SOROCENOLS A AND B, TWO NEW ISOPRENYLATED PHENOLS FROM THE ROOT BARK OF *SOROCEA BONPLANDII* BAILLON[1]

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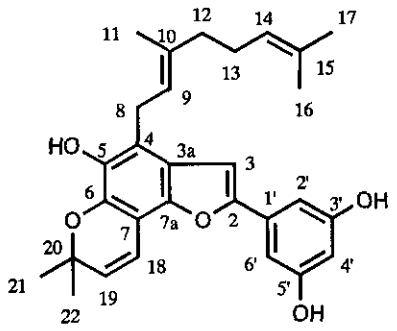
Abstract — From the root bark of *Sorocea bonplandii* Baillon (Moraceae), collected in Paraguay, two new isoprenylated phenols, sorocenols A (**1**) and B (**2**) were isolated along with four known isoprenylated phenols, kuwanon C, artonin D, sorocein B, and kuwanol E. The structures of sorocenols A and B were shown to be **1** and **2**, respectively. Sorocenol B (**2**) is regarded biogenetically as variation of Diels-Alder type adduct between chalcone derivative and dehydroisoprenylated compound.

Previously we reported the structure determination of a series of isoprenylated phenols.[2,3] Some of these compounds showed interesting biological activities such as hypotensive effect,[2] inhibitory activity against arachidonate 5-lipoxygenase,[4] inhibitory activity against testosterone 5α-reductase,[5] and anti-tumor promoting activity.[6] In the course of our studies on the constituents of the moraceous plants, we examined the constituents of *Sorocea bonplandii*, collected in Paraguay. Guarani indians in Paraguay have used the plants of Sorocea species as a folk medicine for a long time.[7] Messana *et al.* reported the structures of five Diels-Alder type adducts named soroceal, soroceins A, B, C, and H along with a prenylated flavanone, sorocein D, from *Sorocea bonplandii* collected in Brazil.[8,9] Furthermore the authors described that sorocein A showed a pharmacological action against several neurotransmitter-induced contractions in the guinea pig ileum and rat uterus *in vitro*.[8,9] This paper deals with the characterization of two new



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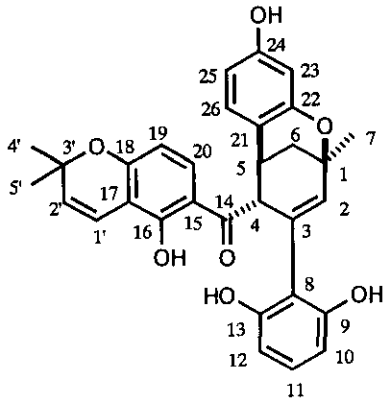

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Figure 1

Table 1 ^{13}C and ^{1}H Nmr data of **1** (δ in acetone-d_6)

	^{13}C	^{1}H		^{13}C	^{1}H
C-2	155.3	7.05 (s)	C-8	26.6	3.57 (2H, br d, J = 7)
C-3	101.8		C-9	123.7	5.37 (m)
C-3a	122.5		C-10	135.5	
C-4	119.5		C-11	16.2	1.85 (3H, br s)
C-5	140.7		C-12	40.5	1.80-2.0 (2H, m)
C-6	139.2		C-13	27.4	1.80-2.0 (2H, m)
C-7	104.9		C-14	125.0	5.06 (m)
C-7a	145.0		C-15	131.7	
C-1'	133.6		C-16	17.7	1.53 (3H, br s)
C-2'	103.8	6.87 (d, J = 2)	C-17	25.8	1.56 (3H, br s)
C-3'	159.8		C-18	116.8	6.82 (d, J = 10)
C-4'	103.4	6.36 (t, J = 2)	C-19	130.8	5.81 (d, J = 10)
C-5'	159.8		C-20	77.8	
C-6'	103.8	6.87 (d, J = 2)	C-21	27.6	1.48 (3H, s)
			C-22	27.6	1.48 (3H, s)

isoprenylated phenols, sorocenols A (**1**) and B (**2**) isolated from the root bark of *S. bonplandii* collected in Paraguai.

