Brosimacutins A−I, Nine New Flavonoids from *Brosimum acutifolium*

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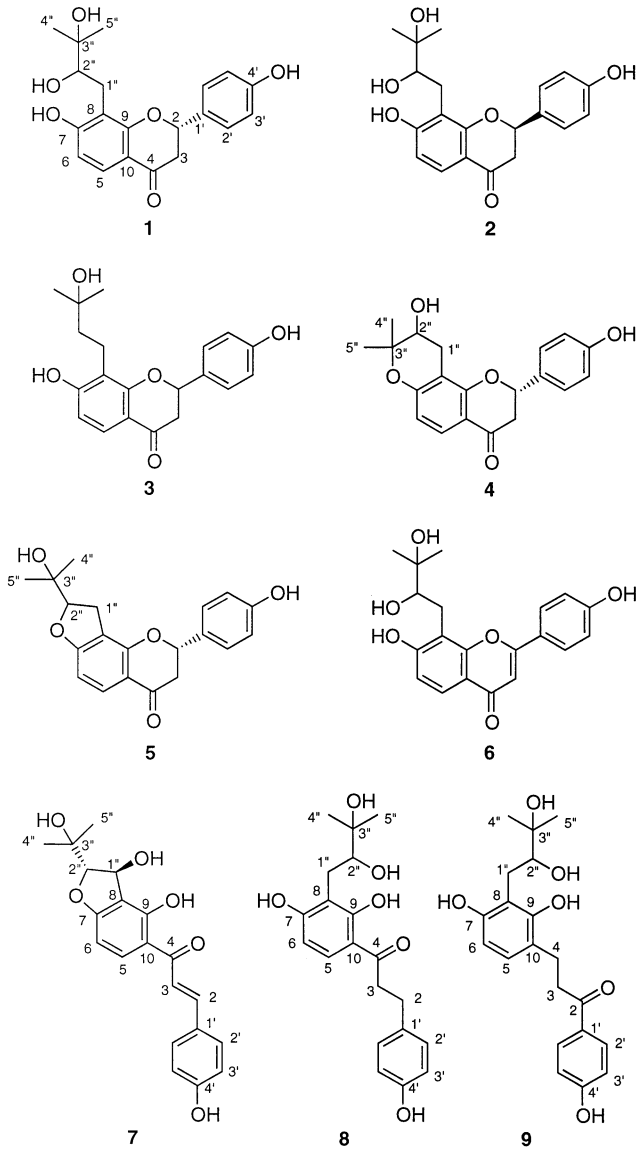
Nine new flavonoids, brosimacutins A−I (**1**−**9**), and four known flavonoids were isolated from the bark of *Brosimum acutifolium*, a Brazilian folk medicine ("Mururé"). Their structures were elucidated by spectroscopic methods, including 2D NMR. Brosimacutins A−I possess differentially functionalized isoprene units at C-8.

Brosimum acutifolium Huber (Moraceae) is a large tree of the Amazonian forests. The bark of this plant is used in Brazilian folk medicine as an anti-inflammatory and anti-rheumatic agent and is commonly known as "Mururé".[1] As part of our program to study the active constituents of Brazilian medicinal plants,[2] we have investigated the bark of *B. acutifolium*. In previous papers, we have reported the isolation and structural elucidation of a new rearranged flavan and five new flavans, acutifolins A−F,[3] as well as three new lignans, mururins A−C,[4] from this plant. Further investigation of extracts of the bark of this plant has led to the isolation of nine new flavonoids, brosimacutins A−I (**1**−**9**). In this paper we describe the isolation and structural elucidation of **1**−**9**.



Results and Discussion

The MeOH extract of the bark of *B. acutifolium* was partitioned with EtOAc and H_2O. The EtOAc-soluble portion was chromatographed over an ODS column and further purified using reversed-phase HPLC to afford brosimacutins A−I (**1**−**9**), together with four known flavonoids, 4′,7-dihydroxyflavone,[5] luteolin,[6] (−)-liquiritigenin,[7] and (−)-naringenin.[8]

