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STUDIES IN ARGENTINE PLANTS. XI. THE PARTIAL STRUCTURE OF ERYSOVINE, ERYSODINE, AND ERYSOPINE

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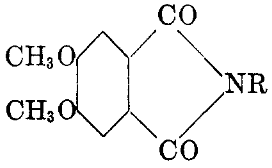
Folkers and Koniuszy (1) isolated from the seeds of many *Erythrina* species, a series of alkaloids that could be extracted by organic solvents only after hydrolysis. Because of the need of this hydrolysis, they were named liberated alkaloids and were represented by the bases erysovine, erysodine, and erysopine. Later, Folkers, Shavel, and Koniuszy (2) added a new member to the series, a base isolated only from *Erythrina costaricensis*, which was named erysonine.

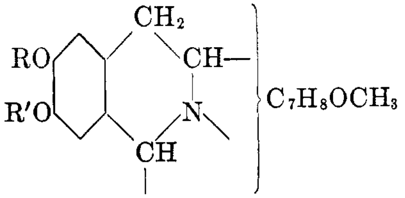
Erysovine and erysodine have the same formula, $C_{18}H_{21}NO_3$, and each has two methoxyl groups and one phenolic hydroxyl. Erysopine with the formula $C_{17}H_{19}NO_3$, has only one methoxyl group but two phenolic hydroxyls were found to be present. None of the bases have N-methyl groups. Koniuszy, Wiley, and Folkers (3) have further studied the structure of erysovine, erysodine, and erysopine. They have presented evidence for the existence in the bases of two double bonds and a four-nucleus ring system. The three bases could be transformed into their N-oxide derivatives, which were methylated with methyl sulphate. After elimination of the N-oxygen, the same fully methylated base was obtained from the three alkaloids. It was named erysotrine and isolated as the picrate. It is evident that the bases have the same ring system with the oxygen atoms and double bonds in the same positions, differing only in the number and position of of O-methyl groups.

Almost simultaneously Prelog, Wiesner, Khorana, and Kenner (4) in a study on the constitution of the *Erythrina* alkaloids, methylated erysodine with methyl sulphate and, without isolating the erysotrine methosulphate formed, oxidized it with potassium permanganate in alkaline solution, obtaining hemipinic acid N-methylimide. The formation of this product established the similarity of structure of one part of the molecule of the liberated alkaloids with that of the free alkaloids of *Erythrina:* erythraline and erythramine. Folkers and Koniuszy (5) have found that erythramine and erythraline give the same hydrogenated derivative and that oxidation of erythraline methohydroxide gives hydrastic acid.

We have been working for some time on the structure of the liberated alkaloids and in a preliminary note (6) have reported that erysovine, erysodine, and erysopine can be methylated with ethereal diazomethane in a methanolic suspension of the alkaloids. In all cases the erysotrine of Koniuszy, Wiley, and Folkers (3), $C_{19}H_{23}NO_3$, was isolated in crystalline condition. Erysovine and erysodine are methylated easily, whereas erysopine, because of its low solubility, takes more time. When erysotrine is oxidized with potassium permanganate, *m*-hemipinic acid imide (I) is obtained. The oxidation of erysotrine methohydroxide gave *m*-hemipinic acid N-methylimide (II).



I R = H
II R = CH_3



III

These results agree with the work of Prelog, Wiesner, Khorana, and Kenner (4) and confirm the partial relationship between the structures of the liberated and some of the free alkaloids of the *Erythrina.*

It follows that the partial structure of the liberated alkaloids can be formulated as III ($R = R' = H$: erysopine; R or R′ = H and R′ or $R = CH_3$: erysovine or erysodine).

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EXPERIMENTAL

Erysodine monobenzoate. One gram of erysodine was dissolved in 8 ml. of 2 *N* sodium hydroxide and while the solution was kept warm on a water-bath, 1 ml. of benzoyl chloride was added slowly with vigorous shaking. A crystalline precipitate formed which increased with time. When the odor of benzoyl chloride had disappeared the suspension was cooled and filtered giving 0.66 g. of solid. The filtrate, which had an alkaline reaction, was treated further with another 1 ml. of benzoyl chloride and an additional 0.42 g. of solid was obtained; total yield, 1.08 g. The product was crystallized from ethanol; m.p. 199°.

Anal. Calc'd for $C_{25}H_{25}NO_4$: C, 74.44; H, 6.45.
Found: C, 74.16; H, 6.29.

Erysodine picrate was prepared in the usual way in ethanol. The solution was decanted and the gummy precipitate was treated with cold ethanol. It solidified and was recrystallized from ethanol, m.p. 200°.

Anal. Calc'd for $C_{18}H_{21}NO_3 \cdot C_6H_3NO_7$: N, 10.66. Found: N, 10.52.

Erysotrine from erysodine. Erysodine (5 g.) was dissolved on heating in 40 ml. of anhydrous methanol and the solution was cooled with shaking so that a fine precipitate was formed. The suspension was cooled to 3° and an ether solution of diazomethane added, while maintaining a continuous agitation. When the yellow color of the diazomethane disappeared more reagent was added until the crystals of erysodine dissolved and a permanent yellow color was obtained. The solution was left overnight in the refrigerator. The excess of diazomethane was destroyed by the addition of a few drops of acetic acid and the ether and 20 ml. of the methanol was distilled. The solution was diluted with water to permanent turbidity and a few ml. of a concentrated potassium hydroxide solution was added to strong alkalinity. On keeping in the refrigerator crystals were obtained; m.p. 96°; yield 5.1 g. Recrystallization from ligroin gave white needles united in rosettes; m.p. 97–98°. The compound can be distilled in a high vacuum without decomposition; $[\alpha]_D^{22}$ +264.3° in ethanol (*c*, 0.7875); $[\alpha]_D^{22}$ +262.1° in 5% HCl (*c*, 0.6790).

