TRANSFORMED STEROIDS.

176. PATHS OF TRANSFORMATION OF 17α-ETHYNYL-17β-HYDROXYANDROSTENES INTO Δ^{16}-21-HYDROXY-20-KETOPREGNENES

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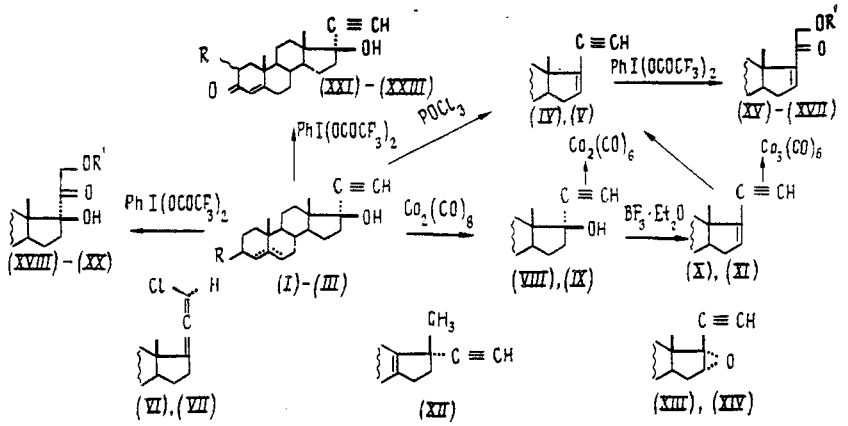
A novel method in steroid chemistry for synthesis of pregna-4,16-dien-3-one-20-yne and pregna-5,16-dien-3β-ol-20-yne, based on the dehydration of Co-complexes of the corresponding 17α-ethynyl-17β-carbinols was investigated. The theoretical possibility of using phenyliodoso trifluoroacetate for the preparative transformation Δ^{16}-17-ethynyl steroids into 21-hydroxy-Δ^{16}-20-ketopregnanes was discovered.

Two approaches to the synthesis of 21-hydroxy-Δ^{16}-20-ketosteroids which are based on the oxidation by phenyliodoso trifluoroacetate (PIFA) [1] of 17α-ethynylcarbinols (I)-(III) and of the Δ^{16}-17-ethynyl steroids (IV), (V) obtained from them by the new method have been studied.

The known methods of the preparation of (IV), (V) from 17α-ethynylcarbinols (I)-(III) are accompanied by rearrangements which lower the yield of the end products or change the course of the reactions. Thus, for example, heating of 17α-ethynylcarbinols (I)-(III) in formic acid proceeds with the aromatization of the D ring and formation of 18-nor-17,17a-dimethyl-$\Delta^{13,15,17}$-trienes [2-5] as the result of a Wagner–Meerwein rearrangement, followed by D-homoannulation [5]. The use of the known method of dehydration of the 17α-ethynylcarbinol (II) by $POCl_3$ in Py [4] gives a low yield of the Δ^{16}-enyne (IV) and, in accordance with our observations, the reaction is complicated by an anionotropic rearrangement [6] and formation of chloroallene (VI). Modification of this method ($POCl_3$ in 2,4-lutidine, heating) leads, according to patent data [7], to the formation of Δ^{16}-enyne (V) in 77% yield. Reproduction of this reaction gave the Δ^{16}-enyne (V) in only 50% yield, while its mother liquor contains an admixture (15%) with similar chromatographic properties which, according to the spectral data (IR, PMR spectra), corresponds to the structure of allene (VII), isolated in the form of geometrical isomers in which the 21β-chloroallene predominates (8:1).



R = OH, Δ^5(I), R = OAc, Δ^5 (II), (IV), (VI), (VIII), (X), (XII), (XIV); R = O, Δ^4 (III);(V), (VII), (IX), (XI), (XIII); R = OAc, Δ^5; R^1 = H (XV); R = OAc, Δ^5; R^1 = $COCF_3$ (XVI), R = O, Δ^4, R^1 = H (XVII), (XX); R = OH, Δ^5; R^1 = H (XVIII); R = OAc, Δ^5, R^1 = $COCF_3$ (XIX); R^1 = $OCOCF_3$ (XXI); R = βOH (XXII), R = βOAc (XXIII).

