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CIRCULAR DICHROISM STUDIES—I

A QUADRANT RULE FOR THE OPTICALLY ACTIVE AROMATIC CHROMOPHORE IN RIGID POLYCYCLIC SYSTEMS

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Abstract—The CD spectra of a number of rigid aromatic compounds containing an asymmetric center adjacent to the aromatic ring are reported. From the CD spectra of compounds of known absolute configuration it has been possible to devise a quadrant rule which predicts the absolute configuration of molecules possessing an asymmetric center adjacent to the aromatic ring. The rule has been tested with representative members of the indole, Amaryllidaceae, morphine, and isoquinoline type alkaloids of known absolute configuration.

MODERN approaches to the determination of the absolute configuration of a dissymmetric molecule include X-ray crystallographic methods, spectral techniques (ORD and CD), and chemical degradation of the substance to a compound of known absolute configuration. While ORD and CD measurements may afford a rapid assignment, the method is frequently prone to misinterpretation. Our original interest in absolute configuration of natural products was stimulated by the observation that (−)-crinane (**1a**) and (+)-powellane (**1b**), although chemically inter-related and known to be of the same absolute configuration, showed optical rotatory dispersion (ORD) spectra which were antipodal from 700 mμ to 300 mμ.[1] With access to ORD and CD instruments which extend considerably further into the ultraviolet, our initial research concentrated on this problem and included other readily available Amaryllidaceae alkaloids. Circular dichroism was chosen to study the Cotton effects associated with the optically active aromatic ring. This approach allows one to examine the effects of a benzylic asymmetric center on the aromatic chromophore in the presence of other overlapping chromophores.[2] With minor exceptions all Amaryllidaceae alkaloids contain an asymmetric benzylic C atom.

The alkaloids of the Amaryllidaceae contain, almost invariably, either an allylic OH or OMe group, and initial assignments of absolute configuration have been based on Mills' rule[3] or on Klyne's modification of the Hudson lactone rule.[4,5] Recent X-ray crystallographic examinations of dihydrolycorine (**2**, no double bond C_3—C_{3a})[6] and galanthamine (**3**)[7] as well as chemical degradations of tazettine (**4b**)[8] have shown the absolute configurations assigned originally by Mills' rule to be correct.

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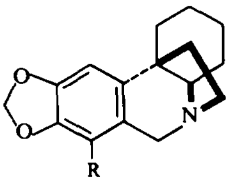
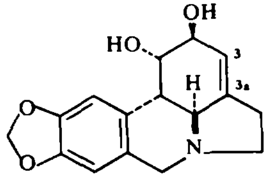


1

a: R = H

b: R = OMe



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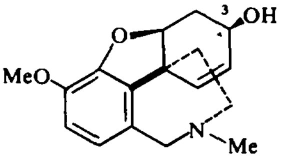

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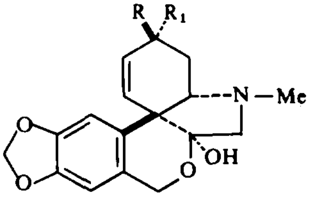

4

a: R = H, R_1 = OMe

b: R = OMe, R_1 = H

RESULTS AND DISCUSSION

The first member of the 5,10b-ethanophenanthridine system to be studied was crinine (**5a**). Crinine and most members of this series containing the methylenedioxyphenyl chromophore give rise to UV maxima at 296 mμ and 240 mμ ($A_{1g} \rightarrow B_{2u}$ and $A_{1g} \rightarrow B_{1u}$ transitions, respectively). The CD spectrum (Fig. 1) of this compound shows a negative max at 295 mμ and a positive max at 240 mμ, both of which correspond to the maxima observed in the UV. In the great majority of compounds we have studied, the benzene ring gives rise to antipodal CD signals for the two bands discussed. We refer to a CD spectrum which shows an antipodal relationship between these aromatic ellipticities as "standard". When ORD and CD spectra do not cross the axis, "non-standard" spectra are obtained which can provide erroneous results.

The amplitude of the aromatic dichroism decreased markedly in progressing from crinine to dihydrocrinine (**5a**, no double bond C_1—C_2) to crinane (**1a**) (Fig. 1). Similar changes are observed in all alkaloids of this ring system when the C_1—C_2 unsaturation is removed. This decrease may be due in part to a conformational change in ring C upon removal of the double bond. However, this structural modification cannot account for the entire magnitude change since there should be no significant conformational alteration of ring C in dihydrocrinine and crinane. NMR data have shown that shielding of the C_1 olefinic proton is due to the increased electron density at this center contributed by the benzene ring. This is particularly noticeable in the C_7-aromatic methoxy compounds. Molecular models show that the double bond and aromatic system are in close proximity.*

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* Removal of what may be a homoconjugated system in crinane may be responsible for this decrease.[9]

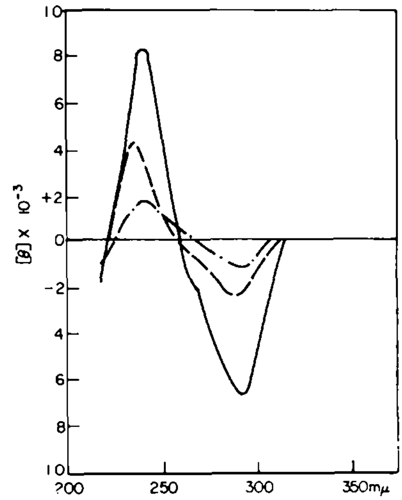
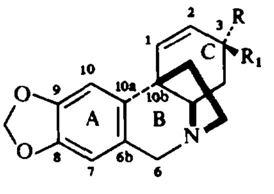
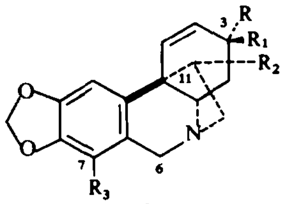


FIG. 1 CD spectra of: ——— crinine, — — — dihydrocrinine, —·—· crinane.



