[Chem. Pharm. Bull. 15(11)1765~1771(1967)]

UDC 582.28 : 581.13 : 547.672.5

226. Eisaku Morishita and Shoji Shibata*1 : Metabolic Products of Fungi. XXVI.*2 Synthesis of racemic Ustilaginoidin A and Its Related Compounds. (1). Synthesis of 2.2′,4.4′,5.5′,7.7′-Octamethoxy-1.1′-binaphthalene (=Product A Octamethyl Ether).

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Octamethyl ether of product A which was derived from ustilaginoidin A by alkaline degradation was synthesized by the Ullmann condensation of dimethyl ether of 5-bromo-6,8-dimethyl-1,3-naphthalenediol (XXI).

Starting from 3,5-dimethoxyphenylacetic acid (IX), the 2-bromo derivative (VII) was prepared which was C-acetylated to afford XX, and then cyclized to form a bromonaphthalene derivative (XXI), whose methyl ether is XXII. The position of C-C linkage connecting two monomeric moieties of ustilaginoidins has unequivocally been established. Rearrangement of bromine atom during the process of methylation of bromohydroxynaphthalenes and cyclization forming the naphthalene nucleus were also discussed.

(Received March 2, 1967)

Previously Shibata, Ogihara, and Ohta[1,2] studied the structures of ustilaginoidins A, B, and C, the pigments of smutted balls growing on the spikes of living rice plant caused by the infection of *Ustilaginoidea virens* (COOKE) TAKAHASHI, and proposed the structures (I), (II), and (III), respectively; accordingly ustilaginoidin A is a dimer of norrubrofusarin (IV).

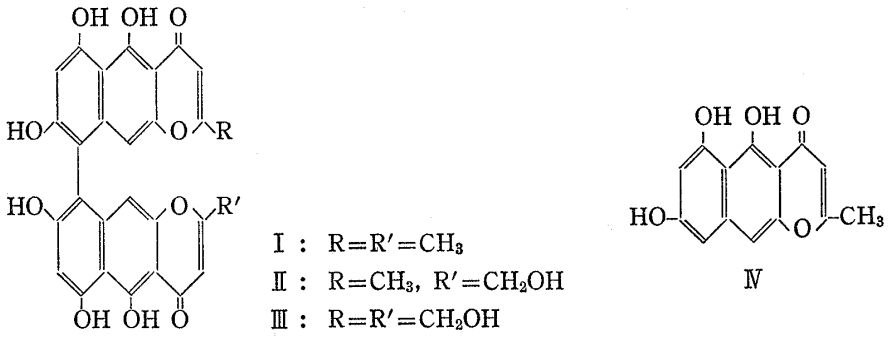


Chart 1.

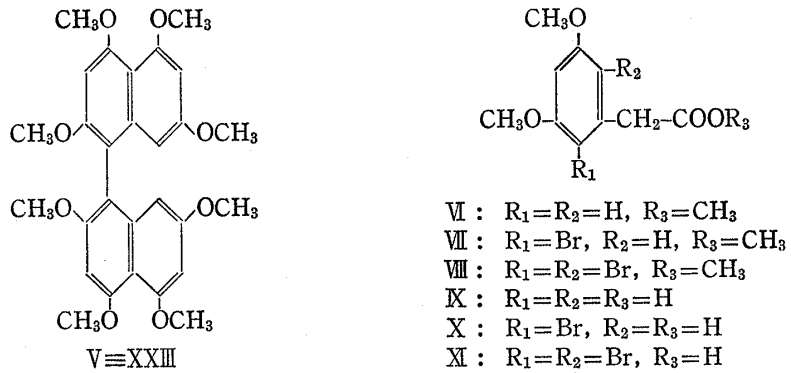


Chart 2.

*1 Hongo, Tokyo (森下顕策，柴田承二).

*2 Part XXV : S. Shibata, E. Morishita, Y. Arima : This Bulletin, **15**, 1757 (1967).

1) S. Shibata, A. Ohta, Y. Ogihara : *Ibid.*, **11**, 1174, 1179 (1963); S. Shibata, Y. Ogihara : *Ibid.*, **11**, 1576 (1963).

2) S. Shibata, Y. Ogihara : Tetrahedron Letters, No. 26, 1777 (1963).

The present paper concerns with the synthesis of octamethyl ether (V) of product A, an alkaline degradation product of ustilaginoidine A, to give a chemical evidence for the position of C-C-linkage connecting two monomeric moieties.

Methyl 3,5-dimethoxyphenylacetate (VI) which was prepared as described in the preceding report*[1] was brominated and subsequently methylated with diazomethane to afford monobromo- (VII) and dibromo- (VIII) derivatives.

