ISOLATION AND CHEMISTRY OF THE ALKALOIDS FROM SOME PLANTS OF THE GENUS *Papaver*. LVII.* **

CHIROPTICAL PROPERTIES AND PREPARATION OF SOME RHOEADINE AND ISORHOEADINE DERIVATIVES

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The chiroptical properties of rhoeadine and related compounds are explained on the basis of the absolute configuration. Some reduction products containing cleaved rings B or/and D have been prepared and their CD-spectra correlated with their stereochemistry.

The relative configuration of rhoeadine alkaloids at $C_{(1)}$ and $C_{(2)}$ was elucidated[1] on the basis of PMR spectra, dissociation constants, and optical rotatory data. These alkaloids form two series of isomers with a *cis*-junction (rhoeadine group) or *trans*-junctions (isorhoeadine group) of rings B and D. On the basis of an analysis of the ORD curves, the absolute configuration of the rhoeadine alkaloids was proposed[2] to be (1*R*, 2*R*) and that of isorhoeadine (1*S*, 2*R*).

In 1M-HCl, the *trans*-bases are isomerized to the thermodynamically more stable *cis*-bases[3,4]. However, different opinions have been expressed in the literature whether this epimerization takes place at $C_{(1)}$ ref.[2,5] or at $C_{(2)}$ ref.[6–8]. A mechanism has been proposed for the latter case[7] which, in our opinion, cannot explain this isomerization because at $C_{(2)}$ two S_N2 steps are involved which must lead to double-inversion, *i.e.* retention. Furthermore, it is assumed that the seven-membered ring opens under formation of a secondary amine; it is highly improbable that it would cyclize again to a seven-membered ring. Pfeifer and coworkers[3,6,9] found that, in diluted (0·004M) methanolic HCl, natural isorhoeadine alkaloids epimerize at $C_{(14)}$ into epiisorhoeadine alkaloids without any change of configuration at $C_{(1)}$ and $C_{(2)}$. From the PMR data it has been concluded[6] that the OR group at $C_{(14)}$ in rhoeadine and epiisorhoeadine alkaloids is in *cis*-position to the hydrogen atom at $C_{(1)}$ and the isorhoeadine group in *trans*-position.

Recently, application of the aromatic chirality method (exciton interaction of two aromatic chromophores[10]) led to the conclusion[5] that the absolute configuration of rhoeadine and iso-

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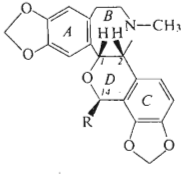
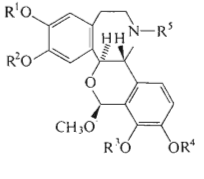
rhoeadine is that one proposed first by Šantavý and coworkers[2]. An unequivocal proof of the relative[11] and absolute[12] configuration of rhoeadine was derived from X-ray analysis of N-methylrhoeagenine iodide by which the (1*R*,2*R*,14*S*) configuration was confirmed.

Very recently Rönsch[39] gave evidence, though, in our opinion, not an unequivocal one for the epimerization at $C_{(1)}$ rather than at $C_{(2)}$ in the rhoeagenine – isorhoeagenine rearrangement. Consequently, the (1*S*)-stereochemistry is used in the following for the isocompounds. The purpose of the present study is to rationalize the CD spectra of rhoeadine and related alkaloids as well as of some of their degradation products.

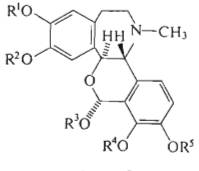
The degradation of rhoeadine methochloride with sodium in liquid ammonia gave the optically active methine *XVIII*. Hofmann degradation of rhoeadine methiodide by the usual procedure yielded a new methine *XXI* besides the already known optically active methine[13] *XVIII*. In the reaction mixture, the methine of stilbene type *XXI* amounted to c. 5%. It could not be converted into the corresponding dihydroderivative by catalytic hydrogenation. Hydrogenation of rhoeadinemethine *XVIII* over Adams catalyst at atmospheric pressure afforded dihydrorhoeadinemethine[13] *XIV*, and acid hydrolysis of the latter dihydrorhoeageninemethine *XIII*. Following reduction of *XIII* with sodium dihydro-bis(2-methoxyethoxy)aluminate in benzene yielded the substance *XXIIIa*. From this compound, the diacetyl derivative *XXIIIc* was pre-



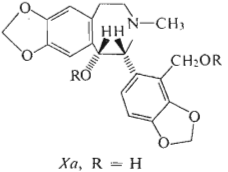
I, R = OH
II, R = OCH_3
III, R = H



IV, $R^1 = R^2 = R^3 = R^4 = CH_2$; R^5 = H
V, $R^1 + R^2 = R^3 + R^4 = CH_2$; $R^5 = CH_3$
VI, $R^1 = R^2 = R^3 = R^4 = R^5 = CH_3$



VII, $R^1 + R^2 = R^4 + R^5 = CH_2$; $R^3 = CH_3$
VIII, $R^1 = R^2 = CH_3$; R^3 = H; $R^4 + R^5 = CH_2$
IX, $R^1 = R^2 = R^4 = R^5 = CH_3$; R^3 = H



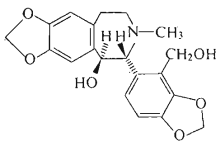
Xa, R = H
Xb, R = $COCH_3$

pared. Attempted hydrogenolysis of *XXIIIc* over 5% $Pd/BaSO_4$ in a 10% ethanolic solution of triethylamine gave, however, only the product of partial hydrolysis, *viz.* the monoacetate *XXIIIb*.

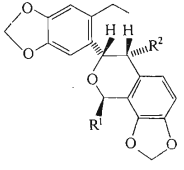
An attempt to obtain substance *XXIIIa* by hydrogenation of *XIII* over Adams catalyst in acetic acid afforded only optically inactive starting material *XIII*. This is analogous to our recent findings that hydrogenation of rhoeagenine (*I*) to rhoeagenidiol (*Xa*) under the same conditions[1] results in partial loss of optical activity, depending on the time of hydrogenation and quality of the catalyst.

The mass spectrum of *XXIIIa* did not exhibit a molecular peak, showed however the presence of a small amount of the ion M-1; without deuteration it is not possible to decide which hydrogen is lost in this fragmentation. Rupture of the central bond between the aromatic rings takes place very easily under formation of the ion *m/e* 208 which undergoes further fragmentation to the ion *m/e* 163. This in turn loses CO to produce an ion *m/e* 135. Evidence for this fragmentation pattern is provided by the presence of metastable peaks at 127·74 (208 → 163) and 111·81 (163 → 135). Similarly, the mass spectrum of the diacetate *XXIIIc* does not exhibit a molecular peak. The base peak at *m/e* 250 corresponds to the acetylated fragment *m/e* 208 in the spectrum of *XXIIIa*. The metastable peaks at 106·28 (250 → 163) and 111·81 (163 → 135) prove the same type of fragmentation. The mass spectrum of the monoacetate *XXIIIb* indicates a very similar fragmentation as that of *XXIIIa* showing no molecular peak; the base peak is again at *m/e* 250.