5

a: $R = OH; R_1 = H$
b: $R = H; R_1 = OH$
c: $R = OMe; R_1 = H$
d: $R = H; R_1 = OMe$



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a: $R,R_2,R_3 = H; R_1 = OH$
b: $R_1,R_2,R_3 = H; R = OH$
c: $R,R_3 = H; R_1 = OMe, R_2 = OH$
d: $R_1,R_3 = H; R = OMe, R_2 = OH$

(—)-Epicrinine (**5b**) has a CD spectrum similar to that found for crinine. However, the magnitudes of the ellipticities are less than those observed in **5a**. This decrease in magnitude appears to be a general phenomenon for alkaloids related to **5** and **6** when the configuration of the substituent at C_3 is changed from *quasi* axial to *quasi* equatorial. The same effect has been observed for a number of epimeric pairs including vittatine (**6a**)-epivittatine (**6b**), haemanthamine (**6c**)-crinamine (**6d**), buphanisine (**5c**)-(—)-epibuphanisine (**5d**),* tazettine (**4b**)-criwelline (**4a**), and powelline (**5a**, —OMe at C_7)-epipowelline (**5b**, —OMe at C_7). This difference in magnitude can be quite useful for the stereochemical assignment of the group at C_3 in these alkaloids, particularly in cases where both epimers are available.

Buphanisine (**5c**) affords a CD spectrum similar in shape to that of crinine but with increased magnitude. This may be due to the OMe group at C_3 contributing to the

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* Neither (—)-epibuphanisine nor (+)-buphanisine has been reported in the chemical literature. The reported spectra result from the inversion of those found for the known (+)-epibuphanisine and (—)-buphanisine. We are indebted to Dr. D. Stauffacher, Sandoz, A.G. Basle for an authentic sample of the former.

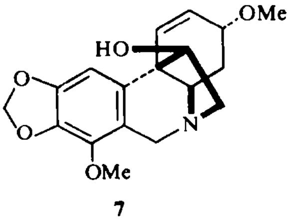
benzene dichroism. The 2000 difference in ellipticity at 294 mμ between buphanisine and crinine suggests that either the bulk or proximity of a functional group may, in certain cases, affect the magnitude of the aromatic dichroism. (−)-Epibuphanisine (**5d**) affords a spectrum of lower magnitude than that of buphanisine. This is in accord with results we have obtained previously for epimeric pairs of alcohols.

Haemanthamine (**6c**) differs from (+)-buphanisine by the presence of an added OH function at C_{11} in the former. The CD spectrum of haemanthamine is of higher magnitude than that of (+)-buphanisine at 300 mμ. This can be attributed to the presence of the C_{11}-OH in **6c**. It is well known that, when functional groups containing non-bonding or π-electrons are removed, the size of the ellipticities decreases.[2] The exact reason for the phenonemon is not yet known.

Crinamine (**6d**) shows a dichroism spectrum which has qualitatively the same shape as that of haemanthamine. However, in agreement with our findings in other C_3-epimeric series, the magnitude of the dichroism is considerably decreased in the crinamine series. Crinamine may also be considered the C_{11}-OH analog of (+)-epibuphanisine. The additional OH group results in increased magnitude for the benzene dichroisms as was observed previously. The dihydro derivatives of haemanthamine and crinamine afford CD spectra with the expected decreased magnitude.

The CD spectrum of powelline (**5a**, —OMe at C_7) is unusual since the ellipticity at 290 mμ is much smaller than the corresponding band in crinine. The ellipticity at 240 mμ is the same as that of crinine within experimental error. As expected, dihydropowelline displays a decreased magnitude relative to that observed for powelline. In addition, it shows a *positive* dichroism at 288 mμ. We consider this a non-standard dichroism spectrum. This result was unexpected since there has been no change in the stereochemistry of the asymmetric center adjacent to the aromatic ring.

Powellane (**1b**) shows a non-standard curve. Both benzene ellipticities are positive and of smaller magnitude than those observed in crinane. These observations demonstrate that the positive ORD spectrum found earlier[1] in powellane is due to a change in the sign of the 288 mμ aromatic ellipticity. Similar trends are observed in other alkaloids and alkaloid derivatives possessing both methylenedioxy and OMe substitution. While the CD spectra of ambelline (**7**), undulatine (**8a**), crinamidine (**8b**),



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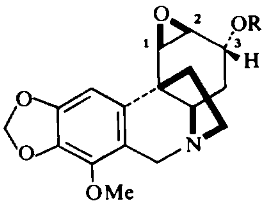
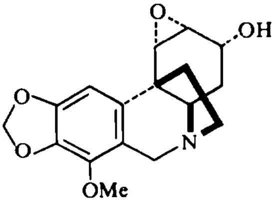


