

Investigación

(\pm)-Bocconarborines A and B, Novel 1,3-Bis-Benzo[c]phenanthridinyl Acetone Alkaloids from *Bocconia arborea*

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Dedicated to Professor Fernando Walls

Abstract. Chemical examination of the aerial parts of *Bocconia arborea* (Papaveraceae), a plant used in traditional medicine, led to the characterization of (\pm)-6-acetonyldihydrosanguinarine (**1**), (\pm)-6-acetonyldihydrochelerythrine (**2**), (\pm)-6-methoxydihydrochelerythrine (**3**), (\pm)-sanguidimerine (**4**), chelidimerine (**5**), and the novel constituents (\pm)-bocconarborine A ((6*R*,6'S + 6*S*,6'R)-13-(6-hydrosanguinarinyl)-15-(6'-hydrochelerythrinyl)-acetone, **6**) and (\pm)-bocconarborine B ((6*R*,6'R + 6*S*,6'S)-13-(6-hydrosanguinarinyl)-15-(6'-hydrochelerythrinyl)-acetone, **7**). The structure and stereochemistry of the novel structures were determined by analyzing the preferred conformations and the spectroscopic data. Antimicrobial evaluations revealed that **3** exhibited activity against *S. aureus*, *S. faecalis* and *C. albicans*.

Keywords: *Bocconia arborea*, medicinal plant, Papaveraceae, alkaloids, benzophenanthridine, bocconarborines A and B, antimicrobial activity.

The genus *Bocconia* (Papaveraceae), which includes ca. nine species, occurs in tropical areas of Mexico, Central and South America [1,2]. Taxonomic considerations indicate a close relationship with the Asiatic genus *Macleaya* and with the North American species *Sanguinaria canadensis* [3]. *Bocconia* species biosynthesize protopine, protoberberine and benzophenanthridine alkaloids [1], which display anti-microbial [4-6], cytotoxic [7], anti-tumor [8-11], anti-viral [12] and anti-inflammatory activities [13], among others. *Bocconia arborea* is a shrub widespread in Mexico that is known as llora sangre (weeping blood), cocoxíhuatl, ahuacachilli, mano de león (lion's hand), palo del diablo (devil's stick), palo amarillo (yellow stick), among many other common names [14,15]. This plant has many different uses in traditional medicine in several regions: as purgative, vermifuge, antitumor and anti-inflammatory agent [14], to heal wounds and dissolve warts [15,16], as a carminative agent, catartic, and analgesic [17].

Previously, the methanolic extract of *B. arborea* showed anti-microbial activity against *S. aureus*, *E. coli*, *P. aeruginosa* and *C. albicans* [18], and the alkaloids dihydrochelerythrine and dihydrosanguinarine were identified as some of the active substances [19]. Now we report the isolation and identification of (\pm)-6-acetonyldihydrosanguinarine (**1**), (\pm)-6-acetonyldihydrochelerythrine (**2**), (\pm)-6-methoxydihydrochelerythrine (**3**),

Resumen. El análisis químico de las partes aéreas de *Bocconia arborea* (Papaveraceae), una planta usada en la medicina tradicional, condujo a la caracterización de (\pm)-6-acetonyldihydrosanguinarine (**1**), (\pm)-6-acetonyldihydrochelerythrine (**2**), (\pm)-6-methoxydihydrochelerythrine (**3**), (\pm)-sanguidimerine (**4**), chelidimerine (**5**), y los compuestos novedosos (\pm)-bocconarborina A ((6*R*,6'S + 6*S*,6'R)-13-(6-hydrosanguinarinyl)-15-(6'-hydrochelerythrinyl)-acetona, **6**) y (\pm)-bocconarborina B ((6*R*,6'R + 6*S*,6'S)-13-(6-hydrosanguinarinyl)-15-(6'-hydrochelerythrinyl)-acetona, **7**). La estructura y la estereoquímica de las estructuras nuevas fueron determinadas mediante el análisis de las conformaciones preferidas deducidas y los datos espectroscópicos. La evaluación antimicrobiana reveló que **3** tiene actividad contra *S. aureus*, *S. faecalis* y *C. albicans*.

Palabras clave: *Bocconia arborea*, planta medicinal, Papaveraceae, alcaloides, benzofenanthridina, bocconarborinas A y B, actividad antimicrobiana.

