THREE NEW FLAVANONE DERIVATIVES FROM THE ROOT BARK OF SOROCEA BONPLANDII BAILLON

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Abstract - Three new flavanone derivatives named sorocein C (2), sorocein D (1) and sorocein H (3) together with the known artonin D, kuwanon C, cyclomorusin , and kuwanon J were isolated from the methanolic extract of the roots of Sorocea bonplandii. The structures were assigned on the basis of spectroscopic evidences.

Sorocea bonplandii is a tree belonging to the Moraceae family. The methanolic extract of the roots collected in Santa Catarina (Brazil) is active in antagonizing responses elicited by different neurotransmitters in smooth muscle preparations.

In a previous paper[1] we reported on the isolation from the extract of three new ketalized Diels-Alder type adducts, named soroceal and soroceins

A and B, toghether with the known betulinic acid, mulberrofuran K and morusin. Sorocein A showed a pharmacological action against several neurotrasmitter-induced contractions in the guinea pig ileum and rat uterus in vitro.[2]

Further purification of the same extract resulted on the isolation of seven minor metabolites : four of them were identified as artonin D,[3] kuwanon C, cyclomorusin, and kuwanon J,[4] the remaining three are new compounds named sorocein C, sorocein D, and sorocein H.

Sorocein D(1), $[\alpha]_D$ + 34°, showed a molecular ion at m/z 504 in the EI mass spectrum. In its ^{1}H nmr spectrum (Table 1) the signals attributable to a chromene ring, two prenyl chains, an aromatic singlet, an ortho coupled system, and a chelated hydroxyl group were present. These data and those of the ^{13}C nmr (Table 1) and uv spectra (see Experimental) suggested for the molecule the structure of a flavanone with an unusual substitution of the C ring. The absence in the ^{1}H nmr spectrum of 1 of the signals attributable to H-2 and H-3 indicated that C-2 and C-3 were fully substituted in 1. A skeleton like sanggenon A,[5] having a prenyl chain at C-3, a OH group at C-2, and a ring closure between C-3 and the 2' OH group, was in agreement with these data. Nevertheless NOE experiments carried out on sorocein D irradiating H-6' evidenced that in 1 the prenyl chain of the C ring was located at C-2. The assignment of the chromene moiety on the A ring was supported by the EI mass fragments at m/z 203 (26%, 1a), and 219 (100%, 1b). The NOE observed irradiating the singlet at δ 5.78 on the resonances attributed to H-10 and H-12 (δ 5.17 and 1.55, respectively) allowed us to discriminate between the two possible structures having C-6 or C-8 substituted. Total assignment of 1 was made by HETCOR and INEPT long-range experiments. Structure (1) was thus demonstrated for sorocein D that is an isomer of sanggenon L.[6]

Sorocein C(2), $[\alpha]_D$ + 427°, showed a pseudo-molecular ion at m/z 757 in

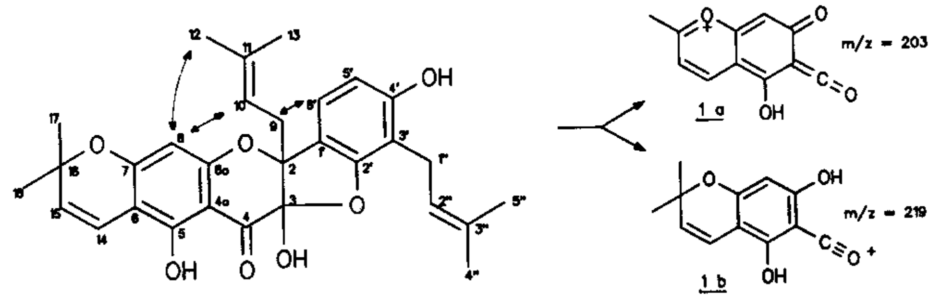
Table 1. ^{1}H and ^{13}C nmr data of compound (1).

