3-Hydroxymethyl-4,5,7-trimethoxy-2-naphthoic Acid γ-Lactone (II)——To a stirred solution of 100 mg. of XII in 30 cc. of $CHCl_3$ was added dropwise a solution of 62 mg. of Br_2 in 30 cc. of $CHCl_3$ at room temperature over a period of 3 hr., and stirring was continued for 1 hr. after the addition was completed. The reaction mixture was washed with $NaHCO_3$ solution and H_2O, and dried over $MgSO_4$. The solvent was removed, and the residue was heated with 100 mg. of LiCl and 5 cc. of dimethylformamide on a boiling water bath for 1 hr. After cooling, 50 cc. of H_2O was added and the whole mixture was extracted with AcOEt. The AcOEt extract was washed with water and dried over $MgSO_4$. A solution of a large excess of CH_2N_2 in Et_2O was added to the AcOEt extract and allowed to stand at room temperature for 2 days. After addition of AcOH to destroy the excess of CH_2N_2, the solution was washed with $NaHCO_3$ solution and H_2O, dried over $MgSO_4$ and evaporated. Recrystallizations of the residue from 10 cc. of EtOH gave 67 mg. (64%) of colorless needles, m.p. 201°. This compound was purified by chromatography using silica-gel and $CHCl_3$ as an eluent. An analytical sample melted at 205°. *Anal.* Calcd. for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15. Found: C, 65.52; H, 5.12. IR: $\nu_{max}^{CHCl_3}$ 1757 cm^{-1} (lactone).

Summary

4-Oxo-5,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthoic acid (VII) is expected to serve as a key intermediate in the synthesis of the proposed structure for α-sorigenin dimethyl ether (3-hydroxymethyl-1,6,8-trimethoxy-2-naphthoic acid γ-lactone (I)). The reported method for VII was improved and the synthesis of 3-hydroxymethyl-4,5,7-trimethoxy-2-naphthoic acid γ-lactone (II) started with VII was carried out. The reaction scheme is shown in chart.

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53. Zen-ichi Horii, Toyoshi Katagi, and Yasumitsu Tamura: Synthetic Studies on Sorigenins. VI.1) Synthesis of γ-Lactone of 3-Hydroxymethyl-1,6,8-trimethoxy-2-naphthoic Acid (α-Sorigenin Dimethyl Ether). (1).[*1]

(*School of Pharmacy, Osaka University*[*2])

Nikuni, Schmid *et al.*, in 1956, showed that α- and β-sorigenin, aglycons of α- and β-sorinin isolated2) from the bark of *Rhamnus japonica* MAXIM., should have the structural formulas,3,4) 3-hydroxymethyl-6-methoxy-1,8-dihydroxy-2-naphthoic acid γ-lactone (I: R=H, R′=CH_3O) and 3-hydroxymethyl-1,8-dihydroxy-2-naphthoic acid γ-lactone (I: R=R′=H), respectively. Recently, Horii, *et al.* synthesized5) β-sorigenin dimethyl ether (I: R=CH_3, R′=H) and established the structure of β-sorigenin. In this paper, 3-hydroxymethyl-1, 6, 8-trimethoxy-2-naphthoic acid γ-lactone (I: R=CH_3, R′=CH_3O) was synthesized by partial reduction5,6) with lithium alminum hydride of the half ester (VIII)

[*1] Partly reported in Chem. & Ind. (London), **1960**, 1088 as communication.

[*2] Toneyama, Toyonaka-shi, Osaka-fu (堀井善一, 加多木豊之, 田村恭光).

1) Part V: This Bulletin, **11**, 309 (1963).

2) Z. Nikuni: J. Agric. Chem. Soc. Japan, **14**, 352 (1938).

3) R. G. Haber, Z. Nikuni, K. H. Schmid, Yagi: Helv. chim. Acta, **39**, 1654 (1956).

4) Z. Nikuni: J. Agric. Chem. Soc. Japan, **18**, 496 (1942); **17**, 779 (1941); **15**, 109, 283, 1179 (1939).

5) Part II: This Bulletin, **10**, 893 (1962).