8
a: R = Me
b: R = H



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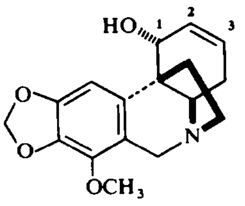
and epoxypowelline (**9**) show normal CD curves, abnormal dichroisms are found in their derivatives when either the double bond is reduced or the oxirane ring is opened. In the case of buphanamine (**10**), the sign of the Cotton effect at 288 mμ was found to be positive even before hydrogenation of the double bond. Since buphanamine has been converted to powellane,[10] *the sign of the aromatic ellipticity at* 288 mμ *in buphanamine is not indicative of the stereochemistry at position* 10b. Oxobuphanamine (**10**, = O instead of OH at C_1) shows a large negative dichroism at 340 mμ which can be assigned to the α,β-unsaturated ketone moiety. The negative max at 290 mμ is attributed to the aromatic chromophore. The sign may be associated with the introduction of a high degree of homoconjugation between the C_1-ketone function and the aromatic ring.[11-13]



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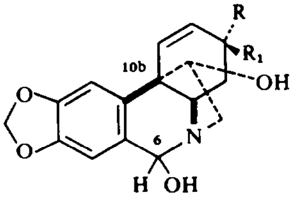

11 a: R = OMe, R_1 = H
b: R = H, R_1 = OMe

6-Hydroxycrinamine (**11a**) possesses *two* asymmetric benzylic carbon atoms. Although it might be expected that the hydroxyl substitution at C_6 would alter the CD curve of **6d**, this was not found to be the case. This observation can be rationalized from the finding that **11a** exists in solution as a pair of equilibrating C_6 epimers;[14] thus the contribution of this center to the CD spectrum might be expected to be slight. The conversion of **11a** to criwelline (**4a**) and haemanthidine (**11b**) to tazettine (**4b**) does not alter the arrangement of atoms about C_{10b} in the original compounds. However, a striking change occurs in the CD spectra and the curves of **11** and **4** are antipodal. The CD spectra of 6-hydroxycrinamine (**11a**) and criwelline (**4a**) are complicated by the abnormal CD curve of criwelline. However, if one assesses CD spectra by the sign of the low wavelength dichroism, the results are consistent.

Since the rearrangement of **11** to **4** does not involve any change in the stereochemistry of the substituents at the benzylic-allylic C atom, it seemed possible that the CD variation in the two compounds was the result of a change in the special distribution of the atoms attached to this center. Such a concept has ample precedent. The octant rule for the CO group in cyclic ketones is based upon a similar premise.[15] There is no theoretical or chemical reason why an octant or similar rule should not exist for other chromophores. The aromatic ring should lend itself to such treatment particularly when it is part of a rigid system. Schellman[16] has predicted the existence of a quadrant rule for the aromatic ring on the basis of symmetry considerations.

Recently, a quadrant rule was suggested which correlates the sign of the 290 mμ ($A_{1g} \rightarrow B_{2u}$) dichroism with the absolute configuration of a number of Amaryllidaceae alkaloids.[17,*] In this paper we propose an alternate rule which encompasses more than seventy correct assignments of absolute configuration to various alkaloid types. As we reported earlier in this paper, the sign of the 290 mμ dichroism *frequently* changes between two closely related compounds known to possess the same absolute

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[*] A number of quadrant and octant rules, using ORD and CD data have been suggested for various chromophores.[17a]

configuration. From the Kuriyama rule one would predict that powelline (θ_{290} = -1600) has an absolute configuration antipodal to that of dihydropowelline (θ_{290} = $+380$) and powellane (θ_{290} = $+800$). Chemical evidence has shown this not to be the case.

The electronic transitions of the aromatic ring which must be examined are the π–π^* excitations. These transitions cannot give rise to optical activity[18] unless an asymmetric center adjacent to the aromatic ring perturbs these transitions in such a way that a mixing of the d_{xy} (aromatic) benzene orbitals occurs. It is known that these perturbations affect the chromophore in a manner depending upon their orientation relative to it. Like the carbonyl group, the benzene ring may be divided by planes through the *p*-orbitals. In our quadrant rule we propose that the aromatic ring and the asymmetric benzylic C atom be placed in plane **a** of Fig. 2. This plane passes through the six nodes of the π-orbitals of the aromatic ring. Plane **b** is the symmetry plane. In compounds where it is difficult to define a symmetry axis, the plane through C atoms 1 and 4 of the aromatic ring and the asymmetric C atom becomes a useful alternative.

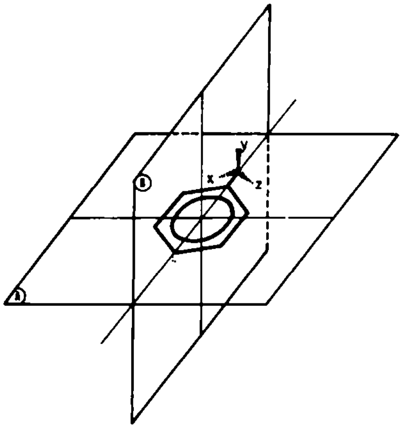


Fig. 2 Quadrant projection of aromatic ring with asymmetric benzylic C atom.

