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Alkaloids of *Geissospermum vellosii*

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A new isolation procedure has been developed for *Geissospermum vellosii* bark that leads to the isolation of crystalline geissospermine in 0.3 to 0.4% yield. No evidence could be found for the presence of pereirine or vellosine in the bark; however, five new alkaloids have been isolated. One of these is identical with geissoschizoline, the indolinic acid cleavage product from geissospermine.

The apocynaceous tree *Geissospermum vellosii*, indigenous to Brazil, has been the object of extended interest over a long period of time, both from the chemical and pharmacological standpoints. Amorphous extracts of its bark, known as pao pereira, have long enjoyed a reputation as a febrifuge[1] in Brazilian folk medicine and recently have been reported to have curare-like activity.[2] The bark is rich in alkaloids, a number of which have been isolated.[1b] As part of a comprehensive study of pereiro bark alkaloids, the previous isolation work has been re-examined, and this report presents an improved isolation procedure, an evaluation of the occurrences reported, and the isolation of some new alkaloids.

Of the three alkaloids reported from *Geissospermum vellosii*, namely, geissospermine, pereirine and vellosine, geissospermine has been found the most frequently and in the largest quantity. The most recent isolation procedure is that of Bertho and Moog[3] who extracted the bark exhaustively with ethanol, dissolved this extractive in dilute acetic acid, and then co-precipitated the alkaloids with lead hydroxide. Extraction of this precipitate gave geissospermine in an improved yield of 0.2%. The improvement was over a previous procedure in which calcium hydroxide had been used and the yield was 0.1%.[1a] A recent application of the lead hydroxide procedure[4] reports the isolation of amorphous material which required chromatography on alumina before crystalline geissospermine could be obtained.

Pereirine was first reported by Hesse[5] as an amorphous gray-white powder. Later material of m.p. 134–35° was isolated[3] from the methanolic geissospermine mother liquors and was called pereirine. Neither the free base nor its salts were crystalline. Indeed, later chromatographic work[6] indicated this pereirine was inhomogeneous.

Vellosine was isolated by Freund and Fauvet[7] and was reported as melting at 189° with the composition $C_{23}H_{28}N_2O_4$. However, it is questionable whether they were working with *Geissospermum vellosii*,[1a,8] and the conclusion was reached[1a] that pereiro bark contains very little if any vellosine.

Our initial attempts to isolate geissospermine were by the Bertho and Moog procedure.[3] However, the best yield we could obtain was 0.1% and this was far from reproducible, particularly with increased scale of operation. The chief difficulty apparently arose in drying the alkaloid–lead hydroxide coprecipitate and indicated a possible action of alkali on geissospermine. Also, only a small fraction of the total alkaloidal content was obtained crystalline by this method, hence a new isolation procedure was sought.

With the small amount of geissospermine at hand from the previous isolation, the partition of geissospermine was determined at various *p*H's and with various solvents. It was found that ether extraction at *p*H 7 removed geissospermine at a slow but reasonable rate; therefore a procedure was built around this observation, and it is shown in Figure 1. It consists in first exhaustively extracting the finely ground bark with ethanol and allowing the ethanol extract to stand in the cold until precipitation is complete. This eliminates considerable non-alkaloidal material, nearly half of the total material initially extracted into the ethanol. The ethanol is then evaporated and replaced with 0.5 *M* phosphate buffer at *p*H 4, resulting in a precipitate of doubtful alkaloidal character which is saved as fraction A. Continuous extraction with ether then removes the weak bases as fraction B which spectrally can be shown to contain indoles.

The remaining alkaloids are separated into moderately strong and very strong bases by extraction first at *p*H 7, which removes geissospermine as well as several other alkaloids, and then at *p*H 10 (fraction F). After the extraction at *p*H 10, the mixture is filtered and the insoluble material is saved as fraction G. Making the aqueous phase more strongly basic (*p*H 12) and extracting further gave very little additional material.

