

PARATOCARPINS A - E, FIVE NEW ISOPRENOID-SUBSTITUTED
CHALCONES FROM *PARATOCARPUS VENENOSA* ZOLL.¹

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Abstract - Five new isoprenoid-substituted chalcones, paratocarpins A (1), B (2), C (3), D (4), and E (5) were isolated from the Indonesian moraceous plant, *Paratocarpus* (= *Artocarpus*) *venenosa* Zoll. The structures of paratocarpins A, B, C, D, and E were shown to be 1, 2, 3, 4, and 5, respectively, on the basis of spectroscopic data.

Previously we reported the structure determination of isoprenoid-substituted phenolic compounds isolated from Indonesian moraceous plant, such as *Artocarpus heterophyllus*,²⁻⁶ *A. communis*,⁷ *A. rigida*,^{8,9} and *Antiaris toxicaria*.¹⁰⁻¹² In the course of our studies on the constituents of the moraceous plants, we examined the constituents of *Paratocarpus* (= *Artocarpus*) *venenosa* Zoll. collected in Bogor, Indonesia. The latex from the seed of the plant contains poison and it has been used for eradication of rats.¹³ This paper deals with the characterization of five new isoprenoid-substituted chalcones, paratocarpins A (1), B (2), C (3), D (4), and E (5) as well as the isolation of a known compound, kanzonol C (6).^{14,15}

Paratocarpin A (1), yellow needles, mp 127 - 128 °C, C₂₅H₂₄O₄, gave a dark brown color with methanolic ferric chloride. The ir spectrum disclosed absorption bands due to hydroxyl, conjugated carbonyl, and benzene ring moieties. The uv spectrum of 1 exhibited maxima at 203, 226, 285, and 388 nm, and was similar to those of chalcones.¹⁶ The ¹H nmr spectrum of 1 showed the signals of the following protons (δ in acetone-*d*₆): two sets of 2,2-dimethylpyran ring protons, δ 1.45, 1.46 (each 6H, s), 5.74, 5.83, 6.47, 6.71 (each 1H, d, *J* = 10 Hz), *ortho*-coupled aromatic protons, δ 6.38, 8.07 (each 1H, d, *J* = 9 Hz), ABX type aromatic protons, δ 6.82 (1H,

