The Absolute Configuration at C(7) of Voacangine Hydroxyindolenine

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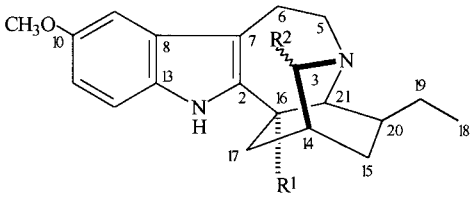
The NMR spectral analysis of voacangine hydroxyindolenine (**2**) and of some synthetic derivatives, together with mechanistic considerations, permitted to establish its absolute configuration at C(7) as (*R*). The configuration at C(7) in hydroxyindolenines of the ibogamine series is also discussed and would be (*S*).

1. Introduction. – Although the absolute configuration of the iboga alkaloids is known [1], the configuration at the chiral centre C(7) (trivial numbering) of the corresponding hydroxyindolenines remains undetermined. In previous works, several approaches to solve this problem have been described [2–4], but none gave any conclusive data. In the present work, we report on some of the chemical behaviour of voacangine hydroxyindolenine (**2**), in particular on the isomerization at C(7) followed by easy de(methoxycarbonylation) in basic media that permitted to establish the (7*R*) configuration of **2** which was also supported by NMR data.

2. Results and Discussion. – Voacangine hydroxyindolenine (**2**) is considered to be an artefact derived from the autoxidation of voacangine (= 12-methoxyiboganine-18-carboxylic acid methyl ester; **1**). In fact, **2** was readily produced by bubbling an air stream through a solution of **1** in $CHCl_3$ [4]. The treatment of compound **2** with Ac_2O in pyridine gave the acetoxyindolenine **3** as the sole reaction product in 54% yield [4] (*Scheme 1*). The use of lead tetraacetate in yohimbinoid alkaloids to give acetoxyindolenines is a well-known reaction used as the first step in the synthesis of 2-acylindole derivatives [5], but when voacangine (**1**) was treated with lead tetraacetate, 3-hydroxyvoacangine (**10**) was obtained as the major product in 52% yield, owing to the oxidation of C(3) of the iboga skeleton [4]. However, when lead tetraacetate was added at once to the solution of **1** in CH_2Cl_2, a small amount of acetoxyindolenine **4** (2% yield) was isolated from the reaction mixture (*Scheme 1*). Surprisingly, the acetoxyindolenines **4** and **3** proved to be epimers at C(7) as suggested by their spectral data.

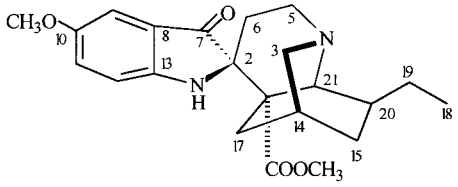
Compounds **3** and **4** show UV maxima at 293 and 284, respectively, and give a yellow colour with $FeCl_3$/$HClO_4$ spray reagent [2] [6]. The MS of **4** is very similar to that of **3**, with peaks at *m/z* 384 (8), 383 (4), 368 (100, $[M - OAc]^+$) and 367 (78); the absence of the molecular ion suggests the loss of the acetoxy group at C(7) of these acetoxyindolenines. The peaks at *m/z* 337 (8) and 353 (20) are due to the loss of an ethyl side chain, and those at *m/z* 136 (47) and 122 (26) are characteristic of iboga alkaloids [7]. The ^{1}H-NMR spectrum of **4** (*Table 1*) displays signals for a tertiary acetate, a methoxycarbonyl and an aromatic methoxy group, an ethyl side chain, and the absence of the NH signal. The remaining peaks of the spectra were assigned by direct comparison with those of compounds **2** and **3**, and confirmed by selective decoupling and ^{1}H-COSY experiments.



