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The nmr spectroscopic studies on methoxybocconine are described. The spectral data indicate bocconine to be 2,3,7,8-bis(methylenedioxy)-10-methoxy-5-methylbenzo[*c*]phenanthridine.

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Bocconine (**1**) is a nematocidal alkaloid isolated from *Bocconia cordata* along with chelerythrine (**2**) and sanguinarine (**3**) by Onda *et al.* in 1965 [2]. Reduction of **1** with sodium borohydride gave dihydrobocconine (**4**), and oxidation with potassium ferricyanide furnished oxybocconine (**5**). Furthermore, **1** was converted into ethoxybocconine (**6**) by treatment with ammonia and then ethanol [1]. These chemical behaviors were the same as those exhibited by a series of reactions of **2** and **3**. It was also shown that **1** is a benzo[*c*]phenanthridine with a methoxyl, an *N*-methyl and two methylenedioxy groups by comparison of the nmr spectra of **4**, **5** and **6** with those of the corresponding derivatives of **2** and **3**. The presence of an

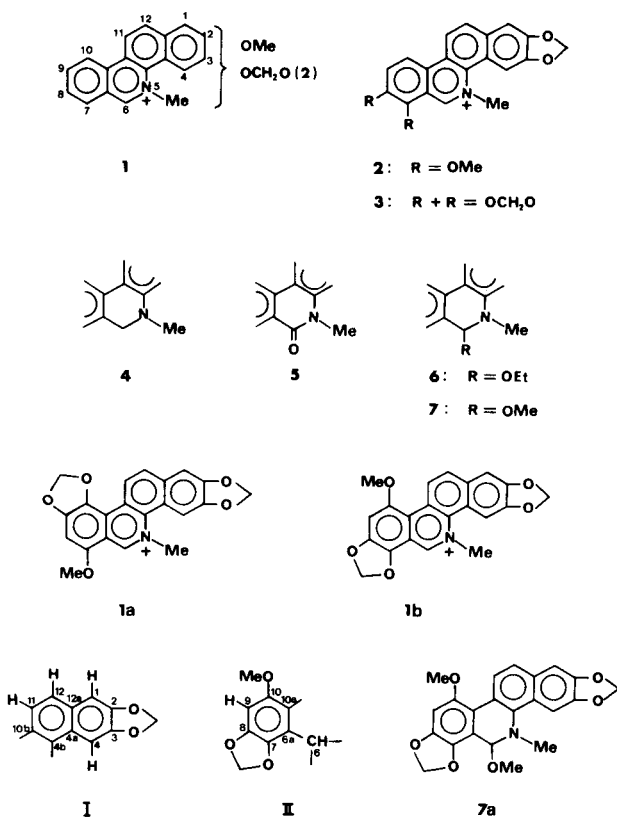
nOe between the methoxyl protons and the highest field singlet aromatic proton (9-H) in **4** and the corresponding absence of an nOe between the methoxyl protons and the lowest field doublet aromatic proton (11-H) led us to a structure with the 7-methoxyl group for **4**, and the structure **1a** was thus proposed for **1** [1]. Later, Ishii *et al.* [3] presented the structure **1b** on the basis of spectral similarity to a synthetic benzo[*c*]phenanthridine. We recently had an opportunity to reinvestigate **1**, and we now independently revise **1a** to be **1b** by means of high field two-dimensional nmr techniques and the others.

A sequence of treatments of **6** with hydrochloric acid, ammonia and methanol gave methoxybocconine (**7**), on which nmr spectroscopic studies were undertaken. The nmr assignments were based on gated decoupling and two-dimensional ¹H-¹³C shift correlation (one-bond and long-range) experiments (Table 1) [4] as well as nOe experiments (Table 2). These data indicated that **7** contains two structural units **I** and **II** [5] with aromatic protons.

Unit I.

One-bond correlation experiments related two singlet (1-H and 4-H) and two doublet aromatic protons (11-H and 12-H) respectively to their corresponding directly attached carbons (Table 1). Long-range correlation experiments established the local heteronuclear environments associated with each of the protons as follows. The 1-proton was long-range coupled to two quaternary carbons (C-2 and C-3), which were observed at δ_c 147.33 and 147.75, respectively. The 1-proton was also long-range coupled to a quaternary carbon (C-4a) at δ_c 126.81, and *via* a *peri* coupling to a methine carbon (C-12) at δ_c 122.93. The 4-proton was long-range coupled to the 2- and 3-carbons, and also to a quaternary carbon (C-12a) at δ_c 130.52. The 11-proton was long-range coupled to the 12a-carbon and a quaternary carbon (C-4b) at δ_c 138.31. The 12-proton was long-range coupled to the 4a-carbon and a quaternary carbon (C-10b) at δ_c 122.53, and *via* a *peri* coupling to the 1-carbon. The distinction between the 4b- and 12a-carbons is ascertained in correlation to the 5(*N*)-methyl protons and the 6-proton (*vide infra*). One-bond and long-range correlation experiments showed that

