Summary

X-ray crystal structure analysis has been made on the securinine hydrobromide dihydrate, which is monoclinic, with two formula units in a cell of dimensions: $a=7.71\,\text{Å}$, $b=14.83\,\text{Å}$, $C=7.04\,\text{Å}$, and $\gamma=112.13°$. The space group is $P2_1$. The determination of the atomic parameters was carried out by the generalized projection methods.

The conclusions may be summed up as follows:

The piperidine ring has a skewed boat form, and the diene part is not co-planar. A dihedral angle of about 10° has been found between the plane passing through C2-, C3-, and C3*a*-atoms and the one involving C3*a*-, C4-, and C5-atoms.

Discussion has been made on the location of the lone electron pair on the nitrogen atom in the free base.

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85. Zen-ichi Horii, Takefumi Momose, and Yasumitsu Tamura: Synthetic Studies on η-Pyrromycinone II.[*1] Synthesis of Methyl 2-Ethyl-5-hydroxy-1-naphthoate.

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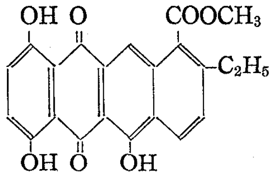
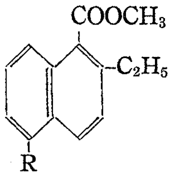
In recent communications,[1,2] the synthesis of η-pyrromycinone (I) has been accomplished *via* the Friedel-Crafts reaction of 3,6-dimethoxyphthalic anhydride and methyl 2-ethyl-5-hydroxy-1-naphthoate (II, R=OH). This paper describes a detail of the experiments for the synthesis of II (R=OH), which was carried out by a similar series of reactions to those for II (R=H) reported in the preceding paper.[*1] The stereochemistries of the intermediate tetralone derivatives are also discussed.



I



II

Condensation of (*m*-methoxyphenyl)acetonitrile[3] with ethyl 2-pentenoate[4] in the presence of one molar equivalent of sodium ethoxide gave ethyl 3-ethyl-4-cyano-4-(*m*-methoxyphenyl)butyrate (III) in 65% yield. A short time alkaline hydrolysis of III gave three products, *i.e.* 3-ethyl-4-cyano-4-(*m*-methoxyphenyl)butyric acid (IV), 3-ethyl-4-carbamoyl-4-(*m*-methoxyphenyl)butyric acid (V) and 2-(*m*-methoxyphenyl)-3-ethylglutaric acid (VI). Refluxing III with 28% aqueous potassium hydroxide for 24 hours gave

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[*1] Part I. Z. Horii, M. Sakamoto, T. Momose, Y. Tamura: Yakugaku Zasshi, **85**, 524 (1965).

[*2] Toneyama, Toyonaka, Osaka-fu (堀井善一, 百瀬雄章, 田村恭光).

1) Z. Horii, T. Momose, Y. Tamura: This Bulletin, **12**, 1262 (1964).

2) *Idem*: *Ibid.*, **13**, 635 (1965).

3) D.K. Banerjee, J. Dutta, A.S. Rao, E.J. Jacob: Tetrahedron, 8, 163 (1960). Cf. W.S. Rapson, R. Robinson: J. Chem. Soc., **1935**, 1533; S.N. Chakravarti, P.L.N. Rao: *Ibid.*, **1938**, 172; M. Asano, N. Fujiwara: Yakugaku Zasshi, **59**, 141 (1939); R.B. Woodward: J. Am. Chem. Soc., **62**, 1478(1940); R. Pschorr: Ann., **391**, 43 (1948); A.W.D. Avison, A.L. Morrison: J. Chem. Soc., **1950**, 1469; D.H. Hey, K.A. Nagdy: *Ibid.*, **1953**, 1894; H. Tsukamoto, H. Yoshimura, S. Toki: This Bulletin, **3**, 239 (1955).

4) R. Tschesche, H. Barkemeyer, G. Heuschkel: Chem. Ber., **88**, 1258 (1955).

VI as a sole product, which did not crystallize and was characterized as the dimethyl ester prepared by action of diazomethane. The glutaric acid (VI) thus obtained is assumed to be a diastereoisomeric mixture from comparison of its infrared spectrum with that of a pure isomer (VIa) prepared by hydrogenolysis of 2-(2-bromo-5-methoxyphenyl)-3-ethylglutaric acid (VIIa) described later.

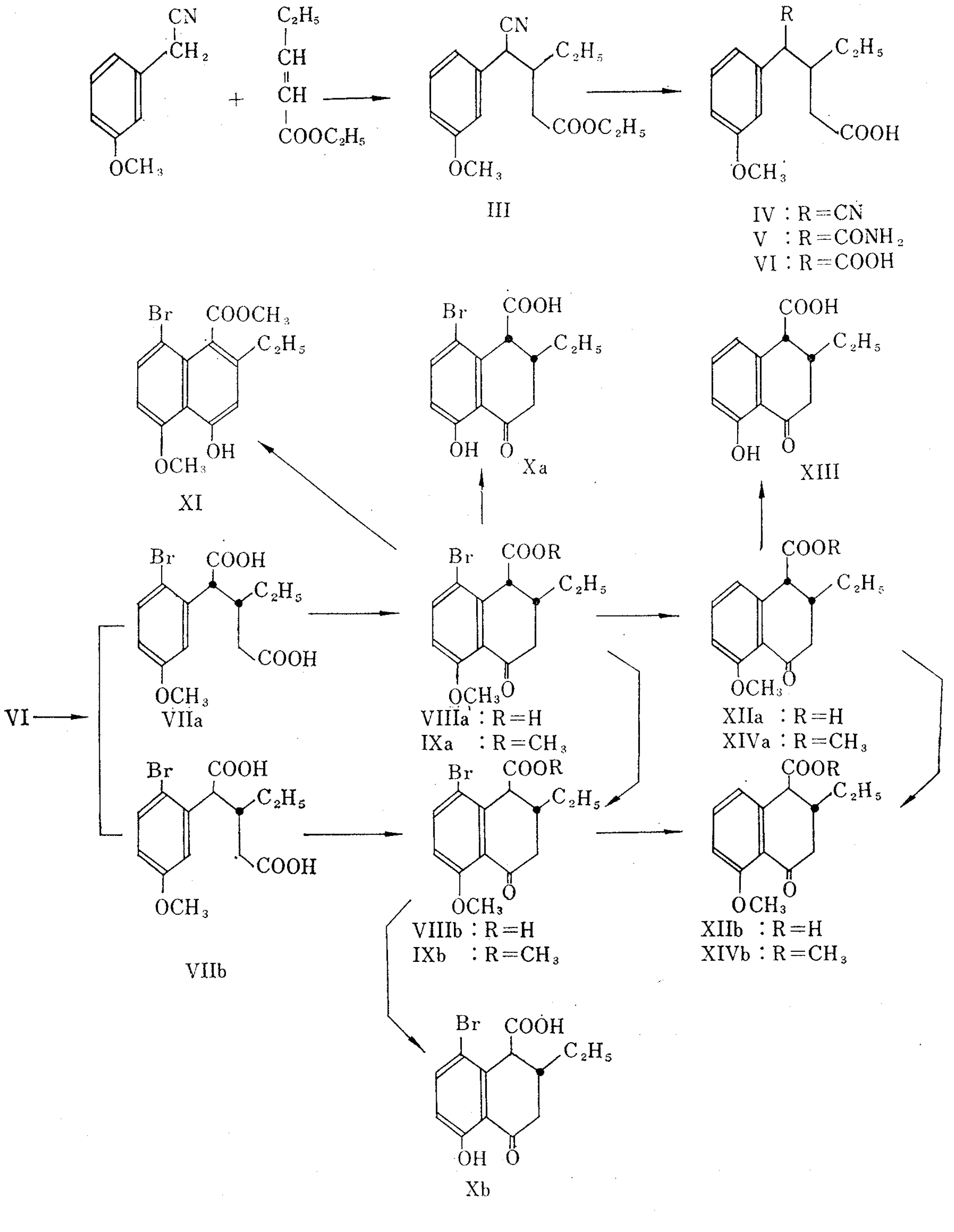

Chart 1.