	δ_C	δ_H		δ_C	δ_H
2	93.1	-	9	32.1	2.76 (1H, dd) (J=6.0 and 15.0 Hz) 3.07 (1H, dd) (J=8.0 and 15.0 Hz)
3	102.0	-			
4	189.2	-			
4a	100.6	-	10	118.7	5.17 (1H, m)
5	158.6	11.55[§](1H, s)	11	136.6	-
6	103.2	-	12	25.8	1.62 (3H, s)
7	164.2	-	13	18.1	1.55 (3H, s)
8	96.4	5.78 (1H, s)	14	115.5	6.59 (1H, d) (J= 10.0 Hz)
8a	162.3	-	15	127.4	5.50 (1H, d) (J= 10.0 Hz)
1'	120.9	-	16	79.4	-
2'	159.5	-	17	28.4[*]	1.44[*] (3H, s)
3'	113.1	-	18	28.5[*]	1.40[*] (3H, s)
4'	159.3	-	1"	23.2	3.34 (2H, m)
5'	109.9	6.51 (1H, d) (J= 8.1 Hz)	2"	122.5	5.27 (1H, m)
6'	123.0	7.19 (1H, d) (J= 8.1 Hz)	3"	131.8	-
			4"	25.9	1.72 (3H, s)
			5"	17.8	1.76 (3H, s)

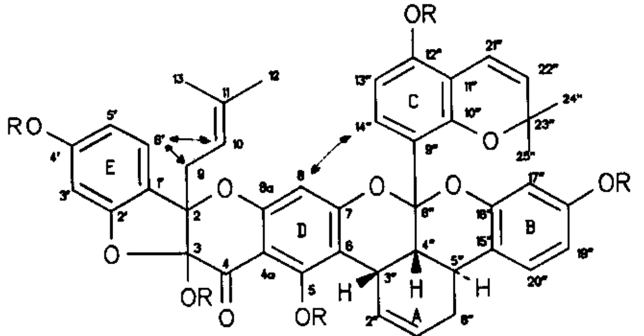
^{1}H nmr solvent: $CDCl_3$; ^{13}C nmr solvent: acetone-d_6 ; * interchangeable

§ OH: exchangeable with D_2O

the positive FAB mass spectrum. ^{1}H and ^{13}C nmr data (Table 2) suggested for 2 the structure of a ketalized Diels-Alder type adduct as sorocein A, sorocein B, and soroceal. Moreover in its ^{13}C nmr spectrum the signals attributable to a modified flavanone skeleton as that one of sorocein D (C-2 at 92.1, and C-3 at 102.3) were present. NOE and INEPT long-range experiments carried out on 2 assigned the prenyl chain of the flavanone moiety at C-2, as in 1. The other moieties of the molecule were identified as a 2,3,4-trisubstituted phenyl ring (C ring), and a 2,4-disubstituted phenyl ring (B ring) that are typical of the ketalized Diels-Alder type adducts isolated up to now. The C ring was located at C-8" on the basis of the observed long-range correlation between the doublet at δ 6.83 (H-14") and the carbon that resonated at 117.0 ppm

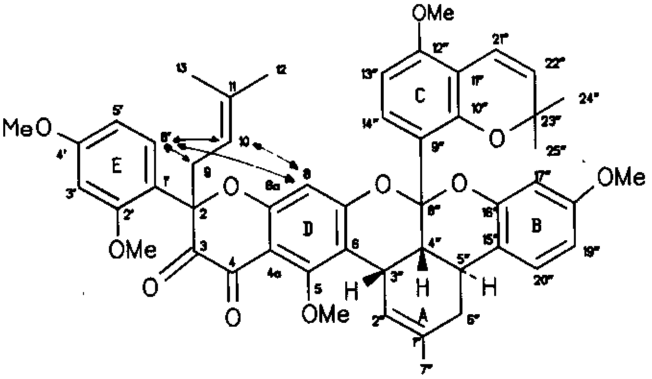


1



2 R = H

2a R = Me



2b

The arrows indicate NOEs observed for compounds (1 , 2 , and 2b).

