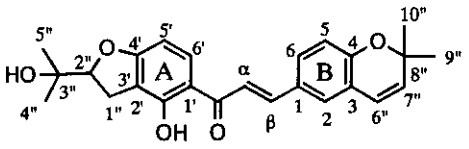
PARATOCARPINS F - L, SEVEN NEW ISOPRENOID-SUBSTITUTED FLAVONOIDS FROM *PARATOCARPUS VENENOSA* ZOLL[1]

Yoshio Hano, Naoyuki Itoh, Akio Hanaoka, and Taro Nomura*
Faculty of Pharmaceutical Sciences, Toho University, 2-2-1, Miyama, Funabashi, Chiba 274, Japan

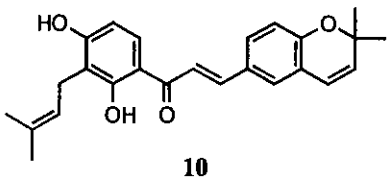
Abstract — Two new isoprenoid substituted chalcones, paratocarpins F (**1**) and G (**2**), along with five new isoprenoid substituted flavanones, paratocarpins H (**3**), I (**4**), J (**5**), K (**6**), and L (**7**), were isolated from the Indonesian moraceous plant, *Paratocarpus* (= *Artocarpus*) *venenosa* Zoll. The structures of paratocarpins F, G, H, I, J, K, and L were shown to be **1**, **2**, **3**, **4**, **5**, **6**, and **7**, respectively, on the basis of spectroscopic and chemical evidence.

Previously we reported the structure determination of five isoprenoid-substituted chalcones, paratocarpins A - E, isolated from *Paratocarpus* (= *Artocarpus*) *venenosa* Zoll.[2] Further extension of studies on the components of *P. venenosa* led to the isolation of two new isoprenoid-substituted chalcones, paratocarpins F (**1**) and G (**2**), along with five new isoprenoid-substituted flavanones, paratocarpins H (**3**), I (**4**), J (**5**), K (**6**), and L (**7**). This paper deals with characterization of these new flavonoids as well as the known compounds, gancaonin Q[3] (**8**) and 6-prenylapigenin (**9**).[4]

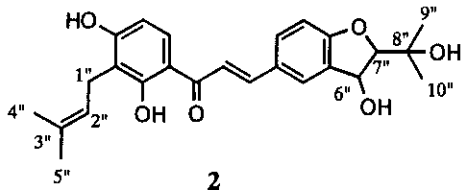
Paratocarpin F (**1**), yellow prisms, mp 89 - 91 °C, $C_{25}H_{26}O_5$, showed positive reaction to methanolic ferric chloride reaction. The ir spectrum disclosed absorption bands due to hydroxyl, conjugated carbonyl, and benzene ring moieties. The uv spectrum of **1** exhibited maxima at 210, 225 (sh), 289, and 377 nm, and was similar to that of paratocarpin C[2] (**10**), indicating that **1** is a 2', 4, 4'-oxygenated chalcone derivative. The ^{1}H nmr spectrum of **1** showed the signals of the following protons (acetone-d_6, 400 MHz): protons in a 2,2-dimethylpyran ring, δ 1.45 (6H, s), 5.83, 6.47 (each 1H, d, J = 10 Hz), *ortho*-coupled aromatic protons, δ 6.40, 8.09 (each 1H, d, J = 9 Hz), ABX type aromatic protons, δ 6.81 (1H, d, J = 8 Hz), 7.60 (1H, d, J = 2 Hz), 7.64 (1H, dd, J = 2 and 8 Hz), two olefinic protons, δ 7.81 (2H, s), proton in a hydrogen-bonded hydroxyl group, δ 13.66 (1H, s), protons in a 2-(1-hydroxy-1-methylethyl)-



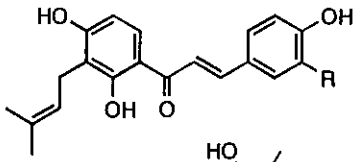
1



10



2



11: R =

12: R =

Figure 1

Table 1 ^{13}C Nmr chemical shifts (ppm) of **1**, **2**, **10**, **11**, and **12** (δ in acetone-d_6)

C	**1**	**2**	**10**	**11**	**12**
C-1	128.8	128.8	128.8	127.6	127.7
C-2	127.8	127.0	127.8	133.6	131.7
C-3	122.4	132.5	122.4	127.7	129.7
C-4	156.5	163.7	156.4	159.9	158.7
C-5	117.5	111.0	117.5	117.5	116.4
C-6	131.4	132.6	131.3	130.1	129.2
C-α	119.2	118.7	119.2	118.3	118.2
C-β	144.8	145.0	144.6	145.2	145.4
C=O	193.0	193.0	193.0	193.1	193.1
C-1'	115.5	114.5	114.5	114.5	114.4
C-2'	168.3	165.2	165.2	165.2	165.2
C-3'	114.7	116.2	116.2	116.2	116.2
C-4'	162.5	162.8	162.8	162.7	162.7
C-5'	102.4	108.1	108.1	108.0	108.0
C-6'	133.2	130.3	130.3	130.2	130.2
C-1"	27.5	22.3	22.3	22.3	22.3
C-2"	92.6	123.3	123.3	123.3	123.3
C-3"	71.5	131.5	131.5	131.5	131.5
C-4"	25.5	17.9	17.9	17.9	17.9
C-5"	26.0	25.9	25.9	25.9	25.9
C-6"	122.3	72.9	122.4	38.7	29.1
C-7"	132.5	98.9	132.4	76.7	123.3
C-8"	78.0	71.1	78.0	148.4	132.8
C-9"	28.4	25.8	28.4	110.8	17.9
C-10"	28.4	26.4	28.4	18.3	25.9

Assignments were performed by 2D ^{13}C-^{1}H shift correlation spectroscopic methods (CHCOSY, COLOC, HMBC).