(\pm)-sanguidimerine (**4**), chelidimerine (**5**), and the new compounds (\pm)-**6** and (\pm)-**7**, named trivially bocconarborines A and B, respectively, from the aerial parts of this plant. In addition, the antimicrobial evaluation revealed that **3** displayed activity.

Results and discussion

Repeated column chromatography of the ethanol extract over silica yielded compounds **1-3**. Compound **1** was a solid which showed physical and spectroscopic characteristics identical to that of (\pm)-6-acetonyldihydrosanguinarine [20], and COSY, DEPT, HMQC and HMBC experiments allowed the complete assignments of the NMR data which confirmed the structure (Table 1). The major constituent from this extract was identified as (\pm)-6-acetonyldihydrochelerythrine (**2**) [21], and (\pm)-6-methoxydihydrochelerythrine (**3**) [21, 22] was isolated as the most polar and minor secondary metabolite from this residue. These structures were identified by comparison with the data published in the literature.

Compound **4**, isolated from the dichloromethane extract as an optically inactive substance, showed well resolved resonances for sixteen hydrogens in the ¹H NMR spectrum (Table

Table 1. ^1H (500 MHz) and ^{13}C (125 MHz) NMR Data of Compound **1^a** in CDCl_3 .

Carbon	^1H mult, J (Hz)	^{13}C
C-1	7.10 s	104.36
C-2	—	147.65*
C-3	—	148.27*
C-4	7.53 s	100.60
C-4a	—	127.48
C-4b	—	139.23
N-CH ₃	2.65 s	43.02
C-6	4.87 dd (10.5,4.0)	54.47
C-6a	—	123.48
C-7	—	144.30
C-8	—	147.21
C-9	6.86 d(8.0)	107.59
C-10	7.33 d(8.0)	116.50
C-10a	—	125.71
C-10b	—	116.03
C-11	7.70 d(8.5)	120.02
C-12	7.49 d(8.5)	124.06
C-12a	—	131.05
C-13 a,b	2.30 dd (15.0,4.0), 2.65 dd (15.0,10.5)	46.62
C-14	—	207.15
C-15	2.06 s	31.20
-OCH ₂ O-	6.03 s	101.07
-OCH ₂ O-	6.04 s	101.53

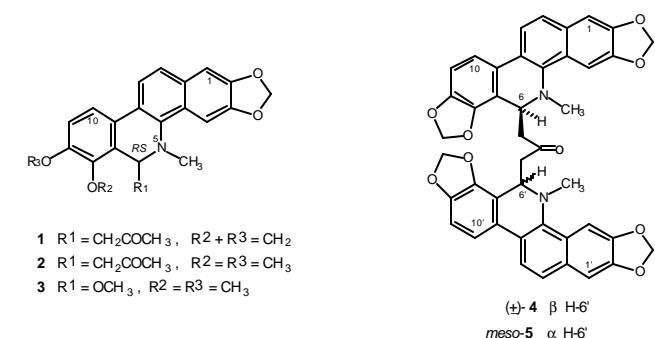
^a Assignments by COSY, DEPT, HMBC and HMQC.^{*} Values may be interchanged.

2), with similar chemical shifts and the same coupling patterns to those observed for (\pm) -6-acetonyldihydrosanguinarine (**1**); the only difference was the absence of the hydrogens for the methyl ketone. This compound gave a molecular ion at m/z 720 by EIMS analysis, consistent with a molecular formula $\text{C}_{43}\text{H}_{32}\text{N}_2\text{O}_9$, which suggested the presence of a substance of dimeric composition with an additional carbonyl group $[(\text{C}_{21}\text{H}_{16}\text{NO}_4)_2\text{CO}]$, in agreement with the number of hydrogens found by ^1H NMR (sixteen) and the absorption at 1712 cm^{-1} (for the ketone) in the IR spectrum. These observations allowed to deduce the structure of 1,3-di(6-hydrosanguinaryl)-acetone for this compound. The two diastereomers for this structure are reported in the literature: (+)-sanguidimerine (**4**) [23] (no spectroscopic data for **4** were published), and chelidimerine (**5**), which is proposed as the *meso*- isomer by preliminary X-ray data [24]. Table 2 shows the ^1H NMR data for **4** and **5**, and comparison of the chemical shifts indicated clear differences, confirming the diastereomeric relationship for these compounds. Therefore, (\pm) -**4** was a natural constituent from *B. arborea*. ^1H NMR analysis of some fractions containing (\pm) -**4** as the major compound, allowed to identify minor signals (*ca.* 3 %) which corresponded to compound *meso*-**5**, which was also a constituent from this species.