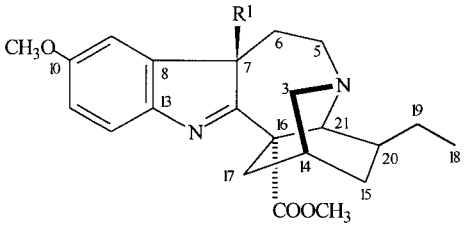
1 $R^1 = COOCH_3$, $R^2 = H$

9 $R^1 = H$, $R^2 = H$

10 $R^1 = COOCH_3$, $R^2 = OH$

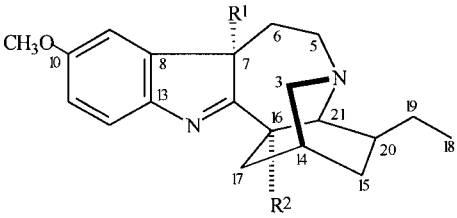


5



2 $R^1 = OH$

3 $R^1 = OAc$



4 $R^1 = OAc$, $R^2 = COOCH_3$

6 $R^1 = OH$, $R^2 = H$

7 $R^1 = OH$, $R^2 = COOH$

8 $R^1 = OH$, $R^2 = COOCH_3$

Important conclusions can be derived from the inspection of the ^{1}H-NMR data of compounds **2**–**4** (*Table 1*). The most significant feature is the great difference in the ^{1}H-NMR chemical shifts of $CH_2(17)$ and H–C(21). Thus, the low-field resonances of the $CH_2(17)$ in **2** (2.74–2.51 ppm) and **3** (2.73–2.53 ppm) as compared to those observed in **4** (2.18–2.00 ppm) could be attributed to the spatial proximity of the O-function at C(7) to the two protons of $CH_2(17)$, consistent with an absolute configuration (7*R*) in **2** and **3**, and (7*S*) in **4**. Similar reasons can be put forward to explain the H–C(21) chemical shift of compound **3** (3.61 ppm) with regard to that of **4** (3.97 ppm), *i.e.*, an opposite configuration of the acetoxy group at C(7). The structure of **4** was further substantiated by comparison of its ^{13}C-NMR data with those of **2** and **3** (*Table 2*).

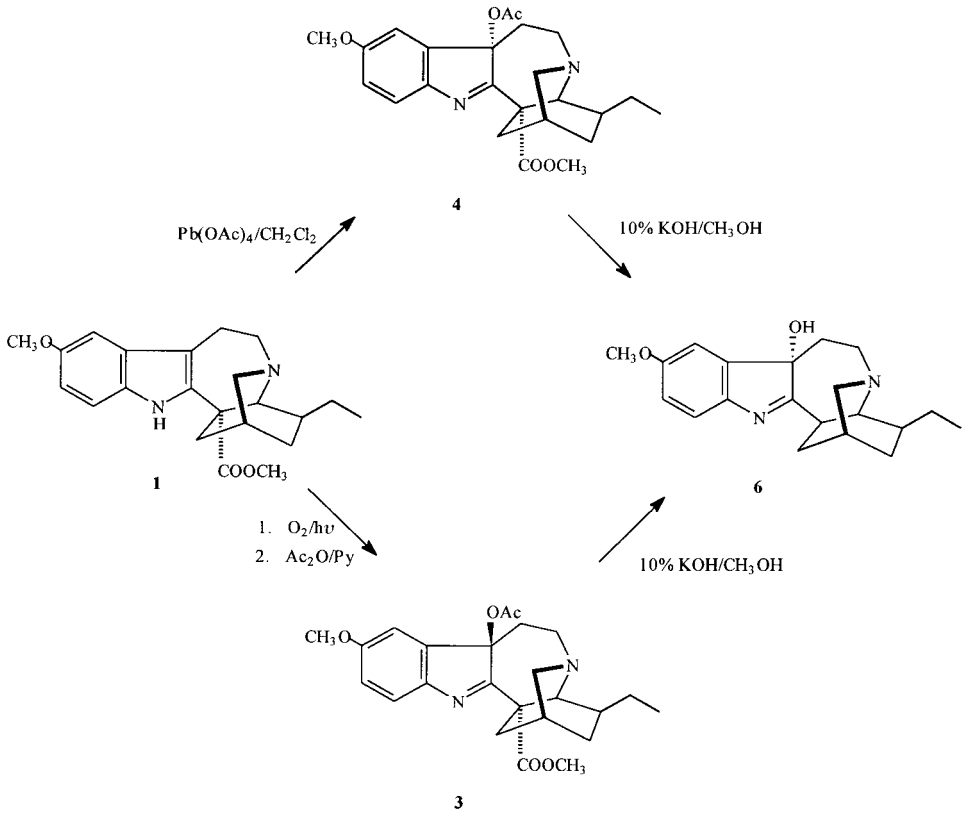
The rearrangement of **2** in basic medium to give voacangine pseudoindoxyl (**5**) was described earlier [2], and the absolute configuration at C(2) was subsequently determined [8]. This configuration has now been confirmed on the basis of a strong correlation between $H_{pro\text{-}R}$–C(17) and NH observed in a NOESY spectrum (*Fig.*), and taking into account the absolute configuration of coronaridine-type alkaloids [1]. The HMQC (*Table 3*) and ^{1}H-COSY spectra allowed us to assign all protons of **5**. Based on the expected retention of configuration of $CH_2(6)$ during the formation of **5** from **2** by a *Wagner-Meerwein* rearrangement [3], the configuration at C(7) of **2** should be (*S*), which is inconsistent with the ^{1}H-NMR data above. This fact can be explained assuming the isomerization at C(7) prior to the rearrangement, as demonstrated by the following experiments.

When **2** was refluxed in the presence of MeONa, a new compound **6** (14% yield) was obtained together with **5** (45% yield). Compound **6** crystallized as colourless prisms from acetone. Its spectral data confirmed the proposed structure and suggested (7*S*) configuration.