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We have developed a new approach to the synthesis of Δ^{16}-enynes (IV), (V), alternative to the available methods and based on the dehydration of dicobaltohexacarbonyl complexes of 17α-ethynylcarbinols (VIII), (IX) by their treatment with $BF_3 \cdot Et_2O$ in CH_2Cl_2 (−78-0°C), followed by removal of the cobalt protection from the compounds (X), (XI) obtained by cerium-ammonium nitrate or iron nitrate in EtOH [8]. The yields of Δ^{16}-enynes (IV), (V) using this method were 55 and 42.7-64%, respectively, based on the starting 17α-ethynylcarbinols (II), (III). In the first case, the reaction is complicated at the (VIII) → (X) stage by the Wagner–Meerwein rearrangement with the formation of the 17β-methyl-17α-ethynyl steroid (XII); variation of the conditions (temperature, concentration, selection of Lewis acids) did not help to eliminate this undesirable process. It is preferred to remove the Co-protection from (XI) by oxidation with $Fe(NO_3)_3 \cdot 9H_2O$ in EtOH, since when $(NH_4)_2Ce^{IV}(NO_3)$ in acetone is used, epoxidation of the Δ^{16}-bond takes place with the formation of 16α,17α-epoxide (XIII). This result was noted for the compounds of the Δ^4-3-keto-series only.

The structure of the Δ^{16}-enynes (IV), (V) was confirmed by comparison with samples obtained by known methods [4, 7] and also by their physicochemical characteristics, while the structure of compounds (VI), (VII), (XII), (XIII) was confirmed by spectral data, compared for close literature analogs [9, 10]; compound (XIII) was also obtained by an independent method of epoxidation of the Δ^{16}-enyne (V) by m-chloroperbenzoic acid. The stereochemistry of the C^{21}-center in allenes (VI), (VII) was ascribed in accordance with the known principle of preferential retention of the stereochemistry in the reactions of 1,3-syn-nucleophilic substitution of the $POCl_3$-solvated propargyl cation formed [6].

For the transformation of the 17-ethynyl group of steroids (I)-(V), PIFA was used which, according to the data in [1, 11], is an effective reagent for a one-step transformation of the acetylene group into an α-hydroxyketonic group, in particular, for the oxidation of the 17α-ethynyl group of mestranol acetate [1] (53%). This is the only known example of the successful application of this method in the chemistry of steroids and therefore the problem of extending this reaction to steroids containing other active groups in the molecule still remains to be resolved. We showed the possibility of a one-step synthesis by this method, giving a 40-50% yield of 21-hydroxy-Δ^{16}-20-ketosteroids (XV), (XVII) from Δ^{16}-enynes (IV), (V) (boiling with 2 mole equivalents or mixing at 20°C with 1 mole equivalent of the reagent in a $CH_2Cl_2/CH_3CN/H_2O$ mixture, followed by chromatography on SiO_2), whereby the presence in (V) of a Δ^4-3-keto group does not substantially influence the yield of the desired end product. However, the two reactions are complicated by the formation of a large number of polar products. Boiling of (IV) with PIFA in anhydrous $CHCl_3$, a rapid treatment, and crystallization of the reaction mixture made it possible to isolate and characterize the 21-trifluoroacetate (XVI) which, in accordance with the postulated mechanism, is an intermediate in this reaction. It is also noteworthy that 16α,17α-epoxide (XIV) was detected among the products of this reaction which indicates an unusual ability of PIFA to selectively epoxidate the enyne grouping.

The oxidation of 17α-ethynylcarbinols (I)-(III) using PIFA in a wide range of various conditions gives ketones (XVIII), (XX) with a very low yield (15-20%). In addition, the reaction with pregnyne (III) is complicated by the formation of trifluoroacetates (XXI) isomeric at C^2. This path, which is probably promoted by impurities in the solvent and an excess of the reagent, becomes the main route when unpurified $CHCl_3$ is used. These facts indicate that the alternative variant of the synthesis of 21-hydroxy-Δ^{16}-20-ketopregnanes (XV)-(XVII), providing an initial oxidation of 17α-ethynylcarbinols (I)-(III) by PIFA and subsequent elimination of the 17β-hydroxy(acetoxy) groups in(XVIII)-(XX), is not practical preparatively.

