Phytochemistry, 1969, Vol. 8, pp. 877 to 881. Pergamon Press. Printed in England

SESQUITERPENE LACTONES OF SOME *AMBROSIA* SPECIES

WERNER HERZ, G. ANDERSON, S. GIBAJA* and D. RAULAIS

Department of Chemistry, The Florida State University, Tallahassee, Florida 32306, U.S.A.

(*Received* 12 *November* 1968)

Abstract—The sesquiterpene lactone content of collections of *Ambrosia ambrosioides* (Cav.) Payne, *A. arborescens* Mill., *A. chenopodiifolia* (Benth.) Payne, *A. confertiflora* (DC.) Rydb., *A. cumanensis* HBK, *A. peruviana* Willd., *A. pumila* (Nutt.) Gray and *A. tenuifolia* Spreng. has been investigated.

THE DISTRIBUTION of sesquiterpene lactones in *Ambrosia* species has been reviewed and its possible utility for clarifying evolutionary relationships has been discussed.[1,2] In the following we describe briefly our work on the isolation of sesquiterpene lactones from four *Ambrosia* species which have not been studied previously. We also report on four species which gave chemical results differing somewhat from those reported by others.

Ambrosia ambrosioides (*Cav.*) *Payne*

No crystalline sesquiterpene lactones could be isolated from two separate Arizona collections of this species. Each collection furnished a small amount of the flavone hispidulin (I). After completion of this work, however, Romo and co-workers[3] reported the isolation of damsin (III) and franserin (IV) from a Sinaloa collection of *Franseria ambrosioides* Cav., a synonym.[4]

Ambrosia arborescens *Mill.*

Two collections of this previously uninvestigated South American "franserioid" species[4] from Peru gave damsin (III), coronopilin (V), psilostachyin (VI), psilostachyin C (VIII) and a small quantity of what appeared to be 11-epidihydropsilostachyin. The relative proportions of the various lactones from the two collections differed somewhat.

Ambrosia chenopodiifolia (*Benth.*) *Payne*

The only crystalline lactone which could be identified in this previously uninvestigated "franserioid" species[4] was damsin (III).

Ambrosia confertiflora (*DC*) *Rydb.*

Our Arizona collection of this species yielded psilostachyin (VI) and psilostachyin C (VIII). Mabry and co-workers isolated confertiflorin (IXa) and desacetylconfertiflorin (IXb)

---

* Facultad de Quimica, Universidad Nacional Mayor de San Marcos, Lima, Peru. Holder of a Ford Foundation Study Award 1967–1968.

[1] W. HERZ, "Pseudoguaianolides in *Compositae*", in *Recent Advances in Phytochemistry* (edited by T. J. MABRY), Vol. 1, pp. 229–269, Appleton-Century-Crofts, New York, N.Y. (1968).

[2] H. E. MILLER, T. J. MABRY, B. L. TURNER and W. W. PAYNE, *Am. J. Botany* **55**, 316 (1968).

[3] J. ROMO, A. ROMO DE VIVAR, A. VELEZ and E. URBINA, *Can. J. Chem.* **46**, 1535 (1968).

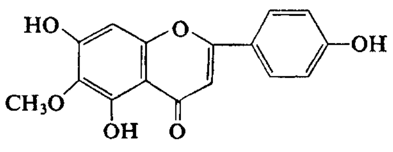
[4] W. PAYNE, *J. Arnold Arboretum* **45**, 401 (1964).

[5] N. H. FISCHER and T. J. MABRY, *Tetrahedron* **23**, 2529 (1967).

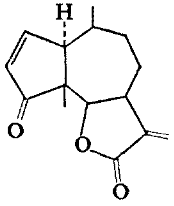
from Texas collections and several germacranolides from a Tamaulipas collection[6] of this species.