The nuclear magnetic resonance (NMR) spectra of VI, VII, and VIII proved the structures of VII and VIII as being methyl 2-bromo-3,5-dimethoxyphenylacetate and methyl 2,6-dibromo-3,5-dimethoxyphenylacetate, respectively.

Table I. NMR Specra in $CDCl_3$ (τ)

	VI	VII	VIII
arom. H	3.62(3H)	3.58(2H)	3.55(H)
arom. $OC\underline{H}_3$	6.25(6H)	6.16(3H) 6.23(3H)	6.13(6H)
$COC\underline{H}_3$	6.33(3H)	6.32(3H)	6.32(3H)
Ph-$C\underline{H}_2$-	6.46(2H)	6.23(2H)	5.82(2H)

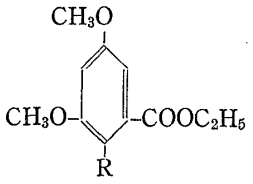
All signals are singlets.

i) The decreasing magnitude of aromatic proton which was observed in VII and VIII by the bromination and esterification of IX showed that the bromine atom is introduced to the benzene ring and not to the phenyl-methylene side chain.

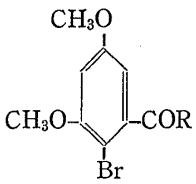
ii) The signals of methoxyl of VI and VIII were singlet showing that the methoxyl is equivalent, while VII gave chemical shift of the non-equivalent methoxyls signal to result two singlets.

Therefore, VIII is 2,6-dibromo and VII is 2-monobromo-derivative. The lower shifting of the phenylmethylene proton signal in the sequence of VI, VII and VIII suggested the deshielding effect of bromine atom at the adjacent position of methylene.

The position of bromine was also proved chemically as follows: Nitration of ethyl 3,5-dimethoxybenzoate[3] (XII) yielded XIII,[4] which was catalytically reduced under pressure with Raney-Ni, and then converted into ethyl 2-bromo-3,5-dimethoxybenzoate (XV).



XII : R=H
XIII : R=NO_2
XIV : R=NH_2
XV : R=Br



XVI : R=OH
XVII : R=Cl
XVIII : R=CHN_2
XIX≡X

Chart 3.

Table 2. NMR Spectra in $CDCl_3$ (τ)

	XII	XIV	XV
arom. H	2.84(2H, d) 3.40(H, d)	3.04(H, d) 3.42(H, d)	3.23(H, d) 3.45(H, d)
$N\underline{H}_2$	——	4.82(2H, s)	——
arom. $OC\underline{H}_3$	6.17(6H, s)	6.14(3H, s) 6.20(3H, s)	6.14(3H, s) 6.20(3H, s)

d: doublet s: singlet

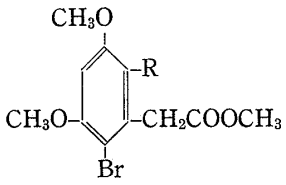
3) Beilstein, **10**, 377, 388, 404.
4) O. Eisleb: D. R. P. 501609 (Chem. Zentr., **1930** (II), 1773). *Idem*: D. R. P. 494434 (Chem. Zentr., **1930** (II), 804).

The NMR spectra of XIV, and XV, giving two non-equivalent methoxyl signals showed that the nitro group is introduced to $C_{(2)}$ of the compound (XII).

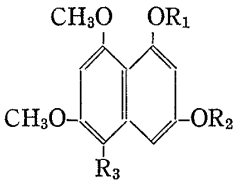
The free acid (XVI) derived from the ester (XV) was converted into the acid chloride (XVII) which was subjected to the Arndt-Eistert reaction to give XIX, m.p. 167°. The identity of XIX with X was established by a mixed fusion and comparison of IR-spectra and thin-layer chromatograms.

The compound (VII) was C-acetylated[5] with acetic anhydride and 60% $HClO_4$ in glacial acetic acid to afford methyl 2-acetyl-6-bromo-3,5-dimethoxyphenylacetate (XX), which was cyclized with sodium methoxide to yield 5-bromo-6,8-dimethoxy-1,3-naphthalenediol (XXI). The dimethyl ether (XXII) of XXI was dimerized by the Ullmann reaction to obtain 2.2′,4.4′,5.5′,7.7′-octamethoxy-1.1′-binaphthalene (XXIII), m.p. 197°, along with the debromination product, 1,3,6,8-tetramethoxynaphthalene (XXIV), m.p. 111°. The compound (XXIV) was identified with methyl ether of 3,6,8-trimethoxy-1-naphthol prepared by Roberts' method.[6]

The product (XXIII) was identified with octamethyl ether (V) of product A by a mixed fusion, and comparison of IR spectra and thin-layer chromatograms.