Codeine (**12**) was chosen as the reference compound for this empirical rule since the absolute configuration of the alkaloid is known;[19] the molecule is relatively rigid and its gross structure resembles that of both galanthamine (**3**) and crinine (**5a**). When placed in the quadrants as described above and viewed through C_2, C_{12}, and C_{13}, codeine is described by Fig. 3. The aromatic ring lies in plane **a** and is bisected by plane **b**. The OMe and epoxide groups lie in plane **a** and are not included in the figure. The 285 and 240 mμ transitions in the CD spectrum of codeine are negative and positive, respectively. Atoms in the upper left and lower right quadrants are considered to make positive contributions to the 240 mμ dichroism, since a majority of the atoms not lying in planes **a** and **b** are in these quadrants. The upper right and lower left quadrants are given opposite values. The signs are reversed when considering the 285 mμ ($A_{1g} \longrightarrow B_{2u}$) transition because of the antipodal natures of "normal" aromatic ellipticities. To test this empirical assignment, it was applied to a number of

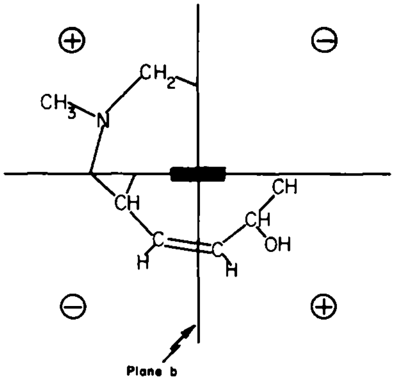
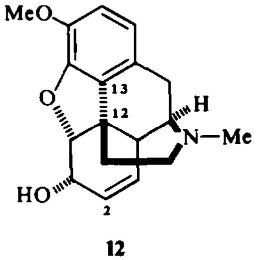


FIG. 3 Quadrant projection of codeine for the 240 mμ ($A_{1g} \rightarrow B_{1u}$) aromatic transition.



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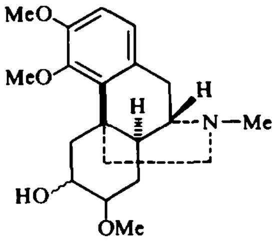

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morphine derivatives of known absolute configuration. These included modifications of the codeine molecule with the dihydrofuran ring opened, with and without aliphatic OH and olefinic unsaturation, as well as compounds in the antipodal sinomenine series (e.g. **13a** and **13b**).[20] The results are given in Table 1. Predictions made from this rule were found correct in all cases.

Application of the quadrant rule to certain members of the Amaryllidaceae alkaloids gave inconsistent results. The absolute configuration of galanthamine (3) has been determined by X-ray analysis.[7] The CD spectrum of this compound was obtained (Fig. 4). The bands at 238 and 285 mμ correspond to those found in the UV spectrum of galanthamine. The negative Cotton effect at 245 mμ has no accompanying band which can be observed in the ultraviolet spectrum of either the free base or the hydrochloride. The 245 mμ ellipticity disappears upon acidification of the solution. This band appears to be a charge transfer band arising from interaction between the pair of electrons of the N atom and the electrons of the double-bond. Bands of this type are known,[23] and both the position and disappearance of these bands upon acidification lend support to this assignment. Application of the quadrant rule (Fig. 4) to galanthamine predicts a positive sign for the 240 mμ ellipticity. This is found experimentally. Since the sign of the 240 mμ aromatic dichroism is not dependent upon the configuration of the C_3—OH function, a positive dichroism is found at 240 mμ in (−)-epigalanthamine (3,α-C_3—OH) as well.

TABLE 1. APPLICATION OF THE QUADRANT RULE TO MORPHINES AND MORPHINANES

Compound	Pred. CD 285 mμ	Pred. CD 240 mμ	Obs. CD 285 mμ	Obs. CD 240 mμ	Pred. ORD 300 mμ	Obs. ORD 300 mμ	Ref.
Codeine	(−)	(+)	(−)	(+)	(−)	(−)	21
Dihydrocodeine	(−)	(+)	(−)	(+)	(−)	(−)	21
Morphine	(−)	(+)	(−)	(+)	...	...	21
O,O-Diacetylmorphine	(−)	(+)	(−)	(+)	...	...	21
Thebaine	(−)	(+)	(−)	(+)	...	...	21
Dihydrothebaine	...	...	...	...	(−)	(−)	20
Tetrahydrothebaine	...	...	...	...	(−)	(−)	20
Dihydrodesoxycodeine D	...	...	...	...	(−)	(−)	20
Dihydrodesoxycodeine C	(−)	(+)	(−)	(+)	...	...	20
3,4-Dimethoxy-6-β,14-β-dihydroxy-N-methylmorphine	(−)	(+)	(−)	(+)	...	...	22
	...	...	...	...	(+)	(+)	20

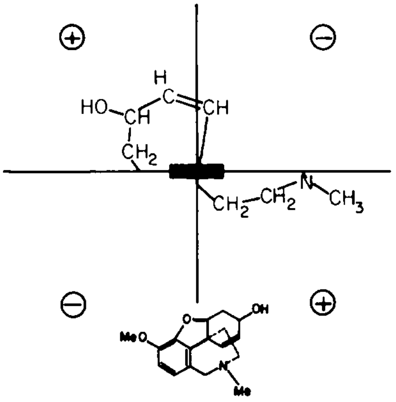


FIG. 4 Quadrant projection of galanthamine for 245 mμ ($A_{1g} \rightarrow B_{2u}$) transition.

The absolute configuration of lycorine (2), assigned originally by Mills' rule,[24] has been verified by the X-ray analysis of dihydrolycorine.[25] The same absolute configuration was also assigned to lycorine from the CD maximum at 291 mμ of 2-oxo derivatives.[26]

The correlation of this max at 291 mμ with the CO chromophore appears questionable since we find a Cotton effect in the same spectral region (290 mμ) and of the same magnitude (−6520 vs −6600 for the parent compound, lycorine). The CO Cotton effect probably is quite small since the aromatic chromophore is β to the CO group. It is known that the magnitude of the Cotton effect decreases very rapidly when the asymmetric center is moved from the α to the β position of a cyclohexanone.[9] A quadrant projection of dihydrolycorine predicts a positive dichroism at 240 mμ. Experimental results are in agreement. Similar CD spectra were observed for other alkaloids (e.g., pluvine, caranine and galanthine) containing the lycorine nucleus and these must be considered to have the same absolute configuration as lycorine.