Brosimacutin A (**1**) was obtained as a colorless amorphous solid with the molecular formula $C_{20}H_{22}O_6$ deduced from HRSIMS [*m*/*z* 359.1478 $(M + H)^+$, Δ −1.5 mmu]. The IR spectrum indicated the presence of the carbonyl group of a γ-pyrone (1653 cm^{-1}) and hydroxyl groups (3200−3600 cm^{-1}). The ^1H and ^{13}C NMR spectra of **1** (Tables 1 and 2) indicated the presence of one ketone carbonyl, six sp^2 quaternary carbons (three of these were bearing oxygen atoms), six sp^2 methines, one sp^3 quaternary carbon (bearing an oxygen atom), two sp^3 methines (bearing oxygen atoms), two sp^3 methylenes, and two methyl carbons. Because seven of 10 unsaturations were thus accounted for, it was concluded that **1** contains three rings. The $^1H-^1H$ COSY, HMBC, and NOESY correlations observed for **1** are shown in Figure 1. The $^1H-^1H$ COSY correlations between H-2 (δ 5.41) and H-3 (δ 2.74 and 3.01) and between H-5 (δ 7.66) and H-6 (δ 6.56) and the HMBC correlations of H-2 to C-4 (δ 194.1), H-3 to C-4 and C-10 (δ 115.3), H-5 to C-4, C-7 (δ 165.0), and C-9 (δ 163.2), and H-6 to C-7, C-8 (δ 115.7), and C-10 revealed the presence of a 2,8-disubstituted 7-hydroxychroman-4-one ring. In turn, the $^1H-^1H$ COSY correlation between H-2′ (δ 7.35) and H-3′ (δ 6.81) and the HMBC correlations of H-2′ to C-2′ (δ 128.9) and C-4′ (δ 158.9) and H-3′ to C-1′ (δ 131.5) and C-3′ (δ 116.3) indicated the occurrence of a 4-hydroxyphenyl group. The HMBC correlations of H-2 to C-1′ and C-2′, H-3 to C-1′, and H-2′ to C-2 (δ 80.8) and the NOESY correla-

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Table 1. ^{1}H NMR Spectral Data of Brosimacutins A−I (δ values, in CD_3OD; J in Hz, in parentheses)

position[a]	1	2	3	4	5	6	7	8	9
2	5.41 dd (13.0, 2.9)	5.39 dd (13.1, 2.8)	5.39 dd (13.0, 2.7)	5.42 dd (13.3, 3.3)	5.43 dd (12.9, 2.9)		7.82 d (15.4)	2.90 t, 2H (7.6)	
3	2.74 dd (16.8, 2.9) 3.01 dd (16.8, 13.0)	2.73 dd (17.0, 2.8) 3.04 dd (17.0, 13.1)	2.75 dd (17.2, 2.7) 3.01 dd (17.2, 13.0)	2.74 dd (16.7, 3.3) 3.06 dd (16.7, 13.3)	2.72 dd (16.7, 2.9) 3.09 dd (16.7, 12.9)	6.69 s	7.64 d (15.4)	3.18 t, 2H (7.6)	3.17 t, 2H (7.5)
4									2.86 t, 2H (7.5)
5	7.66 d (8.7)	7.65 d (8.7)	7.60 d (8.7)	7.62 d (8.7)	7.72 d (8.4)	7.88 d (9.1)	8.11 d (8.9)	7.62 d (9.0)	6.74 d (8.2)
6	6.56 d (8.7)	6.55 d (8.7)	6.51 d (8.7)	6.46 d (8.7)	6.51 d (8.4)	6.96 d (9.1)	6.50 d (8.9)	6.39 d (9.0)	6.29 d (8.2)
2′	7.35 d, 2H (8.6)	7.36 d, 2H (8.6)	7.36 d, 2H (8.4)	7.35 d, 2H (8.5)	7.34 d, 2H (8.4)	7.98 d, 2H (8.6)	7.63 d, 2H (8.6)	7.05 d, 2H (8.5)	7.90 d, 2H (8.8)
3′	6.81 d, 2H (8.6)	6.81 d, 2H (8.6)	6.82 d, 2H (8.4)	6.82 d, 2H (8.5)	6.82 d, 2H (8.4)	6.93 d, 2H (8.6)	6.84 d, 2H (8.6)	6.81 d, 2H (8.5)	6.81 d, 2H (8.8)
1″	2.70 dd (13.8, 10.0) 3.01 dd (13.8, 2.2)	2.71 dd (13.8, 9.8) 2.98 dd (13.8, 2.7)	2.68 m, 2H	2.63 dd (15.0, 6.0) 2.89 dd (15.0, 4.5)	3.10 d, 2H (9.0)	2.63 dd (15.0, 6.0) 2.89 dd (15.0, 4.5)	5.47 d (3.6)	2.68 dd (13.9, 10.1) 3.05 dd (13.9, 2.4)	2.56 dd (14.0, 9.9) 3.28 dd (14.0, 1.6)
2″	3.60 dd (10.0, 2.2)	3.58 dd (9.8, 2.7)	1.65 m, 2H	3.78 dd (6.0, 4.5)	4.74 t (9.0)	3.78 dd (6.0, 4.5)	4.37 d (3.6)	3.58 dd (10.1, 2.4)	3.53 dd (9.9, 1.6)
4″	1.18 s, 3H	1.16 s, 3H	1.18 s, 6H	1.31 s, 3H	1.20 s, 3H	1.31 s, 3H	1.24 s, 3H	1.24 s, 6H	1.24 s, 6H
5″	1.17 s, 3H	1.14 s, 3H		1.32 s, 3H	1.27 s, 3H	1.32 s, 3H	1.26 s, 3H		

[a] For comparison of the NMR data, the same flavone ring numbering was applied to all the compounds including the chalcones.

