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203. Kyosuke Tsuda, Shigeo Nozoe,*1 and Kazuhiko Ohata*2 : Steroid Studies. XLIII.*3 An Aromatization Reaction of a Cross Conjugated Dienone System with Zinc. (8).[1]

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Aromatization of a A-ring of steroids possessing a cross conjugated triply unsaturated ketone, such as 1,4,6-, 1,4,8-, and 1,4,9(11)-trien-3-one system by zinc with concomitant elimination of the C-19 angular methyl group have been reported recently by the present authors.[1] It was also described that the presence of an unsaturation at 9(11)-position besides the 1,4- diene system effected strongly the elimination of the angular methyl group, while 1,4- dien-3-one was converted to *p*-cresol type rearrangement product under the same condition.

In the present paper, authors wish to extend this aromatization reaction to a 1,4, 9(11)-triene-3,12-dione system derived from another natural abundant steroid source.

We have chosen deoxycholic acid (I) as a starting material for synthesis of 19-norskeleton of bile acid. The various synthetic approaches to prepare 3,12-dioxochola-1,4-dienic acid (V) and 3,12-dioxochola-1,4,9(11)-trienic acid from deoxycholic acid were attempted.

Treatment of methyl 3,12-dioxocholanate (II) with two moles of bromine in acetic acid afforded 2,4-dibromo compound (III), which was dehydrobrominated on short boiling with collidine to yield two different isomeric dienone derivatives. Chromatographical separation of these isomers gave methyl 3,12-dioxochola-1,4-dienate (IV), m.p. 137~138°, UV : λ_{max} 243.5 mμ (ε 15,200) and methyl-3,12-dioxo-4,6-choladienate (VI), m.p. 152~164°, UV : λ_{max} 281.5 mμ (ε 25,200).

The structure of former was confirmed by its conversion to the phenolic product, which exhibited characteristic ultraviolet absorption spectrum broad maximum at around 282~286 mμ for 1-hydroxy-4-methyl derivative, although this phenol was failed to be obtained in crystalline form. The structure methyl 3,12-dioxochola-4,6-dienate could be assigned for the latter, since the migration of bromine from 2-position to 6-position during collidine dehydrobromination, to yield a 6-7 double bond, is well known. Similarly, when the 2,4-dibromo derivative (III) in dimethylformamide was treated with lithium bromide and lithium carbonate,[2] IV and VI were obtained as neutral substances. The two free acid derivatives which showed the ultraviolet absorption maxima at 240 mμ, and 280 mμ respectively, were also obtained from the alkaline mother liquor, and these acid derivatives afforded IV and VI by the esterification with diazomethane. Compound (IV) was also obtained on dehydrogenation of methyl 3,12-dioxocholanate (II) with selenium dioxide in *tert*-amyl alcohol.[3]

An attempt to prepare 1,4,9(11)-triene-3,12-dione system by the treatment of 1,4-dien-3-one (IV) with selenium dioxide in acetic acid failed, the starting material being recovered upon refluxing for 18 hours. Then, alternative route was adopted. When

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the methyl 3,12-dioxochol-9(11)-enate (VIII) prepared from deoxycholic acid (I), or cholic acid by Fieser's procedures[4,5] was dehydrogenated with selenium dioxide in *tert*-amyl alcohol, the desired 1,4,9(11)-triene-3,12-dione derivative (IX), m.p. 139~140°, UV : λ_{max} 236 mμ (ε 28,800), was obtained in 33% yield.

This substance (IX) was also obtained by tribromination of II with three moles of bromine in acetic acid at 50~60°, followed by dehydrobromination with collidine. Further, dibromination of VIII in acetic acid and dehydrobromination with collidine afforded IX.