Bromination of VI with one molar equivalent of bromine in chloroform gave two diastereoisomers of 2-(2-bromo-5-methoxyphenyl)3-ethylglutaric acid, (VIIa), m.p. 176∼178°, and (VIIb), m.p. 155∼157°, which were separated by employing a difference of their solubilities in chloroform. Cyclization of VIIa and VIIb was effected by heating with polyphosphoric acid at 90∼100° to give *cis*- and *trans*-2-ethyl-4-oxo-5-methoxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoic acid, (VIIIa) and (VIIIb), respectively. The methyl esters

(IXa) and (IXb) were prepared by treatments of VIIIa and VIIIb with diazomethane. Bathochromic shifts of tetralonecarbonyl bands observed in the infrared spectra of *cis*- and *trans*-2-ethyl-4-oxo-5-hydroxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoic acid, (Xa) and (Xb), which were derived from VIIIa and VIIIb by demethylation with hydriodic acid, proved the location of methoxyl group at C_5 of VIIIa and VIIIb. Isomerization from VIIIa to VIIIb on refluxing with 20% aqueous potassium hydroxide enables us to make the above *cis* and *trans* stereochemical assignments. Further, conversion of IXa to the naphthol (XI) by bromination and subsequent dehydrobromination supported their tetralone structure.

The bromo-acids (VIIIa) and (VIIIb) were hydrogenated[5] in the presence of potassium hydroxide to give *cis*- and *trans*-2-ethyl-4-oxo-5-methoxy-1,2,3,4-tetrahydro-1-naphthoic acid, (XIIa) and (XIIb), respectively. That the tetralone-carboxylic acid (XIIa) isomerized to XIIb on refluxing with 20% aqueous potassium hydroxide and that 2-ethyl-4-oxo-5-hydroxy-1,2,3,4-tetrahydro-1-naphthoic acid (XIII) which was obtained by fusion of XIIa with one molar equivalent of pyridine hydriodide showed a bathochromic shift of a

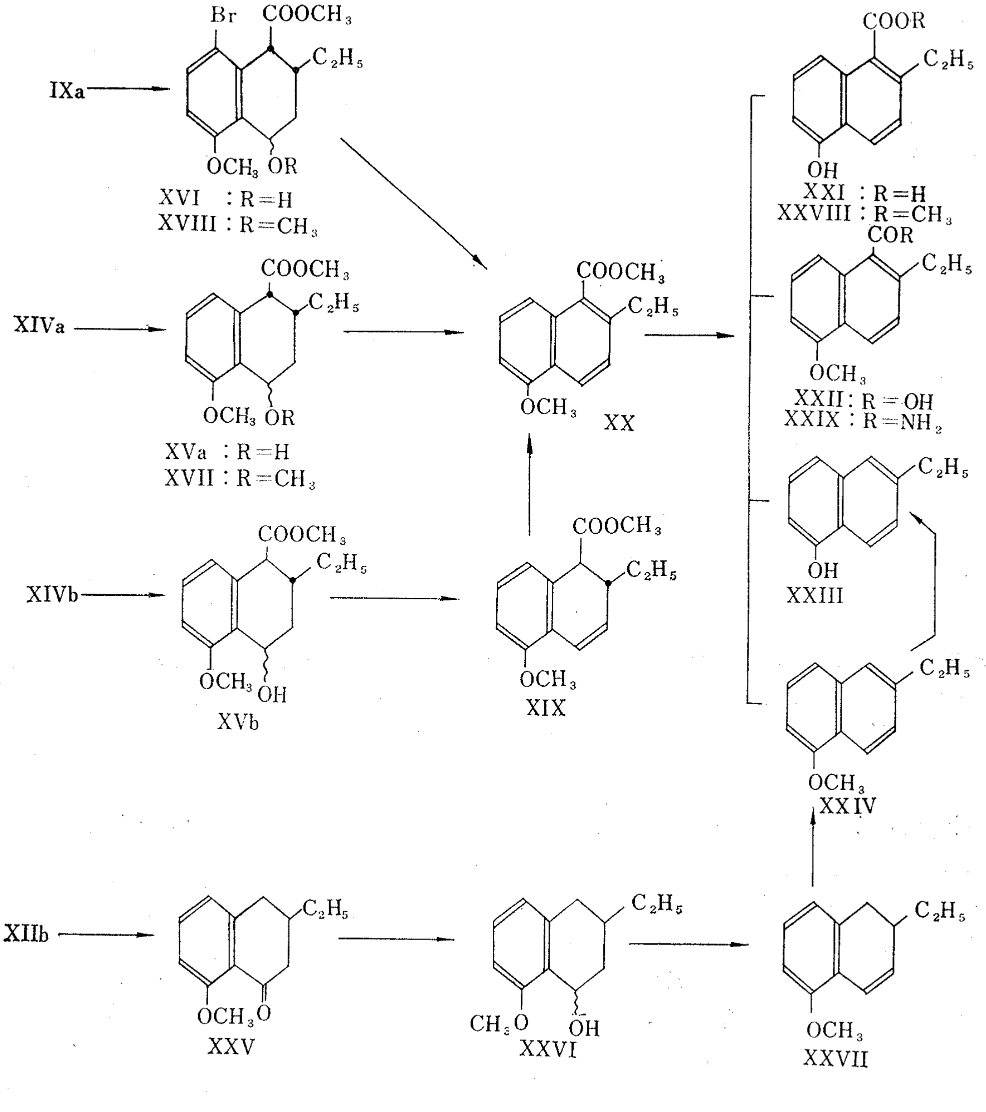

Chart 2.

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[5] K. Hermann, H. Leopold, B. Herwig: Chem. Ber., **91**, 1376 (1958).

tetralone-carbonyl band in its infrared spectrum provided further supports to the structures of XIIIa and XIIIb. Treatment of XIIIa and XIIIb with diazomethane gave the methyl esters, a solid (XIVa) and an oily (XIVb), respectively.

The tetralone-esters (XIVa), (XIVb) and (IXa) were reduced with sodium borohydride in methanol to give methyl *cis*- and *trans*-2-ethyl-4-hydroxy-5-methoxy-1,2,3,4-tetrahydro-1-naphthoate, (XVa) and (XVb), and methyl *cis*-2-ethyl-4-hydroxy-5-methoxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoate (XVI), respectively. Refluxing XVa and XVI with a catalytic amount of *p*-toluenesulfonic acid in methanol gave methyl *cis*-2-ethyl-4,5-dimethoxy-1,2,3,4-tetrahydro-1-naphthoate (XVII) (NMR τ^{CDCl_3} : 6.54 for C_4-OCH_3) and methyl *cis*-2-ethyl-8-bromo-4,5-dimethoxy-1,2,3,4-tetrahydro-1-naphthoate (XVIII) (NMR τ^{CDCl_3} : 6.54 for C_4-OCH_3), respectively, while a similar dehydration of XVb gave methyl *trans*-2-ethyl-5-methoxy-1,2-dihydro-1-naphthoate (XIX). Dehydrogenation of XVa, XVII, and XIX to methyl 2-ethyl-5-methoxy-1-naphthoate (XX), m.p. 69~70°, were achieved by fusing at 220~240° with sulfur in 42, 88, and 71% yield, respectively. Other dehydrogenation methods employing 10% palladium on carbon, chloranil and N-bromosuccinimide were unsuccessful. The bromo-tetralol (XVI) was also dehydrogenated by heating with sulfur to afford XX in 35% yield.

Refluxins XX with a large excess of hydriodic acid in acetic acid gave a mixture of four products, *i.e.* 2-ethyl-5-hydroxy-1-naphthoic acid (XXI) (30%), 2-ethyl-5-methoxy-1-naphthoic acid (XXII) (14%), 6-ethyl-1-naphthol*[3] (XXIII) (33%) and 2-ethyl-5-methoxynaphthalene*[3] (XXIV) (22%). The yield of hydroxy-acid (XXI) was increased to 58% by heating XX with 2.5 molar equivalents of pyridine hydriodide at 230° for 20 minutes. However, employment of one molar equivalent of pyridine hydriodide resulted in the formation of a 80% yield of XXII. Refluxing XX with 10% aqueous potassium hydroxide for 28 hours gave also a quantitative yield of XXII.