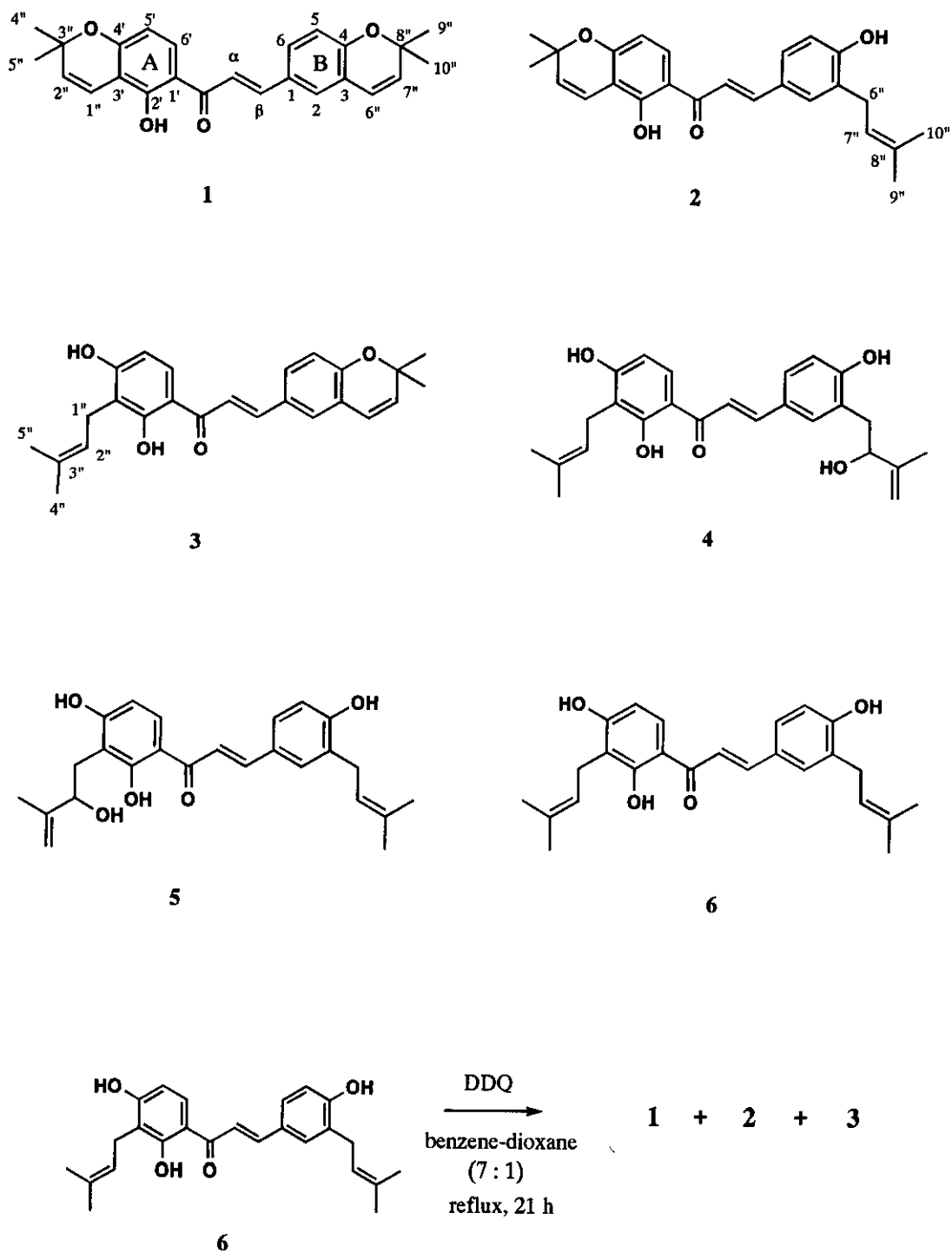


Figure 1

Table 1 ^{13}C Nmr chemical shifts (ppm) of **1**, **2**, **3**, **4**, and **6**

C No.	1	2	3[#]	4[#]	6[#]
C-1	128.7	127.6	128.8	127.6	127.7
C-2	127.9	130.2	127.8	133.6	131.7
C-3	122.4	129.8	122.4	127.7	129.7
C-4	156.6	158.9	156.4	159.9	158.7
C-5	117.6	116.3	117.5	117.5	116.4
C-6	131.5	129.8	131.3	130.1	129.2
C- α	118.8	117.8	119.2	118.3	118.2
C- β	145.3	146.1	144.6	145.2	145.4
C=O	193.2	193.3	193.0	193.1	193.1
C-1'	114.9	114.8	114.5	114.5	114.4
C-2'	161.8	161.7	165.2	165.2	165.2
C-3'	109.9	109.9	116.2	116.2	116.2
C-4'	160.5	160.4	162.8	162.7	162.7
C-5'	108.9	108.9	108.1	108.0	108.0
C-6'	129.3	129.3	130.3	130.2	130.2
C-1''	116.3	116.4	22.3	22.3	22.3
C-2''	132.3	132.2	123.3	123.3	123.3
C-3''	78.6	78.5	131.5	131.5	131.5
C-4''	28.5	28.5	17.9	17.9	17.9
C-5''	28.5	28.5	25.9	25.9	25.9
C-6''	122.3	29.1	122.4	38.7	29.1
C-7''	132.5	123.3	132.4	76.7	123.3
C-8''	78.0	132.8	78.0	148.4	132.8
C-9''	28.4	17.9	28.4	110.8	17.9
C-10''	28.4	25.9	28.4	18.3	25.9

solvent: acetone- d_6

: Assignments of each carbons were established by 2D ^1H - ^{13}C correlation shift spectrometry (CHCOSY, COLOC, HMBC).

d, $J = 8$ Hz), 7.62 (1H, d, $J = 2$ Hz), 7.66 (1H, dd, $J = 2$ and 8 Hz), two olefinic protons, δ 7.80, 7.88 (each 1H, d, $J = 15$ Hz), proton in a hydrogen-bonded hydroxyl group, δ 14.02 (1H, s). The ^{13}C nmr spectrum of **1** was analysed by comparing with that of kanzonol C (**6**) (Table 1). Paratocarpin A (**1**) was derived from **6** by treatment of **6** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ). Thus, the structure of paratocarpin A is characterized as **1**. This compound has been synthesized by Pereira *et al.*¹⁷ To our knowledge, this is the first time that it has been identified as a natural product.