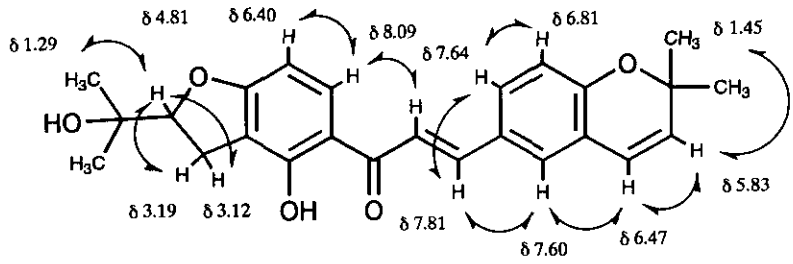


Figure 2 NOESY spectrum of **1**

2,3-dihydrofuran ring,[5] δ 1.24, 1.29 (each 3H, s), 3.12 (1H, dd, J = 10 and 16 Hz), 3.19 (1H, dd, J = 8 and 16 Hz), 4.81 (1H, dd, J = 8 and 10 Hz). The ^{13}C nmr spectrum of **1** was analysed by comparing with that of **10** (Table 1). In the spectrum, the chemical shifts of all the carbon atoms except those of the carbons of the A ring and isoprenoid moiety on the ring were good agreement with those of the relevant carbons of **10**. This result supports that the 2-(1-hydroxy-1-methylethyl)-2,3-dihydrofuran ring locates on the A ring. Furthermore the location of the 2,2-dimethylpyran ring was confirmed by the two dimetional NOE spectroscopy (NOESY) spectrum of **1** as described in Figure 2. From above results, the structure of paratocarpin F is characterized as **1**.

Paratocarpin G (**2**), yellow needles, mp 113 - 116 °C, $C_{25}H_{28}O_6$, showed positive reaction to methanolic ferric chloride reaction. The uv spectrum of **2** exhibited maxima at 204, 240 (sh), 315 (sh), 369 nm, and was similar to those of paratocarpin D (**11**)[2] and kanzonol C (**12**).[6,7] The ^{1}H nmr spectrum of **2** showed the signals of the following protons (acetone-d_6, 400 MHz): protons in a 3,3-dimethylallyl group, δ 1.65, 1.78 (each 3H, s), 3.38 (2H, br d, J = 7 Hz), 5.28 (1H, m), *ortho*-coupled aromatic protons, δ 6.54, 8.00 (each 1H, d, J = 9 Hz), ABX type aromatic protons, δ 6.86 (1H, d, J = 8 Hz), 7.71 (1H, dd, J = 2 and 8 Hz), 7.88 (1H, d J = 2 Hz), two olefinic protons, δ 7.79, 7.87 (each 1H, d, J = 15 Hz), proton in a hydrogen-bonded hydroxyl group, δ 13.97 (1H, s), two methyl protons, δ 1.27, 1.29 (each 3H, s), two methine protons, δ 4.36 (1H, d, J = 4 Hz), 5.45 (1H, dd, J = 4 and 7 Hz), proton in a hydroxyl group, δ 4.84 (1H, d, J = 7 Hz). The ^{13}C nmr spectrum of **2** was analysed by comparing with those of **11** and **12** as described in Table 1. In the spectrum of **2**, the chemical shifts of all the carbon atoms except those of the carbons of the B ring and the isoprenoid moiety on the ring were good agreement with those of the relevant carbons of **12**. The presence of 2-(1-hydroxy-1-methylethyl)-3-hydroxy-2,3-dihydrofuran ring in the structure along with the locations of the ring and the 3,3-dimethylallyl group was confirmed by the HMBC spectrum as described in Figure 3. The relative configuration between 6"-H and 7"-H was

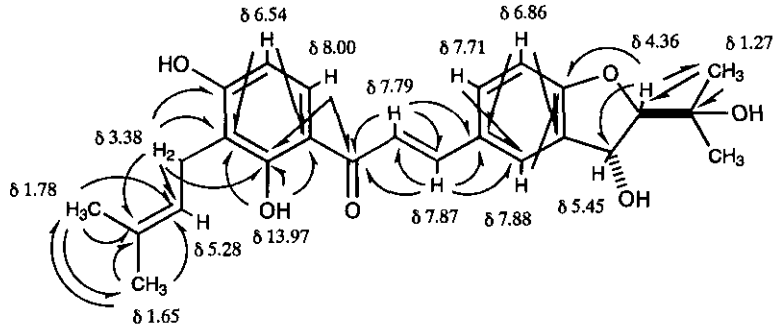


Figure 3 HMBC spectrum of **2** (J_{CCH} = 6 Hz)

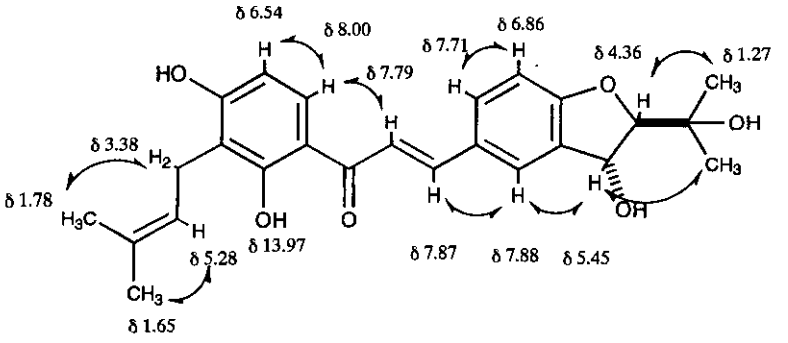
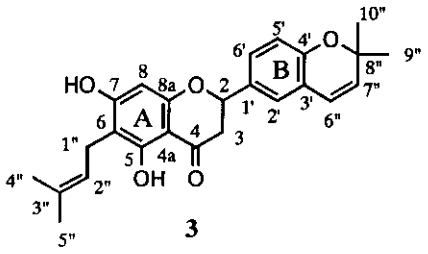


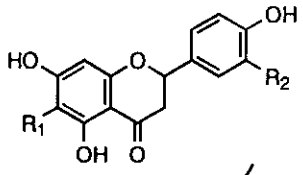
Figure 4 NOESY spectrum of **2**

supported by consideration of the NOESY spectrum of **2** (Figure 4). In the spectrum, the NOE was observed between the 6"-H and the 9"-H as well as the 10"-H. This result supports the relative configuration between 6"-H and 7"-H to be *trans*. From the above results, the structure of paratocarpin G was represented by the formula (**2**).

