0.15 mm. The product was a soft, plastic, nearly colorless material. The infrared absorption spectrum showed absorption at 2.92 and 5.80 μ.

Anal. Calcd. for $C_{21}H_{34}O_5$: C, 68.81; H, 9.35; C-CH_3 (6), 24.5; active H, 1; mol. wt., 366.5. Found: C, 69.05; H, 9.40; C-CH_3, 21.2; active H, 1.09, 0.90; mol. wt., 359.1.

(b) $C_{21}H_{36}O_5$.—The residues from the above distillation were combined and distilled. The fraction boiling at a bath temperature of 190–200° under a pressure of 0.03 mm. was retained. This distillate formed a brittle glassy solid upon cooling. Three and one-tenth grams of this distillate was dissolved in 30 ml. of dry ether. Cooling gave 420 mg. of crystalline solid melting at 196–201°. After two recrystallizations from ethyl acetate the product XIX melted at 215° (capillary). The infrared absorption spectrum showed absorption at 2.93 and 5.85 μ. Only end absorption was present in the ultraviolet.

Anal. Calcd. for $C_{21}H_{36}O_5$: C, 65.59; H, 9.44; O, 24.97; C-CH_3 (7), 27.3; active H, 2; mol. wt., 384.5. Found: C, 65.83; H, 9.47; O, 25.24; C-CH_3, 23.7; active H, 1.86; mol. wt., 384.7 (X-ray crystallographic analysis).

The same product was isolated from several undistilled desulfurization products by crystallization from ethyl acetate.

(c) **Distillation of Foreruns.**—The foreruns from the distillations in part (a) were fractionated twice. The first time the fraction boiling at 119–137° at 0.04 mm. was retained; the second time there was retained the fraction boiling at 130–134° at 0.05 mm., $n^{25}D$ 1.4896. The ultraviolet absorption spectrum showed maxima at 210 mμ, ϵ 5700 and 268 mμ, ϵ 1550. The infrared spectrum showed strong absorption at 5.80 μ.

Anal. Calcd. for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78; mol. wt., 350.5. Found: C, 71.90; H, 9.07; mol. wt., 359.2; active H, 0; >C=C<, 2.4.

The above experimental results were obtained starting with the product from erythralosamine and ethyl mercaptan, but the same products were isolated starting with erythromycin or with the product of 0.005 *N* sodium hydroxide hydrolysis of erythromycin.

Isomerization of XIX.—Four hundred milligrams of XIX was refluxed for 16 hours in a mixture of 20 ml. of methanol and 20 ml. of 2 *N* sodium hydroxide solution. The cooled reaction mixture was acidified with 10% sulfuric acid. A precipitate formed and was removed by filtration. Recrystallization from ethyl acetate gave 70 mg. of the isomeric lactone XX melting at 185–186° (capillary). This depressed the melting point of starting material upon admixture. Further recrystallization from the same solvent caused no change in melting point. The infrared absorption spectrum showed absorption at 2.90 and 5.75 μ. Only end absorption was present in the ultraviolet region.

Anal. Calcd. for $C_{21}H_{36}O_5$: C, 65.59; H, 9.44; mol. wt., 384.5. Found: C, 65.65; H, 9.41; mol. wt., 370.

INDIANAPOLIS, INDIANA

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF PARKE, DAVIS & CO.]

Some New Constituents of *Piscidia erythrina* L.

BY JAMES A. MOORE* AND STANLEY ENG

RECEIVED DECEMBER 29, 1954

A reinvestigation of the constituents of *P. erythrina* has led to the isolation of piscidic acid, rotenone and five apparently new aromatic substances. The characterization of the new substances is described.

The leguminaceous plant *Piscidia erythrina* L., commonly designated and commercially available as Jamaica Dogwood, has been the subject of numerous chemical investigations over the past 70 years. The interest in this species has arisen largely from reports of the analgesic and insecticidal properties of the root-bark as well as its toxicity to fish. The pharmacognosy of the plant and the older literature recently have been reviewed.[1] We now wish to present the results of some further studies on the constituents of this plant.