Table 2. ^{13}C NMR Spectral Data of Brosimacutins A−I (δ values, in CD_3OD)

position[a]	1	2	3	4	5	6	7	8	9
2	80.8	80.9	80.7	81.1	81.0	166.0	146.1	31.1	202.1
3	44.8	44.7	44.9	44.7	44.9	104.7	118.4	40.9	40.3
4	194.1	194.1	194.2	193.8	193.4	180.9	194.0	205.9	27.1
5	127.4	127.3	126.7	126.8	129.8	125.1	135.3	131.3	128.9
6	111.5	111.5	110.9	112.6	105.3	116.0	103.3	108.9	108.1
7	165.0	164.9	164.0	161.4	168.9	162.6	168.9	164.3[b]	155.7
8	115.7	115.6	118.0	109.3	115.2	115.9	116.9	114.9	115.8
9	163.2	163.3	163.1	163.0	160.5	163.5	164.0	164.5[b]	155.7
10	115.3	115.3	115.1	115.0	116.2	117.4	116.0	113.9	121.2
1′	131.5	131.4	131.7	131.4	131.2	124.0	127.8	133.2	129.9
2′	128.9	128.9	128.8	128.9	129.1	129.7	131.9	130.4	132.0
3′	116.3	116.3	116.3	116.4	116.4	117.0	117.0	116.2	116.2
4′	158.9	158.9	158.8	159.0	159.1	157.7	161.7	156.7	163.9
1″	26.7	26.7	19.2	26.7	28.2	26.8	71.3	26.0	27.1
2″	80.0	79.9	43.6	69.3	92.7	79.6	100.3	79.9	81.4
3″	74.0	74.0	71.7	79.3	72.4	73.9	71.9	74.0	74.0
4″	24.9	24.9	28.8	21.9	25.3	25.0	25.2	25.2	25.3
5″	25.9	25.9	28.9	25.5	25.3	25.9	25.3	25.6	25.4

[a] For comparison of the NMR data, the same flavone ring numbering was applied to all the compounds including the chalcones. [b] Assignments may be interchanged.

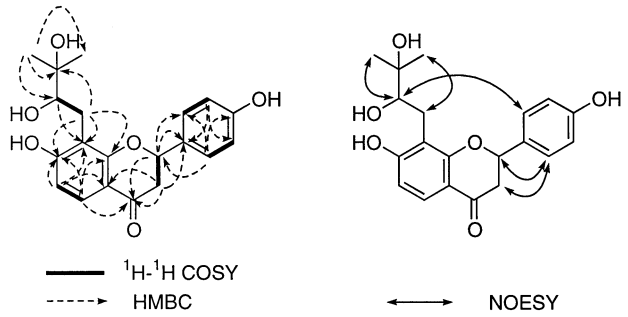

Figure 1. Selected 2D NMR correlations of **1**.

tions between H-2 and H-2′ and between H-3 and H-2′ indicated that the 4-hydroxyphenyl group is attached to C-2 of the chroman-4-one ring. The ^{1}H−^{1}H COSY correlation between H-1″ (δ 2.70 and 3.01) and H-2″ (δ 3.60) and the HMBC correlations of H-4″ (δ 1.18) to C-2″ (δ 80.0), C-3″ (δ 74.0), and C-5″ (δ 25.9), H-5″ (δ 1.17) to C-2″, C-3″, and C-4″ (δ 24.9), and H-1″ to C-3″ revealed the presence of a 2,3-dihydroxy-3-methylbutyl group. The HMBC correlations of H-1″ to C-7, C-8, and C-9 and H-2″ to C-8 indicated that the 2,3-dihydroxy-3-methylbutyl group is attached to C-8 of the chroman-4-one ring. These data suggested that **1** is a flavanone substituted with a 2,3-dihydroxy-3-methylbutyl group at C-8 and with two hydroxy groups at C-7 and C-4′. The absolute configuration at C-2 was confirmed by a positive Cotton effect at 330 nm and a negative Cotton effect at 280−290 nm in the CD spectrum, which is characteristic for the 2*S* configuration of flavanones.[9] Thus, the structure of brosimacutin A (**1**) was determined to be (2*S*)-4′,7-dihydroxy-8-(2,3-dihydroxy-3-methylbutyl)flavanone.

The molecular formula of brosimacutin B (**2**), $C_{20}H_{22}O_6$, was determined by positive-ion HRSIMS [*m*/*z* 359.1465 (M + H)$^+$, Δ −2.8 mmu] and was the same as that of brosimacutin A (**1**). The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) and ^{1}H−^{1}H COSY, HMBC, and NOESY correlations of **2** were also very similar to those of brosimacutin A (**1**) (Tables 1 and 2). However, the CD spectrum of brosimacutin B (**2**) showed a negative Cotton effect at 330 nm and a positive Cotton effect at 280−290 nm, suggesting the configuration at C-2 to be *R*.[9] These results indicated that brosimacutin B (**2**) is (2*R*)-4′,7-dihydroxy-8-(2,3-dihydroxy-3-methylbutyl)flavanone, a diastereomer of brosimacutin A (**1**) at C-2.