Paratocarpin B (**2**), yellow oily substance, $\text{C}_{25}\text{H}_{26}\text{O}_4$, gave a dark brown color with methanolic ferric chloride. The uv spectrum of **2** exhibited maxima at 229, 266, and 378 nm, and was similar to that of **1**. The ^1H nmr spectrum of **2** showed the signals of the following protons: protons in a 2,2-dimethylpyran ring, δ 1.45 (6H, s), 5.73, 6.71 (each 1H, d, $J = 10$ Hz), protons in a 3,3-dimethylallyl group, δ , 1.73, 1.75 (each 3H, s), 3.37 (2H,

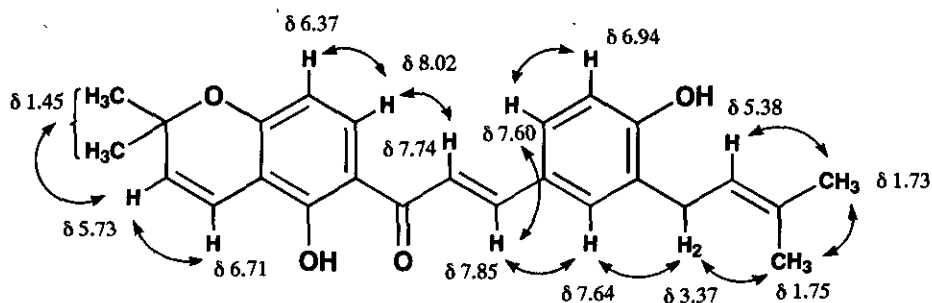


Figure 2 2D NOESY spectrum of 2

br d, $J = 7$ Hz), 5.38 (1H, m), *ortho*-coupled aromatic protons, δ 6.37, 8.02 (each 1H, d, $J = 9$ Hz), ABX type of aromatic protons, δ 6.94 (1H, d, $J = 8$ Hz), 7.60 (1H, dd, $J = 2$ and 8 Hz), 7.64 (1H, d, $J = 2$ Hz), two olefinic protons, δ 7.74, 7.85 (each 1H, d, $J = 15$ Hz), proton in a hydrogen-bonded hydroxyl group, δ 14.08 (1H, s). In the ^1H nmr spectrum of 2, the chemical shifts of the 2,2-dimethylpyran ring and the *ortho*-coupled aromatic protons were similar to those of the relevant protons of 1. The ^{13}C nmr spectrum of 2 was analysed by comparing with those of 1 and 6 (Table 1). In the spectrum, the chemical shifts of all the carbon atoms except those of the carbons of B ring and 3,3-dimethylallyl group were approximately similar to those of the relevant carbons of 1. Furthermore paratocarpin B was derived from 6 by treatment with DDQ. The location of the 3,3-dimethylallyl group on the B ring was supported by the NOESY spectrum as described in Figure 2. Thus, the structure of paratocarpin B is characterized as 2.

Paratocarpin C (3), yellow needles, mp 117 - 118 °C, $\text{C}_{25}\text{H}_{26}\text{O}_4$, gave a dark brown color with methanolic ferric chloride. The uv spectrum of 3 exhibited maxima at 205, 288, and 376 nm and was similar to those of 1 and 2. The ^1H nmr spectrum of 3 showed the signals of the following protons: protons in a 2,2-dimethylpyran ring protons, δ 1.44 (6H, s), 5.81, 6.46 (each 1H, d, $J = 10$ Hz), protons in a 3,3-dimethylallyl group, δ 1.64, 1.78 (each 3H, s), 3.38 (2H, br d, $J = 7$ Hz), 5.28 (1H, m), *ortho*-coupled aromatic protons, δ 6.54, 7.97 (each 1H, d, $J = 9$ Hz), ABX type aromatic protons, δ 6.81 (1H, d, $J = 8$ Hz), 7.57 (1H, dd, $J = 2$ Hz), 7.62 (1H, dd, $J = 2$ and 8 Hz), two olefinic protons, δ 7.77, 7.82 (each 1H, d, $J = 15$ Hz), proton in a hydrogen-bonded hydroxyl group, δ 13.96 (1H, s). The ^{13}C nmr spectrum of 3 was analysed by comparing with those of 1, 2, and 6 (Table 1). Furthermore paratocarpin C was derived from 6 by treatment with DDQ. The location of the 3,3-dimethylallyl group was supported by the NOESY spectrum as described in Figure 3. Thus, the structure of paratocarpin C is characterized as 3.