Bocconarborines A and B were also isolated as optically inactive substances with the same molecular weight ($[\text{M}^+]$ at m/z 736, by EIMS). ^1H NMR data for both compounds (Table 3) showed the same number of hydrogens (eighteen), the same

Table 2. ^1H NMR Data of Compounds (\pm) -**4** and *meso*-**5** (J (Hz)).

H	(\pm) - 4 ^a	<i>meso</i> - 5 ^b
H-1, H-1'	7.05 s	6.98 s
H-4, H-4'	7.43 s	7.42 s
H-9, H-9'	6.81 d (8.4)	6.75 d (8.0)
H-10, H-10'	7.28 d (8.4)	7.58 d (8.0)
H-11, H-11'	7.64 d (8.4)	7.35 d (6.8)
H-12, H-12'	7.43 d (8.4)	7.23 d (6.8)
N-CH ₃	2.53 s	2.60 s
-OCH ₂ O-	5.99 d (1.5)	5.90 m
-OCH ₂ O-	6.04 dd (2.7,1.2)	6.10 m
H-6, H-6'	4.75 dd (9.0,5.0)	4.88 d
H-13 _A , H-15 _A	2.27 dd (15.0,5.0)	2.20 d
H-13 _B , H-15 _B	2.61 dd (15.0,9.0)	2.52 d

^a Taken at 300 MHz, CDCl_3 . ^b Data from reference [24].

coupling systems, and similar chemical shifts. In addition, COSY and NOESY experiments showed the same interactions and crosspeaks, establishing identical chemical connectivity and substitution pattern for both compounds. Bocconarborines A and B showed ^1H NMR signals for two methyls linked to nitrogen, for two methoxyl groups, for three dioxymethylenes, for four AB systems of benzenoid hydrogens in *ortho*-relationship, and for two ABX systems belonging to two methylenes which are linked to methines and to the same carbonyl group. These fragments established the presence of a 1,3-disubstituted acetone; one substituent was a 6-hydrosanguinaryl fragment, and the other substituent corresponded to a 6-hydrochelerythrinyl residue [25], in agreement with the ^{13}C NMR data (see Experimental). Therefore, these substances are diastereomers of molecular formula $\text{C}_{44}\text{H}_{36}\text{N}_2\text{O}_9$, which exist as racemic compounds, due to the lack of optical activity.

From the ^1H NMR data showed in Table 3, it was clear the different chemical shifts for bocconarborines A and B (assigned provisionally as **6** (for the less polar compound) and **7** (for the more polar compound), respectively, devoid of stereochemistry), and the differences ($\Delta\delta = \delta_6 - \delta_7$) are included in the last column. The difference in the chemical shifts of the C(7')-OCH₃ methoxyl group for **6** (less polar) and **7** (more polar), shows a remarkable variation ($\Delta\delta = 0.29$), due presumably to its location in the shielding space of the benzophenanthridine system in (\pm) -bocconarborine A (**6**), and this

Table 3. ^1H NMR (500 MHz, CDCl_3)^a for Compounds (\pm)-**6** and (\pm)-**7**.