The advantages of this extraction procedure are (1) that it is reproducible and easily handled mechanically since for the most part solutions are involved and (2) isolation is accompanied by a fractionation based on both the basicity and partition coefficients of the various alkaloids. After this

(1) See (a) A. Bertho and G. von Schuckmann, *Ber.*, **64**, 2278 (1931), and (b) T. A. Henry, "The Plant Alkaloids," 4th Ed., The Blakiston Co., Philadelphia, Pa., 1949, for complete summaries and references to earlier work on the pharmacology as well as chemistry of this species.

(2) R. Ferreira, *Brasil-med.*, **63**, 131 (1949).

(3) A. Bertho and F. Moog, *Ann.*, **509**, 241 (1934).

(4) K. Wiesner, W. Rideout and J. A. Manson, *Experientia*, **9**, 369 (1953).

(5) O. Hesse, *Ann.*, **202**, 141 (1880).

(6) A. Bertho and H. F. Sarx, *ibid*, **556**, 22 (1944).

(7) M. Freund and C. Fauvet, *Ber.*, **26**, 1084 (1893); *Ann.*, **282**, 247 (1894).

(8) O. Hesse, *ibid.*, **284**, 195 (1895).

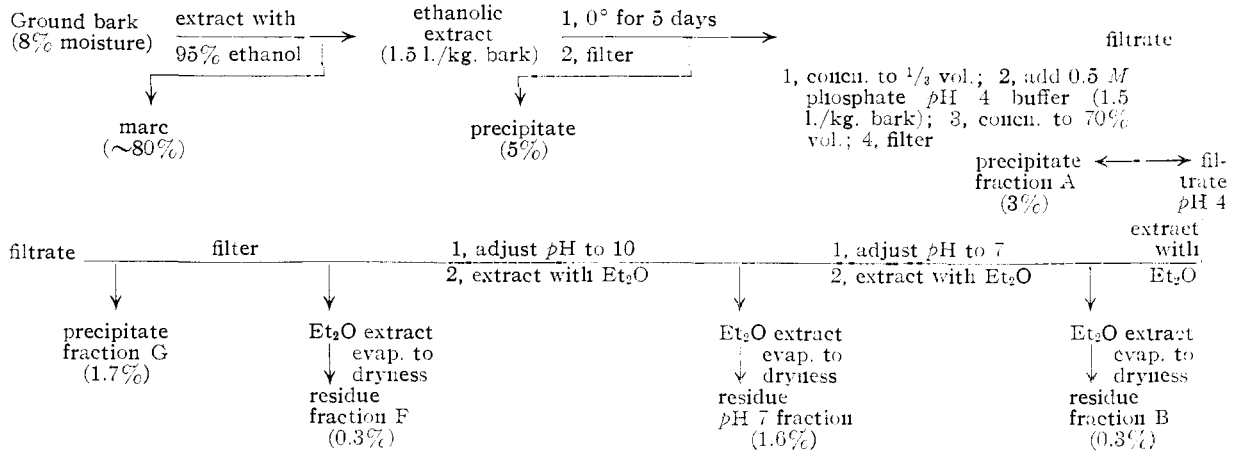

Fig. 1.—Flow sheet of extraction of alkaloids from *Geissospermum vellosii* and separation into main fractions.

crude separation, the various fractions were examined first for the individual alkaloids reported in the literature.

From the *p*H 7 fraction geissospermine was isolated with little difficulty. In most cases, it crystallized in the ether extraction flask during the early stages of the extraction and was obtained quite pure merely by filtering. In those few cases where crystallization did not occur during the extraction, the entire *p*H 7 fraction was chromatographed on alumina and the geissospermine was obtained by cutting the column into zones. Crystallization from aqueous methanol gave consistent yields of 0.3 to 0.4% of material melting at 145–147° for which analysis indicated the dihydrate formulation $C_{46}H_{48}N_4O_3 \cdot 2H_2O$[9] rather than the sesquihydrate,[3,4] and drying gave anhydrous geissospermine, m.p. 206–208°.[3,4]

In spite of a detailed examination of the various fractions for pereirine and vellosine, no evidence for the presence of these alkaloids could be found. In view of our results and the questionable nature of the previous reports, these compounds appear to have no validity.