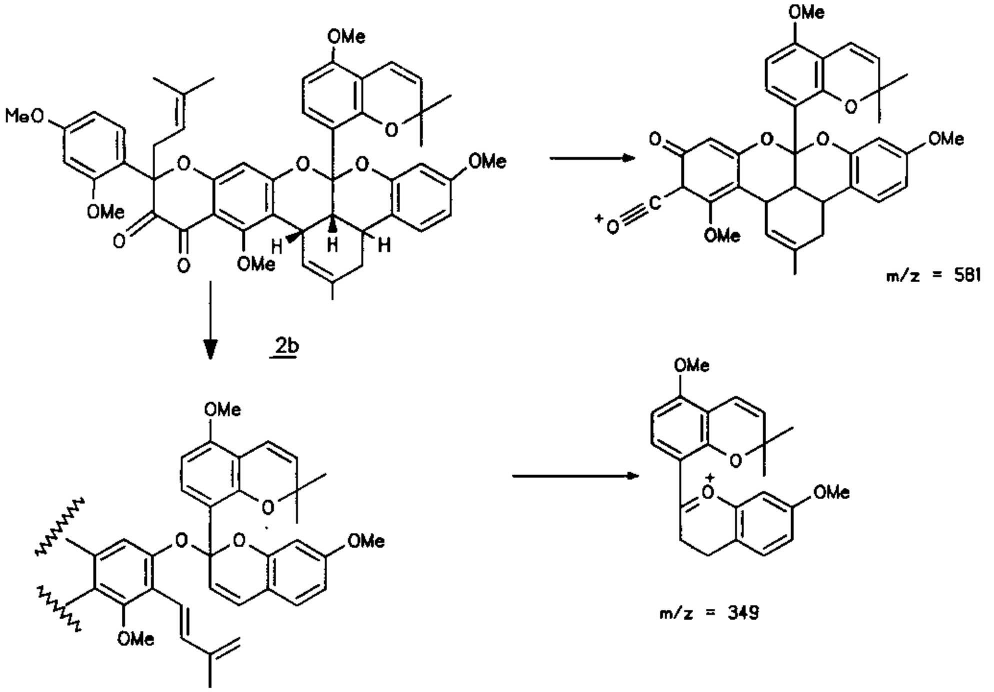
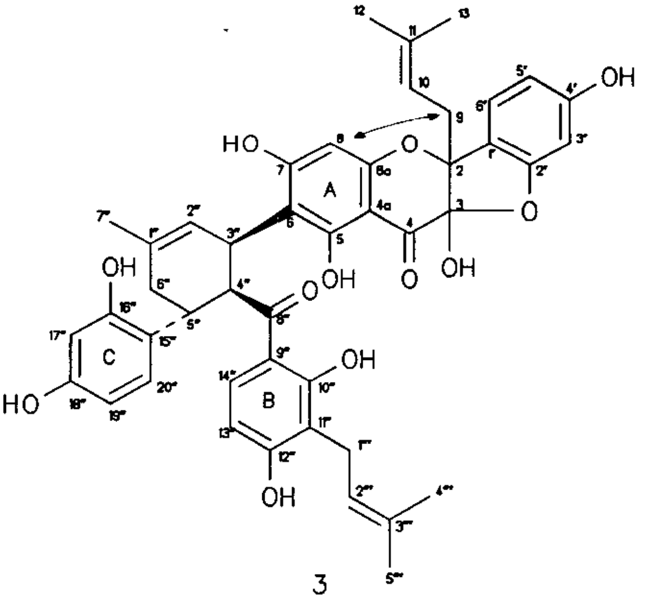


Figure 1



3

The arrows indicate NOEs observed for compound (3).

Table 2. ^{1}H and ^{13}C nmr of compounds(2, 2a, 2b).