When the trienone (IX) was treated with zinc in dimethylformamide containing small amount of water, phenolic product (X), m.p. 167.5~168.5°, was obtained which exhibited ultraviolet absorption maxima at 243 mμ (ε 10,850) and 326 mμ (ε 26,400), analogous to that of 4-hydroxycinnamic acid derivative. The same phenolic product was obtained under similar condition using pyridine or ethanol as a solvent. Acetylation of X afforded acetate (XII), m.p, 164~165°. Infrared spectrum of X clearly showed the presence of hydroxyl group (3280 cm^{-1}), aromatic ring (1610, 1505 cm^{-1}), unsaturated ketone (1678 cm^{-1}) and two adjacent hydrogen atoms on benzene ring (830 cm^{-1}). The nuclear magnetic resonance spectrum showed the absence of the signal corresponding to methyl group on benzene ring. On the basis of above spectral data and elementary analyses of X, XI, and XII, this phenolic product was assumed to be methyl 3-hydroxy-12-oxo-19-norchola-1,3,5(10),9(11)-tetraenate resulted from aromatization of A-ring with concomitant elimination of C_{19} methyl group.

Upon hydrogenation of X with palladium-on-charcoal, two moles of hydrogen was consumed and the product did not crystallize but showed the ultraviolet spectrum maximum at 281.5 mμ (ε 2,100). Hydrolysis of this compound with methanolic potassium hydroxide gave the crystalline free acid (XIII), m.p. 230~231°. This acid showed the same ultraviolet spectrum, characteristic of nonconjugated phenolic chromophore. On the basis of above ultraviolet spectral data, infrared spectra, and elementary analyses of this acid (XIII) and the compound (XIV), m.p. 62~64° obtained with same reduction of XII, XIII was assumed 3,12-dihydroxy-19-norchola-1,3,5(10)-trienic acid, a tetrahydro derivative of XI.

Accordingly, XIV was assumed methyl 3,12-dihydroxy-19-norchola-1,3,5(10)-trienate 3-acetate, which was oxidized with chromic acid-sulfuric acid solution[6] to 3-acetoxy-12-oxo-19-norchola-1,3,5(10)trienic acid methyl ester (XV), m.p. 154~155°.

Reduction of XV with Huang-Minlon method[7] gave 3-hydroxy-19-norchola-1,3,5(10)-trienic acid (XVII), m.p. 209~211°, which was converted to methyl ester (XVIII), m.p. 142~143°, with methanol containing hydrochloric acid.

This 3-hydroxy-19-norchola-1,3,5(10)-trienic acid (XVII) showed an ultraviolet absorption maximum at 281.5 mμ (ε 2,560) analogous to those of estrogens.

Although 3-acetoxy-12-oxo-19-norchola-1,3,5(10),9(11)-tetraenic acid methyl ester (XII) possessed the α,β-unsaturated keto group, this was readily reduced with Huang-Minlon method[7] to 3-hydroxy-19-norchola-1,3,5(10),9(11)-tetraenic acid (XIX), m.p. 184~185°, which exhibited an ultraviolet absorption maximum at 264 mμ (ε 18,500) analogous to those of $\Delta^{9(11)}$ estrogen derivatives.

This acid (XIX) was esterified with methanol containing hydrochloric acid, and then hydrogenated with palladium-on-charcoal to 3-hydroxy-10-norchola-1,3,5(10)-trienic acid methyl ester (XVIII), which was identified with that derived from XV.

