three starches are different in their surface effects.

All these data are consistent with the conclusion that the fatty acids associated with starch are adsorbed.

Summary

1. Potato and defatted corn and rice starches take up palmitic acid from a methanol solution probably by adsorption.

2. A discussion of known facts leads to the conclusion that fatty acids associated with starch are probably adsorbed.

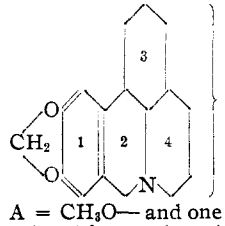
NEW YORK, N. Y. RECEIVED JUNE 1, 1942

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MERCK & CO., INC.]

Erythrina Alkaloids. XIII. Studies on the Constitution of Erythraline, Erythramine, and Erythratine

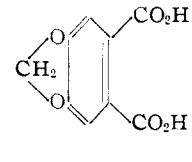
BY KARL FOLKERS, FRANK KONIUSZY AND JOHN SHAVEL, JR.

Studies[1] on the constitution of erythramine and erythraline led to the formulation of the partial structure I with the comment that the presence of

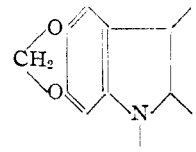


A = CH_3O— and one double bond for erythramine
A = CH_3O— and two double bonds for erythraline

I



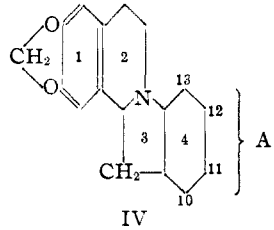
II



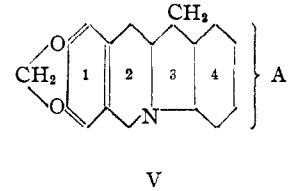
III

one five-atom nucleus was not excluded. The initial studies[2] showed that erythramine, $C_{18}H_{21}NO_3$, contains a methylenedioxy group, a methoxyl group, a tertiary nitrogen atom probably common to two nuclei, and an ethylenic double bond, besides one aromatic nucleus. It consists apparently of four nuclei (exclusive of the methylenedioxy bridge), three being partially or completely saturated and one aromatic. Erythraline, $C_{18}H_{19}NO_3$, differs only in having one more ethylenic double bond since dihydroerythramine and tetrahydroerythraline were found to be identical when the free bases and hydriodides were compared. Ring 1 of the partial structure was established by the formation of hydrastic acid (II) by oxidation of erythraline methohydroxide; and rings 1 and 2 were strongly indicated by the very close similarity between the ultraviolet absorption spectra of dihydroerythramine and 6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline hydrobromides. The hydroindole formulation (III) which might be anticipated because of the accompanying hypaphorine, which is so widely distributed in seeds of species of *Erythrina*, was excluded by the formation of hydrastic acid. Rings 3 and 4 were indicated tentatively because of the tertiary nitrogen atom. It was of interest that these two alkaloids and lycorine and tazettine, of the *Lycoris* alkaloids, possess methoxyl and hydroxyl groups on hydroaromatic nuclei of structures identical for rings 1 and 2.

Recently,[3] new structural studies were presented including experiments performed on β-erythroidine, which led to the isolation of indole from the products of potassium hydroxide fusion. Although β-erythroidine appears to differ considerably from erythraline and erythratine in functional groups and nuclear formulation, it was of interest to examine the products from the fusion of erythraline with potassium hydroxide for the presence of indole. By a modified procedure which involved adding erythraline hydriodide in portions to the molten alkali, pure indole picrate, identical with an authentic specimen, was obtained by appropriate technique. Interpretation of the indole formation suggests erythraline and erythramine actually do



IV



V

A = CH_3O— and >C=C< for erythramine
A = CH_3O— and 2 >C=C< for erythraline
A = CH_3O— and HO— and >C=C< for erythratine

(1) Folkers and Koniuszy, THIS JOURNAL, **62**, 1673 (1940).
(2) Folkers and Koniuszy, *ibid.*, **61**, 3058 (1939).
(3) Folkers, Koniuszy and Shavel, Jr., Abstracts of Papers, meeting of the American Chemical Society, Atlantic City, N. J., Sept., 1941, Division of Organic Chemistry, page 30.

contain one five-atom nucleus, and rings 3 and 4 may be written now as in the C_{16} four-ring structures, IV or V.

