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

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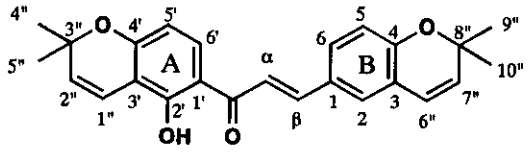
Abstract - Five new isoprenoid-substituted chalcones, paratocarpins A (**1**), B (**2**), C (**3**), D (**4**), and E (**5**) were isolated from the Indonesian moraceous plant, *Paratocarpus* (= *Artocarpus*) *venenosa* Zoll. The structures of paratocarpins A, B, C, D, and E were shown to be **1**, **2**, **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, $C_{25}H_{24}O_4$, 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 ^{1}H 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,



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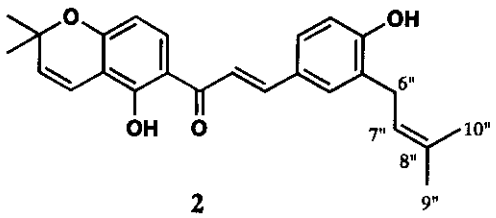

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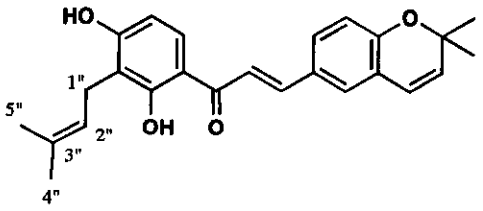

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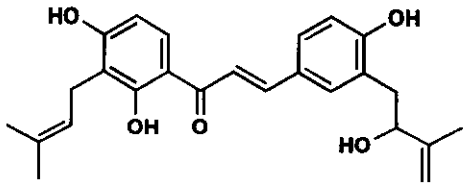

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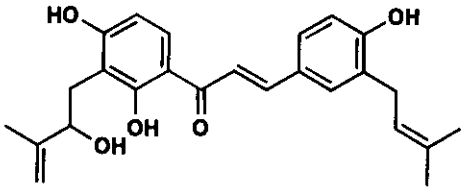

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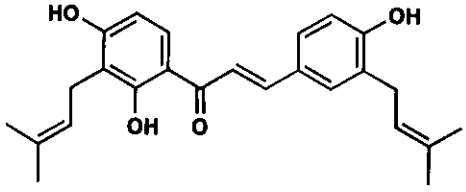

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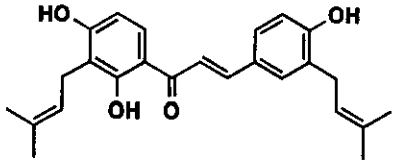

6

DDQ

benzene-dioxane
(7 : 1)
reflux, 21 h

1 + 2 + 3

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 ^{1}H - ^{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, $C_{25}H_{26}O_4$, 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 ^{1}H 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,

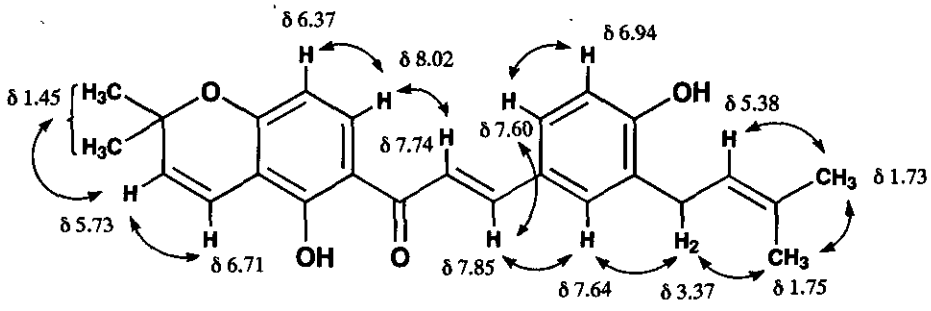

Figure 2 2D NOESY spectrum of **2**

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 ^{1}H 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**.