6) Part I: *Ibid.*, **10**, 887 (1962).

prepared by methanolysis of 1,6,8-trimethoxy-2,3-naphthalenedicarboxylic anhydride (VII), and was shown to be identical with natural α-sorigenin dimethyl ether. Thus, the structural assignment for α-sorigenin presented by Nikuni, Schmid *et al.*⁽³⁾ was proved to be correct.

As the first plan for approaching to the synthesis of I ($R=CH_3$, $R'=CH_3O$), a route via 3-hydroxymethyl-6,8-dimethoxy-3,4-dihydro-1(2*H*)-naphthalenone (XIII) starting from ethyl 4-oxo-5,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthoate (II)⁽¹⁾ by similar procedures to those employed for 1-methoxy-3-hydroxymethyl-2-naphthoic acid γ-lactone reported in the previous paper⁽⁶⁾ was investigated. An attempt to treat II with ethyl orthoformate and reduce the resulting enol ether⁽⁷⁾ with lithium aluminum hydride in a similar manner to that for preparing 3-hydroxymethyl-3,4-dihydro-1(2*H*)-naphthaleneone from the corresponding 3-carboxy derivative⁽⁶⁾ did not give the keto alcohol XIII, but the diol compound, which was characterized as XII formed on distillation. Another attempt to make XIII by partial oxydation of the above diol with manganese dioxide⁽⁶⁾ also failed. II was partially demethylated with a mixture of 20% hydrochloric acid and acetic acid or with anhyd. aluminum chloride in anhyd. benzene to yield XIVa. However, the action of ethylene glycol and *p*-toluenesulfonic acid to the ester XIVb of XIVa yielded XIVc but did not the ketal. Then, an alternative route involving preparation of 3-bromo-4-hydroxy-5,7-dimethoxy-2-naphthoic acid by the method of Shirley⁽⁸⁾ and carboxylation of the 2-bromo-1,6,8-trimethoxy-3-naphthalenemethanol derivative at the 2-position was tried as the second plan. Demethylation of II with 48% hydrobromic acid and acetic acid gave XVa. Esterification followed by acetylation converted XVa to XVc, but dibromination of XVc produced only resinous material. Thus, these plans were given up.

The successful synthesis of I ($R=CH_3$, $R'=CH_3O$) was carried out as shown in Chart. Ethyl 4-oxo-5,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthoate (II) was condensed with diethyl carbonate in anhyd. benzene in the presence of sodium hydride to give diethyl 1-oxo-6,8-dimethoxy-1,2,3,4-tetrahydro-2,3-naphthalenedicarboxylate (III). On monobromination of the diester III at the 2-position, it was initially obserbed that the bromide produced by the usual method⁽⁹⁾⁽¹⁰⁾ was contaminated with a considerable amount of unseparable side product containing more than one bromine atom in the molecule. However, it was overcome by adding dropwise a high dilution of bromine in chloroform to a chloroform solution of III, and thus the resulting bromide afforded considerably pure diethyl 1-hydroxy-6,8-dimethoxy-2,3-naphthalenedicarboxylate (IV) on dehydrobromination employing lithium carbonate and lithium bromide in dimethylformamide. The diester V, prepared from IV by the action of methyl iodide and anhyd. potassium carbonate in acetone, was hydrolyzed by boiling with a potassium hydroxide solution to the corresponding acid VI, m.p. 263°(lit.,⁽⁴⁾ m.p. 263° for oxidation product of natural α-sorigenin dimethyl ether), which was converted to 1,6,8-trimethoxy-2,3-naphthalenedicarboxylic anhydride (VII), m.p. 267°(lit.,⁽⁴⁾ m.p. 263~264°) by means of acetic anhydride. The anhydride was refluxed in methanol for 20 hour and the resulting half ester VIII⁽¹¹⁾ was reduced with lithium aluminum hydride in a mixture of ether and tetrahydrofuran at −60°, giving the lactone I ($R=CH_3$, $R'=CH_3O$), m.p. 185°, ν_{CO} $1754\,cm^{-1}$ (in chloroform), which was shown to be identical with α-sorigenin dimethyl ether derived from natural material by a mixed melting point determination and comparison of their infrared spectra. On the other hand, when the lithium aluminum hydride reduction of the half

