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RIDENTIN-*B*: AN EUDESMANOLIDE FROM *ARTEMISIA TRIPARTITA* SSP. *RUPICOLA**

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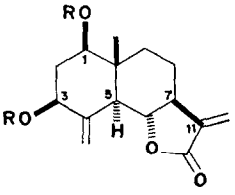
Key Word Index—*Artemisia tripartita*; Compositae; sesquiterpene lactone; eudesmanolide; germacranolide; stereochemistry; conformation; biosynthesis.

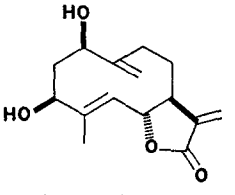
Abstract—Ridentin-*B* (I), a new eudesmanolide, has been isolated from *Artemisia tripartita* ssp. *rupicola*. It is biosynthetically closely allied with ridentin (IV), a germacronolide. The stereochemistry of ridentin is discussed.

INTRODUCTION

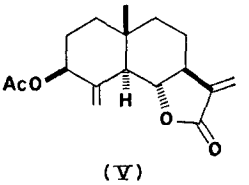
A CRYSTALLINE mixture of ridentin (IV)[1] and ridentin-*B* (I), which was detected as a single spot on TLC, was isolated from *Artemisia tripartita* Rydb. ssp. *rupicola* Beetle. The mixture, consisting principally of ridentin-*B*, could not be purified by recrystallization. It was trimethylsilylated, and the bisTMS ether (II) of ridentin-*B* was isolated chromatographically. Hydrolysis of the ether yielded a small amount of ridentin-*B* (I).



(I) R = H Ridentin-*B*
(II) R = TMS
(III) R = Ac



(IV) Ridentin



(V)

Ridentin (IV) has been isolated in this laboratory from the following species, all of which are members of the section *Tridentatae* Rydb.:[2] *A. tripartita* Rydb. ssp. *rupicola* Beetle, *A. tridentata* Nutt. ssp. *tridentata*, *A. tridentata* Nutt. ssp. *tridentata* f. *parishii* (Gray) Beetle, *A. tridentata* Nutt. ssp. *vaseyana* (Rydb.) Beetle, and *A. cana* Pursh ssp. *cana*.

RESULTS

Ridentin-*B* (I), $C_{15}H_{20}O_4$, had m.p. 188–190° and exhibited IR absorption (Nujol) for hydroxyl groups (3320 cm^{-1}), a γ-lactone (1765 cm^{-1}), and carbon–carbon unsaturation (1660 cm^{-1}). Prominent MS ions of *m/e* 264 (M^+), M−15, M−15–18, and M−18–18 establish its composition and the presence of two hydroxyl groups.

* Contribution No. 3069 from the Department of Chemistry, U.C.L.A.

[1] IRWIN, M. A., LEE, K. H., SIMPSON, R. F. and GEISSMAN, T. A. (1969) *Phytochem.* **8**, 2009.
[2] BEETLE, A. A. (1960) *Univ. Wyom. Agric. Exptl. Sta.* No. 368.

The structure of ridentin-*B* is conveniently considered in terms of the NMR spectrum ($CDCl_3$) of its bisTMS ether (II). The C-10 methyl group gave a singlet at δ 0·76. A pair of doublets (3 Hz), characteristic of the C-11 methylene group, appeared at δ 5·42 and 6·06. The signal of H-7 at δ 2·50, though very broad, showed triplet character due to large (10–11 Hz) interactions with H-6 and H-8. The C-6 proton, coupled equally (11 Hz) with H-5 and H-7, produced a triplet at δ 4·08. The large couplings among H-5, H-6 and H-7 are indicative of their all-*trans*-axial arrangement. The methylene group at C-4 produced signals at δ 4·98 and 5·33, broadened by small geminal and allylic couplings. The signals of protons geminal to trimethylsiloxy groups, H-1 and H-3, were assigned by their downfield shifts on passing to the diacetate (III). The signal of H-3 at δ 4·0 was obscured by that of H-6. Comparison of 60 and 100 MHz spectra showed that H-3, coupled with H-2β (11 Hz) and H-2α (5 Hz), was a quartet, broadened by allylic interaction with the C-4 methylene group. The C-1 proton, coupled with H-2β (11 Hz) and H-2α (5 Hz), gave a quartet at δ 3·02. A β-disposed hydroxyl group at C-9 in ridentin-*B* would also satisfactorily account for this signal, but it is excluded on biosynthetic grounds. The stereochemistry of H-1 and H-3 is clear from the couplings of these protons with those at C-2.