The treatment of **2** under mild conditions with potassium *tert*-butoxide in THF gave only **6** in 49% yield, but the reaction with 10% KOH/MeOH, at room temperature, gave **6** in 51% yield and a small amount of compound **7**. The structure and (7*S*) configuration of **7** were established by its spectroscopic data.

The structure **7** is reasonable in view of the easy de(methoxycarbonylation) of compound **2** in basic medium to give **6**, and **7** seems to be the intermediate between the undetected compound **8** and **6**. However, unequivocal proof of the existence of epimerization at C(7) of **2** under basic conditions was obtained by treatment of the two epimeric acetoxyindolenines **3** and **4** with 10% KOH/MeOH which gave the same hydroxyindolenine **6**. Therefore, two alternative routes can be followed from voacangine (**1**) to give **6** (*Scheme 1*).

Scheme 1



The UV absorption maxima of **6** at 224 and 284 and the intense peak at *m/z* 309(53), $[M-17]^+$ are consistent with a 7-hydroxyindolenine structure. The IR and ^{1}H and ^{13}C-NMR spectra (*Tables 1* and *2*)

Table 1. *^{1}H-NMR* (500 MHz) *Data of Compounds* **2**–**7**[a])

	2	**3**	**4**	**5**	**6**	**7**
H_R–C(3)	2.77 (br. *s*)	2.72 (br. *s*)	2.80 (*dt, J* = 8.6, 3.1)	3.04 (br. *d, J* = 12.2)	2.82 (*dt, J* = 8.4, 2.8)	2.71 (*dt, J* = 8.0, 2.3)
H_S–C(3)	2.77 (br. *s*)	2.72 (br. *s*)	2.65 (*d, J* = 8.6)	2.64 (*dt, J* = 12.1, 2.9)	2.76 (*d, J* = 8.9)	2.57 (*d, J* = 8.5)
H_R–C(5)	3.00 (*dd, J* = 14.7, 4.5)	3.01 (*dd, J* = 14.4, 3.1)	3.11 (*dm, J* = 15.0)	2.76 (*dd, J* = 14.3, 3.7)	2.99 (*dm, J* = 14.7)	3.00 (*dd, J* = 14.2, 3.5)
H_S –C(5)	3.53 (*ddd, J* = 15.0, 15.0, 3.3)	3.43 (*ddd, J* = 13.8, 13.8, 2.9)	3.61 (*ddd, J* = 13.5, 13.5, 2.5)	3.85 (*ddd, J* = 15.9, 15.9, 3.7)	3.47 (*ddd, J* = 13.6, 13.8, 3.1)	3.45 (*ddd, J* = 14.1, 14.1, 3.1)
H_R–C(6)	1.98 (*dt, J* = 13.3, 1.5)	1.96 (*dt, J* = 13.5, 1.7)	2.91 (*dt, J* = 14.1, 2.2)	1.50 (*ddd, J* = 10.4, 2.3, 1.2)	1.87 (*dt, J* = 15.4, 1.0)	2.69 (*dm, J* = 14.9)
H_S–C(6)	1.90 (*ddd, J* = 14.0, 14.0, 4.5)	1.83 (*ddd, J* = 15.1, 15.0, 4.7)	2.23 (*ddd, J* = 13.5, 13.5, 3.8)	2.12 (*ddd, J* = 14.9, 14.9, 5.0)	1.97 (*ddd, J* = 9.3, 9.3, 4.5)	2.03 (*t, J* = 9.0)
H–C(9)	6.94 (*d, J* = 2.5)	6.68 (*d, J* = 2.5)	6.91 (*d, J* = 2.5)	7.06 (*d, J* = 2.7)	6.89 (*d, J* = 2.5)	6.92 (*d, J* = 2.5)
H–C(11)	6.84 (*dd, J* = 8.4, 2.5)	6.80 (*dd, J* = 8.4, 2.5)	6.86 (*dd, J* = 8.4, 2.5)	7.10 (*dd, J* = 8.7, 2.7)	6.82 (*dd, J* = 8.3, 2.5)	6.85 (*dd, J* = 8.3, 2.5)
H–C(12)	7.40 (*d, J* = 8.4)	7.47 (*d, J* = 8.4)	7.46 (*d, J* = 8.5)	6.78 (*d, J* = 8.7)	7.26 (*d, J* = 8.3)	7.39 (*d, J* = 8.3)
H–C(14)	1.95 (br. *s*)	1.91 (br. *s*)	1.89 (br. *s*)	1.90 (br. *s*)	1.86 (br. *s*)	1.90 (br. *s*)
H_R–C(15)	1.80 (br. *m*)	1.70 (*ddd, J* = 11,3, 11.3, 4.7)	1.77 (br. *t, J* = 12.5)	1.72 (*t, J* = 12.0)	1.78 (br. *m*)	1.80 (br. *m*)
H_S–C(15)	1.13 (br. *m*)	1.07 (br. *m*)	1.07 (br. *m*)	1.10 (*dq, J* = 13.1, 3.5)	1.19 (br. *m*)	1.09 (br. *m*)
H–C(16)					3.08 (*dt, J* = 11.5, 1.0)	
H_R–C(17)	2.51 (*dt, J* = 13.7, 2.9)	2.73 (*dm, J* = 12.7)	2.18 (*dd, J* = 11.9, 4.3)	1.66 (*ddd, J* = 13.9, 5.1, 1.6)	2.11 (*dm, J* = 13.5)	1.96 (br. *d, J* = 14.7)
H_S–C(17)	2.74 (*d, J* = 14.1)	2.53 (*d, J* = 13.9)	2.00 (*dt, J* = 13.0, 2.3)	2.66 (br. *m*)	2.21 (*t, J* = 13.5)	1.86 (*d, J* = 13.2)
Me(18)	0.90 (*t, J* = 6.8)	0.92 (*t, J* = 7.1)	0.90 (*t, J* = 7.1)	0.94 (*t, J* = 7.3)	0.96 (*t, J* = 7.0)	0.94 (*t, J* = 7.4)
CH_2(19)	1.47 (*m*)	1.52 (*m*), 1.42 (*m*)	1.54 (*m*), 1.42 (*m*)	1.46 (*m*), 1.66 (*m*)	1.53 (*m*)	1.53 (*m*)
H–C(20)	1.47[b])	1.42[b])	1.42[b])	1.37 (br. *m*)	1.53[b])	1.53[b])
H–C(21)	3.64 (*s*)	3.61 (*s*)	3.97 (*s*)	3.92 (*d, J* = 2.5)	3.52 (*s*)	3.49 (*d, J* = 5.0)
MeO–C(10)	3.85 (*s*)	3.79 (*s*)	3.83 (*s*)	3.80 (*s*)	3.85 (*s*)	3.84 (*s*)
MeOOC	3.74 (*s*)	3.61 (*s*)	3.69 (*s*)	3.33 (*s*)		
Ac		2.09 (*s*)	1.57 (*s*)			
NH				4.28 (br. *s*)		

