### Experimental Section[6]

**Reaction of Deoxyanisoin with 3 Equiv of Aluminum Chloride.**—A mixture of 12.8 g of deoxyanisoin and 20 g of aluminum chloride in 250 ml of benzene was heated under reflux for 1.5 hr. The mixture was then cooled in ice and treated with 200 ml of 2.5 *N* hydrochloric acid. The organic layer was diluted with ether and washed in turn with water and aqueous sodium bicarbonate. Thr organic solution was then extracted with 300 ml of 5% aqueous sodium hydroxide. The solid which was obtained when the extract was acidified was collected on a filter and dried. This was chromatographed on 1 l. of Florisil (elution with 15%, then 25% acetone in Skellysolve B[7]). There was obtained 4.25 g of the monophenol (mp 173–178°) followed by a mixture of mono- and bisphenols.

The former was recrystallized from aqueous methanol to give 4.02 g of *p*-hydroxyphenyl *p*-methoxybenzyl ketone (II), mp 175–178° (lit.[1] mp 175°).

The mixture was recrystallized from aqueous methanol to afford 2.80 g of the bisphenol (III), mp 215–219° (lit.[3] mp 215°).

**Reaction of Deoxyanisoin wih 2 Equiv of Aluminum Chloride.**—A mixture of 1.28 g of deoxyanisoin and 1.33 g of aluminum chloride in 20 ml of benzene was heated at reflux for 18 hr. The mixture was allowed to cool and treated with 15 ml of 2.5 *N* hydrochloric acid. Ether was added and the mixture shaken until the solid had all dissolved. The organic layer was separated and washed with water. This solution was extracted with 5% sodium hydroxide. Acidification of the extract afforded 0.85 g of the crude phenol. This was recrystallized twice from aqueous methanol to afford 0.60 g of *p*-hydroxybenzyl *p*-methoxyphenyl ketone (IV), mp 152–155°, $\nu_{max}$ 3400 and 1680 $cm^{-1}$.

*Anal.* Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83. Found: C, 74.41; H, 6.06.

**Registry No.**—I, 120-44-5; II, 3669-46-3; III, 3669-47-4; IV, 13619-63-1.

(6) Melting points are uncorrected and recorded as obtained on a Thomas–Hoover melting point apparatus. The mass spectra were recorded using an Atlas CH4 instrument equipped with a T04 source; ionizing potential was 70 ev.

(7) A petroleum fraction, by 61–70°, marketed by the Skelly Oil Co.

---

## The Identification of Dehydrocorydalmine and a New Protoberberine Alkaloid, Stepharanine, in *Stephania glabra* Tubers[1]

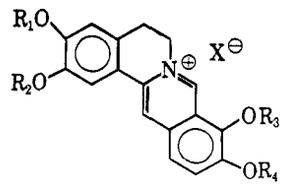
RAYMOND W. DOSKOTCH, M. YOUNAS MALIK, AND JACK L. BEAL

*College of Pharmacy, The Ohio State University, Columbus, Ohio 43210*

*Received April 21, 1967*

Examination of the quaternary alkaloid fraction from the tubers of *Stephania glabra* (Menispermaceae) resulted in the isolation of six crystalline alkaloids.[2] Four of these have been identified as the ubiquitous aporphine magnoflorine and the three protoberberines palmatine (I), jatrorrhizine (II), and columbamine (III). This report is on the characterization of the remaining two optically inactive alkaloids whose isolation and some general properties have been reported. They were previously designated as alkaloids A and B. Alkaloid A has been found to be dehydrocorydalmine (IV) and alkaloid B, a new alkaloid, has been named stepharanine (V).

