[Chem. Pharm. Bull. 12 (4) 473 ~ 479]

UDC 547.92.02

70. **Hiroko Hasegawa and Kyosuke Tsuda :** Stereochemistry of Steroids containing Aromatic A-Ring. IV.[*1],[*2] 9,10β-Epoxysteroid.

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In the previous paper1) of this series, it was reported that bromination of $\Delta^{9(11)}$-estrone acetate (Ib) gave a normal addition product, 9,11-dibromoestrone acetate, while in the case of the methyl ether (Ic) equilenin methyl ether was obtained because of the activation of C_9 position by an electron donating group at C_3 such as methoxyl group. Also epoxidation of $\Delta^{9(11)}$-estrone acetate (Ib) with perbenzoic acid produced stable 9,11α- and 9,11β-epoxyestrone acetates. In this report, epoxidation reaction of $\Delta^{9(11)}$-estrone (Ia) was investigated in order to examine the effect of an electron donating group at C_3.

Treatment of $\Delta^{9(11)}$-estrone (Ia) with three molar equivalents of perbenzoic acid in chloroform afforded an epoxydienone (Ⅱ) in 40~50% and a phenolic compound (Ⅲa) in 3~10% yield.

Epoxydienone (Ⅱ), $C_{18}H_{18}O_4$, showed an ultraviolet absorption maximum at 261.5 mμ (ε 19000) and infrared bands at 1743, 1718, 1663, 1636, and 1604 cm^{-1} which strongly suggested the presence of a 1,4-dien-3-one system, six-membered ring carbonyl group and the absence of a hydroxyl group. The nuclear magnetic resonance[*4] spectrum showed peaks due to three vinyl hydrogens at 6.27~6.70.

When Ⅱ was treated with zinc in acetic acid, 3-hydroxy-9β-estra-1,3,5(10)-triene-11,17-dione (Ⅳa)2) was obtained. The identity was confirmed by mixed melting point and a comparison of its infrared spectra with that of an authentic sample. This result showed that the steroidal skeleton of Ⅱ was unchanged and the carbonyl group of the six-membered ring was at C_{11}. On hydrogenation with 5% palladium-charcoal Ⅱ readily consumed one molar equivalent of hydrogen to afford in high yield a phenolic compound (Ⅴa) showing ultraviolet absorption maxima at 278 mμ (ε 1460) and 284.7 (shoulder). Acetylation of Ⅴa with acetic anhydride in pyridine gave a monohydroxymonoacetate (Ⅴb). The hydroxyl group of Ⅴb was not oxidized by chromic anhydride in pyridine and, thus, might be tertiary. Since Ⅳa was obtained on reduction of Ⅴa with zinc in boiling acetic acid, the tertiary hydroxyl group of Ⅴb was on the carbon adjacent to the C_{11} carbonyl group, *i.e.*, on C_9 because the hydroxyl group of an α-hydroxyketone is eliminated on reduction with zinc in acetic acid.3) Therefore the structure of Ⅴa was determined to be 3,9-dihydroxyestra-1,3,5(10)-triene-11,17-dione, in which the configuration of the hydroxyl group at C_9 was determined as below.

Phenolic compound (Ⅲa), $C_{18}H_{20}O_4$, showed ultraviolet maxima at 275.5 mμ (ε 1340), 282 (1250) and had a six-membered carbonyl group The elemental analysis indicated that Ⅲa was isomeric with Ⅴa. Acetylation of Ⅲa with acetic anhydride in pyridine gave a monohydroxymonoacetate (Ⅲb). The hydroxyl group of Ⅲb was resistant to oxidation

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[*1] This paper constitutes Part XLⅦ of a series entitled "Steroid Studies" by K. Tsuda; Part XLⅦ: This Bulletin, **11**, 1275 (1963).

[*2] This paper will constitute a part of the dissertation to be submitted by H. Hasegawa in partial fulfilment of the requirement for the Doctor's degree.

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[*4] The NMR spectra were measured in $CDCl_3$ with tetramethylsilane as internal standard, using a Varian A-60 instrument. All chemical shifts were reported in p.p.m. as δ value.

1) K. Tsuda, S. Nozoe, Y. Okada : This Bulletin, **11**, 1022 (1963).

2) H. Hasegawa, S. Nozoe, K. Tsuda : *Ibid.*, **11**, 1037 (1963).

3) R. S. Rosenfeld : J. Am. Chem. Soc., **79**, 5540 (1957).

