INTRAMOLECULAR HYDRIDE SHIFT IN OPPENAUER OXIDATION OF SOME DIHYDROXY STEROIDS*

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Oppenauer oxidation of 18,20- and 18a,20-dihydroxy steroids proceeds partly without any change of the oxidation state at the carbon $C_{(20)}$ and partly with an intervention of the 20-keto group which undergoes intramolecular reduction to mainly 20α-hydroxy group derivative. The hydride shift occurs at the stage of the keto aldehyde (Tishchenko reaction) and with 18a,20-dihydroxy derivatives also at the stage of hydroxy carbonyl derivatives (Meerwein–Ponndorf–Oppenauer reaction).

Oxidation of 1,4- and 1,5-diols with various reagents yields γ and δ-lactones in many cases[1-3]. This reaction is usually interpreted in terms of the gradual oxidation at one of the carbinolic centers without any oxidative change of the other one; the ring closure is usually located to the stage of the hydroxy aldehyde[2]. Unique in this respect is the patent of Bellon[4] who explains the Oppenauer oxidation of 18,20-dihydroxy derivative *I* to N-methylparavallarine (*III*) as a formation and redox disproportionation (Tishchenko reaction) of the keto aldehyde *II*. Since the Tishchenko reaction allegedly[5] belongs among reactions of aldehydes only, we decided to reexamine experimentally the mechanism put forward by Bellon.

The starting material [18,18-$^2H_2$]-5α-pregnan-3β,18,20α-triol (*V*) was prepared by the standard reduction of 3β,20α-dihydroxy-5α-pregnan-18-oic acid lactone[6] (*IV*) with lithium aluminum deuteride. On Oppenauer oxidation catalyzed with potassium tert-butoxide this labelled triol yielded a lactone which was identical with an authentic specimen of 3-oxo-20α-hydroxy-5α-pregnan-18-oic acid lactone[6] (*VI*). The mass spectrum revealed the presence of 18·2% of deuterio lactone *VIb*. This result together with the finding that neither the hemiacetal[7] *VII* nor the hemiketal[8] *VIII* suffer the base-catalyzed intramolecular redox isomerization[9,10] indicates that 81·8% of the lactone *VI* isolated was formed by a gradual oxidation at the carbon C_{18} and only 18·2% of the lactone *VI* was formed by the stereospecific hydride ion shift[11-13] from the carbon $C_{(18)}$ to $C_{(20)}$ of the intermediary keto aldehyde of the type *II*. This conclusion is further supported by the result of the oxidation of [18,18-$^2H_2$]-5α-pregnan-3β,18,20β-triol (*X*) prepared from the (20*R*)-lactone[14] *IX* in the usual way. The Oppenauer oxidation, carried out under the same conditions as above afforded

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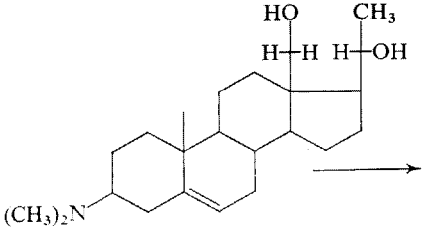
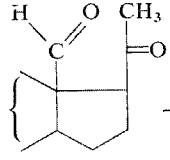
a mixture of non deuterio- and deuteriolactones in a 81·6 : 18·4 ratio (mass spectrometry). The structure of the major component *XI* follows from its ^{1}H-NMR spectrum. (20*S*)-Configuration of the minor component *VIb* was suggested on the basis of the IR spectrum and $[\alpha]_D^{20}$ value of the mixture. Thus the oxidation of the 18,20-diols gives rise to lactones both by gradual oxidation at the carbon $C_{(18)}$ without any change of the configuration at the carbon $C_{(20)}$ and by Tishchenko reaction of the intermediary keto aldehyde of the type *II* which affords (20*S*)-lactones.



