Tetrahedron Letters No. 27, pp 2763 - 2766, 1972. Pergamon Press. Printed in Great Britain.

ABSOLUTE CONFIGURATION OF THE IBOGA AND VOACANGA ALKALOIDS: CHIROPTICAL APPROACH

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(Received in UK 19 May 1972; accepted for publication 31 May 1972)

In the past, much effort has been focused on the solution of the problem of the configurations of the iboga alkaloids[1]. The present knowledge in this field is based on two independent X-ray diffraction studies dealing with cleavamine methiodide[2](prepared[3] from catharanthine (IV))and with the dimeric leurocristine methiodide[4]. The same absolute configuration on the corresponding atoms was found in both compounds. On the other hand, the enantiomeric configuration was suggested for a degradation product of ibogaine (IX) by means of optical rotatory dispersion measurements[5]. However, at that time, this finding was considered not fully convincing. Finally, the series of reactions correlating catharanthine (VI) with coronaridine (I) and ibogamine (VIII) were published[6,7]. Since the optical activity of the resulting coronaridine and ibogamine is not known, these correlations cannot be exploited for the absolute configuration studies.

In the present communication we wish to report on our circular dichroism (CD) studies[x] of several alkaloids with the ibogamine skeleton (Table I) which enabled us to determine the absolute configuration of this class of indole alkaloids. Three groups of Cotton effects can be distinguished on CD curves of the methoxycarbonyl derivatives I - VII. Coronaridine (I), without a methoxyl substituent on the aromatic ring, exhibits a triplet of partially overlapping negative dichroic bands between 295 - 270 nm, a second triplet of positive bands at about 240 - 250 nm and a negative dichroic band at

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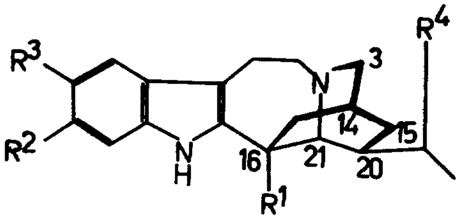
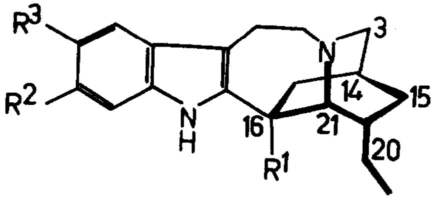
[x] The CD curves were measured on the Dichrograph Jouan 185 (II) in methanol (c = 0.1 - 0.2) using 0.05 - 0.1 cm cells.



Coronaridine (I);	$R^1 = COOCH_3$, $R^2 = R^3 = R^4 = H$, $(16\underline{S}, 20\underline{S})$
Conopharyngine (II);	$R^1 = COOCH_3$, $R^2 = R^3 = OCH_3$, $R^4 = H$, $(16\underline{S}, 20\underline{S})$
Isovoacristine (III);	$R^1 = COOCH_3$, $R^2 = OCH_3$, $R^3 = H$, $R^4 = OH$, $(16\underline{S}, 20\underline{R})$
Isovoacangine (IV);	$R^1 = COOCH_3$, $R^2 = OCH_3$, $R^3 = R^4 = H$, $(16\underline{S}, 20\underline{S})$
Voacangine (V);	$R^1 = COOCH_3$, $R^2 = R^4 = H$, $R^3 = OCH_3$, $(16\underline{S}, 20\underline{S})$
Ibogamine (VIII);	$R^1 = R^2 = R^3 = R^4 = H$, $(16\underline{R}, 20\underline{S})$
Ibogaine (IX);	$R^1 = R^2 = R^4 = H$, $R^3 = OCH_3$, $(16\underline{R}, 20\underline{S})$
Tabernanthine (X);	$R^1 = R^3 = R^4 = H$, $R^2 = OCH_3$, $(16\underline{R}, 20\underline{S})$
Iboxygaine (XI);	$R^1 = R^2 = H$, $R^3 = OCH_3$, $R^4 = OH$, $(16\underline{R}, 20\underline{R})$
Heyneanine (XIII)	$R^1 = COOCH_3$, $R^2 = R^3 = H$, $R^4 = OH$, $(16\underline{S}, 20\underline{R})$



Catharanthine (VI);	$R^1 = COOCH_3$, $R^2 = R^3 = H$, $\Delta^{15,20}$, $(16\underline{R})$
Dihydrocatharanthine (VII);	$R^1 = COOCH_3$, $R^2 = R^3 = H$, $(16\underline{R}, 20\underline{S})$
Epiibogamine (XII);	$R^1 = R^2 = R^3 = H$, $(16\underline{S}, 20\underline{S})$

215 nm. Compounds II - V, substituted in various positions of the aromatic ring with methoxyl groups, display an analogous dichroic absorption pattern with all bands shifted to longer wavelengths. Catharanthine (VI) and its dihydroderivative VII show dichroic bands in the same positions as coronaridine (I) but, surprisingly, all of them with reversed sign. All the natural compounds without the methoxycarbonyl substituent on $C_{(16)}$ which were studied (VIII - XI) show CD curves similar in all respects to those of bases I - V. On the contrary epiibogamine (XII), the product of catalytic hydrogenation[6,8] of catharanthine (VI), exhibits Cotton effects of the same sign as VI and VII.

From these findings we have to conclude that the natural alkaloids I - V, VIII - - XI and all other alkaloids correlated with them stereochemically (e.g. heyneanine[9] (XIII)) possess the enantiomeric absolute configuration to catharanthine (VI), the absolute configuration of which is unequivocally known[2] from anomalous X ray diffraction of cleavamine methiodide.

TABLE 1 CD Characteristics

Alkaloid	λ_{max} ($\Delta\varepsilon$)			
I	-	296(-2.1),288(-5.6), 277(-8.1),272(-9.3)	242(+5.0),231(+2.4) 227(+3.3)	215(-2.6)
II	311(-1.6)	293(-2.5),280(-4.0)	244(+3.8)	225(-2.4)
III	298(-4.0)	285(-2.6),276(-3.8)	249(+3.0),236(+5.7)	219(-1.4)
IV	320(-0.4),316(-1.2), 307(-3.7)	301(-4.4),286(-2.5), 277(-2.9)	250(+4.5),239(+5.7)	217(-1.5)
V	312(+0.7)	281(-5.0)	251(+2.5)	225(-1.5)
VI	-	293(+0.8),286(+1.9), 278(+2.8),270(+3.2)	242(-0.25)	219(+3.3)
VII	-	295(+2.5),281(+3.5), 275(+3.7)	240(-1.6),229(-2.9), 221(-0.7)	217(+1.5)
VIII	-	288(-0.4)	238(+7.5)	218(-8.9)
IX	308(+0.75)	280(-1.9)	242(+13.8)	220(-6.5)
X	-	297(-1.4)	239(+5.7)	221(-5.8)
XI	308(+0.25)	279(-1.0)	238(+6.0)	217(-6.6)
XII	-	292(+0.25)	245(-2.3),236(-6.2)	220(+5.0)

The full paper will be published in Collection of Czechoslovak Chemical Communications.

Acknowledgement: We wish to express our sincere thanks to Prof. N. R. Farnsworth (College of Pharmacy, University of Illinois, Medical Center, Chicago, Illinois) and to Drs M. Gorman and G. H. Svoboda (Eli Lilly and Co., Indianapolis, Indiana) for the generous gift of some alkaloid samples.

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