The structure of compounds (XVI)-(XXIII), some of which were described in the literature [12-15], was confirmed by spectral investigations. In the IR spectra of (XXI), (XXIII), there are bands with ν 2110-2010, 3310-3265 (C≡C–H) and 1620, 1690 cm^{-1} (C=C–C=O), while in their PMR spectra singlet signals are observed with a center at 2.58-2.59 ppm (C≡C–H) and 5.6 (H^4), indicating the retention of both the ethynyl and the Δ^4-3-keto groups.

The presence of a trifluoroacetate group in (XVI), (XXI) is confirmed by mass spectra {408 $[M-HOAc]^+$ for (XVI) and 424 M^+ for (XXI)} and IR spectra ($\nu COCF_3$ 1787-1800 cm^{-1}). Trifluoroacetate (XXI) is obtained in the form of an equivalent mixture of two epimers, one of which (probably the equatorial one) is more readily hydrolyzed by acid in an aqueous-methanolic solution. It was thus possible to obtain 2β-trifluoroacetate (XXIβ) of 80% purity, which was further saponified by K_2CO_3 in aqueous methanol, and the isolated 2β-alcohol

(XXIIβ) was acetylated by the usual method to 2β-acetate (XXIIIβ). The affiliation of compounds (XXIβ), (XXIIβ), (XXIIIβ) to the 2β-series was proved by the PMR spectra: the triplet character of the proton signals at the C^2 atom with a center at 5.6, 4.37, and 5.44 ppm, respectively, and $J_{ea} = J_{ee} = 3$ Hz. In accordance with generally accepted patterns [12], in each pair of the resonance signals of the 19-Me group (1.25 and 1.3 ppm) and the C^2 proton (4.75 and 5.6 ppm) observed in the mixture of 2-trifluoroacetates (XXI), the stronger-field signal should belong to 2β-trifluoroacetate (XXIβ); its 2α-isomer was not isolated.

EXPERIMENTAL

The melting points were determined on a Koffler block. The IR spectra were run on a UR-20 spectrophotometer in KBr tablets. The PMR spectra were recorded on a "Bruker WM-250" spectrometer relative to TMS and the mass spectra on a "Varian MAT CH-6" mass spectrometer with direct introduction of the sample into the ionic source. For the analytical TLC, Silufol plates were used with development by iodine or a $CeSO_4$ solution in dilute H_2SO_4. A KSK brand Soviet-produced SiO_2 and a Silpearl brand SiO_2 were used for the analytical TLC.

3β-Acetoxy-17α-pregn-5-en-20-yl-17β-ol Dicobaltohexacarbonyl (VIII). A solution of 0.72 g of (II) and 0.9 g of $Co_2(CO)_8$ in 20 ml of $CHCl_3$ was stirred at 20-25°C for 3.5 h and then evaporated to dryness under vacuum. The residue was washed several times with hexane and then dissolved in benzene and the benzene solution was passed through an Al_2O_3 layer. The dry residue obtained after the removal of the solvent was crystallized from a benzene–hexane mixture. Yield, 1.26 g of (VIII). IR spectrum (ν, cm^{-1}): 498, 518, 1035, 1272, 1710, 1990, 2000-2040, 2050, 2060, 2090, 3450. PMR spectrum (δ, ppm): 1.04 (18-Me, 19-Me), 2.04 s (3-OAc), 4.6 m (H^3), 5.38 m (H^6), 6.15 s (H^{21}).