From the results of HRSIMS [*m*/*z* 343.1552 (M + H)$^+$, Δ +0.8 mmu], the molecular formula of brosimacutin C (**3**) was deduced as $C_{20}H_{22}O_5$. The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) of **3** were similar to those of brosimacutins A (**1**) and B (**2**) except for the absence of a hydroxyl at C-2″. The ^{1}H−^{1}H COSY correlation between H-1″ (δ 2.68, 2H) and H-2″ (δ 1.65, 2H) and the HMBC correlations of H-4″ or H-5″ (δ 1.18, 6H) to C-2″ (δ 43.6), C-3″ (δ 71.7), C-4″ (δ 28.8), and C-5″ (δ 28.9), H-2″ to C-3″, C-4″, and C-5″, and H-1″ to C-3″, C-7 (δ 164.0), C-8 (δ 118.0), and C-9 (δ 163.1) revealed the presence of a 3-hydroxy-3-methylbutyl group at C-8. Thus, the structure of brosimacutin C (**3**) was determined to be 4′,7-dihydroxy-8-(3-hydroxy-3-methylbutyl)flavanone. Brosimacutin C (**3**) did not show substantial

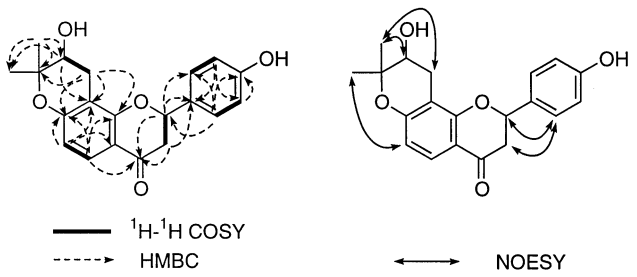

Figure 2. Selected 2D NMR correlations of **4**.

optical activity or Cotton effects. It could be suggested that brosimactin C (**3**) is racemic or a mixture of (2*S*)- and (*2R*)-flavanones.

The molecular formula of brosimacutin D (**4**) was determined as $C_{20}H_{20}O_5$ on the basis of the quasi-molecular ion peak of HRSIMS at *m*/*z* 341.1358 $[M + H]^+$. The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) were also similar to those of brosimacutins A (**1**) and B (**2**) except for the absence of a 2,3-dihydroxy-3-methylbutyl group and the presence of another isoprene unit instead. These NMR data indicated that the molecule possesses a 7,8,4′-trisubstituted flavanone ring, one oxygenated sp^3 quarternary carbon, one oxygenated sp^3 methine, one sp^3 methylene, and two methyl groups. Since its flavanone ring accounted for 10 of 11 unsaturations, it was concluded that **4** contains one more ring in the molecule than in **1** and **2**. The ^{1}H−^{1}H COSY, HMBC, and NOESY correlations observed for **4** are shown in Figure 2. The ^{1}H−^{1}H COSY correlations between H-1″ (*δ* 2.63 and 2.89) and H-2″ (*δ* 3.78) and the HMBC correlations of H-4″ or H-5″ (*δ* 1.31, 3H or 1.32, 3H) to C-2″ (*δ* 69.3), C-3″ (*δ* 79.3), C-4″ (*δ* 21.9), and C-5″ (*δ* 25.5), H-2″ to C-4″, C-5″, and C-8 (*δ* 109.3), and H-1″ to C-3″, C-7 (*δ* 161.4), C-8, and C-9 (*δ* 163.0) revealed the presence of a 2,3-dioxygenated-3-methylbutyl group at C-8. Except for the absence of a 4-methylene carbon and the presence of a 4-carbonyl carbon instead, the NMR data of **4** were similar to those of 4′-hydroxy-7,8-(3″-hydroxy-2″,2″-dimethylpyran)flavan, previously isolated from the title plant.[10] Therefore, it was concluded that **4** possesses a 2,2-dimethyl-3-hydroxy-2,3-dihydro-4*H*-pyran ring. The absence of a NOESY correlation between H-2″ and H-2′, as observed in compound **1**, and the presence of the correlation between H-4″ or H-5″ and H-6 also suggested the presence of a 2,2-dimethyl-3-hydroxy-2,3-dihydro-4*H*-pyran ring fused to C-7 and C-8 of the flavanone ring. The configuration at C-2 was estimated as *S* from the CD spectrum, which showed a positive Cotton effect at 330 nm and a negative Cotton effect at 280−290 nm. Thus, the structure of brosimacutin D (**4**) was elucidated as (2*S*)-4′-hydroxy-7,8-(2,2-dimethyl-3-hydroxy-2,3-dihydro-4*H*-pyrano)flavanone.