The decarboxylated products (XXIII) and (XXIV) were prepared by alternative method as described in Chart 2. The tetralonecarboxylic acid (XIIIb) was decarboxylated by heating with copper powder in quinoline at 200° to 3-ethyl-8-methoxy-1,2,3,4-tetrahydro-1-naphthalenone (XXV). Reduction of XXV with sodium borohydride in methanol followed by dehydration of the resulted tetralol (XXVI) to dihydronaphthalene (XXVII) by refluxing with a small amount of *p*-toluenesulfonic acid in ethanol and subsequent dehydrogenation with sulfur gave XXIV in 42% overall yield. The naphthol (XXIII) was obtained in 65% yield by refluxing XXIV with an excess of hydriodic acid in acetic acid.

Esterification of XXI with diazomethane in ether gave methyl 2-ethyl-5-hydroxy-1-naphthoate (XXVIII), m.p. 95.5~96.5°. 2-Ethyl-5-methoxy-1-naphthamide (XXIX) was prepared in 67% yield from XXII by treating with phosphorus trichloride and then with 28% aqueous ammoia.

Nuclear Magnetic Resonance Evidence for Stereochemistries of Tetralones

The nuclear magnetic resonance (NMR) data of all the tetralones examined and reference compounds cited are listed in Table I. Compounds (XXXa), (XXXb), (XXXIa), and (XXXIb) were prepared as follows. The glutaric acid (VIa) was cyclized by heating with ployphosphoric acid to *cis*-2-ethyl-4-oxo-7-methoxy-1,2,3,4-tetrahydro-1-naphthoic acid (XXXa), m.p. 134~136°, which was led to its methyl ester (XXXIa), m.p. 94~96°, by treating with diazomethane. Hydrolysis of XXXIa by refluxing with 20% aqueous potassium hydroxide gave a *trans*-acid (XXXb), m.p. 150~151°, which gave the methyl ester (XXXIb), $b.p_{0.07}$ 150°, by treating with diazomethane.

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*[3] The synthesis of compounds (XXIII) and (XXIV) *via* 5-methoxy-2-tetralone was reported without a detail of experiments. Cf. W. D. Ollis, I. O. Sutherland, P. L. Veal: Proc. Chem. Soc., **1960**, 349.

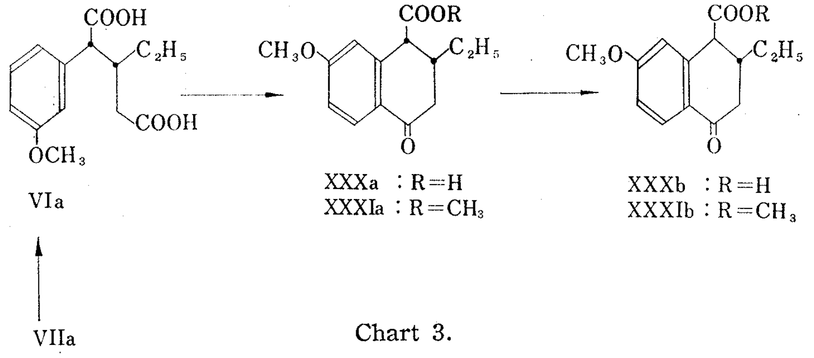

Chart 3.

Examination of the NMR spectra showed that the chemical shifts of the C_1-proton and the value of $J_{1,2}$, as well as the chemical shifts of the C_1-methoxycarbonyl methyl, were well in agreement with those expected for the stereochemistries suggested from the chemical evidences. The results are described below.

a) The C_1-proton signal appeared as a doublet, whose $J_{1,2}$ provided a valuable information concerning the relative configuration at C_1 and C_2. The value for the *cis*-isomer (4.0~4.7 c.p.s) are always smaller than that for the corresponding *trans*-isomer (5.0~6.2 c.p.s.) except in the case of IXb. The difference would be related to the dihedral angle between the protons at C_1 and at C_2. Thus, the *trans*-isomer is assumed to exist preferentially in conformation (XXXIII) in which both protons at C_1 and C_2 are quasi-diaxial, and the *cis*-isomer in either one of both possible conformations (XXXIV) and (XXXV), as illustrated in Fig. 1.

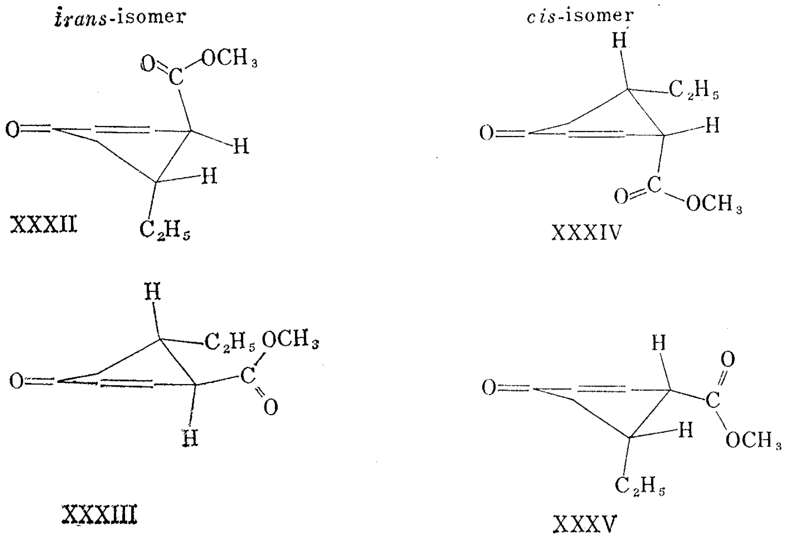

Fig. 1. Conformation of Tetralones

b) The C_1-proton signal in the *cis*-isomer appeared at lower field than that in the *trans*-isomer. On the other hand, the C_1-methoxycarbonyl methyl signal appeared at higher field than that in the *trans*-isomer (Table II). These differences would be due mainly[*4] to the anisotropic shielding effect of the benzene ring of the tetralone. Examination of the conformation of the *cis*- and *trans*-isomer with Dreiding models and the chemical shifts of the C_1-proton or the C_1-methoxycarbonyl methyl led to the conclusion that preferential conformations for the *trans*- and *cis*-isomer would be XXXIII and

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[*4] In the case of the C_1-proton, the diamagnetic shielding effect of the C_2-C_3 bond may also contribute to its chemical shift.

XXXIV, respectively. The conclusion concerning these conformations are not inconsistent with those obtained in section (a).

c) Regarding the exception mentioned in section (a) that the value of $J_{1,2}$ in the *trans*-isomer was extraordinarily smaller than that expected, the following explanation seems to be most reasonable : a considerable steric hindrance operating between the C_8-bromine and C_1-methoxycarbonyl group changes the spacial orientation of the latter and, consequently, allows the dihedral angle between the C_1- and C_2-proton to approach to rectangular.