Among certain of the earlier reports[2] of isolation work on *P. erythrina*,[3] several highly oxygenated neutral and phenolic compounds, a glycoside, an alkaloid, sterols and waxes are very briefly described. A few more fully characterized substances have also been reported. Freer and Clover[4] obtained from an aqueous extract of the root bark an acid, m.p. 182–183°, which they named piscidic acid; this isolation has since been confirmed and the compound has been shown to be *p*-hydroxybenzyltartaric acid.[5] By ligroin extraction these workers isolated two neutral compounds, a substance $C_{21}H_{14}O_5(OCH_3)_2$, m.p. 201°, a substance $C_{20}H_{12}O_4(OCH_3)_2$, m.p. 216°, and a phenolic compound, m.p. 159°. In the most recent investigation, Russell and Kaczka[6] obtained two compounds by extraction of root material with petroleum ether, one of which was identified as rotenone; the other, a neutral substance $C_{21}H_{14}O_5(OCH_3)_2$, m.p. 203–204°, was named ichthynone. It seems quite probable that the substance, m.p. 201°, of Freer and Clover and ichthynone are in fact the same compound. Degradation studies on ichthynone[7] indicate that it is a chromenochromone of the dehydrorotenoid type. Piscidic acid also was isolated in this most recent study.[7]

In the present work, attention has been directed again to the rather highly oxygenated, aromatic compounds which appear to be characteristic of this plant. Although several previous investigators have used hydrocarbon solvents for the extraction of these constituents, thus avoiding the removal of large amounts of tannins, polysaccharides and pigments, we employed ethanol in order to ensure as complete an extraction of the resinoids as possible. The total extract, representing about

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(1) E. C. Auxence, *J. Econ. Botany*, **7**, 270 (1954).

(2) E. Hart, *Am. Chem. J.*, **5**, 39 (1883); P. W. Danckwortt and E. Schütte, *Arch. Pharm.*, **272**, 791 (1934); F. Hauschild, *ibid.*, **274**, 388 (1936).

(3) This plant also has been designated as *P. piscipula* Sarg. and *Ichthyomethia piscipula* A. Hitch.; the equivalence of these names appears to be generally accepted.

(4) P. C. Freer and A. M. Clover, *Am. Chem. J.*, **25**, 390 (1901).

(5) W. Bridge, F. Coleman and A. Robertson, *J. Chem. Soc.*, 257 (1948).

(6) A. Russell and E. A. Kaczka, THIS JOURNAL, **66**, 548 (1944).

(7) E. A. Kaczka, Ph.D. Thesis, Univ. of North Carolina, 1945.

3% of the plant material, was then roughly fractionated in the usual way by distribution between various solvents. Throughout the isolation work, efforts were made to minimize artifact formation or the destruction of sensitive substances; in particular, alkaline treatments were omitted completely and chromatography was carried out rapidly on relatively small amounts of neutral, partially deactivated alumina.

Five crystalline compounds were obtained from the benzene, chloroform and petroleum ether soluble fractions of the alcohol extract; the pertinent information is summarized in Table I. In addition, a mixture of sterols was obtained from the petroleum ether fraction, and a trace of piscidic acid was isolated from the aqueous fraction. As described below, rotenone was identified among the products from another extraction.

TABLE I

Compound	Empirical formula	M.p., °C.	$[\alpha]_D$	Meijer test	Yield, g.[a]
Lisetin	$C_{14}H_{21}O_7(OCH_3)$	285	0[b]	Green-blue	2.1
Jamaicin	$C_{21}H_{15}O_5(OCH_3)$	163, 193	0	Yellow-or.	3.8
Cmpd. D	$(C_{24}H_{22}O_7)$[c]	253	...	Violet	0.04
Cmpd. E	.....	211	...	Yellow-br.	.01
Cmpd. G	$(C_{16}H_{14}O_3)$[c]	219	+20°	Yellow	.02

[a] From 50 pounds bark. [b] Rotation of methyl ether. [c] Provisional formulations, based on single analyses.

None of the substances listed in Table I appear to have been previously described. Two of the compounds, which we have named lisetin and jamaicin, were obtained in quantities which, it is hoped, will permit structural elucidation. The other compounds, designated by letter, must be considered as provisionally characterized at best because of the small amounts of material available. All of the compounds are aromatic, as indicated by the empirical constitutions and the characteristic ultraviolet spectra. The infrared spectra of these aromatic constituents have many points of similarity, among these being a series of strong bands in the 6–7 μ region.

