Characterization of a Monoterpenoid Ether from the Essential Oil of Sagebrush (*Artemisia tridentata*)[1]

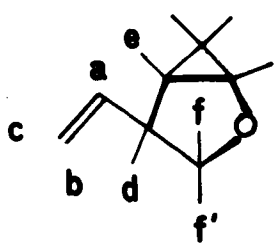
H. BUTTKUS and **R.J. BOSE**, Agriculture Canada Research Station, Summerland, B.C. VOH 1Z0 Canada, and Environment Canada, 6640 N.W. Marine Drive, Vancouver, B.C. V6T 1X2, Canada

ABSTRACT AND SUMMARY

From the essential oil of sagebrush (*Artemisia tridentata*) a component of the general composition $C_{10}H_{16}O$ was isolated. From its nuclear magnetic resonance, mass and infrared spectra an isoprenoid monoterpene, containing a substituted furanyl-cyclopropane fused ring system, 1,6,6-trimethyl-4-ethenyl-*exo*-2-oxabicyclo [3.1.0] hexane, is proposed as its structure.

INTRODUCTION

Analysis for the constituents of the essential oil of sagebrush (*Artemisia tridentata*) has been carried out over the years in different areas of the western U.S. (1-3); however no description of ethers other than 1,8 cineole has been reported. In recent work at this laboratory, chromatography of steam distilled essential oil from sagebrush on alumina columns yielded a fraction (∿13%) of elemental composition $C_{10}H_{16}O$ which according to its nuclear magnetic resonance (NMR) and mass spectral data was not identical to compositional isomers such as neroloxide (4), alpha pinane-2,3-epoxide (5), hop ether (6), or mata biether (7). From analytical data obtained on the fraction of isolated sagebrush oil, the following structures is proposed.



EXPERIMENTAL PROCEDURES

The Na_2SO_4 dried, steam distilled oil obtained from the leaves and young shoots of sagebrush growing in the Okanagan Valley of British Columbia was redistilled at (730 mmHg) in a Quickfit apparatus. A fraction of this oil (2 g) BP 164-185 C was chromatographed on a glass column packed with a 1.8 x 45 cm bed (∿60 g) of neutral alumina, Brockman activity 1, 80-200 mesh. The oil was applied to the column in petroleum ether (BP 35-49 C). Elution was then carried out by the application of 100 ml of petroleum ether and 40 ml each of petroleum ether-benzene 30:10, 20:20, and 10:30. Collecting the eluates in 40 ml fractions the ether was usually contained in fractions 4 and 5 often with some contamination of 1-8 cineole.

The NMR spectrum of the purified ether was recorded in deuterochloroform relative to reference tetramethylsilane with a Varian HA100 instrument. Mass spectra were obtained with a Nuclide 12-90-G mass spectrometer or a Finnigan coupled Gc-Quadrupole mass spectrometer. The column used on this latter instrument was 5 ft (glass) 1/4 in. (OD) packed with 3% OV17 on Chromosorb WHP, 80-100 mesh. Flow rate was 35 ml He/min. Separator and transfer line temperature was 250 C and the mass spectra were obtained with an accelerating voltage of 3000 V with an energy of 70 eV and a scanning time of 1 sec over a mass range of 35-500 m/e. The Nuclide 12-90-G mass spectrometer with direct insertion probe was also operated at 70 eV.

A Beckman 20A spectrophotometer was used to obtain IR spectra of the sample between NaCl plates.

Reduction of the isolated compound was carried out at 20 C in a PtO_2-hexane suspension with water saturated hydrogen.

