Table II.

	Evodol acetate (IV)[a]	Limonin diosphenol acetate (V)
IR ν_{max}^{Nujol} cm^{-1}	1753	1753
	1739	1739
	1695	1695
	1650	1650
UV λ_{max}^{EtOH} mμ (ε)	246 (12300)	245 (12000)
$[\alpha]_D$ (c. in solvent)	− 97° (0.484 $CHCl_3$)	− 101° (1.20 $CHCl_3$)
m.p. (decomp.) (on Kofler)	300～312°	306～313°
	mixed m.p. 299～311°	

a) Evodol acetate (IV), m.p. 298～299° (decomp.) (H_2SO_4 bath)

Experimental

Evodol (I)——Prepared by means of the method of the literature itself.[1,2] It gave brown coloration with $FeCl_3$ in EtOH. *Anal.* Calcd. for $C_{26}H_{28}O_9$: C, 64.45; H, 5.83. Found: C, 64.47; H, 5.86.

Evodol Acetate (IV)——Prepared by means of the method of the literature itself.[4] *Anal.* Calcd. for $C_{29}H_{30}O_{10}$: C, 63.87; H, 5.74; Ac., 8.75. Found: C, 63.77; H, 5.65; Ac., 8.55.

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Katsumi Tanabe and Yasuhiro Morisawa: Steroid Series. XI.[1] Synthesis of B-Norsteroid.

(*Takamine Laboratory, Sankyo Co., Ltd.*[*1])

Lettré and Jahn described the formation of 6-methoxy-5,6-seco-5ξ-cholestane-3β,5-diol 3-acetate 5,6-peroxide (IIa) in 60% yield by ozonization of cholesterol acetate (Ia) in carbon tetrachloride containing methanol.[2] In the course of our studies on B-norsteroid we found that IIa could be obtained in a higher yield under slightly modified reaction conditions, and it proved to be a useful substance for the preparation of 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (IVa), whose synthesis by other procedures and conversion into B-norchlest-5-en-3β-ol acetate have been reported from this laboratory.[3]

When cholesterol acetate (Ia) was treated with an ozonized air in dichloromethane containing 1% of methanol under cooling with dry ice-acetone mixture, there was obtained the peroxidic compound (IIa) of m.p. 151° (decomp.) in 81% yield, which showed a positive potassium iodide test, a negative Criegee test for hydroperoxide with lead tetraacetate, and the presence of a methoxyl group by Zeisel determination. The infrared spectrum in carbon tetrachloride solution exhibiting a band at 3330 cm^{-1} due to a hydroxyl group was superimposable with that described by the German workers.

Reduction of IIa with zinc dust and acetic acid in dichloromethane solution afforded an oily substance, whose infrared spectrum was identical in all regions with that of 3β-hydroxy-5-oxo-5,6-secochlestan-6-al acetate (IIIa) obtained previously.[3]

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*1 Nishishinagawa, shinagawa-ku, Tokyo (田辺克巳, 森沢靖弘).

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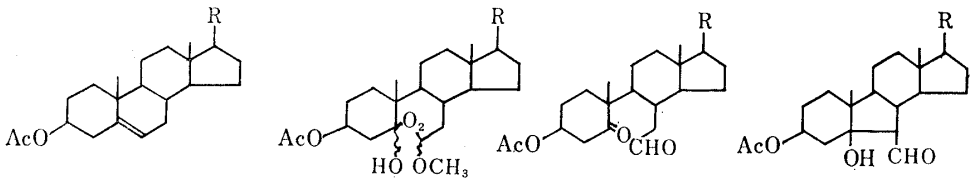

I a, b, c II a, b, c III a, b, c IV a, b, c

a : $R=C_8H_{17}$ b : $R=COCH_3$ c : $R=O$

The intramolecular aldol condensation of the seco-oxoaldehyde (IIIa) into 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (IVa) was effected by stirring of its benzene solution with alumina at room temperature for three hours. The overall yield of IVa from cholesterol acetate (Ia) amounted to 74% of the theoretical.