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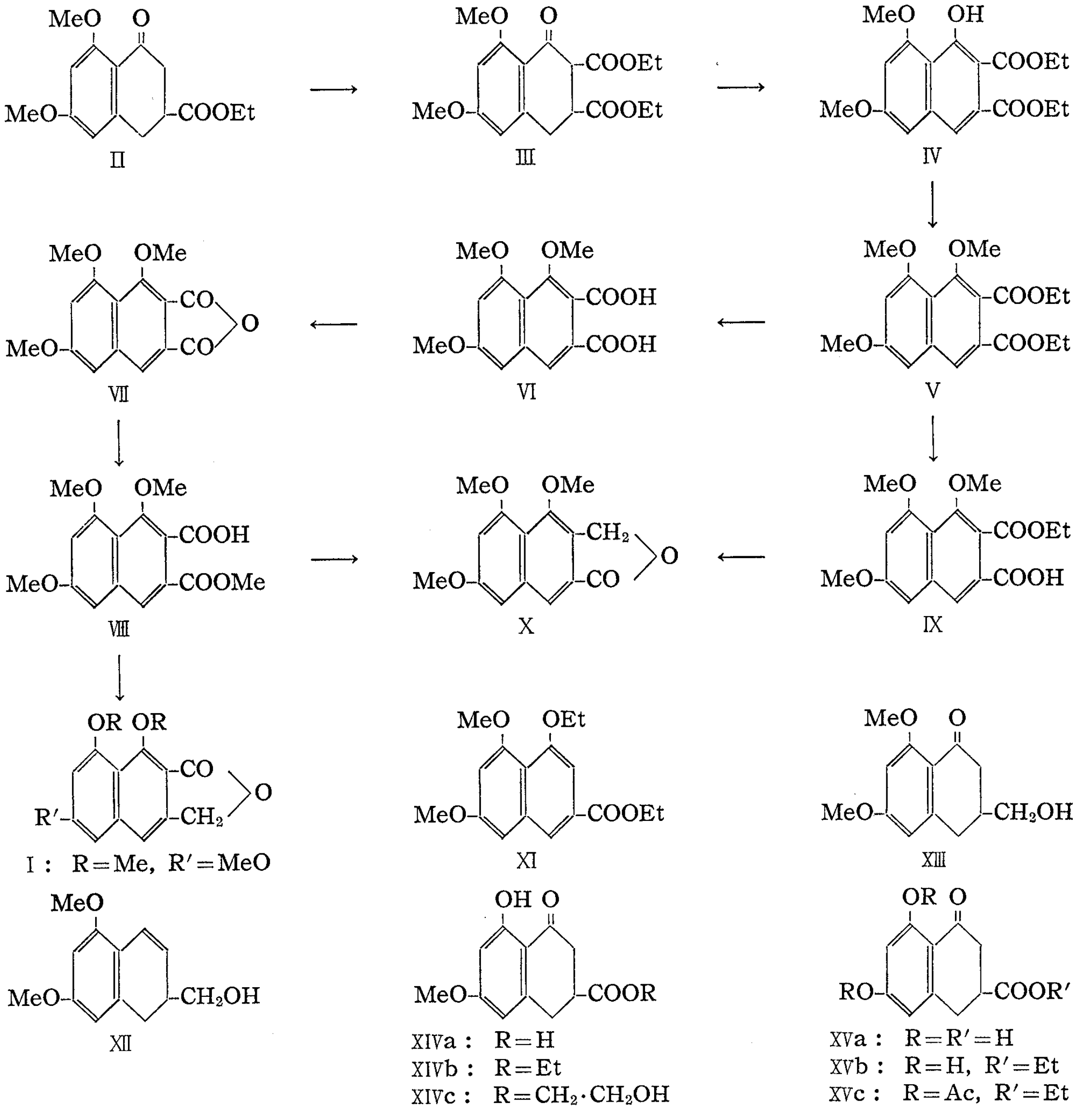
7) E.E. van Tamelen, J. McNary, F.A. Loritzo: J. Am. Chem. Soc., **79**, 1231 (1959).
8) D.A. Shirley, W.L. Dean: *Ibid.*, **79**, 1205 (1957).
9) K. Yagi: J. Agric. Chem. Soc. Japan, **29**, 671 (1955).
10) N.R. Bannerjee, T.R. Seshadri: "The Proceeding of the Indian Academy of Sciences" Vol. 36, p. 134 (1952).
11) E.L. Eliel, A.W. Burgstahler, D.E. Rivard, L. Haefele: J. Am. Chem. Soc., **77**, 5092 (1955).