H	6	7	$\Delta\delta = (\delta_6 - \delta_7)$
H-1	7.02 s	7.06 s	-0.04
H-1'	7.00 s	7.04 s	-0.04
H-4	7.41 s	7.40 s	+0.01
H-4'	7.42 s	7.42 s	0.00
H-9	6.80 d (8.0)	6.83 d (8.0)	-0.03
H-9'	6.91 d (8.7)	6.91 d (8.7)	0.00
H-10	7.25 d (8.0)	7.30 d (8.0)	-0.05
H-10'	7.47 d (8.7)	7.49 d (8.7)	-0.02
H-11	7.57 d (8.5)	7.67 d (8.5)	-0.10
H-11'	7.60 d (8.5)	7.66 d (8.2)	-0.06
H-12	7.37 d (8.5)	7.44 d (8.5)	-0.07
H-12'	7.38 d (8.5)	7.43 d (8.2)	-0.05
(7')-OCH ₃	3.95 s	3.66 s	+0.29
(8')-OCH ₃	3.91 s	3.88 s	+0.03
-OCH ₂ O-	5.93 d (1.0)	5.99 d (1.5)	-0.06
-OCH ₂ O-	5.99 dd (5.0, 1.0)	6.01 d (1.5)	-0.02
-OCH ₂ O-	6.07 dd (3.0, 1.5)	6.03 d (2.5)	+0.04
N-CH ₃	2.63 s	2.53 s	+0.10
N-CH ₃ '	2.59 s	2.46 s	+0.13
H-6	4.99 dd (10.5, 4.0)	4.80 dd (9.0, 5.0)	+0.19
H-13 _A	2.46 dd (15.5, 10.5)	2.35 dd (15.0, 9.0)	+0.11
H-13 _B	2.30 dd (10.5, 4.0)	2.74 dd (15.0, 5.0)	0.44
H-6'	5.09 dd (11.5, 3.5)	4.88 dd (9.0, 3.0)	+0.21
H-15 _A	2.23 dd (15.0, 3.5)	2.17 dd (15.0, 3.0)	-0.06
H-15 _B	2.40 dd (15.0, 11.5)	2.49 dd (15.0, 9.0)	-0.09

^a Assignments were confirmed by COSY and NOESY experiments. *J* in (Hz).

observation could be used as diagnostic for establishing the relative stereochemistry of the diastereomers. In order to determine the relative configurations at the two chiral centers (C-6 and C-6') of **6** and **7**, it was necessary to deduce the preferred conformations for the different fragments of the dimers, and correlate the difference of the chemical shift for the C(7')-O-CH₃ group with its relative location.

Three fragments of bocconarborines A and B can be considered for their conformational analysis: (a) the 1,3-disubstituted acetone, (b) The orientation of the acetyl residue in the dihydropyridine ring, and (c) the topological arrangement of the benzophenanthridines.

Twelve main conformations can be considered for a 1,3-disubstituted acetone, which could be described as anti-, **Y**-anti-, syn-, and **Y**-syn-, according to the orientation of the carbonyl oxygen with the substituent R, and *exo*-and *endo*-, according to the orientation of the substituents with respect to the plane defined by the carbonyl [26]. The three preferred conformations could be considered as the (**Y**-anti /**Y**-syn)-*exo*, (**Y**-anti /**Y**-anti)-*exo* and (**Y**-syn /**Y**-syn)-*exo* arrangements (Fig. 1), where the substituents are located opposite to the plane of the carbonyl group.

The acetyl group linked at C(6) and C(6') of the benzophenanthridine can exist in **Y**-axial or **Y**-equatorial orientations, which may be interconverted via a topomerization process [27]. Considering the planarity of the alkaloid fragment and the steric interactions for the **Y**-equatorial orienta-

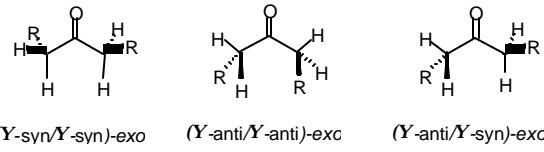


Fig. 1. Preferred conformations for the 1,3-disubstituted acetone fragment.

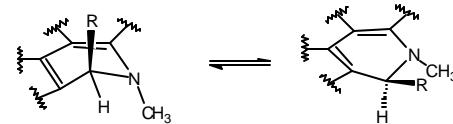
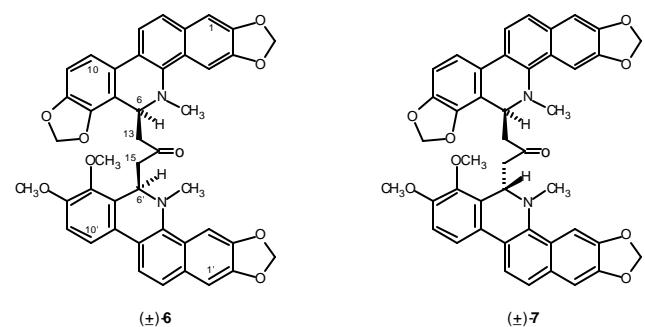


Fig. 2. **Y**-axial \rightleftharpoons **Y**-equatorial Equilibrium of R in the dihydropyridine.



tion of the acetyl residue, the **Y**-axial orientation could be preferred, as depicted in figure 2.