Alkaloid A as the chloride salt, mp 220–221° dec, analyzed for $C_{20}H_{20}NO_4Cl \cdot H_2O$ and for the presence of



I, $R_1$, $R_2$, $R_3$, $R_4$ = $CH_3$
II, $R_1$ = H; $R_2$, $R_3$, $R_4$ = $CH_3$
III, $R_2$ = H; $R_1$, $R_3$, $R_4$ = $CH_3$
IV, $R_4$ = H; $R_1$, $R_2$, $R_3$ = $CH_3$
V, $R_2$, $R_4$ = H; $R_1$, $R_3$ = $CH_3$
VI, $R_3$ = H; $R_1$, $R_2$, $R_4$ = $CH_3$

three methoxy groups. The ultraviolet spectrum was characteristic of the protoberberine alkaloids[3] and the phenolic nature was evidenced by bathochromic shifts in the presence of dilute base. The infrared absorption spectra taken in a KBr pellet supported the presence of a hydroxyl group by the broad absorption bands at 3440 and 3500 $cm^{-1}$.

The nmr spectrum was most informative showing six aromatic protons at $\delta$ 7.10 (1 H, singlet), 7.68 (1 H, s), 7.96 (2 H, s), 8.59 (1 H, s), and 9.58 ppm (1 H, s), three methoxy groups centered at 4.09, 4.15, and 4.28 ppm, and two triplets at 3.42 and 5.02 with $J$ = 6 cps. The nmr spectrum of palmatine (I) determined under the same conditions showed six aromatic protons at 7.09 (1 H, s), 7.69 (1 H, s), 8.07 (2 H, s), 8.60 (1 H, s), and 9.68 (1 H, s), four methoxy peaks at 4.07, 4.13, 4.19, and 4.34, and two triplets at 3.40 and 5.01 ($J$ = 6 cps). These results are consistent with alkaloid A having the same oxygenation pattern as palmatine and possessing three methoxy groups and one phenolic group. Methylation of alkaloid A chloride by dimethyl sulfate in aqueous sodium bicarbonate solution yielded palmatine chloride identical in all respects (infrared, ultraviolet, tlc, and mixture melting point) with an authentic sample and confirming the substitution positions.

The position of the phenolic group remained to be settled. Since jatrorrhizine (II) and columbamine (III), two other monophenolic protoberberines were already known from this source, alkaloid A must be either palmatrubine (VI)[4] or dehydrocorydalmine (IV).[5] Palmatrubine iodide was prepared[6] from palmatine iodide by fusion with urea and found to be different from alkaloid A iodide. Consequently alkaloid A must be dehydrocorydalmine. The iodide salt of our compound melts with decomposition at 195° while Imaseki and Taguchi reported 228–230° dec. We were unable to prepare any other common derivative owing to insufficient material nor were we able to obtain a sample of dehydrocorydalmine for a direct comparison.

Alkaloid B as the chloride salt, mp 274–275° dec, analyzed for $C_{19}H_{18}NO_4Cl \cdot H_2O$ and appeared to be another phenolic protoberberine alkaloid from examination of the ultraviolet and infrared absorption spectra. Again, the nmr spectrum was most informative, showing six aromatic protons at $\delta$ 7.03 (1 H, singlet), 7.71 (1 H, s), 7.94 (2 H, s), 8.52 (1 H, s), and 9.55 ppm (1 H,

(1) Supported by Grant GM-05640 from the National Institutes of Health, U. S. Public Health Service.

(2) M. T. Wa, J. L. Beal, and R. W. Doskotch, *Lloydia*, in press.

(3) A. W. Sangster and K. L. Stuart, *Chem. Rev.*, **65**, 69 (1965).

(4) E. Spath and G. Burger, *Ber.*, **59**, 1486 (1926).

(5) I. Imaseki and H. Taguchi, *J. Pharm. Soc. Japan*, **82**, 1214 (1962).