3β-Acetoxypregna-5,16-dien-20-yne Dicobaltohexacarbonyl (X). A 0.36 ml portion of $BF_3 \cdot Et_2O$ was added with stirring to a solution of 1.26 g of (VIII) in 10 ml of CH_2Cl_2 cooled to −50°C. The mixture was allowed to stand for 1 h, while gradually raising the temperature to −10°C and then 0.2 ml of Et_3N was added. The solvent was evaporated under vacuum, the residue was diluted with water, the precipitate that separated out was filtered off, washed with water, dried, and passed through a layer of Al_2O_3 (elution with benzene). Yield, 1.2 g of product (X), which was contaminated with an admixture of a Co-complex of compound (XII) having similar chromatographic properties. To obtain the spectral characteristics of (X), a solution of 0.18 g of (IV) and 0.23 g of $Co_2(CO)_8$ in 7 ml of $CHCl_3$ was stirred at 20°C for 2 h, the solvent was evaporated under vacuum, the dry residue was washed with hexane, filtered through an Al_2O_3 layer (elution with benzene), and the residue obtained was recrystallized from a $CHCl_3$–C_6H_{14} mixture. Yield, 0.23 g of (X). IR spectrum (ν, cm^{-1}): 500, 520, 1035, 1250, 1372, 1726, 1970, 2006, 2025, 2034, 2050, 2092, 3008. PMR spectrum (δ, ppm): 0.93 s (19-Me), 1.07 s (18-Me), 2.04 s (3-OAc), 4.62 m (H^3), 5.41 m (H^6), 6.17 s (H^{21}).

Pregna-5,6-diene-20-yn-3β-ol 3-Acetate (IV). a) A solution of 0.36 g of (II) and 0.5 g of $Co_2(CO)_8$ in 5 ml of $CHCl_3$ was stirred at 20°C for 2.5 h and the solvent was evaporated under vacuum. The residue was ground with hexane and the precipitate was filtered off. The product obtained (0.71 g) was dissolved in 5 ml of dry CH_2Cl_2. The solution was cooled to −50°C, 0.18 ml of $BF_3 \cdot Et_2O$ was added, the mixture was stirred for 1 h (thus raising the temperature to −10°C) and then 0.2 ml of Et_3N was added. The solvent was evaporated under vacuum, the residue was diluted with water, the precipitate was filtered off, washed with water, and dissolved in 10 ml of Me_2CO. The solution was cooled to −50°C and 2.5 g of $(NH_4)_2Ce^{IV}(NO_3)_6$ was added. The mixture was stirred to complete decoloration, the solvent was then evaporated rapidly under vacuum, and the residue was diluted with water. The precipitate was filtered off (0.34 g), filtered through an SiO_2 layer (benzene–hexane, 1:1, and then benzene). Yield, 0.19 g of (IV), mp 167-177°C (from MeOH–Et_2O) (cf. [4]) and 0.05 g of 3β-acetoxy-17β-methyl-17α-pregna-5,13-dien-20-yne (XII), mp 77-83°C (from MeOH). IR spectrum (ν, cm^{-1}): 640, 1035, 1250, 1730, 2155, 3300. PMR spectrum (δ, ppm): 1.0 s (19-Me), 1.27 s (17-Me), 2.04 s (3-OAc), 2.15 s (H^{21}), 4.62 m (H^3), 5.45 m (H^6). Mass spectrum (m/z): 278 $[M-HOAc]^+$, 263 $[M-HOAc-Me]^+$.

b) A solution of 10 g of (II) and 5.5 ml of $POCl_3$ in 90 ml of Py was boiled for 45 min, then was cooled and poured into 0.5 liter of ice water containing 0.1 liter of concentrated HCl. The mixture was extracted with $CHCl_3$, the extract was washed with water, dried over Na_2SO_4 and evaporated in vacuo. The residue (9 g) was crystallized many times from MeOH.

Yield, 3.2 g of (IV) and 0.95 g of 3β-acetoxy-21β-chloropregna-5,17(20),20-triene (VI), mp 139-141°C (from MeOH–$CHCl_3$). IR spectrum (ν, cm^{-1}): 765, 835, 1035, 1250, 1370, 1738, 1965, 3065. PMR spectrum (δ, ppm): 0.9 s and 1.04 s (18-Me, 19-Me), 2.04 s (3-OAc), 4.61 m (H^3), 5.38 m (H^5), 5.99 t (H^{21}, J = 2.5 Hz); and 4 g of unseparated mixture of (IV) and (VI).