However, a number of new alkaloids were isolated from both the *p*H 7 and 10 fractions. From the geissospermine mother liquors a bright orange alkaloid, D_1, m.p. 237–238°, was obtained in very small amount. It had a complex ultraviolet absorption and showed a strong carbonyl band in the infrared. After removal of D_1, much larger quantities of a second alkaloid, D_2, crystallized. This material melted at 133–135° and had the formula $C_{39}H_{46}N_4O$. It was very similar to geissospermine in its ultraviolet absorption and color test (deep violet-red) with concd. nitric acid. The third new alkaloid found in the *p*H 7 fraction was E_1, m.p. 163–165°, and it was isolated form a fraction moving more rapidly than geissospermine on alumina. Empirically, it had the composition $C_{20}H_{24}N_2$ and its ultraviolet absorption was typical of indoline alkaloids such as ajmaline and rauwolfine.[10]

The *p*H 10 fraction, F, was particularly fruitful. Precipitation as the nitrate easily separated an alkaloid F_1, $C_{17}H_{14}N_2$, which was obtained as the yellow-orange crystalline free base, m.p. 233–235°, by chromatography on alumina. This material has been isolated independently recently[11] as the perchlorate and named flavopereirine. Its structure is the subject of the next paper.[12]

The nitrate-soluble portion of fraction F was converted to free base and chromatographed. Chloroform–benzene eluted a homogeneous fraction which crystallized from chloroform–hexane as the chloroformate, m.p. 105–108°. This compound, F_3, was obtained solvent-free by sublimation after which it melted at 84–87° and had the formula $C_{19}H_{26}N_2O$. Its ultraviolet spectrum was that of an indoline,[10] and it formed a picrolonate and diacetyl derivative.

Concurrent experiments on the structure of geissospermine led to an interesting result with regard to F_3. Previous reports in the literature indicated that the action of concd. hydrochloric acid on geissospermine led to cleavage[3,4,6] of the molecule into two substantial fragments, neither of which had been obtained crystalline. We applied the hydrochloric acid-cleavage reaction to geissospermine and found three crystalline fragments, separable by chromatography on alumina, in yields (by weight) of about 50, 20 and 20%. These compounds have been given the names geissoschizoline ($C_{19}H_{26}N_2O$),[13] geissoschizine ($C_{21}H_{24}N_2O_3$) and apogeissoschizine ($C_{21}H_{22}N_2O_2$), respectively, on the basis of their origin from the splitting of geissospermine, and the fact that geissoschizoline exhibited a typical indoline ultraviolet spectrum whereas geissoschizine and apogeissoschizine were indolic.

A direct comparison of F_3 and geissoschizoline showed them to be identical in all respects (m.p., m.m.p., optical rotation, ultraviolet and infrared absorption) both as the free base and diacetyl derivative. That this coincidence was not an artifact

(9) In spite of numerous analyses it is not possible to exclude H_{50}, but the data are more inclined toward H_{48}.

(10) N. Neuss, "Physical Data of Indole and Dihydroindole Alkaloids," 2nd Ed., Eli Lilly and Co., Indianapolis, Ind., 1956.

(11) O. Bejar, R. Goutarel, M. M. Janot and A. LeHir, *Compt. rend.*, **244**, 2066 (1957).

(12) N. A. Hughes and H. Rapoport, THIS JOURNAL, **80**, 1604 (1958).

(13) A compound of this empirical composition has been isolated previously[4] from the action of acid on geissospermine, but it was amorphous and was characterized as the picrolonate, m.p. 238–240°. We have obtained a picrolonate of our material (see Exptl.) but it differs in m.p., melting at 209–211°.

of the isolation procedure was established by resubmitting geissospermine to the isolation process beginning at the stage prior to concentration at *p*H 4. All the geissospermine was recovered during the *p*H 7 extraction and there was no evidence of any conversion to geissoschizoline.