	2 (acetone d_6)				2a ($CDCl_3$)		2b ($CDCl_3$)	
	δ_C	δ_H	J (Hz)	long-range correlations	δ_C	δ_H	δ_C	δ_H
2	92.1	-	-	H-9, H-10, H-6'	90.5	-	88.6	-
3	102.3	-	-	-	102.1	-	173.7	-
4	189.0	-	-	-	183.2	-	194.9	-
4a	101.4	-	-	H-8	111.6	-	111.6	-
5	164.2	13.33,s[§]	-	H-3"	159.4	-	157.7	-
6	106.2	-	-	H-8, H-3", H-4"	109.9	-	108.4	-
7	163.3	-	-	H-8, H-3"	161.9	-	162.7	-
8	96.1	5.96,s	-	-	97.5	6.35,s	99.8	6.37,s
8a	161.6	-	-	H-8	160.9	-	162.4	-
9	31.7	3.15,dd 2.75,dd	9.0, 15.0 ≈5, 15.0	H-10	31.2	2.66,dd 2.9-3.0,dd	35.7	3.07,br t
10	118.7	5.22,br t	≈7	H-9	118.2	5.0-5.3,br t	116.9	5.11,br t
11	136.7	-	-	H-9	135.0	-	136.8	-
12	25.7	1.46,br s	-	H-10	25.7	1.56[a],s	25.7	1.49[a],s
13	18.2	1.57,br s	-	H-10	18.0	1.65[a],s	18.0	1.53[a],s
1'	121.2	-	-	H-9, H-5'	121.4	-	121.9	-
2'	161.3	-	-	H-6'	160.0	-	161.1	-
3'	103.8	6.37,d	2.5	H-5'	101.3	≈6.6	101.1	6.44,d
4'	161.3	-	-	H-6'	162.5	-	161.7	-
5'	110.2	6.53,dd	2.5, 8.5	H-3'	108.5	6.55,dd	104.9	6.55,dd
6'	125.8	7.41,d	2.5, 8.5	-	125.4	7.37,d	126.9	7.45,d
1"	134.3	-	-	H-3", H-5", H-6"	133.3	-	133.3	-
2"	121.7	6.33,br d	≈6	H-4", H-6"	122.2	6.14,br d	122.5	6.16,br d

3"	33.4	3.23,br dd	5.5, ≈6	H-4", H-5"	33.0	3.26,br t	33.0	3.27,br t
4"	37.3	3.35,dd	5.5, 11.0	H-5", H-6"	36.4	3.21,dd	36.3	3.22,dd
5"	28.1	2.84,m	≈1, 5.0, 11.0, 12.0	H-3", H-4"	29.7	2.9-3.0,m	29.4	2.92,ddd
6"	36.5	2.74,dd 2.05,dd	5.0, 15.0 12.0, 15.0	H-4", H-5"	35.9	2.77,br d 2.05,br t	35.9	2.67,dd 2.05,dd
7"	23.8	1.78,br s	-	H-6"	23.6	1.80,br s	23.6	1.80,br s
8"	117.0	-	-	H-5", H-14"	117.6	-	117.5	-
9"	103.3	-	-	H-4"	104.4	-	n.o.	-
10"	152.4	-	-	H-14", H-21"	151.3	-	151.3	-
11"	111.2	-	-	H-21"	113.7	-	113.7	-
12"	154.9	-	-	H-14", H-21"	156.0	-	156.0	-
13"	107.8	6.29,d	8.5	-	102.6	6.18,d	102.3	6.22,d
14"	128.3	6.83,d	8.5	-	127.7	6.88,d	128.0	6.95,d
15"	118.0	-	-	H-4", H-19"	118.4	-	118.5	-
16"	152.9	-	-	H-5"	152.1	-	152.0	-
17"	99.6	6.43,d	2.5	H-19"	101.7	6.53,d	101.6	6.53,d
18"	157.9	-	-	-	159.4	-	159.3	-
19"	109.8	6.55,dd	2.5, 8.5	H-17"	108.2	≈6.6	108.5	6.61,dd
20"	127.9	7.16,dd	≈1, 8.5	-	126.8	7.15,d	127.6	7.17,d
21"	117.8	6.67,d	10.0	-	117.0	6.62,d	116.7	6.64,d
22"	129.5	5.67,d	10.0	-	129.0	5.55,d	129.1	5.57,d
23"	76.8	-	-	H-21"	76.1	-	76.1	-
24"	27.6^a	1.32^a,s	-	-	27.1^a	1.28^b,s	27.0^a	1.30^b,s
25"	27.5^a	1.31^a,s	-	-	27.6^a	1.30^b,s	27.5^a	1.33^b,s

OMe (^{13}C nmr values) of 2a : 53.0, 55.3, 55.6, 61.1 ; 2b : 55.3, 55.5, 55.6, 61.4.

