Pica pica, Magpie; *Garrulus glandarius*, Jay; *Chloropsis aurifrons*, Goldfronted Leafbird

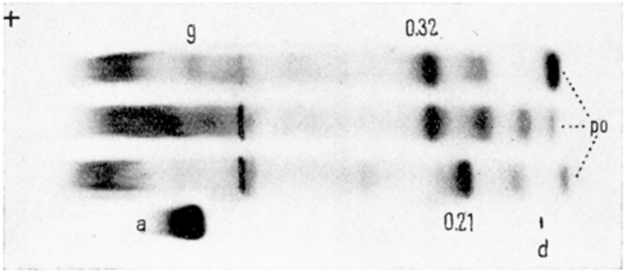

Fig. 4. Muscle pherograms showing the 0.32 and 0.21 mobilities of the myogen and also the myoglobin with peroxydase activity (po).

Turdus merula, Blackbird; *Turdus pilaris*, Fieldfare; *Turdus philomelos*, Song Thrush; *Turdus iliacus*, Redwing

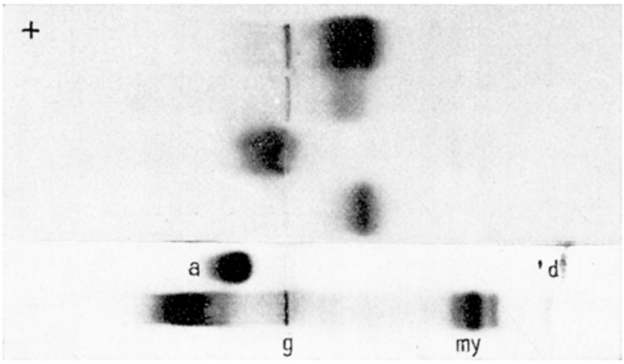

Fig. 5. Muscle pherograms with specific staining for esterases. The lower part of the Figure illustrates a control-strip with serum albumin (a) as a test. It was stained in the usual way with amidoblack, showing also the mobility of the myogen of the Redwing.

oxydase activity. Esterase iso-enzymes and LDH are quite easily detectable in a bird's lens (RABAEY, personal communication) and suitable for mobility measuring. Esterase was detected by using α-naphthyl-acetate as a substrate; LDH by a histochemical method[9], while the substrate was brought in according to an enzymo-electrophoretic method (WIEME, personal communication). Also in the muscle extract of birds, those enzymes are detectable and the esterases are sometimes very specific. This is shown clearly by four *Turdus* species (Figure 5).

Research is being continued on birds of families and orders not yet examined, and also on the comparison of lens proteins by immuno-electrophoretical methods[10].

Résumé. Les protéines solubles de la lentille et des muscles des oiseaux furent examinés au moyen de la micro-électrophorèse en agargel. La mobilité des fractions protéiques s'est présentée comme un caractère systématique important: il y a généralement des différences nettes et constantes, mais parfois aussi des ressemblances, qui indiquent probablement des relations de parenté.

H. GYSELS

Instituut voor Dierkunde, Rijksuniversiteit Gent (Belgium), May 21, 1962.

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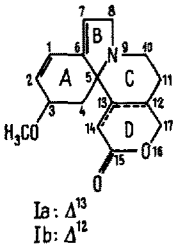
[9] H. J. VAN DER HELM, Lancet II, 108 (1961).

[10] *Acknowledgments.* I am much indebted to the late Prof. Dr. R. VERHEYEN, and to Prof. Dr. M. RABAEY, whose knowledge and councils were of extreme value for me. I wish to thank also Mr. W. VAN DEN BERGH, director of the Antwerp Zoo, and the co-workers of the Belgian Ringing Work, who provided me with so many birds.

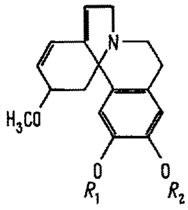
STUDIORUM PROGRESSUS

Absolute Configuration of the Spiro Carbon Atom of the Erythrina Alkaloids: Evidence from Optical Rotatory Dispersion

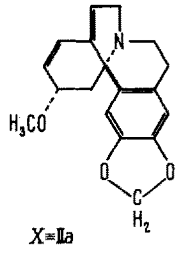
Plants of the genus Erythrina (Leguminosae) produce two groups of dienic alkaloids: the lactones α- and β-erythroidine (Ia and b, resp.), and a number of aromatic bases of the general formula II[1].