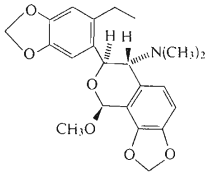
Under modified conditions, Emde degradation of *XIV* leads mainly to the stilbene derivative *XX* which was isolated earlier[13]; in addition, another neutral compound



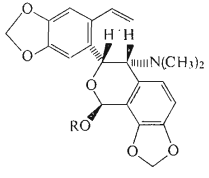
XI



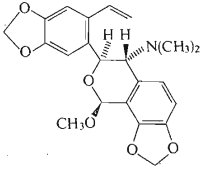
XII, $R^1 = H$; $R^2 = N(CH_3)_2$
XIII, $R^1 = OH$; $R^2 = N(CH_3)_2$
XIV, $R^1 = OCH_3$; $R^2 = N(CH_3)_2$
XV, $R^1 = OCH_3$; $R^2 = H$



XVI



XVII, R = H
XVIII, $R = CH_3$



XIX

TABLE I

PMR Spectral Data of Some Derivatives of Rhoeadine

Compound	$(CH_3)_2N$ (14-H)	CH_3O (Ar.CH_2.O)	2-H (1-H)	O.CH_2.O	Aromatic protons[a]	Others[a]
XIII	2·12 s (6·28 s)	—	3·58 d (5·55 d) J_{AX} = 2·5	5·93 s 6·07 q J_{gem} = 1·2	6·70 s A 7·23 s A 6·73 d B 6·90 d B	Ar.CH_2.CH_3 1·18 t 2·57 q OH, 3·17 s
XIV	2·13 s (5·73 s)	3·47 s	3·57 d (5·40 d) J_{AX} = 2·8	5·93 s 6·03 q J_{gem} = 1·2	6·68 s A 7·28 s A 6·70 d B 6·87 d B	Ar.CH_2.CH_3 1·17 t 2·53 q
XV	(5·75 s)	3·55 s	2·5—3·0 m (5·35 q)	5·93 s 6·03 q J_{gem} = 1·2	6·72 s A 7·10 s A 6·60 d B 6·82 d B	Ar.CH_2.CH_3 1·20 t 2·65 q
XVIII	2·07 s (5·75 s)	3·47 s	3·65 d (5·47 d) J_{AX} = 2·8	5·93 s 6·00 q J_{gem} = 1·2	6·95 s A 7·30 s A 6·70 d B 6·83 d B	vinyl A 5·17 dd M 5·53 dd X 6·83 q
XIX	2·23 s (5·68 s)	3·27 s	4·03 d (5·30 d) J_{AX} = 4·0	5·87 s 6·00 q J_{gem} = 1·2	6·60 s A 6·97 s A 6·85 d B 7·02 d B	vinyl A 5·27 dd M 5·58 dd X 7·32 q
XXI	2·27 s (6·00 s)	3·57 s	6·22 s	5·93 s 6·03 q J_{gem} = 1·2	6·77 s A 6·87 s A 6·60 d B 6·87 d B	Ar.CH_2.CH_2.N 2·65 t 2·83 t

XXV	2·27 s (5·72 s)	3·53 s	(5·30 q)	5·93 s 6·02 q J_{gem} = 1·2	6·70 s A 7·08 s A 6·57 d B 6·80 d B	Ar.CH_2.CH_2.N 2·4—3·1 m
XXIIIa	2·35 s	(4·57 s)	4·13 d (5·18 d) J_{AX} = 10·0	5·83 s 5·93 s	6·50 s A 7·02 s A 6·77 b s	Ar.CH_2.CH_3 1·07 t 2·40 q[b]
XXIIIb	2·30 s	(4·92 d) (5·08 d) (J_{gem} = 12·5)	4·02 d (5·11 d) J_{AX} = 10·0	5·81 q J_{gem} = 1·5 5·92 s	6·47 s A 6·94 s A 6·76 b s	Ar.CH_2.CH_3 1·07 t 2·55 q[c]
XXIIIc	2·28 s	(5·07 s)	4·32 d (6·57 d) J_{AX} = 10·0	5·82 s 5·88 s	6·48 s A 6·82 s A 6·67 b s	Ar.CH_2.CH_3 1·10 t 2·58 q[d]

[a] The coupling constants: *XIII*, J_{ortho} = 8·0; *XV*, J_{ortho} = 8·0; *XVIII*, J_{ortho} = 7·8, J_{AM} = 1·4, J_{AX} = 10·0, J_{MX} = 17·2; *XIV*, J_{ortho} = 8·4; *XXI*, J_{ortho} = 8·0; *XXIIIa—XXIIIc*, J_{ortho} = 8·0. [b] Hydroxyl 2·90 b s. [c] Acetyl 2·02 s. [d] Two acetyls 2·03 s, 2·07 s. s singlet, d doublet, dd doublet of doublets, t triplet, q quartet, m multiplet, b broad.

XV was now obtained. Its structure has been confirmed by the PMR spectrum (Table I). By using the sequence of reactions described earlier[13] for the preparation of rhoeadinemethine *XVIII* and its hydrogenation product *XIV*, isorhoeadine (*V*) has been subjected to Hofmann degradation, leading to *XIX* which was subsequently hydrogenated to *XVI*. The IR spectra of *XVI* and *XIX* are very similar to those of *XIV* and *XVIII*, the PMR spectrum of *XIX* is described in Table I. The

FIG. 1

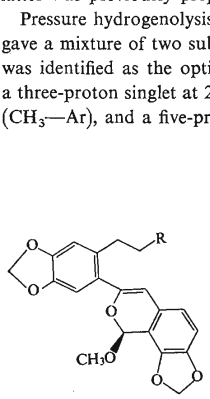
CD Spectra of Rhoeadine (*II*) (———) and Alpininine (*VI*) (·····) in Acetonitril, CD Spectrum of Rhoeadinediol (*Xa*) in Ethanol (– – – –) and Methanolic HCl (–·–·–)

coupling constant of 4·0 Hz between the protons at $C_{(1)}$ and $C_{(2)}$ indicates that the dihydropyran ring of *XIX* is not a regular half-chair, and ring A disposed axially.

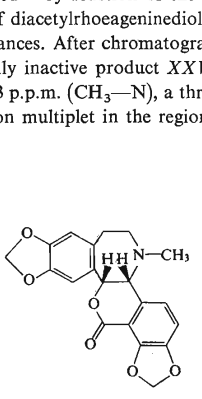
Rhoeagenine (*I*) was converted into its quaternary methiodide. Under these reaction conditions, methylation of the half-acetal OH also takes place. The product obtained is, therefore, the methiodide of rhoeadine. After replacement of the anion by chloride, sodium amalgam reduction gave a mixture of at least four substances. One of them was isolated in crystalline state (yield 65%) and proved to be *XXV*. Its PMR spectrum is very similar to that of *XV* (Table I). The identical chemical shifts of the OCH_3 protons and the protons at $C_{(1)}$ as well as the same sum of coupling constants $|J_{AX} + J_{BX}| = 15$ Hz indicate that in both compounds ring A is equatorially disposed.