Lisetin was obtained by direct crystallization from the defatted resin. The substance is quite sensitive to alkali and was eluted from alumina only in impure form. The compound is phenolic and contains one methoxyl group; it is converted to a dimethoxy derivative with diazomethane. That an additional hydroxyl group or groups are present is indicated by a band at 2.83 μ in the infrared spectrum of the methyl ether. An acetate of uncertain composition was obtained from the methyl ether. Carbonyl derivatives could not be obtained from lisetin. The empirical formula of this compound suggests the presence of at least two aromatic rings; it seems possible that the substance bears some relationship to the rotenoid series.

Jamaicin was the most abundant product encountered, and was obtained from several fractions. It was eluted from alumina with benzene before any of the other constituents, and was readily isolated from amorphous sirups in this way. One of the six oxygen atoms is present as a methoxyl group. The compound formed no hydroxyl or carbonyl derivatives; a test for the methylenedioxy group was negative. A series of products was obtained from the action of alcoholic alkali on jamaicin, indicating the presence of a lactone or pyrone group. Jamaicin furnished a crystalline dibromide. Hydrogenation with palladium catalyst resulted in the uptake of three moles of hydrogen; the reduction product was not crystalline. Further characterization and degradation studies are in progress.

Only the most superficial characterization of compounds D, E and G was possible. Substances D and E were isolated from jamaicin mother liquors and were separated by chromatography. They behaved as homogeneous compounds on crystallization, but no further criterion of purity was available. Compound D contained a phenolic hydroxyl group (infrared band at 2.98 μ); the substance dissolved in alkali with concomitant irreversible change in the ultraviolet spectrum, indicating alteration of the molecule. Substance E showed no hydroxyl band in the infrared, and the ultraviolet spectrum was not significantly changed by alkali. Substance G was isolated from the aqueous fraction by chloroform extraction and subsequent chromatography. The phenolic nature of this compound was revealed by the infrared absorption at 3.00 μ, the large change in the ultraviolet spectrum in alkali, and the formation of a methyl ether with diazomethane. Although the molecular formulas given for compounds D and G must be considered provisional, it seems quite definite that compound G is more closely related in molecular size to the anthoxanthins than to the rotenoids.

Since the first five constituents which we encountered all differed from any of those previously reported from this plant, an abbreviated confirmatory extraction and isolation scheme was carried out. From a methylene chloride extract of the ground bark, lisetin, jamaicin and compound D were again obtained; in addition, rotenone was obtained and positively identified. The isolation of the latter compound was rather fortuitous, in that a nearly pure sample of rotenone was obtained in the course of crystallizing successive crops of jamaicin. It was subsequently found that jamaicin and rotenone cannot be separated effectively on deactivated alumina. No traces of ichthynone were encountered, however; comparison of the ultraviolet spectra[8] established with certainty that none of the compounds isolated by us is a crystal modification of this rotenoid.

Since piscidic acid is perhaps the single most characteristic constituent of this plant, an effort was made to isolate this substance from the aqueous fraction of the extract. After a lengthy procedure which employed the lead salt, a minute amount of material was obtained whose m.p. agreed with the literature value; the yield was much less than that previously reported.[5,7]

The plant material used in this work was a commercial sample, harvested in Jamaica, B.W.I., which had been in storage for at least four years. The identity of the material as the root bark of *P. erythrina*, admixed with some stem bark, was independently confirmed.[9] It appears to be quite impossible to decide which of many possible factors,

(8) We are indebted to Dr. E. A. Kaczka, Merck & Co., for supplying a sample of ichthynone.

(9) We wish to thank Mr. F. F. Woodward, S. B. Penick & Co., for examining a specimen of the bark.

such as different location, harvest time or storage conditions of the plant material may be responsible for the significant differences in our results and those of previous investigators. In this connection, it should be mentioned that some of the constituents encountered in the present work would most probably have been destroyed or escaped detection in some of the earlier isolation procedures. Until further specimens of plant material are examined, a decision as to which, if any, of the constituents thus far isolated are artifacts seems unwarranted.