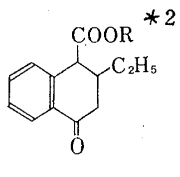
TABLE I. Chemical Shifts of Protons, p.p.m. (δ)[a]

Protons	J, δ	Configuration	Solvent[b]	(1)[c]	(2)[c]	XXXI	XIV	IX	(3)[c]	(4)[c]	(5)[c]
C_1-H	J	*cis*	C		4.3	4.7	4.2	4.1	4.5	4.5	
			P			4.5	4.6	4.0			
		trans	C	5.0	6.0	5.5～5.6	6.0	1.4～2.0	6.5	6.5	7.0
			P			5.4～5.6	5.5	1.5～2.2			
	δ	*cis*	C		4.03	3.98	3.99	4.38	4.72	4.69	
			P			4.12	4.09	4.51			
		trans	C	3.88	3.86	3.81	3.82	4.27	4.62	4.54	4.56
			P			4.01	3.99	4.45			
$COOCH_3$	δ	*cis*	C		3.65	3.70	3.64	3.68	3.70	3.69	
			P			3.59	3.56	3.65			
		trans	C		3.78	3.76	3.73	3.73	3.63	3.61	3.59
			P			3.71	3.69	3.71			
C-CH_3	δ	*cis*	C		1.07	1.06	1.05	1.08			
			P			0.98	0.95	0.99			
		trans	C	0.98	0.96	0.97	0.97	0.97			
			P			0.89	0.83	0.86			

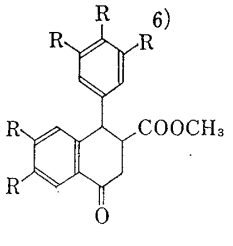
[a] Spectra were determined on about 10% (w/v) solutions in $CDCl_3$ and in pyridine, using tetramethylsilane as internal reference by a Varian A-60 spectrometer operated at 60 Mc.

[b] C : $CDCl_3$; P : pyridine.

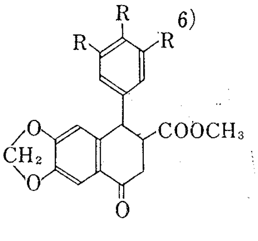
[c]



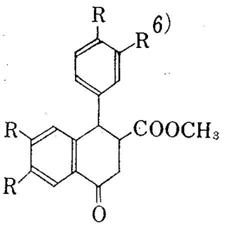
(1), R=H
(2), R=CH_3



(3), R=OCH_3



(4), R=OCH_3



(5), R=OCH_3

TABLE II. $\varDelta=\tau_{cis}-\tau_{trans}$, p.p.m.

Compounds	C_1-H C	C_1-H P	$COOCH_3$ C	$COOCH_3$ P	C-CH_3 C	C-CH_3 P
(2)	−0.17		+0.13		−0.09	
XXXI	−0.17	−0.11	+0.06	+0.12	−0.09	−0.12
XIV	−0.17	−0.10	+0.09	+0.13	−0.08	−0.12
IX	−0.11	−0.06	+0.05	+0.05	−0.11	−0.13
(3)	−0.10		(−0.07)			
(4)	−0.15		(−0.08)			

d) As seen in Table I, the signals of the C_2-terminal methyl in the *trans*-isomer always appeared at a field higher than those in the *cis*-isomer. The same tendency is also observed on the signals of the C_2-methoxycarbonyl methyl in (3) and (4).[6)]

Experimental[*5]

Ethyl 3-Ethyl-4-cyano-4-(*m*-methoxyphenyl)butyrate (III)——(*m*-Methoxyphenyl)acetonitrile was prepared by Banerjee's method[3)] starting from (*m*-methoxybenzaldehyde,[7)] and ethyl 2-pentenoate by Tschesche's method[4)] starting from monoethyl malonate.[8)] To a cold solution of 14.8 g. of Na in 220 ml. of dry EtOH was added a mixture of 94.4 g. of (*m*-methoxyphenyl) acetonitrile and 82.2 g. of ethyl 2-pentenoate under stirring over a period of 2.5 hr. After the addition was complete, the reaction mixture was stirred at room temperature for an additional 1 hr., poured into 1 L. of ice water, acidified with dil. H_2SO_4, saturated with NaCl and extracted with ether (250 ml. × 3). The combined extracts were washed successively with H_2O, satd. aq. $NaHCO_3$, dried over anhyd. Na_2SO_4 and evaporated to give 165 g. of a pale yellow oil, which was fractionated by vacuum distillation. A fraction of b.p$_3$ 165~170° (121.4 g.) was redistilled to give 115.4 g. (65%) of III as an almost colorless oil, b.p$_{0.07}$ 143~147°. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2227 (C≡N), 1724 (C=O). *Anal.* Calcd. for $C_{16}H_{21}O_3N$: C, 69.79; H, 7.69. Found: C, 69.54; H, 7.66.

Hydrolysis of III——A) A mixture of 10 g. of III and 20 ml. of 20% aq. KOH was refluxed until an oily layer disappeared and the mixture became homogeneous (ca. 20 min.). The mixture was cooled, shaken twice with ether, acidified with 10% H_2SO_4 and extracted with ether. The extract was washed with satd. aq. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give 8.8 g. of 3-ethyl-4-cyano-4-(*m*-methoxyphenyl)butyric acid (IV) as a colorless viscous oil, which solidified on standing. The solid was washed with a small amount of CCl_4, giving 3.2 g. of one diastereoisomer of IV as colorless needles, m.p. 103~104°, which was not altered by three recrystallizations from CCl_4. IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 2224 (C≡N), 1695 (C=O). *Anal.* Calcd. for $C_{14}H_{17}O_3N$: C, 67.99; H, 6.93; N, 5.66. Found: C, 67.88; H, 6.92; N, 5.54.

Evaporation of the CCl_4 washing left a viscous oil, which is assumed to be a mixture of diastereoisomers of IV from its IR spectrum.

B) A mixture of 5.2 g. of III, 10 g. of KOH, 10 ml. of EtOH and 20 ml. of H_2O was refluxed for 4 hr. The cooled mixture was acidified with dil. H_2SO_4, and extracted with AcOEt. The extract was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated. The residual solid was washed with ether to give 1.2 g of crystals. Evaporation of the washing gave 3.0 g. of a glassy solid. Three recrystallizations of the crystals from EtOH-H_2O and then twice from H_2O gave 0.9 g. of 3-ethyl-4-carbamoyl-4-(*m*-methoxyphenyl)butyric acid (V) as colorless microneedles, m.p. 150~152°. IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 3425, 3344 (NH), 1692, 1633 (C=O). *Anal.* Calcd. for $C_{14}H_{19}O_4N$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.46; H, 7.14; N, 5.47. [The same sample was obtained from IV as follows. A mixture of 1 g. of IV and 20 ml. of aq. ethanolic (5:1) KOH was refluxed for 4 hr. The cooled mixture was acidified with 20% H_2SO_4, and the deposited crystals were collected. Yield 0.6 g., m.p. 140~152°. Identification with the sample mentioned above was made by IR spectral comparison (in Nujol).] The glassy solid is assumed to be the diacid (VI) contaminated with a small amount of V from its IR spectrum.

C) A mixture of 115.4 g. of III, 200 g. of KOH and 500 ml. of H_2O was refluxed for 24 hr. The cooled mixture was shaken twice with 100 ml. of ether, acidified with dil. H_2SO_4 and extracted with ether (200 ml. × 3). The combined extracts were washed with satd. aq. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give 113.7 g. of a crude diastereoisomeric mixture of 2-(*m*-methoxyphenyl)-3-ethylglutaric acid (VI) as a glassy solid. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1706 (C=O). This acid was characterized by conversion to the dimethyl ester, b.p$_2$ 185° (colorless oil), by treatment with CH_2N_2 in ether. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1724 (C=O). *Anal.* Calcd. for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.22; H, 7.51.

Diastereoisomers of 2-(2-Bromo-5-methoxyphenyl)-3-ethylglutaric Acid (VIIa and VIIb)——To a solution of 259 g. of VI in 800 ml. of dry $CHCl_3$ was added a solution of 156.8 g. of Br_2 in 400 ml. of dry $CHCl_3$ with stirring over a period of 3 hr. After the addition was complete, the mixture was stirred for an additional 6 hr. at room temperature, washed successively with H_2O (100 ml. × 2), 5% aq. $Na_2S_2O_3$ and H_2O, and evaporated without drying. The residual glassy solid (336 g.) containing crystals was washed with $CHCl_3$ to give 166.1 g. of VIIa, m.p. 175~178°. Recrystallization from EtOH and then from EtOH-H_2O gave an analytical sample as colorless short prisms, m.p. 176~178°. IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 1704, 1686 (C=O). *Anal.* Calcd. for $C_{14}H_{17}O_5Br$: C, 48.71; H, 4.96. Found: C, 49.14; H, 5.15.

