colored needles, m. p. 160–164° dec. (see below). The filtrate was taken to dryness and the residue heated briefly on the hot-plate to effect dehydration and put through an alumina–Supercel tower in benzene solution. The hydrocarbon collected from the highly fluorescent filtrate was clarified with Norite in alcohol and crystallized from about 15 cc. of this solvent, giving 50–90 mg. (1.1–1.9%) of material melting at 174–177.5°. Three further crystallizations gave a product of the constant m. p. 181–181.4°; the first crop formed fine, pale orange needles (26–47 mg.) and the mother liquors gave 10 mg. more of good material; yield of pure hydrocarbon, 0.8–1.2%.

Anal. Calcd. for $C_{20}H_{14}$: C, 94.45; H, 5.55. Found: C, 94.25; H, 5.77.

The **trinitrobenzene derivative** when prepared from pure hydrocarbon crystallized from alcohol in bright orange-red needles, m. p. 182.5–183.2°.

Anal. Calcd. for $C_{26}H_{17}O_6N_3$: N, 8.99. Found: N, 9.13.

This derivative is not suitable for use in purifying the hydrocarbon, for when the crude reaction product from the tower was treated with trinitrobenzene the complex was brown-black and melted at about 162° and was not improved on repeated crystallization. The dark red picrate is too unstable to be useful as a derivative.

Many variations were tried in the procedure of conducting the Grignard reaction. In boiling benzene or toluene, in cold benzene, or in ether at −70°, the yield was either as reported or lower. Lithium methyl in ether gave the same yield as the Grignard reagent, and the addition of the crude cyclization product in benzene rather than as a solid lowered the yield. The low yield even under the most favorable conditions seems to be due to extensive and rapid isomerization to the anthranol.

1′,9-Methylene-1,2-benz-10-anthranol (XII).—The material separated from the Grignard reaction mixture by crystallization from benzene proved to be the anthranol in an essentially pure condition. The substance is quite sensitive and rapidly turns red in boiling benzene or in cold dioxane. It is moderately soluble in ether or ligroin (b. p. 80–90°) and on three crystallizations from this solvent-pair formed pale yellow, fibrous needles, m. p. 160–164° with charring. The sample retained ligroin tenaciously and gave a satisfactory analysis only after drying for fifteen hours in high vacuum at 70°.

Anal. Calcd. for $C_{19}H_{12}O$: C, 89.03; H, 4.72. Found: C, 89.08; H, 4.85.

The substance is highly fluorescent in dilute alcoholic solution, and the addition of ferric chloride produces an orange-red coloration. Extensive decomposition occurred on attempted acetylation. The Bucherer reaction was tried at 140, 155, and 180° but gave only water-soluble products. On reduction of the anthranol with zinc and alkali, 1′,9-methylene-1,2-benzanthracene was obtained in 35% yield, and the result was the same using the crude cyclization product. That the yield was lower than from the acetate X is probably because of the great sensitivity of the anthranol and anthrone.

Summary

A synthesis has been developed for 1′,9-methylene-1,2-benzanthracene and its hitherto undescribed 10-methyl and 10-hydroxy derivatives starting with the reaction between *o*-chlorophenylmagnesium bromide and 7-acenaphthenone. A new method was found whereby the ketonic starting material can be produced readily in quantity. This consists in the oxidation of acenaphthene with red lead in acetic acid solution, saponification of the resulting 7-acetoxy compound and oxidation of 7-acenaphthenol to 7-acenaphthenone.

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Erythrina Alkaloids. VII. Isolation and Characterization of the New Alkaloids, Erythraline and Erythratine

BY KARL FOLKERS AND FRANK KONIUSZY

The isolation of erythramine from the seeds of *Erythrina sandwicensis* Deg. and *Erythrina subumbrans* (Hassk.) Merr. was described recently.[1] It was stated in that paper that erythramine had been isolated from other species of *Erythrina*, but that it was found associated with another alkaloid of such similar properties that its isolation was more difficult. This other new alkaloid has been named erythraline.

