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Stereochemistry of Steroid containing Aromatic A-Ring. I.[*3] Reaction of 9(11)-Dehydroestrone.

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As reported before,1) 9(11)-dehydroestrone (I) is now easily obtained by the aromatization reaction of androsta-1,4,9(11)-trien-3,17-dione with zinc and some investigations were made on the reactions and stereochemistry of A-ring phenolic steroids.

Bromination of 9(11)-dehydroestrone methyl ether (II) in carbon tetrachloride afforded equilenin methyl ether (IV) instead of a bromo derivative, by liberation of hydrobromic acid. Bromination of its acetate (III) under the similar condition gave a stable dibromide (V), which on treatment with pyridine did not yield the equilenin-type compound. This showed that the reaction at 9- and 11-position was affected by the substituent at 3-position.

Hydroxybromination of the acetate (III) with N-bromosuccinimide in acetone, in the presence of perchloric acid,2,3) gave a bromohydrin (VI), m.p. 112~113°, in a good yield. Since the treatment of VI with zinc regenerated III, it was clear that VI was a compound formed by addition of bromine atom and hydroxyl group at 9- and 11-position, respectively, or *vice versa.*

There are eight possibilities in consideration of the position of the substituents and their steric configuration and it is assumed that the *trans*-diaxial addition is the most likely.

In general, 4,9(11)-dien-3-one system, under the same condition, should form a bromohydrin having 9α-bromo-11β-hydroxy configuration and treatment of the bromohydrin with alkali is known to give 9β,11β-epoxide compound.2) However, the bromohydrin (VI) of 9(11)-dehydroestrone acetate was recovered unchanged when heated with an excess of acetic anhydride in pyridine or when oxidized with chromium trioxide in acetic acid solution. These results suggested that the hydroxyl group is tertiary, and not the secondary, *i.e.* it must be present at 9-position, thereby excluding four out of eight possibilities. In order to establish the steric configuration of the bromohydrin (VI), following experiments were carried out.

Treatment of the bromohydrin (VI) with potsssium acetate in methanol or zink in ethanol converted it to the epoxide (VII), m.p. 160~162°. However, treatment of VI with sodium methoxide in methanol3) afforded 3-hydroxy-9ξ-estra-1,3,5(10)-trien-11,17-dione (XIV),4) m.p. 194~198° instead of VII, and XIV was also obtained from VII by treatment with acids4,5) or alkali.6)

On the other hand, oxidation of 9(11)-dehydroestrone acetate with perbenzoic acid in chloroform afforded a mixture of an epoxide of m.p. 158~161° in 76% yield and an

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[*3] This paper constitutes Part XLI of a series entitled "Steroid studies" by K. Tsuda.