By attempted hydrogenolytic removal of the benzylic hydroxyl groups of the diol *Xa* or its diacetate *Xb* in neutral or slightly alkaline ethanolic solution over Pd/C or $Pd/BaSO_4$, only the starting material could be recovered. Reduction in acidic medium (Clemmensen reduction, Pd/C in acetic acid and perchloric acid, or direct reduction with $AlCl_3/LiAlH_4$ according to Brewster and coworkers[14]) converted rhoeagenine diol *Xa* into 14-demethoxyrhoeadine[15] (*III*). On an attempt to remove the hydroxyl groups of *Xa via* reduction of its ditosylate with lithiumaluminium hydride, we obtained instead of the diester, besides unreacted diol *Xa*, a quaternary salt which proved to be identical with 7,8-dihydrocoptisinium methochloride. The latter was previously prepared[16] by reaction of the diol *Xa* with thionyl chloride.

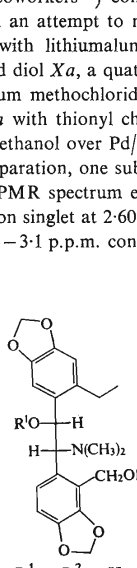
Pressure hydrogenolysis of diacetylrhoeagenine diol *Xb* in ethanol over $Pd/BaSO_4$ gave a mixture of two substances. After chromatographic separation, one substance was identified as the optically inactive product *XXVI*. Its PMR spectrum exhibits a three-proton singlet at 2·03 p.p.m. (CH_3—N), a three-proton singlet at 2·60 p.p.m. (CH_3—Ar), and a five-proton multiplet in the region of 2·5–3·1 p.p.m. containing



XX, R = H
XXI, R = $N(CH_3)_2$

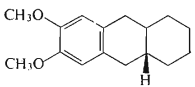


XXII

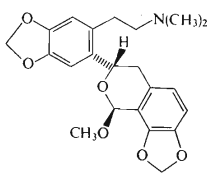


XXIIIa, $R^1 = R^2 = H$
XXIIIb, $R^1 = H$; $R^2 = COCH_3$
XXIIIc, $R^1 = R^2 = COCH_3$

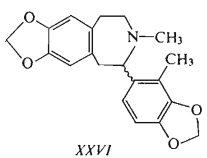
signals of Ar—CH_2—CH_2—N and Ar—CH_2—$\underline{C}H$—N protons. The two-proton multiplet at 3·65 p.p.m. is the AB portion of the ABX system of the Ar—CH_2—CH—N moiety. The signal of the methylenedioxy groups appears as a four-proton singlet at 5·73 p.p.m. The signals at 6·43, 6·47, and 6·50 correspond to four aromatic protons. On the basis of the IR, the PMR, and the mass spectrum, the second optically inactive substance is identical with the already known compound *XXVII* which was obtained earlier by hydrogenation of the "red product of papaverrubine" (ref.[17]). Consequently, hydrogenolysis resulted in cyclization of the methylene group (on ring C) with the tertiary nitrogen and in demethylation of the arising quaternary salt (analogy to Emde degradation).



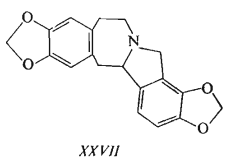
XXIV



XXV



XXVI



XXVII

In Table I, the PMR data of some other compounds are given. The two protons at $C_{(1)}$ and $C_{(2)}$ of *XIII*, *XIV*, and *XVIII* give rise to AX-spectra with $J_{AX} = 2·5$ to 2·8 Hz in agreement with the known stereochemistry. The two protons on the ethylenic bridge of the diol *XXIIIa* as well as its mono- and diacetate produce an AB-quartet with $J_{AB} = 10·0$ Hz which corresponds to an approximate *anti*-periplanar arrangement of these two hydrogens[18,19] and indicates that the preferred torsion angle around the $C_{(1)}$—$C_{(2)}$ bond is the same in all three compounds. In the spectra of the diol *XXIIIa* and its diacetate *XXIIIc*, the signals of the —CH_2OR grouping show up as broad singlets, whereas an AB quartet is found for *XXIIIb* ($J_{gem} = 12·5$ Hz).

The IR spectrum of the diol *XXIIIa* and that of its monoacetate *XXIIIb* exhibit (in dilute solution) an intense band at 3366 cm^{-1} which is attributable to an intramolecular hydrogen bond from the OH at $C_{(1)}$ to the nitrogen atom[21,20]. The band at 3608 cm^{-1} in the IR spectrum of the diol *XXIIIa* corresponds to the free primary hydroxyl group.

Circular Dichroism of Rhoeadine and Related Compounds

The ORD data of several alkaloids of this series have been published earlier[2]; we refer in the following only to the CD data because their interpretation is much easier. All compounds gave a Cotton effect in the range of the ^1L_b-transition, another one within the ^1L_a- and a couplet[22] within the ^1B-absorption. Similar CD spectra have been described in ref.[5]. In most cases, the CD spectra exhibit, however, additional bands. Even if they have opposite signs within one single transition, we do not ascribe them to exciton splitting because the distance between the two benzene rings is too large. Each compound contains two independent aromatic chromophores which, however, absorb approximately at the same wavelengths and the respective CD bands for these two chromophores may have the same or opposite signs (or a stronger band with a shoulder) within one absorption band, in the second case the CD will look similar to a couplet.

The CD spectra of the three stereoisomers glaudine (B/D *trans*, unstable configuration at $C_{(14)}$), its 14-epimer epiglaudine, and the B/D-*cis* analogue oreodine show[5], within the ^1L_b- and ^1L_a-bands, positive and negative Cotton effects, resp., whereas within the ^1B absorption a positive couplet[22] is observed. These data have been interpreted[5] in that sense that, because of the great distance between the two aromatic chromophores and the smaller dipole strength no interaction takes place between the two transitions at lower energy, whereas the allowed ^1B-band gives rise to the Davydov (exciton) splitting. From the sign of the couplet[23], a positive torsion angle between the two long axes (*i.e.* the lines bisecting the two OR-groups) of the aromatic rings has been inferred[10] for all three stereoisomers, which is in agreement with the reported[12] absolute configuration of rhoeadine type alkaloids. Besides the uncertainty which exists with regard to the direction of the electric transition moment vector for the ^1B band, some other arguments are put forward which weaken the reasoning by Shamma and coworkers[5]. The ^1B transition is known to be degenerate in benzene in any case and substitution splits the corresponding band. In chiral compounds, this leads to a couplet even in the absence of a second chromophore as shown *e.g.* by Miles and coworkers[24,25]). A simple example of this is the octahydroanthracene[26] *XXIV*, which (in isooctane solution) shows $\Delta\varepsilon_{max}$ −13 at 205 nm and +14 at 194 nm, nearly at the same wavelengths as found for the three isomeric alkaloids mentioned in ref.[5]. Therefore, in our opinion, the presence of such a couplet cannot be considered as an indication of Davydov splitting between two aromatic chromophores, and hence cannot be used for the determination of the absolute configuration of these alkaloids.