Application of the quadrant rule to the crinine (**5**)-, tazettine (**4**)-, and montanine-type alkaloids gave results at variance with absolute configurations assigned by Mills' rule[27] and degradation.[8] The quadrant projection of crinine (**5a**) for the 240 mμ aromatic band, as viewed either from the symmetry axis (an axis bisecting C_8–C_9 and C_{10a}–C_{6b}) or along the C_8–C_{10a} and C_{10b} axis (dotted) is shown in Fig. 5. This projection is based upon the absolute stereochemistry assigned by Mills' rule. Our quadrant rule predicts a *negative* 240 mμ dichroism. Actually a positive Cotton effect is found at this wavelength. Comparable anomalies were found when the rule was applied to 11-hydroxy- and 6,11-dihydroxy alkaloids derived from **6** as well as to the tazettine and montanine systems. Tazettine (**4b**) and montanine (**14**) have been related by chemical transformation to the 5,10b-ethanophenanthridine ring system.

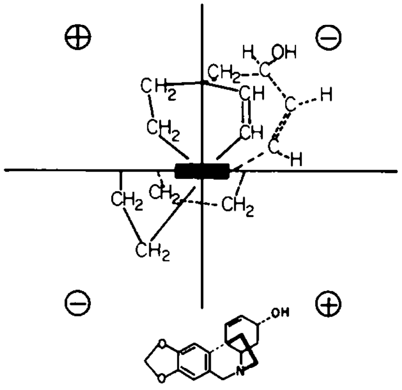


Fig. 5 Quadrant projection of crinine through (a_1 ———) axis of symmetry and (b_1 – – –) symmetry axis for $A_{1g} \rightarrow B_{1u}$ transition.

Although the Amaryllidaceae and Papaveraceae alkaloids are numerous and afford useful examples for CD studies, they represent a somewhat restricted group of compounds containing an asymmetric center adjacent to the aromatic ring. It seemed desirable to test the quadrant rule in more diverse systems. Ajmaline and akuammicine display large dichroisms as predicted qualitatively by the quadrant rule. The very large dichroism ($-89,000$) at 325 mμ of akuammicine is assigned to the α,β-unsaturated ester with asymmetric centers at both the α- and β-positions. Results obtained for these alkaloids as well as dihydrolysergic acid, aspidospermine, brucine, and strychnine are given in Table 2.

The quadrant rule also is applicable to ORD measurements provided *standard dispersion spectra are obtained.* We define such a dispersion curve for an aromatic alkaloid as one which crosses an arbitrary zero axis at or near the center of an aromatic absorption band. The ORD spectrum of crinane is an example of a standard curve while that of powellane is non-standard (Fig. 6). The relationships between ORD and CD are well known,[28] and no ambiguities should arise if one applies the quadrant rule to compounds exhibiting normal ORD curves when CD data are *not* available and standard curves are obtained.

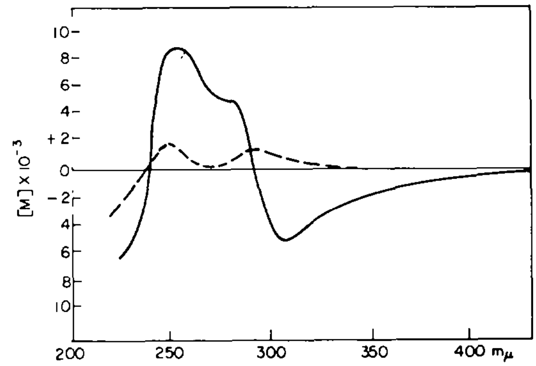
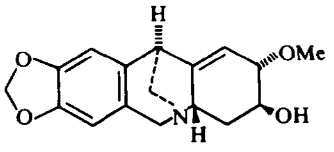


Fig. 6 ORD spectra of (———) crinane and (- - -) powellane



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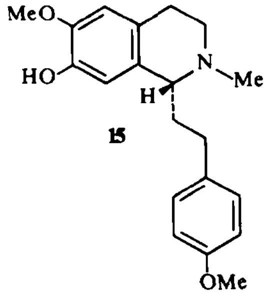

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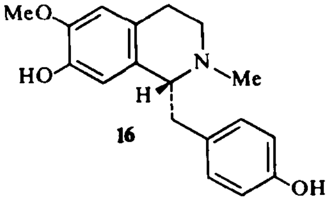

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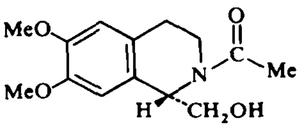
We have examined the ORD spectra of a number of isoquinoline alkaloids of known absolute configuration.[29] Compound **15** as well as **16**[30] were projected upon quadrants, and the empirical predictions agreed with the experimental ORD results. Examination of the Dreiding models of the tetrahydroisoquinolines (**17** and **18**) shows that each may exist in two conformations. In each isomer hydrogen bonding can occur between the OH and CO group in one conformation but not in the other.

17



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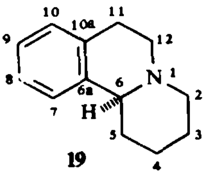

19

When the conformers of **17** and **18** which permit H-bonding are projected onto a set of quadrants for the low energy aromatic band, the predicted sign of rotation agreed with that experimentally observed.[31] The use of CD and ORD for conformational analysis has precedent,[11, 30] and it appears that the proposed quadrant rule also may be useful for this purpose.