By fractional crystallization of the hydriodides from the crude free alkaloids of *Erythrina glauca* Willd., with particular observance of the optical rotations, pure erythraline hydriodide was isolated as the major alkaloid and pure erythramine hydriodide as a minor alkaloid. A second minor alkaloid was also isolated as the hydriodide, and since it has been also characterized as new, it has been named erythratine. It was discovered later that pure erythratine base could be easily obtained directly by crystallization of the crude bases from ethanol, and the yield was twice that

(1) Folkers and Koniuszy, THIS JOURNAL, **61**, 1232 (1939).

obtained by fractional crystallization of the hydriodides. Erythraline and erythramine hydriodides have similar solubilities in ethanol and although prepared in this solvent their separation from it was not satisfactory. However, erythraline hydriodide was less soluble in water than the erythramine and erythratine hydriodides and their separation was satisfactory. The fact that erythraline hydriodide is the least soluble, and therefore the easiest to obtain pure, signifies that this alkaloid would probably be the only one isolated in those cases where only semi-micro quantities of the crude free alkaloid bases were available. It has been desirable to restrict these studies to authentic samples of seeds[2] and, since such samples are generally small, often only semi-micro quantities of bases are available for examination. On this basis, erythraline was isolated as the hydriodide from the seeds of *Erythrina variegata* L. var. *orientalis* (L.) Merr., *Erythrina Folkersii* Kruk. and Mold., *Erythrina velutina* Willd., and *Erythrina macrophylla* DC. The isolation of erythramine and erythratine as minor alkaloids from *Erythrina glauca* was facilitated by the large quantities of seeds of this species which were available.

Because of the close botanical relationship of *Erythrina velutina* forma *aurantiaca* (Ridl.) Kruk. and *Erythrina Grisebachii* Urb. to *Erythrina velutina*, it was considered that erythraline exists also in these, although the hydriodides were not prepared and crystallized after the amount of the free bases present in the seeds was determined.

Erythraline was isolated also from the seeds of *Erythrina fusca* Lour. as the pure free base directly from the crude free alkaloidal fraction. This direct isolation of the free base was considered a manifestation of the freedom of erythraline from its closely related alkaloids in this species and the distinct character of *Erythrina fusca*. In contrast to this was the failure to isolate pure erythraline base directly from the crude free alkaloidal fraction of *Erythrina velutina*. It has been preferred generally to isolate these alkaloids as the hydriodides.

It is to be emphasized from these studies (and others, as yet unpublished) on new *Erythrina* alkaloids that melting points alone of bases and salts (decomposition point for the latter) are unreliable as proof of homogeneity or identity. Mixtures frequently melt at the same temperature as one component. Microanalyses of mixtures of these alkaloids with identical or closely related empirical formulas may be confusing. The optical rotations after crystallizations are the best guide. Consequently, the identity of an individual alkaloid is established best by the combined data of melting points, optical rotations, analyses, and other derivatives if possible.

The results of the microanalyses of the free base, the hydriodide, and the hydrobromide have established the empirical formula of erythraline as $C_{18}H_{19}NO_3$; thus, it differs from erythramine, $C_{18}H_{21}NO_3$, by only two hydrogen atoms.

The microanalyses of the free base hemihydrate, the hydriodide, and the hydrobromide were all in agreement with the empirical formula $C_{18}H_{21}NO_4$ for erythratine.

The initial studies on the constitution of erythramine have been published[3] and their continuance will be described in a forthcoming paper and with new experiments concerning the structure of erythraline.

Hypaphorine was newly isolated from the seeds of *Erythrina glauca*, *Erythrina Folkersii*, *Erythrina fusca*, *Erythrina velutina*, and *Erythrina macrophylla*, and it undoubtedly exists in *Erythrina Grisebachii* and *Erythrina velutina* forma *aurantiaca*. Hypaphorine was re-isolated from *Erythrina variegata* var. *orientalis*.[4]

The relative pharmacological potencies of these *Erythrina* alkaloids are of interest. The threshold dose of erythramine hydrobromide for curare-like paralyzation of frogs was 7 mg./kg., injected intralymphatically.[3] Dr. Klaus Unna of the Merck Institute of Therapeutic Research has reported after preliminary tests that the threshold dose of erythraline hydrobromide was 8 mg./kg. frog, and that of erythratine hydrobromide was 75 mg./kg. frog.