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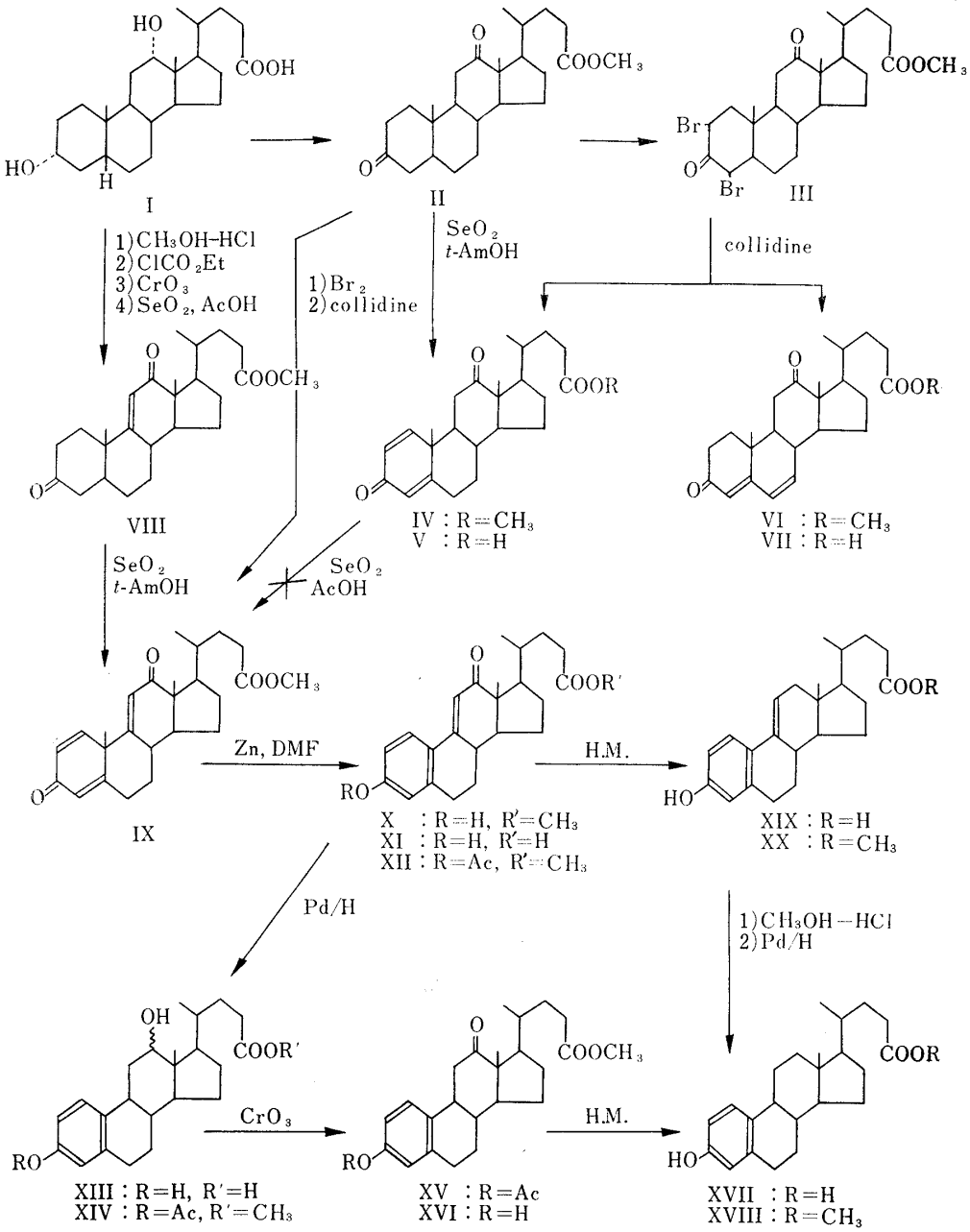

Experimental*4

Methyl 2,4-Dibromo-3,12-dioxocholanate (III)——A solution of 100 g. of deoxycholic acid (I) in 1 L. of MeOH containing 10 g. of HCl was refluxed for 45 min. and condensed *in vacuo* to small volume. The residue was dissolved in Et_2O, and the Et_2O solution was washed with 5% Na_2CO_3 and H_2O, dried over anhyd. Na_2SO_4, and evaporated *in vacuo*. To the solution of the residue in 2 L. of Me_2CO was added with vigorous' stirring 200 ml. of ca. 8*N* CrO_3-H_2SO_4 solution[6] during 3 min. at 30~35°, and after further minutes' stirring, the excess of oxidant was destroyed by addition of MeOH. The solution was poured into 5 L. of H_2O. The precipitated product was filtered, washed well with H_2O, and dried. Recrystallization from AcOEt afforded 95 g. of II as prisms, m.p. 129~130°.