[a]) Chemical shifts in ppm rel. to $SiMe_4$; *J* in Hz. Solvent $CDCl_3$. The *Hanson* system for prochirality was used to identify the protons [9]; H_R and H_S are short forms of $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$, respectively. [b]) Overlapped signals.

Table 2. *^{13}C-NMR* (125 MHz) *Data of Compounds* **2**–**6**[a])

	2[b])	**3**	**4**	**5**	**6**
C(2)	186.8 (*s*)	180.6 (*s*)	184.2 (*s*)	68.5 (*s*)	191.4 (*s*)
C(3)	48.6 (*t*)	48.7 (*t*)	49.5 (*t*)	51.9 (*t*)	49.5 (*t*)
C(5)	49.1 (*t*)	49.4 (*t*)	50.0 (*t*)	47.4 (*t*)	48.9 (*t*)
C(6)	34.2 (*t*)	37.0 (*t*)	31.7 (*t*)	25.7 (*t*)	31.9 (*t*)
C(7)	88.3 (*s*)	90.6 (*s*)	93.5 (*s*)	203.0 (*s*)	87.1 (*s*)
C(8)	144.4 (*s*)	145.1 (*s*)	144.5 (*s*)	153.9 (*s*)	145.4 (*s*)
C(9)	107.9 (*d*)	107.0 (*d*)	107.9 (*d*)	104.5 (*d*)	108.1 (*d*)
C(10)	159.1 (*s*)	158.8 (*s*)	159.2 (*s*)	154.1 (*s*)	158.4 (*s*)
C(11)	113.7 (*d*)	112.7 (*d*)	114.2 (*d*)	126.5 (*d*)	113.5 (*d*)
C(12)	121.3 (*d*)	121.8 (*d*)	121.6 (*d*)	113.8 (*d*)	120.2 (*d*)
C(13)	144.8 (*s*)	141.8 (*s*)	143.3 (*s*)	153.5 (*s*)	143.2 (*s*)
C(14)	27.0 (*d*)	27.8 (*d*)	27.2 (*d*)	26.1 (*d*)	27.3 (*d*)
C(15)	32.0 (*t*)	31.9 (*t*)	29.3 (*t*)	31.1 (*t*)	31.7 (*t*)
C(16)	58.5 (*s*)	57.8 (*s*)	58.6 (*s*)	52.0 (*s*)	43.5 (*d*)
C(17)	34.5 (*t*)	33.6 (*t*)	34.3 (*t*)	30.7 (*t*)	34.0 (*t*)
C(18)	11.5 (*q*)	11.5 (*q*)	11.5 (*q*)	11.9 (*q*)	11.6 (*q*)
C(19)	26.5 (*t*)	26.5 (*t*)	26.8 (*t*)	28.6 (*t*)	27.1 (*t*)
C(20)	37.5 (*d*)	38.4 (*d*)	38.0 (*d*)	35.8 (*d*)	40.6 (*d*)
C(21)	58.5 (*d*)	56.5 (*d*)	55.7 (*d*)	51.0 (*d*)	53.6 (*d*)
MeO–C(10)	55.7 (*q*)	55.6 (*q*)	55.9 (*q*)	55.7 (*q*)	55.6 (*q*)
MeOOC	53.1 (*q*)	52.4 (*q*)	52.6 (*q*)	51.7 (*q*)	
	173.8 (*s*)	172.0 (*s*)	173.0 (*s*)	174.8 (*s*)	
MeCO		21.0 (*q*)	22.5 (*q*)		
		168.1 (*s*)	169.2 (*s*)		