[1]Contribution No. 447

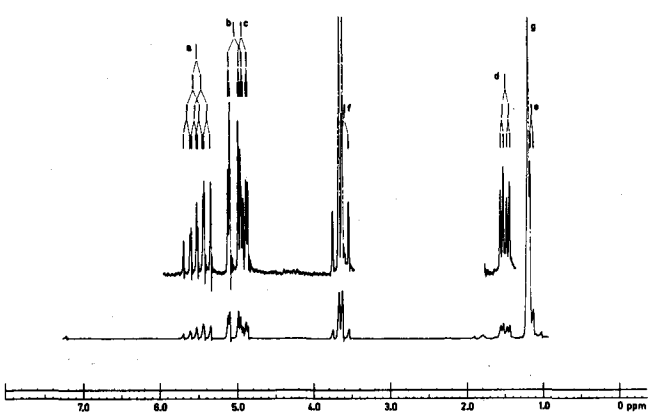


FIG. 1. Nuclear magnetic resonance spectrum of isolated sagebrush ether in $CDCl_3$ at 28.5 C, 100 MHz, chemical shift from tetramethylsilane (TMS).

RESULTS AND DISCUSSION

The terpenoid ether had a gas chromatographic (GC) retention time of 1.0 min on a 5 ft 1/4 in. (OD) 3% OV17 column, 130 C isothermal, 35 ml He/min, while 1,8 cineole, which often accompanied it as a trace impurity, had a retention time of 1.75 min.

The NMR spectrum of the oil in deuterated chloroform, relative to tetramethylsilane (Fig. 1) showed a one proton quintet centered at δ5.53 ppm (1H). This olefinic proton (a) was coupled to the *trans* and *cis* situated protons (b) and (c) of the vinyl group with the respective coupling constants J_{ab} 16.5 and J_{ac} 10 Hz, as well as to the adjacent methine proton (d), J_{ad} 8 Hz. The vinylic protons (b) and (c) appeared as a pair of overlapping quartets centered at δ5.04 and 4.93 ppm (2H) respectively and were coupled to each other J_{bc} and J_{cb} = 2 Hz and to (a) by J_{ba} 16.5 and J_{ca} 10 Hz. Allylic coupling between (c) and (d) with very small coupling constants $J_{al} \cong 0.5$ Hz seemed also present. The resonance signal of proton (d) at δ1.52 ppm (1H) was split into a quartet by interaction with proton (a) J_{da} 8 Hz and (e) J_{de} 4 Hz. The chemical shift value of proton (e) at δ1.15 ppm (1H) is indicative of its being a part of a cyclopropane system. It is coupled to (d) and split into a doublet J_{ed} 4 Hz which was partly buried under a sharp singlet peak at δ1.20 ppm (9H) originating from the protons of three methyl groups.

A quartet, due to the geminal coupling of two non-equivalent methylene protons (J 8.5 Hz), with relative intensities of the inner and outer pairs of lines of 5:1 was centered at δ3.66 (2H). The chemical shift established the

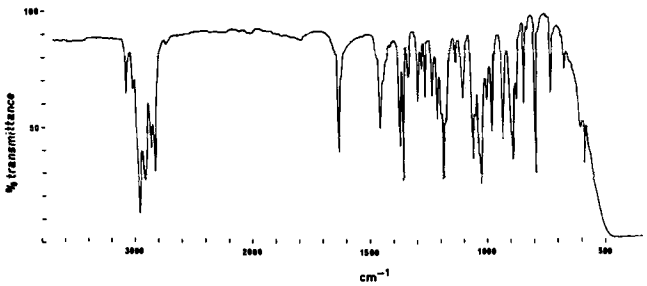


FIG. 2. Infrared spectrum of isolated sagebrush ether (oil) between NaCl plates.

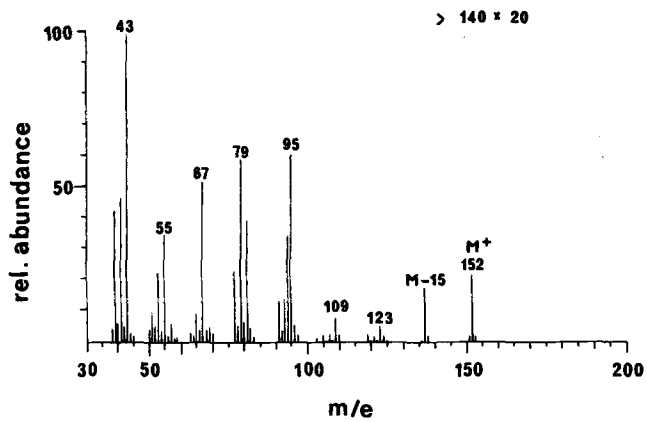


FIG. 3. Mass spectrum of isolated sagebrush ether (oil).