Ia: Δ^{13}
Ib: Δ^{12}



IIa: $R_1 + R_2 = -CH_2-$
b: R_1 or $R_2 = H$
R_2 or $R_1 = CH_3$
c: $R_1 = R_2 = H$



X≡IIa

While the structures of the bases have been unequivocally established, the stereochemistry is only incompletely known. For the lactone base Ia, HILL and SCHAERER[2] have established the absolute configuration at C-12 which is asymmetric in this one alkaloid only; this configuration, however, has not been correlated with those of the two other asymmetric centers, C-3 and C-5, which are present in all Erythrina alkaloids[3]. Since Ia and Ib have been interrelated[4], their configurations at C-3 and C-5

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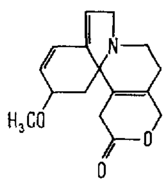
[1] For reviews on these alkaloids, see (a) L. MARION, in *The Alkaloids* (Ed. H. L. HOLMES and R. H. F. MANSKE, Academic Press, Inc., New York 1952), vol. II, p. 499. – (b) V. BOEKELHEIDE, in *The Alkaloids* (Ed. H. L. HOLMES and R. H. F. MANSKE, Academic Press, Inc., New York 1960), vol. VII, p. 201.

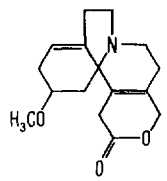
[2] R. K. HILL and W. R. SCHAERER, J. org. Chem. *27*, 921 (1962).

[3] Unpublished evidence on the absolute configuration of C-3 in Ia and Ib is mentioned in [2].

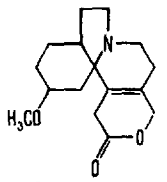
[4] V. BOEKELHEIDE and G. C. MORRISON, J. Amer. chem. Soc. *80*, 3905 (1958).



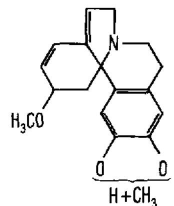
Ib



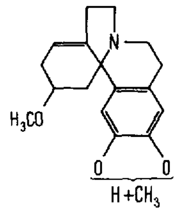
IV



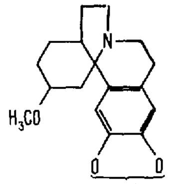
VII



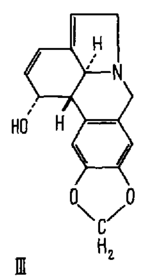
IIb



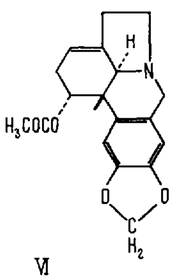
V



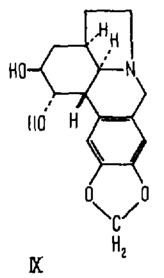
VIII



III



VI



IX

should be the same. X-ray crystallographic investigation[5] of the aromatic base, erythraline (IIa), has established its *relative* configuration: N atom and methoxy group are *cis* to each other with reference to ring A. Since IIa has been correlated[6,7] with the other aromatic bases by reactions which involve removal of the methoxy group but should not alter the configuration at C-5, these bases all should have the *same* stereochemistry at this center. The *absolute* configuration at C-5 remains unknown, however; furthermore, it is not known whether this configuration is the same in both series of alkaloids represented by general formulae I and II. Biogenetic considerations and the uniformly highly positive $[\alpha]_D$ values of all these bases would suggest that this is the case, but experimental proof has not been obtained thus far. The relative configuration at C-3 in all Erythrina alkaloids except IIa is likewise unknown.

Investigation of the rotatory dispersion of several of these alkaloids has now made it possible to determine their absolute configuration at C-5. The approach is based on the fact[8] that a non-planar, conjugated diene is in itself an element of dissymmetry which produces a Cotton effect, the direction of which depends upon the chirality of the diene. The rotational strength of such an inherently dissymmetric chromophore is about one order of magnitude higher than that of an asymmetrically perturbed symmetric chromophore[9]; consequently, it should be the dominating influence on the rotatory dispersion, and the sign of the Cotton effect so produced should give information on the chirality of the diene, which in its turn depends upon the configuration (and conformation) of the molecule. The treatment[8] given originally for *cisoid* dienes only has recently been extended to *transoid* ones[10], the connection between sign of Cotton effect and sense of skewness of the diene in this case being given by the following rule: If a model of the dienic substance is held in such a way that the central single bond and the double bond to its left are horizontal, the double bond pointing *away* from the observer, a positive or negative Cotton effect is predicted if the double bond on the right, pointing toward the observer, extends upwards or downwards, respectively.