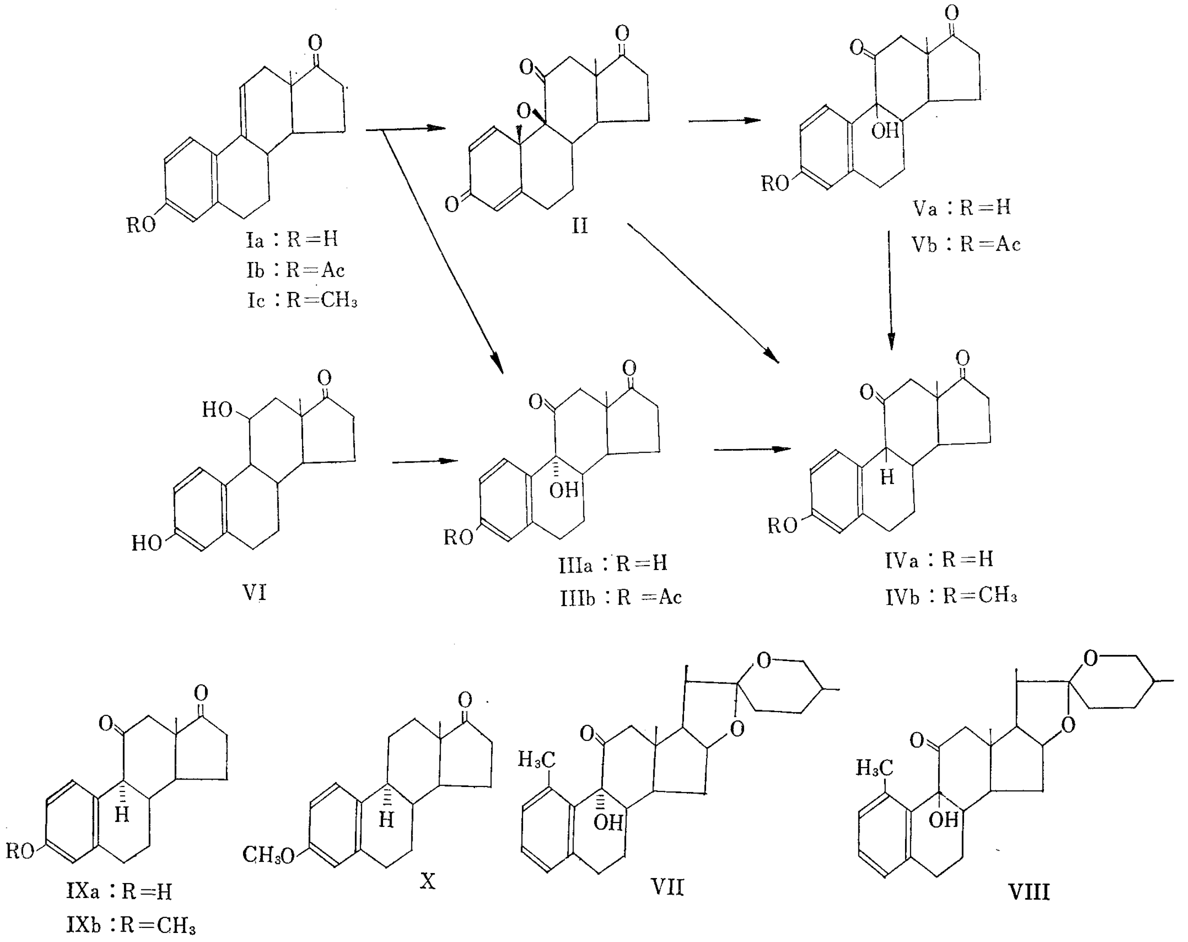

Chart 1.

by chromic anhydride in pyridine and thus might be tertiary. Reduction of IIIa with zinc in acetic acid resulted in hydrogenolysis to yield IVa as did Va.

Accordingly the structure of IIIa was determined to be 3,9-dihydroxyestra-1,3,5(10)-triene-11,17-dione, in which the configuration of hydroxyl group at C_9 was different than Va. Also IIIa was obtained by oxidation of 3,11β-dihydroxyestra-1,3,5(10)-trien-17-one (VI)[4] with chromic anhydride in pyridine.