location of the protons adjacent to oxygen, and spin decoupling experiments confirmed that these protons (f,f') were not coupled to any others in the molecule. In the H_2/PtO_2 reduced molecule the formerly low field signals were now located at δ0.7 to 1.4 ppm and the quartet from the methylene protons at 3.66 had shifted unaltered in pattern to 3.61 ppm. According to a Dreiding model of the compound the stereochemistry of the vinyl group must be *exo*.

The cyclopropane group limits the furan portion of the ether to two possible envelope conformations, each with the methylene group out of the plane of the ring. The dihedral angle $\phi_{d,f}$ approached 90° in the preferred *endo* methylene-cyclopropane conformation ($\phi_{d,f'}$, approached 30°) and $J_{f,d}$ would be expected to be near 0 Hz as observed. The absence of observed coupling between (d) and (f') is less readily explained, but may simply reflect the combined electronegativity values (ΣE) of the geminally situated and reactive vinyl, ether, and cyclopropane substituents in the modified Karplus equation; eg. J = 8.0-1.0 ΣE, as discussed by Abraham and Pachler (8). A similar effect has been described in the literature for 3,4-epoxytetrahydrofuran (9) in which the geminal protons couple only with each other but not with the vicinal methine proton.

An IR spectrum of the compound (Fig. 2) showed medium intensity absorption bands at 3075 and 3020 cm^{-1} due to carbon-hydrogen stretch absorptions of the vinylic bond $-CH=CH_2$, a strong absorption at 1635 cm^{-1} due to C=C stretch and strong peaks at 895, 940, and 985 cm^{-1} due to $-CH=CH_2$ deformations. All of these characteristic absorptions were absent from the spectrum of the H_2/PtO_2 reduced compound in which the CH_3 absorption at 1465 cm^{-1} increased and the doublet due to geminal CH_3 groups (1375 cm^{-1}) remained unchanged. There were no alcohol or ketone functional group absorptions present in either spectrum, and cyclic ether absorptions due to C-O stretch in the 1250-910 cm^{-1} region remained very dominant in the

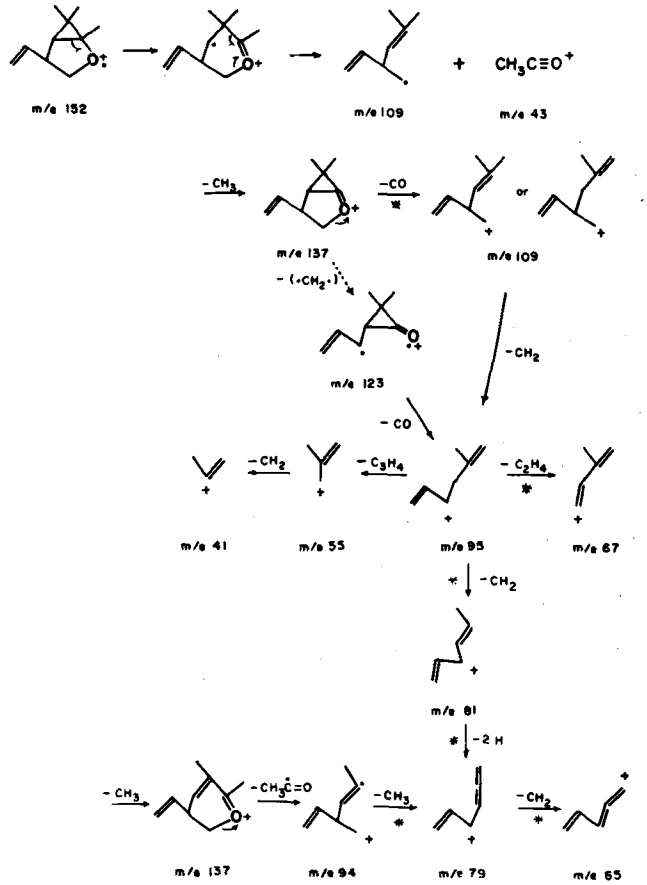


FIG. 4. Scheme for the fragmentation of the sagebrush ether on electron impact.