Ambrosia cumanensis *HBK*

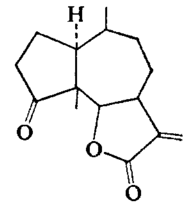
Our Colombian collection of this species gave ambrosin (II), damsin (III) and psilostachyin C (VIII). The three psilostachyins (VI, VII and VIII) or cumanin (X) have been identified[2] in collections from Vera Cruz and Tihautlan, Mexico.[7]



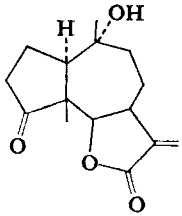
(I)



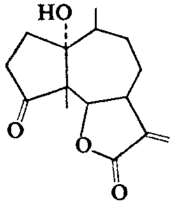
(II)



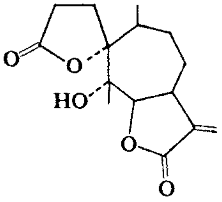
(III)



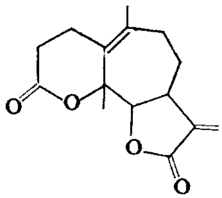
(IV)



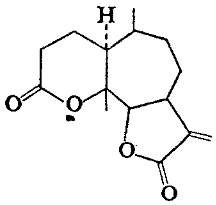
(V)



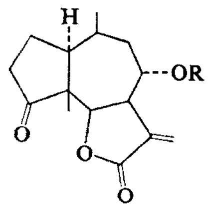
(VI)



(VII)

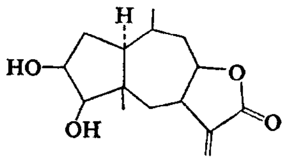


(VIII)

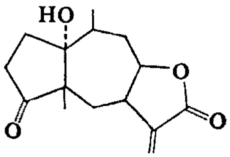


(IXa) R = Ac

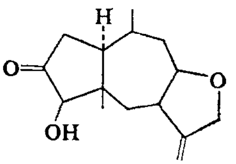
(IXb) R = H



(X)



(XI)



(XII)

---

[6] N. H. FISCHER and T. J. MABRY, *Chem. Commun.* 1235 (1967); N. H. FISCHER, T. J. MABRY and H. B. KAGAN, *Tetrahedron* **24**, 4091 (1968).

[7] J. ROMO, P. JOSEPH NATHAN and G. SIADE, *Tetrahedron* **22**, 1499 (1966), were the first to isolate cumanin from what was claimed to be *A. cumanensis*. In a recent article[8] the species is corrected to *A. psilostachya* DC.

[8] J. ROMO, A. ROMO DE VIVAR and E. DIAZ, *Tetrahedron* **24**, 5625 (1968).

Ambrosia peruvian a *Willd.*

We[9] previously reported the presence of psilostachyin C (VIII) in a 1963 collection from Puerto Rico. Repetition furnished in addition considerable amounts of tetrahydroambrosin which, to our knowledge, has not previously been isolated from a plant source. By contrast, a Hidalgo collection of this species gave peruvin (XI)[10] and peruvinin (XII).[11]

Ambrosia pumila (*Nutt.*) *Gray*

This previously uninvestigated species furnished psilostachyin (VI) and psilostachyin C (VIII) as well as a small amount of an unidentified new lactone.

Ambrosia tenuifolia *Spreng.*

The only crystalline substance isolated from this previously uninvestigated South American species was psilostachyin (VI).

DISCUSSION

Infraspecific variations within these species appear to be greater than differences between species. In the absence of information about minor constituents, it is therefore difficult to see how the above results can be used for chemotaxonomic purposes. The contrast between *Ambrosia arborescens*, whose two populations studied in the course of this work elaborated both mono- and dilactones, and *A. psilostachya* which embraces distinct mono- and dilactone-producing races[2] seems of interest. The single *A. deltoidea* population studied earlier[9] also produces lactones of both types. Since we could not ascertain that our collection of *A. cumanensis* represented a single population, the significance of the observation that both ambrosin II and psilostachyin VI were isolable from it cannot be assessed at this time.

EXPERIMENTAL

M.p.s were determined in capillaries and are uncorrected; NMR spectra were determined using a Varian A-60 spectrometer with tetramethylsilane as internal standard; i.r. spectra using a Perkin Elmer model 257 spectrophotometer; u.v. spectra using a Cary model 14 recording spectrophotometer; ord curves using a Jasco model ORD-5 spectropolarimeter. Light petroleum had b.p. 30–60°, alumina was Alcoa F-20 grade, silicic acid was Mallinckrodt 100 mesh. TLC was carried out on plates coated with silica gel G (Brinkmann). Plant material used for extractions was collected during the flowering season, dried in air, ground and extracted with $CHCl_3$ in the usual fashion.[12] The crude gum obtained after the usual work-up was taken up in benzene and chromatographed over silicic acid. Fractions were monitored by TLC.

