UDC 547.918

141. Zen-ichi Horii, Toyoshi Katagi, Yasumitsu Tamura, Teiji Tanaka, and Yasuhiko Yamawaki: Synthetic Studies on Sorigenins. III.[1] Syntheses of 4-Methoxynaphtho[2,3-*c*]furan-1(3*H*)-one and 5-Methoxynaphtho[1,2-*c*]furan-3(1*H*)-one.

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During our study on the synthesis of α-sorigenin, it was necessary to prepare 4,5,7-trimethoxynaphtho[2,3-*c*]furan-1(3*H*)-one (I), and as a model compound for investigating the preparation of (I), 4-methoxynaphtho[2,3-*c*]furan-1(3*H*)-one (II) was chosen. Although this compound (II) was reported in our previous paper[2] to be obtainable by the partial reduction of 1-methoxy-2,3-naphthalenedicarboxylic anhydride and 4-methoxy-3-carboethoxy-2-naphthoic acid, the methods imply ambiguity concerning the structure of the product. The present work was undertaken to find such a reliable method of preparing (II)[*2] that the structure of (II) could be established uneqivocally. Thus, it was found that (II) was prepared by condensation of ethyl 4-hydroxy-2-naphthoate (IV) with chloral hydrate followed by hydrolysis and decarboxylation, while the methyl ether (V) of (IV) was led to 5-methoxynaphtho[1,2-*c*]furan-3(1*H*)-one (VIII) by the same sequence of reactions.[3]

Preparation of Compound (VIII)——When the methyl ether (V) was treated with chloral hydrate using 90% sulfuric acid, condensation occurred at *para*-position of methoxy group and produced 1-trichloromethyl-5-methoxynaphtho[1,2-*c*]furan-3(1*H*)-one (VI). Compound (VI) was hydrolyzed with an aqueous potassium hydroxide and the resulting acid (VII) was decarboxylated by heating in diethyl phthalate at 185~190° to 5-methoxynaphtho[1,2-*c*]furan-3(1*H*)-one (VIII). In order to prove the structure of (VI) or (VIII), an attempt to prepare (VIII) by more definite method was made. Ethyl 1-methyl-4-hydroxy-2-naphthoate[4] was methylated with methyl iodide and potassium carbonate in acetone and the methyl ether (IX) obtained was transformed by N-bromosuccinimide (NBS) in carbon tetrachloride into ethyl 1-bromomethyl-4-methoxy-2-naphthoate (X). Hydrolysis of the bromide (X) by a mixture of a 2*N* sodium hydroxide and dioxane gave (VIII). Both samples of (VIII) prepared by the two different routes described above were shown to be identical in respects of melting point, mixed melting point and infrared spectrum.

Preparation of Compound (II)——On the other hand, when (IV) was condensed with chloral hydrate using the same condition as that for preparing (VI), the product was the lactone (XI), whose structure was confirmed by converting it to the known compound, 4-methoxynaphtho[2,3-*c*]furan-1(3*H*)-one (II), by the following reactions. Although an attempt to hydrolyze the lactone (XI) with an alkaline solution resulted in producing a resinous material, the corresponding methyl ether (XII), obtained from (XI) by the action of diazomethane, underwent hydrolysis to give 3-oxo-9-methoxy-1,3-dihydronaphtho-