Scheme 1



a methylenedioxy proton at δ_H 6.046 and 6.038, corresponding to a methylene carbon at δ_C 100.92, are long-range coupled to the 2- and 3-carbons. In addition, an nOe (25.6%) was observed between the 1- and 12-protons. Thus, unit **I** was established as a 5,6-disubstituted 2,3-methylenedioxy-naphthalene moiety.

Table 1
 ^1H - and ^{13}C -NMR Data for Methoxybocconine (ppm, Hz)

No	δ_C [a]	Carbon		Correlated Proton	
		$^1J_{CH}$	$>^1J_{CH}$	One-bond [b] J_{HH}	Long-range [b]
1	104.31 Dd	163.4	5.2	7.11 s	12-H
2	147.33 Sm [c]				1-H, 4-H, 2,3-OCH ₂ O
3	147.75 Sdq [c]		7.4, 2.0		1-H, 4-H, 2,3-OCH ₂ O
4	100.44 Ds	175.2		7.72 s	
4a	126.81 St		6.4		1-H, 12-H
4b	138.31 Sm				6-H, 11-H, 5-CH ₃ , 5-CH ₃ , 6-OCH ₃ ,
6	85.98 Dsep	154.0	4.8	5.31 s	6-H
6a	114.88 Sbrs				6-H, 9-H, 7,8-OCH ₂ O
7	139.17 Sdq		7.5, 3.0		9-H, 7,8-OCH ₂ O
8	147.33 Sm				
9	95.78 Ds	161.2		6.68 s	
10	152.48 Squin		4.0		9-H, 10-OCH ₃ ,
10a	113.06 Sdt		3.0, 6.0		6-H, 9-H, 11-H
10b	122.53 Sd		9.6		12-H
11	124.62 Dd	163.7	1.5	8.45 d	9.0
12	122.93 Dd	158.8	4.8	7.46 d	9.0
12a	130.52 Sddd		9.0, 6.0, 2.0		4-H, 11-H, 1-H or 12-H [d]
2,3-OCH ₂ O	100.92 Ts	174.1		6.046 d	1.2
5-CH ₃	40.16 Qd	136.4	2.7	2.74 s	6-H [d]
6-OCH ₃	54.24 Qd	142.0	3.2	3.44 s	6-H
10-OCH ₃	56.68 Qs	144.4		3.89 s	
7,8-OCH ₂ O	101.77 Ts	173.2		6.07 d	1.5
				6.029 d	

[a] Capital and small letters refer to the splittings observed in the off-resonance and the gated decoupled spectra, respectively; s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sep = septet, m = multiplet, br = broad. [b] These data were obtained by two-dimensional ^1H - ^{13}C shift correlation experiments. [c] Assignments may be reversed. [d] Although long-range couplings were not detected in the correlation map, the presence of couplings can be deduced on the basis of the carbon splittings observed in the gated decoupled spectrum.

Table 2
 NOE Data for Methoxybocconine

Irradiated Proton	Observed Proton	nOe (%)
12-H	1-H	25.6
	11-H	22.0
6-OCH ₃	4-H	8.0
	6-H	15.2
10-OCH ₃	9-H	35.7
	11-H	3.3

Unit II.

One-bond correlation experiments related a singlet aromatic proton (9-H) and a singlet methine proton (6-H) respectively to their corresponding directly attached carbons (Table 1). Long-range correlation experiments established the local heteronuclear environments associated with each of the protons as follows. The 9-proton was long-range coupled to four quaternary carbons (C-7, C-8, C-10 and C-10a), which were observed at δ_C 139.17, 147.33, 152.48 and 113.06, respectively. The 6-proton was long-range coupled to the 7- and 10a-carbons, and also to a quaternary carbon (C-6a) at δ_C 114.88. One-bond and long-range correlation experiments showed that a methylenedioxy proton at δ_H 6.072 and 6.029, corresponding to a methylene carbon at δ_C 101.77, is long-range coupled to the 7- and 8-carbons. Also, these experiments revealed that a methoxyl proton at δ_H 3.89, corresponding to a methyl carbon at δ_C 56.68, is long-range coupled to the 10-carbon. In addition, an nOe (35.7%) was observed between the 9-proton and the 10-methoxyl protons. Thus, unit **II** was established as a 3,4-disubstituted 5-methoxy-1,2-methylenedioxybenzene moiety.