Ambrosia ambrosioides (*Cav.*) *Payne*

(A) Above-ground parts, mostly leaves, wt. 6·3 kg, collected by R. J. Barr on 3 September 1964 in Bear Canyon and Sabino Canyon, Pima County, Arizona (Barr No. 64-515, on deposit in Florida State University Herbarium), gave 109 g of crude gum which was chromatographed over 1 kg of silicic acid in 2-l. fractions. Fractions 1–30 (benzene), 31–45 (benzene–$CHCl_3$, 1:1), 46–72 ($CHCl_3$) gave gums only. Fractions 73–75 ($CHCl_3$) and 76–79 ($CHCl_3$–methanol, 99:1), after recrystallization from methanol, yielded 0·145 g of hispidulin, m.p. 291–292°, m.m.p. with authentic material undepressed, i.r., NMR superimposable. The more polar eluates gave gums which could not be induced to crystallize.

(B) Above-ground parts, wt. 3·4 kg, collected by Mrs. Elinor Lehto on 19 April 1965 in a river bed, Cave Creek Road at New River, Maricopa County, Arizona (Lehto No. 4912 on deposit in Arizona State University

---

[9] H. B. Kagan, H. E. Miller, W. Renold, M. V. Lakshmikantham, L. R. Tether, W. Herz and T. J. Mabry, *J. Org. Chem.* **31**, 1629 (1966).

[10] P. Joseph-Nathan and J. Romo, *Tetrahedron* **22**, 1723 (1966).

[11] J. Romo, P. Joseph-Nathan, A. Romo de Vivar and C. Alvarez, *Tetrahedron* **23**, 529 (1967).

[12] W. Herz and G. Högenauer, *J. Org. Chem.* **27**, 905 (1962).

Herbarium), gave 64 g of gum which was chromatographed as before. The only crystalline material, isolated from fractions 78–83 ($CHCl_3$–methanol, 99:1) was 0·315 g of hispidulin.

Ambrosia arborescens *Mill.*

(A) Above-ground parts, wt. 6·7 kg, collected in July 1967 at San Mateo, Peru, at 3000 m altitude by S. Gibaja and R. Ferreyra (voucher on deposit in the Herbarium of the Museo de Historia Natural "Javier Prado" Lima, Peru), gave 147 g of crude gum which was chromatographed over 1 kg of silicic acid in 2-l. fractions. Fractions 1–12 (benzene) gave yellow oils and gums. Fractions 13–25 (benzene) and 26–32 (benzene–$CHCl_3$, 1:1) gave crystalline material mixed with gum. Trituration with ether and boiling with light petroleum furnished relatively pure solid which gave, on recrystallization from acetone–light petroleum, 3·08 g of damsin, m.p. 105–108°, identical with authentic material in all respects. Fractions 33–40 (benzene–$CHCl_3$, 1:1) gave, after recrystallization from diisopropyl ether–CH_2Cl_2, 11·95 g of psilostachyin, m.p. 205°. Fraction 41 ($CHCl_3$) gave crystalline material which was a mixture of three compounds (TLC). Rechromatography over 200 g of silica gel collecting 10 ml fractions gave, in the eluates from fractions 36–57 (ether), 0·42 g of psilostachyin. Fractions 68–101 (ether) gave 0·03 g of a new substance isomeric with dihydropsilostachyin presumably 11-epidihydropsilostachyin, mixed m.p. with authentic dihydropsilostachyin* of m.p. 222–223° depressed, MW (mass spectrum) 280, i.r. bands ($CHCl_3$) at 3590 (OH) and 1770 cm^{-1} (two γ-lactones), NMR signals at 4·56 (H-8), 1·26 (C-5 methyl), 1·25d and 1·10d (7, C-10 and C-11 methyls). Ether–methanol (9:1) eluted 0·23 g of pure psilostachyin C.