[a]) Chemical shifts in ppm rel. to $SiMe_4$. C-Multiplicities were determined by DEPT pulse sequence. Solvent $CDCl_3$. [b]) Recorded at 100 MHz.

confirmed the lack of the methoxycarbonyl group in **6**. The ^{1}H-COSY, HMQC (*Table 3*), and NOESY (*Fig.*) experiments permitted the assignment of all NMR signals, and the δ(H) of CH_2(17) are compatible with a (7*S*) configuration.

Compound **7** displayed UV maxima at 225 and 273 typical for a 7-hydroxyindolenine chromophore [2]. Its ^{1}H-NMR spectrum was very similar to that of **4** (*Table 1*) and did not show signals for the methoxycarbonyl group. Since the ^{1}H-NMR signals for CH_2(17) exhibited the same pattern as for compounds **2**–**4**, and in view of the strong peaks at *m/z* 326(30) and 325(70) in the MS, a COOH group must be located at C(16) of **7**. On the other hand, the high-field signal for CH_2(17) at 1.96–1.86 ppm suggests the (7*S*) configuration at the OH-substituted centre.

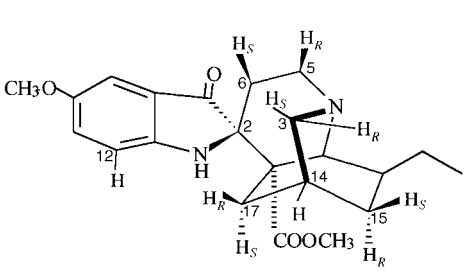
Thus, the autooxidation of voacangine (**1**) [4] would start with the abstraction of the H-atom at N(1) to give two possible pyramidal radicals at C(7), *i.e.*, **11** and **12** (*Scheme 2*). However, the fact that only the (7*R*) isomer **2** of the corresponding voacangine hydroxyindolenine has been isolated from the reaction mixture suggests that the radical species **12** is not sufficiently stable, owing to electronic repulsion between the unpaired electron at C(7) and the very proximal COOMe group at C(16).

The easy de(methoxycarbonylation) of **2** in basic medium indicates an anchimeric assistance of the OH group at C(7), since the COOMe group of **1** was not even hydrolyzed under the same conditions [2]. This can only be explained by prior isomerization at C(7) of **2** to attain spatial proximity of the OH to the COOMe group. The 7-epivoacangine hydroxyindolenine (**8**) should be considered to be a common

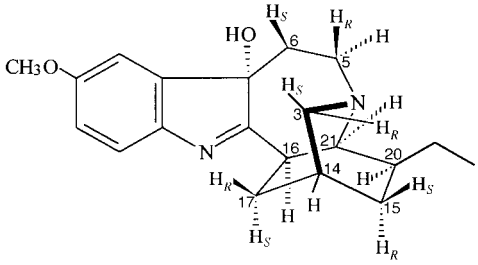
Table 3. *HMQC Data of Compounds* **5** *and* **6**[a])

