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).

(Received June 5, 1961)

UDC 547.91:582.477

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

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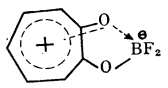
Structural determination and synthesis of β-dolabrin, isolated as a component of the heartwood from *Thujopsis dolabrata* Sieb. et Zucc., besides α- and β-thujaplicins have been already reported by Nozoe, *et al.*[1,2] The β-dolabrin was derived from β-thujaplicin and its details are reported herein.

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)).

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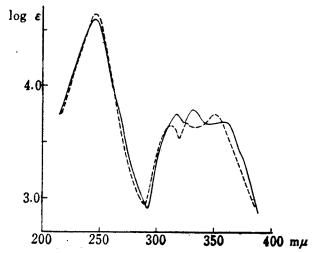
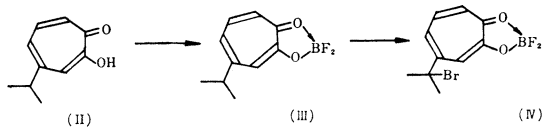


Fig. 1. Ultraviolet Absorption Spectra of (III) and (IV)

------ (III)
——— (IV)

boron compound (VI) of m.p. 116° obtained from 7-bromohinokitiol (V). The infrared absorption bands of (IV) in the C-H out-of-plane region did not differ markedly from that of (III). These facts suggest that (IV) may be either an 8-bromo or 9-bromo compound produced by bromination of the isopropyl side-chain.



Treatment of (IV) in ethanol with tertiary amine, sodium acetate, sodium hydroxide, or pyridine produced free tropolone derivative. Separation and purification of this product as a copper complex afforded a khaki-colored copper complex (VII) of m.p. 198° and a green copper complex (VIII) of m.p. 188°. Melting point, and both ultraviolet and infrared spectra of (VII) were identical well with those of the copper complex of β-dolabrin.

Treatment of (VII) with hydrogen sulfide afforded pale yellow needles (IX), m.p. 58°, which showed no depression of melting point on admixture with β-dolabrin. The ultraviolet and infrared spectra of these two compounds were also in good agreement. The similar treatment of (VIII) with hydrogen sulfide afforded colorless prisms (X), m.p. 48°, whose analytical values were coincident well with the ethoxyl derivative of hinokitiol.

The use of methanol in place of ethanol in the above reaction with alkali and purification as copper complex afforded a green copper complex (XI) of m.p. 230°, besides

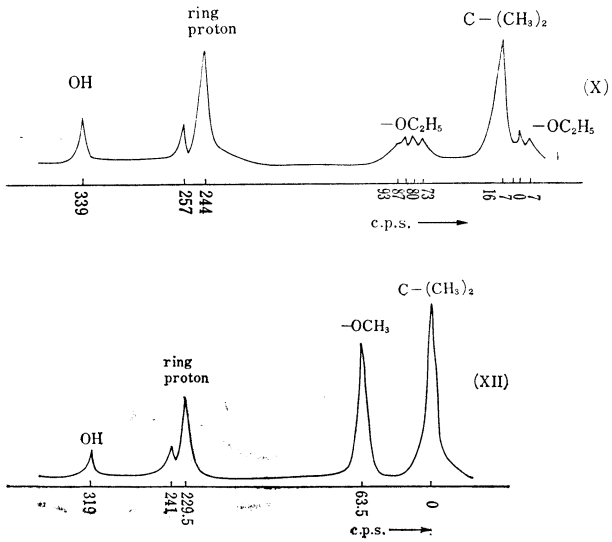


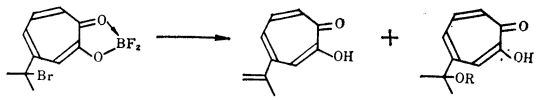
Fig. 2. Proton Magnetic Spectra of (X) and (XII) at 40 Mc. (These spectra were measured under melting condition of (X) at 60°C and (XII) at 80°C.)

(VII). Treatment of (XI) with hydrogen sulfide afforded the methoxyl derivative (XII), m.p. 68°, of hinokitiol.

(IX) was obtained in ca. 30% yield on treatment of (IV) with potassium *tert*-butoxide in *tert*-butanol.