Erythratine,[4] $C_{18}H_{21}NO_4$, has now been found to possess one methylenedioxy group, one methoxyl group and one non-phenolic hydroxyl group. It does not contain $CH_3C\equiv$ or $CH_3N\equiv$ groups. The presence of the non-phenolic hydroxyl group was shown by active hydrogen determination, insolubility in sodium hydroxide solution, and formation of benzoyl and acetyl derivatives. Erythratine is a tertiary base, as evidenced by the formation of a methiodide and methohydroxide of expected properties. Erythratine absorbed one mole of hydrogen over a platinum catalyst at atmospheric pressure to give a dihydroerythratine.

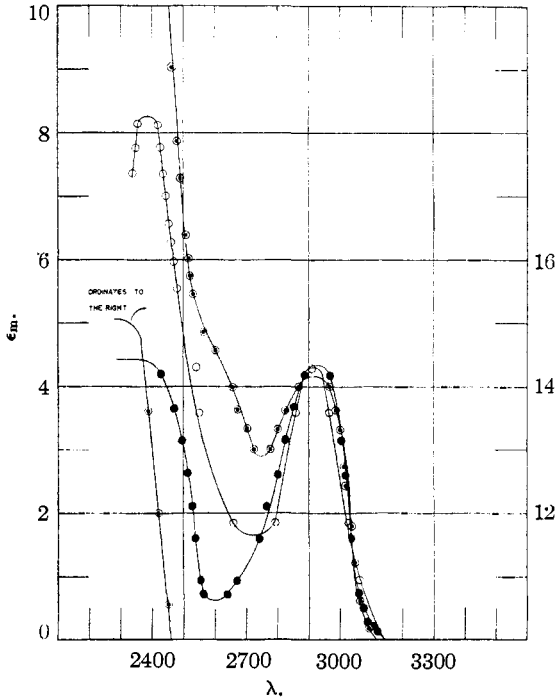
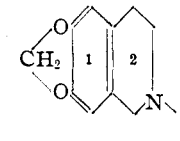
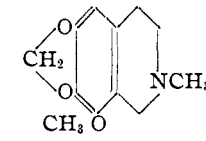


Fig. 1.—Absorption spectra in ethanol for: ●, erythratine; ○, erythramine; ◉, erythraline (note for erythraline that the ordinates are indicated on the right for ϵ_m 10–16). Absorptions are represented in terms of the extinction coefficient computed on the basis of one millimole per liter; wave lengths, in Ångström units.

It is seen from the ultraviolet absorption spectra data[5] in Figs. 1 and 2 that erythratine and dihydroerythratine hydrobromide exhibit a maximum at *ca.* 2930 Å. and ϵ_m 4.3 to 4.8, as is also exhibited by erythramine, erythraline, dihydroerythramine hydrobromide and 6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline hydrobromide. It has been assumed that this band is characteristic of the partial nucleus VI, and it differs considerably from the corresponding band of the spectrum of hydrocotarnine (VII), shown in Fig. 2, which has



VI



VII

a methoxyl group in addition to the methylenedioxy group on the benzenoid nucleus. The spectra as shown in Fig. 1 for erythratine, erythraline and erythramine differ at wave lengths below *ca.* 2900 Å. probably chiefly in accord with the different double bonds and oxygen groups in rings 3 and 4 for the three alkaloids. The absorption of dihydroerythramine and dihydroerythratine parallels that of the known methylenedioxy-tetrahydroisoquinoline derivative as shown in Fig. 2.