Sorocenol A (**1**) is a colorless powder, $C_{29}H_{32}O_5$, and gave a brown color with methanolic ferric chloride. The uv spectrum of **1** exhibited maxima at 212, 264, 300, 324, and 345 nm, and was similar to those of 2-arylbenzofuran derivatives.[2] From this result, compound (**1**) seems to be a 2-arylbenzofuran derivative. The ir spectrum disclosed absorption bands due to hydroxyl group and benzene ring moieties. The ^{1}H nmr spectrum (400 MHz) of **1** showed the signals of the following protons (δ in acetone-d_6): protons in a 2,2-

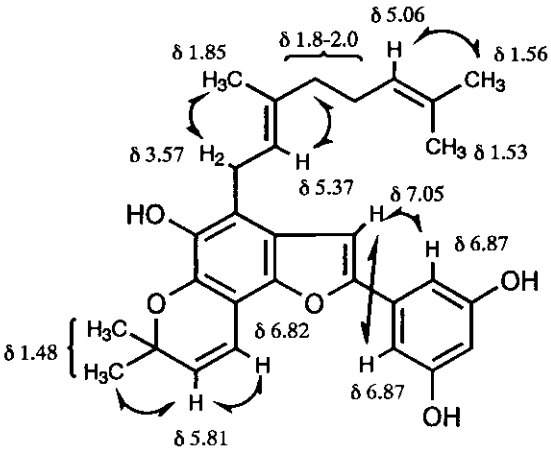


Figure 2 2D NOESY spectrum of **1**

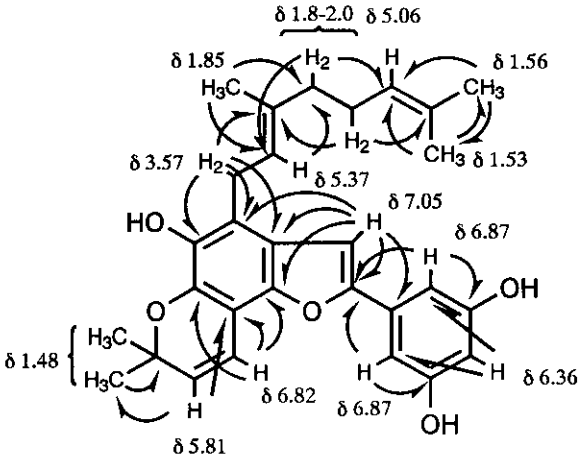


Figure 3 HMBC spectrum (J_{CCH} = 6 Hz) of **1**

dimethylpyran ring, δ 1.48 (6H, s), 5.81, 6.82 (each 1H, d, J = 10 Hz), a geranyl group, δ 1.53, 1.56, 1.85 (each 3H, br s), 1.8 - 2.0 (4H, m), 3.57 (2H, br d, J = 7 Hz), 5.06, 5.37 (each 1H, m), A2B type aromatic protons, δ 6.87 (2H, d, J = 2 Hz), 6.36 (1H, t, J = 2 Hz), an olefinic proton, δ 7.05 (1H, s) and three protons to be exchangeable with D_2O, δ 7.25 (1H, br s), 8.42 (2H, br s). The ^{13}C nmr spectrum of **1** showed the signals of the 29 carbon atoms (Table 1). From the above results, along with the aids of the 2D NOESY spectrum (Figure 2) and the 2D ^{13}C-^{1}H COSY spectrum (Table 1), it was supported that a geranyl group as well as a 2,2-dimethylpyran ring and a symmetrical 1,3,5-trisubstituted aromatic ring were present in the structure of **1**. The location of the geranyl group was revealed with the aid of HMBC spectrum. As can be seen in Figure 3, the quaternary carbon at δ 119.5 (C-4) shows long-range correlations with the olefinic proton at δ 7.05 (3-H) and the methylene protons at δ 3.57 (8-H x 2), while the olefinic proton at δ 7.05 shows long-range correlations with the quaternary carbons at δ 122.5 (C-3a), 145.0 (C-7a), 155.3 (C-2), and 133.6 (C-1'). These results support that the geranyl group locates at the C-4 and the signal at δ 7.05 would be assigned to the proton at C-3 position. The location of the 2,2-dimethylpyran ring was supported by the HMBC spectrum as follows. The quaternary carbon at δ 104.9 (C-7) shows long-range correlations with the olefinic protons at δ 5.81 (19-H) and 6.82 (18-H), while the quaternary carbon at δ 139.2 (C-6) shows a long-range correlation with the olefinic proton at δ 6.82 (18-H). Furthermore the olefinic proton at δ 6.82 (18-H) shows a long-range correlation with the quaternarty carbon at δ 145.0 (C-7a). From the above results, the structure of sorocenol A was represented by the formula (**1**).