The $CHCl_3$ washing was evaporated to give a pale brown glassy solid, which separated 103.4 g. of crystals, m.p. 143~152°, on addition of benzene. Recrystallization from EtOH and then from EtOH-H_2O

[*5] All melting points are uncorrected.

6) E. Schreier: Helv. Chim. Acta, **46**, 75 (1963).

7) R.N. Icke, C.E. Redemann, B.B. Wisegarver, G.A. Alles: Org. Syntheses, Coll. Vol. III, 564 (1955)

8) R.E. Strube: Org. Syntheses, **37**, 34 (1957).

gave 54.5 g. of VIIb as colorless microplates, m.p. 155~157°. IR ν_{max}^{Nujol} cm^{-1}: 1698 (C=O). *Anal.* Calcd. for $C_{14}H_{17}O_5Br$: C, 48.71; H, 4.96. Found: C, 49.21; H, 5.07.

VIa, A Diastereoisomer of VI——A suspension of 5 g. of freshly prepared Raney Ni and 6.7 g. of KOH in 40 ml. of dist. H_2O was shaken in an atmosphere of H_2 at 15° for 30 min. To this was added a solution of 10.4 g. of VIIa in 40 ml. of MeOH, and the whole mixture was hydrogenated. The hydrogenation was stopped when 650 ml. of H_2 was consumed (1740 min.). After fiiltration of the catalyst, MeOH was removed. The residual aqueous solution was acidified with 20% H_2SO_4 and extracted with ether. The extract was washed with satd. aq. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give 8.8 g. of a pale yellow paste, which solidified soon on standing. Washing the solid with 10 ml. of benzene gave 7.9 g. of VIa as colorless crystals, m.p. 116~120°. Recrystallization from benzene-cyclohexane gave an analytical sample as colorless microneedles, m.p. 121.5~122.5°. IR ν_{max}^{Nujol} cm^{-1}: 1704 (C=O). *Anal.* Calcd. for $C_{14}H_{18}O_5 \cdot 1/3C_6H_6$: C, 65.29; H, 7.53. Found: C, 65.54; H, 7.47.

***cis*-2-Ethyl-4-oxo-5-methoxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoic Acid (VIIIa)**——A mixture of 10 g. of VIIa and 225 g. of polyphosphoric acid was heated at 100° for 65 min., and poured onto 200 g. of cracked ice. The deposits were collected by filtration, washed with H_2O and dried in an open air to give 9.4 g. of crystals, m.p. 176~182° (decomp.), which were recrystallized from EtOH to give 7.0 g. of VIIIa as colorless cubics, m.p. 188~190° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3115 (OH), 1731, 1706 (shoulder), 1653 (C=O). *Anal.* Calcd. for $C_{14}H_{15}O_4Br$: C, 51.39; H, 4.62. Found: C, 51.77; H, 4.57.

***trans*-2-Ethyl-4-oxo-5-methoxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoic Acid (VIIIb)**——A mixture of 70 g. of VIIb and 1.1 kg. of polyphosphoric acid was heated at 90~95° for 50 min. and poured onto 1 kg. of cracked ice. The deposits were collected by filtration, washed with H_2O and dried in an open air to give 68.8 g. of crystals, m.p. 168~178° (decomp.), which were recrystallized once from EtOH and then three times from EtOH-H_2O to give 52.4 g. of VIIIb as colorless needles, m.p. 182~184° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3115 (OH), 1724, 1650 (C=O). *Anal.* Calcd. for $C_{14}H_{15}O_4Br$: C, 51.39; H, 4.62. Found: C, 51.21; H, 4.50.

Methyl *cis*-2-Ethyl-4-oxo-5-methoxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoate (IXa)——Esterification of VIIIa with CH_2N_2 in ether gave quantitatively IXa as colorless prisms, m.p. 110~111°, after three recrystallizations from MeOH. IR ν_{max}^{Nujol} cm^{-1}: 1717, 1680 (C=O). *Anal.* Calcd. for $C_{15}H_{17}O_4Br$: C, 52.80; H, 5.02. Found: C, 53.17; H, 4.93.

Methyl *trans*-2-Ethyl-4-oxo-5-methoxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoate (IXb)——Esterification of VIIIb with CH_2N_2 in ether gave quantitatively the methyl ester (IXb) as colorless needles, m.p. 109~110°, after recrystallization from MeOH. IR ν_{max}^{Nujol} cm^{-1}: 1733, 1672 (C=O). *Anal.* Calcd. for $C_{15}H_{17}O_4Br$: C, 52.80; H, 5.02. Found: C, 53.07; H, 5.01.

***cis*-2-Ethyl-4-oxo-5-hydroxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoic Acid (Xa)**——To a solution of 10 g. of VIIIa in 50 ml. of AcOH was added 50 ml. of 52% HI, and the mixture was refluxed for 15 min., poured into 500 ml. of ice water, saturated with NaCl and extracted with ether. The extract was washed with satd. aq. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give 9.0 g. of a pale brown paste, which solidified on standing. Washing the solid with benzene gave 8.5 g. of colorless crystals, m.p. 144~148°. Three recrystallizations from EtOH-H_2O gave 5.7 g. of Xa as colorless plates, m.p. 154~155°, which showed a positive $FeCl_3$ test (reddish purple in EtOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1701, 1639 (C=O). *Anal.* Calcd. for $C_{13}H_{13}O_4Br$: C, 49.86; H, 4.19. Found: C, 49.90; H, 4.07.

***trans*-2-Ethyl-4-oxo-5-hydroxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoic Acid (Xb)**——Demethylation of 5 g. of VIIIb by a similar procedure to that for Xa gave 2.3 g. of Xb as colorless crystals, m.p. 118~119°, after two recrystallizations from benzene. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1703, 1638 (C=O). *Anal.* Calcd. for $C_{13}H_{13}O_4Br$: C, 49.86; H, 4.19. Found: C, 50.39; H, 4.07.

Methyl 2-Ethyl-4-hydroxy-5-methoxy-8-bromo-1-naphthoate (XI)——To a solution of 1.5 g. of IXa in 50 ml. of $CHCl_3$ was added a solution of 0.68 g. of Br_2 in 100 ml. of dry $CHCl_3$ at 15~20° with stirring over a period of 3 hr. The mixture was washed with dil. aq. $Na_2S_2O_3$ and then H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 1.7 g. of a pale brown paste. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1727, 1689 (C=O). The paste was dissolved in 10 ml. of morpholine and heated at 100° for 30 min. After cooling, 30 ml. of ether was added to the mixture and morpholine hydrobromide (weighed 1.0 g.) deposited was removed by filtration. The filtrate was washed with H_2O until morpholine was completely removed, dried over anhyd. Na_2SO_4 and evaporated to give 1.4 g. of a brown viscous oil. The crude oil was dissolved in $CHCl_3$ and purified through 30 g. of alumina to give 1.0 g. of XI as colorless crystals, m.p. 82~83°. Recrystallization from MeOH gave an analytical sample as colorless plates, m.p. 83~85°. IR ν_{max}^{Nujol} cm^{-1}: 3322 (OH), 1712 (C=O), 1625, 1603 (arom.). *Anal.* Calcd. for $C_{15}H_{15}O_4Br$: C, 53.11; H, 4.46; Br, 23.56. Found: C, 52.99; H, 4.58; Br, 23.43.

In another experiment employing 1.5 molar equivalents of Br_2 was obtained a dibromide, presumably 6-bromo-XI, as colorless needles, m.p. 151~152°, after three recrystallizations from MeOH. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3344 (OH), 1718 (C=O), 1622 (weak), 1604 (arom.). *Anal.* Calcd. for $C_{15}H_{14}O_4Br_2$: C, 43.09; H, 3.38; Br, 38.23. Found: C, 42.76; H, 3.26; Br, 37.93.