Conformational analysis leads to the assumption that the conformation of rhoeadine (*II*) in solution is the same as that of its methiodide in crystalline state[11,12], *i.e.* ring B adopting approximately a chair conformation with pseudo-axial arrangement of the dihydropyrane ether oxygen and an equatorial bond to ring C. Ring D in the sofa conformation will have the nitrogen atom axially disposed and the bond to ring A equatorially. The pseudo-axial conformation of a substituent at the benzylic carbon is energetically favoured over the pseudo-equatorial one because of steric

interaction with the *peri*-hydrogen atom. This has been proven for simple tetralins[25,27,28] by CD spectroscopy.

In rhoeadine (*II*), the chromophore of ring A (the A chromophore) is incorporated into an achiral second sphere (ring B)[29] – therefore only third-sphere contributions to the Cotton effect have to be discussed – whereas that of ring C (the C chromophore) is built into a chiral second sphere (ring D) with *M* helicity[30]. The sign of the Cotton effects of homochiral tetralins and related compounds depends on the substitution pattern of the aromatic ring[31–33]. According to these rules within the ^1L_b absorption, *M* helicity leads to a positive Cotton effect for the C chromophore. Third-sphere contributions to the A chromophore will be small because of approximate compensation according to our sector rule[25,32–34]. Third-sphere contributions to the Cotton effect of the C chromophore should be positive[32,33]. This is in excellent agreement with the measured data for this compound (positive CD at 293 nm). The CD within the ^1L_a transition is negative. Previous studies have shown[28,32,33] that this CD is very sensitive to substitution at the benzylic C atoms (pseudo-axial substitution leading to sign inversion by σ–π-interaction), and therefore we refrain from discussing the ^1L_a band CD in detail. The origin of the (positive) couplet at short wavelengths has already been discussed earlier (*vide supra*). In acidic solution, the CD band at 294 nm is increased and a stronger positive shoulder (at approximately 265 nm) appears. Protonation at the nitrogen atom should not change the conformation of the molecule, the change in the CD should therefore be due to a direct contribution of the positive charge. Since there are no simple model compounds available, we cannot predict whether the contributions to the A chromophore, to the C chromophore, or to both have been changed.

The OCH_3 group should not give a very large contribution to the Cotton effects (at least within the ^1L_b band). In agreement with this assumption, the corresponding hydroxy compound rhoeagenine (*I*) and the demethoxy derivative *III* give CD spectra which are very similar to that of rhoeadine (*II*). The *trans*-fused isocompounds *IV*–*VI* with unstable configuration of the OCH_3 group at $C_{(14)}$ also give a positive CD within the ^1L_b transition. Epimerization at $C_{(1)}$ leads to *P* helicity of ring D and, therefore, to a negative contribution of the second sphere of the C chromophore. Third-sphere contributions of the A chromophore are again very small. For the C chromophore, a positive Cotton effect is predicted from the third sphere. Consequently, the sing of the CD cannot be predicted unequivocally. The ^1L_a Cotton effect for isorhoeadine (*V*) is the same as that for rhoeadine (*II*). This is also valid for the ^1B couplet. N-Nor alkaloid papaverrubine A (*IV*) shows, however, a positive Cotton effect within the ^1L_a band whereas alpinine (*VI*) negative and positive Cotton effects within the same absorption band. As in the case of the B,D-*cis* series, also for the *trans* compounds, the OCH_3 group will be of small influence upon the CD and, indeed, the CD spectra of the compounds *VII*–*IX* with stable configuration at $C_{(14)}$ do not significantly deviate from those of their 14-epimers. Alpinigenine (*IX*) shows the

same bisignated* Cotton effect within the ^1L_a transition as alpinine (*VI*) and, for both compounds, the negative part (at longer wavelengths) disappears in acidic solution in favour of the positive part.

Ring B of rhoeageninediol (*Xa*) (in solution) most probably adopts the energetically favoured chair conformation with axial OH and equatorial bond towards ring C, which is in agreement with the coupling constant $J_{1,2} = 2{\cdot}0$ Hz. The second-sphere of the A chromophore is therefore achiral and only third-sphere contributions will determine the Cotton effects. In ethanol solution, the ^1L_b and ^1L_a Cotton effects are negative similarly to the couplet at shorter wavelengths. Obviously, an internal hydrogen bond to the nitrogen stabilizes one definite conformation even in alcoholic solutions because after acidification the ^1L_b Cotton effect decreases strongly and changes sign; the ^1L_a Cotton effect becomes bisignated and within the main CD-band also here sign inversion takes place. For the acetate *Xb*, the CD is similar to that of the diol *Xa* in ethanol solution; it shows only minor changes after acidification. Since several conformations differing in the torsion angle around the bond from $C_{(2)}$ to ring C, which can give rise to hydrogen bonding to the nitrogen, can be built up with molecular models and, because of the presence of two independent aromatic chromophores, it is not possible to assign unequivocally the conformation of this compound. The PMR spectrum of isorhoeageninediol (*XI*) shows that the two substituents at $C_{(1)}$ and $C_{(2)}$ are diequatorially arranged ($J_{1,2} = 8{\cdot}8$ Hz). The chair conformation of ring B is the mirror image to that of rhoeageninediol (*Xa*) (OH again pseudo-axial). Even though the exact conformation is unknown, the change of sign of the Cotton effect within the ^1L_b band can thus be reasonably explained. Within the ^1L_a transition, two Cotton effects of approximately equal rotational strength are observed. This is also in agreement with expectations because the change of configuration of the OH group will be important for the A chromophore but not for the C chromophore.

For the dihydropyran derivative *XII*, the coupling constant $J_{1,2}$ suggests a torsion angle of approximately 60° along the $C_{(1)}-C_{(2)}$ bond. This is in agreement with a sofa or half-chair conformation of the heterocyclic ring. If we assume that the N-dimethyl grouping at the benzylic position $C_{(2)}$ is again located pseudo-axially, and ring A equatorially, the resulting *M* helicity of this chiral second sphere would lead to a positive Cotton effect within the ^1L_b band. Actually, a small negative CD is found for both the ^1L_b and the ^1L_a transition, and a negative couplet within the ^1B transition. The positive Cotton effect arising from second-sphere contributions must therefore be overcompensated by the third-sphere contributions of both chromophores. The CD spectra of *XXIIIa–c* show that indeed such a third-sphere effect can be relatively strong. Furthermore, the bulky $N(CH_3)_2$ group may also experience a stronger

* The term has been coined by Prof. W. Klyne for such curves which show partial bands of opposite signs.

steric hindrance in the pseudo-equatorial conformation. Acidification leads to bisignated CD curves within both the ^1L_b and the ^1L_a transitions.

Introduction of an OR-group at $C_{(14)}$ (*XIII*, *XIV*, *XXV*) increases the negative ^1L_b-CD and leads to a bisignated CD within the ^1L_a transition already in neutral medium. The latter bisignated CD curve is enantiomorphous to the corresponding curve of *XII* in acidic medium. Acidification changes appreciably the CD of *XIII*, *XIV*, and *XXV* though the coupling constant $J_{1,2}$ of *XIV* is only insignificantly changed by protonation at the nitrogen. For *XIII*, two positive CD bands appear within the ^1L_b band and the bisignated CD within the ^1L_a transition changes sign and is then the same as for *XII*. A similar change takes place for *XIV* and *XXV* but the CD within the ^1L_b band is also here bisignated as for *XII*. The two positive CD partial bands within the ^1L_b transition of *XIII* (acidic solution) are a strong argument against the assumption that the bisignated curves observed for these compounds are due to exciton splitting; these two bands are therefore ascribed to the two independent aromatic chromophores.