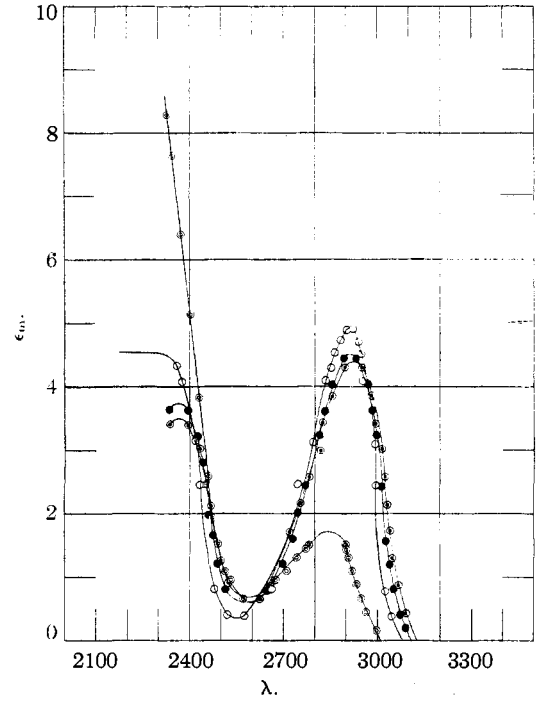
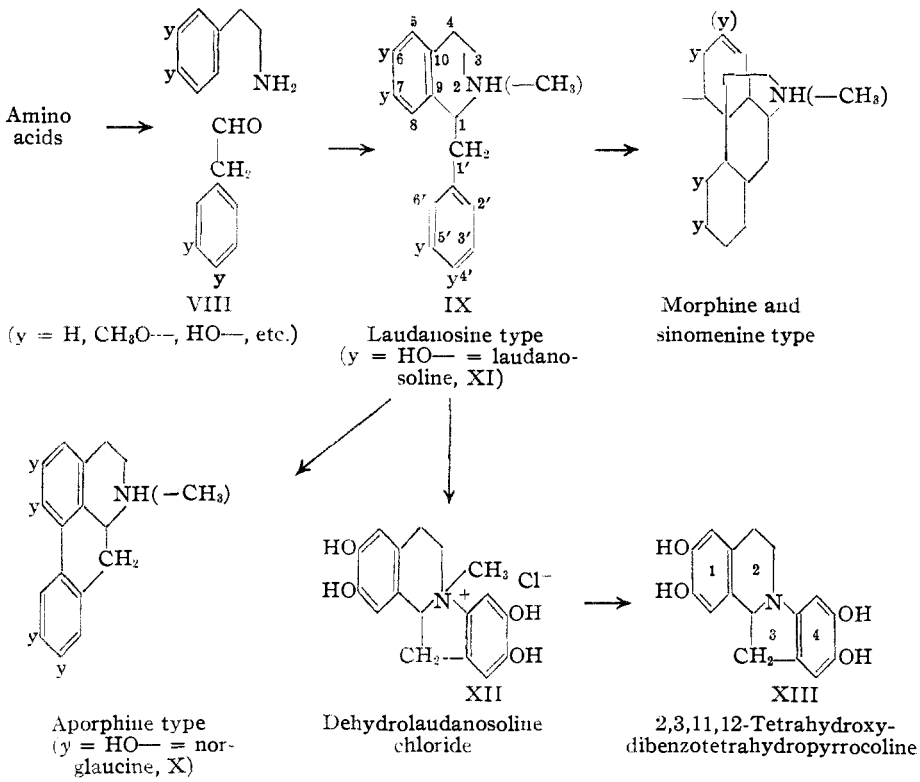


Fig. 2.—Absorption spectra in ethanol for: ○, dihydroerythratine hydrobromide; ●, dihydroerythramine hydrobromide; ◉, 6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline hydrobromide; hydrocotarnine represented by curve with concentric circles.