I



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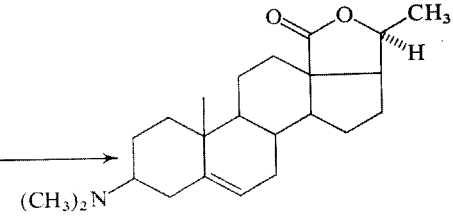

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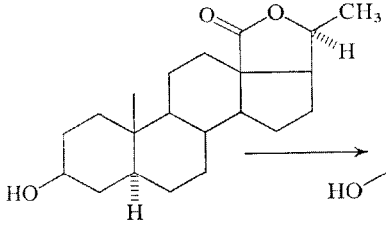
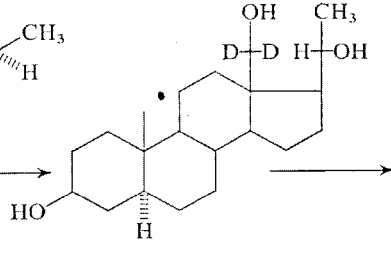
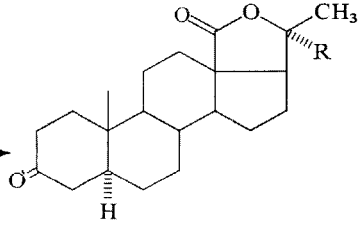


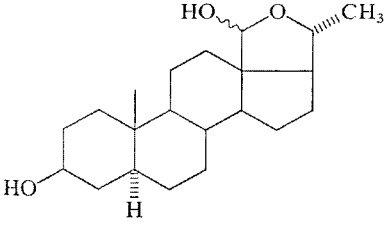
IV



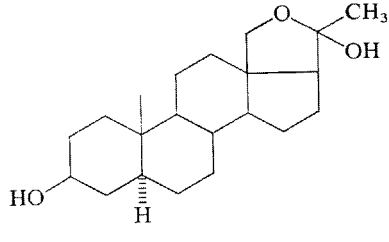
V



VIa, R = H
VIb, R = D



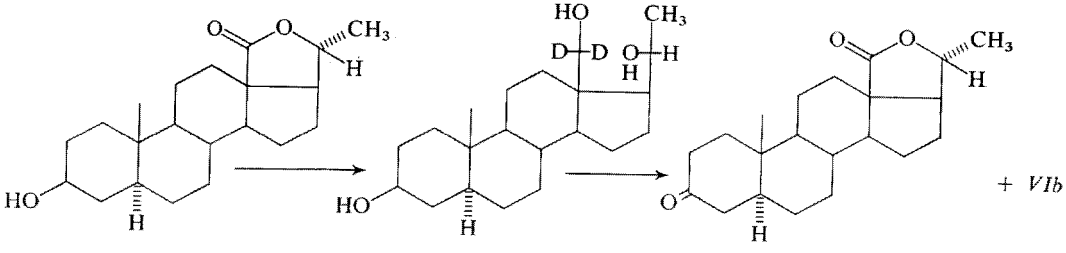
VII



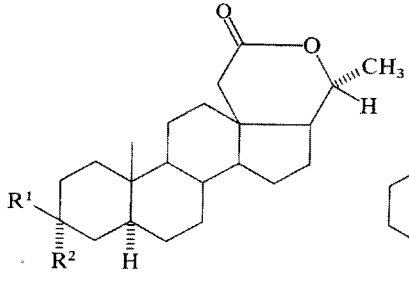
VIII

Further we investigated the utilisability of this oxidation for the synthesis of δ-lactones (see ref.[15]). The starting material was prepared from the 3β,20β-dihydroxy--5-pregnen-18-carboxylic acid lactone[16], which was transformed into dihydro-