17α-Pregna-4-en-3-on-17β-ol-20-yne Dicobaltohexacarbonyl (IX). A solution of 6.4 g of (III) and 9.8 g of $Co_2(CO)_8$ in 40 ml of CH_2Cl_2 was allowed to stand for 5 h at 25°C, then was evaporated under vacuum, the residue was ground with heptane and the insoluble part was filtered off. Yield, 12.8 g of (IX). IR spectrum (ν, cm^{-1}): 1612, 1660, 1990, 2010, 2025, 2042, 2060, 2100, 3080, 3420. PMR spectrum (δ, ppm): 1.06 s (18-Me), 1.19 s (19-Me), 5.72 br. s (H^4), 6.12 s (H^{21}).

Pregna-4,16-dien-3-on-20-yne Dicobaltohexacarbonyl (XI). A 0.25 ml portion of $BF_3 \cdot Et_2O$ was added at −78°C to a solution of 0.65 g of (IX) in 10 ml of CH_2Cl_2. The mixture was stirred for 15 min and, after the temperature rose to 0°C in the course of 30 min, it was neutralized with Et_3N and evaporated under vacuum. The residue was diluted with water, the precipitate that separated out was filtered off, dried (0.62 g), and filtered through a SiO_2 layer (benzene). Yield, 0.45 g of (XI). IR spectrum (ν, cm^{-1}): 1617, 1670, 1975, 2010, 2020, 2040, 2060, 2099. PMR spectrum (δ, ppm): 0.96 s (18-Me), 1.23 s (19-Me), 5.75 br. s (H^4), 6.17 br. s (H^{16} and H^{21}).

Pregna-4,16-dien-3-on-20-yne (V). a) A 2-g portion of $(NH_4)_2Ce^{IV}(NO_3)_6$ was added gradually to a cooled (0°C) solution of 0.62 g of (XI) in 10 ml of Me_2CO. The mixture was stirred to complete decoloration and evaporated under vacuum for 15 min. The residue was diluted with water, the precipitate that separated out was filtered off. Yield, 0.3 g of a product which was partitioned on a column (SiO_2, benzene) to give 0.18 g of (V), mp 170-172°C (from MeOH), cf. [7]. By subsequent elution with MeOH, 0.13 g of a product was obtained from which 0.03 g of the epoxide (XIII) described below, mp 250-257°C, was isolated by TLC.

b) $Fe(NO_3)_3 \cdot 9H_2O$ (14 g) was added in portions to a cooled (0°C) solution of 0.62 g of (XI) in 15 ml of EtOH. The mixture was stirred at 0°C for 4 h and then was poured into a saturated NaCl solution and extracted with Et_2O. Yield 0.27 g of (V).

21ξ-Chloropregna-4,17(20),20-trien-3-one (VII). A suspension of 1 g of (III) in 7 ml of toluene, 3 ml of 2,4-lutidine and 1 ml of $POCl_3$ was stirred at 100°C for 4 h, then cooled and poured into 18 ml of ice water containing 4 ml of conc. HCl. The mixture was stirred for 1 h and extracted with $CHCl_3$ and the extract was washed with water and dried over $MgSO_4$. The residue after the separation of the solvent was crystallized from MeOH to yield 0.52 g of (V), mp 157-165°C. The mother liquor was partitioned by TLC (benzene–Me_2CO, 6:1) to give, together with 0.05 g of (V) (the lower part of the band), 0.12 g of (VII) in the form of oil. IR spectrum (ν, cm^{-1}): 732, 858, 950, 1190, 1230, 1270, 1330, 1352, 1375, 1430, 1450, 1615, 1670, 1960, 3300. PMR spectrum (δ, ppm): 0.93 s and 0.98 s (18-Me), 1.2 s and 1.27 s (19-Me), 5.75 s (H^4), 6.0 t and 7.05 t (H^{21}, J = 3 Hz). Integration of the H^{21} and methyl proton signals gives a ratio of the 21β-Cl isomer to the 21α-Cl isomer equal to 8:1.