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

To a solution of 10 g. of II in 300 ml. of AcOH and several drops AcOH saturated with HBr was added 100 ml. of AcOH which contained 7.61 g. of Br_2, during a period of 2 hr. at room temperature, and stirring was continued for more 10 min. The reaction solution was poured into 1 L. of H_2O. Filtration afforded 13.55 g. of crude (III), m.p. 168°(decomp.). Recrystallization from Me_2CO-EtOH raised melting point to 180°(decomp.), as needles. $[\alpha]_D^{25}$ +50.0°. IR ν_{max} cm^{-1}: 1756, 1730, 1709. *Anal.* Calcd. for $C_{25}H_{36}O_4Br_2$: C, 53.58; H, 6.47; Br, 28.52. Found: C, 53.72; H, 6.61; Br, 29.42.

Dehydrobromination of III——i) With collidine: A solution of 6.63 g. of III in 52 ml. of collidine was refluxed for 20 min., cooled and diluted with benzene. Filtrate was washed with H_2O, dil. HCl, dil. $NaHCO_3$ and H_2O. Benzene solution was evaporated and the residue dissolved in benzene-petr. ether (1:1), was chromatographed on 120 g. of alumina. Recrystallization from MeOH of the crystalline fraction eluted with benzene afforded 353 mg. of VI, as prisms, m.p. 152~164°. $[\alpha]_D^{25}$ +38.4°. UV: λ_{max} 281.3 mμ (ε 25,200). IR ν_{max} cm^{-1}: 1730, 1719, 1670, 1618, 1590. *Anal.* Calcd. for $C_{25}H_{34}O_4$: C, 75.34; H, 8.60. Found: C, 75.18; H, 8.56.

Recrystallization from MeOH of the crystalline fraction eluted with benzene, Et_2O afforded 1.262 mg. of IV, as plates, m.p. 137~138°, $[\alpha]_D^{25}$ +70.0°. UV: λ_{max} 243.5 mμ (ε 15,200). IR ν_{max} cm^{-1}: 1740, 1713, 1671, 1630, 1606. *Anal.* Calcd. for $C_{25}H_{34}O_4$: C, 75.34; H, 8.60. Found: C, 75.28; H, 8.61.

ii) With LiBr and Li_2CO_3: Under atmosphere of N_2, 5 g. of III, 5 g. of LiBr and 5 g. of Li_2CO_3 were added into 100 ml. of dimethylformamide warmed to 100°, and then refluxed for 1 hr. After cooling, 100 ml. of H_2O was added to reaction solution. The crystalline products were filtered and washed with H_2O. Recrystallization from MeOH gave 573 mg. of the mixture of IV and VI, m.p. 126~141°, UV: λ_{max} 280~240 mμ, and 629 mg. of IV contaminated with VI, m.p. 126~137°, UV λ_{max} mμ: 244, 280 (shoulder).

Filtrate of the crude products was acidified with dil. HCl. The precipitated product was filtered and washed well with H_2O. Filtration gave 90 mg. with UV λ_{max} mμ: 244, 280 (shoulder). This crude product dissolved in MeOH, was esterified with diazomethane, and recrystallization from MeOH afforded 60.597 mg. of the mixture of IV and VI, m.p. 131~133°, UV λ_{max} mμ: 244.5, 280 (shoulder).

Dehydrogenation of Methyl 1,12-dioxocholanate (II) with Selenium Dioxide——A mixture of 30 g. of II and 2.7 g. of SeO_2 in 150 ml. of *tert*-AmOH and 1.5 ml. of AcOH was refluxed under atmosphere of N_2 for 8 hr., and after addition of more 2.7 g. of SeO_2, refluxed for further for 10 hr.