This behavior indicates that the remainder of the alkaloidal structures is not influencing the absorption spectrum of these compounds to any pronounced degree. Thus, erythratine also appears

(4) Folkers and Koniuszy, THIS JOURNAL, **62**, 436 (1940).

(5) Acknowledgment is hereby made to Mr. W. A. Bastedo, Jr., of this Laboratory for the measurements of the absorption spectra.



to contain the methylenedioxy-tetrahydroisoquinoline nucleus (VI) and the methoxyl and hydroxyl groups elsewhere. Taking into account the benzenoid nucleus, one ethylenic double bond, and the functional groups in erythratine, the molecule consists apparently of four fused nuclei (exclusive of the methylenedioxy bridge), three being partially or completely saturated and one being aromatic.

When erythratine was degraded by fusion with potassium hydroxide, and after purification chromatographically of the solvent fraction bases over aluminum oxide, indole was isolated and identified as such and as its picrate. When all these related facts on erythramine, erythraline and erythratine are considered, it appears that erythratine is also represented by structure IV or V when A signifies a methoxyl and hydroxyl group and one carbon–carbon double bond.

Structure IV, rather than V, would be preferred for these alkaloids on the basis of several biogenetical relationships. The nuclei 1, 2 and 4 of IV are inherently a benzyl-tetrahydroisoquinoline derivative dehydrogenated between nuclei 2 and 4 to give the fourth nucleus 3, as may be seen from the following relationships. The generally accepted origin of benzyl-tetrahydroisoquinoline alkaloids (IX) from substituted phenylethyl amines and phenylacetaldehydes (VIII) both *via* amino acids, proposed from the studies of Winterstein and Trier, Barger,[6] and Robinson[7] is shown in the scheme according to VIII → IX. Dehydrogenation with ring closure between atoms 8 and 2′ of IX leads to the aporphine type of alkaloid. Dehydrogenation with ring closure between atoms 10 and 6′ leads to the morphine and simomenine type of alkaloid. Although this formal relationship between the benzylisoquinoline type and the aporphine and morphine types has not been achieved experimentally as yet by oxidative or dehydrogenative reagents, such studies have been made.[8] Of particular interest to these three *Erythrina* alkaloids are the experiments of both Robinson[9] and Schöpf[10] to convert laudanosoline (XI) into norglaucine (X) or to convert directly a benzylisoquinoline type into an aporphine type. The product of several reagents (chloranil, potassium ferricyanide, air, and oxygen over platinum) on XI was dehydrolaudanosoline chloride (XII) which is a quaternary dihydroindole deriva-

(6) Barger, *IX Congreso Internacional de Quimica, Conferencias de Introduccion*, Madrid, 1934, p. 97.
(7) Robinson, *ibid.*, p. 168; *J. Chem. Soc.*, 1079 (1936).
(8) For protosinomenine, Robinson, *J. Chem. Soc.*, 1079 (1936).
(9) Robinson and Sugasawa, *ibid.*, 789 (1932).
(10) Schöpf and Thierfelder, *Ann.*, 497, 22 (1932).

tive. Instead of effecting ring closure between atoms 8 and 2′, the closure took place between atoms 2 and 2′. Reaction in boiling acetic anhydride converted XII into the tetraacetyl derivative of the pyrrocoline derivative, XIII. Proof of structure XII was established through Hofmann and Emde degradations.

If structure IV represents these three *Erythrina* alkaloids, then Robinson and Schöpf, failing to convert a benzylisoquinoline type directly into an aporphine type, have achieved its conversion into an *Erythrina* type *before* natural alkaloids of this hydropyrrocoline class were recognized!

