectrum (δ, ppm): 0.85 s (18-Me), 1.37 s (19-Me), 3.07 s (H^{21}), 5.56 m (H^{11}, $\Delta W_{\frac{1}{2}}$ = 11 Hz), 5.76 d (H^4, J = 1.3 Hz), 6.13 t (H^{16}, J = 2.5 Hz). Mass spectrum, m/z: 292 M^+, 277 $[M - Me]^+$.

9α,11α-Epoxypregna-4,16-dien-3-on-20-yne (XVII). A sample of 0.18 g $(NH_4)_2Ce(NO_3)_6$ was added to a solution of 0.047 g (XIV) at 0°C and evaporated for 10 min in vacuum. The residue was diluted with water. The precipitate formed was filtered off and purified by thin-layer chromatography on silica gel using 1:2 acetone–hexane as the eluent to give 0.02 g (XVII), mp 175-182°C (from acetone–hexane). IR spectrum (ν, cm^{-1}): 1620, 1674, 2090, 3240, 3260, 3280. PMR spectrum (δ, ppm): 0.92 s (18-Me), 1.48 s (19-Me), 3.04 s (H^{21}), 3.23 d (H^{11}, $J_{11\beta,12\beta}$ = 5.3 Hz), 5.84 d (H^4, J = 1.5 Hz), 6.07 q (H^{16}, J = 2.1 and 3.4 Hz). Mass spectrum, m/z: 308 M^+, 293 $[M - Me]^+$, 290 $[M - H_2O]^+$, 275 $[M - H_2O - Me]^+$, 264 $[M - H_2O - C{\equiv}CH]^+$, 249 $[M - H_2O - Me - C{\equiv}CH]^+$.

9β,11β-Epoxypregna-4,16-dien-3-on-20-yne (XVIII). Decomplexation of 0.1 g (XV) according to the above procedure gave 0.04 g (XVIII), mp 58-63°C (from ether–hexane). IR spectrum (ν, cm^{-1}): 1617, 1668, 2096, 3250-3280. PMR spectrum (δ, ppm): 1.04 s (18-Me), 1.48 s (19-Me), 3.08 s (H^{21}), 3.41 t (H^{11}, $J_{11\alpha,12\beta}$ = 2.5 Hz), 6.06 q (H^{16}, J_1 = 2, J_2 = 3.3 Hz). Mass spectrum, m/z: 308 M^+, 293 $[M - Me]^+$, 275 $[M - H_2O - Me]^+$, 265 $[M - H_2O - C{\equiv}CH]^+$.

9α,11α,16α,17α-Diepoxypregn-4-en-3-on-20-yne (XIX). a. A solution of 0.025 g (XVI) in 5 ml CH_2Cl_2 containing 0.043 g m-chloroperbenzoic acid was stirred for 5 h at 20°C, treated as described above and purified by thin-layer chromatography on silica gel using 1:2 acetone–hexane as the eluent to give 0.015 g (XIX), mp 254-256°C (from methanol). IR spectrum (ν, cm^{-1}): 1615, 1655, 1669, 2110, 3270. PMR spectrum (δ, ppm): 0.98 s (18-Me), 1.46 s (19-Me), 2.43 s (H^{21}), 3.23 d (H^{11}, $J_{11\beta,12\beta}$ = 5.5 Hz), 3.65 s (H^{16}), 5.83 d (H^4, J = 2 Hz). Mass spectrum, m/z: 324 M^+, 309 $[M - Me]^+$, 291 $[M - H_2O - Me]^+$, 281 $[M - H_2O - C{\equiv}CH]^+$.

b. A solution of 0.017 g (XVII) in 2 ml CH_2Cl_2 and 0.015 g m-chloroperbenzoic acid was stirred for 3.5 h at 20°C. The reaction mixture was treated by analogy to the above procedure to give 0.011 g (XIX).

9β,11β,16α,17α-Diepoxypregn-4-en-3-on-20-yne (XX). A solution of 0.03 g (XVIII) in 4 ml CH_2Cl_2 with 0.02 g m-chloroperbenzoic acid was stirred for 4.5 h at 20°C. The reaction mixture was treated by analogy to the above procedure to give 0.01 g (XX), mp 229-234°C (from methanol). IR spectrum (ν, cm^{-1}): 1618, 1668, 3040, 3302. PMR spectrum (δ, ppm): 1.13 s (18-Me), 1.45 s (19-Me), 2.44 s (H^{21}), 3.43 br.s (H^{11}, $\Delta W_{\frac{1}{2}}$ = 5.3 Hz), 3.67 s (H^{16}), 5.79 s (H^4). Mass spectrum, m/z: 324 M^+, 309 $[M - Me]^+$, 291 $[M - H_2O - Me]^+$, 281 $[M - H_2O - C{\equiv}CH]^+$.

LITERATURE CITED

1. A. M. Turuta, T. M. Fedeeva, A. V. Kamernitskii, and Lyu Dyk Hu, Izv. Akad. Nauk SSSR, Ser. Khim., No. 12, 2810 (1989).
2. A. M. Turuta, T. M. Fadeeva, A. V. Kamernitskii, et al., Izv. Akad. Nauk SSSR, Ser. Khim., No. 3, 675 (1990).
3. V. Vanrheenen and K. P. Shephard, J. Org. Chem., **44**, No. 9, 1582 (1979).
4. Japanese Patent No. 53-127455 (1978); Chem. Abstr., **91**, 747811 (1979).
5. K. M. Nicholas, Acc. Chem. Res., **20**, 207 (1987).
6. USA Patent No. 4,582,644 (1986); Chem. Abstr., **105**, 7.9230t (1986).
7. Organic Reactions in Steroid Chemistry, Vol. 2 (1972), p. 21.
8. K. Tori, T. Komeno, and T. Nakasawa, J. Org. Chem., **29**, No. 57, 1136 (1964).
9. N. S. Bhacca and D. H. Williams, Application of NMR Spectroscopy in Organic Chemistry, Holden-Day, San Francisco (1964).