The species names used in this paper are in accord with the recent taxonomic revision of *Erythrina* by Mr. B. A. Krukoff.[5,6]

Experimental Part

Isolation of Erythraline and Hypaphorine

Erythrina fusca Lour. (Tamesis 9345).—The 980 g. of seed powder was extracted first with 1500 ml. of petroleum

(2) The identity of the *Erythrina* seeds used in these studies was established either by accompanying herbarium material, which was determined by Mr. B. A. Krukoff at the New York Botanical Garden, or by other evidence which left no doubt regarding the identity.

(3) Folkers and Koniuszy, THIS JOURNAL, **61**, 3053 (1939).

(4) Maranon and Santos, *Philippine J. Sci.*, **48**, 563 (1932).

(5) Krukoff, *Brittonia*, **3**, No. 2, 205 (1939).

(6) Krukoff, *J. Arnold Arboretum*, **20**, 225 (1939).

ether for six hours in a Soxhlet. After distillation of the solvent, the yield of the yellow fat fraction was 77 g. (7.8%). The extraction of the seed powder was then continued for thirty-six hours with two 1500 ml. portions of methanol. This extract was concentrated by distillation and finally pumped out at 30° and 18 mm. to remove the last of the methanol. The 150 g. (15.8%) of gum-like residue was dissolved in 700 ml. of water, treated with 14 ml. of concentrated hydrochloric acid, and freed of residual emulsified oil droplets by extracting first with petroleum ether, then with chloroform. The clear aqueous solution was made just alkaline with sodium bicarbonate and extracted with ten 100 ml. portions of chloroform. The yield of crude erythraline, after complete solvent removal at 30° and 18 mm., was 1.829 g. (0.19%).

The hypaphorine may be isolated by treating the alkaline aqueous solution with hydrochloric acid, etc., as described for its isolation from *Erythrina sandwicensis*.[1] Data on hypaphorine from *Erythrina fusca* are in Table III.

Erythraline Base.—The 1.829 g. of crude alkaloids was recrystallized from absolute ethanol. The first crystallization yielded 1.348 g. of gummy crystals, the second yielded crystals of m. p. 55–65° and the third yielded crystals of m. p. 106–107°. Subsequent crystallizations did not alter the melting point; it remained constant at 106–107°. The yield was 0.6731 g. (0.068%). These white crystals of pure erythraline showed $(\alpha)^{27}D$ + 211.8, C = 0.944, absolute ethanol. They were dried at 60° and 2 mm. for thirty minutes before analysis.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.55; H, 6.33; N, 4.88.

Erythraline base was much more stable than erythramine base and was stored in a black vial at ordinary temperatures and pressures.

Mixed melting points of erythraline (m. p. 106–107°) and erythramine (m. p. 103–104°) were as follows: 10 parts and 1 part, respectively, m. p. 88–94°; 5 parts and 5 parts, m. p. 90–96°; 1 part, and 10 parts, m. p. 93–97°

Erythraline Hydriodide.—A quantity of 94.4 mg. of analytically pure erythraline base was dissolved in 2 ml. of absolute ethanol and 47.5 mg. of sodium iodide was added. The solution was acidified with the calculated amount of glacial acetic acid. Yellow crystals of the hydriodide formed at 25°. They melted at 252–253° with decomposition and this constant was not changed by further recrystallizations. This melting or decomposition point varies somewhat with the rate of heating the bath. In the same bath, pure erythramine hydriodide melted at 245–245.5°, and the mixed salts melted at 247–249°, each with decomposition. Erythraline hydriodide showed $[\alpha]^{31}D$ + 177°, C = 0.322, water. A sample was dried at 25° and 2 mm. before analysis.

Anal. Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74; N, 3.29. Found: C, 51.01; H, 4.78; N, 3.38.

Erythraline Hydrobromide.—A quantity of 100 mg. of analytically pure erythraline was dissolved in 3 ml. of absolute methanol, acidified with 40% hydrobromic acid, and brought to the crystallization point with anhydrous ether. After twelve hours at 10°, white, granular crystals formed. They melted at 243° and showed $[\alpha]^{27}D$ +216.6, C = 0.500, water. The salt was dried at 25° and 30 mm. before analysis.