1) K. Tsuda, E. Ohki, S. Nozoe, N. Ikekawa : J. Org. Chem., **26**, 2614 (1961); K. Tsuda, E. Ohki, S. Nozoe : *Ibid.*, **28**, 786 (1963).
2) J. Fried, E.F. Sabo : J. Am. Chem. Soc., **79**, 1130 (1957).
3) D. Taub, R.D. Hoffsommer, H.L. Slates, C.H. Kus, L.N. Wendler : *Ibid.*, **82**, 4012 (1960).
4) R.E. Parker, N.S. Issacs : Chem. Revs., **59**, 737 (1959).
5) R.C. Cookson, J. Hudec : Proc. Chem. Soc., **1957**, 24.
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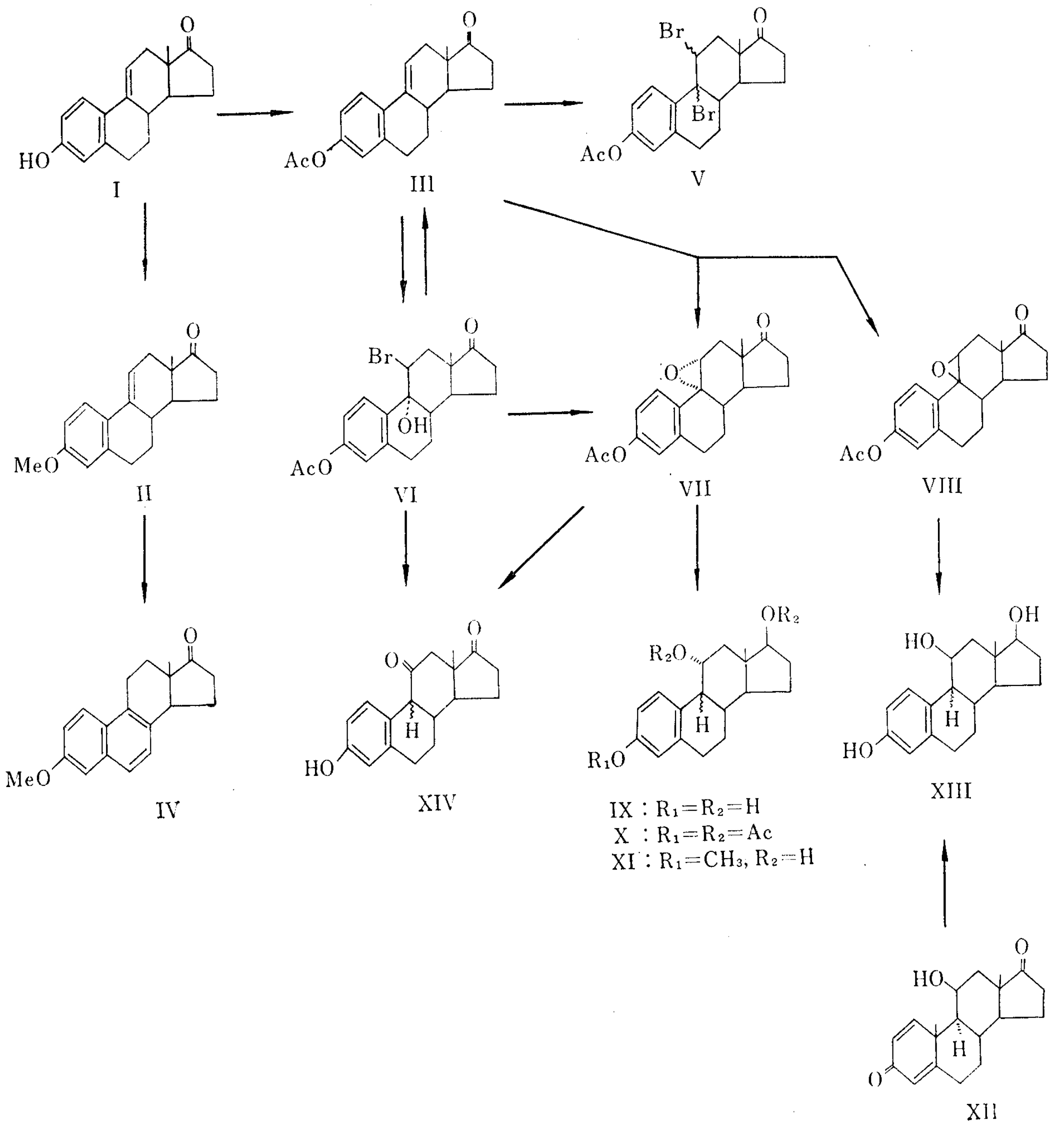

epoxide of m.p. 149～151° in 1.2% yield. The epoxide obtained as the major product was identified with the epoxide (VII) obtained from the foregoing bromohydrin (VI) by the mixed melting point determination and comparison of infrared spectra.

The reductive cleavage of the epoxide (VIII), m.p. 149～151°, obtained as the minor product, with lithium aluminum hydride in tetrahydrofuran[7] gave a triol (XIII) m.p. 289～291°.

Hogg and others[8] reported the synthesis of 9α-estra-1,3,5(10)-triene-3,11β,17β-triol (XIII) by the pyrolysis of 11β-hydroxyandrosta-1,4-dien-3,17-dione (XII), followed by reduction with lithium aluminum hydride. The triol obtained as above showed properties identical with the triol obtained by Hogg and others. The structure of this triol (XIII) was established by the direct comparison with the compound synthesized according to the Hogg's method.

