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STEREOCHEMISTRY OF EVONINE, NEO-EVONINE, EUONYMINE, AND NEO-EUONYMINE, ALKALOIDS OBTAINED FROM *EUONYMUS SIEBOLDIANA* BLUME

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We have recently established the structures of four alkaloids, evonine **1**, neo-evonine **2**, euonymine **3**, and neo-euonymine **4**, obtained from *Euonymus Sieboldiana* Blume.[1] In this paper the stereochemistry of these alkaloids is presented. The configurations of two asymmetric centers in the evoninic acid moiety were already determined by Pailer and Libiseller.[2]

Stereochemistry of evonine **1** *and neo-evonine* **2**. The C-ring is necessarily attached to the B-ring by two axial bonds at C-6 and C-10 of the B-ring on steric ground. Regarding the A/B ring juncture two configurations (*cis* and *trans*) are possible, and it was proved by the intramolecular nuclear Overhauser effects (NOE) on pentadesacetylevonine acetonide diacetate (prepared by acetylation of pentadesacetylevonine acetonide[1a] with Ac_2O/pyridine) that the ring juncture is *trans*: i) irradiation of the 11-methylene group (δ 4.27) caused an increase (20%) in the signal intensity of 5-H (δ 6.35), and ii) an enhancement (8%) of the signal intensity of 5-H was detected on irradiation of 12-Me (δ 1.67). These results of NOE indicate not only the *trans* nature of the A/B ring juncture, but that these three groups (5-H, 11-CH_2, and 12-Me) are axial in each chclohexane ring which is necessarily in a chair conformation. Since the acetyl migration from C_1-OH to C_{11}-OH was observed during the $Pb(OAc)_4$ oxidation of a derivative of **1**,[1b] the C-11 methylene group and C_1-OH are in a *cis* arrangement. The coupling constant between 1-H and 2-H is in a range of 3.2 - 3.8 Hz on a variety of derivatives of **1**, indicating that these vicinal hydrogens are *cis*. The *cis* relationship between 3-H and 12-Me was deduced from the observation of the NOE between 3-H and 12-Me: on irradiation of the 12-Me signal (δ 1.67) the intensity of the 3-H signal (δ 4.79) was increased ($\sim$15%).

Formation of an acetonide (pentadesacetylevonine acetonide[1a]) between C_{11}-OH and C_8-OH revealed that the 11-methylene group and C_8-OH are *cis*. The NOE was observed between 8-H and 14-Me: when the 14-Me signal (δ 1.57) was irradiated on neo-evonine methylether[1c], an increase (30%) of the 8-H signal intensity (δ 4.91) occurred, demonstrating the configuration of 14-Me as shown in 1. The stereochemistry of evonine and neo-evonine is thus established as 1 and 2, respectively.

Stereochemistry of euonymine 3 and neo-euonymine 4. The $LiAlH_4$ reduction of 1 afforded two polyhydroxy compounds diastereoisomeric at C-7 (euonyminol[1a] and iso-euonyminol[1a]), one of which (euonyminol) was shown to be identical with the sesquiterpene part of euonymine.[1c] Since the coupling constant of 8-H was 6.0 Hz in euonyminol octaacetate[1a,1c] and 10.0 Hz in iso-euonyminol octaacetate,[1a,1c] 7-H and 8-H are cis (equatorial-axial) for the former, and trans (axial-axial) for the latter. Further, the NOE was observed between 5-H and 7-H in iso-euonyminol octaacetate (13% increase). The stereochemistry of euonymine and neo-euonymine was determined as 3 and 4.

Some aspects of the NMR spectra of evonine 1 and the derivatives. In the NMR spectra of 1 and the derivatives, characteristic signals were observed, presumably owing to the complex and rigid skeleton and the presence of many functional groups. A doublet ($J \approx 1.0$ Hz) due to 5-H appeared at δ 6.72 and the signal of 15-methylene group was observed as an AB quartet (δ 3.76 and 6.04, J = 11.7 Hz) separated by 2.3 ppm in 1: the presence of a pyridine ring in the molecule seems to be partly responsible for the phenomena ($CDCl_3$, 100 MHz).

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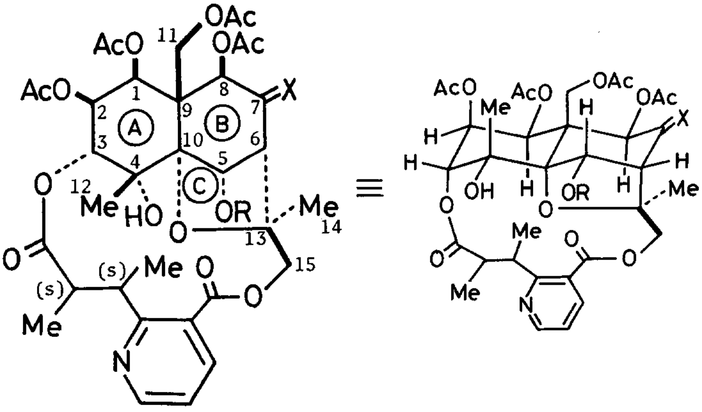

1: evonine	R=Ac,	X=O
2: neo-evonine	R=H,	X=O
3: euonymine	R=Ac,	$X=<^{OAc}_{H}$
4: neo-euonymine	R=H,	$X=<^{OAc}_{H}$

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