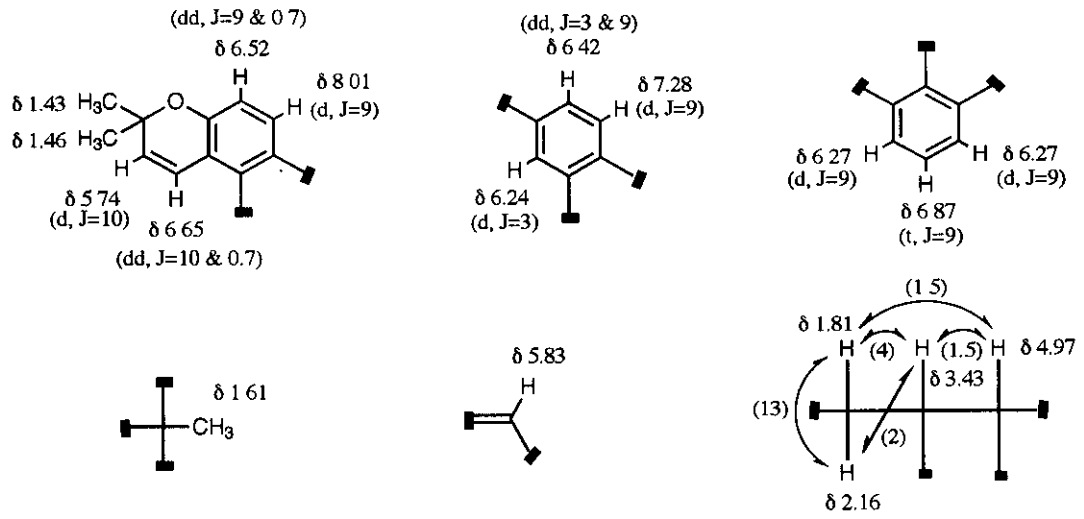


Figure 4 Partial structures of **2** on the basis of ^{1}H nmr data

Table 2 ^{13}C and ^{1}H Nmr data of **2** (δ in acetone-*d6*)

	^{13}C	^{1}H		^{13}C	^{1}H
C-1	71.5		C-15	113.2	
C-2	136.5	5.83 (br s)	C-16	161.2	
C-3	133.0		C-17	110.2	
C-4	55.4	4.97 (t-like, J = 1.5)	C-18	161.4	
C-5	36.6	3.43 (ddd, J = 1.5, 2, 4)	C-19	110.1	6.52 (dd, J = 0.7, 9)
C-6	30.3	1.81 (ddd, J = 1.5, 4, 13)	C-20	132.8	8.01 (d, J = 9)
		2.16 (dd, J = 2, 13)	C-21	123.3	
C-7	27.4	1.61 (3H, s)	C-22	155.5	
C-8	117.3		C-23	104.2	6.24 (d, J =3)
C-9	155.8		C-24	158.3	
C-10	107.9	6.27 (d, J = 9)	C-25	109.1	6.42 (dd, J = 3, 9)
C-11	129.8	6.87 (t, J = 9)	C-26	130.3	7.28 (d, J = 9)
C-12	107.9	6.27 (d, J = 9)	C-1'	115.9	6.65 (dd, J = 0.7, 10)
C-13	155.8		C-2'	129.7	5.74 (d, J = 10)
C-14	207.8		C-3'	79.0	
			C-4'	28.5	1.46 (3H, s)
			C-5'	28.6	1.43 (3H, s)

Sorocenol B (**2**), colorless powder, $C_{31}H_{28}O_7$, $[\alpha]_D$ + 137.5°, showed positive reaction to methanolic ferric chloride. The ^{13}C nmr spectrum indicated the presence of 31 carbon atoms (Table 2). The uv spectrum of **2** exhibited maxima at 216 (sh), 258 (sh), 275, and 317 nm and showed the presence of a benzoyl chromophore in the structure. The ir spectrum disclosed absorption bands due to hydroxyl,