It therefore follows that the minor product (VIII) of epoxidation has 9β,11β-configuration, whereas the major product (VII) has the 9α,11α-epoxide configuration and that the epoxidation of the 9-11 double bond in steroids with an aromatic A-ring chiefly

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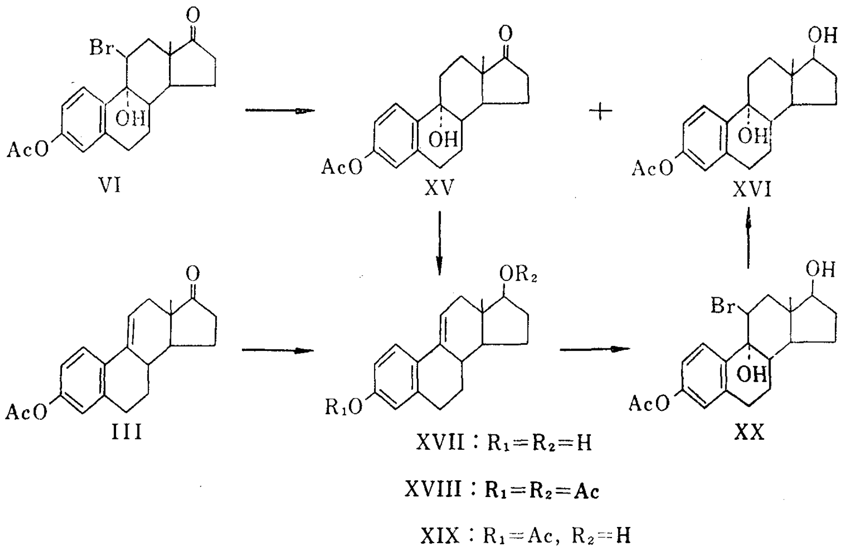
7) J. A. Zedric, Ma. E. Cabezas Rivera, D. C. Limon: J. Am. Chem. Soc., 82, 6373 (1960).

8) B. J. Magerlein, J. A. Hogg: *Ibid.*, **80**, 2220 (1958).

occurs from the α-side. These facts have proved the hydroxyl group in the bromohydrin (VI) has α-configuration. Further support for evidence of α-configuration of the epoxide was provided as follows. The triol (IX), m.p. 254~255°, obtained by the reductive fission[5,11] of the epoxy ring of VII with lithium aluminum hydride[7] formed a triacetate (X), m.p. 127~128°, by acetylation. The melting points of the triol and its derivatives were similar to those reported by Hogg and others[8] for 9ξ-estra-1,3,5(10)-triene-3,11α,17β-triol, although the configuration of the 9-position has not been confirmed yet.



Reduction of the bromohydrin (VI) with Raney-nickel[9] gave debromination products, XV and XVI as major and minor product respectively. Acetylation and oxidation with chromium trioxide[10] of XV, m.p. 167~168°, recovered the starting material unchanged. The hydroxyl group in XV was easily dehydrated and XV changed to a compound with ultraviolet absorption maximum 263 mμ on being heated to above 120°. Treatment of XV with lithium aluminum hydride afforded a small amount of a diol (XVII) which was found to be identical with estra-1,3,5(10),9(11)-tetraene-3,17β-diol by the direct comparison with an authentic sample. The minor product (XVI), m.p. 178~180°, was deduced to be the 17-hydroxyl compound of XV from its spectroscopic data. β-configuration of 17-hydroxyl group in XVI was synthetically proved as follows. 17-Carbonyl group of 9(11)-dehydroestrone 3-acetate (III) was reduced to 17β-hydroxyl compound (XIX) by treatment with sodium borohydride in tetrahydrofuran.[11] Subsequent hydroxybromination and reductive debromination of XIX was carried out as the same manner for III which gave an identical compound with XVI by the melting point and the infrared spectra comparison.

From the foregoing experimental facts and from the formation mechanism, 9α-hydroxy-11β-bromo configuration was proposed for the bromohydrin (VI).[12] The configurations of 9-position in the compounds (XIV) and (IX) are now being examined and will be reported in a forthcoming paper.

Experimental*4

Equilenin Methyl Ether (IV)——To a solution of 145 mg. of 9(11)-dehydroestrone methyl ether (II) in 20 ml. of CCl_4 was added 90 mg. of Br_2 in 10 ml. of CCl_4 dropwise at 0°. There was an immediate

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9) J. Schmidlin, A. Wettstein : Helv. Chim. Acta., **36**, 1241 (1953).
10) P. Bladon, J.E. Fabian, H.B. Hembest, H.P. Koch, G.W. Word : J. Chem. Soc., **1951**, 2402.
11) H.J. Ringold, B. Löken, G. Rosenkranz, F. Sondheimer : J. Am. Chem. Soc., **78**, 816 (1956).
12) R. Livingstone : J. Chem. Soc., **1962**, 76.