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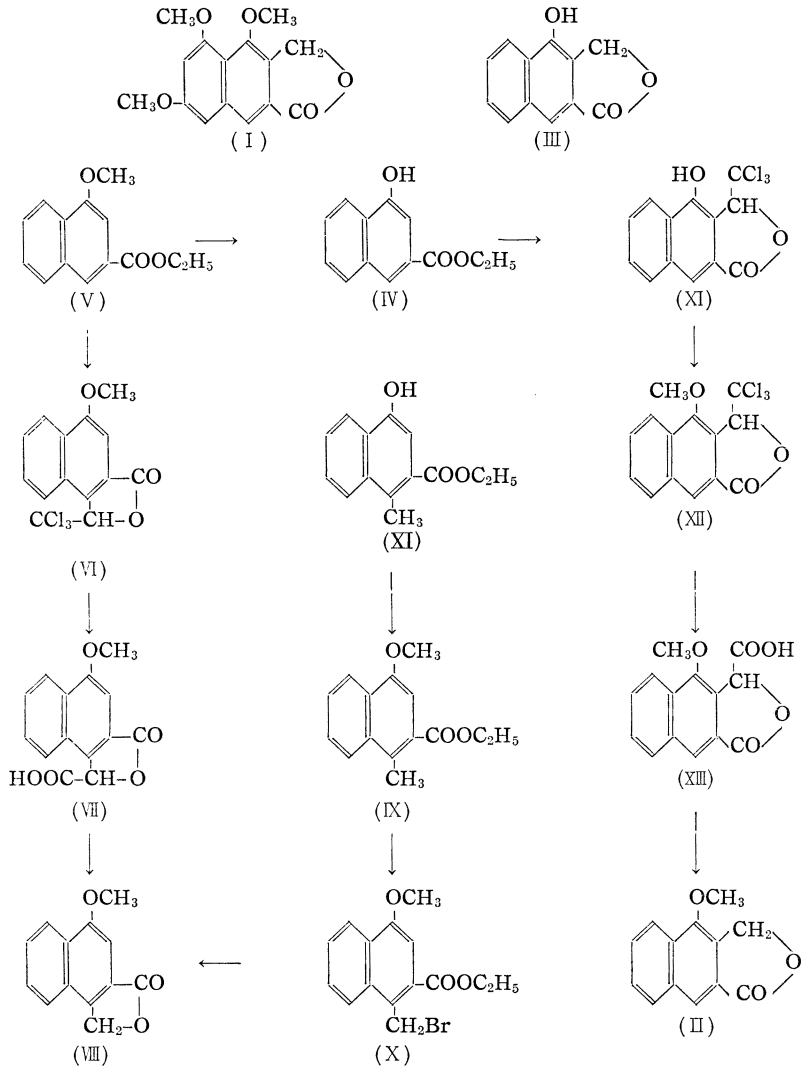
*2 It was reported by K. Yagi that hydroxymethylation of 4-hydroxy-2-naphthoic acid using a 37% formaldehyde solution in an acidic medium afforded 4-hydroxynaphtho[2,3-*c*]furan-1(3*H*)-one (III). Compound (III) would be converted to (II) by the action of diazomethane. Authors attempted to synthesize (II) by this method, but failed to isolate the compound that coincided with an authentic sample of (II). [K. Yagi: J. Agric. Chem. Soc. Japan, **24**, 313 (1950)].

1) Part II: This Bulletin, **10**, 893 (1962).
2) Part I: *Ibid.*, **10**, 887 (1962).
3) P. Fritsch: Ann., **296**, 344 (1897); H. Brockmann: Chem. Ber., **90**, 2302 (1957).
4) Studies on Oxytetracycline and Related Compounds XV. Horii, Sakai, Tamura: This Bulletin, **9**, 455(1961).

[2,3-*c*]furan-1-carboxylic acid (XIII). Compound (XIII) was not decarboxylated by heating it in diethyl phthalate but by heating it with quinoline in the presence of copper powder at 150~160° to yield 4-methoxynaphtho-[2,3-*c*]furan-1(3*H*)-one (II). Compound (II) was identified with a sample naphtho[2,3-*c*]furan-1(3*H*)-one (II) which had been reported in a previous paper.[2] Thus, it was obvious that the condensation of (IV) with chloral hydrate occurred undoubtedly at *ortho*-position of hydroxyl group. Further, this work provided the direct confirmation for the structure of 4-methoxynaphtho[2,3-*c*]furan-1 (3*H*)-one (II) reported in a previous paper.



Experimental

Ethyl 4-methoxy-2-naphthoate (V)——A mixture of 7.5 g. of ethyl 4-hydroxy-2-naphthoate (IV), 7.2 g. of K_2CO_3, 29.6 g. of MeI and 80 cc. of anhyd. Me_2CO was heated under reflux for 15 hr. After cooling, the inorganic salts were filtered from the reaction mixture and the solvent was removed. The residue was extracted with Et_2O, the Et_2O extract was washed with water and dried over Na_2SO_4. Removing the solvent left yellow oil, which solidified slowly on standing at room temperature. Crystal lization from petr. benzin gave 4.8 g. (60%) of ethyl 4-methoxy-2-naphthoate (V), m.p. 66~68° or

b.$p_{0.02}$ 121°. *Anal.* Calcd. for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found : C, 72.50; H, 5.66. IR : $\nu_{max}^{CHCl_3}$ 1698 cm^{-1}.

1-Trichloromethyl-5-methoxynaphtho[1,2-*c*]furan-3(1*H*)-one (VI)——To a mixture of 2 g. of (V) and 1.4 g. of chloral hydrate was added 10 g. of 90% H_2SO_4 and the mixture was stirred at room temperature for 5 hr., during which time it became a dark green paste. Ice-water was poured into the reaction mixture, the deposited white precipitate was collected and washed thoroughly with water to remove H_2SO_4. Recrystallization from Et_2O gave 1.1 g (39%) of colorless plates, m.p. 143.5~144.5°. *Anal.* Calcd. for $C_{14}H_9O_3Cl_3$: C, 50.71; H, 2.74. Found : C, 50.91; H, 2.83. IR : $\nu_{max}^{CHCl_3}$ 1773 cm^{-1}.