conjugated carbonyl, and benzene ring moieties. The ^{1}H nmr spectrum of **2** showed the signals of the following protons (acetone-*d*6): protons in a 2,2-dimethylpyran ring, δ 1.43, 1.46 (each 3H, s), 5.74 (1H, d, J = 10 Hz), 6.65 (1H, dd, J = 0.7 and 10 Hz), A2B type aromatic protons, δ 6.27 (2H, d, J = 9 Hz), 6.87 (1H, t, J = 9 Hz), ABX type aromatic protons, δ 6.24 (1H, d, J = 3 Hz), 6.42 (1H, dd, J = 3 and 9 Hz), 7.28 (1H, d, J = 9Hz), *ortho*-coupled aromatic protons, δ 6.52 (1H, dd, J = 0.7 and 9 Hz), 8.01 (1H, d, J = 9 Hz), methyl protons, δ 1.61 (3H, s), a set of methylene protons, δ 1.81 (1H, ddd, J = 1.5, 4 and 13 Hz), 2.16 (1H, dd, J = 2 and 13 Hz), two methine protons, δ 3.43 (1H, ddd, J = 1.5, 2 and 4 Hz), 4.97 (1H, br s, t-like), an olefinic proton, δ 5.83 (1H, s), and four protons to be exchangeable with D_2O, δ 7.32 (2H, s), 8.17 (1H, s), 12.78 (1H, s). In the ^{1}H nmr spectrum, the long-range coupling (J = 0.7 Hz) between the olefinic proton at δ 6.65 and the aromatic proton at δ 6.52 was observed. From the above results, along with the aid of the 2D ^{1}H-^{1}H COSY spectrum, the presence of the partial structures described in the Figure 4 was supported in the structure of **2**. The correlations between the carbons and the protons were confirmed with the aid of HMQC spectrum as described in Table 2. To correlate the partial structures in Figure 4, HMBC spectrum of **2** was measured. As can be seen in Figure 5, the presence of a methylcyclohexene ring in the structure was supported. Furthermore the location of the three aromatic sub-

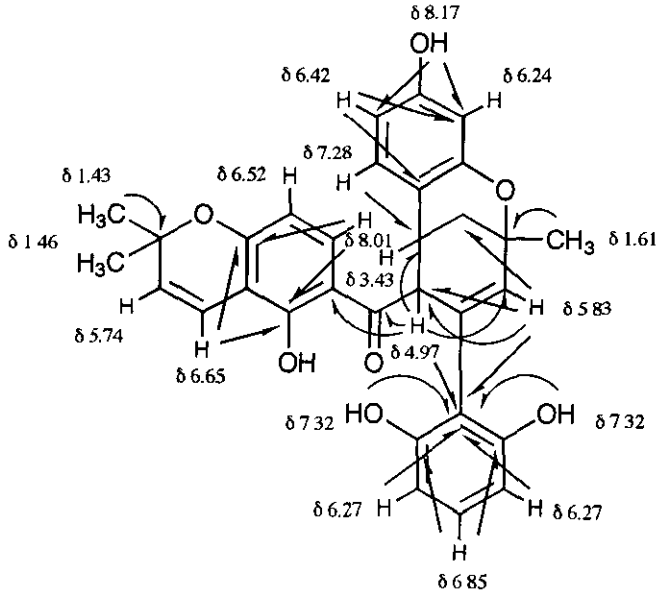
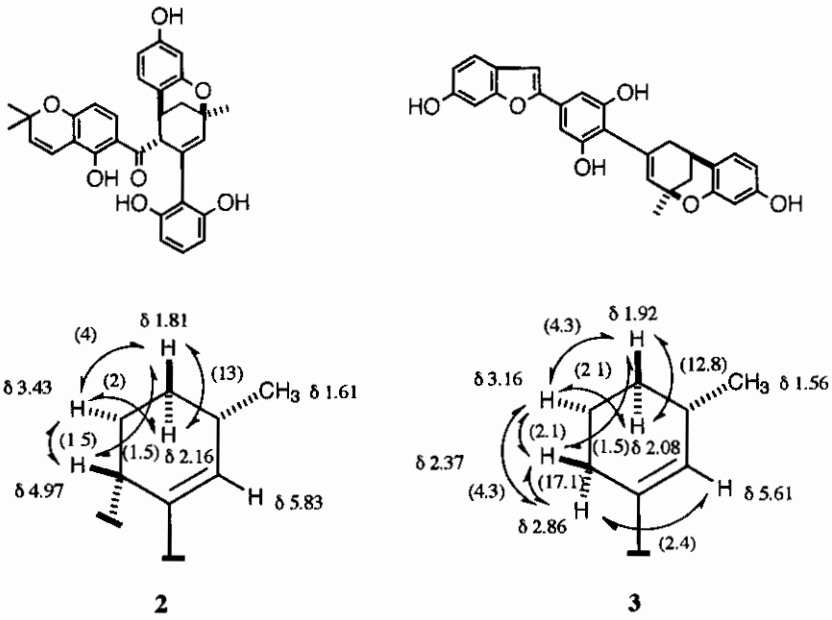