The methoxyl group of erythramine and erythraline is probably at position 12, on the basis of tyrosine as the precursor.[6] Similarly, the methoxyl and hydroxyl groups of erythratine are probably at positions 11 and 12, as in XIII, although positions 12 and 13 are possible.[6] The ethylenic double bonds in structure IV appear to be in ring 4 and not 3, because the pure alkaloids do not show the Ehrlich color test for indole derivatives. Of course, the pyrrocoline derivative, XIII, and these *Erythrina* alkaloids, if so related, would show some different properties because the natural products are partially saturated in ring 4. Nevertheless, the tetramethyl ether of XIII gave a weak blue color with Ehrlich's reagent, whereas its dehydro (ring 3) derivative gave an intense indole reaction, and an aged specimen of erythratine (better for comparison because it has two oxygen atoms on ring 4 to enhance reactivity) gave a blue color at 25° and a strong royal blue color at 90°. A new specimen of erythratine gave only a slight positive test; presumably, the aged specimen had undergone slight atmospheric oxidation in ring 3. A solution of erythraline with Ehrlich's reagent slowly developed a deep pink color.

Whereas the threshold dose of erythratine hydrobromide for curare-like paralyzation of frogs was 75 mg./kg. injected intralymphatically,[11] the threshold dose of erythratine methiodide was found by Dr. Klaus Unna of the Merck Institute for Therapeutic Research to be 100 mg./kg. frog. As for erythramine and erythraline and their respective methiodides,[1,2] the conversion of the tertiary base, erythratine, into its quaternary methiodide did not enhance its curare-like physiological activity. The threshold dose of dihydroerythratine hydrobromide was 300 mg./kg., but the frogs did not recover.

(11) Folkers and Koniuszy, THIS JOURNAL, 62, 486 (1940).

Experimental Part

Indole from the Fusion of Erythraline with Potassium Hydroxide.—When 1.07 g. of erythraline hydriodide was ground with 25 g. of potassium hydroxide and fused, only 9 mg. of residue was obtained from the solvent extraction. It gave the color test for indole. It appeared by this procedure[12] that partially decomposed alkaloid floated as a film on the molten alkali during the fusion and the degradation was not satisfactory. After a second similar fusion, on 1.2 g. of erythraline base, only a few mg. of an impure picrate was obtained. Successful characterization of indole was accomplished only after fusion of larger quantities by the following modified procedure.

When 4.28 g. of pure erythraline hydriodide (from *E. glauca* Willd.) was added slowly to 30 g. of well-stirred molten potassium hydroxide, a vigorous reaction ensued with each addition of alkaloid. After all of it had been added, the homogeneous melt was heated for another ten minutes to insure complete reaction. The melt was then carefully poured on 200 g. of ice, and the resulting solution extracted continuously with ether for ten hours.

The ether extract was concentrated carefully to a volume of about 5 ml. by distillation through a Widmer column. The residual ether solution was then concentrated to a moist residue by distillation at 10° at a somewhat reduced pressure. The residue had an indole odor and gave the pink color test with *p*-dimethylaminobenzaldehyde. The picrate (23 mg.) made from this residue showed the m. p. 166.5–168°. After two recrystallizations from benzene in a centrifuge cone, 12 mg. of red indole picrate, m. p. 172–172.5°, was obtained. A mixed melting point with freshly prepared authentic indole picrate, m. p. 172–172.5°, showed no depression of the melting point.

Extraction of the acidified aqueous solution by ether and chloroform yielded residues too small for the isolation of other degradation products.

Indole from the Fusion of Erythratine with Potassium Hydroxide.—A quantity of 8.27 g. of erythratine (newly isolated from *E. glauca* Willd.) was slowly added to 50 g. of well-stirred molten potassium hydroxide. The reaction was quite vigorous, and the melt was heated for another ten minutes, in which time it started to froth considerably. The melt was then carefully poured on 300 g. of ice, and the resulting alkaline solution was extracted continuously with ether for ten hours.

The ether extract was concentrated to a small volume by careful distillation through a Widmer column to minimize the loss of the volatile indole. The residual ether solution was concentrated to a gummy moist residue at 10° at a somewhat reduced pressure.