	5		**6**	
	δ(H)	HMQC	δ(H)	HMQC
H_R–C(3)	3.04 (*br d, J* = 12.2)	51.9 (*t*)	2.82 (*dt, J* = 8.4)	49.5 (*t*)
H_S–C(3)	2.64 (*dt, J* = 12.1, 2.9)	51.9 (*t*)	2.76 (*d, J* = 8.9)	49.5 (*t*)
H_R–C(5)	2.76 (*dd, J* = 14.3, 3.7)	47.4 (*t*)	2.99 (*dm, J* = 14.7)	48.5 (*t*)
H_S–C(5)	3.85 (*ddd, J* = 15.9, 15.9, 3.7)	47.4 (*t*)	3.47 (*ddd, J* = 13.6, 13.8, 3.1)	48.5 (*t*)
H_R–C(6)	1.50 (*ddd, J* = 10.4, 2.3, 1.2)	25.7 (*t*)	1.87 (*dt, J* = 15.4, 1.0)	31.9 (*t*)
H_S–C(6)	2.12 (*ddd J* = 14.9, 14.9, 5.0)	25.7 (*t*)	1.97 (*ddd, J* = 9.3, 9.3, 4.5)	31.9 (*t*)
H–C(9)	7.06 (*d, J* = 2.7)	104.5 (*d*)	6.89 (*d, J* = 2.5)	108.1 (*d*)
H–C(11)	7.10 (*dd, J* = 8.7, 2.7)	126.5 (*d*)	6.82 (*dd, J* = 8.3, 2.5)	113.5 (*d*)
H–C(12)	6.78 (*d, J* = 8.7)	113.8 (*d*)	7.26 (*d, J* = 8.3)	120.2 (*d*)
H–C(14)	1.90 (br. *s*)	26.1 (*d*)	1.86 (br. *s*)	27.3 (*d*)
H_R–C(15)	1.72 (*t, J* = 12.0)	31.3 (*t*)	1.78 (br. *m*)	31.7 (*t*)
H_S–C(15)	1.10 (*dq, J* = 13.1, 3.5)	31.3 (*t*)	1.19 (br. *m*)	31.7 (*t*)
H–C(16)			3.08 (*dt, J* = 11.5, 1.0)	43.5 (*d*)
H_R–C(17)	1.66 (*ddd, J* = 13.9, 5.1, 1.6)	30.7 (*t*)	2.11 (*dm, J* = 13.5)	34.0 (*t*)
H_S–C(17)	2.66 (br. *m*)	30.7 (*t*)	2.21 (*t, J* = 13.5)	34.0 (*t*)
H–C(18)	0.94 (*t, J* = 7.3)	11.9 (*q*)	0.96 (*t, J* = 7.0)	11.6 (*q*)
CH_2-(19)	1.46 (*m*), 1.66 (*m*)	28.6 (*t*)	1.53 (*m*)	27.1 (*t*)
H–C(20)	1.37 (br. *m*)	35.8 (*d*)	1.53[b])	40.6 (*d*)
H–C(21)	3.92 (*d, J* = 2.5)	51.0 (*d*)	3.52 (*s*)	53.6 (*d*)
MeO–C(10)	3.80 (*s*)	55.7 (*q*)	3.85 (*s*)	55.6 (*q*)
MeCOO	3.33 (*s*)	51.7 (*q*)		

[a]) Chemical shifts in ppm rel. to $SiMe_4$ (= 0); solvent $CDCl_3$. H_R and H_S are short forms of $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$, respectively. [b]) Overlapped signals.