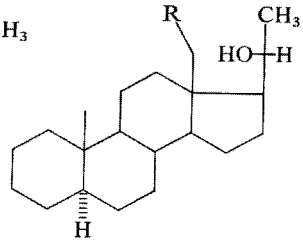
derivative *XII*, ketone *XIII*, thioketal *XIV* and deoxylactone *XV* by standard procedures. The last mentioned compound was reduced by lithium aluminum hydride and deuteride to give diols *XVI* and *XVII* and by tri-tert-butoxylithium aluminum hydride to afford hemiacetal *XVIII*. The selective oxidation of the 20β-hydroxy group of the diol *XVI* was accomplished after protecting the primary hydroxy group by tritylation; having recovered the hydroxy group, we isolated 18a-hydroxy-18-homo-5α-pregnan-20-one, the solution of which exhibits only the infrared absorption of hemiketal *XX*.



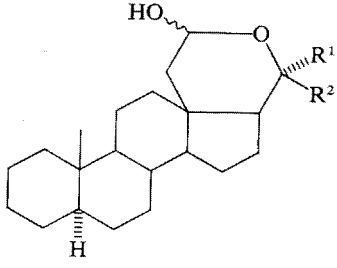
IX *X* *XI* + *VIb*



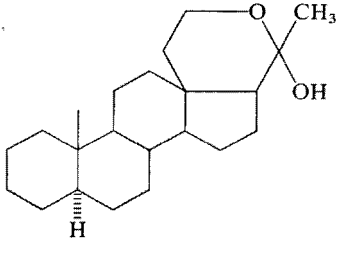
XII, $R^1 = OH$, $R^2 = H$
XIII, $R^1 + R^2 = O$
XIV, $R^1 + R^2 = SCH_2CH_2S$
XV, $R^1 = R^2 = H$



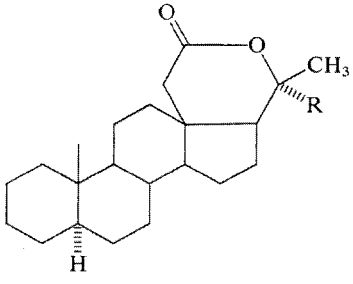
XVI, $R = CH_2OH$
XVII, $R = CD_2OH$
XIX, $R = (C_6H_5)_3COCH_2$



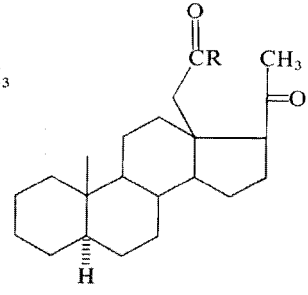
XVIII, $R^1 = CH_3$, $R^2 = H$
XXII, $R^1 = H$, $R^2 = CH_3$