Heating of (IV) with dimethyl sulfoxide for a short time resulted in a formation of the difluoroboron compound (XIII), m.p. 155°, of β-dolabrin, though in a very poor yield. If (IV) were the difluoroboron compound of 9-bromohinokitiol, its alcoholysis should produce 4-(1-alkoxypropyl)tropolone by rearrangement of the methyl group or 9-alkoxyhinokitiol.

The nuclear magnetic resonance spectra of (X) and (XII) are shown in Fig. 2 and there is one characteristic line in those of (X) and (XII) with appropriate height and position corresponding to $-\overset{1}{C}-(CH_3)_2$ group. Consequently, (X) and (XII) should be 8-alkoxyl derivatives of hinokitiol.



(VI) (IX) (X) R=C_2H_5 (XII) R=CH_3

These facts were also supported by the failure to obtain hinopurpurin derivative by treatment of the azo compound (XIV) of m.p. 139°, obtained from (XII) and *p*-toluene diazonium chloride in dilute acid. These results indicated that (IV) was difluoroboron compound of 8-bromohinokitiol.

Treatment of (IV) in sodium hydroxide solution failed to give the product in purified form and formation of 8-bromohinokitiol from (IV) was also unsuccessful.

Experimental*5

Difluoroboron Compound (III) of Hinokitiol——To a solution of 1 g. of hinokitiol (II) dissolved in a mixture of 1 cc. each of benzene and Et_2O, 850 mg. of $BF_3 \cdot Et_2O$ was added. The reaction mixture was cooled with ice during the addition and the reaction proceeded with an evolution of HF and colorless crystals were deposited. They were collected and recrystallized from a mixture of benzene and $CHCl_3$ to colorless scales (III), m.p. 178~179°. Yield, 1.4 g. *Anal.* Calcd. for $C_{10}H_{11}O_2 \cdot BF_2$: C, 56.60; H, 5.18. Found: C, 56.53; H, 5.01. UV λ_{max}^{MeOH} mμ(log ε): 246(4.64), 310(3.66), 325(3.66), 353 (3.76).

Reaction of (III) and Bromine——a) A solution of 4.5 g. of (III) and 4 g. of freshly prepared Br_2 in 150 cc. of $CHCl_3$ was irradiated under sunlight without moisture desiccated through $CaCl_2$ tube. The reaction occurred with vigorous evolution of HBr and colorless scaly crystals began to seperate out after 5~10 hr. The irradiation was continued until crystals were no longer deposited. These crystals were collected and recrystallized from $CHCl_3$ to 5.1 g. of (IV), m.p. 188~189°(decomp.). The mother liquor, kept standing after separation, afforded another crops of 500 mg. of (IV). *Anal.* Calcd. for $C_{10}H_{10}O_2Br \cdot BF_2$: C, 41.24; H, 3.43. Found: C, 41.56; H, 3.24. UV λ_{max}^{MeOH} mμ(log ε): 245(4.67), 317(3.73), 330(3.79), 355(3.69).

b) A solution of 5 g. of (III) and 5 g. of Br_2 dissolved in 60 cc. of $CHCl_3$ was refluxed on a water bath for 5 hr., with a vigorous evolution of HBr and colorless scaly crystals were separated. The crystals were collected after cooled and 5.4 g. of (IV) was obtained. Further 1 g. of (IV) was obtained from its filtrate.

Difluoroboron Compound (VI) of 7-Bromohinokitiol (V)——(V) was treated in exactly the same manner as the preparation of (III) from (II) and (VI) was obtained as colorless scales of m.p. 115~116°. *Anal.* Calcd. for $C_{10}H_{10}O_2Br \cdot BF_2$: C, 41.24; H, 3.43. Found: C, 39.98; H, 3.16. UV λ_{max}^{MeOH} mμ(log ε): 260(4.50), 317(3.75), 380(3.78).

Reaction of (IV) and a Base——a) Reaction of (IV) and AcONa in EtOH: A mixture of 1.5 g. each of (IV) and AcONa suspended in 20 cc. of EtOH was heated for 50 min. and the suspension turned

*5 All m.p.s were not corrected.

pale yellow. EtOH was evaporated from the reaction mixture, to the residue 10 cc. of water was added, and the mixture was heated for 10 min., separating an oil. pH of the solution was adjusted to 3 with dil. HCl and extracted with $CHCl_3$. After drying the extract over anhyd. Na_2SO_4, $CHCl_3$ was evaporated and an addition of aqueous solution of $(AcO)_2Cu$ to the oily residue afforded ca. 1.15 g. of greenish brown Cu complex. Repeated fractional recrystallization of this Cu complex from EtOH gave 50 mg. of khaki-colored Cu complex (VII) of m.p. 196~198°, undepressed on admixture with Cu complex of β-dolabrin. From the easily soluble portion, 600 mg. of green needles (VIII), m.p. 188~189°, was obtained. *Anal.* Calcd. for $C_{12}H_{15}O_3Cu_{1/2}$: C, 60.24; H, 6.32. Found : C, 59.85; H, 6.38.

