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LONGILOBOL, A NEW SESQUITERPENE TRIOL FROM *ARTEMISIA LONGILOBA* (OSTERHOUT) BEETLE*

F. Shafizadeh and N. R. Bhadane

Wood Chemistry Laboratory, Department of Chemistry and
School of Forestry, University of Montana
Missoula, Montana 59801 U.S.A.

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The sesquiterpene constituents of *Artemisia longiloba* (Osterhout) Beetle were studied as part of this laboratory's program on chemical investigation of sagebrush in Montana.[1] Extraction of areal parts of the plant collected in Montana, extensive column chromatography of the extract and further preparative thin layer chromatography resulted in the isolation of two crystalline compounds. One of these compounds was highly unstable and decomposed on further treatments. The other compound which was obtained in 0.02% yield proved to be a new sesquiterpene that was named longilobol. This compound was shown to have the structure I on the basis of the following consideration.

Longilobol, m.p. 176-177°, $[\alpha]_D^{20}$ + 95° (MeOH, *c* = 0.77) behaved as a pure product (t.l.c. and g.l.c. as trimethylsilylether) and analyzed for $C_{15}H_{26}O_3:2H_2O$. Its i.r. spectrum exhibited bands for -OH (3240, 3330 and 3500 cm^{-1}) and unsaturation (1640 cm^{-1}). The mass spectrum showed peaks at *m/e* 254 (M^+), 236 (M-18), 221(M-18-15), 218 (M-18-18) and 203 (M-18-18-15).

The n.m.r. spectrum (C_5D_5N) showed signals at 0.95 (3H,S, CH_3-C<), 1.28 (6H,S, >C(CH_3)$_2$), 1.93 (1H,S, OH) and a complex pattern from 4.60 to 6.00 ppm.

The n.m.r. spectrum ($CDCl_3$) of the trimethylsilyl derivative (Ia) obtained by treatment of longilobol with Tri-Sil reagent showed two broad singlets at 5.12 and 4.77 ppm (1 H each, $W_{1/2}$ = 3 Hz, a characteristic of unconjugated exomethylene protons, C4 = CH_2); a partly mixed signal at 4.62 ppm (1 H, C8-H); a sharp singlet at 1.17 (6H, C7-C(CH_3)$_2$) and a sharp singlet at 0.77 ppm, (3H, C10-CH_3). Integration of the methyl signals of the trimethylsilyl group appearing at 0.07 and 0.13 ppm indicated the presence of three hydroxyl groups in longilobol.

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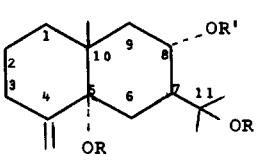
*Part VIII in the series on "Chemical Composition of Sagebrush". Part VII, R. G. Kelsey, M. S. Morris, N. R. Bhadane, and F. Shafizadeh, *Phytochemistry*, in press.

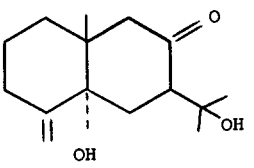
Acetylation of longilobol, under normal conditions gave a monoacetate (Ib); $C_{17}H_{28}O_4$; m.p. 115-116°. The monoacetate showed i.r. peaks at 3340, 3480 (OH), 1725 and 1250 (acetate) cm^{-1} and had mass spectral peaks at *m/e* 236 (M-60), 221 (M-60-15), 218 (M-60-18), 203 (M-60-18-15) and 200 (M-60-18-18). Active hydrogen determination and presence of two n.m.r. signals exchangable by D_2O showed the presence of two free hydroxyl groups in the monoacetate. Longilobol thus has three hydroxyl groups, one of which is secondary.

Longilobol was not oxidized by periodate indicating that there are no vicinal hydroxyl groups in the molecule. The presence of only one secondary hydroxyl group in longilobol was also confirmed by oxidation to a ketone, dehydrolongilobol (II).