After cooling, the precipitated Se was filtered and washed with AcOH. The filtrate was condensed *in vacuo*, and the residue dissolved in benzene was washed with H_2O, dil. $NaHCO_3$ and H_2O, and then dried. Benzene solution was evaporated and the residue dissolved in benzene-petr. ether (2:1) was chromatographed over 100 g. of alumina. Recrystallization from MeOH of the fraction eluted with benzene afforded 530 mg. of IV as plates, m.p. 136~137°. This compound was identified with the compound (IV) which was obtained from dehydrobromination of III with collidine by their IR spectra and mixed melting point determination.

Methyl 3,12-Dioxochol-9(11)-enate (VIII)——Three grams of deoxycholic acid was esterified in 30 ml. of MeOH by usual way. The residue was dissolved in 15 ml. of dioxane and 2.4 ml. of pyridine. To this solution was added 3 ml. of ethyl chlorocarbonate dropwise under cooling. After standing for 30 min. at room temperature, to the reaction mixture was added 36 ml. of H_2O containing 1.5 ml. of 36% HCl, and heated on steam bath for 30 min. Cooling, extraction with Et_2O and evaporation of solvent afforded the crude methyl 3-ethoxycarbonyloxy-12-hydroxycholanate. To a solution of this crude product in 70 ml. of Me_2CO was added dropwise 6.8 ml. of ca. 8*N* CrO_3-H_2SO_4 solution at 30~35° during a period of 3 min. and after further few minutes' stirring, the excess of oxidant was destroyed by addition of MeOH.

The solution was diluted with H_2O. The precipitated product was collected, washed with H_2O and dried. This crude methyl 3-ethoxycarbonyloxy-12-oxocholanate was dissolved in 30 ml. of AcOH and added 1.5 g. of SeO_2 and refluxed for 18 hr. The precipitated Se was filtered and washed with AcOH. Filtration afforded the crude methyl 3-ethoxycarbonyloxy-12-oxochol-9(11)-enate. A solution of this crude product in 40 ml. of MeOH containing 20 ml. of 10% KOH was refluxed for 90 min. MeOH was evaporated *in vacuo*, the residue dissolved in H_2O and acidified with dil. HCl. Filtration afforded the crude 3-hydroxy-12-oxochol-9(11)-enic acid. This dried crude product was esterified with HCl-MeOH. This crude ester was oxidized in Me_2CO with ca. 8*N* CrO_3-H_2SO_4 solution by usual way. Recrystallization from H_2O-MeOH gave 2.39 g. of VIII, m.p. 117~127°. Recrystallization from Et_2O-petr. ether afforded analytical sample as prisms, m.p. 129.5~130.5°, $[\alpha]_D^{25}$ +86.4°. UV: λ_{max} 240 mμ (ε 10,000). IR ν_{max} cm^{-1}: 1756, 1725, 1688, 1611. *Anal.* Calcd. for $C_{25}H_{36}O_4$: C, 74.96; H, 9.06. Found: C, 74.78; H, 8.86.

Methyl 3,12-Dioxochola-1,4,9(11)-trienate (IX)——i) Bromination of II and dehydrobromination with collidine: To a solution of 10 g. of II in 30 ml. of AcOH which contained few drops of AcOH saturated with HBr was added with stirring 2/3 of 1.4 g. of Br_2 in 15 ml. of AcOH during a period of 40 min. at room temperature, and added 1/3 of Br_2 solution during a period of 100 min. at 50~55°. The solution mixture was stirred further for 3 hr., cooled, poured into 160 ml. of ice H_2O, and extracted with $CHCl_3$. $CHCl_3$ layer was washed with dil. $NaHCO_3$ and H_2O, dried, dissolved in 8 ml. of collidine, and

refluxed for 1 hr. The reaction mixture was diluted with Et_2O, the precipitated products were filtered and washed with Et_2O. The Et_2O solution was washed with H_2O, dil. HCl, dil. $NaHCO_3$, and H_2O. Et_2O was removed *in vacuo*, and the residue was chromatographed on 16.5 g. of alumina. Recrystallization from MeOH of the fraction eluted with benzene afforded IX. UV : λ_{max} 236.3 mμ (ε 28,800). IR ν_{max} cm^{-1} : 1749, 1682, 1669, 1627, 1616, 1600. *Anal.* Calcd. for $C_{25}H_{32}O_4$: C, 75.72; H, 8.13. Found : C, 75.50; H, 7.98.