H_2S was passed through a solution of 90 mg. of (VIII) dissolved in $CHCl_3$ and the precipitated CuS was filtered off. $CHCl_3$ was evaporated from the filtrate, the oily residue was dissolved in benzene, and the solution was passed through a column of silica gel. The colorless crystals obtained from its effluent were recrystallized from petr. ether (b.p. 50~60°) to 30 mg. of colorless prisms (X), m.p. 47~48°. *Anal.* Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found : C, 69.35; H, 7.52. UV λ_{max}^{MeOH} mμ (log ε) : 240 (4.44), 325 (3.95).

Similar treatment of (VII) gave crystals (IX) of m.p. 58°, undepressed on admixture with β-dolabrin.

b) Reaction of (IV) and Triethylamine in EtOH : A mixture of 500 mg. of (IV), suspended in 7 cc. of EtOH and 340 mg. of triethylamine was heated on a water bath for 30 min., and the solids began to dissolve into a pale yellowish and transparent solution. After evaporation of EtOH, 5 cc. of H_2O was added and the mixture was heated for 10 min. Treatment of the product as in (a) afforded 200 mg. of (VII), m.p. 198°, and 130 mg. of (VIII), m.p. 185~188°.

c) Reaction of (IV) and Pyridine in EtOH : A mixture of 200 mg. of (IV) suspended in 2 cc. of EtOH and 0.2 cc. of pyridine was heated and a similar treatment as above gave 60 mg. of (VIII).

d) Reaction of (IV) and EtOH solution of NaOH : A suspension of 500 mg. of (IV) in 5 cc. of EtOH, added with 10 cc. of 5% EtOH-H_2O (4:1) solution of NaOH, was stirred for 1 hr. and (IV) dissolved gradually. EtOH was evaporated in a reduced pressure, to which 2 cc. of H_2O was added, and neutralized with dil. HNO_3. This was extracted with $CHCl_3$, the oily residue obtained after evaporation of the $CHCl_3$ extract was treated with aqueous solution of $CuSO_4$. The Cu complex thereby obtained from EtOH furnished 200 mg. of (VIII), m.p. 188°.

e) Reaction of (IV) and MeOH solution of NaOH : A solution of 7 g. of NaOH dissolved in a mixture of 70 cc. of MeOH and 20 cc. of H_2O was added to the suspension of 11 g. of (IV) in 30 cc. of MeOH and the mixture was stirred at room temperature for 1 hr. MeOH was evaporated in a reduced pressure, 10 cc. of H_2O was added to the residue, and the mixture was neutralized with dil. HNO_3. This was extracted with $CHCl_3$, the residual oil obtained on evaporation of $CHCl_3$ was treated with aqueous solution of $CuSO_4$, and greenish brown Cu complex was separated out. Recrystallization from MeOH afforded 6 g. of green needles (XI), m.p. 228~230°. *Anal.* Calcd. for $C_{11}H_{13}O_3Cu_{1/2}$: C, 58.66; H, 5.86. Found : C, 58.78; H, 5.40.

Treatment of (XI) with H_2S, in a similar manner to the case of (VIII), gave colorless prisms (XII), m.p. 67~68°. *Anal.* Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found : C, 67.41; H, 6.55. UV λ_{max}^{MeOH} mμ (log ε) : 240 (4.42), 325 (3.91).

f) Reaction of (IV) and *tert*-BuOK : A solution of 700 mg. of K dissolved in 10 cc. of *tert*-BuOH, added with 1 g. of (IV), was stirred for 1 hr. at a room temperature by which the solution colored yellow. *tert*-BuOH was evaporated in a reduced pressure, 10 cc. of H_2O was added to the residue, and this was neutralized with dil. HCl. This was extracted with $CHCl_3$, the extract was dried over anhyd. Na_2SO_4, and $CHCl_3$ was evaporated. The oily residue thereby obtained was sublimated at 100° (bath temp.) and at 2 mm. Hg, and the sublimate was recrystallized from petr. ether to 200 mg. of (IX), m.p. 58°.