OMe (^{1}H nmr values) of 2a : 3.72, 3.73, 3.75, 3.76, 3.79 ; 2b : 3.59, 3.71, 3.76, 3.78, 3.81.

^{a,b} interchangeable; §OH : exchangeable with D_2O

(C-8"), whereas the B ring was located at C-5" as a long-range coupling exhisted between H-5" and H-20". The flavanone residue was thus located at C-3".

By treatment with dimethyl sulfate in anhydrous acetone, sorocein C gave two different pentamethyl derivatives, (2a and 2b) with the same molecular ion peak at m/z 826. Compound (2b) is the methyl derivative of the ketonic form of the flavanone residue. INEPT long-range experiments carried out on 2b showed a correlation between H-10, H-6' and the carbon that resonates at 88.6 ppm (C-2, Table 2) in agreement with the position assigned to the prenyl chain. The aromatic proton of the D ring (δ 6.37, singlet) was located at C-8 in 2b on the basis of the NOE effect observed on the resonance at δ 6.37 irradiating H-6' and H-10 . NOE experiments also showed the proximity of H-6' with H-10 and one of the methylene protons of the prenyl chain. The methoxy group belonging to the C ring was located at C-12" on the basis of the ^{13}C nmr spectrum of 2b that showed the presence of only a methoxy group ortho disubstituted [7] (61.4 ppm, C-5 OMe). The same substitution of the C ring was assigned to 2a on the basis of ^{13}C nmr data. Thus the OH group of the C ring of sorocein D should be located at C-12". In Figure 1 the major fragments observed in the mass spectrum of 2b are reported.

The relative configurations, between H-3" and H-4" to be cis and between H-4" and H-5" to be trans were determined on the basis of the coupling constant values of H-3", H-4" and H-5".[4]

Sorocein H (3), $[\alpha]_D$ + 235° showed a pseudo-molecular ion at m/z 777 in the positive FAB mass spectrum. ^{1}H and ^{13}C nmr data (Table 3), as well as NOE experiments, indicated for 3 the structure of a Diels-Alder type adduct having the methylcyclohexene ring substituted by a flavanone residue identical to that of 2, a 2,4-dihydroxyphenyl moiety and a 2,4-dihydroxy-3-prenylbenzophenone moiety. The flavanone residue was assigned at C-3" on the basis of the FAB mass spectrum that showed the

Table 3. ^1H and ^{13}C nmr data of compound (3).

	δ_C	δ_H		δ_C	δ_H
2	91.7	-	4"	47.9	4.56 (1H, t) (J=5.6 Hz)
3	102.4	-	5"	32.4	3.85 (1H, m)
4	188.0	-	6"	33.3	2.23 (1H, m)
4a	99.7	-			2.41 (1H, m)
5	163.7*	12.79§(1H, s)	7"	23.5	1.88 (3H, s)
6	108.9	-	8"	208.8	-
7	167.6	-	9"	113.3	-
8	96.4	5.75 (1H, s)	10"	163.2*	12.09§(1H, s)
8a	161.6*	-	11"	115.5	-
9	31.8	2.73 (1H, dd) (J=6.0 and 14.6 Hz)	12"	164.2*	-
		3.10 (1H, dd) (J=8.6 and 14.6 Hz)	13"	107.3	6.44 (1H, d) (J=8.8 Hz)
10	118.3	5.19 (1H, br m)	14"	128.7	8.28 (1H, d) (J=8.8 Hz)
11	136.5	-	15"	121.0	-
12	25.6	1.60 (3H, s)	16"	156.3*	-
13	17.8	1.70 (3H, s)	17"	103.5	6.32 (1H, d) (J=2.2 Hz)
1'	121.9	-	18"	157.6*	-
2'	161.0*	-	19"	107.9	6.28 (1H, dd) (J=2.2 and 8.2 Hz)
3'	99.4	6.47 (1H, d) (J=2.0 Hz)	20"	131.6	6.94 (1H, d) (J=8.2 Hz)
4'	160.9*	-	1"'	21.9	3.24 (2H, d) (J=7.3 Hz)
5'	109.5	6.48 (1H, dd) (J=2.2 and 8.2 Hz)	2"'	123.0	5.14 (1H, br m)
6'	125.3	7.32 (1H, d) (J=8.2 Hz)	3"'	131.2	-
1"	134.6	-	4"'	17.6	1.51 (3H, s)
2"	122.6	5.53 (1H, br s)	5"'	25.7	1.59 (3H, s)
3"	35.7	4.08 (1H, br s)			