Paratocarpin H (**3**), colorless prisms, mp 211 - 212 °C, $C_{25}H_{26}O_5$, showed positive reaction to methanolic ferric chloride reaction, magnesium-hydrochloric acid test, and sodium borohydride test.[8] The uv spectrum exhibited maxima at 225, 294, 340 (sh) nm, and was similar to that of naringenin (**13**).[9] The ^{1}H nmr spectrum of **3** showed the signals of the following protons (acetone-*d*6, 400 MHz): protons in a 3,3-dimethylallyl group, δ 1.64, 1.75 (each 3H, s), 3.25 (2H, br d, *J* = 7 Hz), 5.24 (1H, m), protons in a 2,2-dimethylpyran ring, δ 1.42 (6H, s), 5.77, 6.44 (each 1H, d, *J* = 10 Hz), ABX type protons, δ 2.73 (1H, dd, *J* = 3 and 17 Hz), 3.16 (1H, dd, *J* = 13 and 17 Hz), 5.41 (1H, dd, *J* = 3 and 13 Hz), an aromatic proton, δ 6.04 (1H, s), ABX type aromatic protons, δ 6.78 (1H, d, *J* = 8 Hz), 7.23 (1H, d, *J* = 2 Hz), 7.29 (1H, dd, *J* = 2 and 8 Hz), proton in a hydrogen-bonded hydroxyl group, δ 12.46 (1H, s). The ^{13}C



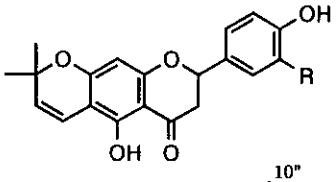
3

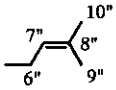


7: $R_1 = R_2 =$ 

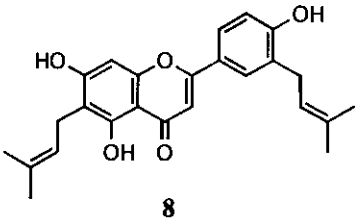
9: $R_1 =$  $R_2 = H$

13: $R_1 = R_2 = H$

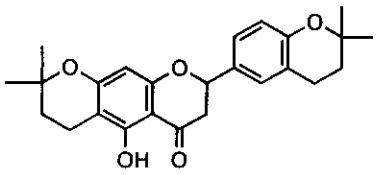


4: R = 

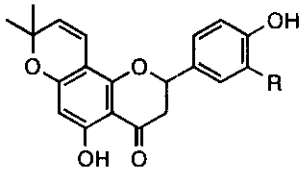
6: R = H



8

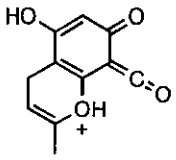


5

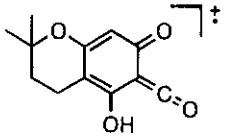


14: R = 

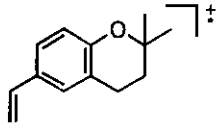
19: R = H



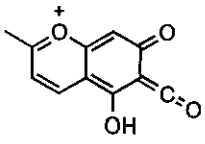
15



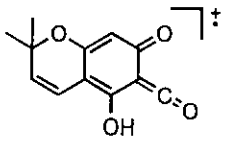
17



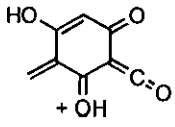
18



16



20



21

Figure 5

Table 2 ^{13}C Nmr chemical shifts (ppm) of **3**, **4**, **5**, **6**, and **7**

C	3[a]	4[b]	5[a]	6[b]	7[a]
C-2	79.7	79.1	79.9	78.9	80.1
C-3	43.6	43.2	43.7	43.2	43.7
C-4	197.2	196.1	197.6	196.0	197.4
C-4a	103.3	102.9	103.0	102.9	103.2
C-5	162.3	162.5	162.2	162.4	162.3
C-6	109.1	103.0	102.6	103.1	109.4
C-7	164.8	158.4	161.7	158.5	164.8
C-8	95.3	96.3	96.6	96.3	95.4
C-8a	162.0	162.1	163.6	162.2	162.1
C-1'	132.4	130.5	131.0	130.7	131.0
C-2'	125.7	128.2	129.0	128.0	129.1
C-3'	122.2	127.3	121.9	115.7	129.0
C-4'	154.2	154.9	155.4	156.1	156.2
C-5'	117.0	116.0	118.0	115.7	115.8
C-6'	128.4	125.7	126.6	128.0	126.2
C-1"	21.6	115.3	16.3	115.3	21.7
C-2"	123.6	126.2	32.4	126.3	123.5
C-3"	131.3	78.3	75.1	78.3	131.2
C-4"	25.9	28.4	26.8	28.4	25.9
C-5"	17.8	28.4	27.0	28.4	17.9
C-6"	122.7	29.9	23.1		29.1
C-7"	132.2	121.2	33.3		123.6
C-8"	77.2	135.4	77.0		132.7
C-9"	28.2	25.8	27.1		25.9
C-10"	28.2	17.9	27.1		17.9

Assignments were performed by 2D shift correlation spectroscopic methods (CHCOSY, COLOC, HMBC)

Solvent: a; acetone-*d6* b; $CDCl_3$

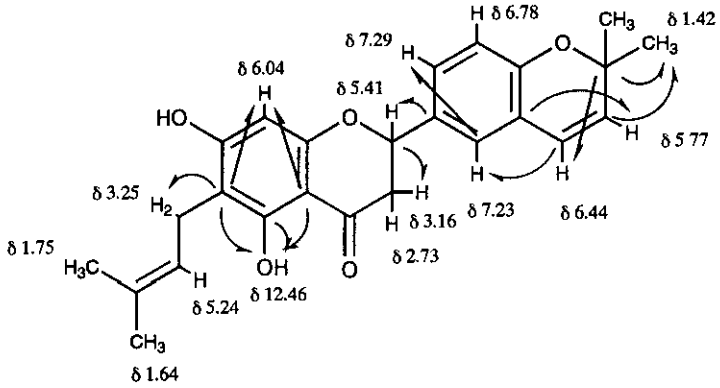


Figure 6 COLOC spectrum of **3** (J_{CCH} = 6 Hz)

nmr spectrum of **3** was analysed by comparing with those of flavanone derivatives[10] (Table 2). From above results, compound **3** is a 5,7,4'-oxygenated flavanone derivative. The location of the 3,3-dimethylallyl group and the 2,2-dimethylpyran ring was confirmed by the COLOC spectrum (Figure 6). From the above results, the structure of paratocarpin H is characterized as **3**.