decolorisation of the solution and no further change in solution color at the end of the addition and the generation of HBr was followed. After the generation of HBr had stopped, the solution was poured into ice-H_2O and the separated CCl_4 layer was well washed to neutral, dried over anhyd. Na_2SO_4 and evaporated *in vacuo*. The resulted residue was crystallized from Et_2O to give 50 mg. of equilenin methyl ether (IV). Further recrystallization from Et_2O gave 18 mg. of analytically pure crystals as plates, m.p. 191~193°(Lit.,[13] 196~196.5°), UV λ_{max} mμ (ε): 230 (61100), 267 (4420), 280 (3800), 287 (3650), 322 (2200), 337 (1150). IR ν_{max} cm^{-1}: 1732, 1620, 1595, 1583, 854, 818. *Anal.* Calcd. for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.83. H, 7.10.

3-Acetoxy-9ξ,11ξ-dibromoestra-1,3,5(10)-trien-17-one (V)——To a solution of 150 mg. of 9(11)-dehydroestrone acetate (III) in 15 ml. of CCl_4 was added 80 mg. of Br_2 in 5 ml. of CCl_4 dropwise at 0°. After the addition had finished, N_2 was passed for 30 min. maintaining the temperature at 0°. Evaporation of CCl_4 *in vacuo* afforded a yellow oil, which was crystallized from Et_2O to give 60 mg. of dibromide (V) as prisms, m.p. 105~106°(decomp.). *Anal.* Calcd. for $C_{20}H_{22}O_3Br_2$: C, 51.08; H, 4.72. Found: C, 51.06; H, 4.66.

3,9α-Dihydroxy-11β-bromoestra-1,3,5(10)-trien-17-one 3-Acetate (VI)——To a solution of 155 mg. of III and 125 mg. of N-bromosuccinimide in Me_2CO was added 0.81 ml. of 0.2 *N* $HClO_4$ solution with stirring at 0~3° over a period of 15 min., and further stirred for 30 min. at 0°. 10% $Na_2S_2O_3$ solution was dropped with stirring until KI-starch paper was no longer blue. A large amount of H_2O was added slowly, the separated crystalline product was filtered, washed with H_2O and dried to afford 160 mg. of bromohydrin (VI), m.p. 88~93° (decomp.). Recrystallization from Et_2O gave prisms, m.p. 112~113° (decomp.) and its Beilstein test was positive. $[\alpha]_D$ $+220°$ (c=1.25), UV λ_{max} mμ (ε): 260.5 (430), 274.5 (380). IR ν_{max} cm^{-1}: 3520, 1767, 1733, 1610, 1585, 1494, 900, 820. *Anal.* Calcd. for $C_{20}H_{23}O_4Br$: C, 58.98; H, 5.69. Found: C, 59.23; H, 5.67.

9(11)-Dehydroestrone Acetate (III) from Bromohydrin (VI)——A solution of bromohydrin (VI) in 5 ml. of glacial AcOH was treated with Zn dust for 2 hr. at 60°. Filtration, and dilution with H_2O precipitated the product. This was collected and dried. Recrystallization from MeOH afforded 9(11)-dehydroestrone acetate (III), m.p. 105~107°. The IR spectrum of the product was identical with that of the authentic sample.

3-Acetoxy-9α,11α-epoxyestra-1,3,5(10)-tetraen-17-one (**VII**)——i) To a solution of 330 mg. of anhyd. AcOK in 3.3 ml. of absolute MeOH, heated just below the boiling point, was added 406 mg. of bromohydrin (VI) in 1.55 ml. of dioxane, and the reaction mixture was refluxed for 40 min. After cooling the precipitated KBr was filtered off. The filtrate was concentrated to one-third volume, diluted with H_2O and refrigerated. The obtained crystals were collected and recrystallized from Et_2O affording 9α,11α-epoxide (VII) as prisms, m.p. 160~162°, $[\alpha]_D$ $+189°$(c=0.7). UV λ_{max} mμ (ε): 268 (690), 296 (610). IR ν_{max} cm^{-1}: 1768, 1742, 1612, 1596, 814. *Anal.* Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.71; H, 6.71.

ii) A solution of 630 mg. of bromohydrin (VI) in 180 ml. of EtOH and 30 ml. of H_2O was stirred with 7.0 g. of Zn dust in a dark place at 0~5° for 48 hr. At the end of this period Zn dust was filtered off and washed with EtOH. The combined solution was concentrated *in vacuo* below 40° to afford the colorless gummy residue, which was crystallized on adding Et_2O to give needles of m.p. 143~147°. After recrystallization, it was identified with 9α,11α-epoxide (VII), by their IR spectra and mixed melting point determination. Additional 9α,11α-epoxide was obtained from the benzene-Et_2O elution of Al_2O_3 chromatogarphy of the mother liquor.