The configuration of the hydroxyl group of IIIb and Vb was assigned by measurement of intramolecular hydrogen bonding in the infrared spectra. The hydroxyl and carbonyl absorption bands in dilute carbon tetrachloride solution (c=0.0004*M*, 1=50 mm.) of IIIb and Vb were observed at 3609, 1730 and 3483, 1713 cm^{-1}, respectively.[*5] The latter indicated the presence of intramolecular hydrogen bonding between C_9-hydroxyl and C_{11}-carbonyl group, while the former did not. Inspection of Dreiding Model as shown in Chart 2 indicates that the 9β-hydroxy isomer (A) should exhibit hydrogen bonding, while the 9α-hydroxy isomer (B) can not. Thus the α- and β-configuration was assigned to the hydroxyl group of IIIb and Vb, respectively. Igarashi[5] also reported that

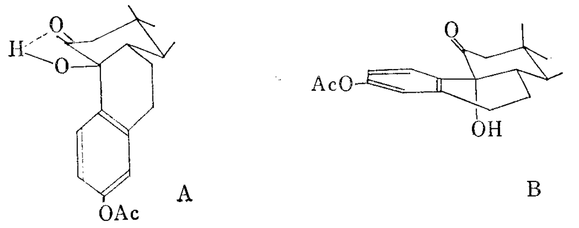

Chart 2.

[*5] Parkin-Elmer Model 221 NaCl and grating was used for measurement of the IR spectra.

4) E. G. Magerlein, J. A. Hogg: J. Am. Chem. Soc., **80**, 2220 (1958).

5) K. Igarashi: This Bulletin, **9**, 729 (1961).

9α-hydroxy isomer (VII) of meteogenone derivatives don't show intramolecular hydrogen bonding between C_9-hydroxy and C_{11}-carbonyl in infrared spectra, whereas the 9β-hydroxy isomer (VIII) do.

This configurational assignment was supported by comparison of the chemical shifts in the nuclear magnetic resonance spectrum of the C_1 hydrogen of IIIb and Vb with