The molecular formula of brosimacutin E (**5**), $C_{20}H_{20}O_5$, determined by HRSIMS [*m*/*z* 341.1393 $(M + H)^+$, Δ +0.5 mmu], was the same as that of brosimacutin D (**4**). The ^{1}H and ^{13}C NMR spectra of **5** were also similar to those of brosimacutin D (**4**) (Tables 1 and 2). These data indicated that brosimacutin E (**5**) is an isomer of brosimacutin D (**4**). Since its NMR data were similar to those of 4′-hydroxy-7,8-[2-(2-hydroxyisopropyl)dihydrofuran]flavan, previously isolated from the title species,[11] except for the absence of a 4-methylene carbon and the presence of a 4-carbonyl carbon, it was concluded that **5** possesses a 2-(1-hydroxy-1-methylethyl)-2,3-dihydrofuran ring. The absolute configuration at C-2 was deduced to be *S* from the result of CD measurement. Thus, the structure of brosimacutin E (**5**) was elucidated as (2*S*)-4′-hydroxy-7,8-[2-(1-hydroxy-1-methylethyl)-2,3-dihydrofurano]flavanone.

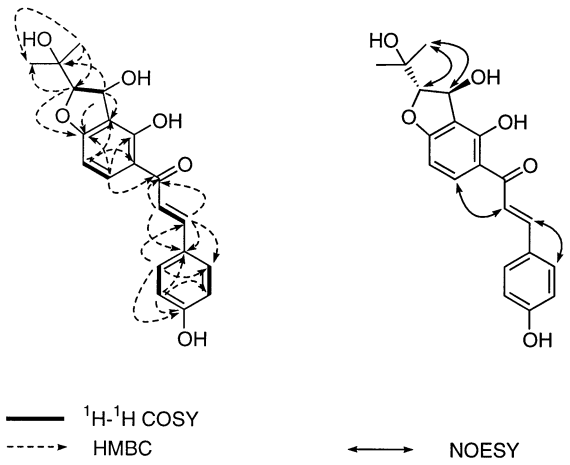

Figure 3. Selected 2D NMR correlations of **7**.

The molecular formula of brosimacutin F (**6**) was determined as $C_{20}H_{20}O_6$ by positive-ion HRSIMS [*m*/*z* 357.1352 $(M + H)^+$, Δ +1.5 mmu]. The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) were also similar to those of brosimacutins A (**1**) and B (**2**) except for the absence of 2-methine and 3-methylene carbons and the presence of a sp^2 quaternary and a sp^2 methine carbon. It can be suggested that **6** is a flavone substituted with a 2,3-dihydroxy-3-methylbutyl group at C-8 and with two hydroxy groups at C-7 and C-4′. Thus, the structure of brosimacutin F (**6**) was determined to be 4′,7-dihydroxy-8-(2,3-dihydroxy-3-methylbutyl)flavone.

The HRDCIMS of brosimacutin G (**7**) gave a molecular ion peak at *m*/*z* 356.1259, which corresponds to the molecular formula $C_{20}H_{20}O_6$ (Δ −0.1 mmu). Its ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) indicated the presence of one ketone carbonyl, six sp^2 quaternary carbons (three of these were bearing oxygen atoms), eight sp^2 methines, one sp^3 quaternary carbon (bearing an oxygen atom), two sp^3 methines (bearing oxygen atoms), and two methyl carbons. Because eight of 11 unsaturations were thus accounted for, it was concluded that **7** contains three rings. The ^{1}H−^{1}H COSY, HMBC, and NOESY correlations obtained for **7** are shown in Figure 3. The ^{1}H−^{1}H COSY correlations between H-5 (*δ* 8.11) and H-6 (*δ* 6.50) and between H-1″ (*δ* 5.47) and H-2″ (*δ* 4.37) and the HMBC correlations of H-5 to C-7 (*δ* 168.9) and C-9 (*δ* 164.0), H-6 to C-8 (*δ* 116.9) and C-10 (*δ* 116.0), H-1″ to C-7 and C-8, and H-2″ to C-7 revealed the presence of a 2,5-disubstituted 3,4-dihydroxy-2,3-dihydrobenzofuran ring. The ^{1}H−^{1}H COSY correlation between H-2′ (*δ* 7.63) and H-3′ (*δ* 6.84) and the HMBC correlations of H-2′ to C-2′ (*δ* 131.9), C-4′ (*δ* 161.7), and C-2 (*δ* 146.1) and H-3′ to C-1′ (*δ* 127.8), C-3′ (*δ* 117.0), and C-4′ revealed the presence of a 4-hydroxyphenyl group. The ^{1}H−^{1}H COSY correlation between H-2 (*δ* 7.82) and H-3 (*δ* 7.64) and the HMBC correlations of H-2 to C-4 (*δ* 194.0), C-1′, and C-2′ and H-3 to C-4 and C-1′ indicated that the 4-hydroxyphenyl group was attached to C-3 of a 2-propen-1-one unit. The large coupling constant (*J* = 15.4 Hz) between H-2 and H-3 indicated the *trans* geometry of a double bond of this 2-propen-1-one moiety. The HMBC correlation of H-5 to C-4 and the NOESY correlation between H-3 and H-5 indicated that a *p*-coumaroyl group was attached to C-5 of the 2,3-dihydrobenzofuran ring. The HMBC correlations of H-4″ (*δ* 1.24) to C-3″ (*δ* 71.9) and C-5″ (*δ* 25.3) and H-5″ (*δ* 1.26) to C-3″ and C-4″ (*δ* 25.2) suggested that a 1-hydroxy-1-methylethyl group was present. The HMBC correlations of H-1″ to C-3″ and H-2″ to C-4″ and C-5″ indicated that the 1-hydroxy-1-methyethyl