3-Hydroxy-9ξ-estra-1,3,5(10)-triene-11,17-dione (XIV)——i) With sodium methoxide: To a stirred slurry of 160 mg. of bromohydrin (VI) in 5 ml. of abs. MeOH covered with N_2 atomosphere was added 53 mg. of MeONa in 1 ml. of abs. MeOH. After all the steroid had dissolved (red solution), color of the solution gradually changed from red to pale yellow-green. After 15 min. AcOH was added to neutralize the solution and the solution was concentrated to 1~2 ml. *in vacuo*. The crystalline product was precipitated on dilution with H_2O and 30 mg. of the crude product was obtained after filtration, washing and drying. Additional same product was obtained from the mother liquor by extraction with Et_2O. Recrystallization from Et_2O afforded diketone (XIV), m.p. 194~198°, $[\alpha]_D$ $+244°$ (c=0.76, dioxane). UV: λ_{max} 280.5 mμ (ε 1700). IR ν_{max} cm^{-1}: 3370, 1730, 1700. 1610, 1502, 866, 822. *Anal.* Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.33; H, 6.77.

ii) From 9α,11α-epoxide (VII): A solution of 100 mg. of epoxide (VII) dissolved in 10 ml. of 5% KOH solution and 10 ml. of MeOH was heated under reflux for 30 min. The reaction mixture was treated as described above to give a crystalline product, identical with the sample prepared above by the IR spectrum comparison.

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*4 All melting points are uncorrected and unless noted otherwise, all rotations were measured in chloroform solution at 25°. Methanol was used for the UV spectra and nujol paste for the IR spectra.

13) W.G. Dauben, L. Ahnamjian, J. Am. Chem. Soc., 78, 633 (1956).

iii) From 9α,11α-epoxide (VII) by treatment with acid: In a solution of 80 mg. of VII in 5 ml. of $CHCl_3$ was passed the dry HCl gas for 30 min. cooling in ice-bath. The $CHCl_3$ solution was well washed with H_2O, dried and evaporated *in vacuo* to give a crystalline product. Recrystallization from Et_2O afforded 30 mg., of crystals, m.p. 195~200°. There was no depression on admixture with XIV and its IR spectrum was identical with that of XIV.

The same product was also obtained by treatment VII with HBr and HF.

Epoxidation of 3-Acetoxyestra-1,3,5(10),9(11)-tetraen-17-one (III)——A solution of 5.58 g. of 3-acetoxyestra-1,3,5(10),9(11)-tetraen-17-one (III) in 20 ml. of $CHCl_3$ was added dropwise to 35.5 ml. of $CHCl_3$ solution containing 2.96 g. of perbenzoic acid and the mixture was allowed to remain in refrigerator. Iodometric titration after 24 hr. indicated the consumption of 0.94 molar equivalents of perbenzoic acid. The mixture was followed by two extractions with 50 ml. of 5% KOH solution, washings with H_2O and drying over anhyd. Na_2SO_4. Concentration *in vacuo* below 35° gave a residue, which was crystallized from Et_2O to yield 5.26 g. of crystals, m.p. 153~155°. Recrystallization from Me_2CO-hexane gave 4.0 g. of prisms, m.p. 158~161°. From the mother liquor, 720 mg. of crystals, m.p. 124~127° were obtained, which consists of two kinds of crystals, needles and prisms. They were mechanically separated and recrystallized respectively from Me_2CO-hexane to give 440 mg. of prisms with m.p. 157~159° and 70 mg. of needles with m.p. 146~150°. IR spectrum of the major product, m.p. 158~161°, was identical with that of the epoxide (VII) obtained from bromohydrin (VI) and the mixed melting point with VII did not show the depression. Further recrystallization of the minor product (VIII) for analysis raised the melting point to 149~151°, $[\alpha]_D$ +38°(c=1.06). UV λ_{max} mμ (ε): 268.5 (630), 275 (560). IR ν_{max} cm^{-1}: 1775, 1746, 1614, 1592, 1500, 819. *Anal.* Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.59; H, 6.68.