Figure 5 HMBC spectrum (J_{CCH} = 6 Hz) of **2**



2 **3**

Figure 6 Chemical shifts (ppm) and coupling constants (Hz) of methylcyclohexene rings of **2** and **3**

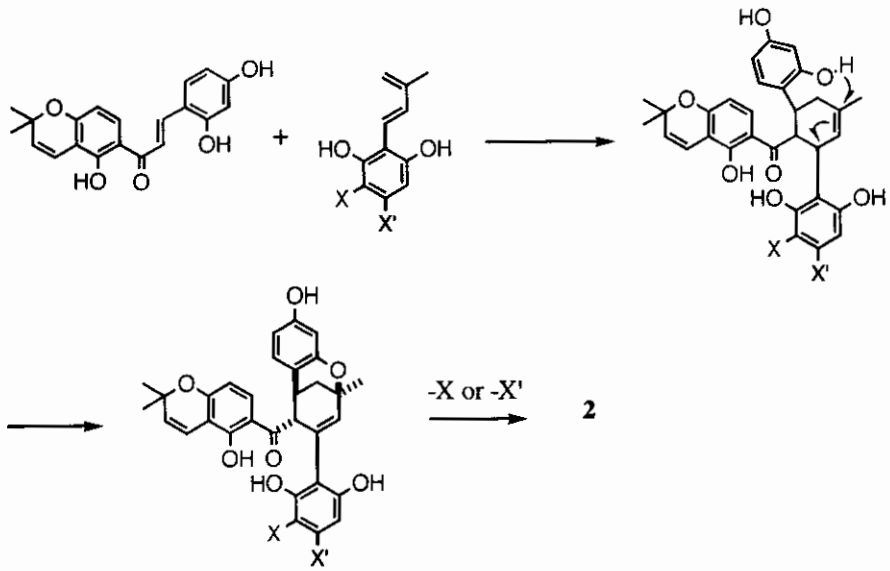


Figure 7 Hypothetical biosynthesis of **2**. X and X' are leaving groups such as COOH, CHO and so on.

stituents on the methylcyclohexene ring was supported as follows. The methine proton at δ 4.97 (4-H) shows long-range correlations with the carbonyl carbon at δ 207.8 (C-14), the methine carbon at δ 36.6 (C-5), the olefinic carbon at δ 136.5 (C-2) and with the two quaternary carbons at δ 113.2 (C-15) and 117.3 (C-8). The aromatic proton at δ 7.28 (26-H) shows long-range correlation with the methine carbon

at δ 36.6 (C-5). From the above results, the structure of sorocenol B was represented by the formula (**2**) (except the relative configurations). The relative configurations between H-4, H-5, and C-1-CH_3 were determined by the comparative examination of the ^1H nmr spectra of **2** and mulberrofuran H (**3**).[10] As described in Figure 6, the coupling constants of the proton signals of the methylcyclohexene ring of **2** were good agreement with those of the relevant signals of the methylcyclohexene ring of **3**. This results suggest that the relative configuration between C-1-CH_3 and H-5 seems to be *cis* and H-4 and H-5 to be *trans*. Furthermore the relative configuration between C-1-CH_3 and H-5 to be *cis* was supported by the examination of Dreiding model. Thus, the structure of sorocenol B is characterized as **2**.

While sorocenol B (**2**) seems to be a unique phenolic compound, biogenetically **2** may be a derivative induced from the Diels-Alder type adduct between a chalcone derivative and a dehydroisoprenylated phenolic compound through the oxidative reaction as described in Figure 7.

EXPERIMENTAL

Abbreviations: s = singlet, d =doublet, dd = double doublet, t = triplet, m = multipet, br = broad, sh = shoulder. The general procedures and instruments used in our previous papers.[3,12]

Plant material: Bark of *Sorocea bonplandii* Baillon was collected in the suburbs of Encarnacion city, Itapua prefecture, Paraguay, in March 1990, and identified by Prof. I. Basualdo, Faculty of Chemistry, Asuncion National University. The sample was deposited in the Herbarium of Toho University.