It is noteworthy that the signals of the C-4 methylene group in ridentin-*B*, as measured in pyridine-d_5, are located at δ 5·22 and 5·84. The exceptionally low field of the proton at δ 5·84 is due to the proximity of the C-3 hydroxyl group, which lies in the plane of the methylene group. The deshielding by the hydroxyl group is enhanced by the solvent effect of pyridine.[3]

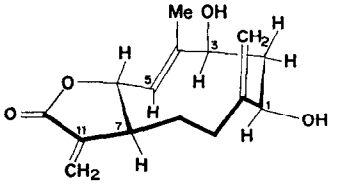
Further support for the structure of ridentin-*B* (I) was found in the good correspondence, except for the signals associated with the C-1 substituent, between the NMR spectra of ridentin-*B* diacetate (III) and the derivative (V) of novanin.[4]

The structure of ridentin was originally proposed without stereochemistry.[1] Several lines of evidence now suggest that it possesses the stereochemistry indicated in structure IV. A negative Cotton effect at 258 nm accords with a *trans*-fusion of the C-6/C-7 lactone (C-7/C-11 bond β-disposed).[5] The NMR spectrum ($CDCl_3$) of the monoTMS ether of ridentin (location of TMS group not known) can be interpreted in terms of the conformational structure VI. The C-6 proton, coupled equally (10 Hz) with H-7 and H-5, gave a triplet at δ 4·46. The C-5 proton produced a doublet (10 Hz) at δ 5·30, broadened by allylic coupling with the C-4 methyl group. The large coupling between H-5 and H-6 indicates that they are *trans*-diaxially related. The protons at C-1 and C-3 produced overlapping quartets at δ 4·03 (10 and 5 Hz) and 4·12 (10 and 4 Hz), the analysis of which was facilitated by comparison of 60 and 100 MHz spectra. The magnitudes of the couplings are in accord with a *trans*-diaxial relationship between H-2β and H-1 and with a *cis*-equatorial-axial relationship between H-2α and H-1. The proton at C-3 is similarly related to the C-2 protons. The C-10 methylene group gave slightly broadened signals at δ 4·88 and 5·20. The signal of the C-7 proton at δ 2·85, though very diffuse, showed triplet character due to large couplings (10–11 Hz) with H-6 and H-8β. The C-4 methyl group gave a doublet (1·2 Hz) at δ 1·71 and the C-11 methylene group a pair of doublets (3 Hz) at δ 5·45 and 6·18.

The chromatographic similarity of ridentin (IV) with ridentin-*B* (I) suggests that their hydroxyl groups are similarly disposed. The disposition expressed in VI closely matches