5 NOESY: NH / H–C(12), H_R–C(17);
H_S–C(3) / H_R–C(5), H_S–C(6);
H_R–C(3) / H–C(14), H_S–C(15)

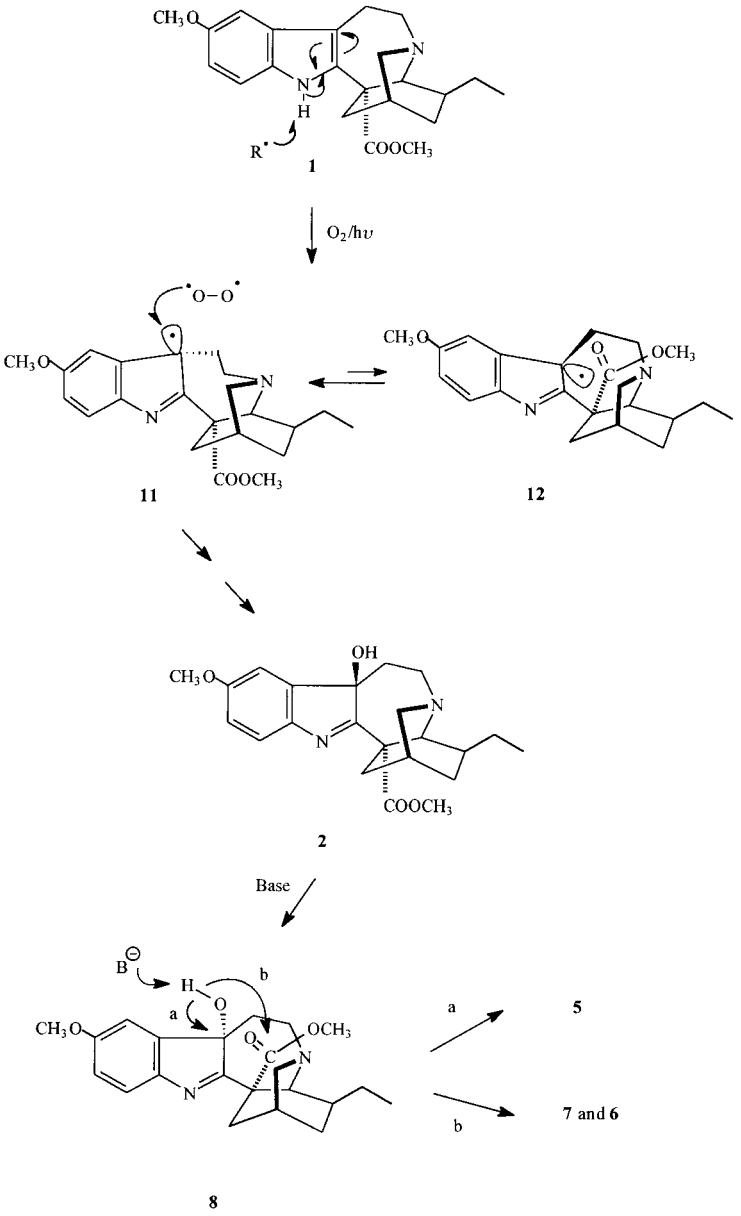


6 NOESY: H_S–C(3) / H_R–C(5), H_S–C(6), H_R–C(17);
H_R–C(3) / H_S–C(15);
H_S–C(5) / H–C(21);
H_R–C(15) / H_S–C(17);
H–C(16) / H_S–C(17), H–C(20)

Figure. *NOESY Data of* **5** *and* **6** *supporting their absolute configuration.* $H_R = H_{pro\text{-}R}$, $H_S = H_{pro\text{-}R}$.

intermediate in the reactions leading to the rearranged compound **5** and the de(methoxycarbonylated) hydroxyindolenine **6** (*Scheme 2*), and the fact that it was not detected in the reaction mixtures indicates that it could not persist under basic conditions. This behaviour contrasts with that encountered for **2** which was slowly transformed into **6** under the same conditions.

Scheme 2



In view of the above considerations, the autooxidation of the iboga alkaloids with a methoxycarbonyl group gave the (7*R*)-hydroxyindolenines. Nevertheless, the straightforward epimerization at C(7) of **2** to give **6**, and considering that, in the autooxidation of the iboga alkaloids without the COOMe group at C(16), the side of the corresponding radical intermediate leading to the (7*S*)-alcohol is sterically less hindered, strongly

suggest the (*S*)-configuration at C(7) of the corresponding hydroxyindolenines. This hypothesis is supported by the fact that the autooxidation of ibogaine (**9**) [2] afforded a hydroxyindolenine whose m.p., and IR, EI-MS, and UV spectra were identical with those obtained from compound **6**.

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Experimental Part

1. *General*. Yields are given on reacted reagents. Column chromatography (CC): alumina *150* (neutral, *Merck*, type *T*, Art. 1101). TLC: *Polygram-Alox-N* chromatoplates; R_f measured using hexane/AcOEt 7:3 as the mobile phase; detection by a UV lamp and with *Dragendorff* and $FeCl_3/HClO_4$ spray reagents. M.p.: *Reichert-Thermovar* apparatus; uncorrected. UV Spectra: *Hewlett-Packard-HP-8254-A* diode array spectrophotometer; λ_{max} in nm, ε in $mol^{-1} \cdot l \cdot cm^{-1}$. IR Spectra: *Nicolet-5PC-FT* IR spectrometer; ν_{max} in cm^{-1}. NMR: *Bruker-AMX-400* (^1H at 400 and ^{13}C at 100 MHz) or *Bruker-AMX-500* (^1H at 500 and ^{13}C at 125 MHz) spectrometers; δ values in ppm, in $CDCl_3$ rel. to internal $SiMe_4$ (= 0 ppm); *J* values in Hz. Mass spectra (*m/z* (rel%)): *VG-Micromass-ZAB-2F* spectrometer at 70 eV.

2. *Oxidation of* **1** *to* **4**. To a stirred soln. of **1** (155 mg) in CH_2Cl_2 (1.7 ml), $Pb(OAc)_4$ (187 mg; molar ratio 1:1) was added at once. After 45 min, a 10% $NaHCO_3$ soln. was poured into the mixture, and after extraction with CH_2Cl_2, a crude residue (160 mg) was obtained. CC (2×5 cm column, hexane/AcOEt 17:3) yielded a mixture (16.6 mg) which was separated by prep. TLC. Hexane/AcOEt 17:3 eluated **1** (4.1 mg) and **4** (2.9 mg, 2%), and further elution with hexane/AcOEt 7:3 yielded **10** as a 3-epimer mixture (66 mg, 42%).