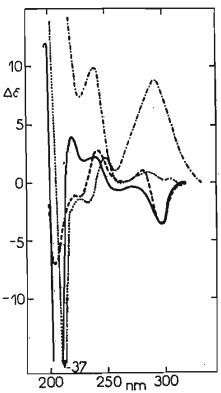


FIG. 2

CD Spectra of *XIII* in Ethanol (———) and Methanolic HCl (·····), CD Spectrum (– – – –) and UV Spectrum (–·–·–·–) of *XV* in Ethanol

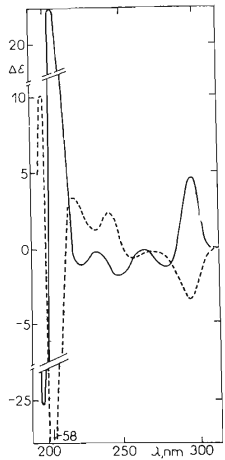


FIG. 3

CD Spectra of Dihydrorhoeadinemethine (*XVI*) (———) and Dihydrorhoeadinemethine (*XIV*) (– – – –) in Ethanol

Epimerization at $C_{(1)}$ and $C_{(14)}$ (*XVI*) leads to the appearance of an apparent positive couplet within the ^1L_b transition whereas within the ^1L_a transition only one Cotton effect is observed. The CD of the substance *XVI* resembles somewhat a mirror image of the CD of dihydrorhoeadinemethine (*XIV*) (Fig. 3). Removal of the $N(CH_3)_2$ group *XV* gives a CD curve which, in the region of 350–220 nm, is not changed by acidification as can be expected; this curve resembles the CD of *XIV* in acidic solution. From this it seems as if the *M* helicity of ring D for *XII* to *XIV*, *XXV* were more preferred in acidic solution than in neutral medium. This may be explained by electrostatic attraction between the aromatic π-system and the positive charge on nitrogen.

Introduction of a double bond into the aliphatic side chain of *XIV* gives the styrene derivative *XVIII*, which modification should not change appreciably the conformation of the whole molecule and, indeed, the coupling constants $J_{1,2}$ are both the same. Since the molecular models do not suggest any reason for a deviation from coplanarity of the styrene system, the corresponding absorption bands will acquire optical activity only by third-sphere effects and not from a chirality of the first sphere. The conjugation will, however, introduce some red shift for the benzene bands. The (negative) ^1L_b-CD band is indeed shifted from 295 to 303 nm, indicating again that the negative Cotton effect comes mainly from the A chromophore. Acidification also here brings forth a bisignated CD curve within the ^1L_b absorption as was the case with *XIV*.

The CD of the free half acetal *XVII* is practically identical with that of *XVIII* in both neutral and acidic media. Inversion of the stereochemistry at $C_{(1)}$ and $C_{(14)}$ (*XIX*) leads to a complete change of the CD curve which, however, resembles somewhat that of the corresponding dihydro derivative *XVI*, save a bathochromic shift of the CD bands at longer wavelengths than 240 nm. The two stilbene derivatives *XX* and *XXI* give only relatively weak Cotton effects which resemble each other. The weak CD indicates that in these compounds the deviation from coplanarity of the C=C—Ar moiety within the heterocyclic system is not pronounced. The "styrene rule"[35] cannot be applied because of the uncertainty in assigning a band of the CD spectrum to this partial chromophore.

The CD spectrum of oxyrhoeagenine (*XXII*) shows a long-wavelengths band at about 325 nm which is characteristic for aromatic lactones of this substitution type[25]. A direct comparison with the corresponding band of phthalidetetrahydroisoquinoline alkaloids[25] is, however, not possible because of difference in ring size of the lactone. Acidification leaves the CD spectrum almost unchanged as was the case with many other compounds with an intact ring system of rhoeadine alkaloids.

The PMR spectra of the three diphenylethane derivatives *XXIIIa–c* already indicated (*vide supra*) that at least the preferred torsion angle around the $C_{(1)}-C_{(2)}$ bond (numbering of the rhoeadine alkaloid skeleton) is the same for the diol *XXIIIa* and its mono (*XXIIIb*) and diacetate (*XXIIIc*). The CD spectra of all three com-

pounds above 230 nm are also very similar to each other and are almost independent on the solvent or on the protonation at nitrogen. One of the two possible conformations allowing for a hydrogen bond to the nitrogen must therefore also be the preferred one in case of the acetates. This is in agreement with the findings on similar simpler diphenylethane derivatives with OH and $N(CH_3)_2$ substitution at the aliphatic part by Munk and coworkers[19,21]. Furthermore, the independence of the CD on the medium proves that also the torsion angles around the two bonds from $C_{(1)}$ and $C_{(2)}$ to the respective aromatic rings are rather fixed. This is further seen from the fact that the CD within the ^1L_b band is relatively strong. The third-sphere contributions of the two aromatic chromophores have opposite signs because, within each UV absorption band, bisignated CD curves are observed. On the basis of hitherto existing evidence it is, however, not possible to decide unequivocally which band corresponds to which chromophore.

EXPERIMENTAL

The melting points have been determined on the Kofler block and are uncorrected; range of error ±2° below 200°C. Column chromatography was carried out on Al_2O_3 (Brockmann activity II, Reanal, Hungary), and thin-layer chromatography on silica gel CH (Spolana Neratovice, ČSSR) with 10% gypsum, using the solvent systems cyclohexane–diethylamine (8 : 2) (S_1) and xylene–2-butanone–methanol–diethylamine (46 : 45 : 7 : 2) (S_2). Solutions in organic solvents were dried over anhydrous sodium sulphate. For physical measurements, the samples were dried for one hour at 60°C/1 Torr. The mass spectra were measured on an AEI MS-9 instrument and the PMR spectra on a Varian T-60 spectrometer in 5% w/v concentration in deuteriochloroform with 1% tetramethylsilane as internal standard. The chemical shifts are given in δ-values (p.p.m.). The infrared spectra were recorded in chloroform on an Infrascan H-900, the ultraviolet spectra in 95% ethanol, and the hydroxyl frequencies in tetrachloromethane (*c* 5 . 10^{-3}M, 4·00 cm silica cells) in the region of 3 700–3 100 cm^{-1} on a Unicam SP. 700. The optical rotatory values of the studied substances were recorded on a Hilger & Watts polarimeter. The CD curves were measured on a Roussel-Jouan dichrograph (Model 185) at 20°C in cells of 0·01 to 2·00 cm thickness and at concentrations of about 1 mg/g. All the values are given as $\lambda_{max}(\Delta\varepsilon)$, shoulders are denoted by sh.