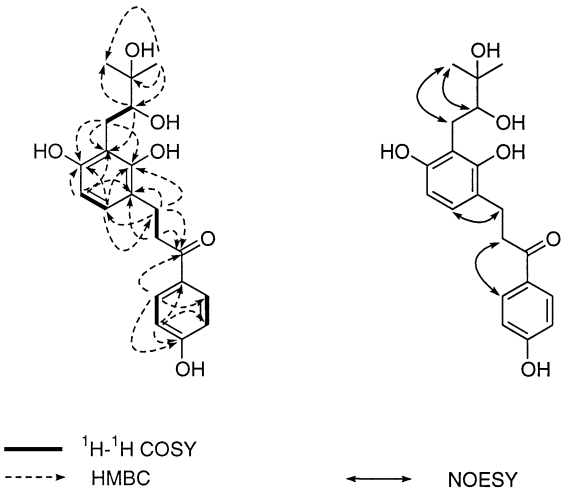

Figure 4. Selected 2D NMR correlations of **9**.

group was attached to C-2 of the 2,3-dihydrobenzofuran ring. These results suggested that **7** is a 2′,4-dihydroxychalcone with a 2-(1-hydroxy-1-methylethyl)-3-hydroxy-2,3-dihydrobenzofuran ring at C-3′ and C-4′. The relative stereochemistry of the substituents on the dihydrofuran ring was elucidated on the basis of the ^{1}H NMR and NOESY experiments of **7**. The small coupling constants (J = 3.6 Hz) of H-1″ (δ 5.47) and H-2″ (δ 4.37) and the absence of NOE enhancement between these two methine proton signals indicated a *trans*-relationship of a hydroxyl group and a 1-hydroxy-1-methylethyl group substituted on the dihydrofuran ring.[12] On the basis of these results, the relative structure of brosimacutin G (**7**) was elucidated as 1-[2,3-*trans*-3,4-dihydroxy-2-(1-hydroxy-1-methylethyl)-2,3-dihydrobenzofuran-5-yl]-3-(4-hydroxyphenyl)-*E*-propenone, leaving the absolute stereochemistry undetermined.

The molecular formula, $C_{20}H_{24}O_6$, of brosimacutin H (**8**) was determined by positive-ion HRSIMS [*m*/*z* 361.1636 (M + H)$^+$, Δ −1.4 mmu]. The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) were also similar to those of brosimacutins A (**1**) and B (**2**) except for the absence of a 2-methine carbon and the presence of a methylene carbon instead. It could be suggested that **8** is a dihydrochalcone substituted with a 2,3-dihydroxy-3-methylbutyl group at C-3′ and with three hydroxyl groups at C-2′, C-4, and C-4′. Thus, the structure of brosimacutin H (**8**) was determined to be 2′,4,4′-trihydroxy-3′-(2,3-dihydroxy-3-methylbutyl)dihydrochalcone.

The molecular formula of brosimacutin I (**9**), $C_{20}H_{24}O_6$, established by HRSIMS [*m*/*z* 361.1665 (M + H)$^+$, Δ +1.5 mmu] was the same as that of brosimacutin H (**8**). The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) were also similar to those of brosimacutin H (**8**) except for an upfield shift of H-5 (δ 6.74) and a downfield shift of H-2′ (δ 7.90, 2H). These data indicated that brosimacutin I (**9**) is an isomer of brosimacutin H (**8**). The ^{1}H−^{1}H COSY, HMBC, and NOESY correlations observed for **9** are shown in Figure 4. The HMBC correlations of H-4 (δ 2.86, 2H) to C-5 (δ 128.9), C-9 (δ 155.7), C-10 (δ 121.2), and C-2 (δ 202.1) and H-2′ to C-2 and the NOESY correlations between H-4 and H-5 and between H-3 (δ 3.17, 2H) and H-2′ revealed that **9** is a 2-keto-4-methylene isomer of **8**. Thus, the structure of brosimacutin I (**9**) was determined to be 2,4,4′-trihydroxy-3-(2,3-dihydroxy-3-methylbutyl)dihydrochalcone.