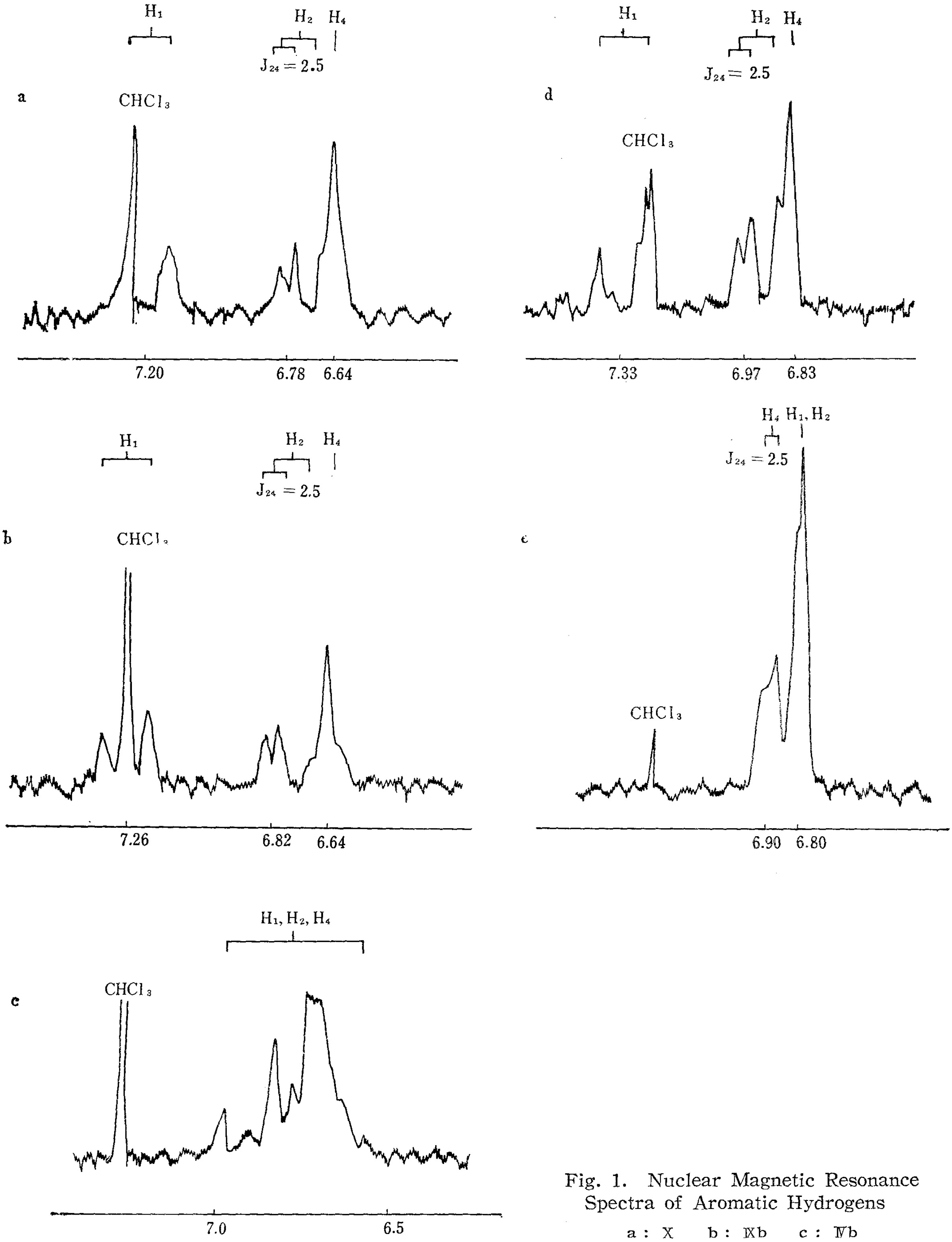

Fig. 1. Nuclear Magnetic Resonance Spectra of Aromatic Hydrogens

a : X b : IXb c : IVb
d : IIIb e : Vb

those of 3-methoxyestra-1,3,5(10)-triene-11,17-dione (Ⅸb)[2] and 3-methoxy-9β-estra-1,3,5(10)-triene-11,17-dione (Ⅳb)[2] which possess no hydroxyl group at C_9. As shown in Fig. 1, the doublet of the C_1 hydrogen of the 9α-isomer (Ⅸb) was observed at 7.25, $J_{12}=8$ c.p.s., at a slightly lower field as compared with that of estrone methyl ether (Ⅹ) (7.20), while that of the 9β-isomer (Ⅳb) was observed at a higher field by more than 0.2 p.p.m. overlapping with C_2 and C_4 hydrogens. This chemical shift difference of the C_1 hydrogens due to B/C ring juncture was also observed in the case of isomers (Ⅲb and Ⅴb). The former had the signal at 7.33, $J_{12}=8$ c.p.s., while the latter at a higher field, 6.80, overlapping with C_2 hydrogen. This difference seemed to be caused by either anisotropy of the carbon-carbon bonds of C ring[6] or an anisotropic shielding of the C_{11} carbonyl group[6] which has little effect on the chemical shift in the case of B/C-trans juncture as mentioned above.

Since the structure of Ⅴa was shown to be 3,9β-dihydroxy-9β-estra-1,3,5(10)-triene-11,17-dione, the structure of Ⅱ was assigned to 9,10β-epoxy-9β-estra-1,4-diene-3,11,17-trione. Accordingly, conversion of Ia into Ⅱ is an oxidative phenol-dienone rearrangement.[*6]

Interestingly, the ultraviolet absorption maximum at 261.5 mμ of Ⅱ was unusual as compared with 244 mμ of similar 1,4-dien-3-one system of steroid with methyl group at C_{10}.[7] The bathochromic shift by 17.5 mμ was apparently caused by additional conjugation of the epoxy group with the 1,4-dien-3-one. Cyclopropane and epoxy rings are known to cause bathochromic shift[8] by conjugation with π-bonds. Recently Winstein, *et al.*[9] found that the bathochromic shift for the cyclopropane ring of spiro[2.5]octa-1,4-dien-3-one was 32 mμ.

The mechanism of this reaction with perbenzoic acid might be rationalized as shown in Chart 3. Epoxidation initially takes place at the 9,11-double bond to C and then cleavage[*7] of the epoxy group at C_9 by the electron releasing character of the 3-hydroxy group to an enol form (D) *via* a benzilic carbonium ion. Further attack of D with perbenzoic acid yields E, which is converted to methylenequinone (F) or to Ⅲa. Finally epoxidation of 9,10-double bond of F gives Ⅱ. Since Ⅸa as well as Ⅳa were unchanged when treated with the same reagent, they were shown not to be intermediates in this reaction. A reaction using a slight excess of perbenzoic acid with $\Delta^{9(11)}$-estrone (Ia) gave a lower yield of Ⅱ (23%) and also Ⅸa (3%), whereas the reaction using two moles afforded Ⅱ (30%), Ⅲa (6%) and Ⅳa (6%). Compounds (Ⅸa and Ⅳa) might be formed from D.