Dreiding models of the Erythrina alkaloids show that all these compounds contain a moderately skewed diene, and that such conformational mobility as is possible modifies the *degree*, but not the *direction*, of the skewness of this conjugated system. Consequently, the chirality of the diene, and hence the absolute configuration of the C-N skeleton, i.e. essentially that at C-5, can be derived from the rotatory dispersion of the compounds. Ib and erysodine (IIb) were chosen for study as representatives of types I and II, respectively.

Since one, as yet unexplained, exception from the rule connecting the chirality of a *transoid* diene with the sense of the Cotton effect has been observed[10], it was essential to obtain additional independent evidence for the applicability of this rule in the present case. This was feasible through investigation of the optical rotatory dispersion of dehydrolycorine[11] (III), a compound of known absolute configuration[12] containing a transoid diene chromophore identical with that present in the Erythrina alkaloids in a structure closely resembling that of the alkaloids of type II. The agreement of the observed Cotton effect with that predicted from the skewness of the diene in models of III (see below) corroborates the reliability of the rule for transoid dienes of the type present in the Erythrina alkaloids.

In order to separate the influence of the diene from that of other chromophores, the rotatory dispersions of Ib, IIb, and III were compared with those of the corresponding dihydro (IV, V, and VI = acetylcaranine[14a]) and tetrahydro (VII, VIII, and IX = dihydrolycorine[14b]) derivatives or analogues. This was especially important in the case of the aromatic compounds, IIb and III, where the presence of the benzene ring might complicate the issue. It has been shown in the structurally related morphine series that this chromophore produces a Cotton effect of moderate intensity around 300 mμ[15], and stronger ones at shorter wave-

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[5] W. Nowacki and G. F. Bonsma, Z. Krist. *110*, 89 (1958).

[6] K. Folkers, F. Koniuszy, and J. Shavel jr., J. Amer. chem. Soc. *73*, 589 (1951).

[7] M. Carmack, B. C. McCusick, and V. Prelog, Helv. chim. Acta *34*, 1601 (1951).

[8] A. Moscowitz, E. Charney, U. Weiss, and H. Ziffer, J. Amer. chem. Soc. *83*, 4661 (1961). The $\pi \rightarrow \pi^*$ transition in α,β-unsaturated ketones, isoelectronic with that of dienes, has been subjected to a similar theoretical treatment, resulting in rules, verified experimentally, which are essentially identical with those for *cisoid* and *transoid* dienes: C. Djerassi, R. Records, E. Bunnenberg, K. Mislow, and A. Moscowitz, J. Amer. chem. Soc. *84*, 870 (1962).

[9] A. Moscowitz, Tetrahedron *13*, 48 (1961).

[10] E. Charney, H. Ziffer, and U. Weiss, manuscript in preparation.

[11] H. M. Fales and W. C. Wildman, J. Amer. chem. Soc. *80*, 4395 (1958).

[12] The assignment of absolute configurations to the alkaloids of the lycorine series rests ultimately upon the application of Mills' rule to lycorine and 2-epilycorine by Nakagawa and Uyeo[13]. Consequently, our use of III and its relatives VI and IX (see below) for corroboration of the rotational evidence for the absolute configurations of the Erythrina alkaloids is predicated upon the assumption that Mills' rule is valid in the case of lycorine.

[13] Y. Nakagawa and S. Uyeo, J. chem. Soc. *1959*, 3736.

[14] (a) Acetylcaranine: E. W. Warnhoff and W. C. Wildman, J. Amer. chem. Soc. *79*, 2192 (1957). The stereochemistry of caranine is given through multiple interrelations with lycorine; see, *inter alia*, [13]. (b) Dihydrolycorine: for constitution and relative stereochemistry, see K. Takeda and K. Kotera, Chem. and Ind. *1956*, 347, and references quoted there.

[15] J. M. Bobbitt, U. Weiss, and D. D. Hanessian, J. org. Chem. *24*, 1582 (1959).

lengths[16]; the latter effects might be expected to interfere with those produced by the diene chromophore of the Erythrina alkaloids (λ_{max} 235–240 mμ[1b]).