Paratocarpin D (4), yellow plates, mp 167 - 169 °C, $[\alpha]_D -5.5^\circ$, $\text{C}_{25}\text{H}_{28}\text{O}_5$, gave a dark brown color with methanolic ferric chloride. The uv spectrum of 4 exhibited maxima at 203, 240 (sh), and 375 nm, and was

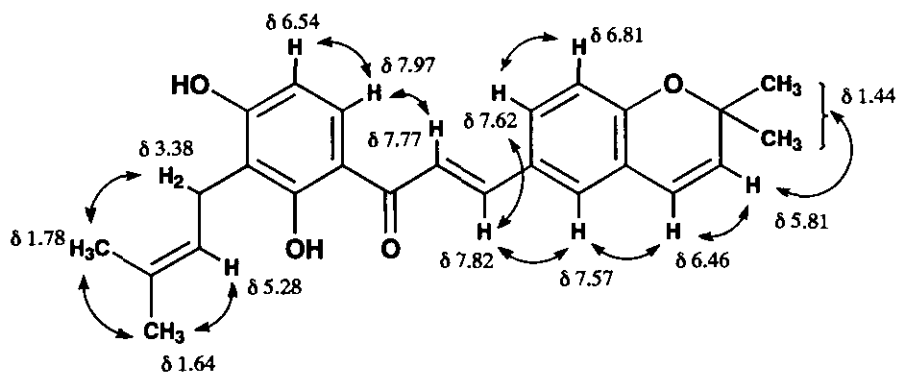
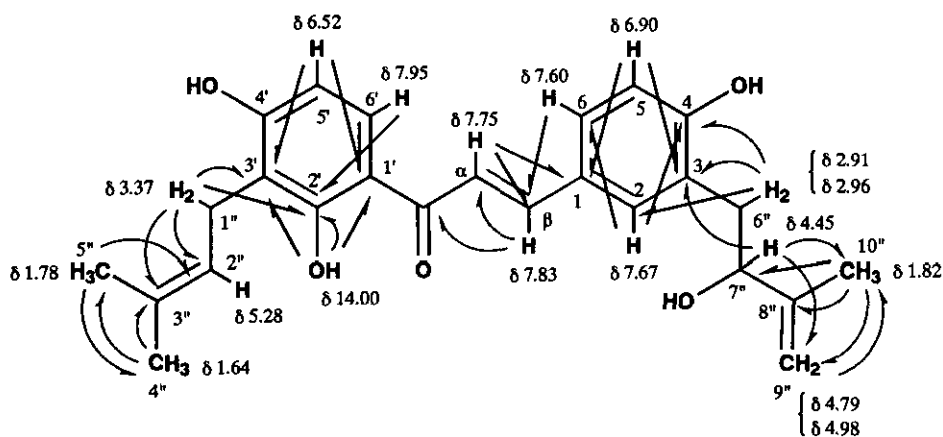


Figure 3 2D NOESY spectrum of 3

similar to that of 6. The ^1H nmr spectrum of 4 showed the signals of the following protons: protons in a 3,3-dimethylallyl group, δ 1.64, 1.78 (each 3H, s), 3.37 (2H, br d, $J = 7$ Hz), 5.28 (1H, m), *ortho*-coupled aromatic protons, δ 6.52, 7.95 (each 1H, d, $J = 9$ Hz), ABX type aromatic protons, δ 6.90 (1H, d, $J = 8$ Hz), 7.60 (1H, d, $J = 2$ and 8 Hz), 7.67 (1H, d, $J = 2$ Hz), two olefinic protons, δ 7.75, 7.83 (each 1H, d, $J = 15$ Hz), proton in a hydrogen-bonded hydroxyl group, δ 14.00 (1H, s), methyl protons, δ 1.82 (3H, s), methylene protons, δ 2.91 (1H, dd, $J = 4$ and 13 Hz), 2.96 (1H, dd, $J = 7$ and 13 Hz), a methine proton, δ 4.45 (1H, dd, $J = 4$ and 7 Hz), terminal methylene protons, δ 4.79, 4.98 (each 1H, br s). The ^{13}C nmr spectrum of 4 was analysed by comparing with that of 6 (Table 1). In the spectrum, the chemical shifts of all the carbon atoms except those of the B ring and five aliphatic carbons were in good agreement with those of the relevant carbons of 6. The presence of the 2-hydroxy-3-methyl-3-butenyl moiety in the structure and the location of the moiety were confirmed by the

Figure 4 HMBC spectrum ($J_{\text{CCH}} = 6$ Hz) of 4

^1H and ^{13}C nmr spectra as well as the ^1H - ^1H COSY and the HMBC spectra as described in Figure 4. Thus, the structure of paratocarpin D is characterized as 4.