16α,17α-Epoxypregn-4-ene-3-one-20-yne (XIII). A solution of 0.5 g of (V) in 8 ml of $CHCl_3$ containing 0.5 g of m-chloroperbenzoic acid was stirred at 20°C for 3 h, was then evaporated under vacuum to 1/3 of its volume, and the precipitate that separated out was filtered off (0.25 g) and washed with $CHCl_3$. The chloroform solution (~30 ml) was successively washed with an aqueous solution of $Na_2S_2O_3$, $NaHCO_3$, and water, then dried over $MgSO_4$. After evaporation of the solution, 0.57 g of a residue was obtained, the crystallization of which from MeOH gave 0.37 g of (XIII), mp 250-257°C. IR spectrum (ν, cm^{-1}): 1065, 1615, 1665, 3268, 3415. PMR spectrum (δ, ppm): 0.95 s (18-Me), 1.19 s (19-Me), 2.41 s (H^{21}), 3.62 br. s (H^{16}), 5.72, br. s (H^4).

3β-Acetoxypregna-5,16-dien-21-ol-20-one (XV). a) A solution of 0.1 g of (IV) and 0.26 g of $PhI(OCOCF_3)_2$ in 10 ml of a $CH_2Cl_2/CH_3CN/H_2O$ (8:1:1) mixture was boiled for 2 h and then allowed to stand overnight. The solvent was evaporated under vacuum to 1/3 of its volume and the residue was held for two days on a filter with SiO_2, then eluted with Et_2O and purified by TLC (benzene–EtOAc, 9:1). Yield, 0.04 g of (XV), mp 176-177°C (from MeOH, cf. [13]).

b) A solution of 0.2 g of (IV) and 0.5 g of $PhI(OCOCF_3)_2$ in 6 ml of dry CH_2Cl_2 was boiled for 4 h and then evaporated under vacuum. The residue was dissolved in aqueous CH_3CN (10:1), the solution was allowed to stand for 20 h at 20°C and evaporated under vacuum. The residue was diluted with water and neutralized with $NaHCO_3$. The precipitate that separated out was filtered off and partitioned by TLC (SiO_2, benzene–EtOAc, 1:20). Yield, 0.06 g of (XV) and 8 mg of 3β-acetoxy-16α,17α-epoxypregn-5-en-20-yne (XIV), mp 215-221°C (from MeOH). IR spectrum (ν, cm^{-1}): 1035, 1248, 1380, 1730, 3250. PMR spectrum (δ, ppm): 0.92 s and 1.05 s (18-Me, 19-Me), 2.04 s (3-OAc), 2.4 s (H^{21}), 3.62 s (H^{16}), m (H^3),* 5.77 m (H^6). Mass spectrum (m/z): 354 M^+, 294 $[M-HOAc]^+$, 279 $[M-HOAc-Me]^+$, 261 $[M-HOAc-Me-H_2O]^+$, 235.

3β Acetoxypregna-5,16-dien-21-ol-20-one 21-Trifluoroacetate (XVI). A solution of 0.2 g of (IV) and 0.38 g of $PhI(OCOCF_3)_2$ in 6 ml of dry $CHCl_3$ was boiled for 3.5 h. It was then neutralized by NH_4OH, washed rapidly with water and dried over $MgSO_4$. After evaporation of the solvent, ~1 ml of hexane was added to the residue and the insoluble precipitate was filtered off and recrystallized from an Et_2O–hexane mixture. Yield, 0.03 g of (XVI) mp 190-198°C. IR spectrum (ν, cm^{-1}): 1040, 1148, 1180, 1220, 1260, 1380, 1440, 1590, 1688, 1732, 1800. PMR spectrum (δ, ppm): 0.95 s and 1.06 s (18-Me, 19-Me), 2.05 s (3-OAc), 4.61 m (H^3), 5.13 d and 5.27 d (H^{21}, J = 16 Hz), 5.38 m (H^6), 6.8 m (H^{16}). Mass spectrum (m/z): 408 $[M-HOAc]^+$, 393 $[M-HOAc-Me]^+$, 341 $[M-CH_2OCOCF_3]^+$, 337, 312, 300, 281.