Finally, the relative topology of the planes defined by the two benzophenanthridinyl substituents may be described as *endo-endo*, *exo-endo*, and *exo-exo*, according to their orientation with respect to the carbonyl group [28], and these three extreme possible arrangements are depicted in figure 3.

The comparison of the chemical shifts of the hydrogens of the dimers with respect to those of the corresponding monomeric fragments indicates that there is a shielding effect in the dimers. Table 4 shows the chemical shifts for the hydrogens of bocconarborines A and B (assigned also as **6** and **7**, respectively, in Table 4) with respect to the monomer (\pm)-6-acetyl dihydroanguinarine (**1**), and the same table shows the chemical shifts for the prime hydrogens of the dimers with (\pm)-6-acetyl dihydrochelerythrine (**2**). The difference $\Delta\delta = \delta\text{H}_{\text{monomer}} - \delta\text{H}_{\text{dimer}}$ is included in Table 4 and the constancy of the positive differences was in agreement with an *endo-endo* arrangement of the benzophenanthridines (Fig. 3) [29]. An *endo-exo* arrangement would presumably produce both shielding and deshielding effects, while the *exo-exo* arrangement would produce deshielding effects in the chemical shifts, which are not observed.

Comparative structural analysis of the molecular models for both diastereomers considering the preferred conformations deduced above (the *exo*- arrangements for the 1,3-disubstituted acetone (Fig. 1), **Y**-axial orientation of the ace-

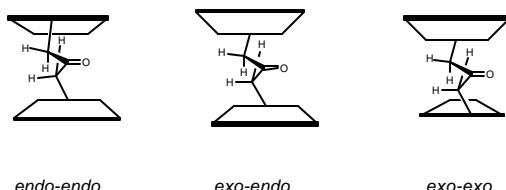
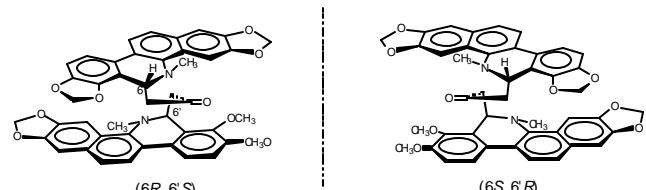


Fig. 3. The three extreme arrangements of the benzophenanthridines with respect to the acetone.

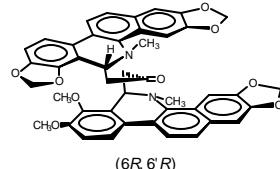
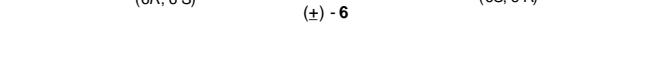
tonyl residue linked to the dihydropyridine (Fig. 2), and the *endo-endo*- arrangement of the benzophenanthridines (Fig. 3), allowed to identify the structures depicted in figure 4 [30]. From this conformational projections it could be proposed that the methoxyl groups in bocconarborine A (**6**) tend to be out of the space comprised between the two benzophenanthridines, while the same groups in bocconarborine B (**7**) are located inside this space. Therefore, the *6R,6'S + 6S,6'R* configuration could be assigned to the (\pm) -**6** diastereomer (methoxyl hydrogens at lower field), while the *6R,6'R + 6S,6'S* configuration could be assigned to the (\pm) -**7** diastereomer (methoxyl hydrogens at higher field).

Antimicrobial evaluation of the extracts, fractions and compounds **1-4** (see the experimental section), allowed to identify that compound **3** exhibited activity against *S. aureus*, *S. faecalis* and *C. albicans* (MIC: 25, 25 and 12 $\mu\text{g}/\text{ml}$, respectively), in agreement with the activity of some benzophenanthidine alkaloids, and with some of the traditional uses of this species.