ester VIII was carried out at 0～−5° of the half ester IX,[5,6] prepared by partial hydrolysis of diethyl 1, 6, 8-trimethoxy-2,3-naphthalenedicarboxylate (V) with an ethanolic potassium hydroxide solution, was reduced with lithium aluminum hydride at −30°, the product was 3-hydroxymethyl-4,5,7-trimethoxy-2-naphthoic acid γ-lactone (X), m.p. 203°, ν_{CO} 1757 cm^{-1} (in chloroform), which was identified with an authentic sample of X prepared in the previous paper.[1] These results provide the synthetic confirmation for the structural formulae I (R=H, R′=CH_3O) of α-sorigenin.



Experimental

Diethyl 1-Oxo-6,8-dimethoxy-1,2,3,4-tetrahydro-2,3-naphthalenedicarboxylate (III)——A mixture of 7.3 g. of ethyl 4-oxo-5,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthoate (II),[1] 15 g. of diethyl carbonate, 1.3 g. of NaH and 50 cc. of anhyd. benzene was heated under reflux in an oil bath for 3 hr. The reaction mixture was poured into ca. 100 cc. of ice-HCl and extracted with benzene. The benzene extract was washed with H_2O successively, $NaHCO_3$ solution and H_2O before being dried over $MgSO_4$. After removing the solvent, the residue was distilled under reduced pressure, giving 5 g. of a yellow oil, b.p$_{0.03}$ 195～200°. The oil was dissolved into Et_2O (10 cc.), kept in a refrigerator for 3 days and then the precipitate was collected. Recrystallization from Et_2O gave 2.8 g. (30.5%) of colorless crystals, m.p. 93~95°. After keeping the mother liquid in a refrigerator for 3 weeks, further 0.5 g. of crude III precipitated. The total yield was 36%. An analytical sample was obtained by recrystallizations from Et_2O, colorless prisms, m.p. 97°. *Anal.* Calcd. for $C_{18}H_{22}O_7$: C, 61.70; H, 6.33. Found : C, 61.66; H, 6.31.

Diethyl 1-Hydroxy-6,8-dimethoxy-2,3-naphthalenedicarboxylate (IV)——To a stirred solution of 1.0 g. of III in 10 cc. of $CHCl_3$ was added dropwise a solution of 0.45 g. of Br_2 in 50 cc. of $CHCl_3$ at room temperature over a period of 4 hr. Stirring was continued at the same temperature for 1 hr. after the addition of Br_2 was completed. The reaction mixture was washed with H_2O, 5% $NaHCO_3$, 5% $NaHSO_3$ and H_2O, and dried over $MgSO_4$. Evaporation of $CHCl_3$ left a crude oily bromide. The crude bromide was heated under stirring with a mixture of 1 g. of LiBr, 1 g. of Li_2CO_3 and 5 cc. of dimethylformamide on a boiling H_2O bath for 5 hr. After cooling, Et_2O (20 cc.) and H_2O (10 cc.) were added to the reaction mixture. The Et_2O layer was washed thoroughly with H_2O and dried over $MgSO_4$. The solvent was removed and the residue was recrystallized from petr. benzin, giving 0.6 g. (63.6%) of IV, m.p. 97°. After several recrystallizations from Et_2O-petr. ether, colorless needles, m.p. 101°, were obtained. *Anal.* Calcd. for $C_{18}H_{20}O_7$: C, 62.06; H, 5.79. Found : C, 62.09; H, 5.86.