We have previously noted that the best symmetry axis of the aromatic ring should be used whenever possible. When the (−)-benzylisoquinolizidine (**19**) was projected onto quadrants, it was difficult to decide which atoms would determine the sign of the Cotton effect if the C_9, C_{6a}, C_6 axis was used (i.e., three carbons vs one nitrogen). However, when the symmetry axis through C_{8-9}–C_{10a-6a} was used, the problem was resolved because the majority of atoms were situated in a positive quadrant when the 275 mμ Cotton effect was examined and in a negative quadrant when the 214 mμ band was considered. The predicted Cotton effect signs at 275 and 214 mμ agree with those observed experimentally,[31] utilizing the CD spectrum. Results obtained from the ORD spectrum were equivocal. It should be stressed that these examples represent one of the few, but important, cases where the symmetry axis afforded unambiguous results. Undoubtedly similar situations will arise as the quadrant rule is further used and tested.

TABLE 2. APPLICATION OF THE QUADRANT RULE TO VARIOUS ALKALOIDS

Compound	Pred. CD 285 mμ	Pred. CD 245 mμ	Obs. CD 285 mμ	Obs. CD 245 mμ	Pred. ORD 300 mμ	Obs. ORD 300 mμ	Ref.
Aspidospermine	(−)	(+)	(−)	(+)	...	...	21
Akuammicine	(−)	(+)	(−)	(+)	...	...	21
Brucine	(+)	(−)	(−)	(−)	...	...	21
Strychnine	...	(−)	...	(−)	...	...	21
Dihydrolysergic Acid	(−)	(+)	(−)	(+)	...	...	21
15	...	...	...	...	(−)	(−)	29
Coclaurine	...	...	...	...	(+)	(+)	30
18	...	...	...	...	(−)	(−)	31
19	(+)	(−)	(+)	(−)	...	...	31
Galanthamine	(−)	(+)	(+)	(+)	...	...	21
Epigalanthamine	(−)	(+)	(+)	(+)	...	...	21
Lycorine	(−)	(+)	(−)	(+)	(−)	(−)	21
Dihydrolycorine	(−)	(+)	(−)	(+)	(−)	(−)	21

Table 2 includes both the predicted and observed ORD and CD signs at the appropriate wavelengths for the compounds listed. As can be seen, complete agreement exists in all cases between the predicted sign of the Cotton effect by the quadrant rule and that observed experimentally.[*] The absolute configurations of all the compounds studied were known except those members of the Amaryllidaceae related to the 5,10b-ethanophenanthridine ring system. In the latter, the predictions are invariably the opposite of those expected from the presently accepted absolute stereochemistry. If the quadrant rule is a valid concept, the absolute configurations of the 5,10b-ethanophenanthridine alkaloids, as well as the interrelated tazettine-, criwelline-, and montanine-types should be examined further in spite of chemical evidence to the contrary.[8] The quadrant rule also states that the absolute configurations assigned to the lycorine- and galanthamine-type alkaloids are correct.

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[*] It should be pointed out that complete agreement exists only for the $A_{1g} \rightarrow B_{1u}$ aromatic transition (ca. 230–250 mμ) which has been of constant sign and is therefore more reliable as a means of assigning the absolute stereochemistry at the asymmetric benzylic position. The $A_{1g} \rightarrow B_{2u}$ band should be used only when normal CD and/or ORD data are available.

EXPERIMENTAL[*]

Complete spectral tabulations for the compounds described in the figures is given below. A tabulation of more than 90 CD spectra of these alkaloids may be found in the Ph.D. thesis of G.D.A.

Ajmaline: CD (*c*, 0·023); $(\theta)_{312}$ 0·0, $(\theta)_{292}$ −3520, $(\theta)_{270}$ 0·0, $(\theta)_{250}$ +34,800, $(\theta)_{230}$ 0·0, $(\theta)_{225}$ −3500.

Akuammicine: CD(*c*, 0·031); $(\theta)_{370}$ 0·0, $(\theta)_{325}$ −89,000, $(\theta)_{292}$ 0·0, $(\theta)_{283}$ +6250, $(\theta)_{270}$ 0·0, $(\theta)_{240}$ +49,500, $(\theta)_{220}$ 0·0.

Ambelline: CD(*c*, 0·135); $(\theta)_{305}$ 0·0, $(\theta)_{279}$ −1350, $(\theta)_{260}$ 0·0, $(\theta)_{245}$ +1300.

Aspidospermine: CD(*c*, 0·068); $(\theta)_{285}$ 0·0, $(\theta)_{255}$ −57,500, $(\theta)_{230}$ 0·0, $(\theta)_{255}$ +37,000, $(\theta)_{220}$ 0·0.

Brucine: CD(*c*, 0·048); $(\theta)_{305}$ 0·0, $(\theta)_{300}$ −4530, $(\theta)_{290}$ −2250, $(\theta)_{265}$ −14,800, $(\theta)_{260}$ −11,600, $(\theta)_{255}$ −24,400 (slit width at 255 mμ, 1·4 mm).

Buphanamine: CD(*c*, 0·158); $(\theta)_{294}$ 0·0, $(\theta)_{288}$ +520, $(\theta)_{275}$ 0·0, $(\theta)_{260}$ 0·0, $(\theta)_{248}$ +11,300, $(\theta)_{245}$ 0·0.

(−)-*Buphanisine*: CD(*c*, 0·08); $(\theta)_{315}$ 0·0, $(\theta)_{295}$ −9300, $(\theta)_{255}$ 0·0, $(\theta)_{245}$ +10,700.