Anal. Calcd. for $C_{18}H_{19}NO_3 \cdot HBr$: C, 57.15; H, 5.32. Found: C, 57.30; H, 5.28.

Isolation of Erythraline, Erythramine and Erythratine

Erythrina glauca Willd. (Wortley 9242.)—A 10-kg. quantity of powdered seeds was extracted. The fourteen hours of extraction with petroleum ether yielded 940 g. (9.4%) of the fatty fraction. The thirty-three hour extraction with methanol yielded 1660 g. (16.6%) of a thick green gum. This gum was dissolved in 6 liters of water, made just acid to congo red with 100 ml. of concentrated hydrochloric acid, and clarified first with petroleum ether and then chloroform. Five liters of the clear solution was made alkaline with sodium bicarbonate at 10–15° and then extracted continuously with chloroform for five hours. The chloroform residue, which was pumped out at 30° and 2 mm. for four hours, weighed 19.3 g. (0.15%).

The 19.3 g. of crude alkaloidal bases was dissolved in 40 ml. of absolute ethanol and treated with 9.65 g. of sodium iodide and 3.86 g. of glacial acetic acid. After standing at 10° for twelve hours, 9.31 g. of mixed yellow hydriodides were obtained. Recrystallization of these hydriodides from 95% ethanol gave the following results: first crop, Fraction A, 5.45 g., m. p. 242–244.5°; $[\alpha]^{27}D$ +196.4; second crop, Fraction B, obtained by concentrating the mother liquor to one-half the volume, 0.341 g., m. p. 241–243°; $[\alpha]^{27}D$ +200.8; third crop, Fraction C, obtained by concentrating the mother liquor to one-half the volume, 0.99 g., m. p. 242°; $[\alpha]^{26}D$ +119°. The third crop or Fraction C was not only markedly different in optical rotation, but was white in color whereas the first two crops were yellow-orange in color. Table I contains the data on the fractional crystallization of 238.3 mg. of Fraction A.

TABLE I

CRYSTALLIZATIONS ON FRACTION A

Crystallization from water	Starting amt., mg.	Amt. recov., mg.	$[\alpha]^{25-28}D$, water	M. p., °C.	Fraction
First	238.3	188.0	+191.3	242	
	2nd Crop	13.8	+221	242	D
Second	168.0	132.0	+187.9	245	
Third	106.0	102.0	+176.9	249	E
Fourth	73.0	70.0	+177	249	F

Fraction D was shown by the physical constants to be pure erythramine hydriodide.[1] Larger amounts of erythramine hydriodide were obtained from the balance of Fraction A. A yield of 0.003% was obtained (based on seed powder).

Fractions E and F were shown by the physical constants to be pure erythraline hydriodide. A yield of 0.03% was obtained. A sample for analysis was dried at 25° and 2 mm.

Anal. Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74; N, 3.29. Found: C, 50.68; H, 4.77; N, 3.16.

Fraction B was found to be a mixture of erythraline and erythramine hydriodides.

The data on Fraction C are in Table II.

Erythratine Hydriodide.—Fraction G of Table II, which had constant properties, was recognized as a new

TABLE II

CRYSTALLIZATIONS ON FRACTION C

Solvent	Starting amt., mg.	Amt. recov., mg.	$[\alpha]^{25-28}D$, water	M. p., °C.	Fraction
95% ethanol	99.0	79.2	+110.2	242–242.5	
Water	75.2	61.0	+108.4	242–242.5	
Water	56.1	47.9	+109.0	242–242.5	G

alkaloid and the base was named erythratine. A yield of 0.007% was obtained.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot HI$: C, 48.66; H, 4.99; N, 3.15. Found: C, 48.67; H, 5.10; N, 3.13.