Refluxing methanol converted Ⅱ into a phenolic product in good yield. The molecular formula, $C_{19}H_{22}O_5$, suggested the addition of 1 mole of methanol and infrared spectra lacked six-membered ring carbonyl absorption. The methanol adduct possessed only one hydroxyl group, which was acetylated and methylated with diazomethane

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[*6] For another phenol-dienone rearrangement in steroidal phenol see : *a*) A. M. Gold, E. Schwenk : J. Am. Chem. Soc., **80**, 5683 (1958). *b*) F. Mukawa : Tetrahedron Letters, **14**, 17 (1959). *c*) J. S. Mills, T. Barrera, E. Olivares, H. Garcia : J. Am. Chem. Soc., **82**, 5882 (1960). *d*) R. Barner, J. Borgulya, G. Proctor, H. Schmid : Chimia (Switz.), **15**, 492 (1961). *e*) E. Schwenk, C. G. Castle, E. Joachim : J. Org. Chem., **28**, 136 (1963).

[*7] Regarding the direction of cleavage of the epoxy ring, an electron releasing group facilitates the breaking of the C-O bond to which it is attached. R. E. Parker, N. S. Isaacs : Chem. Revs. 773 (1959).

6) L. M. Jackman : "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry" Chapter 7 (1959), Pergamon Press, New York.

7) L. F. Fieser, M. Fieser : "Steroids" p. 20 (1959), Reinhold.

8) T. W. Campbell, S. L. Linden, S. Godshalk, W. G. Young : J. Am. Chem. Soc., **69**, 880 (1947); M. T. Rogers : *Ibid.*, **69**, 2544 (1947); R. H. Eastman : *Ibid.*, **76**, 4115 (1954).

9) R. R. Baira, S. Winstein : *Ibid.*, **85**, 567 (1963).

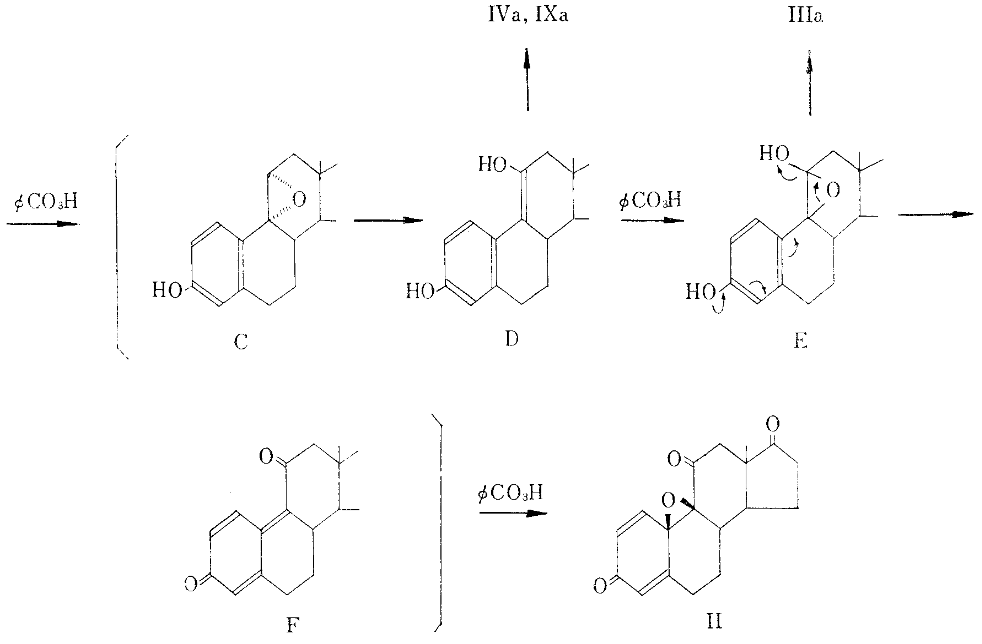

Chart 3.

yielding a monoacetate and a methyl ether, respectively. An analogous ethanol adduct was obtained by refluxing II with ethanol. Also II was converted into a phenolic product in boiling aqueous dioxane. The structures of these products are now being investigated.