The results of the present and earlier investigations on this plant[3,10,11] indicate that the bark of *Brosimum acutifolium* is a rich source of 8-prenylated flavonoids with various modifications of their prenyl substituent groups. Acutifolins D and E[3] and brosimacutins A (**1**), H (**2**), L (**6**), N (**8**), and O (**9**), seven new flavonoids isolated from this plant, have a 2,3-dihydroxy-3-methylbutyl group at C-8. Lonchocarpol B has been reported as the first 8-(2,3-dyhydroxy-3-methylbutyl)flavonoid from *Lonchocarpus minimiflorus*.[13] Acutifolins D and E and brosimacutins A (**1**), H (**2**), L (**6**), N (**8**), and O (**9**) are the second examples of 8-(2,3-dihydroxy-3-methylbutyl)flavonoids as far as we know.

Experimental Section

General Experimental Procedures. Optical rotations were determined on a JASCO DIP-370 digital polarimeter. CD data were recorded on a JASCO J-820 spectropolarimeter. UV and IR spectra were obtained on Shimadzu UV-260 and JASCO FT/IR-5300 spectrometers, respectively. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AMX500 spectrometer using tetramethylsilane as the internal standard. Mass spectra were obtained on a Hitachi M-2000A (SIMS) or JEOL JMS-700 (DCIMS) spectrometer.

Plant Material. The bark of *Brosimum acutifolium* was purchased in Sao Paulo, Brazil, in July 1995. The plant was identified by Dr. K. Yoneda (Osaka University), and a voucher specimen with the identification number B 158 has been deposited at the Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University.

Extraction and Isolation. The MeOH extract (52.12 g) of the bark of *B. acutifolium* (1.5 kg) was partitioned between EtOAc and H_2O. The EtOAc-soluble fraction (12.56 g) was subjected to reversed-phase column chromatography (MCI Gel ODS IMY, Mitsubishi Chemical Corp., step gradient with H_2O−CH_3CN) to give six fractions. The third fraction (3.51 g) was eluted with H_2O−CH_3CN (60:40) and further chromatographed over ODS (MCI Gel ODS IMY, step gradient with H_2O−MeOH) to give nine fractions. The fifth fraction (600 mg), the sixth fraction (860 mg), and the seventh fraction (650 mg), which were eluted with H_2O−MeOH (55:45, 50:50, and 45:55, respectively) were purified by reversed-phase HPLC (Capcellpak C_{18} UG 80, Shiseido, H_2O−CH_3CN) to afford bromisacutins A (**1**, 24.8 mg, 0.0017%), B (**2**, 17.4 mg, 0.0012%), C (**3**, 1.1 mg, 0.000073%), D (**4**, 2.1 mg, 0.00014%), E (**5**, 4.7 mg, 0.00031%), F (**6**, 2.5 mg, 0.00017%), G (**7**, 1.5 mg, 0.00010%), H (**8**, 8.3 mg, 0.00055%), I (**9**, 7.3 mg, 0.00049%), 7,4′-dihydroxyflavone (4.8 mg, 0.00032%),[5] luteolin (1.0 mg, 0.000067%),[6] (−)-liquiritigenin (1.0 mg, 0.000067%),[7] and (−)-naringenin (2.2 mg, 0.00015%).[8]

Brosimacutin A (1): colorless amorphous solid; $[\alpha]^{22}_D$ −31.1° (*c* 0.27, MeOH); CD (*c* 0.027, MeOH) $\Delta\epsilon^{25}$ (nm) 8.5 (332), 0 (320), −12.9 (299), 0 (256), 12.8 (236), 2.5 (228), 34.7 (215); UV (MeOH) λ_{max} (log ϵ) 282 (4.45), 310 (sh, 4.19) nm; IR (KBr) ν_{max} 3412 (br), 2980, 1653, 1589, 1518, 1445, 1331, 1263 cm^{-1}; ^{1}H NMR (Table 1); ^{13}C NMR (Table 2); HRSIMS *m*/*z* 359.1478 [M + H]$^+$ (calcd for $C_{20}H_{23}O_6$, 359.1493).

Brosimacutin B (2): colorless amorphous solid; $[\alpha]^{22}_D$ +29.4° (*c* 0.43, MeOH); CD (*c* 0.025, MeOH) $\Delta\epsilon^{25}$ (nm) −3.3 (333), 0 (320), 4.9 (302), 0 (265), −2.3 (238), 3.3 (227), −4.3 (214); UV (MeOH) λ_{max} (log ϵ) 282 (4.46), 310 (sh, 4.17) nm; IR (KBr) ν_{max} 3399 (br), 2980, 1655, 1586, 1518, 1445, 1331, 1273 cm^{-1}; ^{1}H NMR (Table 1); ^{13}C NMR (Table 2); HRSIMS *m*/*z* 359.1465 [M + H]$^+$ (calcd for $C_{20}H_{23}O_6$, 359.1493).