Solvent : acetone-d_6 ; * interchangeable ; § OH: exchangeable with D_2O

peaks due to the characteristic retro Diels-Alder fragmentation. The NOE observed on the methylene protons of the prenyl chain irradiating the aromatic singlet at δ 5.75 assigned the site of substitution of the A ring at C-6.

The ^{1}H nmr chemical shifts and coupling constants of the protons of the methylcyclohexene ring compared with those of other Diels-Alder type adducts [4] allowed us to locate the benzophenone and the phenyl moieties at C-4" and C-5" , respectively, and also to assign the relative configurations of H-3", H-4" and H-5".

EXPERIMENTAL

^{1}H and ^{13}C nmr spectra were registred at 400 and 100 MHz, respectively, on a Varian XL 400.

Plant material, extraction and purification

See reference 1.

Sorocein D (1). $C_{30}H_{32}O_7$. Amorphous powder (15 mg). EIms, m/z (%): 504 (M^+, 8), 436 (16), 421 (12), 407 (4), 393 (4), 379 (8), 365 (11), 351 (8), 285 (4), 230 (8), 219 (100), 203 (26). $[\alpha]_D$ + 34° (c 0.1, $CHCl_3$). Uv (MeOH), λ_{max} nm (logε): 230sh (4.20), 277 (4.31), 318 (3.94), 380 (3.00). ^{1}H and ^{13}C nmr data: see Table 1.

Sorocein C (2). $C_{45}H_{40}O_{11}$. Amorphous powder (130 mg). FABms, m/z : 757 (M + H)$^+$. $[\alpha]_D$ + 427° (c 0.1, MeOH). Uv (MeOH), λ_{max} nm (log ε): 308 (4.24), 286 (4.23), 226 (4.67). ^{1}H and ^{13}C nmr data: see Table 2.

Methylation of 2. Sorocein C (57 mg), dimethyl sulphate (0.4 ml), and K_2CO_3 (5 g) were refluxed in anhydrous acetone (40 ml) for 2 h. The reaction product, worked up as usual, was purified on SiO_2 using hexane/ethyl acetate (2 : 1) to give 2a (11 mg) and 2b (7 mg). Compound 2a, $C_{50}H_{50}O_{11}$, was obtained as an amorphous powder. EIms, m/z (%): 826 (M^+, 56), 757 (26), 581 (100), 349 (28). ^{1}H and ^{13}C nmr data: see Table 2.

Compound 2b. $C_{50}H_{50}O_{11}$. Amorphous powder. EIms, m/z (%): 826 (M^+, 65), 758 (65, $[M-C_5H_8]^+$), 581 (45), 349 (100) . ^1H and ^{13}C nmr data: see Table 2.

Sorocein H (3). $C_{45}H_{44}O_{12}$. Amorphous powder (30 mg). FABms, m/z : 777 ($M + H$)$^+$, 709, 436, 341. Uv (MeOH), λ_{max} nm(logε): 298(4.32), 288(4.36), 218 (4.69). ^1H and ^{13}C nmr data: see Table 3.

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