Therefore geissoschizoline as isolated from the bark does not come from geissospermine breakdown during extraction. There is a strong possibility that geissospermine is formed in the plant through the union of geissoschizoline and geissoschizine, or that partial breakdown of geissospermine to these two "halves" occurs in the plant. So far, our efforts have failed to reveal geissoschizine or apogeissoschizine as naturally occurring, although the possibility exists that they or very similar compounds may be present in the B and *p*H 7 fractions.

Experimental[14]

Isolation of Alkaloids from *Geissospermum vellosii*. A. Separation into Main Fractions.—A 6.87-kg. batch of *Geissospermum vellosii* bark, ground to a fineness of 0.5 mm., was extracted for one week with 95% ethanol in a modified Soxhlet-type apparatus. The alcoholic extract (*ca.* 10 liters) was allowed to stand at 0° for five days, the mixture was filtered, and the filtrate was concentrated at reduced pressure to 4 liters. To this solution was added 12 liters of 0.5 *M* sodium dihydrogen phosphate, the *p*H was adjusted to 4 by addition of phosphoric acid, the acid solution was concentrated at reduced pressure to 10–11 liters, and the cooled solution was now filtered, saving the insoluble material as fraction A. Using a 12-liter continuous extraction apparatus, the filtrate was extracted at *p*H 4 with ether for 7 days, at *p*H 7 for 11 days, and at *p*H 10 for 7 days. Each *p*H adjustment was made with satd. sodium hydroxide solution, and after extraction at *p*H 10 the aqueous phase was filtered to remove considerable insoluble material, saved as fraction G. Making the filtrate strongly alkaline (to *p*H 12–13) and continuing the ether extraction gave very little additional material. Each ether extract was concentrated to 200 ml., 200 ml. of chloroform was added and the organic phase was washed with satd. sodium chloride solution (50 ml.), dried over sodium sulfate and evaporated to constant weight to obtain each crude fraction.

B. Recovery of Geissospermine from *p*H 7 Fraction.—In most cases, crystalline geissospermine precipitated from the ether extract during the first two days of extraction at *p*H 7. It was removed by filtration and the ethereal filtrate was concentrated to a gummy residue as described above. In those extractions where geissospermine did not crystallize from the ether, the entire extract was reduced to a gummy residue. Further purification was achieved by chromatography of this residue on alumina (Merck, 200 g. per g. of residue) using benzene for development of the chromatogram into three fractions, *viz.*, a dark brown upper fraction (C), an orange center fraction (D), and a lower fraction (E) showing only a slight blue fluorescence when viewed in ultraviolet light. After the solvent had passed through the column, the alumina was extruded and cut into the three fractions above, each fraction being further examined separately.

Fraction D was digested with methanol, the mixture was filtered, and the filtrate was evaporated to dryness. The residue was dissolved in 1 *N* acetic acid and the solution was washed with a half-volume portion of benzene, concentrated *in vacuo* to 80% of its initial volume, and made alkaline with ammonium hydroxide. Crystallization of the resulting precipitate from methanol–water (4:1) gave pure geissospermine as the dihydrate, m.p. 145–147°, in 0.3–0.4% yield from ground bark.

Anal. Calcd. for $C_{40}H_{48}N_4O_3 \cdot 2H_2O$: C, 71.8; H, 7.8; N, 8.4. Found: C, 72.0; H, 8.0; N, 8.6.

On drying the dihydrate at 130° (0.1 mm.) for 12 hours, the anhydrous form was obtained, m.p. 206–208° (reported m.p. 210–212°,[3] 217–219°[4]).

Anal. Calcd. for $C_{40}H_{48}N_4O_3$: C, 75.9; H, 7.7. Found: C, 75.8; H, 7.7.

C. Other Alkaloids from *p*H 7 Fraction.—The aqueous methanolic mother liquors from crystallization of the geissospermine, on standing for one day at room temperature, deposited a small amount of orange crystals which on recrystallization from methanol melted at 237–238°. This material, **alkaloid D_1**, was obtained in very small yield (2×10^{-4}%) and was characterized only by its infrared absorption in chloroform (strong band at 5.83 μ) and its ultraviolet spectrum (λ_{max}^{EtOH} 230, 290, 380, 475 mμ).