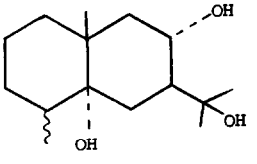
Longilobol on hydrogenation over 5% Pd/C catalyst absorbed one mole of hydrogen and gave a mixture of two compounds which showed no olefinic proton in the n.m.r. spectrum. Attempted separation of the mixture, however, resulted in the isolation of a few mg of one of the two compounds (upper spot). The mass spectrum of this material showed peaks at *m/e* 238 (M-18), 220 (M-18-18) and 205 (M-18-18-15) indicating that it is dihydrolongilobol (III). Longilobol thus has only one unsaturation and a bicyclic structure.



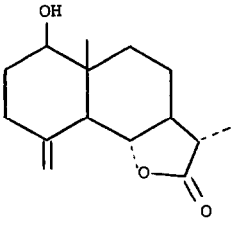
I, R = R' = H
Ia, R = R' = TMS
Ib, R' = Ac, R = H



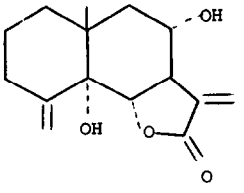
II



III



IV



V

The above data and particularly the appearance of the quaternary methyl signal in the n.m.r. spectrum of longilobol (I), the trimethylsilyl derivative (Ia) and the acetate (Ib) suggests the eudesmane skeleton for longilobol*.

In the n.m.r. spectrum of longilobol (I) and the trimethylsilyl derivative (Ia) the methyl groups of the C7-isopropyl side-chain appear as a 6 proton singlet at 1.28 and 1.18 ppm respectively suggesting that there is no proton at the C11 position. Therefore, one of the tertiary hydroxyl groups should be located at this position. The other tertiary hydroxyl group has to be at either C5 or C7, the only other tertiary positions available in the eudesmane skeleton. Position C7 can be ruled out by the fact that longilobol is not oxidized by periodate, leaving C5 as the site for the second tertiary hydroxyl group.

The above considerations also exclude the C6 position as a possible location for the secondary hydroxyl group. The proton of the carbon atom holding this hydroxyl group appeared as a mixed signal around 5.1-5.2 ppm in the n.m.r. spectrum of longilobol (I). In the n.m.r. of monoacetate ($CDCl_3$), however, this proton appeared as a broad triplet at 5.71 ppm with a large coupling constant (J = 9.5 Hz). The magnitude of this constant suggests that the proton is axial and is coupled with two axial and probably one equatorial neighboring protons; a situation that only exists at C8**. Therefore, the secondary hydroxyl group seems to be located at this position. This conclusion is confirmed by the following considerations.

Longilobol (I) on oxidation with Jones reagent gave a ketone, dehydrolongilobol (II): $C_{15}H_{24}O_3:H_2O$; m.p. 230-235° along with many other products, none of which could be isolated in pure form. Dehydrolongilobol (II) showed i.r. bands at 3410 and 3560 (OH) and 1710 ($\geq C = O$, cyclohexanone) cm^{-1}. The absence of a high intensity u.v. band around 240 nm, characteristic of α,β-unsaturated ketones, in dehydrolongilobol also rules out the possibility of the secondary hydroxyl group being at C3. The C1 and C9 positions can also be ruled out because an axial proton under the secondary hydroxyl group at these positions should show a doublet of doublets as observed for a known C1 hydroxylated eudesmanolide[3] (IV); whereas the spectrum of longilobol shows a broad triplet for this proton.

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*The genus *Artemisia* has so far yielded only guaiane, eudesmane and germacrane type sesquiterpenes[2]. The eudesmanes can easily be distinguished from other two types by the appearance of a quaternary methyl signal (Angular methyl at C10) in their n.m.r. spectrum.

**C1, C3, C6 and C8 are the most generally oxidized positions in sesquiterpenes isolated from the genus *Artemisia*.[4]

The *trans* stereochemistry of the A/B rings in I was assumed in analogy with the known eudesmane sesquiterpenes isolated from this genus.[6-8]

Plants of the genus *Artemisia* contain a variety of sesquiterpene lactones which according to the current concepts of biogenetic pathyways are formed by oxidation of the corresponding alcohols.[5] Rothin-B (V) found in several species of *Artemisia*[6,7] could have been derived from the biological oxidation of longilobol. A similar eudesmane sesquiterpene triol has been recently isolated from *Artemisia pygmea*.[7,8]

ACKNOWLEDGEMENTS

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