The residue was dissolved in 5 ml. of ethyl ether and passed over a 1 × 3 cm. column of aluminum oxide Merck (Brockmann). A 2-mm. band of brown decomposition products appeared at the top, while the solution passing through was colorless. The column was developed further with 25 ml. of ether.

To the eluate was added 5 ml. of petroleum ether and after partial concentration on the steam-bath, 163 mg. of crystals of m. p. 52° was obtained. Besides the identity of the melting point with that of indole, they gave with *p*-

(12) Barger and Scholz, *Helv. Chim. Acta*, 16, 1352 (1933).

dimethylaminobenzaldehyde the pink color reaction characteristic for indole.

Anal. Calcd. for C_8H_7N: C, 82.04; H, 6.02. Found: C, 81.83, 81.86; H, 6.08, 6.09.

On converting a portion of the crystals to the picrate, red needle-like crystals were obtained, m. p. 172–173°. These crystals were mixed with freshly prepared indole picrate (m. p. 172–172.5°) and there was no melting point depression.

Further extractions with ether and chloroform of the original aqueous solution, after acidification, yielded very small residues, which did not satisfactorily permit the isolation of other degradation products.

The Oxygen Atoms of Erythratine.—A Friedrich determination on the hydriodide showed 6.78% —OCH_3 group and no =NCH_3 group; calcd. for one —OCH_3 group, 6.98%. When compared with erythramine and hydrastine, erythratine gave a positive result when tested for the presence of a methylenedioxy group.[13] Erythratine was insoluble in 10% sodium hydroxide solution at 25°. A 117.2 mg. quantity of the base was dissolved in 4 ml. of ethanol, treated with 10 ml. of 10% sodium hydroxide solution, and the mixture was refluxed four hours. Crystals separated on cooling and, by chloroform extraction, a total of 94% of the erythratine was recovered. An active hydrogen determination gave 1.23 to 1.35 active hydrogen atoms for the erythratine hemihydrate base. It is apparent that the fourth oxygen atom exists as a non-phenolic hydroxyl group.

Erythratine does not contain a $CH_3C\equiv$ group as shown by a Kuhn–Roth determination.

O-Benzoyl-erythratine Dihydrate.—To 10 ml. of dry pyridine was added 90 mg. of erythratine and 4 drops of redistilled benzoyl chloride. The solution was refluxed for five minutes and the straw-colored liquid was then poured into 100 ml. of ice and water. A white precipitate and a few oil globules appeared. The oil globules disappeared on the addition of 250 mg. of sodium bicarbonate, but most of the precipitate remained, even after vigorous shaking. Extraction of the mixture by six 25-ml. portions of chloroform dissolved all of the precipitate and concentration of the extracts to dryness *in vacuo* left 104 mg. of transparent gum. The addition of 3 ml. of water caused a partial transformation into a white amorphous solid. A total of 50 ml. of a mixture of ethyl ether and acetone was required to dissolve the solid and gum. The solvent solution was concentrated to 4 ml. which caused immediate crystallization of brown colored needles. They were filtered and washed once with 2 ml. of absolute ethanol; the brown crystals immediately dissolved, leaving 63 mg. of brilliant white needles of m. p. 247–249° (decomp.). These crystals were recrystallized twice from hot absolute ethanol (not very soluble) but the melting point remained at 248–249° (decomp.). A sample was dried for one hour at 100° *in vacuo*, then analyzed. The melting point did not change. The O-benzoyl-erythratine was a dihydrate.

Anal. Calcd. for $C_{25}H_{25}NO_5$: C, 71.65; H, 6.01; N, 3.33. Calcd. for $C_{25}H_{25}NO_5 \cdot 2H_2O$: C, 65.98; H, 6.42; N, 3.07. Found: C, 65.66; H, 6.30; N, 3.22.

