ON ALKALOIDS. XXVI.*

CHIROPTICAL PROPERTIES OF 2-ACYLINDOLE ALKALOIDS, THE SUBGROUP OF 5,16-CYCLO-3,4-SECOCORYNANE

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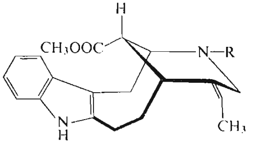
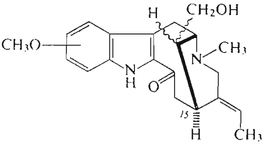
Circular dichroism spectra of vobasine (*I*), dregamine (*II*), tabernaemontanine (*III*), perivine (*IV*), periformyline (*V*), and pelirine (*VI*) were measured. All these alkaloids possess the same absolute configuration and all lack any perceivable transannular interaction between the carbonyl group and the $N_{(4)}$ nitrogen atom.

In connection with systematic investigations on chiroptical properties of indole alkaloids[1-5], the circular dichroism (CD) of some naturally occurring 2-acylindoles of the subgroup of 5,16-cyclo-3,4-secocorynane (for nomenclature and numbering[6,7]) was measured, namely, of vobasine[8] (*I*) and its epimeric dihydro derivatives dregamine[8] (*II*) and tabernaemontanine[8] (*III*), then perivine[9,10] (*IV*), periformyline[11,12] (*V*), and pelirine[13] (*VI*; the structure has not been fully elucidated[14]). The accordance of the dichroic band data (Table I) of substances *I* – *V* confirms the identi-



I-V



VI

I, R = CH_3
II, R = CH_3; 19,20-dihydro; 20 αH
III, R = CH_3; 19,20-dihydro; 20 βH
IV, R = H
V, R = CHO

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* Part XXV: Lloydia *35*, 61 (1972).

TABLE I

Dichroic Bands of Alkaloids *I*–*VI*

Compound	λ, nm (Δε)						
I	359 (+0·65)	348 (−0·82)	308 (−5·90)	265 (+0·25)	248 (−2·54)	234 (+0·75)	214 (+6·11)
II	360 (+0·55)	348 (−0·8)	309 (−10·0)	267 (+0·4)	248, 244 (−2·6, −2·4)	230 (−1·2)	—
III	363 (+0·5)	350 (−0·85)	309 (−7·75)	266 (+0·9)	248 (−5·1)	—	—
IV	362, 357 (+0·19, +0·43)	348 (+0·14)	306 (−3·75)	265 (+0·11)	247 (−2·10)	—	—
V	357 (+1·2)	348 (+0·65)	307 (−8·4)	270, 263[a] (0·7, −0·25)	248 (−6·5)	233 (+2·7)	229 (+2·1)
VI	370 (+0·50)	356 (−1·69)	336 327 (−9·95) (−10·9)	272 261 (+2·20) (+2·45)	246[b] (+2·5)	238 (+2·0)	208 (+25·0)

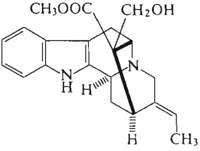
[a] Positive Cotton effect; [b] positive minimum.

TABLE II

Principal Maxima in Ultraviolet Spectra of Compounds *I*–*VI* in Methanol

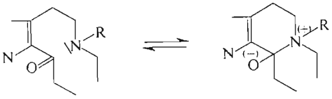
Compound (ref.)	*I* (ref.[8])	*II* (ref.[28])	*III* (ref.[29])	*IV* (ref.[23])	*V* (ref.[30])	*VI* (ref.[31])
λ_{max} nm (log ε)	239 (4·19) 315 (4·27)	239 (4·18) 316 (4·27)	238 (4·16) 315 (4·22)	227 (4·20) 240 (4·15) 313 (4·21)	240 (4·18) 314 (4·29)	~230 sh (4·24) 327 (4·34)

cal absolute configuration of these bases as unequivocally determined earlier with the use of chemical intercorrelations[8,10] and allotment[10] to the pentacyclic alkaloid akuammidine (*VII*) the absolute configuration of which has been defined by three-dimensional X-ray analysis[15,16].