ii) Dehydrogenation of VIII with SeO_2 : A solution of 1.0 g. of VIII and SeO_2 in 50 ml. of *tert*-AmOH containing 0.5 ml. of AcOH was refluxed under atmosphere of N_2 for 8 hr., and then, after addition of more 0.6 g. of SeO_2, refluxed for further 10 hr. The reaction mixture was treated by the method of dehydrogenation of II with SeO_2. Recrystallization of the fraction eluted with benzene from MeOH afforded 318 mg. of IX, m.p. 137~139°. This compound was identified with the compound (IX) which was obtained from i) by their IR spectra.

iii) Bromination of VIII and dehydrobromination with collidine : To a solution of 4.0 g. of VIII in 100 ml. of AcOH which contained a few drops of AcOH saturated with HBr was added dropwise with stirring 3.5 g. of Br_2 in 35 ml. of AcOH at room temperature, and stirred for further 10 min. The reaction mixture was poured into 400 ml. of cold H_2O and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with H_2O and evaporated. The resulting residue washed with Et_2O was dissolved in 25 ml. of collidine and refluxed for 20 min. After cooling, the reaction mixture was diluted with AcOEt. Following the method of i), the residue was chromatographed on 40 g. of alumina. Recrystallization from MeOH of the fraction eluted with benzene afforded 321 mg. of IX, m.p. 138~140°. This compound showed no mixed melting point depression with the compound (IX) of i).

3-Hydroxy-12-oxo-19-norchola-1,3,5(10),9(11)-tetraenic Acid Methyl Ester (X)——i) With pyridine : A solution of 200 mg. of IX in 10 ml. of pyridine with 4 g. of Zn dust and 0.1 ml. of H_2O was refluxed with vigorous stirring for 1 hr. After cooling, the reaction mixture was diluted with Et_2O. Zn dust was filtered and washed with Et_2O. Filtrate was washed with H_2O, dil. HCl, dil. $NaHCO_3$ and H_2O, dried, and evaporated *in vacuo*. Recrystallization from MeOH of the resulted residue afforded 147.5 mg. of X, m.p. 166~167°. Recrystallization from MeOH afforded the analytical specimen as needles, m.p. 167.5~168.5°. $[\alpha]_D^{25}$ +299.6°. UV λ_{max} mμ (ε) : 326 (26,400), 243 (10,850). IR ν_{max} cm^{-1} : 3280, 1715, 1678, 1611, 1600, 1580, 1508. *Anal.* Calcd. for $C_{25}H_{30}O_4$: C, 75.36; H, 7.91. Found : C, 75.52; H, 7.95.

ii) With dimethylformamide : A solution of 4.8 g. of IX in 200 ml. of dimethylformamide with 100 g. of Zn dust and 4 g. of H_2O was refluxed with vigorous stirring for 1 hr. Zn dust was filtered and filtrate was condensed *in vacuo* to a small volume. The residue was diluted with Et_2O the solution was washed well and dried. Evaporation and recrystallization from MeOH gave 2.95 g. of IX, m.p. 165~166°.

iii) With EtOH : A solution of 200 mg. of IX in 20 ml. of EtOH with 4 g. of Zn dust and 0.2 ml. of H_2O was refluxed with vigorous stirring for 6 hr. After cooling, Zn dust was filtered. Evaporation and recrystallization from MeOH afforded 155 mg. of X, m.p. 165~166°.

