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THE ABSOLUTE STEREOCHEMISTRY AND CORRECTED STRUCTURE OF THE MONOTERPENE ETHER FROM ARTEMESIA TRIDENTATA.

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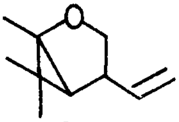
Recently Buttkus and Bose[1] reported the isolation of a monoterpenoid ether from Artemesia tridentata (sagebrush) for which they proposed structure 1. This ether has been isolated previously from sagebrush by Hoegger[2] who proposed structure 2. We have also isolated this compound from sagebrush[3] and on the basis of our work propose structure 4 as the correct one, (1*R*, 5*S*, 6*S*)-1,4,4-trimethyl-6-vinyl-3-oxabicyclo[3.1.0]hexane, for which we propose the trivial name artemeseole.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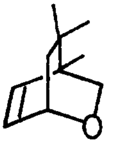
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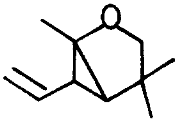
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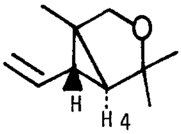

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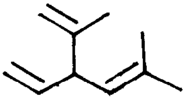
To the IR, NMR and mass spectral data reported by these authors the following ^{13}C NMR data are added ($CDCl_3$, TMS=0, all one carbon) 137.4 δ (d), 115.1 (t), 82.1 (s), 74.0 (t), 41.2 (d), 31.44 (s), 28.77 (d), 26.66 (q), 25.32 (q), 13.61 (q). These data which require a vinyl group ($-CH=CH_2$) and a quaternary carbon bonded to the oxygen ($-\overset{|}{\underset{|}{C}}-O$) disprove 2.

Structure 1 should be considered unlikely on the basis of the NMR as well as biogenetic consideration,[4] and is disproved by chemical means (vide infra). The 'H NMR of the ether contains an AB system at δ3.66 apparently due to geminal hydrogens of a ($-\overset{|}{\underset{|}{C}}-CH_2O$) group, a substructure lacking in 1. Buttkus and Bose account for this AB system by comparing 1 to 3,4-epoxytetrahydrofuran which exhibits no coupling between the C_2 and C_3 hydrogens. Such an explanation in the case of 1 is unlikely, but if such an explanation were feasible it then becomes difficult to explain why the same hydrogens still do not couple in the hydrogenated product. Two structures which contain a ($-\overset{|}{\underset{|}{C}}-CH_2-O$) group and are consistent with all spectra are 3 and 4. Compounds 1, 2, and 3 do not possess any known monoterpene carbon skeleton while 4 has the santolinyl skeleton seen in other monoterpenes 5,[3] 6,[5] and especially 7[6] isolated from Artemesia tridentata.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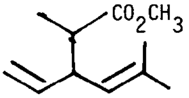

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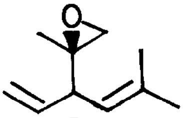
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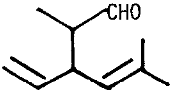

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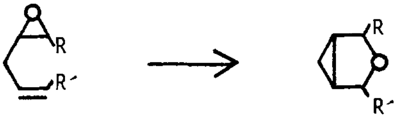
We reasoned mechanistically that one of the diastereomers of 7, the (2R, 3S) isomer, could be the precursor of 4 by an acid catalyzed rearrangement as was seen in the conversion of epoxide 8 to ether 9 in the presence of BF$_3$-etherate.[7] (See Scheme 1)

A mixture of (3S) and (3R) diastereomers of 7, isolated from the essential oils of A. tridentata (Price) was treated with formic acid at room temperature for 15 minutes, yielding two products; aldehyde 10 and ether 4. Compound 4 isolated by preparative glc from the reaction mixture was identical in IR and NMR spectra, glc retention time and specific rotation ($[\alpha]_D$ = $+16.3^{0}$) (1.22, $CDCl_3$) to 4 isolated from the same essential oils.



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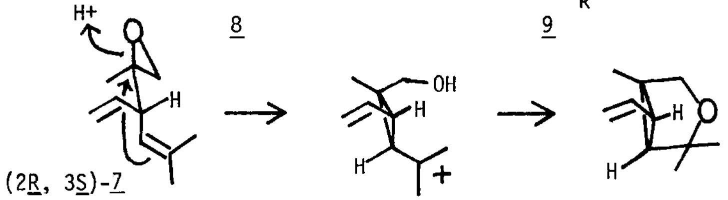
R = $(CH_2)_4CH_3$
R´ = $(CH_2)_7CO_2CH_3$

Scheme 1



Scheme 2

In an identical experiment, pure (3R)-7 yielded only aldehyde 10, showing that (3S)-7 is the source of 4 in the first experiment, and since the C_3 center is not involved in the mechanism of the rearrangement (Scheme 2) 4 must have (6S) stereochemistry as well. The 'H NMR coupling constant $J_{5,6}$ = 3.6 Hz (d of d, δ=1.56) shows that the cyclopropyl hydrogens are trans oriented on the ring,[8] thus giving an overall absolute stereochemistry for 4 as (1R, 5S, 6S).

The relative and absolute stereochemistry of 4 is consistent with the absolute stereochemistry assigned to C_2 of 7 in the previous article. Assuming inversion of configuration at C_2 in Scheme 2, molecular models show that of the two possible diastereomers of (3S)-7 only (2R, 3S)-7 can rearrange to 4 having hydrogens trans on the cyclopropane ring while (2S, 3S)-7 would rearrange to 4 with cis oriented hydrogens.

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