Fractions 42–44 ($CHCl_3$) of the large chromatogram gave crystalline material. Recrystallization afforded 5·48 g of psilostachyin C, m.p. 225–228°. Fractions 45–54 ($CHCl_3$), after recrystallization from acetone–petroleum ether, yielded 5·80 g of coronopilin, m.p. 176–178°, identical in all respects with authentic material. Subsequent fractions gave only gums.

(B) Above-ground parts, collected by S. Gibaja in the locality of Marcacocha (Ollantaytambo, Cuzco, Peru) at about 3000 m altitude in late August 1967 (voucher on deposit in the Herbarium of the Museo de Historia Natural "Javier Prado", Lima, Peru), wt 6 kg, gave 169 g of crude gum which was chromatographed over 1000 kg of silicic acid, the eluate being collected in 2-l. fractions. Fractions 1–4 (benzene) gave a yellow oil, fractions 5–25 (benzene) and 26–33 (benzene–$CHCl_3$ 1:1) gave a mixture of crystalline material and gum. Trituration with ether and recrystallization of the solid residue afforded 18·86 g of damsin, m.p. 108–109°. Fractions 34–35 (benzene–CH_3Cl_3, 1:1) gave 4·64 g of psilostachyin, m.p. 215°. Fractions 36–37 (benzene–$CHCl_3$, 1:1) gave 1·15 g of a 1:1 mixture of psilostachyin and psilostachyin C (TLC), fractions 38–40 (benzene–chloroform 1:1) and 41 ($CHCl_3$) gave 1·98 g of psilostachyin C, fractions 42–43 ($CHCl_3$) gave solid which was triturated with acetone. The insoluble material on recrystallization afforded 0·23 g of psilostachyin C, the acetone extract 0·37 g of coronopilin. Fractions 44–59 ($CHCl_3$) furnished 17·85 g of coronopilin. The later fractions afforded only gums.

Ambrosia chenopodiifolia (*Benth.*) *Payne*

Above-ground parts, wt. 2·2 kg, collected by Mr. R. M. Beauchamp on 9 March 1965 one-half mile above the international boundary at San Ysidro, California, gave 15 g of gum which was chromatographed over 1 kg of silicic acid in 2-l. fractions. Fractions 1–24 (benzene) gave gums, fractions 25 (benzene) and 26–33 (benzene–$CHCl_3$) gave semisolid material, wt. 0·55 g, consisting of two lactones (NMR spectrum) which could not be separated by preparative TLC and were not identified. Fractions 34–40 (benzene–$CHCl_3$ 1:1) gave gums. Fractions 41–42 ($CHCl_3$) gave 0·75 g of recrystallized damsin, m.p. 107–108°, identical with authentic material in all respects. The more polar fractions gave gummy mixtures of several constituents, which could not be separated satisfactorily.

Ambrosia confertiflora (*DC*) *Rydb.*

Above-ground parts, collected by R. J. Barr on 18 October 1964 on the Sabino Canyon Road northeast of Tucson, Pima County, Arizona (Barr No. 64-568, on deposit in Florida State University Herbarium), gave 35 g of gum which was chromatographed over 0·9 kg of silicic acid in 100-ml fractions, the eluates being controlled by TLC. Rechromatography of the gummy benzene, benzene–$CHCl_3$, $CHCl_3$ and $CHCl_3$–methanol (99:1) eluates furnished no solid, The $CHCl_3$–methanol (49:1) eluates were rechromatographed and gave 1·2 g of psilostachyin, m.p. 213–215°, identified by comparison with authentic material. The $CHCl_3$–methanol (19:1) eluates were rechromatographed and gave 0·2 g of psilostachyin C, m.p. 218–222°, identified by comparison with authentic material.