VII : R=H
XX : R=$COCH_3$

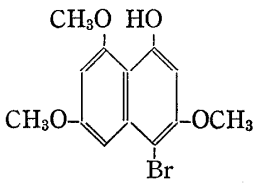


XXI : $R_1=R_2=H$, $R_3=Br$
XXII : $R_1=R_2=CH_3$, $R_3=Br$
XXIV : $R_1=R_2=CH_3$, $R_3=H$
XXV : $R_1=H$, $R_2=CH_3$, $R_3=Br$
XXVII : $R_1=R_3=H$, $R_2=CH_3$

Chart 4.

The position of linkage connecting two monomeric moieties of ustilaginoidins, which was deduced by the NMR analysis, has now been established chemically as being 9 and 9′-positions.

Rearrangement of Bromine Atom in Bromohydroxynaphthalene——Using diazomethane, or dimethyl sulfate and potassium carbonate at room temperature, 5-bromo-6,8-dimethoxynaphthalene-1,3-diol (XXI) was methylated partially to give 5-bromo-3,6,8-trimethoxy-1-naphthol (XXV), m.p. 121° (decomp.) along with an isomer (XXVI), m.p. 131° (decomp.). Both compounds were methylated by usual method to yield 5-bromo-1,3,6,8-tetramethoxynaphthalene, m.p. 116° (XXII).



XXVI

The NMR spectral analysis of XXV and XXVI in comparison with those of XXVII,[6] XXIV, and XXII gave the following results :

Table III. NMR Spectra in $CDCl_3$ (τ)

	XXVII	XXIV	XXV	XXVI	XXII
$C_{(2)}$-H	3.53(d)	3.67(d)	3.53(d)	3.46(s)	3.58(d)
$C_{(4)}$-H	3.34(d)	3.37(2H, d)	3.00(d)	—	2.85(d)
$C_{(5)}$-H	3.37(d)		—	2.95(d)	—
$C_{(7)}$-H	3.67(d)	3.67(d)	3.65(s)	3.68(d)	3.49(s)

d : doublet s : singlet

5) B.W. Bycroft, J.C. Roberts : J. Chem. Soc., **1962**, 2063.
6) *Idem* : *Ibid.*, **1963**, 4868.

The signal of aromatic proton at $C_{(4)\text{ or }(5)}$ of XXV and XXVI shifted to lower field (τ : 3.00 or 2.95) in comparison with those of XXVII. The proton signal corresponding to that of $C_{(5)}$ or $C_{(4)}$ of XXVII and XXIV was not observed in XXV and XXVI, respectively, while the signal of $C_{(7)}$-H in XXV and $C_{(2)}$-H in XXVI appeared as singlets. These results revealed that the by-product of methylation of XXI should be 4-bromo-3,6,8-trimethoxy-1-naphthol (XXVI), which could be formed during the process of methylation by the rearrangement of bromine from $C_{(5)}$ to $C_{(4)}$ or transmethylation from $C_{(8)}$-methoxyl to $C_{(1)}$-hydroxyl.

An attempt to synthesize dimethyl ether (XXVIII)[1] of product B, an alkaline degradation product of ustilaginoidin A hexamethyl ether, was unsuccessful, since the cyclization of the compound XXXI, m.p. 96°, which was prepared by the Claisen or Spassow condensation of XXX and ethyl acetoacetate did not proceed to give the intermediate monomer (XXIX). By the action of polyphosphoric acid at room temperature for 3 hr., XXXI was converted into ethyl 5-bromo-3-hydroxy-6,8-dimethoxy-1-methyl-2-naphthoate, m.p. 137°, (XXXII), while heating at 100° for 5 min., ethyl 4-bromo-3-hydroxy-6,8-dimethoxy-1-methyl-2-naphthoate, m.p. 120°, (XXXIII) and its desbromo derivative (XXXIV)[7] were formed. The NMR spectra of XXXII, XXXIII, and XXXIV were compared to establish the structures.