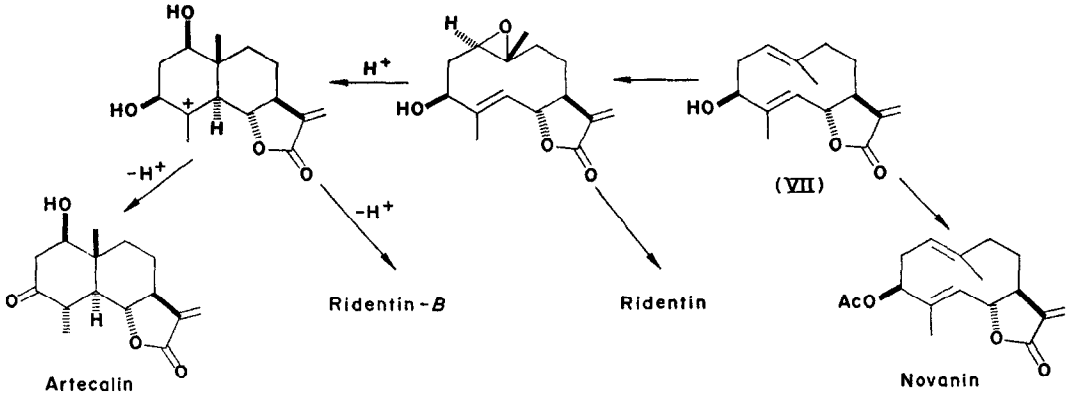
[3] DEMARCO, P. V., FARKAS, E., DODDRELL, C., MYLARI, L. and WENKERT, E. (1968). *J. Am. Chem. Soc.* **90** 5480.
[4] IRWIN, M. A., and GEISSMAN, T. A. (1973) *Phytochem.* **12**, 875.
[5] STÖCKLIN, W., WADDELL, T. G. and GEISSMAN, T. A. (1970) *Tetrahedron* **26**, 2397.

that of ridentin-*B* (I). The biosynthetic hypothesis discussed below provides additional weight for the stereochemistry in structure IV.



(VI)

Ridentin (IV), ridentin-*B* (I) and artecalin[6] were isolated from identical collections of *A. tripartita* ssp. *rupicola*, and novanin,[4] which has been isolated from the chemically closely related species *A. nova* Nels., has been detected (TLC) in *A. tripartita* ssp *rupicola*. A reasonable pathway for the biosynthesis of these compounds from a common precursor (VII) is outlined in Scheme 1. A transformation analogous with that leading from the VII to ridentin-*B* has been carried out *in vitro*.[7]



SCHEME 1. BIOSYNTHETIC PATHWAY OF *Artemisia tripartita* EUDESMANOLIDES.

EXPERIMENTAL

Spectra were measured on: NMR, Varian A-60D and HA-100; IR, Perkin–Elmer 237; MS (70 eV, direct insertion), CEC 21-491.

Ridentin-B (I). The isolation of the mixture (0·5 g, 0·01%) of ridentin-*B* (I) and ridentin (IV) from 4·9 kg of dried plant has been described.[8] The presence of both compounds was confirmed by NMR. Part of the mixture was treated with trimethylchlorosilane and pyridine. The solvent was removed *in vacuo*, and the residue was chromatographed over silica gel eluted with $CHCl_3$ to give the bis-TMS ether (II) of ridentin-*B*. It was further purified by recrystallization and was characterized by NMR. Ridentin-*B* was obtained by treatment of the ether with MeOH containing a trace of HCl and removal of the solvent under vacuum. Recrystallized from EtOAc as microcrystalline lumps, it had m.p. 188–190° (to a glass). Its IR spectrum showed peaks at 3320, 1765 and 1660 cm^{-1} ($CHCl_3$). The MS contained principal ions at *m/e* (rel. int.) 264 (53, M^+), 249 (9), 246 (16), 231 (12), 228 (6), 218 (11), 217 (12), 213 (5) and others including 41 (100). The non- crystalline acetate (III) was prepared with Ac_2O and pyridine and purified by chromatography. Its IR spectrum showed peaks at 1765, 1740 and 1655 cm^{-1} ($CHCl_3$).

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[6] GEISSMAN, T. A., GRIFFIN, T. S. and IRWIN, M. A. (1969) *Phytochem.* **8**, 1297.
[7] SUCHY, M., HEROUT, V. and ŠORM, F. (1966) *Collin Czech. Chem. Commun.* **31**, 2899.
[8] IRWIN, M. A. and GEISSMAN, T. A. (1973) *Phytochem.* **12**, 863.