Experimental*8

Treatment of $\Delta^{9(11)}$-Estrone (Ia) with Perbenzoic Acid——a) To a stirred solution of 2 g. of 3-hydroxyestra-1,3,5(10),9(11)-tetraen-17-one (Ia) in 1 L. of $CHCl_3$ was added, dropwise, 49 ml. of solution of BzO_2H in $CHCl_3$ containing 3 molar equivalents of BzO_2H at 5° in 10 min. and the mixture allowed to stand at 7° for 3 hr. in the dark. The solution was washed successively with cold 1% $Na_2S_2O_3$ solution, saturated $NaHCO_3$ solution and H_2O, and was dried over anhyd. Na_2SO_4. The solvent was removed at 10~20° under vacuum. The residue was triturated with CH_2Cl_2 and CH_2Cl_2 soluble and insoluble portions were separated. The CH_2Cl_2 soluble portions was chromatographed on 200 g. of silica gel. Elution with CH_2Cl_2 (1.060 g.) and crystallization from Me_2CO yielded 973 mg. of II (44%). Recrystallization afforded an analytical sample, m.p. 153~155° (decomp.). $[\alpha]_D$ +405° (c=1.01). UV: λ_{max} 261.5 mμ (ε 19000). IR ν_{max} cm^{-1}: 1743, 1718, 1663, 1636, 1604. *Anal.* Calcd. for $C_{18}H_{18}O_4$: C, 72.46; H, 6.08. Found: C, 72.56; H, 6.19. The CH_2Cl_2 insoluble portion (105 mg.) was recrystallized from MeOH to yield IIIa, m.p. 222~227° (decomp.), $[\alpha]_D$ +409° (c=0.998). UV λ_{max} mμ (ε): 275.5 (1340), 282.2 (1250). IR ν_{max} cm^{-1}: 3530, 3470, 1733, 1720, 1620, 1580, 1500. *Anal.* Calcd. for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.95; H, 6.74.

b) Two grams of Ia was treated with 2 molar equivalents BzO_2H under above condition. The residue was triturated with CH_2Cl_2 and CH_2Cl_2 soluble and insoluble portions were separated. The CH_2Cl_2 soluble portion was chromatographed on 200 g. of silica gel. Elution with CH_2Cl_2 and crystallization from Me_2CO gave 598 mg. of II. Portion eluted with MeOH-CH_2Cl_2 (1:99) gave a crude product (147 mg.). Recrystallization from Me_2CO afforded material, m.p. 203~208° (decomp.), which was identified as IVa[2] by mixed melting point and IR spectrum. Crystallization of the CH_2Cl_2 insoluble portion (302 mg.) from MeOH gave IIIa.

c) To a stirred solution of 500 mg. of Ia in 180 ml. of $CHCl_3$ was added 4.05 ml. of solution of BzO_2H in $CHCl_3$ (1.05 molar equivalent) at 5° and the mixture allowed to stand at 7° for 19 hr. The solution was washed successively with cold 1% $Na_2S_2O_3$ solution, saturated $NaHCO_3$ solution and H_2O, and was

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*8 All melting points were uncorrected. Optical rotations were measured in dioxane unless otherwise stated. Infrared spectra were obtained with Nujol and ultraviolet spectra were measured in MeOH. The work-up meant washing with 5% HCl saturated $NaHCO_3$ solution and H_2O, successively, and then drying over anhyd. Na_2SO_4.

dried over anhyd. Na_2SO_4. The solvent was removed at 10~20° under vacuum. The residue was chromatographed on 35 g. of silica gel. The first portion eluted with CH_2Cl_2 gave 125 mg. of Ⅱ and the second portion eluted with CH_2Cl_2 afforded 30 mg. of crude Ⅸa. Crystallization from Me_2CO yielded Ⅸa,2) m.p. 199~203°(decomp.). The identity was confirmed by mixed melting point and the comparison of IR spectra with that of an authentic sample.

Reduction of II with Zinc in Acetic Acid——A mixture of 60 mg. of Ⅱ, 2 g. of Zn and 6 ml. of AcOH was refluxed for 2 hr. with stirring. After the filtration of Zn, removal of AcOH, and trituration with H_2O, the resulting precipitate was filtered and dried to afford 30 mg. of material (173~197°). Recrystallization from Me_2CO yield 9 mg. of Ⅳa (203~208°).