9α-Estra-1,3,5(10)-triene-3,11β,17β-triol (XIII)——i) From epoxide (VIII): Reductive fission of 37 mg. of epoxide (VIII) in 2 ml. of anhyd. tetrahydrofuran at reflux for 24 hr. with 45 mg. $LiAlH_4$ in 2 ml. of anhyd. tetrahydrofuran was carried out. After excess $LiAlH_4$ was decomposed with Me_2CO, the mixture was diluted with 5% HCl solution and extracted with AcOEt. The extract was washed with dilute $NaHCO_3$ solution, dried and evaporated to leave a crystalline product. Recrystallization from Me_2CO afforded 15 mg. of triol (XIII), as needles with m.p. 289~291°. The mixed melting point showed no depression and the IR spectrum was identical with that of the authentic sample.

ii) From pyrolysis product, 11β-hydroxyestrone (XII): To a solution of 70 mg. of 11β-hydroxyestrone (XII) in 3 ml. of anhyd. tetrahydrofuran was added 70 mg. of $LiAlH_4$ in 2 ml. of anhyd. tetrahydrofuran, and the reaction mixture was allowed to stand overnight at room temperature. After decomposition of excess $LiAlH_4$ with Me_2CO, 5% HCl solution was added to precipitate 53 mg. of a crystalline product. Recrystallization from Me_2CO gave 40 mg. of needles, m.p. 286~289°. λ_{max} mμ (ε): 276 (1940), 283 (shoulder). IR ν_{max} cm^{-1}: 3450, 3310, 3260, 3230 (broad), 1619, 1589, 1500, 865, 826.

9ξ-Estra-1,3,5(10)-triene-3,11α,17β-triol (IX)——As described above, 1.18 g. of 9α,11α-epoxide (VII) was treated with 1.18 g. of $LiAlH_4$ in 60 ml. of anhyd. tetrahydrofuran refluxing for 24 hr. Usual working up gave the crystalline product, which was recrystallized from Me_2CO to afford 600 mg. of triol (IX) as prisms, m.p. 254~255°, $[\alpha]_D$ −52°(c=1.03, dioxane). UV: λ_{max} 279 mμ (ε 1700). IR ν_{max} cm^{-1}: 3400, 3285, 3180, 1617, 1587, 1498, 876, 822. *Anal.* Calcd. for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.89; H, 8.31.

Triacetate (X) of IX——Acetylation of 50 mg. of triol (IX) with Ac_2O and pyridine was carried out at room temperature. Usual processing afforded the crystalline product, which was crystallized from MeOH to yield the triacetate (X) as leaflets, m.p. 127~128°, $[\alpha]_D$ −113°(c=0.96). UV λ_{max} mμ (ε): 255.5 (1120), 270.5 (1030). IR ν_{max} cm^{-1}: 1758, 1726, 1610, 1597, 1494, 886, 804. *Anal.* Calcd. for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30. Found: C, 69.57; H, 7.29.

Methyl Ether (XI) of IX——To a stirred suspension of 390 mg. of triol (IX) in 10 ml. of EtOH was added 1.07 ml. of 15*N* NaOH solution, and 1.49 ml. of Me_2SO_4 was added dropwise, the reaction was occurred with boiling. This operation was repeated four times. After the last addition was finished, the solution was stirred for further 15 min. The reaction mixture was poured into a large amount of H_2O and the separated precipitate was filtered. Recrystallization from Et_2O gave 235 mg. of XI as silky needles, m.p. 130~137°. Additional 100 mg. of XI was obtained by concentration of the mother liquor. Further recrystallizations for analysis raised melting point to 145~146°, $[\alpha]_D$ −58°(c=0.62). UV λ_{max} mμ (ε): 280 (2000), 287 (shoulder). IR ν_{max} cm^{-1}: 3540, 3300 (broad), 1612, 1574, 1495, 868, 815. *Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.34; H, 8.59.