The starting materials for chemical transformations were rhoeadine (*II*), m.p. 251–253°C (ethyl acetate) (ref.[1]), isorhoeadine (*V*), m.p. 159–161°C (ether) (ref.[1]), rhoeagenine (*I*), m.p. 236–238°C (methanol) (ref.[1]). Rhoeageninediol *Xa*, m.p. 131–133°C (ethyl acetate), diacetylrhoeageninediol *Xb*, m.p. 107–108°C (ethanol), and isorhoeageninediol *XI*, m.p. 153–155°C were prepared according to ref.[1]. Rhoeadinemethine *XVIII*, m.p. 160–162°C (ethyl acetate) and dihydrorhoeadinemethine *XIV*, m.p. 147–148°C (methanol) were prepared according to ref.[13]. The isolation of the alkaloids alpinine (*VI*) and alpinigenine (*IX*) has been described in ref.[36], that of papaverrubine A (*IV*) in ref.[37], and that of glaucamine (*VIII*) in ref.[38].

Dihydrorhoeageninemethine XIII: Methyl acetal *XIV* (1·58 g) was heated with 0·2M-HCl (40 ml) for 3 h on a water bath, made alkaline with ammonia, and extracted with 200 ml of ether–chloroform (9 : 1). After evaporation, crude *XIII* (1·25 g) was obtained which on crystallization from ether gave 455 mg (29%) of pure material. The mother liquors were purified by chromatography on Al_2O_3 with benzene–chloroform (7 : 3) to yield another crop of 570 mg (38%) *XIII*, m.p. 170–171°C, $[\alpha]_D^{25}$ −63° ± 2° (*c* 0·60 in chloroform). Mass spectrum: molecular ion *m/e*

385; *m/e* 368, 367, 339, 221, 208, 207, 206, 192, 177, 163, and 135. λ_{max} 212, 237, and 290 nm (log ε 4·30, 4·03, and 3·94); λ_{min} 227 and 261 nm (log ε 4·00 and 3·25).

Emde degradation of dihydrorhoeadinemethine XIV: The methiodide prepared from 200 mg of *XIV* was dissolved in methanol (30 ml), mixed with freshly prepared silver chloride, shaken for 5 h, filtered, and evaporated to dryness *in vacuo*. The residue was dissolved in water (15 ml) and 4% sodium amalgam (2 g) was added. After heating the reaction mixture on a water bath for 3 h, the aqueous solution was extracted with 40 ml of ether to give 70 mg of *XX*, a Dragendorff-negative blue fluorescing substance, m.p. 136—137°C (ether) which was identical with authentic material of m.p. 135—137°C (ethyl acetate–ether) (ref.[13]). Acidification of the aqueous layer with 1M-HCl and extraction with ether afforded 40 mg of another Dragendorff-negative substance *XV*, m.p. 207—209°C (ether), $[\alpha]_D^{25}$ +49° ± 2° (*c* 0·765 in chloroform). In the mass spectrum, the peak M^+ 356·1257 corresponds to the empirical formula $C_{20}H_{20}O_6$ (356·1259). λ_{max} 211, 238, and 290 nm (log ε 4·29, 4·00, and 3·95); λ_{min} 225 and 256 nm (log ε 3·87 and 3·00).

Isorhoeadinemethine XIX *and its dihydroderivative* XVI: A solution of isorhoeadine (*V*) (80 mg) in 5 ml acetonitril was refluxed for 3 h with 2 ml of methyl iodide and left standing overnight at room temperature. The unreacted methyl iodide and the solvent were removed. The residue was dissolved in 2 ml of 50% aqueous methanol, shaken with freshly prepared moist silver oxide, filtered, and the solution concentrated to half of its volume *in vacuo*. After addition of solid potassium hydroxide (1 g), the mixture was heated for 2 h at 120°C, diluted with water, and extracted with ether. After evaporation of the ether, oily methine *XIX* (30 mg) was obtained, $[\alpha]_D^{25}$ −25° ± 4° (*c* 0·068 in ethanol). λ_{max} 270 and 294 sh nm (log ε 3·91 and 3·81); λ_{min} 256 nm (log ε 3·81).

Hydrogenation of XIX: A solution of *XIX* (20 mg) in methanol (2 ml) was hydrogenated for 2 h under atmospheric pressure at room temperature over Adams catalyst. After filtration and evaporation of the solvent, an oily substance *XVI* (15 mg) was obtained whose infrared spectrum was practically identical with that of dihydrorhoeadinemethine *XIV*. Mass spectrum: *m/e* 398 (M^+-1), 383, 368, 354, 323, 295, 266, 221, 206, 177, and 163. λ_{max} 241 and 292 nm (log ε 3·74 and 3·89); λ_{min} 262 nm (log ε 3·00).

Degradation of rhoeadine methochloride with sodium in liquid ammonia: To the methiodide of rhoeadine (*II*) (940 mg) in ethanol (200 ml), silver chloride (prepared from 800 mg of silver nitrate) was added. The mixture was shaken for 5 h, filtered, evaporated *in vacuo*, and the residue dissolved in 70 ml of freshly redistilled ammonia. Sodium was added until the mixture turned blue and left standing for 1 h at −70°C. Crystalline iron(III) nitrate and solid ammonium chloride were added. After evaporation of ammonia, the residue was dissolved in water and this solution extracted with chloroform. The solvent was removed and the residue crystallized from n-hexane to give 430 mg of rhoeadinemethine *XVIII*, m.p. 155—157°C (ref.[13], m.p. 160 to 162°C (ethyl acetate)), $[\alpha]_D^{25}$ −50° ± 2° (*c* 0·44 in ethanol).

Rhoeadinemethine XXI: The residue (1·3 g) from mother liquors obtained after crystallization of rhoeadinemethine *XVIII*, prepared by Hofmann degradation according to ref.[13], was chromatographed on Al_2O_3 with benzene–chloroform (9 : 1) to give 0·79 g of the substance *XVIII*, 0·25 g of a mixture of the two methines *XVIII* and *XXI*, and 0·20 g of rhoeadinemethine *XXI*, m.p. 135—136°C (benzene), $[\alpha]_D^{25}$ +49° ± 2° (*c* 0·84 in chloroform). Mass spectrum: molecular ion *m/e* 397; *m/e* 382, 366, 352, 320, 279, 192, and 163. λ_{max} 202, 292, and 314 nm (log ε 4·51, 4·15, and 4·09); λ_{min} 253 nm (log ε 3·79).

Dihydrorhoeägeninemethinediol XXIIIa: The substance *XIII* (0·50 g, 1·3 mmol) was dissolved in benzene (20 ml), and 1·5 ml (3·25 mmol) of a 53% solution of sodium dihydro-bis(2-methoxyethoxy)aluminate in benzene was added. The reaction mixture was refluxed for 2 h and then

treated with a 20% solution of sodium hydroxide. After removal of benzene, the aqueous layer was extracted with 150 ml of chloroform. The residue of this chloroform extract was dissolved in benzene and chromatographed on Al_2O_3 to give 0·48 g (95%) of chromatographically pure diol *XXIIIa* which could not be crystallized, $[\alpha]_D^{25}$ +85° ± 2° (*c* 0·61 in chloroform). λ_{max} 213, 236, and 291 nm (log ε 4·30, 3·90, and 3·85); λ_{min} 230 and 260 nm (log ε 3·88 and 3·07).