All the Erythrina alkaloids and their hydrogenation products were investigated as the hydrobromides in aqueous solution. For the model compounds in the lycorine series, this was not feasible because of the very low solubility of the hydrobromide of VI; hence, the rotatory dispersions of III, VI, and IX were measured on methanolic solutions of the free bases. To establish whether it is permissible to compare these two sets of data, III and IX were also investigated as the hydrobromides in water. It was found that their curves in both media are negative throughout the range of wavelengths studied and quite similar in shape, although the [M] values of the bases in methanol are consistently higher than those of the hydrobromides in water. Since the sense rather than the intensity of the rotation is significant for our purpose, the results obtained for III, VI, and IX can be used to support the conclusions reached for the Erythrina alkaloids.

Results. The findings of our investigation of Ib, IIb, and their respective di- and tetrahydro derivatives are shown in Figures 1 and 2. While the Cotton effects produced by the diene chromophore were not reached because of the intense absorption of the compounds in the significant spectral region[17], it is obvious from the curves obtained that this chromophore contributes *dextro*-rotation in both instances (cf. the difference between Ib and VII[18], and between IIb and VIII), while that of III (Figure 3) causes a *negative* effect, in agreement with predictions from the chirality of its diene.

From examination of Dreiding models it is clear that chirality of the diene compatible with the observed dextrorotatory contribution is produced by that absolute configuration at C-5 which is exemplified for Ib in Figure 4. In the Cahn-Ingold-Prelog notation, this configuration is (5*S*) for Ib, and (5*R*) for the aromatic bases; the model for IIb would be identical except for ring D. (In Figure 4 it is arbitrarily assumed that the methoxyl at C-3 has the same orientation relative to the N atom which it is known[5] to have in IIa.) Our results thus establish that both Ib and IIb have this absolute stereochemistry at C-5; in addition, comparison of the rotatory dispersion curves of IIa, IIb, and IIc (Figure 5) shows convincingly that IIa and IIc likewise have this (5*R*) configuration, and hence that the Erythrina alkaloids of both types I and II belong to the same stereochemical series. In the case of IIa, this result, together with the earlier ones from X-ray crystallography[5], establishes the complete absolute stereochemistry: IIa has the absolute configuration (3*S*:5*R*) (X). For the other Erythrina bases, the configuration at C-3 remains unknown (but cf. ref. 3).

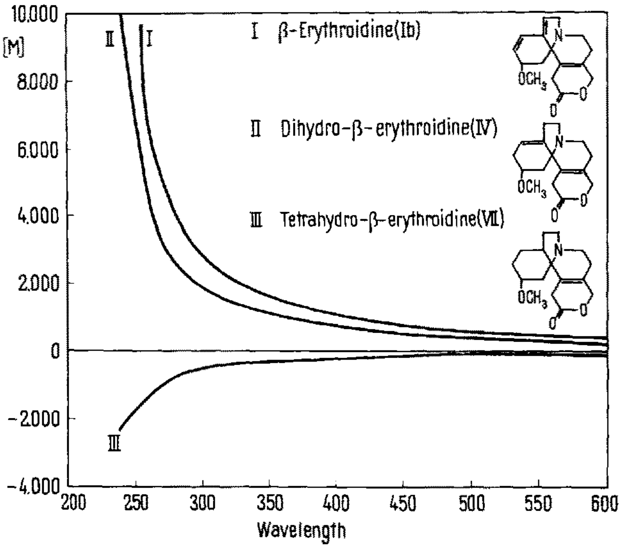

Fig. 1. Optical rotatory dispersion of β-erythroidine (Ib) and its hydrogenation products (IV, VII), as the hydrobromides in water.

The intense dextrorotation (Figure 1) shown by IV in spite of the absence of the diene chromophore is in line with recent findings[20] on the rotatory dispersion of homoconjugated systems with rigid geometrical orientation (e.g., the case of (+)-5-methylene-bicyclo-[2, 2, 1]-hept-2-ene).

Experimental. The rotatory dispersions were measured with a Rudolph Recording Spectropolarimeter. The Erythrina bases were investigated as the hydrobromides in aqueous solution, the lycorine-type alkaloids as the bases in methanol[21].

