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THE STRUCTURE OF CHAMISSONIN

M. F. L'Homme and T. A. Geissman
Department of Chemistry, University of California,
Los Angeles, 90024[1,2]

H. Yoshioka, T. H. Porter, W. Renold and T. J. Mabry
The Cell Research Institute and Department of Botany
University of Texas at Austin, 78712

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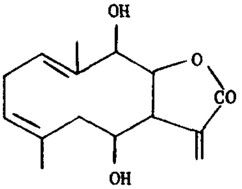
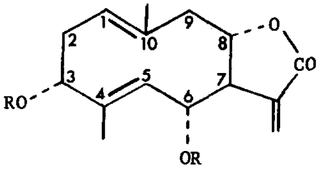
Chamissonin, the principal sesquiterpene lactone of Ambrosia chamissonis Less. ssp. bipinnatsecta[3] and of some populations of A. acanthicarpa (Hook.) Cov.,[4] was first formulated as I by interpretation of its chemical behavior and spectral characteristics.[3] During the course of studies on related lactones since that time, it was found that certain behavior that chamissonin would have been expected to exhibit was not in fact observed. Furthermore, n.m.r. spin-decoupling experiments on diacetylchamissonin (now formulated as IIb) indicated that chamissonin could not be represented by structure I: irradiation of the H-7 signal in the diacetate altered the complex signal for the C-8 proton into another complex signal instead of a doublet as would have been expected if an oxygen function were located at C-9 as in structure I. Therefore, additional studies were undertaken to establish the structure of chamissonin.

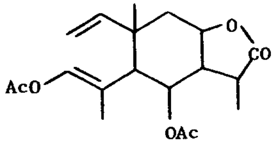


I

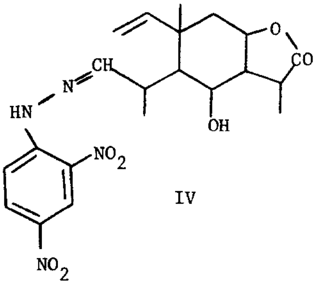


IIa R = H

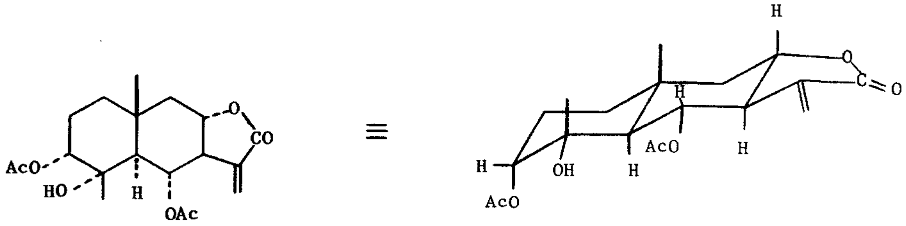
IIb R = Ac



III



IV



V

Chamissonin diacetate can be hydrogenated to yield di-, tetra-, and hexa-hydro derivatives, thus further establishing its germacranolide structure.[3] Dihydrodiacetylchamissonin, m.p. 142°, yielded after pyrolysis (210° for 6 minutes) a Cope product which exhibited an n.m.r. spectrum in accord with structure III[5] (without stereochemistry): the C-3 enolic proton signal (δ 6.94) showed only allylic coupling, the C-1 olefinic signal (δ 5.78) was coupled to the two terminal C-2 olefinic protons (J = 18 and 10) and a singlet for the C-10 tertiary methyl group was observed at δ 1.20. The Cope product was characterized as a desacetyl-2,4-DNP derivative, m.p. 214°.

The following data confirms the skeletal features of chamissonin diacetate and, in addition, establishes the stereochemistry as shown in IIb. When chamissonin diacetate, $C_{19}H_{24}O_6$, is treated with perchloric acid solution there is formed a compound (V), m.p. 234-5°, $C_{19}H_{26}O_7$, which (by n.m.r.) is still a diacetoxylactone. This compound is clearly the product of an acid-catalyzed cyclization of IIb and contains the elements of water in addition to the $C_{19}H_{24}O_6$ of chamissonin diacetate. The IR spectrum of V showed the presence of a hydroxyl group, and on t.l.c. compound V shows an R_f value much below that of IIb and about the same as those of coronopilin and farinosin, both compounds containing one tertiary hydroxyl group.

The 100 mc n.m.r. spectrum of V establishes its structure and stereochemistry as shown.

The two methyl groups (C-4, C-10) appear as sharp singlets at δ 1.46 and 1.21, and the protons of the exocyclic $=CH_2$ group as the characteristic doublets (1H, J = 2 cps) at δ 5.50 and 6.20. The most significant features of the spectrum are the signals for the protons at positions, 3, 6, 7 and 8, all of which are clearly discernable; these (all 1H) are, respectively, δ 4.81 (narrow triplet, J about 2 cps); 5.71 (triplet, J = 12 cps); 2.97 (triplet, J = 12 cps, with small additional splitting due to coupling to $=CH_2$); and 4.18 (triplet of doublets, J = 12, 2 cps). These data show that the protons at C-8, C-7 and C-6 are trans-diaxially disposed, and that the proton at C-3 is equatorial (β). Moreover, the circular dichroism curve of V shows the positive Cotton effect which has been shown[6] to be characteristic of the trans-fused C-7/C-8 lactones in this series. The configuration of the methyl group at C-4 and the stereochemistry of the ring junction were assumed to be as formulated in V, principally, because the acid-catalyzed ring closure that leads from IIb to V would be expected to proceed with the steric results expressed in V. This assignment has been confirmed by study of the nuclear Overhauser effects associated with the axial methyl group at C-4 and the axial proton at C-6.[7]

The formation and structures of III and V clearly indicate that chamissonin can be formulated as IIa.

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References

1. Contribution No. 2395 from the Department of Chemistry, U.C.L.A.
2. All compounds gave satisfactory elemental analytical values, and mass spectral data were in agreement with molecular weights and expected principal fragments.
3. T. A. Geissman, R. J. Turley and S. Murayama, J. Org. Chem., 31, 2269 (1966).
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5. Similar compounds have been investigated by N. H. Fischer and T. J. Mabry, Chemical Comm., 1235 (1967) and N. H. Fischer, T. J. Mabry and H. B. Kagan, Tetrahedron, 24, 4091 (1968).
6. T. G. Waddell, W. Stöcklin, and T. A. Geissman, Tetrahedron Letters, 1313 (1969).
7. We are indebted to Professor F.A.L. Anet for examining the NOE of III.