From a biogenetic point of view, the presence of the alkaloids (\pm) -**4**, *meso*-**5**, (\pm) -**6** and (\pm) -**7** clearly correlate structurally with the acetyl derivatives (\pm) -**1** and (\pm) -**2**. Considering the number of possible monomeric fragments reported in the literature, many additional combinations of 1,3-bis-benzophenanthridinyl acetone alkaloids may be found in *Bocconia* and taxonomically related species.



(\pm) - **6**



(\pm) - **7**

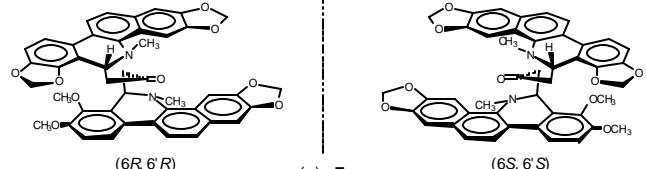


Fig. 4. The enantiomeric pairs of **6** and **7**.

Experimental section

General Experimental Procedures. Melting points were determined on a Fisher-Johns apparatus and are not corrected. Optical rotations were measured on a JASCO DIP 360 polarimeter. IR spectra were recorded on a FT-IR Nicolet Magna 750. MS were measured on a JEOL JMS-AX505HA mass spectrometer and NMR spectra were taken on Unity 300 and Unity Plus 500 instruments. TLC was performed on silica gel 60 Macherey Nagel Duren, Alugram SilF/UV 254, and silica gel 60 0.04-0.063/230-400 mesh ASTM and mesh 70-230 were used for the column chromatographies. Compounds were visualized on UV light or spraying with a 1 % solution of $(\text{NH}_4)_4\text{Ce}(\text{SO}_4)_4$ in sulfuric acid 2N.

Plant Material. Leaves and stems of *B. arborea* S. Watson were collected in Morelos State, México, in February, 1996. A voucher specimen (MEXU 822267) is deposited in the

Table 4. $\Delta\delta$ for the hydrogens of **6** and **7** with respect to those of **1** and **2**.

H	1	2	6	7	$\Delta\delta_1$	$\Delta\delta_2$	$\Delta\delta_3$	$\Delta\delta_4$
H-1	7.10		7.02	7.06	+0.08	+0.04		
H-1'		7.10	7.02	7.04			+0.08	+0.06
H-4	7.53		7.41	7.40	+0.12	+0.13		
H-4'		7.51	7.42	7.42			+0.09	+0.09
H-9	6.86		6.80	6.83	+0.06	+0.03		
H-9'		6.95	6.91	6.91			+0.04	+0.09
H-10	7.33		7.25	7.30	+0.08	+0.03		
H-10'		7.54	7.47	7.49			+0.07	+0.05
H-11	7.70		7.57	7.67	0.13	+0.03		
H-11'		7.71	7.60	7.66			+0.11	+0.05
H-12	7.49		7.37	7.44	+0.12	+0.05		
H-12'		7.48	7.38	7.43			+0.10	+0.05
C(7)-OCH ₃ '	3.95	3.95	3.66				0.0	+0.29
C(8)-OCH ₃ '	3.92	3.91	3.88				+0.01	+0.04
N-CH ₃	2.65		2.63	2.53	+0.02	+0.12		
N-CH ₃ '		2.64	2.59	2.46			+0.05	+0.18

$\Delta\delta_1 = \delta_1 - \delta_6$; $\Delta\delta_2 = \delta_1 - \delta_7$; $\Delta\delta_3 = \delta_2 - \delta_6$; $\Delta\delta_4 = \delta_2 - \delta_7$.

National Herbarium (MEXU), Instituto de Biología de la Universidad Nacional Autónoma de México.