Debromination of Bromohydrin (VI) with Raney Nickel——A solution of 530 mg. of bromohydrin (VI) and 10 ml. of Raney-Ni(W-4) in 10 ml. of dioxane and 14 ml. of Et_2O was stirred in a dark place at 0~5° for 8 hr. At the end of the period, Ni ws filtered off and washed with Et_2O. The combined solution was evaporated *in vacuo* in the water bath below 50°. The resulted residue was crystallized on adding Et_2O to give 300 mg. of crude product. Recrystallization from Me_2CO-hexane gave 220 mg. of XV as needles, m.p. 167~168°. $[\alpha]_D$ +113°(c=0.58). UV λ_{max} mμ (ε): 266 (480), 273 (440). IR ν_{max} cm^{-1}: 3470, 1775, 1753, 1735, 1608, 1585, 1495, 820. *Anal.* Calcd. for $C_{20}H_{24}O_4\cdot\frac{1}{2}H_2O$: C, 71.19; H, 7.47. Found: C, 71.11; H, 7.42.

Chromatography of 150 mg. of the crude product on 5 g. of silica gel afforded XV from the elution with benzene-Et_2O (99:1～98:2) as the first fraction, which was recrystallized from Et_2O giving 80 mg. of pure material. From the elution with benzene-Et_2O (95:5) was obtained 20 mg. of XVI as prisms, m.p. 178～180°, as the second fraction. UV λ_{max} mμ (ε): 265.5 (600), 273 (530). IR ν_{max} cm^{-1}: 3510, 3400, 1757, 1608, 1585, 1490, 820. *Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.33; H, 7.74.

9(11)-Dehydroestradiol (XVII)——To a solution of 200 mg. of XV in 1 ml. of anhyd. tetrahydrofuran was added 200 mg. of $LiAlH_4$ in 1 ml. of anhyd. tetrahydrofuran under cooling in an ice-bath and the mixture was allowed to stand overnight at room temperature. Usual working up afforded 130 mg. of crystals as needles, m.p. 178～182°. Further recrystallization from Et_2O raised melting point to 184～186°. UV: λ_{max} 262.5 mμ (ε 19300). IR ν_{max} cm^{-1}: 3395, 3130 (broad), 1628, 1612, 1576, 1492, 808..

3,17β-Diacetate of XVII——i) Acetylation of 100 mg. of diol (XVII) with Ac_2O and pyridine afforded a diacetate as leaflets. Recrystallization from MeOH gave 80 mg. of pure material, m.p. 148～149°. $[\alpha]_D$ +94°(c=0.85). UV: λ_{max} 258 mμ (ε 18700). IR ν_{max} cm^{-1}: 1768, 1732, 1626, 1606, 1576, 1491, 900, 818. *Anal.* Calcd. for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.68; H, 7.36.

ii) From Dehydroestrone 3-acetate (III): As described above, 146 mg. of III was treated with 150 mg. of $LiAlH_4$ in 4 ml. of anhyd. tetrahydrofuran at room temperature. Usual working up afforded the crystalline product, which was recrystallized from Et_2O, m.p. 180～183°. Its IR spectrum was identical with that of diol (XVII).

3,17β-Diacetate: Crystals obtained from the mother liquor described above were acetylated with Ac_2O in pyridine to give a crystalline product. Recrystallization from MeOH afforded the diacetate as leaflets, m.p. 147～149°. There was no depression on admixture with XVIII and the IR spectrum was identified with that of XVIII.

Estra-1,3,5(10)-triene-3,9α,17β-triol 3-Acetate (XVI)——According to the Sondheimer's condition, 500 mg. of 9(11)-dehydroestrone 3-acetate (III) was treated with $NaBH_4$ in tetrahydrofuran. After recrystallization 440 mg. of XIX was obtained, m.p. 123～126°, IR ν_{max} cm^{-1}: 3435 (broad), 1760, 1622, 1603, 1578, 1492, 818. Hydroxybromination with N-bromosuccinimide was carried out at -8～-5° on 300 mg. of XIX and gave 220 mg. of the crude bromohydrin, m.p. 80～83°(decomp.). This bromohydrin was successively debrominated with Raney-Ni by usual manner. Usual processing gave the debromination product with m.p. 177～180°, which showed the same IR spectrum of that of XVI.

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Summary

Bromination of 3-methoxy-9(11)-dehydroestrone (II) gave equilenin methylether (IV). Hydroxybromination of 3-acetoxy-9(11)-dehydrostrone (III) with N-bromosuccinimide in the presence of perchloric acid afforded a bromohydrin (VI), whose structure was assigned 3,9α-dihydroxy-11β-bromoestra-1,3,5(10)-trien-17-one 3-acetate, on the basis of the resistance of hydroxyl group to acetylation and oxidation, and by leading to 9α,11α-epoxide (VII) and triol (IX).

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