Combination of Units I and II.

The 11-proton was related to the 10a-carbon by long-range correlation experiments, and an nOe (3.3%) was observed between the 10-methoxyl protons and the 11-proton, suggesting that units **I** and **II** are bonded by the 10a- and 10b-carbons. Assignments of protons and carbons in 5(*N*)-methyl and the 6-methoxyl groups were made by one-bond correlation experiments. The positions of these groups were decided by long-range correlation experiments as follows. The 6-proton, which was related to the 6-methoxyl carbon, was long-range coupled to the 4b-carbon, and the 5(*N*)-methyl protons to the 4b- and 6-carbons. These observations show that the 5(*N*)-methyl group connects between the 4b- and 6-carbons, forming a dihydrobenzo[*c*]phenanthridine system.

Thus, the structure of **7** was straightly established as **7a** without any comparison with the nmr data for related compounds, and as a result, **1** was decided to be 2,3,7,8-bis-(methylenedioxy)-10-methoxy-5-methylbenzo[*c*]phenanthridine.

A ratio of the nOe's observed between the 9-proton and the 10-methoxyl protons, and between the 10-methoxyl protons and the 11-proton suggests that the 10-methoxyl group in **7** is predominantly directed toward the 9-hydrogen atom due to a steric interaction with the 11-hydrogen atom. This conformational situation is the same as that in **4** (*vide supra*). This is the reason why we erroneously proposed the structure **1a** for **1**.

EXPERIMENTAL

Elemental analysis was performed on a Perkin-Elmer 240B. MS was taken on a JEOL JMS DX-300.

The ^1H - and ^{13}C -nmr spectra were recorded on a Varian XL-400 at 400 and 100.6 MHz, respectively. The solutions were 0.102 mmole ml^{-1} in deuteriochloroform. For the nOe spectra, the degassed solutions were used. All spectra were taken at probe temperature, 20°C, using a 5 mm tube.

The 90° ^1H and the 90° ^{13}C pulses were calibrated at 31.0 and 9.1 mseconds, respectively, in two-dimensional ^1H - ^{13}C shift correlation experiments. A single experiment was run for each of the one-bond and long-range correlations under the following conditions. One-bond correlation: sweep width, 2800 Hz in the F_1 domain (^1H) (memory size, 0.5K) and 12121 Hz in the F_2 (^{13}C) (memory size, 2K); digital resolution, 0.17 Hz per point; quadrature collection; receiver phase, echo; J_{1XH} , 140 Hz; Δ_1 and Δ_2 , 1.33 seconds and 140 Hz; number of scans, 128 (transients, 64); size of final data points, 2K; acquisition time, 0.084 second. Long-range correlation: sweep width, 2600 Hz in the F_1 domain (^1H) (memory size, 0.5K) and 12563 Hz in the F_2 domain (^{13}C) (memory size, 2K); digital resolution, 0.75 Hz per point; quadrature collection; receiver phase, echo; J_{NXH} , 7.0 Hz; Δ_1 and Δ_2 , 1.33 seconds and 7.0 Hz; number of scans, 128 (transients, 256); size of final data points, 2K; acquisition time, 0.082 second.

The nOe spectra were recorded by means of nOe difference techniques. The pre-irradiation time of each resonance was 4 seconds. The irradiation data sets were not interleaved to cancel drift and changing magnet homogeneity [6]. Prior to subtraction to compute the difference spectra, these spectra were transformed by the difference between two free induction decays.

Methoxybocconine (7).

A solution of 37 mg (0.0908 mmole) of **5** in 2 ml of 5% hydrochloric

acid and 30 ml of water was made alkaline with 5% ammonia, and then the mixture was extracted with ethyl acetate. The organic phase was washed with water and dried over anhydrous sodium sulfate. After removal of the solvent *in vacuo*, the resulting residue was recrystallized from chloroform-methanol to yield 20 mg (55.5%) of colorless needles, mp 197-200° (uncorr); ms: m/z M^+ , 393.122 (M , 393.121).

Anal. Calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_6 \cdot 1/3\text{H}_2\text{O}$: C, 66.16; H, 4.96; N, 3.51. Found: C, 66.13; H, 4.75; N, 3.46.

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- [5] The numberings refer to those of **7a**.
- [6] Interleaving techniques are not necessary on a Varian XL-400 under the employed conditions.