A similar ozonization reaction was applied to 3β-hydroxypregn-5-en-20-one acetate (Ib) and 3β-hydroxyandrost-5-en-17-one acetate (Ic) t giv eo6-methoxy-3β,5-dihydroxy-5,6-seco-5ξ-pregnan-20-one 3-acetate 5,6-peroxide (IIb), m.p. 155~156° (decomp.), and 6-methoxy-3β,5-dihydroxy-5,6-seco-5ξ-androstan-17-one 3-acetate 5,6-peroxide (IIc), m.p. 147~148° (decomp.), respectively. Reduction of IIb and IIc to the seco-oxo-aldehyde (IIIb) and (IIIc) with zinc dust and acetic acid, followed by cyclization reaction with alumina gave the known 3β,5-dihydroxy-6β-formyl-B-nor-5β-pregnan-20-one 3-acetate (IVb), m.p. 184~185°, and 3β,5-dihydroxy-6β-formyl-B-nor-5β-androstan-17-one 3-acetate (IVc), m.p. 132~134°,[3] respectively.

Experimental

6-Methoxy-5,6-secocholestane-3β,5-diol 3-Acetate 5,6-Peroxide (IIa)——A solution of 2 g. of cholesterol acetate (Ia) in 160 cc. of CH_2Cl_2 containing 1% of MeOH was treated with a stream of an ozonized air (0.33 mmole of O_3/min.) until the solution turned to pale blue. The solvent was removed below 30° under a reduced pressure and the residual crystals were recrystallized from MeOH to afford 1.93 g. (81%) of 6-methoxy-5,6-secocholestane-3β,5-diol 3-acetate 5,6-peroxide (IIa) as needles of m.p. 151~152° (decomp.), (lit.[2] m.p. 145~146° (decomp.)). *Anal.* Calcd. for $C_{30}H_{52}O_6$: C, 70.83; H, 10.30; OCH_3, 6.09. Found : C, 70.80; H, 10.28; OCH_3, 5.83. IR ν_{max}^{Nujol} cm^{-1} : 3250 (OH), 1740, 1250 (OAc). IR $\nu_{max}^{CCl_4}$ cm^{-1} : 3320 (OH), 1742, 1243 (OAc).

6β-Formyl-B-nor-5β-cholestane-3β,5-diol 3-Acetate (IVa)——To an ozonized solution of 5 g. of cholesterol acetate (Ia) prepared as above was added 10 g. of Zn dust and to this mixture 40 cc. of AcOH was dropwise added under stirring and cooling at 0°. After the addition was completed, the mixture was stirred for additional half an hour to show a negative KI test. Zn dust was separated by filtration and washed with CH_2Cl_2 several times. The combined organic solution was washed with aq. 2% $NaHCO_3$ solution and water until neutral and dried over Na_2SO_4. Evaporation of the solvent gave an oily residue (IIIa), which was dissolved in 250 cc. of benzene and stirred with 50 g. of neutral alumina at room temperature for 3 hr. The alumina was separated by filtration and washed well with $CHCl_3$. The combined filtrate was condensed to dryness under a reduced pressure, the residue was recrystallized from MeOH to afford 3.8 g. (74%) of 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (IVa) of m.p. 91~92°. The structure was confirmed by mixed melting point determination and comparison of the IR spectra with the authentic sample.[3] *Anal.* Calcd. for $C_{29}H_{48}O_4$: C, 75.60; H, 10.50. Found : C, 75.72; H, 10.64.

6-Methoxy-5,6-secopregnane-3β,5-diol 3-Acetate 5,6-Peroxide (IIb) and 3β,5-Dihydroxy-6β-formyl-B-nor-5β-pregnan-20-one 3-Acetate (IVb)——A solution of 5 g. of 3β-hydroxypregn-5-en-20-one 3-acetate (Ib) in 400 cc. of CH_2Cl_2 containing 1% of MeOH was treated with an ozonized air as described for the cholestane series. One tenth of the mixture ozonized was taken up and the solvent was removed to leave a crystalline product, which was recrystallized from hexane-acetone to give 6-methoxy-3β,5-dihydroxy-5,6-secopregnan-20-one 3-acetate 5,6-peroxide (IVb) of m.p. 155~156° (decomp.) as needles. *Anal.* Calcd. for $C_{24}H_{38}O_7$: C, 65.73; H, 8.73; OCH_3, 7.07. Found : C, 65.77; H, 8.73; OCH_3, 6.82. IR ν_{max}^{Nujol} cm^{-1} : 3250 (OH), 1740, 1250 (OAc), 1705 (20-CO).