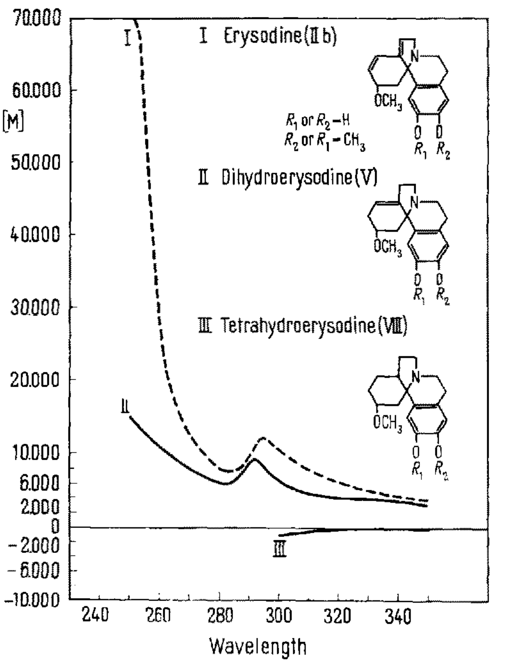

Fig. 2. Optical rotatory dispersion of erysodine (IIb) and its hydrogenation products (V, VIII), as the hydrobromides in water.

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[16] U. WEISS and H. ZIFFER, unpublished observations.

[17] The peak ($\lambda \sim$ 250 mμ) of a Cotton effect apparently centered at approximately 238 mμ, and hence ascribable to the diene, was observed in the case of IIa, when the rotatory dispersion was investigated with the help of a very thin cell (path length 2 mm). The rotations observed under these circumstances were too small to permit calculation of significant [M] values, which, however, seem to be of the order of magnitude usually found for conjugated dienes ($\sim 5 \times 10^4$).

[18] It is noteworthy that two different preparations of VII gave rotatory dispersion curves which are weakly *negative* throughout the entire range of wavelengths investigated. Yet the $[\alpha]_D$ of the β-isomer of tetrahydro-β-erythroidine (as the hydrobromide, m.p. 240° dec.) is given[19] as + 65.2°. Data on the rotation of the other isomer seem to be lacking.

[19] K. FOLKERS and F. R. KONIUSZY, Brit. Pat. 596976; Chem. Abstr. *42*, 3914a (1948).

[20] K. MISLOW, Ann. New York Acad. Sci. *93*, 457 (1962).

[21] Samples of Erythrina alkaloids were kindly furnished by Drs. K. FOLKERS and A. F. WAGNER (Merck, Sharp and Dohme, Inc., Rahway, New Jersey), Prof. V. PRELOG (Eidgenössische Technische Hochschule, Zürich), Mr. R. SALKIN (S. B. Penick and Co., Jersey City, New Jersey), and Dr. I. H. SLATER (Eli Lilly and Co., Indianapolis), those of III, VI, and IX by Drs. H. M. FALES and W. C. WILDMAN (National Heart Institute).

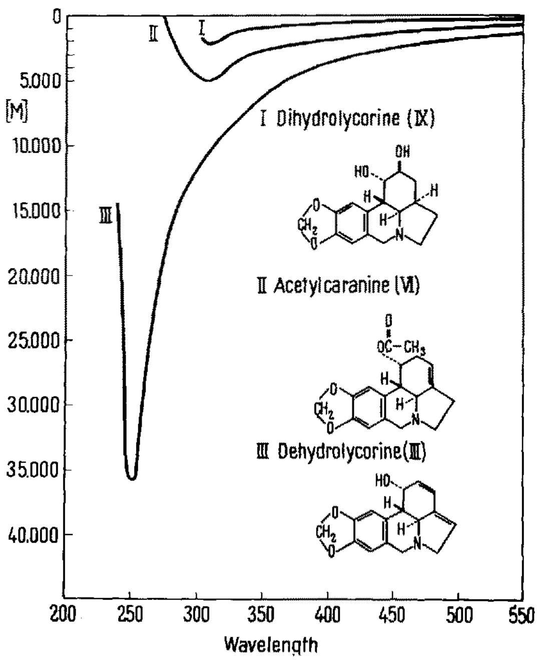

Fig. 3. Optical rotatory dispersion of dehydrolycorine (III), acetylcaranine (VI) and dihydrolycorine (IX) as the bases in methanol.