3-Oxo-5-methoxy-1,3-dihydronaphtho[1,2-*c*]furan-1-carboxylic Acid (VII)——A suspension of 1.2 g. of (VI) in 75 cc. of 20% KOH was heated in a boiling water bath under stirring for 6 hr. until solution resulted. After cooling, the resulting pale yellow solution was washed with Et_2O and acidified with dil. HCl. The precipitated colorless needles were recrystallized from dil. EtOH yielding 0.7 g. (75%) of (VII), m.p. 180°(decomp.). *Anal.* Calcd. for $C_{14}H_{10}O_5$: C, 65.12; H, 3.90. Found : C, 65.34; H, 3.87. IR ν_{max}^{Nujol} cm^{-1} : 3125 (broad), 1739.

Ethyl 1-Methyl-4-methoxy-2-naphthoate (IX)——A mixture of 4 g. of ethyl 1-methyl-4-hydroxy-2-naphthoate, 3.6 g. of MeI, 2.3 g. of anhyd. K_2CO_3 and 100 cc. of anhyd. Me_2CO was refluxed for 6 hr. The reaction mixture was filtered and Me_2CO was removed from the filtrate. The residue was dissolved in water and extracted with benzene. The benzene extract was washed with dil. NaOH and then water, dried over Na_2SO_4 and evaporated. Recrystallization from petr. benzin gave 2.6 g. (67%) of colorless scales, m.p. 63°. *Anal.* Calcd. for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found : C, 73.83; H, 6.60. IR : $\nu_{max}^{CHCl_3}$ 1706 cm^{-1}.

Ethyl 1-Bromomethyl-4-methoxy-2-naphthoate (X)——A solution of 1 g. of (IX) and 0.52 g. of NBS in 30 cc. of CCl_4 was refluxed for 6 hr. The reaction mixture was filtered and the solvent was removed from the filtrate. The residue was crystallized from petr. benzin, giving 1.2 g. (50%) of colorless needles, m.p. 126°. *Anal.* Calcd. for $C_{15}H_{15}O_3Br$: C, 55.74; H, 4.68. Found : C, 55.87; H, 4.66.

5-Methoxynaphtho[1,2-*c*]furan-3(1*H*)-one (VIII) i) From (VII)——A solution of 0.2 g. of (VII) in 1 cc. of diethyl phthalate was heated at 185~190° under a nitrogen atmosphere until an evolution of CO_2 ceased. The reaction mixture was allowed to cool to room temperature and a small amount of MeOH was added. The insoluble material was recrystallized from dil. EtOH, giving 0.1 g. (63%) of (VIII), m.p. 180.5°. *Anal.* Calcd. for $C_{13}H_{10}O_3$: C, 72.89; H, 4.71. Found : C, 73.05; H, 4.75. IR : $\nu_{max}^{CHCl_3}$ 1749 cm^{-1}.

ii) From (X)——In a mixture of 3 cc. each of 2*N* NaOH and dioxane, 150 mg. of (X) was dissolved and the mixture was refluxed for 3 hr. Most of dioxane was removed by distillation and the residual alkaline solution was acidified with dil. HCl. The acidic solution was warmed on a water bath for 20 min. and was allowed to cool to room temperature. The precipitated crystals were collected and recrystallized from MeOH to give 90 mg. (90%) of colorless needles, m.p. 180.5°. The melting point of this compound was not depressed on admixture with the sample prepared in i). Their IR spectra were identical.

3-Trichloromethyl-4-methoxynaphtho[2,3-*c*]furan-1(3*H*)-one (XII)——To a mixture of 1.8 g. of (IV) and 1.4 g. of chloral hydrate was added 9 g. of 90% H_2SO_4 and stirred at room temperature for 6.5 hr. The reaction mixture was treated in the same manner as described above for the preparation of (VI). Crystallization of the product from Et_2O gave 1.5 g. (57%) of 3-trichloromethyl-4-hydroxynaphtho[2,3-*c*]furan-1(3*H*)-one (XI), m.p. 250°(decomp.) as colorless needles. This material was used for the preparation of (XII).

An Et_2O solution containing large excess of CH_2N_2 was added to a solution of 1.5 g. of (XI) in 30 cc. of AcOEt and the mixture was kept for a week in a refrigerator. AcOH was added to the reaction mixture to destroy the excess of CH_2N_2. The solution was successively washed with water, $NaHCO_3$ solution and water, and dried over Na_2SO_4. After removing the solvent, the residue was recrystallized from Et_2O to give 1.3 g. (84%) of colorless plates, m.p. 184.5~185.5°. *Anal.* Calcd. for $C_{14}H_9O_3Cl_3$: C, 50.71; H, 2.74. Found : C, 50.90; H, 2.96. IR : $\nu_{max}^{CHCl_3}$ 1786 cm^{-1}.