XX



XXIa, R = H
XXIb, R = D



XXIIIa, R = H
XXIIIb, R = D

The Oppenauer oxidation of diol *XVI* afforded, under catalysis with potassium tert-butoxide, an unseparable mixture of lactones (80%). The ^{1}H-NMR and IR spectra of this mixture indicated that the major product was the (20*R*)-lactone *XV* accompanied by the (20*S*)-epimeric *XXI*. An analogous oxidation of deuteriodiol *XVII* yielded a similar mixture composed of almost equal amounts of lactones of molecular masses 330 and 331 (mass spectrometry). The ^{1}H-NMR spectrum of this mixture is a superposition of the spectra of lactone *XV* and deuteriolactone *XXIb*. Since both respective intermediates, *i.e.* the hemiacetal *XVIII* and the hemiketal *XX*, were found to suffer isomerization to the hemiacetal *XXII* when exposed to the basicity of the oxidation studied, we were not able to decide at which stage the observed intramolecular hydride shifts from the carbon $C_{(18a)}$ to $C_{(20)}$ occur. Therefore we submitted both possible intermediates to Oppenauer oxidation and analyzed the isolated lactones by means of CD, IR and ^{1}H-NMR spectrometry. The results obtained as summarized in the Table I, may be interpreted as follows: the oxidation of diol *XVI* catalyzed by potassium tert-butoxide proceeds in two parallel sequences of which the one, begun by preferential oxidation of the primary hydroxy group[17,18] (sequence *A*) plays the more important role. The hemiacetal *XVIII* formed in this way undergoes further oxidation at carbon $C_{(18a)}$ leading to the lactone with the unchanged configuration at carbon $C_{(20)}$ and to a lesser extent it is oxidized to keto aldehyde *XXIII* which is isomerized (Tishchenko reaction) mainly to (20*S*)-lactone *XXI*. The hemiacetal *XVIII* may be also first isomerized to hemiketal *XX* and hemiacetal *XXII* and then oxidized to the lactone *XXI*. The sequence *B* is characterized by preferentical oxidation of the secondary hydroxy group of the diol *XVI* and the ensueing hemiketal *XX* is further oxidized and isomerized or isomerized and oxidized under predominant formation of lactone *XXI*. When the labelled diol *XVII* is oxidized under the conditions described, the concentration of the 20-deuteriolactone in the lactone mixture reflects the degree of the intramolecular deuteride ion shift whether it was realized at the stage of a hydroxy carbonyl or a dicarbonyl intermediate. The fact that deuterium is not lost* in the process of isomerization supports the conclusion that a substantial proprotion of the isolated compound *XXIb* is a product of Tishchenko reaction of the intermediary keto aldehyde *XXIII*. The aluminum tert-butoxide catalyzed oxidation of diols *XVI* and *XVII* proceeds again mainly by the sequence *A*, but the yields of (20*S*)-lactone formed by intramolecular redox reaction are superior to those given above (see Table I). This fact is undoubtedly connected with the higher coordination ability of aluminum alkoxides. Experimental data do not permit exact assessment of the

* In the case of a substantial intervention of the equilibrium *XVIII* $\rightleftarrows$ *XX* $\rightleftarrows$ *XXII* in the course of the reaction, deuterium would survive[19] at the carbon $C_{(18a)}$ of the hemiacetal *XXII*, but it would be lost through the direct oxidation to the (20*S*)-lactone *XXIa* that would very likely follow. Table I (entry 2) shows that the content of the (20*S*)-lactone is not higher than the concentration of the deuteriolactone.

role of the catalyst in the course of the reaction though it is very likely that in this series of experiments the Oppenauer–Meerwein–Ponndorf reaction of intermediary hemiacetals heavily contributes to the formation of the (20*S*)-lactone *XXI* (see Table I, entry 6 and 8).

In this paper 4 examples of the intramolecular hydride shift are given (the formation of lactones from keto aldehydes, the formation of *XXII* from both *XX* and *XVIII*). The predominance of the products with the (20*S*)-configuration in all these cases is to be understood in the light of stereochemical requirements of the hydride ion addition to a carbonyl group[20]. The most likely conformation of the 17β-acetyl group[21–25] is favourable to intramolecular hydride ion shift under the formation of (20*S*)-derivatives.

EXPERIMENTAL

The melting points are determined on a Kofler block and are uncorrected. Analytical samples were dried at 50°C and 0·2 Torr for 2 hours over phosphorus pentoxide. Optical rotations were measured in chloroform and circular dichroism in methanol (Roussel-Jouan Dichrograph).

TABLE I

t-Butoxide Catalyzed Oppenauer Oxidation of 18a,20-Disubstituted Pregnane Derivatives
Composition of the lactone fraction based on molecular elipticity.

Entry	Starting material	Proportion of the (20*R*)-lactone %	Proportion of the (20*S*)-lactone %
	Potassium tert-butoxide		
1	diol *XVI*	54·6	45·4
2	diol *XVII*[a]	56·2	43·8
3	hemiacetal *XVIII*	85·1	14·9
4	hemiketal *XX*	13·3	86·7
	Aluminum tert-butoxide		
5	diol *XVI*	18·6	81·4
6	diol *XVII*[b]	16·5	83·5
7	hemiacetal *XVIII*	25·5	74·5
8	hemiacetal *XVIII*[c]	24	76

[a] Proportion of $C_{(20)}$-deuteriolactone: 47·7% (mass spectrometry); [b] proportion of $C_{(20)}$-deuteriolactone: 79·8%; [c] compound *XVIII* was treated with aluminum tert-butoxide in xylene and oxidized to a mixture of lactones according to Jones.

