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DIMERIC INDOLINE ALKALOIDS OF A NEW BIPHENYL TYPE [1,2]

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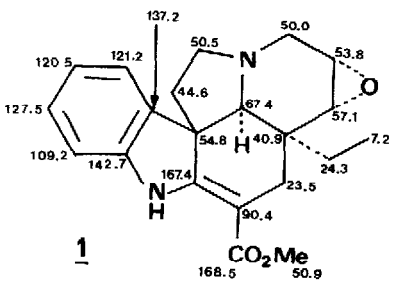
Abstract: A ^{13}C NMR analysis of lochnericine and the new alkaloids peceyline, peceylanine and pelankine is presented and the structures of the indoline dimers described.

The Apocynaceae plant Petchia ceylanica Wight, indigenous to the lowlands of Sri Lanka, has yielded inter alia lochnericine (1)[3] and the new alkaloids peceyline, peceylanine and pelankine.[4] In view of an earlier ^{13}C NMR analysis of pachysiphine (2) (tabersonine β-epoxide)[5] it was of interest to inspect lochnericine (1) (tabersonine α-epoxide) by the same spectroscopy. As the chemical shifts on the formulas 1 and 2 portray,[6] the epoxide stereochemistry change causes several shift alterations. However, the shielding of the aminomethine and of the methylene of the ethyl sidechain by the epoxide oxygen in lochnericine is stereochemically most diagnostic.



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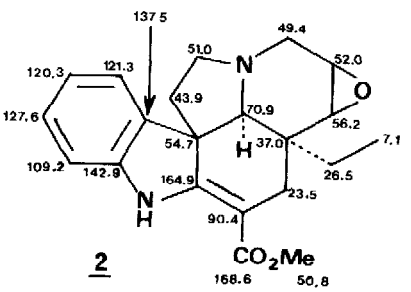

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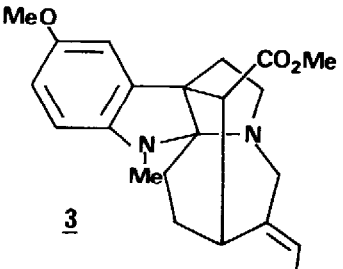
Peceyline, peceylanine and pelankine are dimeric indoline alkaloids whose structure analysis by ^{13}C NMR spectroscopy is the subject of the present communication. Their ^{1}H NMR spectra had shown each compound to exhibit four aromatic hydrogen singlets, one olefinic hydrogen multiplet and sets of two carbomethoxy singlets, N-methyl singlets and C-methyl doublets.[4] The ^{13}C NMR spectra now revealed a half of the non-aromatic carbon resonances to be common to the three sustances, indicative of the presence of a common monomer unit. The trisubstituted double bond carbon resonances were identified by the residual long-range coupling to aliphatic hydrogens in the SFORD spectra[7] (aromatic methines remaining sharp one-bond doublets at all values of J_R) and the assignment of the olefinic methine confirmed

by ^{1}H-^{13}C cross-correlations.[8] The latter experiment revealed also the attachment of the C-methyl group to the olefinic methine.

In addition to the thus-discovered ethylidene unit and O-and N-methyl groups the saturated carbons found common to the three alkaloids corresponded to two aminomethylenes, three dialkylmethylenes, two methines and two non-protonated carbon sites. The chemical shift (97.5 ppm) of one of the latter carbons was characteristic of a center attached to two heteroatoms. All these facts were reminiscent of the structure of vincorine (3). Comparison of the non - aromatic carbon shifts of the latter[9] with the non - aromatic carbon signals present in the spectra of each of the dimeric alkaloids identified one monomer unit as the vincorine system and showed it to be attached to the other half of the molecular framework through its aromatic ring.