After removal of D_1, the geissospermine mother liquors were allowed to evaporate at room temperature and atmospheric pressure to about one-half the initial volume. This resulted in the appearance of a large number of plate-like crystals which were recrystallized from 4:1 methanol–water to constant melting point, 133–135°. The yield of **alkaloid D_2** was about 0.03%, $[\alpha]^{25}D$ +74° (*c* 1.0, ethanol); $\lambda_{max}^{CHCl_3}$ 2.84(w), 6.23(m) μ; λ_{max}^{EtOH} 250, 284, 292 mμ.

Anal. Calcd. for $C_{39}H_{46}N_4O \cdot {}^1/_2H_2O$: C, 78.6; H, 8.0; N, 9.4; O, 4.0. Found: C, 78.6; H, 8.1; N, 9.7; O, 3.9.

The bottom portion (*ca.* 0.5 cm.) of chromatographic fraction E (described above in the recovery of geissospermine) had a slight yellow appearance and was examined separately. The alumina was digested with methanol and the filtered methanol solution was evaporated to dryness. Several crystallizations of the residue from hexane gave colorless needles of **alkaloid E_1** in about 0.001% yield, m.p. 163–165°, $[\alpha]^{24}D$ −51° (*c* 1.0, ethanol); $\lambda_{max}^{CHCl_3}$ 2.92(m), 6.05(w), 6.23(s), 11.00(s) μ; λ_{max}^{EtOH} 245, 300 mμ.

Anal. Calcd. for $C_{20}H_{24}N_2$: C, 82.2; H, 8.3; N, 9.6; mol. wt., 292. Found: C, 82.1; H, 8.6; N, 9.6; mol. wt. (Rast), 280.

D. Separation of *p*H 10 Fraction (F) into F_1 (Flavopereirine) and F_3 (Geissoschizoline).—A 20-g. portion of the residue designated above as F and obtained by continuous ether extraction of the aqueous solution at *p*H 10 and evaporation of the ether was dissolved in 250 ml. of ethanol and 800 ml. of 0.25 *N* hydrochloric acid was added with stirring. After being clarified by filtration, the solution was treated with a saturated solution of sodium nitrate with stirring until precipitation was complete and then was kept at 0° for 12 hours. The mixture then was centrifuged and the precipitate and supernatant were examined separately.

The precipitate was suspended in 1% sodium nitrate solution and the suspension was centrifuged, giving an orange precipitate and a supernatant solution. Addition of sodium hydroxide and chloroform extraction of this supernatant gave, on evaporation of the chloroform, a small residue (F_2) which was not investigated further. The orange solid was suspended in 600 ml. of water, 100 ml. of 1 *N* potassium hydroxide solution was added slowly with stirring which was continued for 30 minutes, and the mixture was extracted continuously with chloroform for four hours. Evaporation of the dried chloroform extract gave 5 g. of a crude residue which was redissolved in 50 ml. of chloroform and introduced onto a column (40 × 4 cm.) of alumina (Merck). Continued elution with chloroform left a brown band at the top of the column and removed an orange band. This orange material, obtained as a gum on evaporation of the chloroform, was dissolved in 50 ml. of acetone. Cooling gave 2.1 g. of crystalline **flavopereirine (F_1)**, m.p. 233–235°, unchanged on repeated crystallization. It was optically inactive.

Anal. Calcd. for $C_{17}H_{14}N_2$: C, 83.0; H, 5.7; N, 11.4; equiv. wt., 246. Found: C, 83.0; H, 5.8; N, 11.4; equiv. wt., 246.