The ^{1}H-NMR spectra were measured on a Varian HA-100 instrument in deuteriochloroform using tetramethylsilane as internal standard. The mass spectra of the deuterioderivatives (AEI MS 902) were evaluated after comparison with the spectra of compounds devoid of deuterium.

[18,18-$^2H_2$]-5α-Pregnane-3β,18,20α-triol (*V*)

3β,20α-Dihydroxy-5α-pregnan-18-oic acid lactone[6] (*IV*, 150 mg) was reduced by four hours refluxing with lithium aluminum deuteride (about 200 mg) in dioxan (5 ml). The excess hydride was destroyed with a few drops of a saturated solution of sodium sulfate in water and the mixture was dried with anhydrous sodium sulfate. Inorganic material was filtered off and extracted with chloroform. The filtrate was evaporated and crystallized. M.p. 220–223°C (chloroform, heptane, 95 mg), $[\alpha]_D^{20}$ +37° (*c* 0·6). For $C_{21}H_{34}D_2O_3$ (338·5) calculated: 74·51% C, 11·31% H; found: 10·90% H, 74·66% C.

[18,18-$^2H_2$]-5α-Pregnane-3β,18,20β-triol (*X*)

3β,20β-Dihydroxy-5α-pregnan-18-oic acid lactone[14] (*IX*, 100 mg) was reduced under the conditions given above. M.p. 235–236°C (dichloromethane, benzene, 76 mg) $[\alpha]_D^{20}$ 0° (*c* 0·6); IR spectrum (nujol): 3310 cm^{-1}, mass spectrum: $[M-1]^+ = 337$. For $C_{21}H_{34}D_2O_3$ (338·5) calculated: 74·51% C, 11·31% H; found: 74·30% C, 10·96% H.

18-Homo-5α-pregnane-18α,20β-diol (*XVI*)

Lactone *XV* (300 mg) was reduced by lithium aluminum hydride to yield diol *XVI*, m.p. 199 to 200°C (chloroform, benzene), $[\alpha]_D^{20}$ −5° (*c* 0·6); IR spectrum ($CHCl_3$): 3610 cm^{-1}. For $C_{22}H_{38}O_2$ (334·5) calculated: 78·92% C, 11·45% H; found: 78·62% C, 11·59% H.

[18a,18a-$^2H_2$]-18-Homo-5α-pregnane-18a,20β-diol (*XVII*)

Lactone *XV* (100 mg) was reduced with lithium aluminum deuteride under the same conditions as above. M.p. 199–200°C (chloroform, benzene), $[\alpha]_D^{20}$ −8° (*c* 1·2); mass spectrum: $[M-15]^+ = 321$, $[M-44]^+ = 292$. For $C_{22}H_{36}D_2O_2$ (336·5) calculated: 78·52% C, 11·97% H; found: 78·26% C, 12·10% H.

3β,20β-Dihydroxy-5α-pregnane-18-carboxylic Acid Lactone (*XII*)

3β,20β-Dihydroxy-5-pregnane-18-carboxylic acid lactone[16] (4 g) was hydrogenated in acetic acid (100 ml) on platinum oxide (0·5 g). After 18 hours the catalyst was filtered off, the filtrate evaporated *in vacuo* and crystallized. M.p. 213–215°C (2·7 g, aqueous ethanol), $[\alpha]_D^{20}$ +74° (*c* 1·0); IR spectrum ($CHCl_3$): 1730, 1265, 1256, 3610, 1035 cm^{-1}. For $C_{22}H_{34}O_3$ (346·5) calculated: 76·26% C, 9·89% H; found: 76·23% C, 9·86% H;