O-Acetyl-erythratine.—A 500-mg. quantity of erythratine base was dissolved in 5 ml. of acetic anhydride. After the solution was refluxed ten minutes, it was poured into 100 ml. of ice and water. The solution was made alkaline with sodium bicarbonate and extracted ten times with chloroform, etc. A yield of 503 mg. of pale yellow gum was obtained which was quite soluble in ether and did not crystallize. It was sublimed at 125° and 10^{-4} mm. The sublimate was a white brittle solid which softened at 43 and melted at 55°. In another experiment, the sublimate was resublimed to give a crystalline product melting at 128°. Since the analyses on these products were not entirely satisfactory, the reaction was repeated on larger scale for better purification of the product.

A solution of 2 g. of erythratine in 25 ml. of acetic anhydride was refluxed for twenty minutes, cooled, and poured into 250 ml. of ice and water. Shaking of this mixture caused disappearance of the excess acetic anhydride, and after making the solution alkaline with sodium bicarbonate, it was extracted with ten 25-ml. portions of chloroform. Distillation of the solvent and pumping *in vacuo* left 2.1 g. of acetylated erythratine as a clear gum. Although this erythratine problem was suspended for two years, the acetylated product remained unchanged in physical appearance. It was then sublimed twice at 10^{-4} mm. and 130°. The sublimate was crystalline, m. p. 128–129°.

Anal. Calcd. for $C_{20}H_{23}NO_5$: C, 65.88; H, 6.35; N, 3.92; CH_3CO—, 11.80. Found: C, 66.04; H, 6.35; N, 3.88; CH_3CO—, 12.08 (alkaline hydrolysis), 11.79 (Kuhn–Roth $CH_3C\equiv$ determination).

The check acetyl determination by the Kuhn–Roth method for $CH_3C\equiv$ groups was done to be sure that the product was not an N-acetyl-O-acetyl-erythratine. An N-acetyl group would be expected to be more resistant to hydrolysis, if the formation of one had resulted from a nitrogen ring cleavage in boiling acetic anhydride, as has been observed for the conversion of chelidonine into N-acetyl-anhydrochelidonine.[14,15]

Hydrolysis of O-Acetyl-erythratine.—The following hydrolysis of the O-acetyl derivative to erythratine confirms the absence of nuclear change in the acetylation reaction. A solution of 25 mg. of O-acetyl-erythratine in 4 ml. of 95% ethanol and 10 ml. of 4% hydrochloric acid was refluxed four hours. After diluting to 50 ml. with water, extracting with six 20-ml. portions of chloroform, and the solvent removal, 9.3 mg. of gum was obtained. Addition of one drop of ether caused crystallization; m. p. 170–171°, $(\alpha)_D$ +145°. Addition of sodium bicarbonate and chloroform extraction eventually yielded 12.8 mg. of gum, which crystallized on adding a drop of ether; m. p. 169–170°, $(\alpha)_D$ +145°. Thus, erythratine was recovered, and its extraction from an acid solution is indicative of its low basicity.

Erythratine Methiodide.—A 50-mg. quantity of erythratine ($(\alpha)^{25}_D$ +146.0) was dissolved in 25 ml. of anhydrous ethyl ether and treated with 0.5 ml. of redistilled methyl iodide. The clear liquid became progressively turbid, but no crystals were immediately apparent. The turbid solution was allowed to stand overnight at 25°. This resulted in tiny white crystals that appeared somewhat amorphous; m. p. 121–125°, $(\alpha)^{25}_D$ +109.7, C, 0.164, water.

(13) Gadamer and Winterfeld, *Arch. pharm.*, **262**, 601 (1924).

(14) Gadamer, *ibid.*, **262**, 265 (1924).

(15) Späth and Kuffner, *Ber.*, **64**, 375 (1931).

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot CH_3I \cdot {}^1/_2H_2O$: C, 48.96; H, 5.40. Found: C, 48.85; H, 5.36.

After drying for two hours at 100° *in vacuo*, the methiodide was fairly well dehydrated; m. p. 135–136°, $(\alpha)_D$ +110.4.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot CH_3I$: C, 49.94; H, 5.29. Found: C, 49.56; H, 5.39.

