

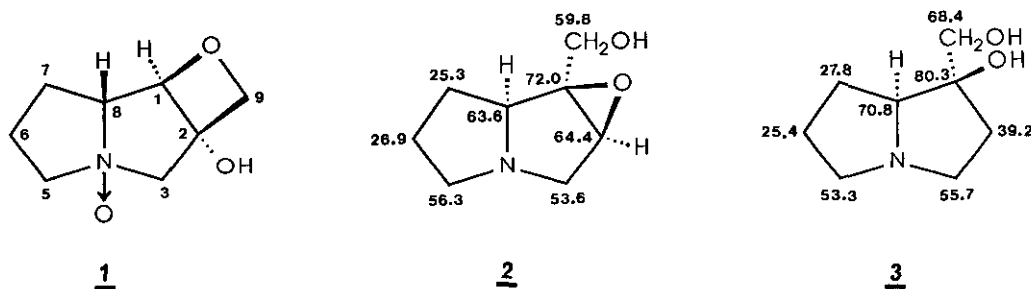
THE STRUCTURE OF SUBULACINE-N-OXIDE

Tammo Winkler* and Roland Heckendorn

CIBA-GEIGY AG, CH-4002 Basel, Switzerland

Abstract — The nmr spectra reported for subulacine-N-oxide are shown to be those of 1 β ,2 β -epoxy-1 α -hydroxymethyl-8 α -pyrrolizidine.

Subulacine-N-oxide, the major alkaloid of *Heliotropium subulatum*, was recently reported¹ in this journal to possess structure 1, a pyrrolizidine system with an anellated oxetane ring. But the chemical shifts given for the oxetane protons (3.55 and 3.77 ppm) and the geminal coupling constant (12.7 Hz) for the oxetane OCH₂ group indicate immediately, that structure 1 cannot be correct (for a summary of ¹H-nmr characteristics of oxetanes see e.g. lit.²).

Scheme

Instead, a comparison of the reported¹ ¹H-nmr data of subulacine-N-oxide with those of 1 β ,2 β -epoxy-1 α -hydroxymethyl-8 α -pyrrolizidine (2)³ (table) shows that the two spectra are identical.

Table ¹H-nmr chemical shifts of 1 β ,2 β -epoxy-1 α -hydroxymethyl-8 α -pyrrolizidine (2) in CDCl₃.

	H-2	H-3	H-5	H-6,7 (average)	H-8	H-9
authentic <u>2</u> ³	3.60	2.93; 3.09	2.6; 3.0	1.8	3.52	3.81
subulacine-N-oxide ¹	3.55	2.89; 3.03	2.54; 2.93	1.7	3.48	3.77

The small, constant shift difference of ca. 0.06 ppm is probably due to the higher temperature and concentration used in a 60 MHz instrument with an iron magnet as compared to a 400 MHz instrument with a superconducting magnet.

The carbon chemical shifts reported for subulacine-N-oxide (cf. scheme, data and signal assignments from lit.¹) are in good agreement with 2 as can be seen by a comparison with those of the related compound 3⁴. Moreover, N-oxidation would cause a downfield shift of C(3), C(5) and C(8) of 15-20 ppm⁵ as compared with the shifts of these carbons in the tertiary base^{4,5}. The absence of this downfield shift again rules out N-oxide structure 1. As N-oxidation imparts high crystallinity and water solubility to pyrrolizidine alkaloids⁵, an N-oxide group is also improbable for chemical reasons (subulacine-N-oxide was isolated as a chloroform-soluble oil¹). Furthermore, the reported absorption in the ir spectrum at 1180-1280 cm⁻¹ (typical rather for heteroaromatic N-oxides) can not be attributed to an N⁺—O⁻ group since aliphatic N-oxides absorb at 950-970 cm⁻¹ (cf. lit.⁶).

Thus, the origin of the peak at 171 m/z in the mass spectra reported¹ for subulacine-N-oxide and the cause of the resistance of this hydroxymethylated alkaloid to acetylation and oxidation¹ remain open. Since the N-oxide of 2 as well as its acetate have not been described in the literature, continuation of the research on the alkaloids of Heliotropium subulatum seems warranted.

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