Diethyl 1,6,8-Trimethoxy-2,3-naphthalenedicarboxylate (V)——A mixture of 0.54 g. of IV (m.p. 97°), 5 g. of MeI, 1 g. of anhyd. K_2CO_3 and 10 cc. of pure Me_2CO was refluxed for 14 hr. After cooling, K_2CO_3 was filtered from the reaction mixture and washed well with Me_2CO. The filtrate and washings were combined and evaporated, giving an oily residue which solidified slowly on standing at room temperature for one day. Recrystallization from ether-petr. ether gave 0.40 g. (71%) of colorless needles, m.p. 73°. An analytical sample was obtained by several recrystallizations from Et_2O-petr. ether, m.p. 75°. *Anal.* Calcd. for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12. Found : C, 63.10; H, 5.92. IR : $\nu_{\max}^{CHCl_3}$ 1712 cm^{-1} (CO_2Et).

1,6,8-Trimethoxy-2,3-naphthalenedicarboxylic Acid (**VI**)[4]——A mixture of 780 mg. of V, 800 mg. of KOH and 10 cc. of H_2O was refluxed for 2 hr. After cooling, the reaction mixture was washed with Et_2O, acidified with dil. HCl and extracted with AcOEt. The AcOEt extract was washed with H_2O and dried over $MgSO_4$. The solvent was removed, giving 640 mg. (97%) of yellow crystals, m.p. 257~259°. Recrystallizations from EtOH gave light yellow needles, m.p. 261~263°. *Anal.* Calcd. for $C_{15}H_{14}O_7$: C, 58.82; H, 4.61. Found : C, 58.70; H, 4.50.

1,6,8-Trimethoxy-2,3-naphthalenedicarboxylic Anhydride (**VII**)[4]——A solution of 260 mg. of VI in 10 cc. of Ac_2O was refluxed for 30 min. and allowed to cool to room temperature. The deposited yellow needles were collected, washed with Ac_2O and dried, 155 mg. (63%), m.p. 265~267°. Recrystallization from Ac_2O gave an analytical sample, m.p. 267°. *Anal.* Calcd. for $C_{15}H_{12}O_6$: C, 62.50; H, 4.20. Found: C, 62.72; H, 4.17.

3-Hydroxymethyl-1,6,8-trimethoxy-2-naphthoic Acid γ-Lactone (**α-Sorigenin Dimethyl Ether**) (**I**)——**a**) Prepared by methylation of α-sorigenin according to the method of Nikuni,[2] m.p. 185°. *Anal.* Calcd. for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15. Found : C, 65.58; H, 5.24. IR : $\nu_{\max}^{CHCl_3}$ 1754 cm^{-1} (lactone).

b) **From VII**——A suspension of 55 mg. of VII in 10 cc. of MeOH was heated under reflux for 20 hr. until solution was completed. The solvent was removed and the residue was dissolved in $NaHCO_3$ solution. The alkaline solution was washed with Et_2O, acidified with dil. HCl and extracted with Et_2O. The Et_2O extract was washed with H_2O, dried over $MgSO_4$ and evaporated. The residue was recrystallized from benzene-petr. benzin to give 3-methoxycarbonyl-1,6,8-trimethoxy-2-naphthoic acid (VIII) as a yellow powder, IR $\nu_{\max}^{CHCl_3}$ cm^{-1} : 1718 ($MeCO_2$), 1701 (CO_2H). This melted once and solidified again at ca. 170° to give the material (probably VII) which melted at 262°.