Acknowledgments.—We wish to thank Mr. C. E. Childs and associates for the microanalyses, Dr. J. M. Vandenbelt and Mrs. C. H. Spurlock for the ultraviolet spectra, and Mr. R. B. Scott and Mr. E. Schoeb for the infrared spectra.

Experimental

Alumina was either Merck, washed to *p*H 7.8 and reactivated at 180°, or Woelm, neutral grade; the alumina was partially deactivated before use by washing with methanol and air drying.[10]

Alcohol Extraction.—Shredded root bark (50 lb.) was saturated with 70% ethanol for three weeks and fresh solvent was then drained through the percolator until the effluent was nearly colorless. The extract, 24 l., was evaporated *in vacuo* to 5-l. volume. The dark brown aqueous solution was decanted from a gummy green precipitate which had separated and was then extracted successively with petroleum ether and chloroform. The precipitate was dissolved in alcohol and the solution was extracted with petroleum ether and evaporated, giving 104 g. of green resin. The combined petroleum ether extracts were concentrated and extracted exhaustively with 90% methanol; the methanol layers gave 14 g. of green resin and the petroleum ether layers gave 24 g. of oil. Chromatography of this oil on 70 g. of fully activated alumina furnished 1.1 g. of crystalline material, m.p. 135–160°, which gave positive digitonin and color reactions typical of sterols.

Lisetin.—The 104 g. of defatted precipitate was dissolved in 150 cc. of methanol, and after standing several days, crystals which had formed in the thick sirup were filtered and washed with methanol. The sticky solid was dissolved in hot acetone, filtered through Celite and concentrated to give 2.1 g. of light tan crystals, m.p. 273–280° dec. Several recrystallizations from acetone–methanol mixtures gave colorless prisms, m.p. 284–285° dec. The compound gave a brilliant blue-green color with the Meijer reagent[11]; ultraviolet spectrum: λ_{max}^{EtOH} (mμ) 214 ($\epsilon \times 10^{-3}$ 39.8), 258 (39.4), 284 (23.2), 338 (13.9); $\lambda_{max}^{0.1\ N\ NaOH}$ 274 (30.7), 306 (28.2), 368 (15.5); infrared spectrum (μ) 2.83, 3.10, 6.05, 6.17, 6.61, 7.79, 8.59, 9.67, 11.58, 12.91.

Anal. Calcd. for $C_{24}H_{21}O_7(OCH_3)$: C, 66.36; H, 5.35; OCH_3, 6.83. Found: C, 66.17, 66.27; H, 5.40, 5.26; OCH_3, 7.58.

The compound gave a magenta color with ferric chloride and became yellow in contact with sodium carbonate solution. It dissolved in 1 *N* sodium hydroxide to give a yellow solution which rapidly became brownish-black. The compound was recovered unchanged after 30 min. refluxing with hydroxylamine.

Lisetin was converted to the **methyl ether** by two-hour treatment with diazomethane. The derivative was crystallized from methanol, m.p. 217–218°, $[\alpha]_D$ 0.0° ± 2 (chf.); Meijer reaction blue-green, ferric chloride reaction negative. The ultraviolet and infrared spectra closely resembled those of lisetin, the 3.10 μ infrared spectrum band was absent. The compound was insoluble in alkali.

Anal. Calcd. for $C_{24}H_{20}O_6(OCH_3)_2$: C, 66.94; H, 5.62; OCH_3, 13.31. Found: C, 67.02; H, 5.47; OCH_3, 13.26.

A sample of the methyl ether was acetylated with acetic anhydride–pyridine. The derivative, which crystallized from the warm reaction mixture, was recrystallized from acetone, m.p. 230–233°; λ_{max}^{EtOH} 255 mμ (E_1^1, 701), 280 (475), 308 (infl.). Analysis indicated a tri- or tetraacetate.

Anal. Calcd. for $C_{32}H_{32}O_{11}$: C, 64.86; H, 5.44. Calcd. for $C_{34}H_{34}O_{12}$: C, 64.35; H, 5.40. Found: C, 64.59; H, 4.88.