The supernatant solution recovered from the initial centrifugation was made strongly alkaline with sodium hydroxide before being extracted thoroughly with chloroform. Evaporation of the dried extracts left 5 g. of residue which was chromatographed on alumina (120 g., Merck) using 4% chloroform–benzene followed by 10 and 25% chloroform–benzene for elution. The 3 g. of material which was eluted with 10 and 25% chloroform–benzene was crystallized from chloroform–hexane and **geissoschizoline (F_3)** was obtained as the crystalline **chloroformate**, m.p. 105–108° after drying at room temperature and 1 mm. pressure overnight, $[\alpha]^{25}D$ +24° (*c* 1.0, ethanol).

(14) All melting points are corrected and those above 200° were taken in evacuated capillaries; microanalyses were performed by the Microchemical Laboratory, University of California, Berkeley.

Anal. Calcd. for $C_{19}H_{26}N_2O \cdot CHCl_3$: C, 57.5; H, 6.5; N, 6.7; O, 3.8; Cl, 25.5. Found: C, 57.7; H, 6.6; N, 6.6; O, 4.1; Cl, 25.6.

The free base was obtained by sublimation of the chloroformate at 140° (10 μ) and melted at 84–87°, $[\alpha]^{25}D$ +32° (c 1.0, ethanol); ultraviolet spectrum in ethanol, λ_{max} 247 mμ (ϵ 8500), 301 (3900).

Anal. Calcd. for $C_{19}H_{26}N_2O$: C, 76.5; H, 8.8; N, 9.4; O, 5.4. Found: C, 76.6; H, 8.7; N, 9.3; O, 5.8.

Geissoschizoline picrolonate was prepared in absolute ethanol and was recrystallized from absolute ethanol, m.p. 209–211°.

Anal. Calcd. for $C_{19}H_{26}N_2O \cdot C_{10}H_8N_4O_5$: C, 61.9; H, 6.1. Found: C, 62.0; H, 6.0.

Diacetylgeissoschizoline was prepared by heating a solution of 500 mg. of geissoschizoline and 5 ml. of acetic anhydride in 25 ml. of pyridine on the steam-bath for three hours. This solution was poured onto 100 ml. of ice and extracted with three 150-ml. portions of chloroform after being made alkaline with concd. potassium hydroxide. Evaporation of the chloroform and crystallization of the residue from 25 ml. of acetone gave 340 mg. of diacetylgeissoschizoline, m.p. 196–197°; ultraviolet spectrum in ethanol: λ_{max} 253 mμ (ϵ 13,500), 283 (3,800), 291 (3,300).

Anal. Calcd. for $C_{23}H_{30}N_2O_3$: C, 72.2; H, 7.9; N, 7.3; O, 12.6; acetyl, 22.5. Found: C, 72.4; H, 7.8; N, 7.4; O, 12.7; acetyl, 22.4.

Acid Cleavage of Geissospermine.—Addition of 1 g. of geissospermine to 5 ml. of concd. hydrochloric acid at room temperature led to a homogeneous solution after three minutes. After five more minutes, the solution was poured into 200 ml. of cold, 1 N aqueous ammonia, and the mixture was extracted with three 200-ml. portions of chloroform. Drying and evaporating the chloroform left a residue which was chromatographed on alumina (Merck, 35 g.). Elution with benzene removed 200 mg. of apogeissoschizine as the first fraction, then 15% chloroform in benzene removed 450 mg. of geissoschizoline, and finally 10% methanol in chloroform removed 250 mg. of geissoschizine.

Geissoschizoline was crystallized from chloroform–hexane, m.p. 105–108°, and was found to be identical with alkaloid F_3 in every property described above. Mixtures of F_3 and geissoschizoline, and of the diacetyl derivatives, showed no melting point depression, and the infrared spectra were identical.

Geissoschizine was obtained from the 10% methanol–chloroform eluted fraction by digesting the residue with 30 ml. of methanol and filtering after thorough cooling. The crystalline material was recrystallized three times from ethanol (long reflux necessary for complete solution), m.p. 180–182°; ultraviolet spectrum in ethanol, λ_{max} 268 mμ (ϵ 14,600), 290 (7,800).

Anal. Calcd. for $C_{21}H_{24}N_2O_3$: C, 71.6; H, 6.8; N, 8.0; O, 13.6; equiv. wt., 352. Found: C, 71.9; H, 6.8; N, 8.0; O, 13.3; equiv. wt., 351.

