THE CRYSTAL AND MOLECULAR STRUCTURE OF

BROMOAMBROSIN*

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The sesquiterpene lactones ambrosin (I), originally

isolated from Ambrosia maritima L. (1), and parthenin (II),

the main constituents of Parthenium hysterophorus L. (2), were

the first substances in which the existence of the no·· widely

distributed pseudoguaianolide carbon skeleton was recognized (3).
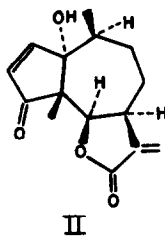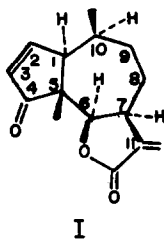
I   II

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Our proposal for the absolute configurations inherent in I
and II was based on degradation of parthenin to $S(+)$-α-methyl-
glutaric acid which fixed the absolute configuration of C_{10},
chemical transformations and optical data and was supported by
the mechanism invoked to explain the acid-catalyzed transforma-
tion of coronopilin (2,3-dihydroparthenin) to coronopilic acid
(4). We herein report the result of an X-ray analysis of
3-bromoambrosin (1) which confirms the proposed configurations
and simultaneously establishes those of many compounds which have
been related to ambrosin.

Single crystals of bromoambrosin were obtained by recrystal-
lization from ethanol. A selected crystal was prepared for
X-ray studies by cutting and grinding into an ellipsoid with
major and minor axes of 0.27 mm and of 0.21 mm. Preliminary
photographic X-ray data showed that the crystal was monoclinic
with unit cell dimensions of a = 8.697 $\pm$ 0.060 $\overset{o}{A}$, b = 15.550
$\pm$ 0.110 $\overset{o}{A}$, c = 12.458 $\pm$ 0.090 $\overset{o}{A}$ and β = 122.45° $\pm$ 0.5°. The
symmetry of the Patterson map indicated that the space group
was $P2_1$. This assignment was confirmed by the observation of
(0,k,0) systematic extinctions (8). The crystal density was
measured by the buoyancy method using a solution of zinc
chloride in water. The density was found to be 1.511 $\pm$ 0.002
gm/cc which is consistent with 4 molecules per unit cell. These
are arranged so that two molecules form the asymmetric unit in
the unit cell.

The X-ray diffraction data used for the structure analysis
was collected on an X-ray diffractometer at Harvey Mudd

College.* Of the 3000 reflections in the unique segment of the
sphere of reflection, 1638 were strong enough to be observed and
measured. X-ray structure calculations were carried out on an
IBM 709 computer using the University of Washington X-ray 63
system programs. The bromine atom positions for the two mole-
cules in the asymmetric unit were obtained from the three dimen-
sional Patterson map. These were then used to calculate an
approximate set of phases and the first three dimensional
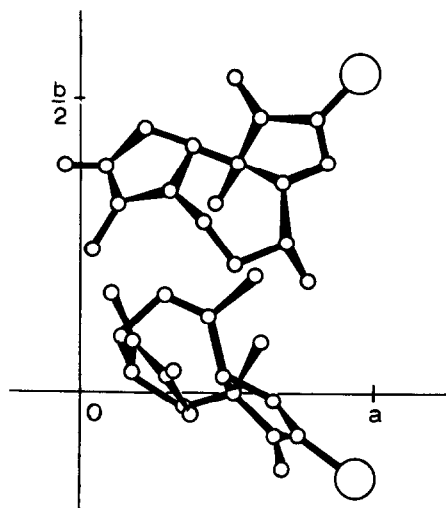electron density map. The positions of ten other atoms and

FIGURE I

PROJECTION OF ASYMMETRIC UNIT OF BROMOAMBROSIN

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*X-ray data was collected by R. W. Witters.

improved positions of the bromines were obtained from this map.
The error of the Fc's using the two bromine atom positions was
R = 0.44.   Structure refinement proceeded smoothly.   The seventh
Fourier map gave all atom positions in the asymmetric unit and
allowed identification of the oxygen atoms.   At this point R was
0.26.   Four cycles of diagonal least squares refinement reduced
the R value to 0.132.   The projection of the asymmetric unit*
on a plane perpendicular to the C axis of the crystal is shown
in Figure I.   One molecule of **Bromoambrosin** (III) is displaced
behind the other approximately one fourth of a unit cell
along the C axis.

Since the relative configuration of ambrosin is the same as
that of parthenin at every asymmetric center including C_1 and
C_{10} (3,5) and since the absolute configuration of parthenin
is C_{10}-methyl β (3), the representation of Figure I depicts the
absolute configuration as well.   The absolute configuration of
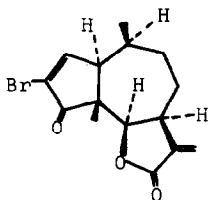
III

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*A table of atomic positions and temperature factors is not in-
cluded.   This information will be supplied by the authors on
request.

such compounds as the psilostachyins (6) and others which have
been correlated with ambrosin or parthenin, follows naturally.

It is noteworthy that the absolute configuration at C_{10}
of all pseudoguaianolides isolated from <u>Ambrosia</u> and related
species, in which the lactone ring is closed to C_6, differs
from the absolute stereochemistry at C_{10} of the second known
class of pseudoguaianolides from <u>Helenium</u> and related species
(7) in which the lactone ring is closed to C_8. The biogenetic
significance of this is not clear.

<div align="center">Acknowledgment</div>

<div align="center">References</div>

1. H. Abu-Shady and T.D. Soine, <u>J. Am. Pharm. Assoc.</u>, <u>42</u>,
    387 (1953); <u>43</u>, 365 (1954).

2. H.V. Arny, <u>J. Pharm.</u>, 121 (1890); 169 (1897).

3. W. Herz, H. Watanabe, M. Miyazaki and Y. Kishida, <u>J. Am.
    Chem. Soc.</u>, <u>84</u>, 2601 (1962).

4. T.A. Geissman and R.J. Turley, <u>J. Org. Chem.</u>, <u>29</u>, 2553 (1964).

5. A. Romo de Vivar, L. Rodriguez-Hahn, J. Romo, M.V.
    Lakshmikantham, R.N. Mirrington, J. Kagan and W. Herz,
    <u>Tetrahedron</u>, <u>22</u>, -- (1966).

6. T.J. Mabry, H.E. Miller, H.B. Kagan and W. Renold,
    <u>Tetrahedron</u>, <u>22</u>, 1139 (1966); H.B. Kagan, H.E. Miller,

W. Renold, M.V. Lakshmikantham, L.R. Tether, W. Herz and
T.J. Mabry, J. Org. Chem., 31, -- (1966).

7. D. Rogers and Mazhar-ul Haque, Proc. Chem. Soc., 92 (1963);
    M.T. Emerson, C.N. Caughlan and W. Herz, Tetrahedron Letters
    621 (1964); W. Herz and M.V. Lakshmikantham, Tetrahedron,
    21, 1711 (1965).

8. "International Tables for X-Ray Crystallography", International
    Union of Crystallography, the Kynoch Press, Birmingham,
    England, 1952, Vol. I.