3-Oxo-9-methoxy-1,3-dihydronaphtho[2,3-*c*]furan-1-carboxylic Acid (XIII)——Alkaline hydrolysis of (XII) was carried out by the method described for the preparation of (VII). Crystallization from benzene gave colorless needles of m.p. 197~198°. Yield was 85%. *Anal.* Calcd. for $C_{14}H_{10}O_5$: C, 65.12 : H, 3.90. Found : C, 65.12; H, 3.90. Found : C, 65.22 : H, 3.94. IR ν_{max}^{Nujol} cm^{-1} : 1777, 1730.

4-Methoxynaphtho[2,3-*c*]furan-1(3*H*)-one (II)——A solution of 300 mg. of (XIII) in 2 g. of quinoline was heated in an oil bath in the presence of a small amount of copper powder. CO_2 gas began to evolve at about 120°. The reaction mixture was kept at 150~160°, at which temperature vigorous foaming was observed, until an evolution of CO_2 completed. After cooling, copper powder was removed by filtration and the filtrate was taken up in AcOEt. The AcOEt solution was washed with dil. HCl, water and $NaHCO_3$ solution, and dried over Na_2SO_4. Removing the solvent and recrystallization of the residue from benzene-petr. benzin gave 76 mg. (31%) of needles, m.p. 168°. *Anal.* Calcd. for $C_{13}H_{10}O_3$: C, 72.89; H, 4.71. Found : C, 73.12; H, 4.71. IR : $\nu_{max}^{CHCl_3}$ 1757 cm^{-1}.

Summary

Condensation of ethyl 4-hydroxy-2-naphthoate (IV) and chloral hydrate with sulfuric acid followed by methylation, alkaline hydrolysis and decarboxylation gave 4-methoxynaphtho[2,3-*c*]furan-1(3*H*)-one (II). On the other hand, the methyl ether (V) of (IV) was transformed to 5-methoxynaphtho[1,2-*c*]furan-3(1*H*)-one (VIII) by a similar sequence of reactions. Synthesis of (VIII) by another route starting from ethyl 1-methyl-4-hydroxy-2-naphthoate gave a synthetic confirmation to the structure of (VIII).

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142. Shuichi Seto,*1 Shingo Matsumura,*1 and Katsuo Ro*2 : Synthesis of β-Dolabrin from β-Thujaplicin (Hinokitiol).*3

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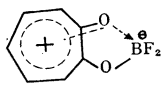
Structural determination and synthesis of β-dolabrin, isolated as a component of the heartwood from *Thujopsis dolabrata* Sieb. et Zucc., besides α- and β-thujaplicins have been already reported by Nozoe, *et al.*[1,2] The β-dolabrin was derived from β-thujaplicin and its details are reported herein.

In the difluoroboron compound (I) of tropolone, the co-ordinated bond would be formed between oxygen atom of the carbonyl group and boron atom, thus the seven-membered ring would possess cationic nature. Consequently, (I) is likely to be unreactive with cationoid reagents. The fact that only (I) is obtainable by the Friedel-Crafts reaction of tropolone using boron trifluoride[3] and that (I) is inert to heating with bromine*4 showed the unreactivity.



(I)

β-Thujaplicin (Hinokitiol) (II) was reacted easily to form difluoroboron compound (III), m.p. 179° with boron trifluoride diethyl ether. The methine group in the isopropyl sidechain of (III) is likely to be activated by the cationic effect of seven-membered ring. Based on these considerations, reaction of (III) with bromine was examined.

Irradiation of sunlight over a chloroform solution of (III) with an excess of bromine at room temperature resulted in a vigorous evolution of hydrogen bromide and monobromo compound (IV), m.p. 189°(decomp.), was obtained fairly in a good yield. (IV) was also obtained by heating a solution of (III) and bromine in chloroform. The ultraviolet spectrum of (IV), as shown in Fig. 1, showed a slightly bathochromic shift in its maximum absorption from that of the starting (III). (IV) was not identical with the difluoro-

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*3 This Paper presented at the 12th Annual Meeting of the Chemical Society of Japan, 1959.
*4 Tropolone and hinokitiol react easily with bromine to form ring-substituted derivatives (cf. T. Nozoe *et al.* : Proc. Japan Acad., **27**, 152 (1951); *ibid.*, **27**, 224 (1951)).

1) T. Nozoe, K. Takase, M. Ogata : Chem. & Ind. (London), **1957**, 1070.
2) T. Nozoe, T. Mukai, T. Asao : Bull. Chem. Soc. Japan, **33**, 1452 (1960).
3) J. W. Cook, R. A. Raphael, A. I. Scott : J. Chem. Soc., **1952**, 4416.