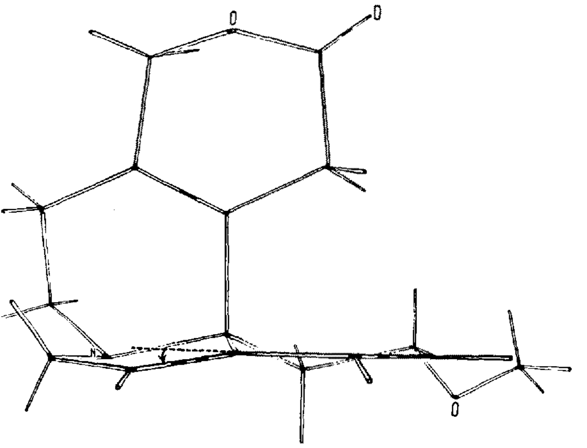

Fig. 4. Dreiding model of β-erythroidine, with angle of skewness of diene indicated.

Compounds IV, V, and VIII were prepared by catalytic hydrogenation of Ib[22] and IIb[23], resp. One sample of VII hydrobromide was prepared by us through catalytic reduction (PtO_2) of Ib[19,24]; m.p. 239–243°. Another sample was obtained from a beautifully crystalline picrate (m.p. 215–216°) of unknown history, kindly furnished by Dr. W. C. Wildman; m.p. of the hydrobromide, 238–240°. The IR spectra of both samples were essentially identical.

Gas-chromatography. β-Erythroidine (Ib) and its reduction products were analyzed by means of a Barber-Colman Model 15 gas chromatograph, containing a six foot 1% QF-1 column at 201°. Retention times relative to Ib are: IV, 0.77; VII, 0.72. Erysodine (IIb) and its hydrogenation products were studied in the same instrument, using a twelve foot 1% SE-30 column at 201°. Retention times relative to IIb are: V, 0.91; VIII, 1.07.

Numerical values of optical rotation ([M] values of extrema, and of lowest wavelength investigated): (A) Series of β-erythroidine (as hydrobromides in water): Ib, (c 0.0817), $[M]_{254}$ + 9100°; IV, (c 0.018), $[M]_{254}$ + 8800°; VII, (c 0.1), $[M]_{230}$ – 2100°. (B) Series of erysodine (as hydrobromides in water): IIb, (c 0.1), $[M]_{295}$ + 11,400°; $[M]_{285}$ + 7500°; $[M]_{252}$ + 70000°; V, (c 0.04), $[M]_{292}$ + 8300°; $[M]_{285}$ + 2260°; $[M]_{240}$ + 13500°; VIII, (c 0.137), $[M]_{300}$ – 730°. (C) Series of dehydrolycorine (as bases in methanol): III, (c 0.01), $[M]_{250}$ – 35800°; $[M]_{235}$ – 15000°; VI, (c 0.1), $[M]_{305}$ – 4400°; (c 0.01), $[M]_{275}$ ± 0°; IX, (c 0.1), $[M]_{315}$ – 2000°; $[M]_{305}$ – 1900°. (D) Erythraline, erysopine (as hydrobromides in water): IIa (c 0.0156), $[M]_{298}$ + 15500°; $[M]_{285}$ + 9900°; (c 0.003), $[M]_{250}$ + 70000°; IIc (c 0.1), $[M]_{294}$ + 12200°; $[M]_{280}$ + 7130°; $[M]_{256}$ + 42000°[25].

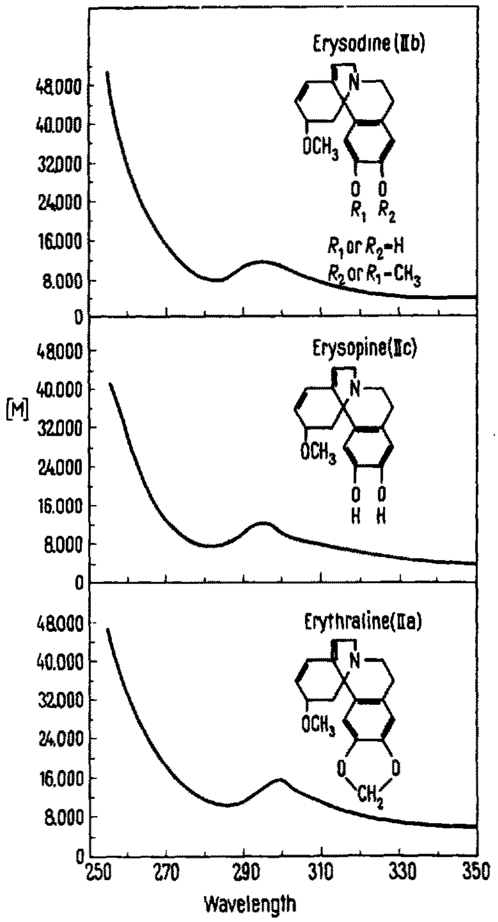

Fig. 5. Optical rotatory dispersion of erythraline (IIa), erysodine (IIb), and erysopine (IIc) as the hydrobromides in water.