Ambrosia cumanensis *HBK*

Above-ground parts, wt. 0·8 kg, collected by Mr. Umberto Jimenez in the vicinity of Bogota, Colombia, in July 1964 gave 9 g of gum which was chromatographed over 200 g of silicic acid in 250-ml fractions. Fractions 1–20 (benzene) and 21–32 (benzene–$CHCl_3$) gave gums. Fractions 34–36 (benzene–$CHCl_3$, 1:1) gave 0·235 of

---

* We wish to thank Professor T. J. Mabry for a specimen of this substance.

recrystallized damsin, m.p. 108–111°, identical in all respects with authentic material. Fractions 37–41 ($CHCl_3$) gave 0·161 g of recrystallized ambrosin, m.p. 136–138°, fractions 42–43 ($CHCl_3$) gave gums. Fractions 44–50 ($CHCl_3$) gave 0·235 g of psilostachyin C, m.p. 218–223°. Fractions 51–53 ($CHCl_3$) gave gums, fraction 54 gave a minute quantity of non-identified solid, m.p. 184–187° (dec.). Subsequent fractions gave gums which could not be resolved satisfactorily.

Ambrosia peruviana *Willd.*

Above-ground parts, wt. 28·5 kg, collected by Mr. B. Cancel Collazo near Mayaguez, Puerto Rico, in 1965, yielded 145 g of gum which was dissolved in benzene–$CHCl_3$ (2:1) and chromatographed over 1 kg of silicic acid. Fractions 1–3 (benzene–$CHCl_3$, 2:1, 1 l. each) gave gums, fraction 4–15 (benzene–$CHCl_3$, 2:1, 1 l. each) gave 8·8 g of recrystallized tetrahydroambrosin, m.p. 127–128°, $[\alpha]_D + 86{\cdot}6°$ (95% ethanol, 0·0113 g/ml), $[\alpha]_b + 82{\cdot}7°$ ($CHCl_3$, 0·0109 g/ml), identical with authentic material in all respects. Rechromatography of the mother liquors furnished an additional 6·75 g of tetrahydroambrosin. Fractions 16–18 (benzene–$CHCl_3$, 1:1 1 l. each), 19–21 (benzene–$CHCl_3$, 1:2, 1 l. each), 22–25 (2 l. each) and 26 ($CHCl_3$, 2 l.) gave gums. Fractions 27–29 ($CHCl_3$) gave 2·97 g of recrystallized psilostachyin C after rechromatography, m.p. 225–228°, identical in all respects with authentic material, fractions 30–33 ($CHCl_3$) gave gums, and fraction 34–38 ($CHCl_3$–methanol, 49:1) gave 45 mg of hispidulin after rechromatography. Subsequent fractions gave gummy mixtures which could not be resolved satisfactorily.

Ambrosia pumila (*Nutt.*) *Gray*

Above-ground parts, wt. 1·2 kg, collected by Mr. R. M. Beauchamp in April 1965 at Balboa Park, San Diego, California, gave 42 g of gum which was chromatographed over 0·6 kg of silicic acid in 1 l. fractions. Fractions 1–25 (benzene) and 26–36 (benzene–$CHCl_3$, 1:1) gave gums, fractions 37 (benzene–$CHCl_3$, 1:1) gave 0·67 g of a semisolid mixture. Preparative TLC gave 0·2 g of amorphous material which melted over the range 120–158°. The NMR spectrum indicated that this lactone or mixture of lactones was structurally similar to psilostachyin B. Fraction 38–40 (benzene–$CHCl_3$, 1:1) and 41–44 ($CHCl_3$) gave gums. Fractions 45–48 ($CHCl_3$) gave 1·83 g of a 1:1 mixture of psilostachyin and psilostachyin C. The later fractions gave gummy mixtures which could not be resolved satisfactorily.

Ambrosia tenuifolia *Spreng*

Above-ground material collected by Mr. P. R. Legname and A. R. Cuezza along the road from Las Talas to Bella Vista, Department of Famailla, Province of Tucuman, Argentina (voucher No. 5679 C on deposit in the Herbarium of Instituto Miguel Lillo, Tucuman, Argentina), gave 29 g of gum which was chromatographed over 1 kg of silicic acid in 2-l. fractions. Fractions 1–25 (benzene), 26–40 (benzene–chloroform, 1:1) 41–42 ($CHCl_3$) gave gums. Fractions 43–53 ($CHCl_3$) yielded 4·34 g of recrystallized psilostachyin, m.p. 213–215°, m.m.p. undepressed, i.r., NMR spectra superimposable. The more polar fractions were gummy mixtures which would not be resolved satisfactorily.

Acknowledgement—This work was supported in part by a grant from the United States Public Health Service (GM-5814).