Coccinine: CD(*c*, 0·103); $(\theta)_{305}$ 0·0, $(\theta)_{295}$ −3300, $(\theta)_{270}$ 0·0, $(\theta)_{240}$ −38,000, $(\theta)_{230}$ −21,700, $(\theta)_{225}$ −45,000.

Codeine: CD(*c*, 0·028); $(\theta)_{297}$ 0·0, $(\theta)_{282}$ −8600, $(\theta)_{265}$ 0·0, $(\theta)_{243}$ 41,000, $(\theta)_{232}$ 0·0, $(\theta)_{231}$ −8000.

Crinamidine: CD(*c*, 0·067); $(\theta)_{300}$ 0·0, $(\theta)_{282}$ −1600, $(\theta)_{265}$ 0·0, $(\theta\ )_{260}$ +1600.

Crinamine: CD(*c*, 0·053); $(\theta)_{315}$ 0·0, $(\theta)_{297}$ +6520, $(\theta)_{257}$ 0·0, $(\theta)_{245}$ −5730, $(\theta)_{238}$ 0·0.

Crinane: CD(*c*, 0·145); $(\theta)_{305}$ 0·0, $(\theta)_{290}$ −1500, $(\theta)\ _{270}$ 0·0, $(\theta)_{260}$ 0·0, $(\theta)_{245}$ +2010, $(\theta)_{235}$ 0·0.

Crinine: CD(*c*, 0·039); $(\theta)_{308}$ 0·0, $(\theta)_{290}$ −7300, $(\theta)_{265}$ 0·0, $(\theta)_{255}$ 0·0, $(\theta)_{240}$ +8200, $(\theta)_{235}$ 0·0.

Criwelline: CD(*c*, 0·148); $(\theta)_{310}$ 0·0, $(\theta)_{290}$ +1560; (*c* 0·049); $(\theta)_{255}$ 0·0, $(\theta)_{239}$ +26,100, $(\theta)_{225}$ +21,500.

Dihydroambelline: CD(*c*, 0·285); $(\theta)_{295}$ 0·0, $(\theta)_{285}$ +440, $(\theta)_{265}$ 0·0, $(\theta)_{250}$ +585.

Dihydrocodeine: CD(*c*, 0·096); $(\theta)_{300}$ 0·0, $(\theta)_{280}$ −10,550, $(\theta)_{255}$ 0·0, $(\theta)_{245}$ +18,100 $(\theta)_{230}$ 0·0.

Dihydrocrinamine: CD(*c*, 0·112); $(\theta)_{310}$ 0·0, $(\theta)_{290}$ +4900, $(\theta)_{255}$ 0·0, $(\theta)_{245}$ −3900.

Dihydrocrinine: CD(*c*, 0·120); $(\theta)_{310}$ 0·0, $(\theta)_{295}$ −2680, $(\theta)_{260}$ 0·0, $(\theta)_{250}$ +2500.

Dihydroepicrinine: CD(*c*, 0·064); $(\theta)_{310}$ 0·0, $(\theta)_{292}$ −2140, $(\theta)_{265}$ 0·0, $(\theta)_{250}$ +2670.

Dihydroepipowelline: CD(*c*, 0·1); $(\theta)_{288}$ 0·0, $(\theta)_{276}$ +870, $(\theta)_{260}$ +260, $(\theta)_{255}$ +1425.

Dihydro-6-hydroxycrinamine: CD(*c*, 0·030); $(\theta)_{310}$ 0·0, $(\theta)_{295}$ +5700, $(\theta)_{265}$ 0·0, $(\theta)_{240}$ −4270, $(\theta)_{230}$ 0·0.

Dihydrolycorine: CD(*c*, 0·114); $(\theta)_{310}$ 0·0, $(\theta)_{290}$ −3100, $(\theta)_{260}$ 0·0, $(\theta)_{255}$ 0·0, $(\theta)_{240}$ +2160, $(\theta)_{230}$ 0·0.

Dihydrolysergic acid: CD(*c*, 0·133); $(\theta)_{292}$ 0·0, $(\theta)_{280}$ −645, $(\theta)_{265}$ 0·0, $(\theta)_{235}$ +4050, $(\theta)_{230}$ 0·0.

Dihydropowelline: CD(*c*, 0·32); $(\theta)_{320}$ 0·0, $(\theta)_{295}$ −360, $(\theta)_{288}$ 0·0, $(\theta)_{282}$ +380, $(\theta)_{270}$ 0·0, $(\theta)_{245}$ +2840, $(\theta)_{240}$ 0·0.

Dihydroundulatine: CD(*c*, 0·285; $(\theta)_{290}$ 0·0, $(\theta)_{280}$ +300, $(\theta)\ _{265}$ +100, $(\theta)_{248}$ +1550, $(\theta)_{240}$ 0·0.

(−)-*Epicrinine*: CD(*c*, 0·096); $(\theta)_{315}$ 0·0, $(\theta)_{295}$ −5400, $(\theta)_{245}$ 0·0, $(\theta)_{250}$ +2700.

Epigalanthamine: CD(*c*, 0·070); $(\theta)_{305}$ 0·0, $(\theta)_{288}$ +2750, $(\theta)_{265}$ 0·0, $(\theta)_{250}$ −485, $(\theta)_{245}$ 0·0, $(\theta)_{240}$ +8250, $(\theta)_{238}$ 0·0. CD(*c*, 0·070; CH_3OH, HCl); $(\theta)_{305}$ 0·0, $(\theta)_{286}$ +1360, $(\theta)_{269}$ 0·0, $(\theta)_{250}$ 0·0, $(\theta)_{242}$ +14,300, $(\theta)_{238}$ 1570 (slit width at 239·5 was 1·8 mm, at 240, 1·4 mm).