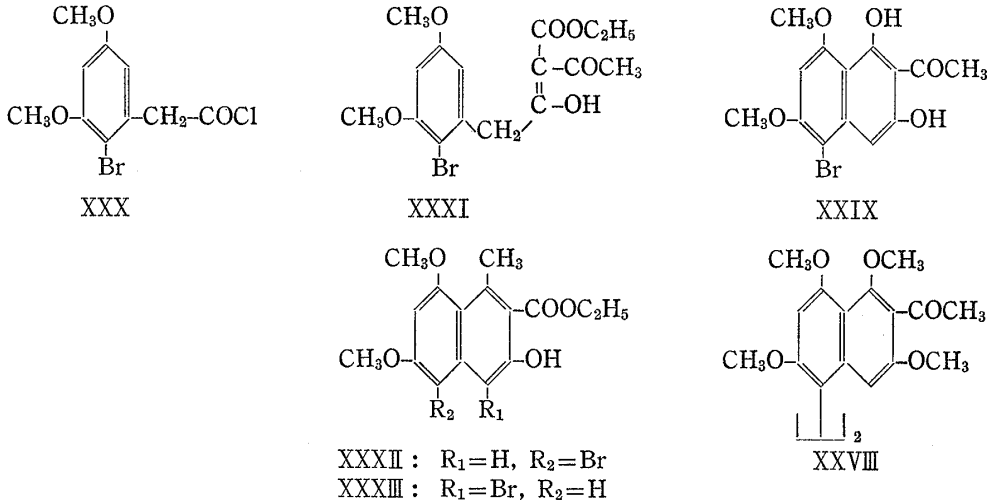


Chart 5.

TABLE IV. NMR $CDCl_3$ (τ)

	XXXIV	XXXII	XXXIII
C_3-OH	0.55(s)		1.55(s)
C_4-H	2.97(s)	2.43(s)	
C_5-H	3.44(d)		3.07(d)
C_7-H	3.62(d)	3.58(s)	3.77(d)
$-OCH_2-CH_3$	5.49(q)	5.52(q)	5.59(q)
OCH_3	6.09(6H, s)	6.02(s), 6.09(s)	6.12(s), 6.15(s)
$Ar-CH_3$	7.06(s)	7.12(s)	7.28(s)
$-OCH_2-CH_3$	8.57(t)	8.60(t)	8.60(t)

s : singlet d : doublet t : triplet q : quartet

The aromatic protons of $C_{(4)}$ and $C_{(7)}$ in XXXII appeared at τ : 2.43 and 3.58 in singlets, whereas those of $C_{(5)}$ and $C_{(7)}$ in XXXIII appeared at τ : 3.07 and 3.77 as doublets

7) S. Shibata, *et al.* : This Bulletin, **15**, 1757 (1967).

by the meta coupling. The rearrangement of bromine as described above has also been observed in this case.

Experimental

Methyl 2-Bromo-3,5-dimethoxyphenylacetate (VII)——To a suspension of IX[7] (20 g.) and $CaCO_3$ (5.6 g.) in dried $CHCl_3$ (400 ml.), the solution of Br_2 (18 g.) in dried $CHCl_3$ (800 ml.) was added dropwise very slowly below 0° for 7 hr. under vigorous stirring. It was necessary to keep a reaction temperature below 0° using ice and salt. The reaction mixture was decomposed with ice water, acidified with conc. HCl and taken to $CHCl_3$. After evaporation, the residue was recrystallizd from 50% EtOH to give colorless needles, m.p. 155~159° (28 g., 91%), which were methylated with CH_2N_2 [made from N-nitrosomethylurea (20 g.)] in ether to afford colorless needles, m.p. 105~106° [from petroleum benzine (b.p. 80~90°)] (18.7 g., 66.8%). A small amount of VIII (m.p. 137~138°) was obtained from the mother liquor by repeated recrystallization from EtOH. *Anal.* Calcd. for $C_{11}H_{13}O_4Br$: C, 45.68; H, 4.50; Br, 27.68. Found: C, 45.60; H, 4.29; Br, 27.93. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1745 (C=O).

2-Bromo-3,5-dimethoxyphenylacetic Acid (X)——A suspension of VII (10 g.) in 15% NaOH (50 ml.) was heated at 130° for 2 hr. in a sealed tube and then the reaction mixture was treated by the usual method. The resulting solids were recrystallized from 50% EtOH to give colorless needles, m.p. 166~167° (9 g., 95%). *Anal.* Calcd. for $C_{10}H_{11}O_4Br$: C, 43.63; H; 4.00; Br, 29.1. Found: C, 43.41; H, 4.16; Br, 28.9. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1723 (C=O).

2,6-Dibromo-3,5-dimethoxyphenylacetic Acid (XI)——Bromination of IX (0.5 g.) with Br_2 (0.9 g., 2 moles) at 10° by the same method as described above produced a dibromo-compound, colorless prisms (from EtOH), m.p. 231~232° (0.61 g., 67.6%). *Anal.* Calcd. for $C_{10}H_{10}O_4Br_2$: C, 33.96; H, 2.82; Br, 45.67. Found: C, 33.93; H, 3.00; Br, 45.33.