To a vigorously stirred solution of 40 mg. of VIII in 5 cc. of dehyd. tetrahydrofuran was added dropwise a solution of 30 mg. of $LiAlH_4$ in 10 cc. of anhyd. Et_2O at −60° over a period of 10 min. After the addition was completed, the mixture was stirred at the same temperature for 1 hr. AcOEt was added to destroy the excess reagent and the solvent under reduced pressure. To the residue was added 10% H_2SO_4 and extracted with Et_2O (30 cc. × 3). The Et_2O extract was washed with H_2O, dil. $NaHCO_3$ and then H_2O, and dried over $MgSO_4$. Evaporation of the solvent gave 17 mg. (50%) of needles, m.p. 182~184°, which was raised up to 185° by further recrystallizations from EtOH. The melting point was undepressed on admixture with an authentic sample of I, derived from natural α-sorigenin. Their IR spectra in $CHCl_3$ were identical. *Anal.* Calcd. for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15. Found : C, 65.76; H, 5.11. IR $\nu_{\max}^{CHCl_3}$ 1754 cm^{-1} (lactone). From the $NaHCO_3$ washing, 20 mg. of unchanged VIII was recovered after acidification with HCl.

3-Hydroxymethyl-4,5,7-trimethoxy-2-naphthoic Acid γ-Lactone (X). **a**) **From VII**——3-Methoxycarbonyl-1,6,8-trimethoxy-2-naphthoic acid (VIII) was prepared from VII and a solution of 34 mg. of VIII in 2 cc. of dehyd. tetrahydrofuran was reduced with a solution of 30 mg. of $LiAlH_4$ in 10 cc. of anhyd. Et_2O at 0~−5° by the same procedure as described for the preparation of I ($R=CH_3$, $R'=OCH_3$) from VII. The crude product (15 mg., 52%, m.p. 196°) was recrystallized from EtOH to give colorless needles of X, m.p. 202°, IR : $\nu_{\max}^{CHCl_3}$ 1757 cm^{-1} (lactone), which was identified with an authentic sample of X obtained at the previous paper.[1]

b) **From V**——A mixture of 86 mg. of V, 15.8 mg. of KOH, 3 cc. of EtOH and a few drops of H_2O was heated under reflux for 7 hr. EtOH was removed, the residue was dissolved in H_2O and the resulting aqueous solution was washed with AcOEt. The aqueous solution was acidified with dil. HCl under ice-cooling and extracted with AcOEt. The AcOEt extract was washed with H_2O and dried. Removing the solvent gave 75 mg. (79%) of 3-ethoxycarbonyl-4,5,7-trimethoxy-2-naphthoic acid (IX) as colorless crystals, IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1} : 1721 ($EtCO_2$), 1692 (CO_2H). This melted once and solidified again at ca. 210° to give the material (probably VII) which melted at 263°.

A solution of 50 mg. of the half ester IX in 6 cc. of dehyd. tetrahydrofuran was reduced with a solution of 200 mg. of $LiAlH_4$ in 20 cc. of anhyd. Et_2O at −30° by the same method as described in a). The crude product (m.p. 197°, 32 mg.) was recrystallized from EtOH to give colorless needles, m.p. 203°. This compound was shown to be identical with authentic samples of X prepared in a) and in the preceding paper[1] by a mixed melting point determination and comparison of their IR spectra.

1,2-Dihydro-5,7-dimethoxy-2-naphthalenemethanol (XII)——The ester II (6.2 g.) was dissolved in a mixture of 3.7 g. of ethyl orthoformate, 1 cc. of anhyd. EtOH and 2 drops of conc. H_2SO_4. The mixture was kept at 40~45° for 3 hr. before being allowed to stand at room temperature over night. The reaction mixture was diluted with 10 cc. of anhyd. Et_2O and the resulting solution was added dropwise to a vigorously stirred solution of 2.6 g. of $LiAlH_4$ in 150 cc. of anhyd. Et_2O at room temperature during a period of 30 min. Stirring was continued for 1 hr. after the addition was completed. To the mixture was added dil. H_2SO_4 to decompose the excess of $LiAlH_4$. The Et_2O layer was washed with H_2O, dil. $NaHCO_3$ and H_2O, and dried over $MgSO_4$. The solvent was removed and the residue was distilled to give 2.1 g. of a pale yellow oil, b.p$_{0.08}$ 154°. *Anal.* Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found : C, 70.66; H, 7.43.