Pregna-4,16-dien-21-ol-3,20-dione (XVII). a) A solution of 0.1 g of (V) and 0.14 g of $PhI(OCOCF_3)_2$ in 10 ml of a $CH_2Cl_2/CH_3CN/H_2O$ (8:1:1) mixture was stirred at 20°C for 5 days, then washed with water and dried over $MgSO_4$. The residue after evaporation of the CH_2Cl_2 was partitioned by TLC (C_6H_6–Me_2CO, 6:1), holding preliminarily the material for 2 days on a plate. Yield, 0.05 g of (XVII), mp 177-189°C, after crystallization from aqueous MeOH, mp 202-204°C, cf. [14].

b) A solution of 0.05 g of (V) and 0.18 g of $PhI(OCOCF_3)_2$ in 5 ml of a $CH_2Cl_2/CH_3CN/H_2O$) (8:1:1) mixture was heated for 10 h, then evaporated under vacuum, the residue was held on a filter with SiO_2 for 2 days and then was eluted with Et_2O and partitioned by TLC. Yield, 0.03 g of (XVII).

17α-Pregn-5-ene-3β,17β,21-triol-20-one (XVIII). A solution of 0.15 g of (I) in 1 ml of dry $CHCl_3$ was boiled for 7 h and then 0.4 g of $PhI(OCOCF_3)_2$ was added in portions. The mixture was evaporated to dryness, the residue was dissolved in 2 ml of aqueous MeOH, and the solution was allowed to stand for 18 h at 20°C. It was then evaporated under vacuum and the residue was dissolved in $CHCl_3$. The solution was neutralized with NH_4OH, washed with water, and dried over $MgSO_4$. The residue after evaporation of the $CHCl_3$ was partitioned by TLC (SiO_2, benzene–EtOAc, 2:1). Yield, together with 0.02 g of (I), 0.04 g of (XVIII), mp 198-204°C (from EtOAc). IR spectrum (ν, cm^{-1}): 1010, 1013, 1070, 1095, 1710, 3385, 3490. Mass spectrum (m/z): 348 M^+, 330, $[M-H_2O]^+$, 318, 299, 289, 271.

3β,21-Diacetoxy-17α-pregn-5-en-17β-ol-20-one (XIX). Acetylation of (XVIII) with Ac_2O in Py (20°C, 24 h) gave (XIX), mp 158-160°C (from Me_2CO–C_6H_{14}). IR spectrum (ν, cm^{-1}): 1040, 1240, 1260, 1380, 1730, 1750 sh, 3480. PMR spectrum (δ, ppm): 0.9 s and 1.02 s (18-Me, 19-Me), 2.03 s (3-OAc), 2.18 s (21-OAc), 4.58 m (H^3), 4.87 d and 5.24 d (H^{21}, J = 17.8 Hz), 5.36 m (H^6). Mass spectrum (m/z): 432 M^+, 372 $[M-HOAc]^+$, 354 $[M-HOAc-H_2O]^+$, 342, 312.

17α-Pregn-4-en-17β,21-diol-3,20-dione (XX). A solution of 0.2 g of (III) in 3 ml of $CHCl_3$ was boiled for 13 h and then 0.68 g of $PhI(OCOCH_3)_2$ was added in portions. After the above-described treatment, together with 0.03 g of (III), 0.034 g of (XX) was obtained, mp 194-198°C (from Me_2CO–C_6H_{14}). IR spectrum (ν, cm^{-1}): 1085, 1615, 1660, 1710, 3300, 3400. PMR spectrum (δ, ppm): 0.99 s (18-Me), 1.18 s (19-Me), 4.43 d and 4.58 d (H^{21}, J = 19 Hz). Mass spectrum (m/z): 346 M^+, 328 $[M-H_2O]^+$, 314, 297, 287.

17α-Pregn-4-ene-2ξ,17β-diol-20-yn-3-one 2ξ-Trifluoroacetate (XXI) (mixture of epimers). A solution of 0.5 g of (I) and 1.7 g of $PhI(OCOCF_3)_2$ in 32 ml of $CHCl_3$ was boiled for 8.5 h. It was then evaporated under vacuum and the residue was partitioned by TLC (benzene, and then benzene–EtOAc, 8:1). Yield, together with 0.13 g of (I), 0.13 g of (XXI) which, according to the PMR spectrum data, is a mixture (1:1) of epimers, mp 106-124°C. IR spectrum (ν, cm^{-1}): 1065, 1130, 1155, 1175, 1230, 1390, 1460,1620, 1690, 1787, 2110, 3310, 3450. PMR