Paratocarpin I (**4**), pale yellow oily substance, $C_{25}H_{26}O_5$, showed positive reaction to methanolic ferric chloride reacion, magnesium-hydrochloric acid test, and sodium borohydride test. The uv spectrum exhibited maxima at 203, 226, 272, 294, 305 (sh), 360 nm, and was similar to euchrenone a_2 (**14**).[11] The ^{1}H nmr spectrum of **4** showed the signals of the following protons (acetone-*d*6, 400 MHz): protons in a 3,3-dimethylallyl group, δ 1.78 (6H, s), 3.38 (2H, br d, *J* = 7 Hz), 5.32 (1H, m), protons in a 2,2-dimethylpyran ring, δ 1.43, 1.44 (each 3H, s), 5.50, 6.62 (each 1H, d, *J* = 10 Hz), ABX type protons, δ 2.76 (1H, dd, *J* = 3 and 17 Hz), 3.08 (1H, dd, *J* = 13 and 17 Hz), 5.31 (1H, dd, *J* = 3 and 13 Hz), an aromatic proton, δ 5.95 (1H, s), ABX type aromatic protons, δ 6.84 (1H, d, *J* = 8 Hz), 7.18 (1H, d, *J* = 2 Hz), 7.19 (1H, dd, *J* = 2 and 8 Hz), proton in a hydrogen-bonded hydroxyl group, δ 12.31 (1H, s). Comparative examination of the EI-mass spectra of **3** and **4** was carried out. The EI-mass spectrum of **3** showed the fragment ion at *m/z* 205 (**15**), while that of **4** showed at *m/z* 203 (**16**). This result supports the 2,2-dimethylpyran ring to be on the A ring. The ^{13}C nmr spectrum of **4** was analysed (Table 2). Fukai, *et al* reported that the chemical shift of the C-1 atom of the 3,3-dimethylallyl group was depend on the substituents located at the adjacent positions.[12] The signal of the C-1 atom of the 3,3-dimethylallyl group

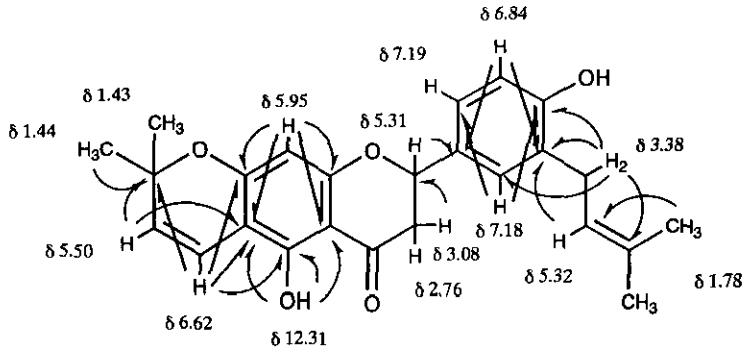


Figure 7 HMBC spectrum of **4** (J_{CCH} = 6 Hz)

of **4** was observed at δ 29.9. This result suggests that one of the *ortho*-positions to the 3,3-dimethylallyl group is replaced by the oxygenated substituent, and the group locates at the C-3' position. The location of the 2,2-dimethylpyran ring was confirmed by the HMBC spectrum of **4** (Figure 7). Thus, the structure of paratocarpin I is characterized as **4**.

Paratocarpin J (**5**), colorless oily substance, $C_{25}H_{28}O_5$, showed positive reaction to methanolic ferric chloride reaction, magnesium-hydrochloric acid test, and sodium borohydride test. The uv spectrum exhibited maxima at 204, 213 (sh), 228 (sh), 294, 330 (sh) nm, and was similar to that of **13**. The ^{1}H nmr spectrum of **5** showed the signals of the following protons (acetone-*d*6, 400 MHz): protons in two sets of 2,2-dimethyldihydropyran ring, δ 1.32 (12H, s), 1.83, 1.84, 2.58, 2.85 (each 2H, t, J = 7 Hz), ABX type protons, δ 2.75 (1H, dd, J = 3 and 17 Hz), 3.18 (1H, dd, J = 13 and 17 Hz), 5.40 (1H, dd, J = 3 and 13 Hz), an aromatic proton, δ 5.85 (1H, s), ABX type aromatic protons, δ 6.76 (1H, d, J = 8 Hz), 7.23 - 7.25 (2H, m), a proton in a hydrogen-bonded hydroxyl group, δ 12.56 (1H, s). The EI-mass spectrum of **5** showed the fragment ion at *m/z* 220 (**17**) and 188 (**18**). The location of the 2,2-dimethyldihydropyran ring in the A ring was confirmed by the HMBC spectrum (Figure 8). Thus, the structure of

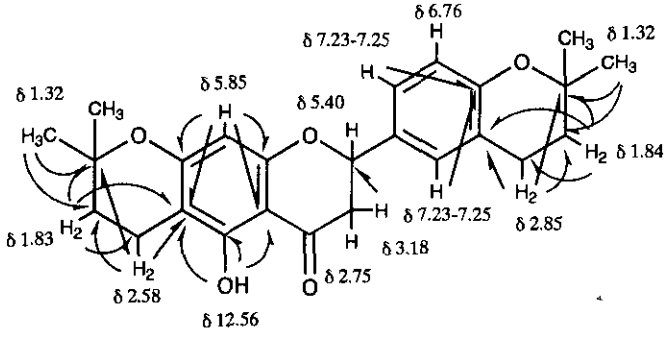


Figure 8 HMBC spectrum of **5** (J_{CCH} = 6 Hz)

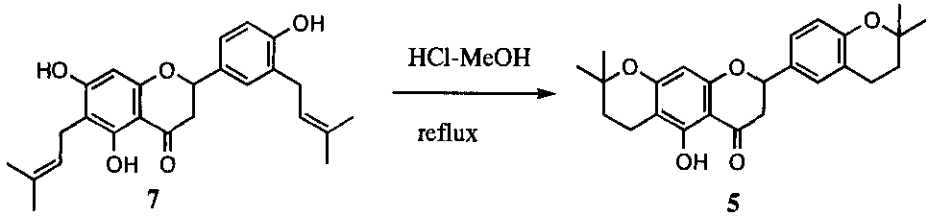


Figure 9 Chemical correlation of compound (**7**) to compound (**5**)

paratocarpin J is characterized as **5**. The structure (**5**) was confirmed by the derivation from paratocarpin L (**7**) (Figure 9). This compound (**5**) has been synthesized by Mitscher *et al.*[13] To our knowledge, this is the first time that it has been identified as a natural product.

