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THE STEREOCHEMISTRY OF SPIROPACHYSINE

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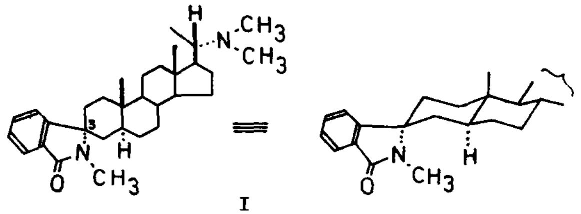
In the previous paper (1) the structure of spiropachysine, a novel alkaloid from Pachysandra terminalis SIEB. et ZUCC., was assigned to the formula I. However, the stereochemistry at the 3-position was remained uncertain. Now a study of circular dichroism (CD) has enabled the C_3 configurational assignment to be made for spiropachysine.

As seen in Table, the CD spectra of both spiropachysine (I) and deoxospiropachysine (II), a $LiAlH_4$ reduction product of spiropachysine, exhibit multiple Cotton effects due to the aromatic transition in about 300-230 mμ region.

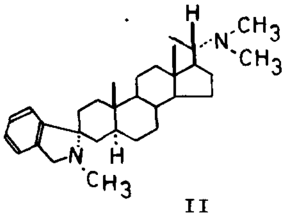
An ORD study on hydrastine-narcotine alkaloids (IIIa, IIIb, IVa and IVb) having a phthalide system, which can be regarded as an analogous system to the phthalimidine moiety in spiropachysine, has been reported by Ohta et al. who found that the longest wavelength Cotton effect centered at about 310 mμ was negative for IIIa and IIIb in contrast to the positive sign for IVa and IVb, reflecting the absolute configuration at C_9 (2). The lactone oxygen atom in the phthalide moiety of these compounds and the lactam nitrogen in spiropachysine would have the similar contribution to the $\pi-\pi^*$ aromatic transition since they locate at the same position in a five membered ring of almost planar conformation. Also two methoxyl substituents on the phthalide would be expected to exert no influence on the sign of the longest wavelength Cotton effect. It is therefore expected that the same steric relationship at the benzylic asymmetric carbon atoms will give the same sign for the longest wavelength Cotton effect.

In order to make a direct comparison we measured CD curves of the above compounds (Table) and obtained a result in accord with the Ohta's observation (2): i.e., the longest wavelength Cotton effects of IIIa and IIIb having the 9S configuration are negative whereas those of IVa and IVb with 9R configuration are positive. Since spiropachysine presents the negative sign for the corresponding Cotton effect (279 mμ), it can reasonably be related with IIIa and IIIb, thus being assigned to the structure I (C_3-C_4 bond is more bulky than C_3-C_2 bond) (3).

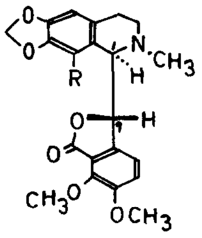
A support for this assignment was obtained by the comparison with the CD spectra of oxindole alkaloids. It has been reported that the sign of the longest wavelength Cotton effect (about 290 mμ) in a series of oxindole alkaloids is governed by the configuration of C_7 spiro carbon atom; for instance, isomitraphylline (V) gives the negative Cotton effect at 285 mμ while mitraphylline (VI) the positive one at 290 mμ (4,5,6). Since the nature of the longest wavelength transition of aromatic chromophore in oxindoles is considered as similar to that of phthalimidine chromophore in spiropachysine, the configuration of the C_3 spiro carbon atom in the latter base would be assigned as the same as the C_7 configuration in isomitraphylline (V) with the same negative Cotton effect (C_7-C_3 bond is more bulky than C_7-C_6 bond): hence the phenyl group in spiropachysine is β.



I

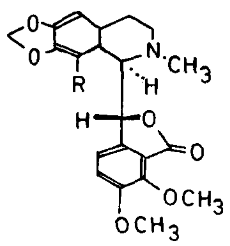


II



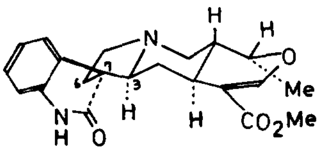
IIIa: R=H

IIIb: R=OCH_3

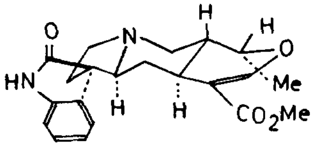


IVa: R=H

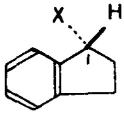
IVb: R=OCH_3



V



VI



VII

Table

CD data*

Compound	Solvent	Molecular Ellipticity λ_{max}(mμ) ($[\theta]$)
Spiropachysine (I)	M	279(-1680) 274^{sh}(-700) 250(+1960)
Deoxospiropachysine (II)	D	273(-590) 266(-560)
1-β-Hydrastine (IIIa)	M	315(-10900) 304(-12100) 273(-12000) 220(+48000)
1-α-Narcotine (IIIb)	M	313(-14000) 252^{sh}(-13500) 240(-37800)!
1-α-Hydrastine (IVa)	M	302(+10000) 278(-4000) 256(+3000) 235(-61000) 216(-118000)
1-β-Narcotine (IVb)	M	318(+2600) 270(+3400) 240(-29200)

* The CD spectra were recorded on a JASCO ORD UV-5 spectropolarimeter.
M: methanol; D: dioxane; ! : last reading

We further examined the CD curve of deoxospiropachysine (II) (Table) in comparison with those of optically active 1-R-substituted indanes (VII: X=NH_2, $NHCH_3$, $N(CH_3)_2$, CH_2OH, COOH, OH, etc.). A recent study by Brewster et al. (7) has revealed that these compounds possess the multiple Cotton effects in the region 300-250 mμ and the Cotton effects associated with the longest wavelength band (α-band) at about 270 mμ are positive.

The optical nature of α-band of the isoindoline nucleus in deoxospiropachysine (II) would be the same as that of indane (VII) because the nitrogen atom in the five membered ring in II locates on the local symmetry axis of the aromatic chromophore. It follows that the opposite sign for the above two chromophores suggests the opposite stereochemistry at the benzylic asymmetric carbon. Deoxospiropachysine (II) with negative Cotton effect at 273 mμ can therefore be related to 1-S-indanes; supporting the 3β-phenyl configuration at C_3.

These observations confirm the structures of spiropachysine and deoxospiropachysine as represented by I and II, respectively.

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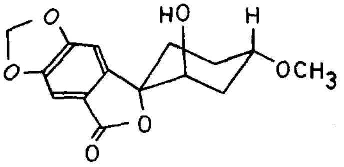
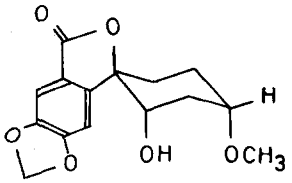
3) It should be noted in this connection that Highet et al. obtained two lactones (VIIIa, VIIIb) by the performic acid treatment of *d*-6-(4'-methoxycyclohexenyl)-piperonylic acid and showed their ORD curves of opposite character, but it seems that the correct structures of the two lactones are their enantiomeric forms respectively; see R. J. Highet, J. C. N. Ma, and P. F. Highet, *J. Org. Chem.*, **33**, 3096 (1968).



VIIIa: + Cotton effect



VIIIb: – Cotton effect

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