Phytochemistry, 1973, Vol. 12, pp. 853 to 855. Pergamon Press. Printed in England.

ARBUSCULIN-*D* FROM *ARTEMISIA ARBUSCULA* SSP. *ARBUSCULA**

M. A. Irwin and T. A. Geissman

Department of Chemistry, University of California, Los Angeles, CA 90024, U.S.A.

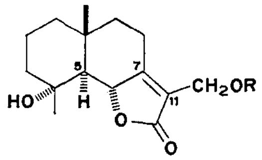
(*Received* 10 *October* 1972. *Accepted* 21 *October* 1972)

Key Word Index—*Artemisia arbuscula*; Compositae; sesquiterpene lactone; eudesmanolide; structure; stereochemistry.

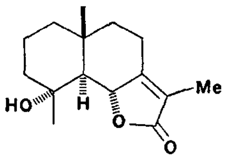
Abstract—Arbusculin-*D* (I), a new eudesmanolide, has been isolated from *Artemisia arbuscula* Nutt. ssp. *arbuscula* and is present also in *A. arbuscula* Nutt. ssp. *thermopola* Beetle. It represents a structural variant in the lactone grouping.

The isolation of arbusculin-*A*, -*B* and -*E* from *Artemisia arbuscula* ssp *arbuscula* has been described.[1] Arbusculin-*D* (I), alluded to in that paper as a non-crystalline fraction from the chromatographic separation, has now been further purified and crystallized. It has m.p. 170–172°, and the composition $C_{15}H_{22}O_4$. Its UV spectrum showed a maximum at 218 nm (ϵ 13 400), indicating that it did not contain the common structural feature of its cogeners, the α-methylene-γ-lactone grouping.[1] Its IR spectrum contained peaks at 3545, 3420, 1745 and 1675 cm^{-1}. The UV and IR spectra show the characteristic absorption of an α,β-unsaturated-γ-lactone containing an endocyclic double bond. This was confirmed by the evidence described in the following.

The MS showed the molecular ion (m/e 266) at low voltage only; the 70 eV spectrum exhibited principal ions at M−15, M−18, M−15–18, M−18–18 and M−15–18–18. These data, and the elemental analysis, establish that arbusculin-*D* contains two hydroxyl groups.



(I) R = H
(II) R = OAc



(III)

The NMR spectrum (Table 1) of arbusculin-*D* is readily interpretable in terms of structure I. The C-10 and C-4 methyl groups were seen as 3-proton singlets at δ 1·07 and 1·40, respectively. The C-11 $-CH_2O-$ grouping, equally coupled (0·9 Hz) with H-6 and H-8β, gave a narrow 2-proton triplet at δ 4·39. This signal was shifted downfield to δ 4·81 on acetylation to II. The methine proton, H-6, of the lactone grouping, coupled with H-5, gave a doublet (12 Hz) at δ 4·98, slightly broadened by homoallytic coupling. The C-5 proton,

---

* Contribution No. 2948 from the Department of Chemistry, U.C.L.A.

[1] Irwin, M. A. and Geissman, T. A. (1969) *Phytochem.* **8,** 2411. Arbusculin-*C* has been described: Irwin, M. A. and Geissman, T. A. (1971) *Phytochem.* **10,** 637.

spin-isolated from all but H-6, gave a sharp doublet (12 Hz) at δ 1·48. Irradiation of either H-5 or H-6 collapsed the other to a singlet. The large H-5/H-6 coupling is consistent with a *trans*-diaxial relationship between these protons.

TABLE 1. NMR SPECTRA OF ARBUSCULIN-*D* AND DERIVATIVES

Compound	4-Me	5-H	6-H	10-Me	$-CH_2O^-$
I	1·40	1·48 (12·1)	4·98 (11·7)	1·07	4·39 (0·9/0·9)
II*	1·41	1·47 (11·8)	5·00 (11·9)	1·19	4·81 (br)
III	1·41		4·93 (12)	1·07	1·82 (1·6/1·6)†

* Acetyl Me, 2·07.
† 11-Me. Values are δ (*J* Hz), measured in $CDCl_3$.