20β-Hydroxy-3-oxo-5α-pregnane-18-carboxylic Acid Lactone (*XIII*)

Hydroxy lactone *XII* (2·5 g) was oxidized in acetone according to Jones. After the standard work-up the product was crystallized from acetone and heptane. M.p. 201–202°C, $[\alpha]_D^{20}$ +106° (*c* 1·3); IR spectrum ($CHCl_3$): 1711, 1730 cm^{-1}. For $C_{22}H_{32}O_3$ (334·5) calculated: 76·70% C, 9·36% H; found: 76·70% C, 9·41% H.

20β-Hydroxy-5α-pregnane-18-carboxylic Acid Lactone (*XV*)

Keto lactone *XIII* (2·4 g) was dissolved in ethane-1,2-dithiol (3·5 ml) and boron trifluoride etherate (3·5 ml) was added. After 15 minutes the mixture was diluted with chloroform (60 ml) and set aside for 18 hours at room temperature. The mixture was washed with a saturated solution of sodium chloride in water, dried over sodium sulfate and evaporated. The raw thioketal *XIV* was refluxed with Raney nickel (25 g) in ethanol (100 ml). After 18 hours the inorganic material was filtered off and washed, and the filtrate was evaporated and purified by column chromatography on silica gel (benzene). M.p. 144—146°C (cyclohexane, 1·7 g), $[\alpha]_D^{20}$ +85° (*c* 1·0); IR spectrum: 1734 cm^{-1} ($CHCl_3$); $\Delta\varepsilon_{218nm} = 3{\cdot}70$; mass spectrum: $M^+ = 330$; ^{1}H-NMR spectrum: 0·785 (s, 3 H, $C_{(19)}$-protons), 1·357 (c, $J = 6{\cdot}5$ Hz, 3 H, $C_{(21)}$-protons), 3·99 (quintet, $W = 28$ Hz, 1 H, $C_{(20)}$-proton), 2·16 and 2·46 (AB system, $J = 15$ Hz, $C_{(18)}$-protons) p.p.m. For $C_{22}H_{34}O_2$ (330·5) calculated: 79·95% C, 10·37% H; found: 78·89% C, 10·39% H.

18a,20β-Epoxy-18-homo-5α-pregnan-18aξ-ol (*XVIII*)

From a solution of lactone *XV* (144 mg) in toluene (30 ml) 10 ml of azeotropic mixture was distilled off, and lithium tri-tert-butoxy aluminum hydride (450 mg) was added. The mixture was refluxed for 20 minutes and poured onto an aqueous solution of sodium potassium tartrate. The product was extracted with benzene, dried over sodium sulfate and purified by thin layer chromatography on silica gel with 25% of ether in benzene. After detection with morin in acetone a single zone (R_F 0·5) was eluted with ether. M.p. 142—146°C (dichlormethane, heptane, 90 mg), IR spectrum (CCl_4): 3600, 1109, 1087, 1020, 1003 cm^{-1}. For $C_{22}H_{36}O_2$ (332·5) calculated: 79·46% C, 10·91% H; found: 79·15% C, 10·88% H.

18a-Triphenylmethoxy-18-homo-5α-pregnan-20-one (*XIX*)

Diol *XVI* (95 mg) was treated with triphenylmethyl chloride (600 mg) in refluxing pyridine (5 ml). After 3 hours the mixture was evaporated *in vacuo* and purified by thin layer chromatography on alumina (act. III—IV, 30% of benzene in light petroleum). The more polar zone was eluted with ether and the product (460 mg) oxidized according to Jones without further purification. The usual work-up afforded ketone *XIX* which after thin layer chromatography on silica gel (5% of ether in light petroleum) and crystallization melted at 86—88°C (acetone, —60°C, 190 mg), $[\alpha]_D^{20}$ +32° (*c* 1·2); IR spectrum (CCl_4): 1705, 1357, 1218, 1068 cm^{-1}; ^{1}H-NMR spectrum: 0·87 (s, 3 H, $C_{(19)}$-protons), 1·69 (s, 3 H, $C_{(21)}$-protons), 7·2 (mt, 15 H, aromatic protons) p.p.m.