(6) Palmatrubine iodide, mp 234–236° dec, was prepared from palmatine iodide by fusion with urea according to Spath and Burger,[4] but the temperature was maintained between 170 and 180°. Methylation of the product with dimethyl sulfate gave palmatine iodide and reduction with sodium borohydride gave tetrahydropalmatrubine, mp 146–148° (lit.[4] mp 148–149°).

s), as well as, two triplets at 3.38 (2 H) and 4.99 (2 H) with $J = 6$ cps, a result compatible with the substitution pattern found in palmatine. The spectrum differed significantly only in the methoxy region, showing two peaks at 4.08 (3 H) and 4.27 (3 H). The remaining two oxygens must be present as phenolic groups as methylation with dimethyl sulfate gave palmatine chloride, identical in all respects (infrared, ultraviolet, tlc, and mixture melting point) with an authentic sample.

The arranging of two methoxy groups and two phenolic groups on the protoberberine skeleton having the oxygenation pattern of palmatine gives a total of six possible structures. The position of the phenolic groups was determined by methylation of alkaloid B with 1 equiv of dimethyl sulfate and examination of the monophenolic products formed. This was accomplished by separating the reaction mixture by preparative thin layer chromatography utilizing silica gel G and methanol–ammonium hydroxide–water (8:1:1), removing the colored bands, and crystallizing the material from these bands as the chloride salts. There was isolated in this manner palmatine, alkaloid B (starting material), columbamine (III), and dehydrocorydalmine (IV). Identification of the reaction products was by direct comparison of the ultraviolet and infrared spectra and the mobility in the thin layer chromatographic system with authentic samples. Alkaloid B must therefore have the structure V, a new natural product which we have named stepharanine.

### Experimental Section

Melting points were determined on a Kofler hot stage and are uncorrected. Infrared spectra were recorded in KBr windows on a Perkin-Elmer Model 237 spectrophotometer. Ultraviolet spectra were determined in ethanol on a Cary Model 15 spectrophotometer. Proton magnetic resonance spectra were obtained in trifluoroacetic acid with tetramethylsilane as internal standard on a Varian A-60A apparatus. Thin layer chromatography was performed on silica gel G (Merck) plates with methanol–ammonium hydroxide–water (8:1:1) as the solvent with detection by visual examination as the alkaloids are colored.

**Methylation of Dehydrocorydalmine (Alkaloid A) to Palmatine.**—Dehydrocorydalmine chloride (20 mg) was dissolved in 20 ml of water and 2 ml of a saturated sodium bicarbonate solution was added. The solution immediately turned orange and 4 mg of dimethyl sulfate was added. The reaction mixture was stirred at room temperature for 6 hr and then evaporated to dryness at reduced pressure. The residue was dissolved in 10 ml of hot water and on cooling overnight deposited fine yellow needles which after collecting, washing with cold water, and drying weighed 15 mg, mp 203–205°. When this product was admixed with authentic palmatine chloride, it had mp 203–205° and the infrared spectra of the two were superimposable. Mobility in the thin layer system was $R_f$ 0.12.

**Methylation of Stepharanine (Alkaloid B) with Dimethyl Sulfate (1 Equiv).**—Stepharanine chloride (50 mg) was dissolved in 40 ml of water and 4 ml of a saturated sodium bicarbonate solution was added. The precipitate that formed was redissolved by warming on the steam bath. Dimethyl sulfate (18 mg) was added and the solution was stirred magnetically for 2 hr at room temperature. The reaction mixture was evaporated to dryness under reduced pressure. The residue was dissolved in 10 ml of absolute ethanol, filtered, and the filtrate reduced to 2 ml to be spotted on thin layer plates. Five silica gel G thin layer plates (20 × 20 cm) were poured to a thickness of 1 mm, then dried and activated in an oven at 150°. The 2-ml reaction mixture solution was streaked evenly over the five plates and developed by methanol–ammonium hydroxide–water (8:1:1). Examination of the developed plates under daylight and ultraviolet light showed four major zones at $R_f$ 0.12, 0.16, 0.60, and 0.67 corresponding to palmatine, columbamine, dehydrocorydalmine, and stepharanine, respectively.