*As in Russian Original — Editor.

spectrum (δ, ppm): 0.94 s and 0.95 s (18-Me), 1.25 s and 1.3 s (19-Me), 2.58 s and 2.59 s (H^{21}), 4.75 (H^{2a}, $\Delta W_{1/2}$ = 8.3 Hz), 5.6 t (H^{2e}, J = 3 Hz), 5.89 s and 6.01 s (H^4). Mass spectrum (m/z): 424 M^+, 380, 365, 310. UV spectrum: λ_{max} 242 nm, log ε 4.06.

17α-Pregn-4-ene-2β,17β-diol-3-on-20-yne 2β-Trifluoroacetate (XXIβ). A solution of 0.05 g of a mixture of epimers of (XXI) in 5 ml of a MeOH–water (10:1) mixture containing 0.09 ml of 5% HCl was allowed to stand for 17 h at 20°C. The mixture was then neutralized with NH_4-OH, evaporated under vacuum, the precipitate that separated out was filtered off and washed with water to give 0.042 g of a product which was partitioned by TLC (benzene). Yield, 0.015 g of an 80% pure (XXIβ), mp 110-125°C. IR spectrum (ν, cm^{-1}): 1065, 1130, 1165, 1175, 1220, 1385, 1620, 1689, 1785, 2010, 3310, 3450. PMR spectrum (δ, ppm): 0.95 s (18-Me), 1.31 s (19-Me), 2.59 s (H^{21}), 5.6 t (H^{2e}, J = 3 Hz), 6.01 s (H^4).

17α-Pregn-4-ene-2β,17β-diol-3-on-20-yne (XXIIβ). A solution of 0.03 g of the above-obtained (XXIβ) in 1.5 ml of MeOH and 0.3 ml of water containing 6 mg of K_2CO_3 was allowed to stand for 43 h at 20°C. The solvent was evaporated under vacuum, the residue was washed with water, and then it was partitioned by TLC (SiO_2, benzene–EtOAc, 13:1, twice). Yield 0.01 g of (XXIIβ), mp 260-266°C (Me_2CO–benzene). IR spectrum (ν, cm^{-1}): 1068, 1620, 1665, 2010, 3265, 3400, 3590. PMR spectrum (δ, ppm): 0.94 s (18-Me), 1.41 s (19-Me), 2.59 s (H^{21}), 4.37 t (H^{2e}, J = 3 Hz), 5.83 s (H^4). Mass spectrum (m/z): 328 M^+, 310 $[M-H_2O]^+$, 295 $[M-H_2O-Me]^+$, 292 $[M-2H_2O]^+$, 277 $[M-2H_2O-Me]^+$, 267 $[M-2H_2O-C\equiv CH]^+$. UV spectrum: λ_{max} 238 nm, log ε 4.2.

2β-Acetoxy-17α-pregn-4-en-17β-ol-3-on-20-yne (XXIIIβ). A solution of 8 mg of (XXIIβ) in 0.5 ml of Py and 0.1 ml of Ac_2O was allowed to stand for 18 h at 20°C. The mixture was then evaporated under vacuum with heptane to dryness, the residue was purified by TLC (SiO_2, EtOAc–benzene, 1:5). Yield, 7 mg of (XXIIIβ), mp 80-84°C. IR spectrum (ν, cm^{-1}): 1020, 1070, 1232, 1376, 1460, 1620, 1672, 1736, 2110, 3300, 3416. PMR spectrum (δ, ppm): 0.96 s (18-Me), 1.32 s (19-Me), 2.07 s (3-OAc), 2.59 s (H^{21}), 5.44 t (H^{2e}, J = 3 Hz), 5.97 s (H^4). Mass spectrum (m/z): 370 M^+, 328 $[M-COCH_2]^+$, 310 $[M-HOAc]^+$, 303 $[M-COCH_2-C\equiv H]^+$, 295 $[M-HOAc-Me]^+$, 292 $[M-HOAc-H_2O]^+$. UV spectrum: λ_{max} 237 nm, log ε 4.0.

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