Methyl 2,6-Dibromo-3,5-dimethoxyphenylacetate (VIII)——On methylation with an ethereal CH_2N_2 by the usual method, XI (0.35 g.) afforded VIII as colorless prisms (from EtOH), m.p. 137~138° (0.2 g., 58%). *Anal.* Calcd. for $C_{11}H_{12}O_4Br_2$: C, 35.87; H, 3.27; Br, 43.48. Found: C, 36.04; H, 3.58; Br, 43.20. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1748 (C=O).

Ethyl 3,5-Dimethoxybenzoate (XII)——Ethylation of 3,5-dimethoxybenzoic acid[7] with ethanolic HCl gave an ester as a viscous oil, $b.p_7$ 160°, which solidified by ice cooling to colorless needles, m.p. 26~27°. IR ν_{max}^{Cap} cm^{-1}: 1730 (C=O).

Ethyl 3,5-Dimethoxy-2-nitrobenzoate (XIII)[4]——Nitration of XII (20 g.) by O. Eisleb's method yielded pale yellow prisms (from EtOH), m.p. 128° (20 g., 82.5%). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (C=O).

Ethyl 2-Amino-3,5-dimethoxybenzoate (XIV)——A suspension of XIII (20 g.), Raney Ni (10 g.) in EtOH (250 ml.) was hydrogenated catalytically under high pressure (90 Atm → 75 Atm) at 80~100° for 3 hr. After filtration and evaporation, the residue was dissolved in ether and extracted with 5% HCl. The acidic layer was made alkaline and extracted with ether. After removal of solvent, the product was purified by vacuum distillation to afford a yellow oil, $b.p_4$ 142~145° (14 g., 79.4%), which solidified on cooling to give pale yellow prims, m.p. 44° (from 50% EtOH). IR $\nu_{mxa}^{CCl_4}$ cm^{-1}: 3570, 3410 (NH_2), 1700 (C=O).

Ethyl 2-Bromo-3,5-dimethoxybenzoate (XV)——A mixture of XIV (10 g.) in 48% HBr (13.5 ml.) was diazotized at 0° with $NaNO_2$ (3.7 g.) in H_2O (6.7 ml.) and the reaction mixture gave a purple color. The above diazonium solution was added dropwise quickly to a suspension of freshly prepared CuBr (5 g.) in 48% HBr (5 ml.). Under refluxing, the reaction proceeded smoothly under the evolution of N_2. After 30 min., the reaction mixture was poured into water and extracted with $CHCl_3$. The purification by chromatography on neutral Al_2O_3 (Wohlem) using $CHCl_3$ as the developing solvent and by the subsequent vacuum distillation yielded a pale yellow oil, $b.p_4$ 140~150°, which solidified on cooling. Recrystallization from 60% MeOH afforded colorless needles, m.p. 32~33° (6.8 g., 53%). *Anal.* Calcd. for $C_{11}H_{13}O_4Br$: C, 45.70; H, 4.50. Found: C, 46.05; H, 4.51. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 (C=O).

2-Bromo-3,5-dimethoxybenzoic Acid (XVI)——Hydrolysis of XV (6.8 g.) with 15% NaOH (40 ml.) in EtOH (15 ml.) at 120~130° for 2 hr. in a sealed tube gave the acid (XVI) as colorless needles (from EtOH), m.p. 199.5~200.5° (5.3 g., 86.7%). *Anal.* Calcd. for $C_9H_9O_4Br$: C, 41.40; H, 3.45. Found: C, 41.60; H, 3.63.

2-Bromo-3,5-dimethoxybenzoyl Chloride (XVII)——The compound (XVI) (6.4 g.) was refluxed with $SOCl_2$ (10 ml.) for 1 hr. After removal of the excess $SOCl_2$ *in vacuo*, the residue was recrystallized from petroleum benzine (b.p. 60~80°) to yield colorless needles, m.p. 84.5~85.5° (5.5 g., 95%). This was characterized as an amide, colorless needles (from EtOH), m.p. 171~172°. *Anal.* Calcd. for $C_9H_{10}O_3NBr$: C, 41.60; H, 3.84; N, 5.38. Found: C, 41.77; H, 4.05; N, 5.13. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3445, 3210 (NH_2), 1690, 1650 (C=O).