Paratocarpin K (**6**), pale yellow prisms, mp 165 - 166 °C, $C_{20}H_{18}O_5$, showed positive reaction to methanolic ferric chloride, magnesium-hydrochloric acid test, and sodium borohydride test. The uv spectrum exhibited maxima at 227, 272, 295, 307, 360 nm, and was similar to those of **4** and citflavanone (**19**).[14] The ^{1}H nmr spectrum of **6** showed the signals of the following protons ($CDCl_3$, 400 MHz): protons in a 2,2-dimethylpyran ring, δ 1.43, 1.44 (each 3H, s), 5.50, 6.62 (each 1H, d, J = 10 Hz), ABX type protons, δ 2.78 (1H, dd, J = 3 and 17 Hz), 3.07 (1H, dd, J = 13 and 17 Hz), 5.34 (1H, dd, J = 3 and 13 Hz), A_2B_2 type aromatic protons, δ 6.88, 7.32 (each 2H, d, J = 8 Hz), an aromatic proton, δ 5.95 (1H, s), a proton in a hydrogen-bonded hydroxyl group, δ 12.29 (1H, s).. The EI-mass spectrum of **6** showed the fragment ion m/z 218 (**20**). The ^{13}C nmr spectrum of **6** was analysed by comparing with that of **4** (Table 2). In the spectrum, the chemical shifts of all the carbon atoms except those of the B ring carbons were similar to those of the relevant carbons of **4**. From the above results, the structure of paratocarpin K is characterized as **6**. While the compound (**6**) has been synthesized by Jain *et al*,[15] this is the first time that it has been identified as a natural product.

Paratocarpin L (**7**), colorless needles, mp 169 - 170 °C, $C_{25}H_{28}O_5$, gave a dark blue color with methanolic ferric chloride. The uv spectrum of **7** exhibited maxima at 207, 228 (sh), 292, 334 (sh) nm, indicating that **7** is a flavanone derivative.[9] The ^{1}H nmr of **7** showed the signals of the following protons (acetone-*d6*, 400 MHz): protons in two sets of 3,3-dimethylallyl groups, δ 1.64 (3H, s), 1.71 (6H, s), 1.75 (3H, s), 3.25, 3.35 (each 2H, br d, J = 7 Hz), 5.23, 5.35 (each 1H, m), ABX type protons, δ 2.70 (1H, dd, J = 3 and 17 Hz), 3.15 (1H, dd, J = 13 and 17 Hz), 5.39 (1H, dd, J = 3 and 13 Hz), an aromatic proton, δ 6.02 (1H, s), ABX type aromatic protons, δ 6.88 (1H, d, J = 8 Hz), 7.20 (1H, dd, J = 2 and 8 Hz), 7.28 (1H, d, J = 2 Hz), a proton in a hydrogen-bonded hydroxyl group, δ 12.47 (1H, s). The ^{13}C nmr spectrum of **7** was analysed by comparing with those of flavanones, indicating that **7** is a 5,7,4'-trioxygenated flavanone derivative (Table 2). The EI-mass spectrum of **7** showed the fragment ion at m/z 220 and 165 (**21**). These results suggest that the structure of paratocarpin L is characterized as **7** or **7a**. Paratocarpin L was identified with **7** which was derived from 2-hydroxy-4,6-dimethoxymethoxy-5-prenylacetophenone (**22**)[16] and 4-methoxymethoxy-3-prenylbenzaldehyde (**23**)[17] (Figure 10). Thus, the structure of paratocarpin L was represented by formula (**7**).

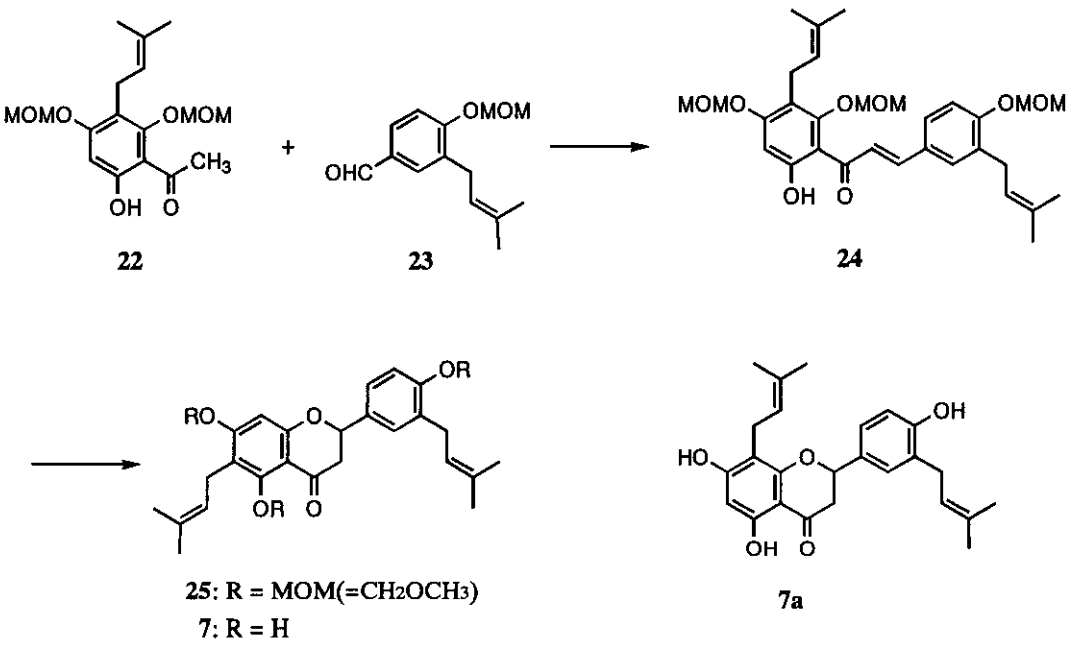


Figure 10 Synthesis of compound (7)

EXPERIMENTAL

Abbreviations: s = singlet, d = doublet, dd = double doublet, m = multiplet, br = broad, sh = shoulder. The general procedures followed and the instruments used in our previous paper.[2]

Isolation of Paratocarpins F (1), G (2), H (3), I (4), J (5), K (6), and L (7)

The dried bark of *P. venenosa* (3.4 kg) was extracted at room temperature with *n*-hexane (9 l, three times), benzene (9 l x 3), and acetone (9 l x 3), successively (each 3 days). Evaporation of the *n*-hexane, benzene and acetone solutions to dryness yielded 60 g, 55 g, and 95 g of the residues, respectively.[2]

The *n*-hexane extract (30 g) was chromatographed over silica gel (300 g) using *n*-hexane, *n*-hexane - ethyl acetate (97 : 3, 95 : 5, 4 : 1), and then ethyl acetate to prepare frs. 1 - 46.[2] The fraction eluted with *n*-hexane - ethyl acetate (95 : 5, frs. 25 and 26, 18 mg) was fractionated by preparative tlc (benzene) to give paratocarpin J (**5**, 2 mg). The fraction eluted with ethyl acetate (frs. 41 - 46, 5 g) was rechromatographed over silica gel (150 g) with *n*-hexane containing increasing amount of ethyl acetate as an eluent (frs. 1' - 58'). The fraction eluted with *n*-hexane - ethyl acetate (4 : 1, frs. 20' - 24', 540 mg) was fractionated by preparative tlc [*n*-hexane - acetone (2 : 1)] to give paratocarpin L (**7**, 36 mg).