Direct Isolation of Erythratine Base.—It was discovered later that when the crude free alkaloidal fraction of *Erythrina glauca* (Wortley 9242) was dissolved in 95% ethanol, and allowed to stand, the erythratine base crystallized in a fairly pure condition. The 23.7 g. of crude alkaloidal bases from 12 kg. of seeds was dissolved in 72 ml. of 95% ethanol. On standing, crystals formed; yield, 2.7542 g. of m. p. 167.5–168° and $[\alpha]_D$ +138.6, absolute ethanol. They were recrystallized twice by dissolving in 20 ml. of absolute ethanol, distilling to 8 ml., and adding petroleum ether to incipient crystallization. The final yield of pure erythratine hemihydrate base was 2.16 g. (0.018%); m. p. (and mixed with base derived from the isolated hydriodide) 170°; $[\alpha]^{28}D$ +145.5, C = 0.371, absolute ethanol. The sample was dried at 100° and 0.01 mm. for twenty minutes for analysis.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot {}^1/_2H_2O$: C, 66.66; H, 6.83. Found: C, 66.46; H, 7.02.

Erythratine hemihydrate base was more stable than either erythramine or erythraline, the crystals remaining pure on standing for over six months.

Erythratine Hemihydrate Base.—A sample of 296.9 mg. of pure erythratine hydriodide was converted to the free base by dissolving in water, adding sodium bicarbonate, and extracting with chloroform. Experiments with the *Erythrina* free bases are best done with bases so obtained. The pumped out base (210.6 mg.) was a clear gum. It was dissolved in 30 ml. of anhydrous ether and 10 ml. of petroleum ether was added. Flocculent material was filtered, and after concentration to 10 ml., white crystals formed. They melted at 168–169° and through four recrystallizations from anhydrous ether the constant value, m. p. 170–170.5°, was obtained. The crystals were dried at 25° and 2 mm. for analyses, $[\alpha]^{25}D$ +144.9, C = 0.159, absolute ethanol.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot {}^1/_2H_2O$: C, 66.66; H, 6.83; N, 4.31. Found: C, 66.21; H, 6.61; N, 4.53.

The erythratine hemihydrate could not be converted to the anhydrous base by drying at 140° and 0.01 mm. for four hours. Less drastic conditions did not materially dehydrate the hemihydrate.

A sample of the pure erythratine hemihydrate was converted back to the hydriodide, and the properties were the same as those of the starting hydriodide; $[\alpha]^{26}D$ +113.3.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot HI$: C, 48.66; H, 4.99; I, 28.65. Found: C, 48.49; H, 5.08; I, 28.82.

Erythratine Hydrobromide.—A sample of 50 mg. of pure erythratine hemihydrate was dissolved in 1 ml. of absolute ethanol and the solution was acidified with two drops of concentrated hydrobromic acid. The yield of hydrobromide was 39 mg., m. p. 241°. Recrystallization yielded 21.4 mg. of m. p. 241° also, $[\alpha]^{25}D$ +158.7, C = 0.258, water. The salt was dried at 25° and 30 mm. for analysis.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot HBr$: C, 54.56; H, 5.59;