Isomerization of VIIIa——A mixture of 1 g. of VIIIa, 10 g. of KOH and 40 ml. of H_2O was refluxed for 12 hr., cooled, acidified with 20% H_2SO_4 and extracted with AcOEt (20 ml. × 3). The combined extracts were washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 1.0 g. of a pale brown paste, which crystallized on addition of ether. Washing the product with a small amount of ether gave 0.55 g. of colorless crystals, m.p. 160～175°, whose IR spectrum was superimposed with that of the *trans*-isomer (VIIIb) (in Nujol).

cis-2-Ethyl-4-oxo-5-methoxy-1,2,3,4-tetrahydro-1-naphthoic Acid (XIIa)——A suspension of 5 g. of Raney Ni in KOH solution from 4 g. of KOH and 30 ml. of H_2O was saturated with H_2 for 200 min. To this was added a solution of 7 g. of VIIIa in 30 ml. of MeOH, and the whole mixture was hydrogenated under an atmospheric pressure of H_2. The absorption of H_2 subsided after 60 min. (477 ml. of H_2). After filtration of the catalyst, MeOH was evaporated from the mixture under a reduced pressure. The aqueous solution was acidified with 20% H_2SO_4 and extracted with ether. The extract was washed with satd. aq. NaCl and evaporated. The residue was dried at 100° for 1 hr. *in vacuo* to give a paste, which solidified on addition of a small amount of ether. Washing the solid with ether gave 4.2 g. of crystals, m.p. 145～152°. Three recrystallizations from EtOH-H_2O gave 3.1 g. of XIIa as colorless microprisms, m.p. 158～159°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 3081 (OH), 1720, 1703 (shoulder), 1649 (C=O). *Anal.* Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found : C, 67.65; H, 6.69.

trans-2-Ethyl-4-oxo-5-methoxy-1,2,3,4-tetrahydro-1-naphthoic Acid (XIIb)——Compound VIIIb (35 g.) was hydrogenated in a similar manner to that for XIIa. The H_2-uptake subsided after 295 min. (2545 ml. of H_2). Crystals (21.4 g.) of m.p. 156～164° was obtained. Three recrystallizations from EtOH-H_2O gave 16.7 g. of XIIb as colorless microneedles, m.p. 169～171°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 1721, 1638 (C=O). *Anal.* Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found : C, 67.99; H, 6.70.

Isomerization of XIIa——A mixture of 1 g. of XIIa, 5 g. of KOH and 20 ml. of H_2O was refluxed for 12 hr. and worked up in a similar manner to that for VIIIa to give 0.6 g. of colorless crystals, m.p. 120～133°, whose IR spectrum was completely superimposed with that of the *trans*-isomer (XIIb) (in Nujol).

cis-2-Ethyl-4-oxo-5-hydroxy-1,2,3,4-tetrahydro-1-naphthoic Acid (XIII)——A mixture of 2 g. of XIIa and 2 g. of pyridine hydriodide was heated at 200～205° for 5 min., cooled and triturated with AcOEt in the presence of conc. HCl. The aqueous layer was extracted with AcOEt. The AcOEt layer and extract were combined and shaken with satd. aq. $NaHCO_3$. The alkaline layer was acidified with conc. HCl and extracted with AcOEt. The extract was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 1.5 g. of a brownish solid, which crystallized on addition of CCl_4. Washing the crystals with CCl_4 gave 1.4 g. of crystals, m.p. 166～173°. Three recrystallizations from EtOH-H_2O gave 0.6 g. of XIII as colorless long needles, m.p. 175～177°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 3120 (OH), 1711, 1641 (C=O); $\nu_{\max}^{CHCl_3}$ cm^{-1} : 3460 (OH), 1704, 1639 (C=O). *Anal.* Calcd. for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found : C, 66.63; H, 6.09.

A neutral fraction weighed 0.4 g., a brown oil, and was presumed to be decarboxylated XIII from its IR spectrum.*[6]

Methyl _cis_-2-Ethyl-4-oxo-5-methoxy-1,2,3,4-tetrahydro-1-naphthoate (XIVa)——To a suspension of 30.4 g. of XIIa in 100 ml. of ether was added a solution of CH_2N_2 in ether under ice-cooling. The precipitated crystals of XIVa (20.2 g.), m.p. 97～98°, were collected by filtration. The filtrate, after an addition of AcOH to destroy an excess of CH_2N_2, was washed with satd. aq. $NaHCO_3$, dried over anhyd. Na_2SO_4 and evaporated to give 11.5 g. of a colorless viscous oil, which solidified on standing. Washing the solid with a small amount of ether gave 7.2 g. of the second crops of XIVa, m.p. 97～98°. Recrystallization from hexane gave an analytical sample as colorless plates, m.p. 98～99°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 1720, 1669 (C=O). *Anal.* Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found : C, 68.74; H, 7.07.

Methyl _trans_-2-Ethyl-4-oxo-5-methoxy-1,2,3,4-tetrahydro-1-naphthoate (XIVb)——Methylation of 20 g. of XIIb with CH_2N_2 in 100 ml. of ether by a similar procedure to that described for XIVa gave 20 g. of a colorless viscous oil, b.p.$_2$ 178～179°, which did not solidify. IR $\nu_{\max}^{CCl_4}$ cm^{-1} : 1736, 1686 (C=O). *Anal.* Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found : C, 68.52; H, 6.89.

Methyl _cis_-2-Ethyl-4-hydroxy-5-methoxy-1,2,3,4-tetrahydro-1-naphthoate (XVa)——To a stirred and ice-cooled solution of 5.7 g. of $NaBH_4$ in 80 ml. of MeOH was added a solution of 26.2 g. of XIVa in 160 ml. of MeOH-ether (1 : 1), and the mixture was stirred under ice-cooling for 2 hr. and at room temperature for another 1.5 hr. The reaction mixture was poured into 500 ml. of ice water, saturated with NaCl and extracted with ether (100 ml. × 3). The combined extracts were washed three times with satd. aq. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give 26.0 g. of a viscous oil, which solidified on standing. The product was recrystallized from hexane to give 23.1 g. of colorless long prisms, m.p. 81～82°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 3484 (OH), 1725 (C=O). *Anal.* Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found : C, 67.95; H, 7.50.

Methyl _trans_-2-Ethyl-4-hydroxy-5-methoxy-1,2,3,4-tetrahydro-1-naphthoate (XVb)——The keto-ester (XIVb) (24.3 g.) was reduced with 5.3 g. of $NaBH_4$ in a similar manner to that for XVa to give 24.5 g. of XVb as a colorless viscous oil, b.p.$_{0.3}$ 173～175°, which did not solidify and decomposed partially on distillation. IR $\nu_{\max}^{CCl_4}$ cm^{-1} : 3534 (OH), 1733 (C=O).

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*[6] The IR spectrum of the neutral fraction lacks bands due to COOH group.

Methyl *cis*-2-Ethyl-4-hydroxy-5-methoxy-8-bromo-1,2,3,4-tetrahydro-1-naphthoate (XVI)——The keto-ester (IXa) (13.3 g.) was reduced with 2.3 g. of $NaBH_4$ to give 13 g. of a viscous oil, which solidified on standing. The product was recrystallized twice from MeOH-H_2O to give 11 g. of XVI as colorless plates, m.p. 110～112°. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3546 (OH), 1724 (C=O). *Anal.* Calcd. for $C_{15}H_{19}O_4Br$: C, 52.49; H, 5.58. Found: C, 52.79; H, 5.60.

Methyl *cis*-2-Ethyl-4,5-dimethoxy-1,2,3,4-tetrahydro-1-naphthoate (XVII)——A mixture of 20.3 g. of XVa, 0.4 g. of TsOH and 100 ml. of MeOH was refluxed for 2 hr. After removing MeOH, the mixture was taken in 100 ml. of benzene, washed with satd. aq. $NaHCO_3$ and then H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 19.1 g. of an oil, which crystallized on standing. The product was recrystallized three times from hexane to give 17.5 g. of XVII as colorless prisms, m.p. 65～66°. IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 1724 (C=O). *Anal.* Calcd. for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.26; H, 8.09.