The benzene extract (25 g) was chromatographed over silica gel (300 g) using *n*-hexane, *n*-hexane - ethyl acetate (99 : 1, 98 : 2, 96 : 4, 95 : 5, 9 : 1, and 85 : 15) to prepare frs. 1" - 98".[2] The fraction eluted with *n*-hexane - ethyl acetate (98 : 2, frs. 19" and 20", 70 mg) was fractionated by preparative tlc (benzene) to give paratocarpin J (**5**, 2 mg). The fraction eluted with *n*-hexane - ethyl acetate (95 : 5, fr. 37", 150 mg) was fractionated by preparative tlc [*n*-hexane - ethyl acetate (5 : 1)] to give paratocarpin H (**3**, 10 mg). The fraction eluted with *n*-hexane - ethyl acetate (95 : 5, frs. 39" - 43", 200 mg) was fractionated by preparative tlc [*n*-hexane - ethyl acetate (5 : 1)] to give paratocarpin I (**4**, 6 mg). The fraction eluted with *n*-hexane - ethyl acetate (9 : 1, frs. 60" - 65", 210 mg) was fractionated by preparative tlc [*n*-hexane - acetone (2 : 1)] to give paratocarpin F (**1**,

6 mg). The fraction eluted with *n*-hexane - ethyl acetate (9 : 1, frs. 66" - 69", 200 mg) was fractionated by preparative tlc [*n*-hexane - ethyl acetate (3 : 1)] to give paratocarpin K (**6**, 7 mg). The fraction eluted with *n*-hexane - ethyl acetate (85 : 5, frs. 74" and 75", 800 mg) was fractionated by preparative tlc [*n*-hexane - ethyl acetate (2 : 1)] to give paratocarpin L (**7**, 210 mg). The acetone extract (30 g) was chromatographed over silica gel (300 g) using benzene, benzene - acetone (95 : 5, 92 : 8, and 8 : 2) to prepare frs. 1"' - 55"'. The fraction eluted with benzene (fr. 6"', 210 mg) was fractionated by preparative tlc [*n*-hexane - acetone (3 : 1)] to give paratocarpins H (**3**, 5 mg) and I (**4**, 3 mg). The fraction eluted with benzene - acetone (95 : 5, fr. 12"', 95 mg) was fractionated by preparative tlc [*n*-hexane - acetone (2 : 1)] to give gancaonin Q[3] (**8**, 9 mg). The fraction eluted with benzene - acetone (92 : 8, fr. 17"', 164 mg) was fractionated by preparative tlc [$CHCl_3$ - MeOH (50 : 1)] to give 6-prenylapigenin (**9**, 14 mg). The fraction eluted with benzene - acetone (8 : 2, fr. 31"', 120 mg) was fractionated by preparative tlc [$CHCl_3$ - MeOH (10 : 1)] to give paratocarpin G (**2**, 26 mg). The known compound, gancaonin Q[3] (**8**), was identified by direct comparison with the authentic sample. 6-Prenylapigenin (**9**) was identified by comparison with the published data[4] and the authentic sample (**9a**) which was derived from naringenin[18] (**13**).

Paratocarpin F (1)

Compound (**1**) was recrystallized from MeOH - H_2O (2 : 1) to give yellow prisms, mp 89 - 91 °C. $FeCl_3$ test: positive (dark brown). $[\alpha]_D^{22}$-6.9° (*c* = 0.1, MeOH). Uv λ_{max}^{MeOH} nm (log ε): 210 (4.53), 225 (sh 4.42), 289 (4.20), 377 (4.59). EI- ms: *m/z* (rel. int.) 406 (M^+, 24), 391 (100), 373 (3), 347 (4), 338 (8), 203 (6), 187 (6), 171 (31). HR-ms: *m/z* 406.1759 (M^+, $C_{25}H_{26}O_5$ requires 406.1780), 391.1516 ($C_{24}H_{23}O_5$ requires 391.1546). Ir ν_{max}^{KBr} cm^{-1}: 3430, 2975, 2930, 1640, 1600, 1560, 1490, 1430.

Paratocarpin G (2)

Compound (**2**) was recrystallized from MeOH to give yellow needles, mp 113 - 116 °C. $FeCl_3$ test: positive (dark brown). $[\alpha]_D^{22}$0° (*c* = 0.1, MeOH). Uv λ_{max}^{MeOH} nm (log ε): 204 (4.66), 240 (sh 4.23), 315 (sh 4.23), 369 (4.62). EI- ms: *m/z* (rel. int.) 424 (M^+, 37), 407 (2), 406 (2), 381 (11), 369 (4), 348 (19), 333 (7), 305 (67), 293 (23), 204 (23), 203 (23), 189 (18), 187 (28), 161 (42), 149 (100). HR-ms: *m/z* 424.1855 (M^+, $C_{25}H_{28}O_6$ requires 424.1886), 305.0796 ($C_{19}H_{13}O_4$ requires 305.0814). Ir ν_{max}^{KBr} cm^{-1}: 3430, 2930, 1630, 1610, 1560, 1490, 1440.