2-Bromo-3,5-dimethoxybenzoyldiazomethane (XVIII)——A solution of XVII (5 g.) in dried benzene was added to an ethereal CH_2N_2 [prepared from N-nitrosomethylurea (4 g.)] under stirring at 0°. After standing overnight, the solvent was removed *in vacuo* and the residue was recrystallized from petroleum benzine-benzene (9:1) to form pale yellow needles, m.p. 86~87° (4.9 g., 96%). *Anal.* Calcd. for $C_{10}H_9O_3N_2Br$: C, 42.10; H, 3.16; N, 9.83. Found: C, 42.07; H, 3.03; N, 9.82. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2130 ($COCHN_2$).

2-Bromo-3,5-dimethoxyphenylacetic Acid (XIX)——To a suspension of Ag_2O (2 g.), $Na_2S_2O_3 \cdot 5H_2O$ (2.9 g.) and Na_2CO_3 (1.25 g.) in H_2O (55 ml.), a solution of XVIII (4.5 g.) in dioxane (20 ml.) was added dropwise at 80~85°. The reaction mixture was kept at 90~95° for further 1 hr. and added with H_2O. After removal of Ag_2O, the filtrate was acidified with conc. HNO_3, to separate pale yellow solid which was recrystallized from 50% EtOH to give colorless needles, m.p. 166~167° (2.7 g., 62.2%), which was identified with X by a mixed fusion. *Anal.* Calcd. for $C_{10}H_{11}O_4Br$: C, 43.63; H, 4.00; Br, 29.1. Found : C, 43.21; H, 4.03; Br, 28.5.

Methylation of this product with ethereal CH_2N_2 gave an ester (VII), m.p. 105~106° (85%).

Methyl 2-Acetyl-6-bromo-3,5-dimethoxyphenylacetate (XX)——To a solution of VII (6 g.) in a mixture of AcOH (50 ml.) and Ac_2O (24 ml.), twenty drops of 60% $HClO_4$ was added slowly at 65° on a water bath under occasional shaking and then the mixture was poured into ice-water. The separated solid was washed with 5% $NaHCO_3$ and H_2O. On recrystallization from MeOH, coloress needles, m.p. 141~142° (5 g., 73%) were obtained. *Anal.* Calcd. for $C_{13}H_{15}O_5Br$: C, 47.13; H, 4.53. Found : C, 47.06; H, 4.55. IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 1740, 1690 (C=O). NMR $\tau_{Me_4Si}^{CDCl_3}$: 3.52 (H, arom. H), 6.06, 6.12 (6H, $OC\underline{H}_3$), 6.09 (2H, $-C\underline{H}_2-$), 6.28 (3H, $COOC\underline{H}_3$), 7.50 (3H, $COC\underline{H}_3$).

5-Bromo-6,8-dimethoxy-1,3-naphthalenediol (XXI)——A solution of XX (8.5 g.) in dried benzene (67 ml.) was added dropwise to a boiling solution of Na (1.28 g.) in abs. MeOH (57 ml.) under N_2-stream. After boiling for a further 20 min., the reaction mixture was cooled and poured into a solution of 10% H_2SO_4 (43 ml.) and H_2O (300 ml.) for decomposition. The separated crystals were recrystallized from 60% MeOH to yield colorless needles, m.p. 250° (darken from 120°), (6.53g., 85%). It is soluble in 5% Na_2CO_3 to give an orange red solution and gives a red color with Gibbs' reagent. This substance is unstable on standing for a long time or heating. *Anal.* Calcd. for $C_{12}H_{11}O_4Br$: C, 48.16; H, 3.68. Found : C, 48.29; H, 3.88. IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 3590, 3400 (OH).

4-Bromo-1,3,6,8-tetramethoxynaphthalene (XXII)——XXI (5 g.) was methylated by refluxing for 5 hr. in Me_2CO (125 ml.) with Me_2SO_4 (5 ml.) and K_2CO_3 (5 g.). A methyl ether was yielded as a pale yellow solid, which was purified by chromatography using $CHCl_3$ as the solvent on silica gel and recrystallized from MeOH–petroleum benzine to yield colorless needles, m.p. 115~116° (3 g., 55%). *Anal.* Calcd. for $C_{14}H_{15}O_4Br$: C, 51.38; H, 4.59. Found : C, 51.62; H, 4.47. UV λ_{max}^{EtOH} mμ (log ε) : 217 (4.31), 242 (4.74), 307 (3.81), 330 (3.76).