Hydrolysis of X——After a solution of 100 mg. of X in 7 ml. of MeOH and 3 ml. of 10% KOH was refluxed for 1 hr., MeOH was evaporated *in vacuo*. The residue was dissolved in H_2O and acidified with dil. HCl. The crystallized product was filtered and washed with H_2O to furnish 86 mg. of the crude 3-hydroxy-12-oxo-19-norchola-1,3,5(10),9(11)-tetraenic acid (XI), m.p. 225~232°. Recrystallization from Me_2CO–H_2O (4:1) gave the analytical specimen as prisms, m.p. 236~238°. $[\alpha]_D^{25}$ +307.9° (in EtOH). UV λ_{max} mμ (ε) : 326 (25,000), 242.5 (9,200). *Anal.* Calcd. for $C_{23}H_{28}O_4$: C, 74.97; H, 7.66. Found : C, 74.66; H, 7.88.

Acetylation of X——A solution of 100 mg. of X in 0.5 ml. of pyridine and 0.5 ml. of Ac_2O was allowed to stand overnight at room temperature. To the reaction mixture was added H_2O slowly. Filtration gave 107 mg. of the crude acetate (XIII), m.p. 162~164°. Recrystallization from MeOH gave the analytical specimen as fine needles, m.p. 164~165°. $[\alpha]_D^{25}$ +213.7°, UV λ_{max} mμ (ε) : 296 (18,000), 229 (83.50). IR ν_{max} cm^{-1} : 1770, 1740, 1672, 1618, 1591, 1490. *Anal.* Calcd. for $C_{26}H_{32}O_5$: C, 73.56; H, 7.60. Found : C, 73.39; H, 7.49.

Hydrogenation of X——A solution of 574 mg. of X in 50 ml. of MeOH was shaken with 60 mg. of 5% Pd-C under atmosphere of H_2. Filtration and evaporation of solvent gave 576 mg. of the crude product which could not be crystallized. A solution of 200 mg. of this crude product in 20 ml. of MeOH containing 6 ml. of 10% KOH was refluxed for 1 hr. Evaporation, acidification and crystallization from Me_2CO–H_2O (4:1) afforded 100 mg. of XIII as prisms, m.p. 230~231°, $[\alpha]_D^{25}$ +76.4° (in MeOH), UV : λ_{max} 281.5 mμ (ε 2,136). IR ν_{max} cm^{-1} : 3500, 1716, 1615, 1517. *Anal.* Calcd. for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found : C, 74.08; H, 8.60.

Hydrogenation of XII——A solution of 323 mg. of XII in 60 ml. of MeOH was hydrogenated over 5% Pd-C by the same manner that of X. Recrystallization afforded 206.8 mg. of methyl 3,12-dihydroxy-19-norchola-1,3,5(10)-trienate 3-acetate (XIV) as needles, m.p. 62~65°, $[\alpha]_D^{25}$ +59.6, UV λ_{max} mμ (ε): 275 (714), 268 (722). *Anal.* Calcd. for $C_{26}H_{36}O_5$: C, 72.87; H, 8.47. Found : C, 72.73; H, 8.48.

3-Acetoxy-12-oxo-19-norchola-1,3,5(10)-trienic Acid Methyl Ester (XV)——A solution of XIV in 20 ml. of Me_2CO was oxidized with ca. 8*N* CrO_3–H_2SO_4 solution by usual way. Recrystallization from

MeOH afforded 165 mg. of XV as fine needles, m.p. 154~155°, $[\alpha]_D^{25}$ +90.0°, UV λ_{max} mμ (ε): 275(640). 268.5(640). IR ν_{max} cm^{-1}: 767, 1748, 1710, 1616, 1585, 1500. *Anal.* Calcd. for $C_{26}H_{34}O_5$: C, 73.21; H, 8.04. Found: C, 73.46; H, 8.07.