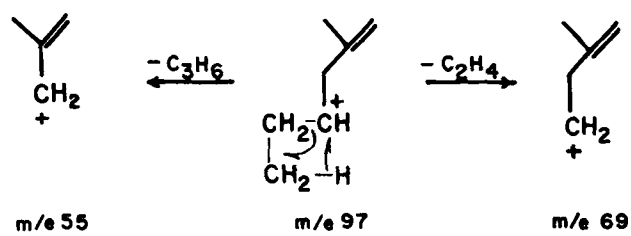


FIG. 5. Scheme for hydrogen rearrangement and fragmentation of ion m/e 97 from reduced cyclic sagebrush ether.

reduced compound, particularly at 920, 1040, 1080, 1120, 1160, 1180, and 1210 cm^{-1}. Characteristic epoxy ring vibrations in the vicinity of 835 cm^{-1} did not seem to be present.

An ultraviolet spectrum of the compound showed an absorption maximum at 213 nm, $E_M = 2.7 \times 10^3$.

Microanalytical results gave the elemental formula $C_{10}H_{16}O$ for the isolated compound which reacted with one mole of hydrogen to form $C_{10}H_{18}O$.

The mass spectrum of the isolated compound (Fig. 3) displayed the molecular ion (M^+) at m/e 152 with the corresponding M^+-15 peak at 137 (18%) while the base peak was at m/e 43. The relative intensity of M^+ was 1.0% in the isolated and 0.6% in the H_2/PtO_2 reduced compound which is within the range of alkyl ethers of molecular weights between 130 to 185 (10). A rationale for the formation of the principal peaks in the spectrum by charge site as well as radical site initiation and the major pathways of fragmentation are outlined (Fig. 4).

Loss of acylium ion $CH_3C{\equiv}O^+$ from M^+ led to the formation of the base peak m/e 43 and a radical (M-43). The primary involvement of the acylium ion instead of

$C_3H_7^+$ was favored by the presence of the corresponding m/e 43 + 2 ion (1%) to which ^{18}O and ^{13}C isotope containing ions contributed 0.212% while the m/e 44/43 ratio was 2.3 indicative of a C_2 ion. Characteristic minor peaks (less than 5% relative abundance) were formed by rearrangements involving hydrogen transfer and displacement reactions leading to such ions as M^+-29-18 (C_2H_5, H_2O) at m/e 105 (2%); M^+-15-18 (CH_3, H_2O) at m/e 119 (2%); and M^+-15-30 (CH_3, CH_2O) at m/e 107 (2%).

In the spectrum of the reduced compound (M^+=m/e 154) all the prominent, as well as the above minor ion peaks, were shifted up by two mass units except in the low molecular weight region, i.e. m/e 43, the predominant leaving ion ($CH_3C{\equiv}O^+$) still formed the base peak and m/e 55 (72%) was now present at higher relative abundance as was also the reduced $(M\text{-}15)^+$ ion now at m/e 139 (75%). Further proof for the proposed structure of the ether comes from the fragmentation of the secondary carbonium ion m/e 97 which can still eliminate C_2H_4(28) by hydrogen transfer to generate m/e 69 (45%) but will more readily lose C_3H_6 (42) forming ion m/e 55 (72%). Predictably the latter fragmentation step takes place more readily than the elimination of C_3H_4(40) from m/e 95 of the isolated compound to generate the same m/e 55 ion at only 35% relative abundance. The detailed mechanism for hydrogen rearrangement and fragmentations of ion m/e 97 from the reduced sagebrush ether is shown in Figure 5.

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