2.2',4.4',5.5',7.7'-Octamethoxy-1,1'-binaphthalene (XXIII) (Product A Octamethyl Ether)——A mixture of XXII (0.3 g.) and Cu bronze (0.3 g.) was heated at 260~280° for 30 min. in N_2-stream. The reaction mixture was extracted with $CHCl_3$ and chromatographed on Al_2O_3 using $CHCl_3$–acetone (1:1) as a solvent to obtain a colorless oily substance removing resinous by-products. The resulting oil was purified by repeated chromatography on silica gel using $CHCl_3$ as the solvent. From the bottom fluoresent band, colorless prisms, m.p. 111° (0.03 g., 13.5%) were isolated. It was identified with 1,3,6,8-tetramethoxynaphthalene (XXIV). The second fluorescent band was eluted and recrystallized from MeOH to give colorless needles, m.p. 197° (0.03 g., 13.5%), which showed no melting point depression on admixture with product A octamethyl ether. *Anal.* Calcd. for $C_{28}H_{30}O_6$: C, 68.02; H, 6.07. Found : C, 67.78; H, 6.11. UV λ_{max}^{EtOH} mμ (log ε) : 242 (4.96), 316 (4.13), 330 (4.09).

5-Bromo-3,6,8-trimethoxy-1-naphthol (XXV) and 4-Bromo-3,6,8-trimethoxy-1-naphthol (XXVI)——1) A partial methylation of XXI with CH_2N_2 : To a solution of XXI (0.45 g.) in ether (10 ml.) and MeOH (2 ml.), an ethereal solution of CH_2N_2 [prepared from N-nitrosomethylurea (1 g.)] was added dropwise. After standing overnight and evaporation of the solvent, the residue was chromatographed on silica gel using $CHCl_3$ as the solvent. From the bottom band, XXVI, m.p. 130~131°, was obtained. The second band was eluted and recrystallized from MeOH to give colorless needles, m.p. 120~121° (decomp.) (0.2 g., 42.5%) (XXV). It gives a violet color with Gibbs' reagent and darkens on heating *in vacuo*. *Anal.* Calcd. for $C_{13}H_{13}O_4Br$: C, 49.84; H, 4.15. Found : C, 50.02; H, 4.10. UV λ_{max}^{EtOH} mμ (log ε) : 217 (4.25), 245 (4.92), 310~320 (3.79), 334 (3.74). IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 3386 (OH).

Acetate——Acetylation of XXV (0.25 g.) with Ac_2O (2 ml.) and pyridine (0.5 ml.) produced colorless needles (from benzene), m.p. 188~189° (decomp.) (0.25 g., 88%). *Anal.* Calcd. for $C_{15}H_{15}O_5Br$: C, 50.70; H, 4.23. Found : C, 50.86, H, 4.23. IR $\nu_{max}^{CHCl_3}$: 1767 (C=O).

2) A partial methylation of XXI with a mixture of Me_2SO_4 and K_2CO_3 : XXI (1 g.) was methylated with Me_2SO_4 (0.5 ml.) and K_2CO_3 (1 g.) in Me_2CO (25 ml.) at room temperature for 2.5 hr. After treating by the usual method, the product was purified by chromatography as described above. From the first band, colorless needles (from benzene–MeOH), m.p. 130~131° (decomp.) (0.225 g., 26.3%) was separated. It is insoluble in 5% NaOH and gives a light blue color with Gibbs' reagent. *Anal.* Calcd. for $C_{13}H_{13}O_4Br$: C, 49.84; H, 4.15. Found : C, 50.15; H, 4.12. UV λ_{max}^{EtOH} mμ (log ε) : 217 (4.32), 248 (4.77), 310~320 (3.78), 333 (3.74). IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 3390 (OH). From second band, XXV, m.p. 120~121° (decomp.) (from MeOH) (1.2 g., 57.5%) was obtained as above.

4-Bromo-1,3,6,8-tetramethoxynaphthalene (XXII)——Methylation of both XXV (0.2 g.) and XXVI (0.2 g.) with a mixture of Me_2SO_4 (0.2 ml.) and K_2CO_3 (0.5 g.) in Me_2CO (10 ml.) gave colorless needles (from MeOH), m.p. 115~116° in a good yield (0.18 g., 83.2%). This was proved to be identical with XXII by a mixed fusion (mixed m.p. 115~116°).

3-Bromo-3,5-dimethoxyphenylacetyl Chloride (XXX)——A solution of X (3 g.) and PCl_3 (0.63 ml.) in abs. benzene (20 ml.) was refluxed for 1 hr. After filtration removing insoluble substance, the mixture was evaporated *in vacuo* to obtain a yellow syrupy oil. On addition of a small amount of petroleum benzine under ice-cooling, colorless needles (3 g., 93%), which were characterized as the corresponding amide, m.p. 189~190°, were separated. *Anal.* Calcd. for $C_{10}H_{12}O_3BrN$: C, 43.80; H, 4.38; N, 5.11. Found: C, 44.23; H, 4.53; N, 5.03. IR ν_{max}^{KBr} cm^{-1}: 3398, 3253 (NH_2), 1663 (CO).