18a,20-Epoxy-18-homo-5α-pregnan-20ξ-ol (*XX*)

A solution of triphenylmethoxy ketone *XIX* (130 mg) in aqueous acetic acid (90%, 30 ml) was refluxed for 10 minutes and evaporated. The product was purified by thin layer chromatography on silica gel (20% of ether in benzene). After detection with morin in acetone the more polar zone (R_F approx. 0·4) was eluted with ether. M.p. 200—207°C (dichloromethane, heptane); IR spectrum (CCl_4): 3595, 3580, 1027 cm^{-1}. For $C_{22}H_{36}O_2$ (332·5) calculated: 79·46% C, 10·91% H; found: 79·19% C, 11·16% H.

Attempted Isomerization of 3β,18-Dihydroxy-5α-pregnan-20-one (*VIII*)

a) Hemiketal *VIII* (2 mg) was treated with a saturated solution of potassium tert-butoxide in tert-butanol at 90°C. After 1 hour's reaction the mixture was diluted with benzene, washed with dilute hydrochloric acid and water, dried over sodium sulfate and evaporated. The product

appeared to be unchanged on thin layer chromatogram (50% of ether in benzene). The product was oxidized according to Jones and thin layer chromatography revealed the presence of 3,20-diketo-5α-pregnan-18-oic acid without detectable amounts of lactones *VI* or *IX*.

b) Hemiketal *VIII* (20 mg) was treated with potassium tert-butoxide (13 mg) in refluxing xylene (4 ml). After 20 hour's treatment the mixture was diluted with benzene and worked up as above: a redox isomerization of the starting compound *VIII* was not observed.

Attempted Isomerization of 3β,20β-Dihydroxy-5α-pregnan-18-ol (*VII*)

Hemiacetal *VII* (20 mg) was treated with potassium tert-butoxide in xylene as above. Thin layer chromatography of the product of Jones oxidation proved that no redox isomerization occurred: all the material was oxidized to lactone *VI* or *XI*.

Isomerization of 18a,20-Epoxy-18-homo-5α-pregnan-20ξ-ol (*XX*)

Hemiketal *XX* (10 mg) was treated with potassium tert-butoxide in tert-butanol at 80°C. After 6 hours the mixture was diluted with chloroform and washed with dilute hydrochloric acid and water. After evaporation the product was oxidized according to Jones and separated by means of thin layer chromatography on silica gel (15% of ether in benzene). The zone corresponding to lactone *XXI* was eluted with ether affording 4 mg of lactones. IR spectrum ($CHCl_3$): 1730 cm^{-1}. $\Delta\varepsilon_{219nm}$ −0·70.

Isomerization of 18a,20β-Epoxy-18-homo-5α-pregnan-18aξ-ol (*XVIII*)

From the solution of the hemiacetal *XVIII* (10 mg) in xylene (12 ml) 4 ml of azeotropic mixture was distilled off and then the mixture was refluxed with aluminum tert-butoxide (60 mg) for 8 hours under nitrogen. Working up as above afforded 5 mg of lactones *XV* and *XXI*. $\Delta\varepsilon_{220nm}$ −0·71.

Oxidation According to Oppenauer

A solution of a steroid (45 mg) and 9-fluorenone or N-methyl-4-piperidone (250 mg) was dried by removal of 3 ml of an azeotropic mixture and then treated with potassium or aluminum tert-butoxide (35 mg). An additional 5 ml of xylene were distilled off in the course of the reaction. The mixture was cooled and diluted with benzene, washed with dilute hydrochloric acid and water. The solvents were removed by steam distillation (about 10—20 minutes only) and the products were taken up into chloroform and purified by thin layer chromatography with 10—20% of ether in benzene, detection with morin in methanol. The zone with the R_F value identical with that of the authentic lactone was eluted with ether and analyzed by IR, CD, ^{1}H-NMR and mass spectrometry. The yields are given in weight per cents (see Table II).