Jamaicin.—The methanol was removed from the thick sirup remaining after the separation of lisetin, and the resin was thoroughly extracted with warm benzene, giving 53 g. of benzene-soluble material which was chromatographed on 450 g. of alumina. The fractions eluted with benzene gave crystals from ether solution, which after several recrystallizations from methanol–ether gave 1.86 g. of prisms, m.p. 193–194°, and 0.46 g. of less pure material, m.p. 189–192°. The fractions eluted from alumina with methanol gave an additional 50 mg. of lisetin, m.p. 270–285°, green Meijer test.

The 14 g. of resin from the methanol-soluble portion of the petroleum ether extracts was chromatographed on 190 g. of alumina from benzene–petroleum ether solution (chromatogram B). The first fractions of this chromatogram, eluted with petroleum ether and benzene, furnished 0.85 g. of jamaicin. An additional 1.1 g. of jamaicin was obtained by rechromatography of the combined crystallization mother liquors.

Jamaicin crystallized in characteristic prisms from methanol, m.p. 193–194°. In some cases, a crystal modification was obtained which either underwent a transition at 160–163° or, occasionally, complete melting at 160–163°, followed by resolidification (on scratching) and remelting at 190–193°; ultraviolet spectrum: λ_{max}^{EtOH} (mμ) 231 (ϵ 10^{-3} 30.5), 263 (34.7), 306 mμ (14.5); infrared spectrum: (μ) 6.12, 6.65, 6.72, 7.15, 7.81, 7.90, 8.37, 8.52, 8.92, 9.59, 10.72, 12.05, 12.89; $[\alpha]_D$ −0.7 ± 1° (chf.).

Anal. Calcd. for $C_{21}H_{15}O_5(OCH_3)$ (378.36): C, 69.83; H, 4.79; OCH_3, 8.20. Found: C, 69.85, 70.15; H, 4.97, 4.77; OCH_3, 8.38; mol. wt. (isothermal dist.), 362.

Jamaicin was insoluble in alkali and the ultraviolet spectrum was unchanged in the presence of alkali, the ferric chloride color was negative, Meijer test yellow-green turning to brown. The compound was recovered unchanged from attempted oxime formation, attempted acetylation (pyridine, acetic anhydride, 100°), attempted methylation with diazomethane and boiling with 20% sulfuric acid. No color developed on warming a solution of jamaicin in 70% sulfuric acid with chromotropic acid. Under the same conditions, a sample of narcotine gave a deep violet color, showing the presence of a methylenedioxy group.

Jamaicin dibromide was prepared from 25 mg. of jamaicin in chloroform solution and 0.7 cc. of 0.1 *M* bromine in chloroform. The solution was evaporated *in vacuo* to a yellow oil which crystallized from ether in white prisms, m.p. 181–183° dec.; λ_{max}^{EtOH} 221 mμ (E_1^1, 487), 251 mμ (378), 394 mμ (295).

Anal. Calcd. for $C_{22}H_{18}O_6Br_2$: C, 49.09; H, 3.37. Found: C, 48.98; H, 3.66.

Compounds D and E.—These substances were obtained from the fractions of chromatogram B (methanol-soluble fraction of the petroleum ether extract) which were eluted with chloroform and chloroform–methanol mixtures, respectively. Further quantities of compound D were obtained from the chloroform eluates of subsequent chromatograms of jamaicin mother liquors.

Compound D crystallized in light yellow felted needles from chloroform, m.p. (rapid heating) 249–253° dec. It was very sparingly soluble in other solvents, the Meijer reaction was bright violet. Ultraviolet spectrum: λ_{max}^{EtOH} 239 mμ (E_1^1 650), 277 (607), 307 (446); infrared spectrum: (μ) 2.98, 6.10, 6.25, 6.60, 6.90, 7.08, 7.75, 8.25, 8.65, 9.01, 9.41, 11.41, 12.69.

Anal. Calcd. for $C_{24}H_{22}O_7$ (422.42): C, 68.23; H, 5.25. Found: C, 67.87; H, 5.28; mol. wt. (Rast), 424.

Although the ultraviolet spectrum was unchanged by addition of alkali, the compound dissolved in 1 *N* potassium hydroxide giving a yellow solution, λ_{max} 283 mμ.