TABLE III

DATA ON THE ISOLATION OF ALKALOIDS FROM SPECIES OF *Erythrina*

Plant	Collectors' names, specimens, numbers and source	Seeds, g.	Fatty fraction, %	Alcohol residue, %	Hypaphorine hydrochloride, %	Crude free alkaloid fraction,[a] %	Identity and authenticity of alkaloids
E. glauca Willd.	Haigh 9170 (Ceylon)	200.0	13.3	14.0[b]	0.16	0.40[c]	*d*
E. glauca Willd.	P. Campos Porto 9199 (Brazil)	9.4	8.8	18.2[e]	..	.33[f]	..
E. glauca Willd.	A. Dugand 9203 (Colombia)	50.7	9.9	15.9[e]	0.9	.38[c]	..
E. glauca Willd.	Wortley 9242 (Trinidad)	10 kg.	9.4	16.6[e]	..	.19[f]	*g*
E. glauca Willd.	Wortley 9242 (Trinidad)	12 kg.	7.7	19.7[e]	..	.19[f]	..
E. glauca Willd.	Wortley 9242 (Trinidad)	5 kg.	8.6	..	..	.25[f]	..
E. Folkersii Kruk. and Mold.	Kinloch 9163 (British Honduras)	63.0	15.0	10.3[b]	1.3	..	..
E. Folkersii Kruk. and Mold.	Kinloch 9167 (British Honduras)	200.0	15.3	12.0[b]	2.2	..	..
E. Folkersii Kruk. and Mold	Kinloch 9167 (British Honduras)	650.0	15.4	16.3[e]	..	.074[f]	*h*
E. variegata L. var. *orientalis* (L.) Merr.	Otero 9131 (Puerto Rico)	100.0	12.4	6.4[b]	2.2	.04[c]	*i*
E. variegata L. var. *orientalis* (L.) Merr.	Canicoza 9152 (Philippine Is.)	586.2	10.9	4.8[b]	1.3	.009[c]	*i*
E. variegata L. var. *orientalis* (L.) Merr.	H. Smith 9176 (Tahiti)	370.0	*k*	15.4	..	*k*	..
E. variegata L. var. *orientalis* (L.) Merr.	*j*	700.0	13.4	17.4[e]	..	0.035	*l*
E. fusca Lour.	Philippine Forest Service 9153	150.0	6.8	8.1[b]	0.94	.071[f]	..
E. fusca Lour.	Tamesis 9345 (Philippine Is.)	980.0	7.8	15.8[e]	..	.19[f]	*g*
E. velutina Willd.	Vasconcellos Sobrinho 9263	650.0	9.2	20.0[e]	2.0	.321[f]	*m*
E. velutina Willd.	(Brazil)	650.0	14.4	16.3[e]	..	.290[f]	*n*
E. velutina Willd.	Gomez Parente 9169 (Brazil)	50.0	9.6	13.0[b]	1.72	.195[c]	..
E. velutina forma *aurantiaca* (Ridl.) Kruk.	Rocha 9272 (Brazil)	50.0	15.2	22.4[e]	..	.255[f]	*o*
E. Grisebachii Urb.	Walsingham 9316 (Cuba)	50.0	12.0	12.6[e]	..	.195[f]	*o*
E. macrophylla DC.	Armstrong 9442/52, 53	800.0	12.2	24.0[e]	3.5	.225[f]	*p*

[a] It is recommended that the crude free alkaloid fraction be extracted before the hypaphorine hydrochloride is removed exactly as described in detail for *E. fusca* and *E. glauca*. This method is called the "preferred procedure" and the percentage figure obtained for the crude free alkaloid fraction expresses quite accurately the amount actually present. The