4-Oxo-5-hydroxy-7-methoxy-1,2,3,4-tetrahydro-2-naphthoic Acid (XIVa)——a) A mixture of 1.4 g. of II, 10 cc. of AcOH and 40 cc. of 20% HCl was refluxed for 3 hr. After cooling, the precipitate was collected and washed with water, giving 1.0 g. (84%) of crude XIVa, m.p. 165~169°. The melting point was raised up to 172° by recrystallization from H_2O. *Anal.* Calcd. for $C_{12}H_{12}O_5$: C, 61.01; H, 5.12. Found : C, 61.08; H, 5.32.

b) To a solution of II in 50 cc. of anhyd. benzene was added 3 g. of anhyd. $AlCl_3$ and the mixture was refluxed for 5 hr. The reaction mixture was poured into 100 cc. of ice-H_2O to decompose $AlCl_3$ and extracted with AcOEt. The AcOEt solution was shaken with 5% $NaHCO_3$ and the alkaline extract was acidified with dil. HCl. The precipitate was collected, 0.94 g. (55%), m.p. 170~171°. The melting point was raised up by recrystallizations from H_2O to 172°, which was not depressed on an admixture with a sample of XIVa prepared in a).

Ethyl 4-Oxo-5-hydroxy-7-methoxy-1,2,3,4-tetrahydro-2-naphthoate (XIVb)——A mixture of 1.0 g. of XIVa, 30 cc. of EtOH and a few drops of conc. H_2SO_4 was heated under reflux for 5 hr. After evaporating EtOH, the residue was dissolved in 50 cc. of Et_2O. The Et_2O solution was washed with 5% $NaHCO_3$ and H_2O, dried over $MgSO_4$ and evaporated. The residue was recrystallized from 30 cc. of petr. ether (b.p. 30~40°) to give 0.75 g. (67%) of colorless needles, m.p. 56°. *Anal.* Calcd. for $C_{14}H_{16}O_5$: C, 63.62; H, 6.10. Found : C, 63.95; H, 6.12. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1} : 3322~2632 (broad) (OH), 1724 ($EtCO_2$), 1626 (CO).

2-Hydroxyethyl 4-Oxo-5-hydroxy-7-methoxy-1,2,3,4-tetrahydro-2-naphthoate (XIVc)——A solution of 350 mg. of XIVb, 50 mg. of *p*-toluenesulfonic acid and 10 g. of dehyd. ethylene glycol was heated on a boiling water bath under slightly reduced pressure for 15 hr. After cooling, the reaction mixture was poured into ice-$NaHCO_3$ solution and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. Removing the solvent left 295 mg. of solid, m.p. 80°, which was recrystallized from benzene to give colorless prisms, m.p. 85.5°. *Anal.* Calcd. for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75. Found : C, 59.77; H, 5.76. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1} : 3571, 3472 (OH), 1733 (CO_2R), 1626 (CO).

4-Oxo-5,7-dihydroxy-1,2,3,4-tetrahydro-2-naphthoic Acid (XVa)——A mixture of 5.0 g. of II, 50 cc. of 48% HBr and 30 cc. of AcOH was refluxed in an oil bath for 8 hr. Most of the solvent was removed under reduced pressure and the residue was poured into ice-H_2O. The precipitate was collected and recrystallized from AcOEt to give 2.7 g. (67%) of colorless crystals, m.p. 230°. An analytical sample was obtained by several recrystallizations from AcOEt, m.p. 233°. *Anal.* Calcd. for $C_{11}O_{10}O_5$: C, 59.46; H, 4.54. Found : C, 59.62; H, 4.88.

Ethyl 4-Oxo-5,7-dimethoxy-1,2,3,4-tetrahydro-2-naphthoate (XVb)——A mixture of 1.2 g. of XVa, 30 cc. of EtOH and 0.2 cc. of conc. H_2SO_4 was refluxed for 7 hr. The solvent was removed, the residue was dissolved in AcOEt. The AcOEt solution was washed with $NaHCO_3$ solution and H_2O, and evaporated. Recrystallization of the residue from AcOEt-petr. benzin gave 1.05 g. (77%) of colorless needles, m.p. 163~165°. An analytical sample was prepared by several recrystallizations from AcOEt-petr. benzin, m.p. 165°. *Anal.* Calcd. for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found : C, 62.44; H, 5.59.