Data of 7-Epivoacangine Acetoxyindolenine (= *9α-Acetoxy-16,17-didehydro-9,17-dihydro-12-methoxy-ibogamine-18-carboxylic Acid Methyl Ester;* **4**): TLC: R_f 0.54 (yellow with $FeCl_3/HClO_4$). UV (MeOH): 284 (7943). ^1H-NMR (500 MHz): *Table 1*. ^{13}C-NMR (125 MHz): *Table 2*. EI-MS: 384 (8), 383 (4), 368 (100, $[M-OAc]^+$), 367 (78), 353 (20), 337 (7), 307 (14), 283 (12), 244 (30), 184 (23), 136 (47), 122 (26), 57 (47), 55 (75). HR-EI-MS: 368.210228 ($C_{22}H_{28}N_2O_3^+$; calc. 368.209993), 367.202377 ($C_{22}H_{27}N_2O_3^+$; calc. 367.202168).

3. *Treatment of* **2** *with Bases*. A soln. of **2** (22.1 mg) in 3 ml of a soln. of Na (103 mg) in MeOH (10 ml) was refluxed for 1 h. Then H_2O was added and the mixture extracted with $CHCl_3$. Prep. TLC (hexane/AcOEt 4:1) of the crude material (14.6 mg) provided **2** (5.4 mg), **5** (7.5 mg, 45%) and **6** (2 mg, 14%).

A mixture of **2** (17.5 mg), THF (1.5 ml), and *t*-BuOK (7 mg) was heated for 30 min in a water-bath at 55° while stirring. An additional amount of *t*-BuOK was added and the mixture left at r.t. for 3 h. Then H_2O was added and the mixture extracted with AcOEt to give a residue (13.6 mg) which, after prep. TLC (hexane/AcOEt 4:1), gave **2** (6.4 mg) and **6** (4.6 mg, 49%). A soln. of **2** (6.9 mg) and 10% KOH/MeOH (1 ml) was stirred at r.t. for 24 h. Then H_2O was added, the mixture neutralized with dil. HCl, soln. and extracted with $CHCl_3$, the extract evaporated, and the residue (5 mg) submitted to prep. TLC (hexane/AcOEt 4:1): traces of **2**, **6** (3 mg, 51%), and **7** (0.5 mg, 7%).

Data of Voacangine Pseudoindoxyl (= *Voaluteine*; **5**). Crystallized from MeOH as yellow needles. M.p. 190–194°. TLC: R_f 0.13. ^1H-NMR (500 MHz): *Table 1*. ^{13}C-NMR (125 MHz): *Table 2*. EI-MS: 384 (89, M^+), 368 (33), 355 (3), 325 (27), 244 (14), 209 (30), 162 (4), 136 (43), 122 (46), 109 (57), 55 (92).

Hydroxyindolenine **6** (= *16,17-Didehydro-9,17-dihydro-12-methoxyiboganin-9α-ol*). Crystallized from acetone as colourless prisms. M.p. 105–110°. TLC: R_f 0.28. UV (MeOH): 224 (12589), 284 (6309), 260 (sh), 290 (sh), 313 (sh). IR ($CHCl_3$): 3690, 3589, 3024, 2958, 2934, 2859, 1601, 1561, 1474, 1435, 1361, 1281, 1226, 1205, 1157, 1098, 1029, 979. ^1H-NMR (500 MHz): *Table 1*. ^{13}C-NMR (125 MHz): *Table 2*. EI-MS: 326 (100, M^+), 309 (53, $[M-OH]^+$), 269 (6), 225 (8), 202 (19), 189 (14), 136 (18), 122 (17), 94 (8), 55 (6). HR-EI-MS: 326.199455 ($C_{20}H_{26}N_2O_2^+$; calc. 326.199428), 309.193657 ($C_{20}H_{25}N_2O^+$; calc. 309.196689).

Hydroxyindolenine **7** (= *16,17-Didehydro-9,17-dihydro-9α-hydroxy-12-methoxyiboganine-18-carboxylic Acid*). TLC: R_f 0.072. UV (MeOH): 225 (5011), 273 (1995), 280 (sh), 310 (sh). ^1H-NMR (500 MHz): *Table 1*. EI-MS: 326 (30, $[M-CO_2]^+$), 325 (69, $[M-COOH]^+$), 314 (15), 309 (9), 308 (4), 217 (21), 205 (17), 190 (5), 174 (40), 162 (8), 135 (72), 122 (27), 109 (100), 55 (17). HR-EI-MS: 326.205376 ($C_{20}H_{26}N_2O_2^+$; calc. 326.199428), 325.198395 ($C_{20}H_{25}N_2O_2^+$; calc. 325.191603).

4. *Hydroxyindolenine* **6** *from* **3** *or* **4**. Compound **3** (2.3 mg) or **4** (2.0 mg) was treated with 10% KOH/MeOH (1 ml) for 3 and 7 days, resp., at r.t. with stirring. Both mixtures were extracted with $CHCl_3$, and the product was purified by prep. TLC (hexane/AcOEt 4:1): **6** (1.2 mg (40%) and 0.9 mg (35%), resp.).

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