Diacetyldihydrorhoeageninediolmethine XXIIIc: The diol *XXIIIa* (0·30 g) in pyridine (5 ml) and acetanhydride (5 ml) was left standing overnight at room temperature. Pyridine and acetanhydride were removed *in vacuo*, the residue was dissolved in chloroform, and the solution shaken with 10% $NaHCO_3$. After evaporation of the chloroform layer, the residue gave 383 mg (90%) of an oily diacetyl derivative *XXIIIc*, $[\alpha]_D^{25}$ −55° ± 2° (*c* 0·62 in chloroform). λ_{max} 213, 238, and 291 nm (log ε 4·30, 3·89, and 3·87); λ_{min} 231 and 262 nm (log ε 3·88 and 3·18).

Monoacetyldihydrorhoeageninediolmethine XXIIIb: The diacetate *XXIIIc* (0·18 g) and 5% $Pd/BaSO_4$ (0·18 g) in 6 ml of 10% ethanolic solution of triethylamine were treated with hydrogen gas at atmospheric pressure and room temperature for 8 h. After filtration and concentration to dryness *in vacuo*, a mixture of two substances (0·15 g) was obtained. This mixture was chromatographed on Al_2O_3 with benzene–chloroform (8 : 2) to give 90 mg of the starting material *XXIIIc*, 7 mg of a mixture of *XXIIIc* and *XXIIIb*, and 40 mg of pure monoacetate *XXIIIb*, m.p. 155–157°C (ethyl acetate), $[\alpha]_D^{25}$ +48° ± 2° (*c* 0·74 in chloroform). λ_{max} 238 and 293 nm (log ε 3·93 and 3·92); λ_{min} 230 and 261 nm (log ε 3·91 and 3·10).

Emde degradation of rhoeagenine (I) *to* XXV: The methiodide of rhoeadine (*II*) was prepared from 0·40 g of rhoeagenine (*I*) and dissolved in methanol (50 ml). Freshly prepared silver chloride was added, the slurry stirred for 5 h, filtered, and the filtrate evaporated *in vacuo*. The residue was dissolved in water (15 ml) and 4% sodium amalgam (4 g) was added. The mixture was heated for 3 h on a boiling water bath, diluted with water, and extracted with ether to give 0·35 g of crude material. Thin-layer chromatography shows that it is a mixture of at least four substances — R_F 0·78; 0·67; 0·59; 0·31 (S_1). Column chromatography on Al_2O_3 with benzene gave 226 mg of the substance *XXV*, m.p. 134–135°C (ethyl acetate), R_F 0·59 (S_1), optically active. In the mass spectrum the peak M^+ 399·1678 corresponds to the empirical formula $C_{22}H_{25}NO_6$ (399·1681). λ_{max} 238 and 291 nm (log ε 3·98 and 3·93); λ_{min} 225 and 259 nm (log ε 3·87 and 3·10).

Hydrogenolysis of diacetylrhoeageninediol Xb: The diol *Xb* (0·30 g) was hydrogenated for 6 h at 100°C (initial hydrogen pressure 50 atm) with 5% $Pd/BaSO_4$, in 15 ml of ethanol, left standing overnight at room temperature, filtered, and evaporated *in vacuo*. The residue was dissolved in water, extracted with chloroform, and the solvent removed to give 150 mg of a mixture of two substances which were chromatographed on Al_2O_3, with benzene–cyclohexane (1 : 1). The first fractions gave 60 mg of an optically inactive substance *XXVI*, m.p. 153–154°C (benzene–cyclohexane). Mass spectrum: molecular ion *m/e* 339; *m/e* 324, 308, 296, 281, 190, and 148. λ_{max} 235 sh and 291 nm (log ε 3·99 and 3·94); λ_{min} 257 nm (log ε 3·12). The next fractions afforded 27 mg of a mixture of the substances *XXVI* and *XXVII*, and the following ones 42 mg of pure optically inactive *XXVII*, m.p. 205–206°C (benzene). The infrared and the PMR spectral data show that this substance is identical with the substance which was obtained[17] by hydrogenation of the "red product of papaverrubine".

CD Data of Rhoeadine and Related Compounds

Rhoeagenine I: acetonitrile: 292·5 (+3·09), 254 (−1·79), 246 (−1·85), 225 sh (+3·90), 207·5 (+38), 197 (−32); HCl/methanol: 293 (+5·30), 270 sh (+1·07) 249 (−0·87), 232 sh (+2·70), 209 (+53), 198 (−41); dioxane: 292 (+3·78), 255 (−2·19), 245 (−2·69), 226 sh (+3·98),