"alternative procedure," which consisted of the removal of the hypaphorine hydrochloride before the extraction of the crude free alkaloids, gives a slightly high value for the percentage of the crude free alkaloids because of the introduction of other substances. [b] Extracted with 95% ethanol. [c] By the "alternative procedure." See note *a*. [d] Erythraline hydriodide; m. p. 247°; $[\alpha]^{28}D$ +179.2, water. *Anal.* Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74. Found: C, 50.72; H, 5.18. Thus, the alkaloid in the seeds from Ceylon does not differ from the alkaloid in the seeds from Trinidad. The mother liquors from erythraline hydriodide were not examined further because of the small amount available. [e] Extracted with absolute methanol. It is generally preferred because of greater extracting power. [f] By the "preferred procedure." See note *a*. [g] See Expt. Part. [h] The 481.2 mg. of crude free alkaloids was dissolved in 0.4 ml. of absolute ethanol and treated with 240 mg. of sodium iodide and 94 mg. of glacial acetic acid. The 80.1 mg. of mixed hydriodides containing a little sodium acetate was recrystallized; yield, 20 mg., m. p. 239.5–241°, $[\alpha]^{28}D$ +197.2. *Anal.* Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74. Calcd. for $C_{18}H_{21}NO_3 \cdot HI$: C, 50.60; H, 5.15. Found: C, 51.01; H, 5.38. These properties are those of mixed erythraline and erythramine hydriodides. Two more recrystallizations from water yielded pure erythraline hydriodide, $[\alpha]^{26}D$ +178. The first mother liquor from the 20 mg. yielded crude erythramine hydriodide of $[\alpha]^{26}D$ +211.1. The accepted value is $[\alpha]D$ +220. The material was now exhausted. [i] A crystalline hydriodide was not obtained from the 40 mg. of crude free alkaloid. [j] The following three samples were combined: 363 g., Belaev 9220, Philippine Islands; 164 g., Haigh 9172, Ceylon; 211 g. Acuna 9164, Cuba. A sample of 700 g. was used after grinding. [k] The fatty fraction and the alcohol extractives were removed together by extracting for twenty-eight hours with methanol. The alcohol residue was dissolved in 300 ml. of water, made acid with hydrochloric acid, and extracted fifteen times with petroleum ether for removal of the fatty fraction. However, after making alkaline with sodium bicarbonate and extracting with chloroform, it was found that the expected semi-micro quantity of alkaloids was badly contaminated with extraneous material. This extraction experiment demonstrated that the "preferred procedure" described for *E. fusca* should be followed when semi-micro quantities of alkaloids are being extracted, and that chloroform extraction should follow the petroleum ether in the clarification step. [l] The 247.8 mg. of crude bases yielded 70.2 mg. of crude hydriodides, m. p. 234–238°. One recrystallization yielded 35.6 mg., m. p. 242–243°, $[\alpha]^{28}D$ +212.4. Two more recrystallizations yielded pure erythraline hydriodide, m. p. (and mixed) 249–250°, $[\alpha]D$ +177.4, 0.0035% yield. *Anal.* Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74. Found: C, 50.98; H, 5.06. The last 1 mg. of mother liquor hydriodides showed $[\alpha]D$ +238.5°. [m] The 2.087 g. of crude bases yielded 0.9784 g. of mixed hydriodides, m. p. 234–235°. Recrystallization yielded 0.744 g., m. p. 243–244°, $[\alpha]D$ +189.6°. One more recrystallization from water yielded pure erythraline hydriodide, m. p. (and mixed) 249°, $[\alpha]D$ +176.0, 0.056% yield. [n] An attempt was made to crystallize the crude free bases from ethanol as was done for the crude bases from *E. fusca*. However, pure erythraline could not be obtained because it could not be crystallized away from the accompanying alkaloids. The inseparable mixture showed m. p. 101–102°, $[\alpha]^{28}D$ +213 whereas pure erythraline showed m. p. 106–107° and $[\alpha]D$ +211. There was no depression in mixed melting points when this impure erythraline was mixed with pure erythramine or erythraline. [o] See discussion in the introduction of this paper. [p] The 1.8298 g. crude bases yielded 1.5928 g. mixed hydriodides, m. p. 229–230°, $[\alpha]D$ +148.3. After fractional crystallizations, only pure erythraline hydriodide was obtained as the major free alkaloid, although related alkaloids were present. It showed m. p. 249–250°, $[\alpha]D$ +176.6, 0.06% yield. *Anal.* Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74; N, 3.29; I, 29.86. Found: C, 50.54; H, 4.91; N, 3.13; I, 29.99.

N, 3.53; Br, 20.17. Found: C, 54.53; H, 5.31; N, 3.55; Br, 20.21.

Isolation of Alkaloids from Other Species of *Erythrina*.—The technique of fractional crystallization of the hydriodides of erythraline, erythramine, and erythratine from the seeds of *Erythrina glauca* has been described in detail. The significant data on the alkaloids as isolated from other species of *Erythrina* are summarized in Table III. In general, the amount of the crude free alkaloidal fraction was 0.2–0.4% for all of the species of *Erythrina* mentioned in Table III with the exception of *Erythrina variegata* var. *orientalis* and *Erythrina Folkersii*. These two species contained only traces of this alkaloid fraction. The 0.2–0.4% amount of this fraction was also true for *Erythrina sandwicensis* and *Erythrina subumbrans*.

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Summary

Erythramine and two new alkaloids, named erythraline and erythratine, have been isolated from the seeds of *Erythrina glauca* Willd. Erythraline was also isolated from the seeds of *Erythrina fusca* Lour., *Erythrina Folkersii* Kruk. and Mold., *Erythrina variegata* L. var. *orientalis* (L.) Merr., *Erythrina velutina* Willd., and *Erythrina macrophylla* DC.

Hypaphorine was isolated from all of the above mentioned species and all for the first time, with the exception of *Erythrina variegata* var. *orientalis* from which it had been previously isolated by others.

Erythraline and hypaphorine undoubtedly

exist also in *Erythrina velutina* forma *aurantiaca* (Ridl.) Kruk. and *Erythrina Grisebachii* Urb.