Paratocarpin H (3)

Compound (**3**) was recrystallized from *n*-hexane - $CHCl_3$ (1 : 1) to give colorless prisms, mp 211 - 212 °C. $FeCl_3$ test: positive (dark brown). Mg - HCl test: positive (violet). $NaBH_4$ test: positive (orange). $[\alpha]_D^{22}$ -26.1° (*c* = 0.1, MeOH). Uv λ_{max}^{MeOH} nm (log ε): 225 (4.57), 294 (4.14), 340 (sh 3.39). EI- ms: *m/z* (rel. int.) 406 (M^+, 37), 391 (93), 363 (6), 351 (9), 205 (20), 171 (100). HR-ms: *m/z* 406.1781 (M^+, $C_{25}H_{26}O_5$ requires 406.1780), 391.1516 ($C_{24}H_{23}O_5$ requires 391.1546). Ir ν_{max}^{KBr} cm^{-1}: 3400 (br), 3140, 2970, 2920, 1650, 1630, 1590, 1490, 1450.

Paratocarpin I (4)

Compound (**4**) was obtained as oily substance. $FeCl_3$ test: positive (dark brown). Mg - HCl test: positive (violet). $NaBH_4$ test: positive (orange). $[\alpha]_D^{22}$0° (*c* = 0.1, MeOH). Uv λ_{max}^{MeOH} nm (log ε): 203 (4.63), 226 (4.26), 272 (4.48), 294 (4.00), 305 (sh 3.89), 360 (3.50). EI- ms: *m/z* (rel. int.) 406 (M^+, 22), 391 (79), 375 (34), 293 (3), 203 (100), 187 (67). HR-ms: *m/z* 406.1771 (M^+, $C_{25}H_{26}O_5$ requires 406.1780), 391.1542 ($C_{24}H_{23}O_5$ requires 391.1546). Ir ν_{max}^{KBr} cm^{-1}: 3430 (br), 2930, 1650, 1570, 1500, 1450.

Paratocarpin J (5)

Compound (**5**) was obtained as oily substance. $FeCl_3$ test: positive (dark brown). Mg - HCl test: positive (violet). $NaBH_4$ test: positive (orange). $[\alpha]_D^{22}$0° (c = 0.1, MeOH). Uv λ_{max}^{MeOH} nm (log ε): 204 (4.55), 213 (sh 4.31), 228 (sh 4.25), 294 (4.13), 330 (sh 3.21). EI- ms: *m/z* (rel. int.) 408 (M^+, 37), 353 (3), 220 (12), 205 (6), 188 (62), 175 (100), 165 (37), 149 (9). HR-ms: *m/z* 408.1949 (M^+, $C_{25}H_{28}O_5$ requires 408.1937). Ir ν_{max}^{KBr} cm^{-1}: 3440 (br), 1640, 1580, 1500, 1480, 1440.

Formation of 5 from 7

A mixture of **7** (50 mg) and 35% HCl (3 ml) - MeOH (15 ml) solution was refluxed for 2 h, and treated as usual. The product was purified by preparative tlc (benzene) to give **5** (15.5 mg). The compound (**5**) was identified with **5** by comparing the phisical data of **5** with those of **5**.

Paratocarpin K (6)

Compound (**6**) was recrystallized from *n*-hexane - $CHCl_3$ (1 : 1) to give yellow proisms, mp 165 - 166 °C. $FeCl_3$ test: positive (dark brown). Mg - HCl test: positive (violet). $NaBH_4$ test: positive (orange). $[\alpha]_D^{22}$0° (c = 0.1, MeOH). Uv λ_{max}^{MeOH} nm (log ε): 227 (4.15), 272 (4.51), 295 (3.97), 307 (3.87), 360 (3.33). EI- ms: *m/z* (rel. int.) 338 (M^+, 13), 323 (49), 218 (3), 203 (100), 147 (3), 135 (2), 120 (5) HR-ms: *m/z* 338.1131 (M^+, $C_{20}H_{18}O_5$ requires 338.1155), 203.0354 ($C_{11}H_7O_4$ requires 203.0344). Ir ν_{max}^{KBr} cm^{-1}: 3430 (br), 2930, 1650, 1570, 1520, 1450.

Paratocarpin L (7)

Compound (**7**) was recrystallized from *n*-hexane - ethyl ether (1 : 1) to give pale yellow needles, mp 169 - 170 °C. $FeCl_3$ test: positive (dark brown). Mg - HCl test: positive (violet). $NaBH_4$ test: positive (orange). $[\alpha]_D^{22}$ -11° (c = 0.04, EtOH). Uv λ_{max}^{MeOH} nm (log ε): *205 (4.35), 210 (4.31), 228 (4.14), 295 (3.99), 336 (3.27).* EI- *ms: m/z (rel. int.)* 408 (M^+, 100), 393 (3), 365 (18), 353 (27), 220 (25), 205 (45), 192 (25), 175 (19), 165 (56). HR-ms: *m/z* 408.1936 (M^+, $C_{25}H_{28}O_5$ requires 408.1929), 165.0175 ($C_8H_5O_4$ requires 165.0186). Ir ν_{max}^{KBr} cm^{-1}: 3450, 3150, 1640, 1600, 1500.

Formation of 24 from 2-hydroxy-4,6-dimethoxymethoxy-5-prenylacetophenone (22) and 4-methoxymethoxy-3-prenylbenzaldehyde

A mixture of **22**[16] (110 mg) and **23**[17] (95 mg) in EtOH solution (3 ml) and 25% KOH aqueous solution (1 ml) was kept at room temperature for 15h, and treated as usual. The product was purified by preparative tlc [*n*-hexane - acetone (5 : 1)] to give **24** (21 mg). Compound (**24**) was obtained as yellow oily substance. HR-ms: *m/z* 540.2687 (M^+, $C_{31}H_{40}O_8$ requires 540.2712). ^1H Nmr (acetone-d_6, 400 MHz): δ 1.65, 1.75, 1.76, 1.81 (each 3H, s), 3.39 (4H, br d, J = 7 Hz), 3.47 (6H, s, -$OCH_2OC\underline{H}_3$ x 2), 3.50 (3H, s, -$OCH_2OC\underline{H}_3$), 4.96 (2H, s, -$OC\underline{H}_2OCH_3$), 5.33 (4H, s, -$OC\underline{H}_2OCH_3$ x 2), 5.23, 5.35 (each 1H, m), 6.48 (1H, s), 7.16 (1H, d, J = 8 Hz), 7.58 (1H, dd, J = 2 and 8 Hz), 7.59 (1H, d, J = 2 Hz), 7.80 (2H,s), 12.99 (1H, s).