Compound E crystallized from the chloroform–methanol eluates with m.p. between 196–204°. The combined crystalline material gave 9 mg. of white prisms, m.p. 209–211°, after recrystallizing from chloroform–methanol. The Meijer test was yellow-brown; ultraviolet spectrum, λ_{max}^{EtOH} 268 mμ (E_1^1 1080); infrared spectrum (μ) 3.33, 6.05, 6.35, 6.57, 6.83, 7.26, 7.60, 7.83, 8.27, 8.67, 8.94, 9.64, 11.94, 12.32, 12.71, 13.01, 13.84.

(10) L. B. Norton and R. Hansberry, THIS JOURNAL, **67**, 1609 (1945).

(11) T. M. Meijer, *Rec. trav. chim.*, **55**, 954 (1936).

Compound G.—The chloroform extract of the aqueous phase from the original extraction gave, on evaporation, 57 g. of brown resin. This was extracted with warm benzene to give 3 g. of benzene-soluble gum which was chromatographed on 40 g. of alumina. The fractions eluted with benzene gave a total of 18 mg. of cream colored prisms on crystallization from methanol–ether. Recrystallization from acetone–petroleum ether gave slender colorless prisms, m.p. 216–219°; $[\alpha]_D$ +20 ± 2° (An); ultraviolet spectrum: λ_{max}^{EtOH} 240 mμ ($\epsilon \times 10^{-3}$ 14.8), 279 (10.8), 339 (7.4); $\lambda_{max}^{EtOH + NaOH}$ 259 mμ (9.1), 356 (25.1); infrared spectrum (μ): 3.00, 6.04, 6.17, 6.32, 6.62, 6.79, 6.94, 7.35, 7.71, 8.25, 8.64, 8.93, 9.72, 10.74, 11.49, 12.76, 13.29, 14.30.

Anal. Calcd. for $C_{16}H_{14}O_5$ (286.27): C, 67.13; H, 4.93. Found: C, 66.81; H, 5.11; mol. wt. (Rast), 254.

A small sample of the compound was treated with excess diazomethane. The product was crystallized four times from ether–petroleum ether to give white prisms, m.p. 173–178°. The ultraviolet spectrum in ethanol showed the same maxima as the parent compound with somewhat lower extinctions. In alkali the spectrum was quite different; $\lambda_{max}^{EtOH + NaOH}$ (mμ) 229 (E_1^1 595), 249 (462), 272 (358), 338 (297), 397 (410); λ_{min} 304.

Methylene Chloride Extraction. Isolation of Rotenone.—Seven pounds of shredded root bark was extracted with 9 l. of methylene chloride in six portions. The combined extracts were evaporated, and the residue (18 g.) was dissolved in benzene and chromatographed on 180 g. of alumina. The first fraction eluted with benzene furnished 310 mg. of jamaicin, m.p. 192–194°. The intermediate fractions eluted with chloroform gave no crystals. The final fraction, eluted with methanol, deposited a very small quantity of crystals from chloroform, m.p. 270–280°. This was identified as lisetin by the Meijer test and ultraviolet spectrum.

The mother liquors of the jamaicin from the first fraction were then rechromatographed on 87 g. of alumina. The first fraction, 4.5 g. eluted with petroleum ether–benzene (1:1), furnished a further 66 mg. of jamaicin from methanol. The mother liquors from this crop were stored in the ice-box in methanol–ether solution, and slowly deposited a larger second crop of prism-clusters. This material was twice recrystallized from chloroform–petroleum ether, weight 170 mg., m.p. 163–164°. A mixed m.p. with jamaicin gave a large depression, a mixed m.p. with authentic rotenone gave no depression; the infrared spectrum was superimposable upon that of authentic rotenone. Further crystallization of this fraction then gave a small third crop of crystals which were recrystallized from chloroform–petroleum ether to give 25 mg. of jamaicin, m.p. and mixed m.p. 160° (190–191°).

The fractions of this chromatogram eluted with benzene gave 4 mg. of compound D from chloroform–ether, m.p. 236–255° dec., bright violet Meijer test.