Pratocarpin C (**3**), yellow needles, mp 117 - 118 °C, $C_{25}H_{26}O_4$, 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 ^{1}H nmr spectrum of **3** showed the signals of the followng 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°, $C_{25}H_{28}O_5$, 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

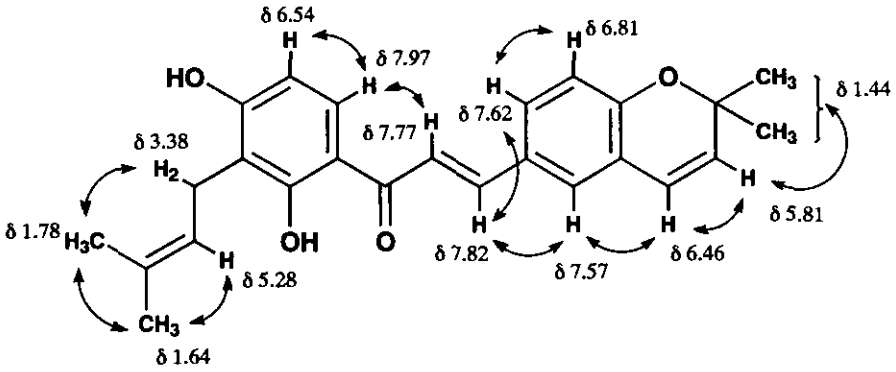

Figure 3 2D NOESY spectrum of **3**

similar to that of **6**. The ^{1}H 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 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

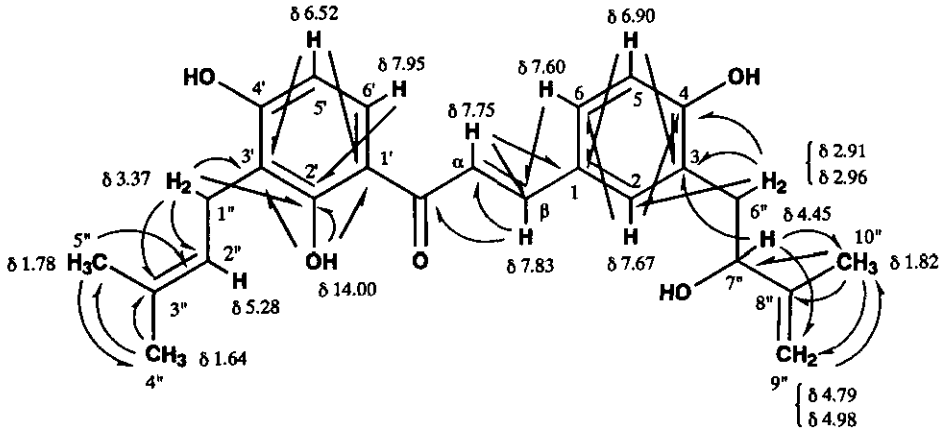

Figure 4 HMBC spectrum (J_{CCH} = 6 Hz) of **4**

^{1}H and ^{13}C nmr spectra as well as the ^{1}H-^{1}H 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, $[\alpha]_D$ 0°, $C_{25}H_{28}O_5$, 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 ^{1}H 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 venenosa* 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. venenosa* (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 ℃. $FeCl_3$ 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^+, $C_{25}H_{24}O_4$ requires 388.1675). Ir ν_{max}^{KBr} cm^{-1}: 3420, 2930, 2850, 1650, 1630, 1580, 1490, 1460, 1360. Uv λ_{max}^{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. $FeCl_3$ 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^+, $C_{25}H_{26}O_4$ requires 390.1831). Ir ν_{max}^{KBr} cm^{-1}: 3420, 1650, 1620, 1560, 1480, 1470, 1440. Uv λ_{max}^{MeOH} nm (log ε): 229 (4.43), 266 (4.40), 378 (4.54).

Pratocarpin C (**3**)

Compound (**3**) was recrystallized from *n*-hexane - $CHCl_3$ (1 : 1) to give yellow needles, mp 117 - 118 ℃. $FeCl_3$ 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^+, $C_{25}H_{26}O_4$ requires 390.1831). Ir ν_{max}^{KBr} cm^{-1}: 3430 - 3250 (br), 2980, 2920, 1650, 1630, 1560, 1490, 1470, 1440. Uv λ_{max}^{MeOH} nm (log ε): 205 (4.52), 280 (4.18), 376 (4.51).

Pratocarpin D (**4**)

Compound (**4**) was recrystallized from MeOH - H_2O (2 : 1) to give yellow plates, mp 167 - 169 ℃, $[\alpha]_D^{22}$ - 5.5° (*c* = 0.1, MeOH). $FeCl_3$ 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^+, $C_{25}H_{28}O_5$ requires 408.1937). Ir ν_{max}^{KBr} cm^{-1}: 3420, 2920, 1610, 1600, 1500, 1430, 1370. Uv λ_{max}^{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, $[\alpha]_D^{22}$ 0° (*c* = 0.1, MeOH). $FeCl_3$ 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 λ_{max}^{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.

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