Methyl *cis*-2-Ethyl-8-bromo-4,5-dimethoxy-1,2,3,4-tetrahydro-1-naphthoate (XVIII)——The tetralol (XVI) (5 g.) was treated with 0.1 g. of TsOH in a similar manner to that for XVII, giving 5 g. of a viscous oil, b.p$_2$ 169～170°, which solidified on standing. The product was recrystallized from petr. ether to give 4.2 g. of XVIII as colorless prisms, m.p. 85～87°. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1721 (C=O). *Anal.* Calcd. for $C_{16}H_{21}O_4Br$: C, 53.79; H, 5.97. Found: C, 53.87; H, 5.97.

Methyl *trans*-2-Ethyl-5-methoxy-1,2-dihydro-1-naphthoate (XIX)——A mixture of 24 g. of XVb, 0.4 g. of TsOH and 100 ml. of MeOH was refluxed for 2 hr. After removing MeOH, the mixture was taken in 100 ml. of benzene, washed with satd. aq. $NaHCO_3$ and then H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 24 g. of an oil. Distillation of the product gave 19.9 g. of XIX as a colorless oil, b.p$_{0.2}$ 141°. IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1735 (C=O), 1633 (C=C). *Anal.* Calcd. for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.24; H, 7.20.

Methyl 2-Ethyl-5-methoxy-1-naphthoate (XX)——A) From XVa: A mixture of 1.3 g. of XVa and 160 mg. of precipitated sulfur was heated at 245～260° for 55 min., during whose time H_2O distilled out at 180～190° and H_2S evolved above 200°. The reaction mixture was cooled and distilled *in vacuo* to give 1.1 g. of a yellow viscous oil, b.p$_3$ 155～175°. Column chromatography on alumina employing benzene as eluent gave 0.6 g. of a viscous oil, which solidified on standing. Three recrystallizations from MeOH-H_2O gave 0.5 g. (42%) of XX as colorless plates, m.p. 68～70°. IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1727 (C=O), 1623, 1599, 1581 (arom.). *Anal.* Calcd. for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.62; H, 6.80.
B) From XVII: A mixture of 19.1 g. of XVII and 2.9 g. of precipitated sulfur was placed in a Claisen flask, and heated with stirring at 200～210° for 30 min., at 210～220° for 20 min. and at 220～230° for 40 min. The reaction mixture was distilled under a reduced pressure to give 16.8 g. of a pale yellow distillate, b.p$_3$ 169～181°, which solidified on standing. Redistillation gave 15 g. (88%) of XX as an oil, b.p$_3$ 170～175°, which was identified with the sample obtained in section A by IR spectral comparison.
C) From XIX: A mixture of 18 g. of XIX and 3 g. of precipitated sulfur was placed in a Claisen flask and heated with stirring at 210～215° for 70 min. and at 220～240° for 40 min. Distillation of the mixture gave 12.7 g. (71%) of XX as a pale yellow distillate, b.p$_{0.2}$ 158～162°, which was identified with the sample obtained in section A by IR spectral comparison.

D) From XVI: A mixture of 0.8 g. of XVI and 75 mg. of precipitated sulfur was heated at 210～220° for 15 min. An evolution of white smoke was observed on elevation of the temperature to 230°. The reaction mixture was cooled to 170° and distilled under a reduced pressure to give 0.3 g. of a pale yellow viscous oil, b.p$_3$ 175°, which showed a negative Beilstein test. The distillate was dissolved in benzene and purified through alumina column to give 0.2 g. (35%) of XX as colorless crystals, m.p. 68～70°, which were identified with the sample obtained in section A by IR spectral comparison.

Demethylation of XX——A) By hydriodic acid: A mixture of 3 g. of XX, 10 ml. of AcOH and 15 ml. of 52% HI was refluxed for 1 hr., poured into 200 ml. of ice water and extracted with AcOEt. The extract was washed with H_2O and shaken with satd. aq. $NaHCO_3$ (30 ml. × 5). The AcOEt layer was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 1.5 g. of a dark brown viscous oli, which gave 0.7 g. (33%) of 6-ethyl-1-napnthol (XXIII) as colorless leaflets, m.p. 64～68°, on sublimation at 100°/3 mm.Hg. IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 3180 (OH); $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 3565, 3442 (OH), on C=O band. The 3,5-dinitrobenzoate: yellow needles, m.p. 177～178°, after three recrystallizations from acetone, IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 1743 (C=O). *Anal.* Calcd. for $C_{19}H_{14}O_6N_2$: C, 62.29; H, 3.85. Found: C, 62.21; H, 3.89.

The unsublimable neutral fraction (0.8 g.) was purified by column chromatography on silica gel employing $CHCl_3$ as eluent to give 0.5 g. (22%) of 2-ethyl-5-methoxynaphthalene (XXIV) as a colorless oil, whose structure was confirmed by alternative preparation as described later.

The $NaHCO_3$ washings were shaken twice with AcOEt, filtered, acidified with dil. H_2SO_4 and extracted with AcOEt. The extract was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 1.2 g. of a pale brown paste. Washing the paste with benzene gave 0.8 g. (30%) of 2-ethyl-5-hydroxy-1-naphthoic acid (XXI) as pale pink crystals, m.p. 158～160°, which were recrystallized twice from H_2O to give an analytical sample as colorless cubics, m.p. 159～160°. IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 3067 (OH, broad), 1712 (C=O). *Anal.* Calcd. for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 71.91; H, 5.48.

The benzene washing gave 0.4 g. (14%) of 2-ethyl-5-methoxy-1-naphthoic acid (XXII) as almost colorless fine crystals, m.p. 123~125°, which were recrystallized from EtOH-H_2O to give an analytical sample as colorless needles, m.p. 125.5~126.5°. IR ν_{max}^{Nujol} cm^{-1}: 1681 (C=O), no OH band. *Anal.* Calcd. for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13. Found: C, 72.77; H, 6.16.

B) By pyridine hydriodide (Py. HI): i) With 1 mole. equiv. of Py. HI: A mixture of 0.8 g. of XX and 0.68 g. of Py. HI was heated at 200~210° for 10 min. and cooled. The mixture was triturated in 50 ml. of 5% H_2SO_4 and extracted with ether (20 ml. x 3). The combined extracts were shaken with satd. aq. $NaHCO_3$ until no more acid was extracted. The alkaline layer was shaken with ether, filtered, acidified with dil. H_2SO_4 and extracted with ether. The extract was washed three times with satd. aq. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give 0.6 g. (80%) pale brown crystals, m.p. 122~124.5°, which were identified with XXII obtained in section A by IR spectral comparison. The neutral fraction (0.1 g.) was obtained as a dark brown viscous oil which was assumed to be XXIV from its IR spectrum.

ii) With 2 mole. equiv. of Py. HI: A mixture of 1 g. of XX and 1.7 g. of Py. HI wash eated at 210° for 10 min., cooled, triturated in 50 ml. of 5% H_2SO_4 and extracted with AcOEt. The extract was treated in a similar manner to that described in i) to give 0.9 g. of XXII and 5 mg. of XXI, which were identified with the corresponding samples obtained in section A) by IR spectral comparison.

iii) With 2.5 mole. equiv. of Py. HI: A mixture of 4.1 g. of XX and 8.7 g. of Py. HI was heated at 230° for 20 min., cooled and treated in a similar manner to that described in i) to give 1 g. of a neutral fraction and 3 g. of an acidic fraction. Trituration of the latter with benzene gave 2.1 g. (58%) of XXI as pale pink crystals, m.p. 157~158°, which were identified with the sample obtained in section A by IR spectral comparison.

Alkaline Hydrolysis of XX——A mixture of 0.5 g. of XX, 5 ml. of MeOH, 0.5 g. of KOH and 5 ml. of H_2O was refluxed for 30 hr. (An oily reaction layer did not completely disappear). After removing MeOH, a solution of 0.5 g. of KOH in 5 ml. of H_2O was added to the reaction mixture, and the mixture was refluxed for 28 hr., cooled, shaken twice with ether, filtered, acidified with dil. H_2SO_4 and extracted with ether. The extract was washed with satd. aq. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give 0.5 g. of pale brown crystals, m.p. 120~123°, which were identified with the sample of XXII obtained in the preceding experiment by IR spectral comparison.