Formation of 25 from 24

A mixture of **24** (17 mg) and sodium acetate (42 mg) in EtOH (5 ml) was refluxed for 2h, and treated as usual. The product was purified by preparative tlc [*n*-hexane - acetone (7 : 1)] to give **25** (5 mg). Compound (**25**) was obtained as yellow oily substance. HR-ms: m/z 540.2699 (M^+, $C_{31}H_{40}O_8$ requires 540.2712). Ir ν_{max}^{KBr} cm^{-1}: 1670, 1600, 1160. ^1H Nmr (acetone-d_6, 400 MHz): δ 1.65, 1.71, 1.73, 1.78 (each 3H, s), 2.67 (1H, dd, J = 3 and 17 Hz), 3.04 (1H, dd, J = 13 and 17 Hz), 3.38,

3.39 (each 2H, br d, J = 7 Hz), 3.45 (6H, s, -$OCH_2OC\underline{H}_3$ x 2), 3.53 (2H, s, -$OCH_2OC\underline{H}_3$), 5.01, 5.14 (each 1H, d, J = 7 Hz, -$OC\underline{H}_2OCH_3$), 5.20 (1H, m), 5.27, 5.31 (each 2H, s, -$OC\underline{H}_2OCH_3$), 5.32 (1H, m), 5.47 (1H, dd, J = 3 and 13 Hz), 6.51 (1H, s), 7.12 (1H, d, J = 8 Hz), 7.34 (1H, dd, J = 2 and 8 Hz), 7.35 (1H, d, J = 2 Hz).

Formation of 7 from 25

A mixture of **25** (10 mg) and 3N HCl solution (0.2 ml) was refluxed for 30 min, and treated as usual. The product was purified by preparative tlc [*n*-hexane - acetone (2 : 1)] to give **7** (3 mg). The compound (**7**) was recrystallized from *n*-hexane - ethyl ether (1 : 1) to give pale yellow needles, mp 170 °C. The compound (**7**) was identified **7** by mixed melting point experiment and comparing the ^{1}H nmr and ir spectral data.

6-Prenylapigenin (9)

Compound (**9**) was recrystallized from *n*-hexane - ethyl ether (1 : 1) to give yellow needles, mp 223 °C. HR-ms: *m/z* 338.1127 (M^+, $C_{20}H_{18}O_5$ requires 338.1149). ^{1}H Nmr(acetone-d_6, 400 MHz): δ 1.65, 1.78 (each 3H, br s), 3.35 (2H, br d, J = 7 Hz), 5.28 (1H, m), 6.61, 6.62 (each 1H, s), 7.02 (2H, d, J = 9 Hz), 7.92 (2H, d, J = 9 Hz), 13.30 (1H, s). ^{13}C Nmr (acetone-d_6, 100 MHz): δ 161.9 (C-2), 104.1 (C-3), 183.2 (C-4), 105.3 (C-4a), 162.5 (C-5), 112.4 (C-6), 164.9 (C-7), 94.1 (C-8), 156.6 (C-8a), 123.5 (C-1'), 129.2 (C-2'and 6'), 116.9 (C-3' and 5'), 160.3 (C-4'), 20.0 (C-9), 123.3 (C-10), 131.7 (C-11), 25.9 (C-12), 17.9 (C-13).

AKNOWLEDGEMENT

We are grateful to Eisai Co., Ltd., and to P.T. Eisai Indonesia Co., Ltd., for their kind offer of facilities to collect the plant material. Authors' thanks are due to the members of Botanical Garden of Bogor, Indonesia, for their identification of plant material.

REFERENCES

1. *Part 25 in the series "Constituents of the Moraceae Plants". Part 24 in the series:* K. Shinomiya, M. Aida, Y. Hano, and T. Nomura, *Phytochemistry*, in press.
2. Y. Hano, N. Itoh, A. Hanaoka, Y. Itoh, and T. Nomura, *Heterocycles*, 1995, **41**, 191, and references cited therein.
3. T. Fukai, Q. -H. Wang, and T. Nomura, *Phytochemistry*, 1991, **30**, 1245.
4. a) F. Bohlmann, C. Zdero, and R. H. King, *Phytochemistry*, 1979, **18**, 1246; b) K. Kajiyama, S. Demizu, Y. Hiraga, K. Kinoshita, K. Koyama, K. Takahashi, Y. Tamura, K. Okada, and T. Kinoshita, *J. Nat. Prod.*, 1992, **55**, 1197; c) T. Fukai and T. Nomura, *Heterocycles*, 1993, **36**, 329.
5. S. Nakahara, S. Tahara, J. Mizutani, and J. L. Ingham, *Agric. Biol. Chem.*, 1986, **50**, 863.

6. T. Fukai, J. Nishizawa, and T. Nomura, *Phytochemistry*, 1994, **35**, 515.

7. S. B. Christensen, C. Ming, L. Andersen, U. Hjfme, C. E. Olsen, C. Cornett, T. G. Theander, and K. Kharazmi, *Planta Med.*, 1994, **60**, 121.

8. R. M. Horowitz, *J. Org. Chem.*, 1957, **22**, 1733.

9. T. J. Mabry, K. R. Markham, and M. B. Thomas, "The Systematic Identification of Flavonoids", Springer-Verlag, New York, 1970.

10. P. K. Agrawal, R. S. Thakur, and M. G. Bonsal, "Carbon-13 NMR of Flavonoids", ed. by P. G. Agrawal, Elsevier, Amsterdam, 1989, p. 95.

11. M. Mizuno, K. Kimura, T. Tanaka, and M. Iinuma, *Phytochemistry*, 1988, **27**, 1831.

12. T. Fukai and T. Nomura, *Heterocycles*, 1989, **29**, 2379.

13. L. A. Mitcher, S. R. Gollapudi, I. K. Khanna, S. D. Drake, T. Hanumaiah, T. Ramaswamy, and K. V. J. Rao, *Phytochemistry*, 1985, **24**, 2885.

14. C. Itoh, M. Omura, M. Jun-ichi, and H. Furukawa, *Chem. Pharm. Bull.*, 1988, **36**, 3292.

15. A. C. Jain, R. C. Gupta, and P. D. Sarpal, *Tetrahedron*, 1978, **34**, 3563.

16. T. Fujimoto, Y. Hano, and T. Nomura, *Planta Med.*, 1985, **47**, 190.

17. K. Kyogoku, K. Hatayama, S. Yokomori, R. Saziki, S. Nakae, M. Sasajima, J. Sawada, M. Ohzeki, and T. Tanaka, *Chem. Pharm. Bull.*, 1979, **27**, 2943.

18. A. Hanaoka, Master thesis, Toho University, 1991, March.

Received, 12th June, 1995