Extraction and Isolation. Dried and powdered plant material (1 kg) was extracted with dichloromethane at room temperature (3 times, 24 h each) and then with ethanol (3 times, 24 h each). Elimination of the solvents at reduced pressure afforded 40 g and 120 g of residues, respectively. Part of the ethanolic extract (26 g) was adsorbed on silica gel (70-230) and chromatographed on a silica gel (230-400) column packed with *n*-hexane-chloroform (20:1), and using increasing amounts of chloroform, and then mixtures of chloroform-methanol as eluting system. The chromatography was developed at reduced pressure [31]. Some fractions were further rechromatographed to give, in order of increasing polarity: (±)-**1** (100 mg), (±)-**2** (310 mg), and (±)-**3** (52 mg). The dichloromethane residue (40 g) was adsorbed on silica gel (70-230) and applied to a column packed with silica gel (230-400) suspended in *n*-hexane. The column was developed at reduced pressure [31] with mixtures of *n*-hexane-EtOAc. Fractions eluted with *n*-hexane-EtOAc (20:1) were rechromatographed using mixtures of *n*-hexane-CHCl₃ as eluent, to give additional amounts of (±)-**1** (100 mg). Fractions eluted with *n*-hexane-EtOAc (9:1) were rechromatographed in an open column using *n*-hexane-CHCl₃-MeOH (1:1:0.1) as constant eluent, and recrystallization of some fractions from MeOH-CHCl₃ provided (±)-**4** (40 mg). ¹H NMR analysis of some fractions indicated the presence of *meso*-**5** (*ca.* 3 % with respect to (±)-**4**). From fractions eluted with *n*-hexane-EtOAc (4:1) of the main column was obtained a residue, which was further rechromatographed in an open column packed with *n*-hexane and eluting with mixtures of *n*-hexane-EtOAc. This column afforded (±)-**6** (40 mg) as the less polar constituent, and subsequent fractions afforded (±)-**7** (45 mg) as the more polar constituent.

(±)-**6 Acetonyldihydrosanguinarine (1).** Colorless powdery solid, mp 190-191 °C (lit [20]: 194-195 °C), R_f 0.58 (*n*-hexane-CHCl₃-MeOH, 1.5:1.5:0.05); [α]_D = 0° (CDCl₃); IR (CHCl₃) ν_{max} 1711, 1470, 870 cm⁻¹; ¹H NMR (500 MHz) and ¹³C NMR (125 MHz), see Table 1.

(±)-**6 Acetonyldihydrochelerythrine (2).** Colorless powdery solid, mp 199-200 °C (lit [21]: 194 °C), R_f 0.53 (*n*-hexane-CHCl₃-MeOH, 1.5:1.5:0.05); [α]_D = 0° (CDCl₃); IR (CHCl₃) ν_{max} 1712, 1604, 1492, 1463, 1417, 1359, 1275, 1083, 1041 cm⁻¹; ¹H (300 MHz, CDCl₃) δ 7.71 (1H, d, 8.4, H-11), 7.54 (1H, d, 9, H-10), 7.51 (1H, s, H-4), 7.48 (1H, d, 8.4, H-12), 7.10 (1H, s, H-1), 6.95 (1H, d, 8.4, H-9), 6.04 (2H, dd, 2.1, 1.2, -OCH₂O-), 5.04 (1H, dd, 11.4, 3.6, H-6), 3.95 (3H, s, (C-7)-OCH₃), 3.92 (3H, s, (C-8)-OCH₃), 2.64 (3H, s, N-CH₃), 2.58 (1H, dd, 15.0, 11.4, H-13_B), 2.25 (1H, dd, 15.0, 3.6, H-13_A), 2.06 (3H, s, -COCH₃).

(±)-**6 Methoxydihydrochelerythrine (3).** Yellow solid, mp 248-250 °C (lit [3]: 210 °C); R_f 0.43 (CHCl₃-MeOH, 2.9:0.1);

[α]_D = 0° (CDCl₃); IR (CHCl₃) ν_{max} 1496, 1464, 1448, 1416, 1275, 1067, 1040, 946 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.78 (1H, d, 8.5, H-11), 7.70 (1H, s, H-4), 7.62 (1H, d, 9.0, H-10), 7.47 (1H, d, 8.5, H-12), 7.12 (1H, s, H-1), 7.04 (1H, d, 9.0, H-9), 6.05 (2H, s, -OCH₂O-), 5.55 (1H, s, H-6), 3.96 (3H, s, (C-7)-OCH₃), 3.93 (3H, s, (C-8)-OCH₃), 3.46 (3H, s, (C-6)-OCH₃), 2.76 (3H, s, N-CH₃); EIMS *m/z* (rel. int.): 379 [M]⁺ (40), 348 (100), 333 (37), 318 (20), 290 (27), 174 (20).