Brosimacutin C (3): colorless amorphous solid; $[\alpha]^{22}_D$ −1.2° (*c* 0.050, MeOH); UV (MeOH) λ_{max} (log ϵ) 283 (4.44), 310 (sh, 4.28) nm; IR (KBr) ν_{max} 3423 (br), 2926, 1655, 1518, 1440, 1383, 1278 cm^{-1}; ^{1}H NMR (Table 1); ^{13}C NMR (Table 2); HRSIMS *m*/*z* 343.1552 [M + H]$^+$ (calcd for $C_{20}H_{23}O_5$, 343.1544).

Brosimacutin D (4): colorless amorphous solid; $[\alpha]^{22}_D$ +63.0° (*c* 0.095, MeOH); CD (*c* 0.028, MeOH) $\Delta\epsilon^{25}$ (nm) 7.6 (332), 0 (319), −10.7 (300), 0 (261), 10.2 (238), −5.3 (226), 16.1 (214); UV (MeOH) λ_{max} (log ϵ) 283 (4.49), 310 (sh, 4.24) nm; IR (KBr) ν_{max} 3422 (br), 2928, 1667, 1601, 1518, 1439, 1335, 1267, 1221 cm^{-1}; ^{1}H NMR (Table 1); ^{13}C NMR (Table 2); HRSIMS *m*/*z* 341.1358 [M + H]$^+$ (calcd for $C_{20}H_{21}O_5$, 341.1388).

Brosimacutin E (5): colorless amorphous solid; $[\alpha]^{22}_D$ −84.0° (*c* 0.23, MeOH); CD (*c* 0.023, MeOH) $\Delta\epsilon^{25}$ (nm) 3.5 (331),

0 (320), −10.8 (296), 0 (256), 5.9 (239), −5.8 (227), 9.6 (213); UV (MeOH) λ_{max} (log ϵ) 286 (4.48), 310 (sh, 4.31) nm; IR (KBr) ν_{max} 3423 (br), 2928, 1667, 1607, 1518, 1454, 1370, 1311, 1269, 1248 cm^{-1}; ^1H NMR (Table 1); ^{13}C NMR (Table 2); HRSIMS *m/z* 341.1393 $[M + H]^+$ (calcd for $C_{20}H_{21}O_5$, 341.1388).

Brosimacutin F (6): colorless amorphous solid; $[\alpha]^{22}_D$ −3.0° (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ϵ) 250 (4.22), 259 (4.24), 330 (4.44) nm; IR (KBr) ν_{max} 3423 (br), 2926, 1628, 1607, 1510, 1439, 1386, 1252 cm^{-1}; ^1H NMR (Table 1); ^{13}C NMR (Table 2); HRSIMS *m/z* 357.1352 $[M + H]^+$ (calcd for $C_{20}H_{21}O_6$, 357.1337).

Brosimacutin G (7): yellow amorphous solid; $[\alpha]^{22}_D$ −0.7° (*c* 0.060, MeOH); UV (MeOH) λ_{max} (log ϵ) 370 (4.43) nm; IR (KBr) ν_{max} 3424 (br), 2926, 1634, 1605, 1561, 1514, 1440, 1366, 1246 cm^{-1}; ^1H NMR (Table 1); ^{13}C NMR (Table 2); HRDCIMS *m/z* 356.1259 $[M]^+$ (calcd for $C_{20}H_{20}O_6$, 356.1260).

Brosimacutin H (8): colorless amorphous solid; $[\alpha]^{22}_D$ +7.0° (*c* 1.1, MeOH); UV (MeOH) λ_{max} (log ϵ) 283 (4.47), 310 (sh, 4.11) nm; IR (KBr) ν_{max} 3416 (br), 2930, 1618, 1516, 1441, 1372, 1260, 1225 cm^{-1}; ^1H NMR (Table 1); ^{13}C NMR (Table 2); HRSIMS *m/z* 361.1636 $[M + H]^+$ (calcd for $C_{20}H_{25}O_6$, 361.1650).

Brosimacutin I (9): colorless amorphous solid; $[\alpha]^{22}_D$ −33.1° (*c* 0.15, MeOH); UV (MeOH) λ_{max} (log ϵ) 282 (4.48) nm; IR (KBr) ν_{max} 3382 (br), 2975, 1655, 1603, 1514, 1453, 1368, 1283, 1213 cm^{-1}; ^1H NMR (Table 1); ^{13}C NMR (Table 2); HRSIMS *m/z* 361.1665 $[M + H]^+$ (calcd for $C_{20}H_{25}O_6$, 361.1650).

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