Paratocarpin E (5), yellow amorphous powder, $[\alpha]_{\text{D}}^{20}$, $\text{C}_{25}\text{H}_{28}\text{O}_5$, gave a dark brown color with methanolic ferric chloride. The uv spectrum of 5 exhibited maxima at 204, 240 (sh), and 375 nm, and was similar to that of 4. The ^1H nmr spectrum of 5 showed the signals of the following protons: protons in a 3,3-dimethylallyl group, δ 1.73, 1.75 (each 3H, s), 3.37 (2H, br d, $J = 7$ Hz), 5.38 (1H, m), *ortho*-coupled aromatic protons, δ 6.47, 7.98 (each 1H, d, $J = 9$ Hz), ABX type aromatic protons, δ 6.94 (1H, d, $J = 8$ Hz), 7.58 (1H, dd, $J = 2$ and 8 Hz), 7.63 (1H, d, $J = 2$ Hz), two olefinic protons, δ 7.75, 7.83 (each 1H, d, $J = 15$ Hz), proton in a hydrogen-bonded hydroxyl group, δ 14.26 (1H, s), protons in a 2-hydroxy-3-methyl-3-butenyl group, δ 1.83 (3H, s), 2.89 (1H, dd, $J = 8$ and 14 Hz), 3.11 (1H, dd, $J = 3$ and 14 Hz), 4.40 (1H, dd, $J = 3$ and 8 Hz), 4.76, 4.95 (each 1H, br s). The signal patterns of all the proton signals of 5 were good agreement with those of the relevant signals of 4. This result supports that paratocarpin E (5) is a structural isomer of 4. Furthermore, the chemical shifts and coupling patterns of the proton signals of the B ring and the 3,3-dimethylallyl group were good agreement with those of the relevant signals of 6. Thus, the structure of paratocarpin E is characterized as 5.

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 papers.²⁻⁶

Plant material: Bark of *Paratocarpus venosus* Zoll. was collected in the Botanical Garden of Bogor, Indonesia, in September 1992, and was identified by the members of Botanical Garden of Bogor.

Isolation of Paratocarpin A (1), B (2), C (3), D (4), and E (5)

The dried bark of *P. venosus* (3.4 kg) was finely cut and 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, acetone solutions to dryness yielded 60 g, 55 g, and 95 g of the residue, respectively.

The *n*-hexane extract (30 g) was chromatographed over silica gel (300 g) using *n*-hexane, *n*-hexane - ethyl acetate (97 : 3, 95 : 5, and 4 : 1), and then ethyl acetate to prepare frs. 1 - 46. The fraction eluted with *n*-hexane - ethyl acetate (97 : 3, fr. 22, 30 mg) was fractionated by preparative tlc (silica gel, solvent, benzene) to give paratocarpin A (1, 4 mg). The fraction eluted with *n*-hexane - ethyl acetate (4 : 1, frs. 33 - 37, 27 mg) was fractionated by preparative tlc [*n*-hexane - acetone (2 : 1)] to give paratocarpin E (5, 4 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 (9 : 1, frs. 10' and 11', 330 mg) was fractionated by preparative tlc [*n*-hexane - ethyl acetate (3 : 1)] to give paratocarpin C (3, 10 mg). The fraction eluted with *n*-hexane - ethyl acetate (85 : 15, frs. 17' - 19', 610 mg) was fractionated by preparative tlc [*n*-hexane - acetone (3 : 1)] to give paratocarpin D (4, 3 mg). The fraction eluted with *n*-hexane - ethyl acetate (4 : 1, frs. 25' - 29', 731 mg) was fractionated

by preparative tlc [*n*-hexane - acetone (2 : 1)] to give kanzonol C (6, 62 mg), which was identified with 6 by comparing with authentic sample.¹⁴

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, 85 : 15) to prepare frs. 1" - 98". The fraction eluted with *n*-hexane (frs. 1" - 12", 340 mg) was fractionated by preparative tlc (benzene only) to give 1 (10 mg). The fraction eluted with *n*-hexane - ethyl acetate (98 : 2, frs. 28" - 36", 770 mg) was fractionated by preparative tlc [*n*-hexane - ethyl acetate (5 : 1)] to give paratocarpin B (2, 2 mg). The fraction eluted with *n*-hexane - ethylacetate (95 : 5, frs. 44" - 47", 690 mg) was fractionated by preparative tlc [*n*-hexane - ethyl acetate (3 : 1)] to give 3 (61 mg). The fraction eluted with *n*-hexane - ethyl acetate (85 : 15, frs. 77" - 81", 1.6 g) was fractionated by preparative tlc [*n*-hexane - acetone (2 : 1)] to give 6 (812 mg).