211 (+25). *Rhoeadine* II: acetonitrile: 293 (+3·27), 253 sh (−2·55), 248 (−2·78), 225 sh (+4·93), 207 (+45), 197 (−28); HCl/methanol: 294·5 (+5·79), 267 sh (+0·72), 248 (−2·78), 230 (+2·91), 211 (+43), 200 (−64); dioxane: 293·5 (+3·61), 256 (−2·65), 245 (−3·09), 226 sh (+4·90), 215 (+14). 14-*Demethoxyrhoeadine* III: ethanol: 289 (+3·39), 270 sh (+0·88), 252·5 sh (−0·81), 242·5 (−2·17), 227 sh (+3·10), 210 (+56), 196 (−70); HCl/methanol: 290 (+4·23), 265 sh (+0·92), 246 (−1·68), 230 sh (+4·12), 212·5 (+67), 200 (−69). *Papaverrubine* A IV: acetonitrile: 296 (+5·09), 247·5 (+1·36), 206 (+78), 195 (−24); dioxane: 296·5 (+5·31), 246·5 (+1·20), 215 (+15). *Isorhoeadine* V: acetonitrile: 296 (+5·68), 276 sh (+0·80), 252 sh (−2·70), 243 (−2·90), 206 (+64), 196 (−31); HCl/methanol: 293 (+7·30), 267 sh (+0·73), 248 (−2·87), 229 sh (+2·60), 210 (+66), 199 (−47); dioxane: 298 (+5·93), 275 sh (+0·43), 255 (−2·69), 241 (−3·66), 215 (+25). *Alpinine* VI: acetonitrile: 287 (+2·66), 272 sh (+0·67), 253 (−1·96), 239·5 (+2·10), 207 (+63), 196 (−42); HCl/methanol: 284 (+3·39), 242 (+3·09), 225 sh (+5·20), 209 (+61), 198 (−38). *Epiisorhoeadine* VII: acetonitrile: 297 (+4·01), 275 sh (+0·19), 255 (−1·42), 242 sh (−1·09), 206 (+57), 195 (−27); HCl/methanol: 294 (+5·28), 270 sh (+0·68), 249 (−1·42), 230 sh (+2·06), 210 (+49), 198 (−54). *Glaucamine* VIII: acetonitrile: 296 (+4·78), 273 sh (+0·40), 255 (−2·55), 240 sh (+1·07), 208 (+89), 195 (−61); HCl/methanol: 289 (+4·83), 270 sh (+0·98), 244 sh (+3·42), 209 (+56), 198 (−58). *Alpinigenine* IX: acetonitrile: 287 (+2·75), 272 sh (+0·33), 253 (−2·79), 239·5 (+2·33), 207 (+65), 196 (−43); HCl/methanol: 284 (+3·09), 241 sh (+5·54), 225 sh (+9·64), 209 (+59). *Rhoeagenineidiol* Xa: ethanol: 295 (−2·55), 249·5 (−5·73), 225 sh (−5·92), 209 (−32); HCl/methanol: 293 (+0·34), 255·5 (−0·27), 243 (+4·55), 226 sh (−4·35), 213·5 (−56), 201 (+16). *Diacetylrhoeagenineidiol* Xb: ethanol: 286 (−0·70), 250 (−4·92), 239 (+0·22), 227 (−3·22), 211 (−39); HCl/methanol: 284 (−0·90), 254·5 (−2·64), 243 (+1·14), 228·5 sh (−2·08), 214 (−37), 200 (+39). *Isorhoeagenineidiol* XI: ethanol: 296 (+1·98), 277 (−0·08), 250 (−3·71), 234 (+5·24), 207 (+18), 198 (−16); HCl/ethanol: 287 (−1·79), 252 (−3·22), 239 (+0·35), 230 (−2·55), 215 (−26), 205 (+17). 14-*Demethoxyrhoeadinemethine* XII: ethanol: 293 (−1·50), 252 (−0·83), 206 (−24), 195 (+11); HCl/ethanol: 295 (−1·24), 278 (+0·54), 248 (+1·78), 229 sh (−1·68), 211 (−32), 196 (+10); cyclohexane: 292 (−2·04), 253 (−1·62), 206 (−29), 192 (+10). *Dihydrorhoeageninemethine* XIII: ethanol: 295 (−3·63), 256 (−0·74), 241 (+2·31), 219·5 (+4·03), 205·5 (−53), 198 (+12); HCl/methanol: 302 (+0·45), 284 (+0·96), 247 (+2·23), 232 (−1·61), 210 (−37). *Dihydrorhoeadinemethine* XIV: ethanol: 295 (−3·45), 255·5 (−0·63), 241 (+2·39), 218 (+3·36), 205 (−58), 195 (+18·32); HCl/methanol: 297 (−1·16), 281·5 (+0·84), 249 (+2·45), 233 (−3·37), 211 (−36), 199 (+31). *Compound* XV: ethanol: 296 (−3·62), 280 (+1·19), 241 (+2·88), 227 (−1·11), 204 (−7), 195 (+8); HCl/ethanol: 296 (−2·36), 279 (+0·68), 241 (+1·70), 228 (−0·91), 196 (+12); cyclohexane: 296 (−3·33), 280 (+1·05), 274 sh (+0·81), 240 (+2·90), 226 sh (−0·93), 204 (−20), 197 (+12). *Dihydroisorhoeadinemethine* XVI: ethanol: 297 (+4·69), 279 (−1·24), 248 (−1·89), 223 (−1·04), 205 (+22), 197 (−25); HCl/ethanol: 297 (+6·14), 279 (−1·11), 247 (−1·90), 220 (−3·50), 210 (+18), 201 (−35). *Rhoeageninemethine* XVII: ethanol: 302·5 (−2·63), 284·5 (0), 276 (−1·00), 250 (+5·02), 226 sh (−4·7); HCl/methanol: 306 (−1·63), 284 (+3·61), 259 (+3·51), 235 sh (−2·72), 214 (−22), 203 (+32). *Rhoeadinemethine* XVIII: ethanol: 303 (−2·90), 276 (−1·00), 251 (+5·29), 223 sh (−5·8), 208 (−23·27), 195 (+12·53); HCl/methanol: 306 (−2·54), 284 (+3·96), 262 (+4·48), 236 sh (−6·3), 214 (−32), 203 (+32). *Isorhoeadinemethine* XIX: ethanol: 323 (−0·23), 302 (+1·17), 278 (−4·16), 268 (−4·16), 234 (+2·70), 210 (−26), 198 (+12); HCl/ethanol: 311 (−0·53), 300 (+0·97), 275 (−5·10), 238 (+2·34), 227 (+2·81), 213 (−47), 200 (+18). *Dihydrorhoeadinebismethine* XX: acetonitril: 326 (−2·75), 290 (+0·68), 280 (+1·17), 260 (−0·27), 246 (+1·19), 230 (−0·62), 209 (+13). *Rhoeadinemethine* XXI: ethanol: 320 (−1·18), 284 (+0·35), 261 (−0·35), 246 (+1·68), 222 (−0·80), 207 (+4); HCl/methanol: no CD detectable; cyclohexane: 323 (−1·83), 284 (+2·00), 247 (+1·72), 231 (−0·45), 206 (+12). *Oxyrhoeagenine* XXII: acetonitrile: 323 (+1·34), 299 (+0·92), 285 sh (−0·31), 256·5 (−5·65), 241·5 (+0·93),

223 (−5·10), 208 (+39); HCl/methanol: 327·5 (+1·74), 305 sh (+1·09), 282 sh (−0·77), 260 (−6·75), 247·5 (+1·59b, 227·5 (−6·87), 211 (+34), 198 (−50); dioxane: 320 (+1·96), 306 sh (+1·61), 283·5 sh (−1·11), 256 (−6·54), 241·5 (+1·63), 222 (−7·02), 215 (+6·20). *Dihydrorhoeageninediolmethine* XXIIIa: ethanol: 298 (+1·66), 281 (−1·25), 249 (−0·57), 230 (+3·79), 205 (+15); HCl/ethanol: 298 (+2·84), 281 (−1·04), 248 (−1·11), 231 sh (+2·96), 209 (+14), 196 (−5); cyclohexane: 298 (+1·76), 282 (−1·11), 231 (+5·63), 205 (+20). *Monoacetyl-dihydrorhoeageninediolmethine* XXIIIb: ethanol: 299 (+1·99), 283 (−1·91), 250 (−0·49), 232 (+4·24), 216 (−3·4), 206 (+15); HCl/ethanol: 300 (+2·86), 283 (−2·11), 250 (−0·75), 232 (+2·86), 211 (+15); cyclohexane: 300 (+1·17), 283 (−2·31), 250 (−1·05), 234 (+3·00), 206 (+15). *Diacetyl-dihydrorhoeageninediolmethine* XXIIIc: ethanol: 302 (+1·16), 285 (−2·77), 249 (−0·85), 237 (+0·47), 215 (−10); HCl/ethanol: 300 (+2·16), 284 (−2·38), 252 (−0·96), 233 (+1·32), 215 (+11); cyclohexane: 303 (+0·80), 285 (−4·89), 251 (−1·64), 216 (−20). *Compound* XXV: ethanol: 296 (−3·50), 279 (+1·39), 241 (+2·74), 227 (−0·87); HCl/ethanol: 297 (−2·10), 279 (+0·97), 243 (+1·50), 230 (−0·90).

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