(±)-**Sanguidimerine (4).** Colorless powdery solid, mp 180 °C (lit [23b]: 174 °C), R_f 0.56 (*n*-hexane-CHCl₃-MeOH, 1.5:1.5:0.05), [α]_D = 0° (CHCl₃), IR (CHCl₃) ν_{max} 2924, 1712, 1602, 1440, 1352, 1250, 1040, 940, 857 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) see Table 2; EIMS *m/z* (rel. int.): 720 [M]⁺, 389 (3), 332 (26), 317 (100), 259 (5), 201 (8), 158 (7).

(±)-**Bocconarborine A (6).** Colorless powdery solid, mp 159-163 °C, R_f 0.43 (*n*-hexane-CHCl₃-MeOH, 1.5:1.5:0.05), [α]_D = 0° (CHCl₃), IR (CHCl₃) ν_{max} 2928, 2900, 2854, 2802, 1713, 1602, 1494, 1463, 1442, 1416, 1361, 1274, 1240, 1103, 1081, 1043, 948, 861 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) see Table 3; ¹³C NMR (CDCl₃, 125 MHz) δ 207.02 (CO), 152.14 (C-8'), 148.08, 148.01, 147.70, 147.50, 147.11, 145.69 (C-7'), 144.28 (C-7), 139.30 (C-4b), 132.57, 130.99, 130.88, 128.39, 127.57, 127.31, 124.86, 123.79, 123.77, 123.36, 123.21, 119.86 (C-11), 119.67 (C-11'), 118.67 (C-10'), 116.41 (C-6a), 116.22 (C-10), 111.46 (C-9'), 107.28 (C-9), 104.30, 104.16, 101.59 (OCH₂O), 100.91 (OCH₂O), 100.75, 100.63, 60.93 (C-7'-OCH₃), 55.80 (C-8'-OCH₃), 54.81 (C-6'), 53.56 (C-6), 47.23 (C-13), 46.79 (C-15), 42.99 (CH₃-N), 42.77 (CH₃-N); HRFABMS *m/z* 736.2404 [M + 1]⁺ for C₄₄H₃₆N₂O₉ (calcd [M + 1]⁺ *m/z*: 736.3421).

(±)-**Bocconarborine B (7).** Colorless powdery solid, mp 181 °C (dec.), R_f 0.41 (*n*-hexane-CHCl₃-MeOH, 1.5:1.5:0.05), [α]_D = 0° (CHCl₃), IR (CHCl₃) ν_{max} 2960, 2898, 2841, 1712, 1602, 1492, 1463, 1442, 1415, 1361, 1101, 1082, 1041, 948, 858 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) see Table 3; ¹³C NMR (CDCl₃, 125 MHz) δ 206.53 (CO), 152.07 (C-8'), 148.11, 148.07, 147.55, 147.17, 145.49, 144.37, 139.35, 131.081, 130.99, 128.34, 127.44, 127.38, 124.86, 123.83, 123.77, 123.47, 123.18, 120.00 (C-11), 119.68, (C-11'), 118.69 (C-10'), 116.45 (C-10), 116.35, 111.50 (C-9'), 107.38 (C-9), 104.21, 104.15, 101.48 (OCH₂O), 100.94 (OCH₂O), 100.78, 100.70, 60.68 (C-8'-OCH₃), 55.77 (C-7'-OCH₃), 54.39 (C-6'), 53.87 (C-6), 47.08 (C-13), 46.54 (C-15), 42.74 (CH₃-N), 42.56 (CH₃-N); EIMS *m/z* (rel. int.): 736 [M]⁺ (5), 405 (3), 389 (7), 348 (100), 332 (60), 317 (7), 290 (6).

Biological Activities. The dichloromethane and ethanol extracts, the main fractions of the column chromatographies, as well as compounds **1-4** were tested against *S. aureus*, *S. faecalis*, *E. coli*, *P. aeruginosa*, *S. sonnei*, *K. pneumoniae*, and *C. albicans*, following the procedures described previously [18, 19]. Bioguided fractionation allowed to identify that **3** displayed activity against *Staphylococcus aureus* (ATCC

29213), *Streptococcus faecalis* (ATCC 29212) and *Candida albicans* (ATCC 10231) (MIC: 25, 25 and 12 $\mu\text{g} / \text{mL}$, respectively, gentamicin: 2.5 $\mu\text{g} / \text{mL}$; nystatin: 5 $\mu\text{g} / \text{mL}$).

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