Anal. Calc'd for $C_{19}H_{23}NO_3$: C, 72.84; H, 7.34; OCH_3, 29.71.
Found: C, 72.28; H, 7.49; OCH_3, 29.31.

Erysotrine picrate. Erysotrine picrate was obtained in the usual way. Recrystallized from ethanol, it melted at 161°, and was identical with that described by Koniuszy, Wiley, and Folkers (3); m.p. 160–161°.

Anal. Calc'd for $C_{19}H_{23}NO_3 \cdot C_6H_3N_3O_7$: C, 55.35; H, 4.79.
Found: C, 55.30; H, 5.02.

Erysotrine from erysovine. The methylation of 0.9 g. of erysovine was carried out as described above for erysodine. Yield, 0.72 g. of crystals of erysotrine, m.p. 98.5°. *Picrate,* m.p. 161°.

Erysotrine from erysopine. Erysopine (3 g.) was finely ground and suspended in 30 ml. of methanol. The suspension was cooled to 3°, agitated continuously, and a diazomethane solution was added to a permanent yellow color. The suspension was then kept in a refrigerator with an excess of diazomethane and shaken from time to time. The crystals dissolved slowly and in a few days passed into solution. The solution was evaporated to 15 ml., water was added to a permanent turbidity, and upon adding a potassium hydroxide solution, 2.7 g. of impure erysotrine crystals were obtained which, after recrystallization from ligroin, had m.p. 97–98° and gave erysotrine *picrate,* m.p. 160–161°.

Erysotrine methiodide. One gram of erysotrine was dissolved in 30 ml. of acetone, 10 ml. of methyl iodide was added, and the solution was boiled for 3 hours and left overnight at room temperature. No precipitate was formed. The solution was evaporated in a vacuum and the oily residue crystallized by the addition of a few drops of ethyl ether followed by scratching with a glass rod. Crystals (1.3 g. m.p. 200–205°) were obtained which, after four crystallizations from ethanol, gave prisms, m.p. 209–210°; $[\alpha]_D^{22}$ +187.7° in water (*c*, 0.4980).

Anal. Calc'd for $C_{20}H_{26}INO_3$: C, 52.74; H, 5.71.
Found: C, 52.92; H, 5.98.

Erysotrine hydrochloride was prepared by dissolving 1 g. of erysotrine in 3 ml. of absolute ethanol, adding concentrated hydrochloric acid to *p*H 3.5, and then ethyl ether to permanent turbidity. Upon leaving in the refrigerator overnight crystals were obtained which were recrystallized from ethanol with the addition of ether; prisms m.p. 205–206°; $[\alpha]_D^{22}$ +241.3° in water (*c*, 0.5490).

Anal. Calc'd for $C_{19}H_{23}NO_3 \cdot HCl$: C, 65.23; H, 6.58.
Found: C, 65.41; H, 6.40.

Oxidation of erysotrine. m-Hemipinic acid imide. A solution of 500 mg. of erysotrine in 50 ml. of acetone was heated to boiling and a hot solution of 2.5 g. of potassium permanganate in acetone was added slowly. When the oxidant was exhausted the manganese dioxide was filtered and the solution evaporated to dryness. The 300 mg. of crystalline residue was digested with cold acetone, filtered, and recrystallized from 96% ethanol; white needles, m.p. 315–320°. They gave no depression with an authentic sample of *m*-hemipinic acid imide and a blue fluorescence in ethanolic solution under Wood's light.

Anal. Calc'd for $C_{10}H_9NO_4$: C, 57.97; H, 4.34.
Found: C, 57.11; H, 4.23.

No definite compound could be obtained from the manganese dioxide when a search was made for other degradation products.

Oxidation of erysotrine methohydroxide. m-Hemipinic acid N-methylimide. One gram of erysotrine was dissolved in 10 ml. of methanol, 2.5 ml. of methyl iodide was added, and the solution was heated to boiling for two hours in a water-bath. The solution was then evaporated and the residue dried well. It was dissolved in 100 ml. of water, brought to alkalinity with potassium carbonate, and 400 ml. of a 2.5% aqueous solution of potassium permanganate was added with continuous agitation at room temperature. A current of sulfur dioxide was passed through and when the manganese dioxide dissolved, crystals were observed in suspension. After keeping at 5° for 24 hours, they were filtered; m.p. 258°. They remained unchanged upon high vacuum sublimation; m.p. 258°, giving a blue fluorescence in ethanolic solution with blue Wood's light. No depression was observed upon mixing them with an authentic sample of *m*-hemipinic acid N-methylimide (m.p. 258°) prepared by evaporation of a solution of the acid in an aqueous methylamine solution and purification of the residue by high vacuum sublimation.

SUMMARY

1. Treatment of the liberated alkaloids of *Erythrina:* erysovine, erysodine, and erysopine, with diazomethane gave the same methylated base, erysotrine, which was obtained in crystalline condition.

2. Oxidation of erysotrine gave *m*-hemipinic acid imide. When erysotrine methohydroxide was oxidized *m*-hemipinic acid N-methylimide was obtained.

3. The constitutional relationship between the liberated alkaloids and the free alkaloids erythramine and erythraline is confirmed.

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