The residual mixture ozonized was reduced with 10 g. of Zn dust and 40 cc. of AcOH, followed by cyclization with 45 g. of neutral alumina in a similar way for the cholestane series to give 3.33 g. (68%) of 6β-formyl-3β,5-dihydroxy-B-nor-5β-pregnan-20-one 3-acetate (IVb) melting at 104~106°, which showed

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no depression of melting point on admixture with the authentic sample.[3] *Anal.* Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.69; H, 8.75.

6-Methoxy-3β,5-dihydroxy-5,6-secoandrostan-17-one 3-Acetate 5,6-Peroxide (IIc) and 6β-Formyl-3β,5-dihydroxy-B-nor-5β-androstan-17-one 3-Acetate (IVc)——A solution of 5 g. of 3β-hydroxyandrost-5-en-17-one acetate (Ic) in 400 cc. of CH_2Cl_2 containing 1% of MeOH was treated with an ozonized air as described above. One tenth of the ozonized mixture was separated, the solvent was removed to give a semisolid product, which was recrystallized from hexane-Me_2CO to yield 6-methoxy-3β,5-dihydroxy-5,6-seco-6-androstan-17-one 3-acetate 5,6-peroxide (IIc) melting at 147~148° (decomp.). *Anal.* Calcd. for $C_{22}H_{34}O_7$: C, 64.37; H, 8.35; OCH_3; 7.55. Found: C, 63.92; H, 8.21; OCH_3, 7.20. IR ν_{max}^{Nujol} cm^{-1}: 3280 (OH), 1730, 1240 (OAc).

The residual mixture ozonized was reduced with Zn dust and AcOH and cyclized with alumina as described above to yield 3.16 g. (64%) of 6ξ-formyl-3β,5-dihydroxy-B-nor-5ξ-androstan-17-one 3-acetate (IVc) of m.p. 132~134°. *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.45; H, 8.21.

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Summary

Cholesterol acetate (Ia), 3β-hydroxypregn-5-en-20-one acetate (Ib) and 3β-hydroxyandrost-5-en-17-one acetate (Ic) were ozonized in dichloromethane containing a small amount of methanol to give the corresponding 3β-acetoxy-5-hydroxy-6-methoxy-5,6-peroxy-5,6-seco steroid compounds (IIa, b, c), which on reduction with zinc dust and acetic acid afforded 3β-acetoxy-5-oxo-5,6-secosteroid-6-als (IIIa, b, c). Cyclization reaction of (IIIa, b, c) was conducted by stirring with alumina in benzene solution to yield 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (IVa), 6β-formyl-3β,5-dihydroxy-B-nor-5β-pregnan-20-one 3-acetate (IVb) and 6β-formyl-3β,5-dihydroxy-B-nor-5β-androstan-17-one 3-acetate (IVc), respectively.

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Toshio Kakimoto, Kyozo Hayashi, and Tomoji Suzuki: Synthesis of Quinoline Derivatives of Amino Acid.

(*Faculty of Pharmacy, Kyoto University*[*1])

One of the main requirements among satisfactory chemotherapeutic agents is desired to penetrate into or to be absorbed readily by micro organisms against which it is directed. It is already known that bacterial growth is inhibited to some extent by 3-(4-quinolyl)alanine and other heterocyclic amino acids.[1] Our principal project has been a little far from investigating competitive growth inhibition by amino acid analogs and rather an effect of compounds in which the side chain of the characteristic 2-aminopropionic acid and 2-aminobutyric acid is attached at its ω-carbon to quinoline and its nucleus substituent has been studied.

*1 Yoshida-Konoe-che, Sakyo-ku, Kyoto (柿本年雄, 林 恭三, 鈴木友二).

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