Apogeissoschizine was found in the benzene-eluted fraction and was best characterized as the hydrochloride. This was prepared by evaporating the benzene, dissolving the residue in hexane, and passing in dry hydrogen chloride until there was no further precipitation. Apogeissoschizine hydrochloride was recrystallized by dissolving it in several ml. of methanol, adding 50 ml. of ethyl acetate, and then adding hexane until the solution became cloudy, m.p. 139–142°; ultraviolet spectrum in ethanol, λ_{max} 273 mμ (ϵ 19,300), 324 (19,000).

Anal. Calcd. for $C_{21}H_{22}N_2O_2 \cdot HCl$: C, 68.0; H, 6.3; N, 7.6; Cl, 9.6. Found: C, 67.7; H, 6.1; N, 7.7; Cl, 9.5.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY]

Flavopereirine, an Alkaloid from *Geissospermum vellosii*

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Flavopereirine, an alkaloid isolated from *Geissospermum vellosii*, has the four-ring indolo[2,3-a]quinolizine (I) chromophore in common with sempervirine, the difference between the two alkaloids arising in the substitution of ring D. Catalytic hydrogenation, which is quite sensitive to acid and alkali, has yielded (1) an octahydro derivative with rings A and D reduced, (2) an octahydro derivative with rings C and D reduced, (3) a tetrahydro derivative with ring D reduced, and (4) a hexahydro derivative in which ring D has undergone hydrogenation and hydrogenolysis. C-Methyl determinations on these hydrogenation products identified the ring D substituent as an ethyl group and located it at positions 1, 2 or 3. Dehydrogenation of the octahydro compound (C and D rings reduced) gave 3-ethyl-2-(5′-ethyl-2′-pyridyl)-indole (desethylalstyrine), thus establishing flavopereirine as 3-ethylindolo[2,3-a]quinolizine. The use of tetrahydroquinoline as solvent and hydrogen donor allowed the dehydrogenation reaction to be applied directly to flavopereirine with excellent results. Critical to the use of this modification was the observation that desethylalstyrine, a base of pK_a' approximately 4.5, was not removed from ether by dilute phosphoric acid.

The bark of *Geissospermum vellosii*, the tree familiarly know as pao pereira in Brazil, is quite rich in alkaloids, and a number in addition to geissospermine have been isolated crystalline.[1] The structure and chemistry of one of these new alkaloids, flavopereirine, is the subject of the present report.[2]

Fractionation of the total crude alkaloids as a function of their basicities and partition coefficients between ether and water led to a strongly basic fraction, termed F, isolated from the aqueous solution by extraction at pH 10. The separation of this fraction into two crystalline alkaloids, F_1 and F_3, has been described in detail.[1] Alkaloid F_1, flavopereirine, was then subjected to a detailed examination.[3]

The empirical formula of flavopereirine, which crystallized as well defined orange rhombs, m.p. 233–235°, was established clearly by analysis of the free base[1] and of a number of salts as $C_{17}H_{14}N_2$. That this (246) rather than any higher multiple was also the molecular formula was definitely indicated by the fact that flavopereirine could be sublimed at 200° and 0.1 mm. pressure. It was optically inactive, had no N-methyl or N-ethyl groups, and showed no C-methyl groups in Kuhn–Roth oxidation.

(1) H. Rapoport, T. P. Onak, N. A. Hughes and M. G. Reinecke, THIS JOURNAL, **80**, 1601 (1958).

(2) Supported in part by a generous grant from Smith, Kline and French Laboratories, Philadelphia, Pa.

(3) After our work had been completed, a short note appeared by O. Bejar, R. Goutarel, M. M. Janot and A. Le Hir, *Compt. rend.*, **244**, 2066 (1957), on the constitution of this alkaloid which they named flavopereirine. Since their material is identical with our F_1, we have adopted their nomenclature. Our conclusion as to the structure of flavopereirine is in agreement with theirs.