3-Hydroxy-19-norchola-1,3,5(10),9(11)-tetraenic Acid Methyl Ester (XX)——After a solution of 350 mg. of XII in 40 ml. of trimethylene glycol and 2 ml. of 80% hyrazine hydrate was refluxed at 130~140° for 30 min., the condenser was removed and a concd. solution of 4 g. of KOH (ca. 60%) was added slowly to the reaction solution. The reaction mixture was diluted with H_2O and then acidified with dil. HCl. The precipitated product was filtered and washed well with H_2O. Recrystallization from Me_2CO-H_2O (4:1) afforded 175 mg. of XIX as prisms, m.p. 184~185°, $[\alpha]_D^{25}$ +83.0°, UV: λ_{max} 264 mμ (ε 18,500).

A solution of 165 mg. of XIX in 50 ml. of MeOH and 1 ml. of 35% HCl was refluxed for 1 hr. Solvents were removed *in vacuo* and the residue was dissolved in Et_2O, and acidic substances were removed with 5% Na_2CO_3. Evaporation and recrystallization from MeOH afforded 148.3 mg. of XX as needles, m.p. 175~176.5°. $[\alpha]_D^{25}$ +89.4, UV: λ_{max} 264 mμ (ε 15,500), IR ν_{max} cm^{-1}: 3310, 1710, 1610, 1507. *Anal.* Calcd. for $C_{24}H_{32}O_3$: C, 78.22; H, 8.75. Found: C, 78.22; H, 8.64.

3-Hydroxy-19-norchola-1,3,5(10)-trienic Acid Methyl Ester (XVIII)——i) From XVI: A solution of 107 mg. of XX in 20 ml. of MeOH was shaken with 1 l mg. of 5% Pd-C under atmosphere of H_2. Filtration, evaporation and recrystallization form MeOH afforded 84 mg. of XVIII as needles, m.p. 145~146°, $[\alpha]_D^{25}$ +55.4°, UV: λ_{max} 281.5 mμ (ε 2560), IR ν_{max} cm^{-1}: 3245, 1710, 1611, 1510. *Anal.* Calcd. for $C_{24}H_{34}O_3$: C, 77.80; H, 9.25. Found: C, 77.81; H, 9.05.

ii) From XVI: By the same method that of XII, 180 mg. of XVI in 25 ml. of trimethylene glycol and 1 ml. of 80% hydrazine hydrate was reduced. Recrystallization from Me_2CO-H_2O (4:1) afforded 130 mg. of XVII, as needles, m.p. 209~211°, $[\alpha]_D^{25}$ +71.8°, UV: λ_{max} 281 mμ (ε 2,700).

A solution of 65 mg. of XVII in 15 ml. of MeOH and 0.3 ml. of 35% HCl was esterified by usual method. Recrystallization from MeOH afforded 56 mg. of XVIII as needles, m.p. 145~146°. This compound showed no mixed melting point depression with the compound (XVIII) of i).

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Summary

Using Methyl 2,4-Dibromo-3,12-dioxocholanate (III) as a starting material Methyl 3,12-dioxochola-1,4-dienate (IV) and methyl 3,12-dioxochola-4,6-dienate (VI) were prepared. Methyl 3,12-dioxochola-1,4,9(11)-trienate (IX) was obtained by bromination and dehydrobromination of methyl 3,12-dioxocholanate (II) or dehydrogenation with selenium dioxide in *tert*-amyl alcohol of methyl 3,12-dioxochol-9(11)-enate (VIII). Aromatization of IX with zinc in pyridine, dimethylformamide, or ethanol afforded 3-hydroxy-12-oxo-19-norchola-1,3,5(10),9(11)-tetraenic acid methyl ester (X). Hydrogenation, followed by chromium-trioxide-oxidation and Huang-Minlon reduction or Huang-Minlon reduction and then hydrogenation of X afforded 3-hydroxy-19-norchola-1,3,5(10)-trienic acid methyl ester (XVIII).

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