The material from the four zones was isolated in the following manner. After removing the colored bands, the substances were dissolved away from the adsorbent with methanol. The solvent was removed by evaporation to dryness under reduced pressure. The residue was dissolved in 1 ml of hot methanol, filtered, and on cooling the filtrate deposited crystalline material. The zone with $R_f$ 0.12 yielded 6 mg of yellow crystals, mp 202–204°, showing infrared and ultraviolet spectra identical with palmatine chloride. The material (5 mg) from the zone with $R_f$ 0.16 melted at 238–241° and showed infrared and ultraviolet spectra identical with columbamine chloride, mmp 238–240°. The $R_f$ 0.60 zone gave 4 mg of a material, mp 219–221°, identical in infrared and ultraviolet spectra with dehydrocorydalmine, mmp 219–221°. The material from the zone with $R_f$ 0.67 was identical with the starting material, stepharanine.

**Registry No.**—IV chloride, 13509-85-8; IV iodide, 13509-86-9; V chloride, 13509-87-0.

---

## Isolation, Structure, and Synthesis of Hymenoxin, a New Flavone from *Hymenoxys scaposa* (Compositae)

M. B. THOMAS AND T. J. MABRY

*The Cell Research Institute and Department of Botany, The University of Texas, Austin, Texas*

*Received May 10, 1967*

An investigation[1] of the infraspecific variation of the flavonoid constituents in the Compositae species, *Hymenoxys scaposa*, has led to the isolation, structure determination, and synthesis of a new member of the rare group of fully oxygenated A-ring flavones.[2] When the A-ring substituents are as shown in **1a** neither proton nuclear magnetic resonance (pmr) nor ultraviolet spectral data will unequivocally locate the positions of all the hydroxyl and methoxyl groups [*cf.* lucidin[3] (5,7-dihydroxy-6,8-dimethoxy-3′,4′-methylenedioxyflavone), nevadensin[4] (5,7-dihydroxy-4′,6,8-trimethoxyflavone), acerosin[5] (3′,5,7-trihydroxy-4′,6,8-trimethoxyflavone), and sudachitin[5] (4′,5,7-trihydroxy-3′,6,8-trimethoxyflavone)].

Methylene chloride extraction of the leaves of *Hymenoxys scaposa* (Family Compositae) collected near Austin, Texas, yielded a crystalline flavone, $C_{19}H_{18}O_8$, mp 211–213°, which we named hymenoxin. The flavone nucleus and the oxygenation pattern were suggested to be the same as those of **1** by the ultraviolet and pmr spectra. The pmr spectrum of hymenoxin trimethylsilyl ether[6] indicated the presence of four methoxyl and two hydroxyl groups, the latter as trimethylsilyl signals. Hymenoxin mono(trimethylsilyl ether) exhibited a pmr singlet at 12.53 ppm, a signal typical for a C-5 hydrogen-bonded hydroxyl group. The ultraviolet spectra of hymenoxin in methanol alone and methanol with diagnostic reagents (sodium methoxide,

(1) P. Seeligmann and R. E. Alston, *Brittonia*, **19**, 205 (1967).

(2) J. B. Harborne, "Comparative Biochemistry of the Flavonoids," Academic Press Inc., New York, N. Y., 1967, pp 42–46.

(3) H. H. Lee and C. H. Tan, *J. Chem. Soc.*, 2743 (1965).

(4) L. Farkas, M. Nogradi, V. Sudarsanam, and W. Herz, *J. Org. Chem.*, **31**, 3228 (1966).

(5) L. Farkas, M. Nogradi, V. Sudarsanam, and W. Herz, *Tetrahedron*, in press.

(6) T. J. Mabry, J. Kagan, and H. Rösler, "Nuclear Magnetic Resonance Analysis of Flavonoids," The University of Texas Publication No. 6418, Austin, Texas, 1964.