3-Ethyl-8-methoxy-1,2,3,4-tetrahydro-1-naphthalenone (XXV)——To a solution of 10 g. of XIIb in 10 g. of quinoline was added 0.15 g. of freshly prepared copper powder,[9] and the mixture was heated at 200° 1.5 hr., cooled, diluted with an excess of 10% H_2SO_4 and extracted with $CHCl_3$ (25 ml. x 3). The combined extracts were washed wit satd. aq. $NaHCO_3$ and then H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 8.9 g. of a pale brown oil, which was fractionated by vacuum distillation. The fraction of b.p$_{8.5}$ 165~167° (6.5 g.) was redistilled to give 6.0 g. (73%) of XXV as a colorless oil, b.p$_3$ 150~151°. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1680 (C=O). *Anal.* Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 77.03; H, 7.87.

2-Ethyl-5-methoxy-1,2-dihydronaphthalene (XXVII)——To an ice-cooled and stirred solution of 2.5 g. of $NaBH_4$ in 40 ml. of MeOH was added dropwise a solution of 8.2 g. of XXV in 20 ml. of ether, and the mixture was stirred under ice-cooling for 1 hr. and at room temperature for another 2 hr., poured into 150 ml. of satd. aq. NaCl and extracted with ether (40 ml. x 3). The combined extracts were washed with satd. aq. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give 8 g. of 2-ethyl-4-hydroxy-5-methoxy-1,2,3,4-tetrahydronaphthalene (XXVI) as a colorless oil, which decomposed partially on distillation and was employed in the next step without further purification. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3528 (OH).

A mixture of 6 g. of XXVI obtained above, 0.1 g. of TsOH and 30 ml. of EtOH was refluxed for 2 hr. After removing MeOH, the mixture was taken in 50 ml. of benzene, washed with satd. aq. $NaHCO_3$ and then H_2O, dried over anhyd. Na_2SO_4 and evaporated. The residue was fractionated *in vacuo* to give 5.4 g. of XXVII as a colorless oil, b.p$_5$ 116°. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1625 (C=C). UV λ_{max}^{EtOH} mμ (ε): 368 (5.25×10^{3})). *Anal.* Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.75; H, 8.53.

2-Ethyl-5-methoxynaphthalene (XXIV)——A mixture of 3.8 g. of XXVII and 0.65 g. of precipitated sulfur was heated at 195°. The temperature was elevated up to 240° during 1.5 hr. The reaction mixture was distilled *in vacuo* to give 3 g. of a pale yellow oil, b.p$_5$ 120~130°, which was purified by column chromatography on alumina employing benzene as eluent to give 2 g. (60%) of XXIV as a colorless oil, b.p$_3$ 122°. M.p. 26.5~27.5°. IR ν_{max}^{film} cm^{-1}: 1631, 1604, 1581 (arom.). *Anal.* Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 84.19; H, 7.60.

6-Ethyl-1-naphthol (XXIII)——A mixture of 2.5 of XXIV, 5 ml. of AcOH and 5 ml. of 52% HI was refluxed for 30 min., poured into 50 ml. of H_2O and extracted with benzene (30 ml. x 2). The combined extracts were washed with satd. aq. $NaHCO_3$ and then H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 2 g. of a pale brown oil, which gave 1 g. of the starting material and 0.9 g. of XXIII on purification by column chromatography on silica gel employing $CHCl_3$ as eluent. This specimen was identified with that obtained on HI-demethylation of XX by IR spectral comparison.

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[9] R. Q. Brewster, T. Groening: Org. Syntheses, Coll. Vol. II, 446 (1948).

Methyl 2-Ethyl-5-hydroxy-1-naphthoate (XXVIII)——Esterification of 0.7 g. of XXI with an excess of CH_2N_2 in ether under ice-cooling gave 0.7 g. of almost colorless crystals, m.p. 87～93°. Two recrystallizations from CCl_4 gave 0.5 g. of XXVIII as colorless plates, m.p. 95.5～96.5°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3330 (OH), 1685 (C=O); $\nu_{\max}^{CCl_4}$ cm^{-1}: 3534, 3401 (OH), 1727 (C=O), 1706 (shoulder). *Anal.* Calcd. for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13. Found: C, 72.81; H, 6.08.

2-Ethyl-5-methoxy-1-naphthamide (XXIX)——To a solution of 0.6 g. of XXII in 15 ml. of dry benzene was added a solution of 0.5 g. of PCl_3 in 15 ml. of dry benzene, and the mixture was heated at 60° for 100 min. After removing benzene and the excess of PCl_3, the residue was added into 20 ml. of 28% aq. NH_3 under vigorous shaking. The precipitates resulted were washed once with a small amount of ether to give 0.4 g. (67%) of XXIX, m.p. 153～157°. Four recrystallizations from MeOH-H_2O gave 0.2 g. of colorless needles, m.p. 160～162°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3372, 3145 (NH), 1629 (C=O). *Anal.* Calcd. for $C_{14}H_{15}O_2N$: C, 73.34; H, 6.59; N, 6.11. Found: C, 72.96; H, 6.83; N, 6.02.

***cis*-2-Ethyl-4-oxo-7-methoxy-1,2,3,4-tetrahydro-1-naphthoic Acid (XXXa)**——A mixture of 2 g. of VIa and 200 g. of polyphosphoric acid was heated at 95° for 1.5 hr., poured onto 500 g. of cracked ice and extracted with ether. The extract was washed with satd. aq. NaCl and evaporated without drying to give 1.85 g. of a pale brown glassy solid, which was purified by column chromatography on silica gel employing $CHCl_3$ as eluent. The first fraction gave 0.9 g. of colorless crystals, m.p. 124～130°. Three recrystallizations from ether-cyclohexane gave 0.6 g. of XXXa as colorless plates, m.p. 134～136°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 1686, 1671 (C=O). *Anal.* Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.95; H, 6.61.

Methyl *cis*-2-Ethyl-4-oxo-7-methoxy-1,2,3,4-tetrahydro-1-naphthoate (XXXIa)——Esterification of XXXa with CH_2N_2 in ether and subsequent recrystallization from hexane gave quantitatively XXXIa as colorless long plates, m.p. 94～96°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 1720, 1668 (C=O). *Anal.* Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.64; H, 6.85.

***trans*-2-Ethyl-4-oxo-7-methoxy-1,2,3,4-tetrahydro-1-naphthoic Acid (XXXb)**——To a solution of 1 g. of KOH in 5 ml. of H_2O was added a solution of 0.5 g. of XXXIa in 1 ml. of MeOH, and the mixture was refluxed until an oily layer disappeared (required 30 min.). After removing MeOH by evaporation, the mixture was refluxed for 2.5 hr., cooled, shaken with ether, acidified and extracted with ether. The extract was washed with H_2O and evaporated to give 0.45 g. of crystals, m.p. 134～150°. Recrystallization from ether gave 0.3 g. of XXXb as colorless crystals, m.p. 150～151°. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 1718, 1638 (C=O); $\nu_{\max}^{CHCl_3}$ cm^{-1}: 1705, 1669 (C=O). *Anal.* Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.41; H, 6.48.

Methyl *trans*-2-Ethyl-4-oxo-7-methoxy-1,2,3,4-tetrahydro-1-naphthoate (XXXIb)——Esterification of XXXb with CH_2N_2 in ether gave quantitatively XXXIb as a colorless oil, b.p$_{0.07}$ 150°. IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 1733, 1680 (C=O). *Anal.* Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.47; H, 6.96.

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Summary

As a part of the investigation on the synthesis of η-pyrromycinone (I), methyl 2-ethyl-5-hydroxy-1-naphthoate (II, R=OH) was synthesized by a series of reactions indicated in Chart 1 and 2. The stereochemistries of the tetralone derivatives obtained as preparative intermediates were discussed from the chemical and nuclear magnetic spectral evidences.

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