20α-Hydroxy-5α-pregnane-18-carboxylic Acid Lactone (*XXI*)

Diol *XVI* (300 mg) was oxidized under the given conditions using aluminum tert-butoxide and N-methyl-4-piperidone. The resulting mixture of lactones *XV* and *XXI* ($\Delta\varepsilon = -1{\cdot}11$) was reduced by means of lithium aluminum hydride and then oxidized once more. The mixture of lactones *XXI* and *XV* (215 mg, $\Delta\varepsilon$ −1·39) was repeatedly crystallized from acetone and heptane. The pure lactone *XXI* melted at 187—189°C (60 mg). $[\alpha]_D^{20}$ +13° (*c* 0·9), $\Delta\varepsilon_{218}$ −2·22;

IR spectrum ($CHCl_3$): 1727; IR spectrum (KBr): 1714 and 1728 cm^{-1}; ^{1}H-NMR spectrum: 0·77 (s, 3 H, $C_{(19)}$-protons), 1·32 (d, $J = 6·5$ Hz, 3 H, $C_{(21)}$-protons), 2·07 and 2·42 (AB system, $J_{AB} = 18$ Hz, $C_{(18)}$-protons), 4·55 (quartet, $W = 19$ Hz, $C_{(20)}$-proton) p.p.m.

For $C_{22}H_{34}O_2$ (330·5) calculated: 79·95% C, 10·37% H; found: 79·91% C, 10·41% H.

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TABLE II

Yields of Lactones from the Oppenauer Oxidation of 18,20-Disubstituted Pregnanes Catalysed with tert-Butoxides

Entry	Starting compound	Reaction time, h	Yield %	Molecular elipticity (wave length, nm)
		Potassium tert-butoxide		
1	*V*[a]	11	23	+1·16 (288), +0·66 (227)
2	*X*[b]	24	20	+1·16 (288), −0·19 (227)
3	*XVI*[c]	8	80	+1·01 (218)
4	*XVII*[d,e]	12	84	+1·11 (218)
5	*XVIII*	5	84	+2·82 (218)
6	*XX*	3	74	−1·43 (217)
		Aluminum tert-butoxide		
7	*XVI*	6	93	−1·11 (218)
8	*XVII*[d,f]	5	76	−1·24 (218)
9	*XVIII*	6	75	−0·71 (218)

[a] M.p. 158–176°C, after crystallization 174–178°C (heptane); ^{1}H-NMR spectrum exhibits signals of the compound *Va* only. Proportion of $C_{(20)}$-deuteriolactone: 18·2% (mass spectrometry); [b] IR spectrum ($CHCl_3$): 1710, 1750 cm^{-1}; $[\alpha]_D^{20}$ +30 (literature values[6,14] of compound *VI* and *XI* are +17° and +35° respectively), ^{1}H-NMR spectrum contains signals of lactone *XI* only (0·96, s, 3 H; 1·4, d, $J = 6·5$ Hz, 3 H; 4·30, q $J = 6·5$ Hz, 1 H p.p.m.). Proportion of $C_{(20)}$-deuteriolactone: 18·4%; [c] IR spectrum ($CHCl_3$): 1740 cm^{-1}, ^{1}H-NMR spectrum contains signals of $C_{(19,20,21)}$-protons of the compounds *XV* and *XXI*; [d] ^{1}H-NMR-spectrum reveals signals of $C_{(19,20,21)}$-protons of compounds *XV* and *XXIb*; [e] Proportion of $C_{(20)}$-deuteriolactone: 47·7%; [f] Proportion of $C_{(20)}$-deuteriolactone: 79·8%.

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