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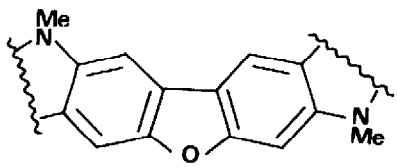

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Peceyline and peceylanine revealed identical non aromatic carbon shifts, except for the latter's extra, two, aromatic methoxy resonances (55-58 ppm), indicative of the identity of the second monomer unit in the two bases. This portion of the skeleta exhibited a striking spectral resemblance, in non-aromatic carbon shifts and multiplicities, to the vincorine unit except for the replacement of the trisubstituted double bond by an oxymethine and a non-proton ated oxycarbon and the consequent shift perturbations of neighboring carbon sites. Since the one-bond, carbon - hydrogen coupling constant (170 $\pm$ 3 Hz) of the oxymethine showed it to be part of a three-membered oxide ring, the second monomer unit of the two alkaloids was vincorine oxide. Whereas the shift data did not permit an unequivocal assignment of the epoxide stereochemistry, it showed the two halves of peceyline and peceylanine to be linked to each other via their benzene rings.

The molecular composition of peceyline,[4] the number, field position and multiplicity of its aromatic carbon resonances and the shielding characteristics of the ortho substituents of its aromatic methines, as revealed by their proton shifts,[4] limited the mode of attachment of the two monomer units to the form of an unsymmetrically substituted dibenzofuran system (4). Hence the structure of peceyline is as depicted in formula 5 or its epoxide/double bond interchange isomer.

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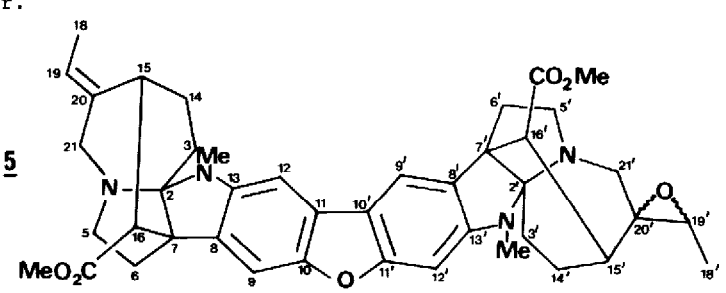
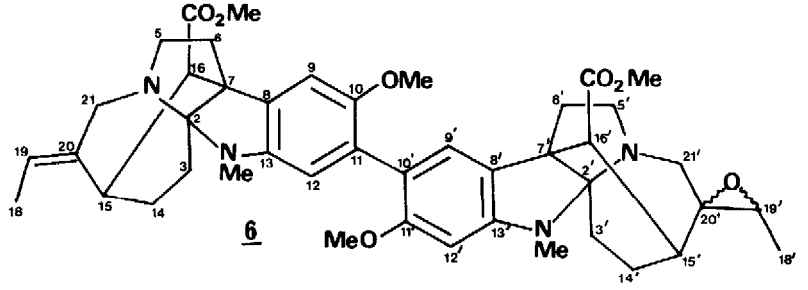


The ^{13}C NMR spectra of peceylanine revealed an aromatic carbon shift pattern similar to that of peceyline. Since the ^{1}H NMR spectra of peceylanine had exhibited an aromatic hydrogen singlet pattern indicative of a lack of symmetry of substitution between the two benzene rings,[4] the methoxy group in one ring had to be para to nitrogen and the methoxy function on the other indoline unit disposed in a meta orientation to its nitrogen. The carbon shifts of the aromatic methines were in accord with this argument.[10] Thus the structure of peceylanine is as illustrated in formula 6 or its epoxide/double bond interchange isomer.



6

Half of the aromatic carbon signals in the spectra of peceyline were reproduced in those of pelankine. This fact, the identity of the molecular composition of the two bases[4] and the aromatic hydrogen singlets pattern of pelankine[4] indicated the latter to possess the unsymmetrically substituted dibenzofuran structure of peceyline, but to differ from its congener by the nature and/or amount of substitution of one or both of the saturated carbons of its non - vincorine indoline moiety. The aromatic carbon shift pattern of pelankine permitted the differentiation of the resonances of the vincorine half from the other monomer unit in this substance and the total aromatic carbon shift assignment for pelankine ans peceyline. Thus, for example, the high field position of the aromatic methines with common shifts(94 and 107 ppm) in the two bases signified o-heteroatom substitution and hence a para relationship between the furan oxygen and indoline nitrogen in the vincorine monomer unit. Similarly, the field positions (ca.91 and 113 ppm) of the remaining aromatic methines, indicative of one with two o-heteroatom substituents and the other with none, showed a meta relationship between the heteroatoms in the non-vincorine moiety.