Further drying with heat initiated slight decomposition.

N-Methyl-erythratine Methine.—A solution of 174 mg. of erythratine methiodide in 20 ml. of water was treated with 500 mg. of silver oxide and the mixture was shaken for three hours at 25°, then filtered. The filtrate gave a negative halogen test, and yielded only 1.8 mg. of chloroform-soluble material when extracted five times. The aqueous erythratine methohydroxide solution was concentrated to dryness at 35° and 20 mm. *in vacuo*, then dried for two hours at 35° and 2 mm. The yield of quaternary base was 135 mg. On heating *in vacuo* in an oil-bath at 150°, rapid effervescence occurred. The bubbling stopped after two minutes, but the heating was continued for another two minutes. The methine was shaken with 25 ml. of water for fifteen minutes, but nothing apparently dissolved. When 5 ml. of chloroform was added, all the methine went into the chloroform layer. Concentration of the chloroform solution to dryness yielded 103.2 mg. of methine that could not be crystallized. Sublimation at 2.5×10^{-4} mm. vacuum and a temperature of 110–125° gave a transparent brittle sublimate.

Anal. Calcd. for $C_{19}H_{23}NO_4$: C, 69.29; H, 7.03. Found: C, 68.96; H, 6.75.

Zn Dust Distillation of N-Methyl-erythraline Methine.—A distillation at 500–560° of 400 mg. N-methyl-erythraline-methine mixed with 40 g. of zinc dust yielded a yellow oil. It was completely soluble in 10% hydrochloric acid solution, and concentration of this solution yielded 91 mg. of gummy hydrochloride which could not be crystallized. From this material, 69 mg. of free base was obtained as a yellow gum which likewise could not be crystallized.

Dihydroerythratine Hydrobromide.—A quantity of 494 mg. of pure erythratine hemihydrate was dissolved in 25 ml. of water containing 1 ml. of 40% hydrobromic acid solution. The hydrogenation was performed over 75 mg. of Adams platinum catalyst and at atmospheric pressure. After two hours, one mole of hydrogen was absorbed. The filtrate was concentrated to dryness at 30° and 18 mm. The residue was dissolved in 5 ml. of absolute ethanol and brought to the crystallization point with 5 ml. of ether. After fifteen hours at 10°, 291.1 mg. of pinkish crystals was obtained. Recrystallization did not alter the melting point of 249°. A sample was dried at 100° and 2 mm. for one hour before analysis.

Anal. Calcd. for $C_{18}H_{23}NO_4 \cdot HBr$: C, 54.31; H, 6.07. Found: C, 54.10; H, 6.06.

After standing at 25° for two to three days, decomposition had taken place.

Acknowledgment.—We wish to express our appreciation to Messrs. Hayman, Reiss, Clark and Boos for the microanalyses.

Summary

Erythraline ($C_{18}H_{19}NO_3$), erythramine ($C_{18}H_{21}NO_3$), and erythratine ($C_{18}H_{21}NO_4$) contain a methylenedioxy group, a methoxyl group, a tertiary nitrogen atom common to two nuclei, and two, one and one ethylenic double bonds, respectively. Erythratine contains an additional nonphenolic hydroxyl group. These alkaloids appear to contain four fused nuclei (exclusive of the methylenedioxy bridge), three being partially or completely saturated and one aromatic. Three of the fused nuclei appear to be identical for each alkaloid, the fourth differing in unsaturation and oxygen groups.

Indole was isolated from the fusion of erythraline and erythratine with potassium hydroxide.

They are structurally formulated as hydropyrrocoline derivatives on the basis of present facts. If this formulation be correct, Robinson and Schöpf, failing to convert directly a benzylisoquinoline type of alkaloid into an aporphine type, have achieved its conversion into an *Erythrina* type, before natural alkaloids of this hydropyrrocoline type were known.

RAHWAY, N. J. RECEIVED JULY 1, 1942