The crystalline erythraline and erythratine bases, their hydrobromides and hydriodides, have been described. Many microanalyses on several samples and from different species have shown that erythraline has the empirical composition, $C_{18}H_{19}NO_3$, and erythratine has the empirical composition $C_{18}H_{21}NO_4$.

Erythraline and erythramine were of comparable activity (7–8 mg./kg.) in causing a curare-like paralysis in frogs, whereas, erythratine had one-tenth of this activity.

RAHWAY, N. J. RECEIVED DECEMBER 5, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Introduction of Substituted Vinyl Groups. V. A Rearrangement Involving the Migration of an Allyl Group in a Three-Carbon System[1]

BY ARTHUR C. COPE AND ELIZABETH M. HARDY[2]

The (dialkylvinyl)-alkylcyanoacetic esters described recently[3] were stable compounds which were not altered in any way during purification. However, in the preparation of ethyl (1-methylpropenyl)-allylcyanoacetate, which was studied but not reported in the previous work, an unstable product was formed, which changed into a stable substance of higher boiling point after several distillations in vacuum. The structures of these compounds and the nature of the rearrangement have now been determined, and are reported in this paper.

The substance formed initially when the sodium derivative prepared from ethyl (1-methylpropylidene)-cyanoacetate was treated with allyl halides proved to be sufficiently stable to be isolated in a pure state if it was distilled at a pressure of 1 mm. Analysis and molecular refraction were in agreement with the structure of the normal alkylation product, ethyl (1-methylpropenyl)-allylcyanoacetate, I.

$$CH_3CH_2C(CH_3){=}C(CN)COOEt \xrightarrow{NaOEt}$$

$$[CH_3CH{=}C(CH_3)C(CN)COOEt]^- Na^+ \xrightarrow{CH_2{=}CHCH_2X}$$

$$\underset{\displaystyle CH_2CH{=}CH_2}{CH_3CH{=}C(CH_3)C(CN)COOEt}$$

I

Structure I was established by quantitative reduction of the compound, which gave ethyl *s*-butyl-propylcyanoacetate, and condensation of the latter with urea, which produced 5-*s*-butyl-5-propyl-barbituric acid.

The ester I was completely rearranged on heating for four hours at 150–160°, or twenty minutes at 260°, into an isomeric substance of approximately 10° higher boiling point (at 16 mm.). The rearrangement product also had a higher index of refraction (n^{25}D 1.4780 compared to 1.4609), and an exaltation in molecular refraction of +1.53. All of these properties indicate the presence of conjugated double bonds. Quantitative reduction proved the presence of two olefinic linkages, and the reduction product was proved to be a substituted cyanoacetic ester by condensation with urea, which gave a barbituric acid derivative. The high melting point of the latter (219.5–220.5°) suggested that it was a monoalkyl barbituric acid. The most probable way in which I could rearrange into a substance which would give a monoalkyl cyanoacetic ester on reduction involves a shift of the allyl group from the alpha to the gamma position, accompanied by a shift of the double bond from the β, γ to the α, β position, giving II.

$$\underset{\displaystyle CH_2CH{=}CH_2}{CH_3CH}{-}C(CH_3){=}C(CN)COOEt$$

II

Formula II was established by cleavage of the compound with concentrated aqueous ammonia[4] to *unsym*-methyl allyl acetone and cyanoacetamide, and verified by synthesis from methyl allyl acetone and ethyl cyanoacetate.

$$II \xrightarrow{NH_4OH} CH_2{=}CHCH_2CH(CH_3)COCH_3 + CH_2(CN)CONH_2$$

(1) Presented at the Eighth National Organic Chemistry Symposium, St. Louis, Mo., December 29, 1939.

(2) Abstracted from the M.A. Thesis submitted to Bryn Mawr College by Elizabeth M. Hardy in May, 1939.

(3) Cope and Hancock, THIS JOURNAL, **60**, 2903 (1938).

(4) Analogous to the cleavage of ethyl isopropylidenemalonate to acetone and malonamide by ammonia reported by Kötz, *J. prakt. Chem.*, [2] **75**, 479 (1907).