Ethyl 2-(2-Bromo-3,5-dimethoxyphenylacetyl)acetoacetate (XXXI)——1) By the Claisen reaction: A solution of ethyl acetoacetate (1.42 g.) in abs. ether (5 ml.) was added gradually at 0° to a suspension of NaH (0.3 g.) in abs. ether (10 ml.) under stirring. The reaction occurred rapidly under evolution of H_2-gas and a syrupy sodium salt was formed. After standing for 1 hr. under stirring a solution of XXX (3 g.) in abs. benzene (30 ml.) was added dropwise to the above reaction mixture below 0° under vigorous stirring. After standing for 1 hr. at room temperature and then refluxing for 3 hr., the reaction mixture was poured into 5% H_2SO_4 and ice. The isolated benzene layer was shaken with 5% $NaHCO_3$ to remove the starting material (X) (0.25 g., 8.35%), washed with H_2O and dried. Evaporation of the solvent left a yellow oil, which was solidified under ice-cooling and recrystallized from EtOH to give colorless needles, m.p. 95~96° (2.35 g., 59.5%). *Anal.* Calcd. for $C_{16}H_{19}O_6Br$: C, 49.61; H, 4.91. Found: C, 49.66; H, 5.06. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705 (C=O). It gives a red color with $FeCl_3$ and forms, by the addition of a saturated aqueous solution of cupric acetate, Cu-salt, pale blue needles (from EtOH), m.p. 158~159°. *Anal.* Calcd. for $C_{16}H_{18}O_6Br \cdot \frac{1}{2}Cu$: C, 45.90; H, 4.31. Found: C, 45.93; H, 4.35.

2) By the Spassow reaction: By the modified Viscontini and Köhler's method, XXXI was produced from X (10 g.), Mg (0.84 g.) and ethyl acetoacetate (4.45 g.) in a yield of 6.1 g. (43.5%).

Ethyl 5-Bromo-3-hydroxy-6,8-dimethoxy-1-methyl-2-naphthoate (XXXII) and Ethyl 4-Bromo-3-hydroxy-6,8-dimethoxy-1-methyl-2-naphthoate (XXXIII)——Ring closure of XXX with PPA.

1) Cyclization at room temperature: A mixture of XXXI (0.5 g.) and PPA [prepared from H_3PO_4 (5 ml.) and P_2O_5 (5 g.)] was allowed to stand for 3 hr. at room temperature. The reaction mixture was poured into ice water and the pale green precipitates were collected and chromatographed on silica gel using $CHCl_3$ as the solvent. The third band from the bottom was eluted and recrystallized from benzene-petroleum benzine to yield colorless plates (XXXII), m.p. 136~137° (0.1 g., 21%). It gives a blue color with Gibbs' reagent and positive Beilstein reaction. *Anal.* Calcd. for $C_{16}H_{17}O_5Br$: C, 52.03; H, 4.61. Found: C, 52.12; H, 4.68. UV λ_{max}^{EtOH} mμ (log ε): 255 (4.66), 315 (3.77). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3250 (OH), 1725, 1670 (C=O).

2) Cyclization at 100° for 5 min.: A mixture of XXXI (4 g.) and PPA (made as described above) was reacted at 100° for 5 min. The reaction mixture was poured into ice water and extracted with $CHCl_3$. The extract was purified by chromatography on silica gel using $CHCl_3$ as the solvent. From the bottom yellow fluorescent band, colorless prisms (XXXIII) (from petroleum benzine), m.p. 119~120° (0.1 g., 2.62%), which gave a dark green color (changed gradually into blue) with Gibbs' reagent, were obtained. *Anal.* Calcd. for $C_{16}H_{17}O_5Br$: C, 52.03; H, 4.61. Found: C, 52.32; H, 4.84. UV λ_{max}^{EtOH} mμ (log ε): 245 (4.65), 307 (3.79). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3520, 3100 (OH), 1737, 1670 (C=O). From the second yellow fluorescent band, colorless needles (from petroleum benzine), m.p. 130~131° (0.2 g., 6.7%), identical with XXXIV[7] (a debromination product of XXXIII) were isolated.

The authors are indebted to Dr. S. Matsuura, Gifu College of Pharmacy for supplying the starting material (α-resorcylic acid). A part of the experiment was carried out by Mr. N. Nishiyama of this Faculty, the microanalysis and UV, IR and NMR spectral measurement were carried out by the members of Microanalytical Laboratory of this Faculty, to whom the authors' thanks are due.