3,9β-Dihydroxyestra-1,3,5(10)-triene-11,17-dione (Va)——9,10β-Epoxyestra-1,4-diene-3,11,17-trione (Ⅱ) (300 mg.) in 70 ml. of MeOH was hydrogenated over 45 mg. of 5% Pd-C. One mole of H_2 was readily consumed. After hydrogenation for 2 hr., the catalyst was removed by filtration and the filtrate evaporated to yield 314 mg. of crude material. Crystallization from Et_2O afforded 150 mg. of Ⅴa. The mother liquior was dried and chromatographed on 10 g. of silica gel. The fraction eluted with CH_2Cl_2 was crystallized to give a further 86 mg. of Ⅴa. Recrystallization afforded an analytical sample, 177° (soften) 187~195° (decomp.), $[\alpha]_D$ +244° (c=1.108). UV λ_{max} mμ (ε): 278.2 (1460), 284.7 (shoulder). IR ν_{max} cm^{-1}: 3540, 3345, 1729, 1717, 1622, 1584, 1495. *Anal.* Calcd. for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.12; H, 6.70.

3,9β-Dihydroxyestra-1,3,5(10)-triene-11,17-dione 3-Acetate (Vb)——A mixture of 84 mg. of Ⅴa, 1 ml. of pyridine and 1 ml. of Ac_2O was allowed to stand at room temperature for 16 hr. The solution was poured into ice H_2O and extracted with Et_2O. The Et_2O solution was worked up and evaporated to afford 77 mg. of Ⅴb. Recrystallization from Et_2O afforded an analytical sample, m.p. 150~151°. UV λ_{max} mμ (ε): 266 (427), 273 (392), 291.5 (164). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3490, 1762, 1750, 1715, 1612, 1583, 1497. *Anal.* Calcd. for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.24; H, 6.52.

Oxidation of Vb——A mixture of 43 mg. of Ⅴb, 1 ml. of pyridine and CrO_3-pyridine complex containing 100 mg. of CrO_3 and 1 ml. of pyridine was allowed to stand at room temperature for 17 hr. The mixture was poured into ice H_2O and extracted with Et_2O. The Et_2O solution was worked up and removed in vacuum to yield 28 mg. of solid. Crystallization from Et_2O gave 16 mg. of starting material, m.p. 149~150°.

3,9α-Dihydroxyestra-1,3,5(10)-triene-11,17-dione (IIIa)——To a solution of 100 mg. of 3,11β-Dihydroxyestra-1,3,5(10)-trien-17-one (Ⅵ)4) in 1 ml. of pyridine was added CrO_3-pyridine complex containing 150 mg. of CrO_3 and 1 ml. of pyridine and allowed to stand at room temperature for 14 hr. The mixture was poured into ice H_2O and extracted with AcOEt. The solution was worked up and evaporated in vacuum to give 60 mg. of product. Recrystallization from Me_2CO gave 15 mg. of material, m.p. 220~227° (decomp.), which was identical with Ⅲa obtained by treatment of Ia with BzO_2H

3,9β-Dihydroxyestra-1,3,5(10)-triene-11,17-dione 3-Acetate (IIIb)——A mixture of 100 mg. of Ⅲa, 1 ml. of pyridine and 1 ml. of Ac_2O was allowed to stand at room temperature for 15 hr. The solution was poured into ice H_2O. The resulting precipitate was filtered and recrystallized from Me_2CO to give 40 mg. of Ⅲb, m.p. 235~243° (decomp.), $[\alpha]_D$ +349° (c=1.030). UV λ_{max} mμ (ε): 264.3 (400), 272.2 (340), 297 (105). *Anal.* Calcd. for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.00; H, 6.57.

Reduction of Va with Zinc in Acetic Acid——A mixture of 120 mg. of Ⅴa and 6 g. of Zn in 18 ml. of AcOH was refluxed for 19 hr. with stirring. Zn was removed by filtration and the filtrate concentrated in vacuum. The residue was triturated with H_2O and the resulting precipitate was filtered (100 mg.). Recrystallization from Et_2O gave 25 mg. of Ⅳa m.p. 204~207° (decomp.).

Reductoin of IIIa with Zinc in Acetic Acid——A mixture of 50 mg. of Ⅲa and 2 g. of Zn in 10 ml. of AcOH was refluxed for 4 hr. with stirring. The mixture was worked up as above. Recrystallization from Et_2O gave 10 mg. of Ⅳa, m.p. 203~207° (decomp.).

Methanol Adduct——A solution of 300 mg. of Ⅱ in MeOH was refluxed for 6 hr. Removal of MeOH and crystallization from Me_2CO yielded 230 mg. of MeOH adduct (m.p. 271~272°). Recrystallization afforded an analytical sample, m.p. 272~274.5° (decomp.), $[\alpha]_D$ +158° (c=1.028). UV λ_{max} mμ (ε): 225.8 (6765), 282.5 (2450). IR ν_{max} cm^{-1}: 3445, 1740, 1620, 1593, 1497. *Anal.* Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.11; H, 6.71; OCH_3, 0.92.