Ethyl 4-Oxo-5,7-diacetoxy-1,2,3,4-tetrahydro-2-naphthoate (XVc)——To an ice-cooled solution of 410 mg. of XVb in 3 cc. of anhyd. pyridine was added 300 mg. of AcCl, and the mixture was kept in a refrigerator for 48 hr. The solution was poured into ice-dil. HCl and extracted with AcOEt. The

AcOEt extract was washed with dil. $NaHCO_3$ and H_2O, dried and evaporated to give 510 mg. of a yellow oil, which solidified spontaneously. Recrystallizations from EtOH gave colorless needles, m.p. 97°. *Anal.* Calcd. for $C_{17}H_{18}O_7$: C, 61.07; H, 5.43. Found : C, 61.07; H, 5.22.

Summary

The lithium aluminum hydride reduction of the half ester Ⅷ, obtained by alcoholysis of 1,6,8-trimethoxy-2,3-naphthalenedicarboxylic anhydride (Ⅶ), afforded two kinds of lactones of m.p. 185° and m.p. 202°, among which the former lactone of m.p. 185° was shown to be identical with natural α-sorigenin dimethyl ether, and the latter lactone of m.p. 202° with 3-hydroxymethyl-4,5,7-trimethoxy-2-naphthoic acid γ-lactone (Ⅹ) prepared in the previous paper. Thus, the structure of α-sorigenin dimethyl ether was proved to be 3-hydroxymethyl-1,6,8-trimethoxy-2-naphthoic acid γ-lactone by synthetic means.

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54. Zen-ichi Horii, Toyoshi Katagi, and Yasumitsu Tamura :

Synthetic Studies on Sorigenins. VII.[1] Synthesis of α-Sorigenin Dimethyl Ether (3-Hydroxymethyl-1,6,8-trimethoxy-2-naphthoic Acid γ-Lactone). (2).

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In the preceding paper,[1] the structure I of α-sorigenin dimethyl ether was proved by synthetic means. That is, of both lactones obtained by the reductions of the half esters of 1,6,8-trimethoxy-2,3-naphthalenedicarboxylic acid with lithium aluminum hydride, one coincided with known 3-hydroxymethyl-4,5,7-trimethoxy-2-naphthoic acid γ-lactone[2] and the other with natural α-sorigenin dimethyl ether. This report describes the synthesis of I by an alternative unequivocal route.

It has been shown, previously, that attempts to prepare 3-hydroxymethyl-6,8-dimethoxy-3,4-dihydro-1(2*H*)-naphthalenone from ethyl 5,7-dimethoxy-4-oxo-1,2,3,4-tetrahydro-2-naphthoate (Ⅱb), for example, through the lithium aluminum hydride reduction of the enol ether or ketal of Ⅱb are not successful.[1] The authors investigated to explore another method for blocking the keto group and reducing the ester group selectively on the lithium aluminum hydride reduction of Ⅱb, and devised an excellent procedure applicable for the synthesis of α-sorigenin dimethyl ether. The method, essentially, consists of the lithium aluminum hydride reduction of ethyl 7,9-dimethoxy-4,5-dihydronaphth[2,1-*d*]isoxazole-4-carboxylate (Ⅳb) and the successive alkaline treatment of the resulting 7,9-dimethoxy-4,5-dihydronaphth[2,1-*d*]isoxazole-4-methanol (Ⅵb) to 1-oxo-3-hydroxymethyl-6,8-dimethoxy-1,2,3,4-tetrahydro-2-naphthonitrile (Ⅷb), which was led to α-sorigenin dimethyl ether by aromatization, methylation and hydrolysis.

In an initial study, the synthesis of 1-hydroxy-3-hydroxymethyl-2-naphthoic acid γ-lactone (Ⅸ) from ethyl 4-oxo-1,2,3,4-tetrahydro-2-naphthoate (Ⅱa) was undertaken.

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[1] Part Ⅵ : This Bulletin, **11**, 312 (1963).

[2] Part Ⅴ : *Ibid.*, **11**, 309 (1963).