Isolation of Sorocenols A (1) and B (2)

The dried root bark of *Sorocea bonplandii* (550 g) was finely cut and extracted for three days at room temperature with *n*-hexane (2.3 l, three times), benzene (2.3 l x 3), and acetone (2.4 l x 3), successively. Evaporation of *n*-hexane, benzene, and acetone solutions to dryness yielded 9.3 g, 3.3 g, and 20.3 g of the residue, respectively.

The acetone extract (20.3 g) was chromatographed over silica gel (250 g) using *n*-hexane, *n*-hexane - ethyl acetate (9 : 1, 85 . 15, 8 : 2, 7 : 3, 3 : 2, 1 : 1), and then ethyl acetate. The fraction eluted with *n*-hexane - ethyl acetate (8 : 2) was evaporated to give the residue (0.1 g), which was fractionated by preparative tlc [benzene - ether (5 : 1), *n*-hexane - acetone (2 : 1)], and followed by preparative hplc [solvent, chloroform - ethyl acetate (6 : 1), column, Senshu Pak SSC Silica 4251-N, 10ϕ x 250 mm, detector, uv 280 nm] to give sorocenols A (**1**, 4 mg) and B (**2**, 1.6 mg).

The fraction (0.1 g) eluted with *n*-hexane - ethyl acetate (7 : 3) was fractionated by preparative tlc [*n*-hexane - ethyl acetate (3 : 1), *n*-hexane - acetone (2 : 1)], and followed by preparative hplc [*n*-hexane - ethyl acetate (3 : 2)] to give kuwanon C (3 mg).[11]

The fraction (1.2 g) eluted with *n*-hexane - ethyl acetate (3 : 2) was rechromatographed over silica gel (50 g) with benzene containing increasing amount of acetone. The fraction (230 mg) eluted with benzene - acetone (9 : 1) was fractionated by preparative tlc [*n*-hexane - acetone (1 : 1), *n*-hexane - acetone (4 : 5)] to give artonin D (8 mg).[12]

The fraction (1.3 g) eluted with *n*-hexane - ethyl acetate (1 : 1) was rechromatographed over silica gel (50 g) with benzene containing increasing amount of acetone. The fraction (86 mg) eluted with benzene - acetone (9 : 1) was fractionated by preparative tlc [benzene - acetone (2 : 1), chloroform - ethyl acetate (1 : 1)], and followed by preparative hplc [chloroform - ethyl acetate (1 : 2)] to give sorocein B (3 mg).[9]

The fraction (130 mg) eluted with benzene - acetone (8 : 2) was fractionated by preparative tlc [benzene - acetone (1 : 1), chloroform - ethyl acetate (1 : 2), *n*-hexane - acetone (2 : 3)], and followed by preparative hplc [*n*-hexane - ethyl acetate (1 : 3)] to give kuwanol E (10 mg).[13] Of the known compounds, sorocein B was identified by comparing with the spectral data of authentic sample, and the identifications of other known compounds, *kuwanon* C, *artonin* D, and kuwanol E, were performed by direct comparisons with authentic samples.

Sorocenol A (1)

Compound **1** was obtained as colorless powder. $FeCl_3$ test: positive (brown). EI-ms: *m/z* (rel. int.) 460 (M^+, 100 %), 445 (47), 377 (12), 337(33), 137(53). HR-*ms*: *m/z* 460.2265 (M^+, $C_{29}H_{32}O_5$, requires 460.2250). Ir ν_{max}^{KBr} cm^{-1}: 3270 (br), 2900, 1600, 1580 (sh), 1520, 1460 (sh), 1420, 1370, 1120. Uv λ_{max}^{MeOH} nm (log ε): 212 (4.44), 264 (sh 4.04), 300 (4.31), 324 (sh 4.12), 345 (4.11).

Sorocenol B (2)

Compound **2** was obtained as a colorless powder. $FeCl_3$ test: positive (dark blue). $[\alpha]_D^{22}$ +137.5° (*c* = 0.016, MeOH). EI-ms: *m/z* (rel. int.) 512 (M^+, 4 %), 494 (14), 479 (29), 385 (7), 309 (22), 203 (100), 187 (11), 161 (21). HR-ms: *m/z* 512.1857 (M^+, $C_{31}H_{28}O_7$ requires 512.1845). Ir ν_{max}^{KBr} cm^{-1}: 3420 (br), 3000, 1640 (sh), 1600, 1500, 1100, 1070 (sh). Uv λ_{max}^{MeOH} (log ε): 216 (sh 4.27), 258 (sh 4.09), 275 (4.16), 317 (3.87).

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