Ethanol Adduct——A solution of 50 mg. of Ⅱ in EtOH was refluxed for 2 hr. Removal of EtOH and crystallization from Et_2O afforded 35 mg. of EtOH adduct, m.p. 236~240° (decomp.), $[\alpha]_D$ +168° (c=0.394). UV λ_{max} mμ (ε): 226 (5967), 283.5 (2540). IR ν_{max} cm^{-1}: 3450, 1740, 1620, 1591, 1495. *Anal.* Calcd. for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.90; H, 7.02.

Acetate of Methanol Adduct——A mixture of 148 mg. of MeOH adduct, 2.5 ml. of Ac_2O and 2.5 ml. of pyridine was allowed to stand at room temperature for 14 hr. The solution was poured into ice H_2O. The resulting precipitate was filtered to give 140 mg. of actate, m.p. 155~157°. Recrystallization from Et_2O afforded an analytical sample, m.p. 157~158.5°, $[\alpha]_D^{15}$ +153° (c=1.032). UV λ_{max} mμ (ε): 268.5 (830), 275 (790), 300 (95). IR ν_{max} cm^{-1}: 1765~1731, 1613, 1595, 1495. *Anal.* Calcd. for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.61; H, 6.58; OCH_3, 0.93.

Methyl Ether of Methanol Adduct——To a solution of 50 mg. of MeOH adduct was added an excess of solution of CH_2N_2 in Et_2O for 6 hr. Removal of solvent and recrystallization from Et_2O afforded 28 mg. of an analytical sample, m.p. 166~169°, $[\alpha]_D^{15}$ +148° (c=1.030). UV λ_{max} mμ (ε): 226.2 (8640), 280.5 (2216), 285.5 (shoulder). IR ν_{max} cm^{-1}: 1735, 1616, 1589, 1496. *Anal.* Calcd. for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 70.00; H, 6.90.

Acetate of Ethanol Adduct——A mixture of 100 mg. of EtOH adduct, 1 ml. of Ac_2O and 1 ml. of pyridine was allowed to stand at room temperature for 20 hr. The mixture was poured into ice H_2O and extracted with Et_2O. The Et_2O solution was worked up and the solvent was removed. Crystallization from Et_2O afforded acetate, m.p. 126~127.5°, $[\alpha]_D^{15}$ +152° (c=0.970). UV λ_{max} mμ (ε): 269.5 (856), 275.3 (810), 301 (83). IR ν_{max} cm^{-1}: 1766, 1743, 1492. *Anal.* Calcd. for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.47; H, 6.62.

Treatment of II with Aqueous Dioxane——A solution of 500 mg. of II in 8 ml. of dioxane and 13 ml. of H_2O was refluxed for 2 hr. The solvent was removed and the result triturated with Et_2O. The Et_2O insoluble powder was filtered (193 mg.) and crystallized from Et_2O. An analytical sample was dried at 110° for 20 hr., m.p. 196.5~200° (decomp.). UV: λ_{max} 294 mμ (ε 12500). IR ν_{max} cm^{-1}: 3385~3350, 1727, 1670, 1647, 1608, 1505. *Anal.* Calcd. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.20; H, 6.49.

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Summary

9,10β-Epoxy-9β-estra-1,4-diene-3,11,17-trione (II) and 3,9α-dihydroxyestra-1,3,5(10)-triene-11,17-dione (IIIa) was synthesized by the treatment of $\Delta^{9(11)}$-estrone (Ia) with perbenzoic acid. 9β-Isomer of IIIa (Va) was obtained from II by the catalytic hydrogenation.

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71. Yoshio Ueno, Shizuo Suzuki, Ikuko Ueno et Takashi Tatsuno: Recherches Enzymatiques du Métabolisme du *Penicillium islandicum* Sopp. I. Préliminaire de la voie Métabolique Principale de *P. islandicum*.

(*Chimie microbiotique à la Fecultè de Pharmacie de Rikadaigaku de Tokyo*[*1])

Parmi les pigments que produit le *Penicillium islandicum* Sopp, la lutéoskyrine est une substance toxique pour le foie. Quand on administre le pigment aux souris ou aux rats, une lésion se forme au foie peu après l'administration et la cirrhose et le cancer y apparaissent à une époque plus tardive.[1~3]

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