Pratocarpin A (1)

Compound (1) was recrystallized from benzene - petrol (3 : 2) to give yellow needles, mp 127 - 128 °C. FeCl₃ test: positive (dark brown). EI-*ms*: *m/z* (rel. int.) 388 (M⁺, 18), 373 (58), 203 (10), 187 (100), 179 (29), 171 (28), 159 (4), 149 (16). HR-*ms*: *m/z* 388.1656 (M⁺, C₂₅H₂₄O₄ requires 388.1675). Ir $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3420, 2930, 2850, 1650, 1630, 1580, 1490, 1460, 1360. Uv $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 203 (4.55), 226 (4.45), 285 (4.36), 380 (4.51).

Pratocarpin B (2)

Compound (2) was obtained as a yellow oily substance. FeCl₃ test: positive (dark brown). EI-*ms*: *m/z* (rel. int.) 390 (M⁺, 12), 375 (28), 203 (13), 187 (100), 163 (3). HR-*ms*: *m/z* 390.1782 (M⁺, C₂₅H₂₆O₄ requires 390.1831). Ir $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3420, 1650, 1620, 1560, 1480, 1470, 1440. Uv $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 229 (4.43), 266 (4.40), 378 (4.54).

Pratocarpin C (3)

Compound (3) was recrystallized from *n*-hexane - CHCl₃ (1 : 1) to give yellow needles, mp 117 - 118 °C. FeCl₃ test: positive (dark brown). EI-*ms*: *m/z* (rel. int.) 390 (M⁺, 39), 375 (100), 357 (2), 347 (29), 335 (7), 203 (4), 171 (13), 161 (4), 149 (10). HR-*ms*: *m/z* 390.1807 (M⁺, C₂₅H₂₆O₄ requires 390.1831). Ir $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3430 - 3250 (br), 2980, 2920, 1650, 1630, 1560, 1490, 1470, 1440. Uv $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 205 (4.52), 280 (4.18), 376 (4.51).

Pratocarpin D (4)

Compound (4) was recrystallized from MeOH - H₂O (2 : 1) to give yellow plates, mp 167 - 169 °C, $[\alpha]_{\text{D}}^{22}$ - 5.5° (*c* = 0.1, MeOH). FeCl₃ test: positive (dark brown). EI-*ms*: *m/z* (rel. int.) 408 (M⁺, 17), 390 (8), 375 (8), 347 (17), 338 (61), 282 (24), 205 (24), 203 (39), 187 (17), 161 (38), 149 (100). HR-*ms*: *m/z* 408.1952 (M⁺, C₂₅H₂₈O₅ requires 408.1937). Ir $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3420, 2920, 1610, 1600, 1500, 1430, 1370. Uv $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 203 (4.44), 240 (sh 3.91), 375 (4.34).

Pratocarpin E (5)

Compound (5) was obtained as a yellow oily substance, $[\alpha]_{\text{D}}^{22}$ 0° (*c* = 0.1, MeOH). FeCl₃ test: positive (dark brown). EI-*ms*: *m/z* (rel. int.) 408 (M⁺, 6), 390 (6), 375 (2), 338 (67), 282 (4), 220 (10), 203 (23), 188 (26), 149 (100). Uv $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 204 (4.44), 240 (sh 3.91), 375 (4.33).

Treatment of Kanzonol C (6) with DDQ

A mixture of **6** (95 mg) and DDQ (18 mg) in benzene - dioxane (7 : 1) solution (30 ml) was refluxed for 21 h and treated as usual. The product was purified by preparative tlc (benzene only) to give **1'** (7 mg), **2'** (8 mg), and **3'** (16 mg). The compounds (**1'**), (**2'**), and (**3'**) were identified with paratocarpins A (**1**), B (**2**), and C (**3**), respectively, by direct comparison with authentic samples.

AKNOWLEDGMENT

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.

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