Epipowelline: CD(*c*, 0·116); $(\theta)_{300}$ 0·0, $(\theta)_{285}$ −1320, $(\theta)_{260}$ 0·0, $(\theta)_{250}$ +4400, $(\theta)_{245}$ 0·0.

Epoxypowelline: CD(*c*, 0·30); $(\theta)_{300}$ 0·0, $(\theta)_{280}$ −910, $(\theta)_{260}$ 0·0, $(\theta)_{250}$ +900.

Galanthamine: CD(*c*, 0·112); $(\theta)_{305}$ 0·0, $(\theta)_{285}$ +8200, $(\theta)_{265}$ 0·0, $(\theta)_{245}$ −2350, $(\theta)_{243}$ 0·0, $(\theta)_{238}$ +2700, $(\theta)_{236}$ 0·0.

Galanthamine hydrochloride: CD(*c*, 0·067); $(\theta)_{275}$ +7700, $(\theta)_{265}$ +2980, $(\theta)_{255}$ +700, $(\theta)_{245}$ +1050, $(\theta)_{241}$ +4030, $(\theta)_{238}$ 0·0.

Haemanthamine: CD(*c*, 0·058); $(\theta)_{310}$ 0·0, $(\theta)_{292}$ +11,900, $(\theta)_{255}$ 0·0, $(\theta)_{240}$ −13,800, $(\theta)_{228}$ 0·0.

Haemanthidine: CD(*c*, 0·078); $(\theta)_{315}$ 0·0, $(\theta)_{290}$ +8320, $(\theta)_{265}$ 0·0, $(\theta)_{242}$ −8700, $(\theta)_{225}$ 0·0.

Heroin: CD(*c*, 0·132); $(\theta)_{295}$ 0·0, $(\theta)_{285}$ −1310, $(\theta)_{255}$ 0·0, $(\theta)_{244}$ +5740, $(\theta)_{237}$ 0·0.

6-Hydroxycrinamine: CD(*c*, 0·053); $(\theta)_{315}$ 0·0, $(\theta)_{290}$ 7400, $(\theta)_{260}$ 0·0, $(\theta)_{245}$ −6400, $(\theta)_{230}$ 0·0.

Lycorine: CD(*c*, 0·167); $(\theta)_{310}$ 0·0, $(\theta)_{290}$ −6600, $(\theta)_{250}$ 0·0, $(\theta)_{245}$ +4600, $(\theta)_{235}$ 0·0.

Montanine: CD(*c*, 0·089); $(\theta)_{310}$ 0·0, $(\theta)_{293}$ −3000, $(\theta)_{260}$ 0·0, $(\theta)_{243}$ −57,500, $(\theta)_{239}$ −27,200, $(\theta)_{235}$ −48,000.

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[*] All CD spectra were measured with a modified Jouan dichrograph.[32] The ORD data were obtained on a Jasco Model 5 ORD/UV spectropolarimeter. Methanol was used as a solvent unless stated otherwise. The temperature of measurement was 25°. The units of ellipticity are degrees-cm^2-decimole.

Morphine: CD(c, 0·020; CH_3OH, NaOH); $(\theta)_{320}$ 0·0, $(\theta)_{293}$ +7700, $(\theta)_{260}$ +760, $(\theta)_{255}$ +40,000, $(\theta)_{240}$ 0·0, $(\theta)_{237}$ −40,000. CD(c, 0·020; CH_3OH, HCl); $(\theta)_{320}$ 0·0, $(\theta)_{293}$ −7500, $(\theta)_{260}$ 0·0, $(\theta)_{245}$ +34,400, $(\theta)_{233}$ 0·0.

Oxobuphanamine: CD(c, 0·36); $(\theta)_{385}$ 0·0, $(\theta)_{345}$ −5800, $(\theta)_{300}$ −2125, $(\theta)_{280}$ −2900, $(\theta)_{240}$ 0·0, $(\theta)_{230}$ +840.

Powellane: CD(c, 0·206); $(\theta)_{290}$ 0·0, $(\theta)_{280}$ +800, $(\theta)_{255}$ 0·0, $(\theta)_{247}$ +1800; more sample provided to complete spectrum; $(\theta)_{240}$ 0·0.

Powelline: CD(c, 0·129); $(\theta)_{300}$ 0·0, $(\theta)_{288}$ −1620, $(\theta)_{260}$ 0·0, $(\theta)_{250}$ +4200, $(\theta)_{240}$ 0·0.

Tazettine: CD(c, 0·069); $(\theta)_{310}$ 0·0, $(\theta)_{286}$ −4950, $(\theta)_{262}$ 0·0, $(\theta)_{238}$ +44,300, $(\theta)_{225}$ +23,100.

Thebaine: CD(c, 0·057); $(\theta)_{315}$ 0·0, $(\theta)_{285}$ −15,200, $(\theta)_{270}$ −6200, $(\theta)_{245}$ −1610, $(\theta)_{238}$ −2320, $(\theta)_{230}$ 0·0, $(\theta)_{223}$ +14,100, $(\theta)_{215}$ +7000.

Undulatine: CD(c, 0·187); $(\theta)_{305}$ 0·0, $(\theta)_{280}$ −450, $(\theta)_{255}$ 0·0, $(\theta)_{245}$ +500.

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