Isolation of Piscidic Acid.—One-half of the aqueous solution remaining after the chloroform extraction, containing about 200 g. of solids, was treated with 400 ml. of saturated lead acetate solution. The resulting dark brown precipitate was filtered, dissolved in warm acetic acid, and reprecipitated with water after Norite treatment. The lead salt was then filtered and decomposed with hydrogen sulfide in alcohol suspension. The alcohol was completely evaporated and the dark brown residue was extracted with warm ethyl acetate. This extract was concentrated and diluted with chloroform to precipitate brown, amorphous impurities. After this process had been repeated several times, the ethyl acetate was evaporated and the oily residue partially crystallized. The solid was separated from the oil and sublimed at 140° (0.05 mm.). Less than 1 mg. of sublimate was obtained, m.p. 181–185°, $\lambda_{max}^{H_2O}$ 223 mμ (A:5.55), 274 mμ (A:0.985); $\lambda_{max}^{0.01\ N\ NaOH}$ 240 mμ (A:6.95), 292 mμ (A:14.8).

DETROIT 32, MICHIGAN

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Senecio Alkaloids. The Composition of "Hieracifoline" and "Jacobine"

BY ROGER ADAMS AND MAURIZIO GIANTURCO

RECEIVED NOVEMBER 10, 1955

The alkaloid "hieracifoline," isolated by Manske from *Erechtites hieracifolia*, is a mixture. By employing a partition chromatographic procedure, the two compounds, namely, senecionine and seneciphylline, were separated. From the alkaloid "jacobine," isolated by Manske[1] from *Senecio jacobea*, senecionine, seneciphylline and a third alkaloid which is identical with Bradbury's and Culvenor's[6] jacobine, were obtained. These same three components in different ratios were present in a sample of *Senecio jacobea* L. of Norwegian origin.

(A) The Alkaloids from *Erechtites hieracifolia*.—Manske[1] reported in 1939 the isolation from *Erechtites hieracifolia* of an alkaloid $C_{18}H_{25}NO_5$ isomeric with senecionine, integerrimine and usaramoensine. This alkaloid, m.p. 227°, $[\alpha]_D$ −89.7°, was named hieracifoline. It gave on hydrolysis the base retronecine and an acid $C_{10}H_{16}O_5$, called hieracinecic acid, isomeric with senecic, integerrinecic, usaramoensenecic and platynecic acids.

From *Senecio aquaticus*, an alkaloid, $C_{18}H_{25}NO_5$, m.p. 220°, $[\alpha]^{15}D$ −83° was reported.[2] This substance, which was named aquaticine, showed characteristics very close to those of the so-called hieracifoline.

Recently Culvenor[3] has shown that the alkaloid pterophine, m.p. 227°, $[\alpha]_D$ −88.5°, obtained first by De Waal[4] from *Senecio pterophus* and *Senecio ilicifolius* is actually a mixture of the two known alkaloids senecionine and seneciphylline. In the same Communication[3] he postulated that hieracifoline is probably a mixture of senecionine and seneciphylline on the basis of the infrared spectra and the R_f values.

The infrared spectra and R_f values, however, do not always permit distinction between stereoisomers. Hieracifoline which was extracted from *Erechtites hieracifolia* was therefore subjected in this Laboratory to further investigation. The melting point and infrared spectrum of the sample available were identical with those of a sample of hieracifoline kindly supplied by Dr. Manske.

Senecionine has a band in the infrared spectrum at 757 cm.$^{-1}$ which was used for identification of this alkaloid in mixtures containing seneciphylline, retrorsine and riddelline.[5] This band, however, is also present in the spectra of the stereoisomers integerrimine and usaramoensine. Moreover, it has now been found that integerrimine, usaramoensine and senecionine all have the same R_f values. For

(1) R. H. F. Manske, *Can. J. Research*, **17B**, 8 (1939).
(2) W. C. Evans and E. T. Evans, *Nature*, **164**, 30 (1949).
(3) C. C. J. Culvenor, *Chemistry and Industry*, 1386 (1954).
(4) H. L. De Waal, *Nature*, **146**, 777 (1940).
(5) R. Adams and T. R. Govindachari, THIS JOURNAL, **71**, 1956 (1949).