VII

The chiroptical properties of substances are often influenced even by small structural changes in the neighbourhood of the chiral chromophore. In this respect, the circular dichroism might be expected to constitute a sufficiently sensitive method to detect in compounds *I*–*V* any transannular interactions[17] between the C=O group and the $N_{(4)}$ atom. Similar interactions have been observed in the case of compounds possessing rings of the medium size, namely, protopine[18–20], N-methylpseudostrychnine[18] or othonecine[21] (for the use of optical rotatory dispersion to detect this effect see ref.[22]). The normal ν(C=O) values in infrared spectra of 2-acylindoles (thus *e.g.*, ν(C=O) of perivine *IV* in chloroform[23] is equal to 1655 cm^{-1}) suggest[14,24] the absence (for some exceptions see voacarpine[25] or epiperivine[10]) of such an interaction in less polar solvents; in more polar solvents (methanol), the proportion of the dipolar form *B* in the equilibrium mixture can be higher[26]. The nucleophilicity of the nitrogen atom is also strongly influenced by the nature of the substituent[27] R. In addition to substances with a tertiary amino group (compounds *I*–*III*, *VI*), we have therefore included into our investigations the analogue *IV* (secondary amino group) and the N-formyl derivative *V* which is supposed to be free of any transannular interaction.



A *B*

The CD curves of substance *I*–*V* (Table I) agree in every respect (except of the sign of some weak bands at 348 nm) and in principal dichroic bands correspond with ultraviolet spectra (Table II). This observation suggests the structural similarity of the chromophoric system and the absence of any transannular interaction in our substances, at least in aqueous methanol. Such conformations[32] which are closely related to that of vobasine (*I*) (determined by three-dimensional X-ray analysis[33]) are probably preferred. The CD curve of pelirine (*VI*) is also very similar to the curves mentioned above. Its principal Cotton effects in the long wavelength region correspond with extrema occurring in the appropriate ultraviolet spectrum[31] (Table II). Because of the substitution by the methoxyl group however, a bathochromic shift may be observed in comparison with the remaining five alkaloids but the sign fully corresponds to the Cotton effects at 309, 348, and 360 nm of other alkaloids. On the basis of these findings, pelirine (*VI*) has the absolute configuration with an α-oriented hydrogen atom at the $C_{(15)}$ carbon atom, *i.e.*, the same configuration as with alkaloids *I* – *V* and almost all alkaloids derived from the non-rearranged secologanine precursor[34].

Materials. Vobasine (*I*), dregamine (*II*), tabernaemontanine (*III*), perivine (*IV*), periformyline (*V*), and pelirine (*VI*) have been reported in the literature[14,24]. The measurements were performed with the use of authentic samples.

Spectroscopic measurements. The CD curves were taken on a Jouan 185 (II) dichrograph in methanol (*c* 0·05) with the use of 0·05 – 1 cm cells.

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Note added in proof: Quite recently we had occasion to measure the CD curves of further alkaloids of the type as studied in the present paper — ochropamine and 16-epiochropamine (formula *I*, methyl group on the indole nitrogen), both kindly supplied by Professor J. Le Men, University of Reims, France. The curves were measured in methanol under the conditions given above. *Ochropamine*: max. 372 nm ($\Delta\varepsilon$ +0·44), 357 (−1·5), 333 (−1·4), max. 310 (−11·3), max. 270 (0, positive band), max. 253 (−3·2), 240 (+2·1), 232 (+2·7), 220 (+10, end value). 16-*Epiochropamine*: 372 (+0·73), 355 (−1·4), 358 (−1·5), max. 326 (−8·8), max. 272 (+2·73), max. 250 (−22), 240 (0, cross point), 230 (+0·8), 220 (+7·0, end value). The over-all similarity of the measured curves of both the recently studied alkaloids with the curves reported in the present paper is evident. We therefore conclude that the absolute configuration of both ochropamine and its 16-epimer is most probably the same as that of vobasine (*I*).