The 100 MHz spectrum revealed the 2 protons at C-8. The H-8α proton, coupled with H-8β (15 Hz), H-9α (5 Hz) and H-9β (2 Hz), gave a multiplet at δ 2·93. The H-8β proton, coupled with H-8α (15 Hz), H-9α (10 Hz) and H-9β (6 Hz), gave a multiplet at δ 2·50. The H-9β signal, detected by irradiation of the C-8 protons, was construed as a multiplet at δ 1·68 with couplings of 13, 6 and 2 Hz. The hydroxyl protons gave a signal at δ 3·1, shifted slightly and sharpened by the addition of trifluoroacetic acid. These observations establish the stereochemistry of arbusculin-*D* (I), if the α-orientation of the C-4 hydroxyl group be assumed by analogy with the known arbusculin-*A*.

Catalytic hydrogenation of arbusculin-*D* or its acetate yielded deoxyarbusculin-*D* (III) by hydrogenolysis of the allylic hydroxyl (or acetoxyl) group at C-13. The 7,11-double bond was resistant to hydrogenation. The NMR spectrum of III shows the newly formed methyl group as a triplet (1·6 and 1·6 Hz) at δ 1·82 and the C-10 and C-4 methyl groups as singlets at δ 1·07 and 1·41, respectively. The 2 protons of C-8 were seen as multiplets at δ 2·2 and 2·7, and the C-6 proton as a broadened doublet (12 Hz) at δ 4·93. It is clear from the above data that arbusculin-*D* can be represented by I, and the deoxy compound by III.

It is seen that arbusculin-*D* differs from arbusculin-*A* only in the nature of the lactone grouping, which in the latter is the familiar α-methylene-γ-lactone. The lactone of the former represents an additional step of oxidation.

EXPERIMENTAL

Spectra were measured on: NMR Varian A-60D and HA-100; MS (70 eV, direct insertion), AEI-MS9; IR ($CHCl_3$), Perkin⁻Elmer 237; UV (abs. EtOH), Cary-14.

Isolation of arbusculin-D (I). The extraction of the *A. arbuscula* ssp *arbuscula* and isolation of the lactone mixture has been described.[1] Arbusculin-*D* (I) was found in fractions following those containing arbusculin-*B*, -*C* and -*A*, was and obtained as a yellow oil (2 g from 1·3 kg of plant). Rechromatography yielded fractions from which arbusculin-*D* was at length obtained as colorless needles, from EtOAc, m.p. 170–172°. The MS showed a weak molecular ion at *m/e* 266 (low eV), and principal fragments of *m/e* (rel. int.) 251 (11), 248 (4·4), 230 (7·9), 205 (5·2), 202 (6·2), 190 (14), 163 (9·2), 117 (7·1), 91 (10), 79 (10), 57 (12), 55 (10), 53 (10), 43 (100), 41 (49) and 39 (30). The IR, UV and NMR spectra have been described above (*Anal.* Calc. for $C_{15}H_{22}O_4$: C, 67·64; H, 8·33. Found: C, 67·77; H. 8·38%).

Arbusculin-D *acetate* (II). The compound, which was prepared with Ac_2O–pyridine and which could not be crystallized, was purified by chromatography and gave a single spot on TLC. Its IR spectrum had peaks at 3555, 3440, 1755 and 1740 (shoulder) cm^{-1}. Its MS showed principal ions at *m/e* (rel. int.) 308 (0·5, M^+), 293 (4·9), 248 (18), 233 (8·2), 230 (17), 215 (11), 190 (20), 163 (36) and 43 (100). Its NMR spectrum has been described above.

Deoxyarbusculin-D (III). A solution of arbusculin-*D* in EtOH was hydrogenated in the presence of 10% Pd/C. After hydrogen uptake caesed, the solution showed only one spot on TLC. The solvent was removed and the residue material chromatographed over silica gel. Fractions containing III were combined and evaporated, yielding deoxyarbusculin-*D* as a pale yellow oil. Its IR spectrum had peaks at 3550, 3400, 1745 and 1675 cm^{-1}. Its MS showed principal ions at *m/e* (rel. int.) 250 (11, M$^+$), 235 (38), 232 (46), 217 (14), 165 (28), 147 (24), 119 (22), 91 (26), 55 (27), 53 (31), 43 (100) and 41 (53). The NMR spectrum has been described above.

Acknowledgements—This study was supported by a research grant GM-14240 from the U.S. Public Health Service. We are grateful to Professors A. A. Beetle and R. O. Asplund, University of Wyoming, and G. H. Ward, Knox College, for providing the plant material and for authenticating its identity. Dr. G. Chmurny assisted in the NMR measurements, and analyses are by Miss Heather King, U.C.L.A.