Zusammenfassung. Durch Messung der Rotationsdispersion wurde die bisher unbekannte absolute Konfiguration

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[22] K. Folkers and F. R. Koniuszy, U.S. Pat. 2370651 (1945); Chem. Abstr. *39*, 5411 (1945).

[23] V. Prelog, K. Wiesner, H. G. Khorana, and G. W. Kenner, Helv. chim. Acta *32*, 453 (1949).

[24] V. Boekelheide, J. Weinstock, M. F. Grundon, G. L. Sauvage, and E. J. Agnello, J. Amer. chem. Soc. *75*, 2550 (1953).

[25] *Acknowledgments.* The authors are much indebted to Mr. H. K. Miller for making available the Rudolph spectropolarimeter, to Drs. H. M. Fales, R. J. Highet, N. E. Sharpless, and Lin Tsai for stimulating discussions, and to Mr. J. R. Mills for helpful technical assistance.

des Spiro-Kohlenstoffatoms (C-5) der Erythrina-Alkaloide ermittelt. Die Methode beruht auf der Tatsache, dass diese Alkaloide ein nicht-coplanares conjugiertes Dien-System enthalten, und dass die Richtung des Cottoneffektes, welcher von einem solchen System erzeugt wird, von dessen Chiralität abhängt[8]; diese ist ihrerseits durch die Konfiguration des Moleküls bedingt. Es ergibt sich, dass beide Haupttypen dieser Alkaloide die gleiche absolute Konfiguration von C-5 besitzen und daher derselben sterischen Reihe zugehören.

U. WEISS and H. ZIFFER

Laboratory of Physical Biology, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda (Maryland, U.S.A.), September 3, 1962.

PRAEMIA

Eidgenössische Technische Hochschule

Fonds für den Ruzicka-Preis

Ausschreibung des Preises für 1963

Aus dem Fonds für den Ruzicka-Preis wird alljährlich einem jungen Forscher für eine hervorragende, veröffentlichte Arbeit auf dem Gebiete der allgemeinen Chemie ein Preis erteilt. Die chemischen Arbeiten, welche mit einem Preis ausgezeichnet werden sollen, müssen entweder in der Schweiz oder von Schweizern im Ausland ausgeführt worden sein.

Kandidaten dürfen in dem Jahre, in welchem sie den Preis erhalten, das 45. Lebensjahr nicht überschritten haben. Sie können dem Kuratorium von dritter Seite vorgeschlagen werden oder sich auch selbst um den Preis bewerben.

Der Preis wird auf den Antrag eines Kuratoriums durch den Schweiz. Schulrat erteilt. Die Überreichung des Preises erfolgt im September 1963.

Bewerbungen und Anträge sind unter Angabe der chemischen Arbeit, für welche der Preis erteilt werden soll, *bis spätestens am Mittwoch, den 29. Mai 1963*, der Kanzlei des Schweiz. Schulrates, Eidg. Technische Hochschule, Leonhardstrasse 33, Zürich 6, einzureichen.

Der Präsident des Schweiz. Schulrates
Prof. Dr. H. PALLMANN

CORRIGENDUM

J. R. PETER: *Intermittierende elektrische Entladungen im Gasraum zwischen zwei Dielektrika*. Exper. vol. XVIII, fasc. 12, p. 543 (1962). Irrtümlicherweise wurden an verschiedenen Stellen Φ (gross Phi) anstelle von φ (klein phi) gesetzt. Auf p. 543, linke Kolonne, Zeile 1 und 2 von unten, rechte Kolonne, Zeile 15 von unten; p. 544, rechte Kolonne, in der Gleichung für w_L sollte überall φ stehen anstatt Φ. Auf p. 544, linke Kolonne, Zeile 6 von unten (in den Gleichungen für A und B) sollte $\Phi_{\alpha,x}$ durch $\varphi_{\alpha,x}$ uud $\Phi_{\beta,x}$ durch $\varphi_{\beta,x}$ ersetzt werden.