The non-aromatic part of the non-vincorine monomer unit of pelankine differed from the other half of the alkaloid skeleton by the replacement of the non-protonated diaminocarbon and a methylene group by two aminomethines. One of the latter exhibited a 79.3 ppm signal reminiscent of the C(2) resonance of ajmaline-like substances.[10] The non-vincorine N-methyl group was deshielded by ca.6 ppm with respect to the like function in the other alkaloids, indicative of less sustitution on the saturated carbon to which the methylamino group was attached. These facts were compatible with a deacetyl deformyl 1-methyl-1,2 β-dihydroakuammiline structure[11] for the non-vincorine monomer unit and leads to the overall structure of pelankine as outlined in formula 7.

The carbon shifts of the three new bis - indoline bases are listed in the Table.

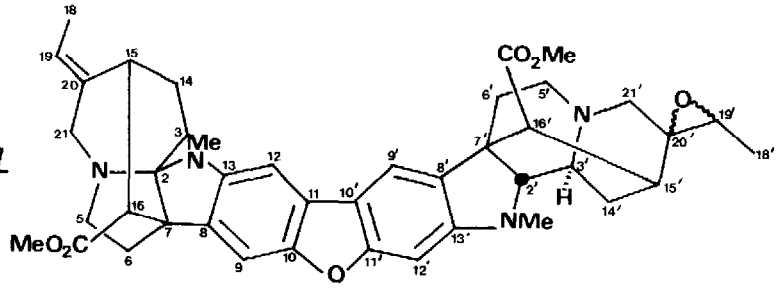


Table . Carbon shifts of Peceyline, Peceylanine and Pelankine[a]

	5	6[b]	7		5	6[b]	7		5	6[b]	7		5	6[b]	7
C(2)	97.5	97.2	97.5	C(13)	145.3	143.2	145.4	C(2')	96.3	96.3	79.3	C(13')	148.7	149.2	152.9
C(3)	41.4	41.4	41.3	C(14)	26.3	26.1	26.3	C(3')	41.4	40.7	53.8	C(14')	25.0	24.9	33.4
C(5)	54.8	54.8	54.9	C(15)	34.6	34.5[d]	34.7	C(5')	54.8	54.8	49.9[e]	C(15')	39.0	38.9	39.3
C(6)	20.5	20,4	20.6	C(16)	50.9[c]	50.7[d]	51.1	C(6')	21.4	21.2	33.1	C(16')	51.1[c]	50.5[d]	47.0
C(7)	57.0	57.2	57.1	C(18)	13.5	13.4	13.5	C(7')	56.1	56.0	42.5	C(18')	14.6	14.4	15.8
C(8)	134.7	135.6	135.1	C(19)	121.9	121.7	122.0	C(8')	131.8	127.6	135.8	C(19')	63.1	63.1	65.5
C(9)	107.1	108.5	107.4	C(20)	138.9	138.0	139.0	C(9')	114.6	126.2	112.5	C(20')	63.7	63.8	65.8
C(10)	148.9	149.2	149.3	C(21)	58.2	58.2	58.3	C(10')	114.1	115.7	116.3	C(21')	56.8	56.8	55.7[e]
C(11)	123.8	127.3	123.5	C=O	173.6	173.5	173.5	C(11')	157.7	156.8	156.7	C = O	173.5	173.3	173.1
C(12)	93.8	110.4	94.1	OMe	51.5	51.3	51.5	C(12')	88.5	89.9	93.1	OMe	51.4	51.3	51.4
				NMe	27.9	27.7	27.8					NMe	27.1	27.1	33.8

[a] In $CDCl_3$ solutions; δ values in ppm downfield form TMS ; δ TMS = δ ($CDCl_3$) + 76.9 ppm [b] Aromatic OMe shifts are 55.5 and 57.3 ppm. [c,d,e] Shifts with identical superscripts may be reversed.

References and Notes

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