Reaction of (IV) and Dimethyl Sulfoxide——A solution of 50 mg. of (IV) dissolved in 0.5 cc. of dimethyl sulfoxide was heated on a water bath for 5 min., dimethyl sulfoxide was evaporated in a reduced pressure, and the crystals precipitated were recrystallized from a mixture of benzene and Et_2O to colorless needles (XIII), m.p. 152~153°, undepressed on admixture with BF_2 compound obtained from β-dolabrin.

Difluoroboron Compound (XIII) of β-Dolabrin——(IX) was treated in exactly the same manner as the preparation of (III) from (II) and (XIII) was obtained as colorless needles of m.p. 153~155°. *Anal.* Calcd. for $C_{10}H_9O_2 \cdot BF_2$: C, 57.17; H, 4.76. Found : C, 57.48; H, 4.53. UV λ_{max}^{MeOH} mμ (log ε) : 240 (4.18), 272 (4.19), 310 (3.57), 325 (3.56), 368 (3.60).

5-Tolylazo-8-methoxyhinokitiol (XIV)——The diazonium chloride prepared from 50 mg. of *p*-toluidine was added to 100 mg. of (XII) solution dissolved in 0.4 cc. of pyridine. Addition of H_2O to this reaction mixture produced precipitates in reddish brown solid, and recrystallization from EtOH-H_2O mixture afforded 80 mg. of (XIV), m.p. 139~140°. *Anal.* Calcd. for $C_{18}H_{20}O_3N_2$: C, 69.21; H, 6.45; N, 8.97. Found : C, 69.43; H, 6.27; N, 9.03. UV λ_{max}^{MeOH} mμ (log ε) : 232 (4.43), 387 (4.46).

Reaction of (XIV) and dil. HCl——A mixture of 50 mg. of (XIV) and 0.5 cc. of dil. HCl heated on a water bath for 20 min., and crystalline residue thus obtained was recrystallized from EtOH-H_2O mixture to recover (XIV).

The authors' thanks are due to Professor T. Isobe and Mr. K. Takahashi, the Institute, for their technical co-operation and discussion on NMR spectra; the Takasago Perfumery Co. for a supply of materials which made this investigation possible. The authors are also indebted to Mr. S. Aono for infrared spectral measurements and to Mr. S. Ohyama and Miss. Y. Endo for elemental analyses.

Summary

Reaction of difluoroboron compound of β-thujaplicin and bromine afforded 8-bromo compound, which gave β-dolabrin and 8-alkoxyhinokitiol by a treatment of base in alcohol.

(Received June 8, 1961)

UDC 547.457.1

143. Masuo Akagi, Setsuzo Tejima, and Masanobu Haga : A New Synthesis of 1,6-Anhydro-β-D-glucopyranose (Levoglucosan).

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Several methods for the preparation of 1,6-anhydro-β-D-hexoses (levoglycosans) have been reported. The pyrolysis of sugars and polysaccharides under reduced pressure have been well known to afford 1,6-anhydrides.[1]

Besides pyrolysis, 1,6-anhydro-β-D-glycopyranoses were also obtainable when aryl-β-D-glycopyranosides,[2] aryl-β-D-thioglucopyranoside,[3] 2,3,4,6-tetra-O-acetyl-β-D-glycopyranosyl trimethylammonium bromide,[4] 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl nitrate,[5] 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl fluoride[6] and 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl azide[6] were treated with hot alkali, respectively.

Moreover, it was reported that, by a treatment with alkaline reagents, the ester derivatives sterically hindered, stevioside[7] and 1-O-(2,4,6-trimethylbenzoyl)-β-D-glucopyranose[8,9] gave 1,6-anhydride.

In addition to the reaction with alkaline, the methods of preparing 1,6-anhydro-β-D-glucopyranose by treating 1,2,3,4-tetra-O-acetyl-β-D-glucopyranose[10] and 6-O-trityl-1,2,3,4-tetra-O-acetyl-β-D-glucopyranose[11] with acidic reagents were reported.

The mechanism of 1,6-anhydro ring formation from phenyl-β-D-glucopyranoside

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