

STUDIES ON PEROXIDES OF ARTEMISIA LANCEA

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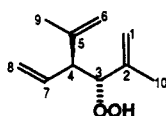
ABSTRACT.—Two novel monoterpene peroxides, along with the known sesquiterpene peroxide qinghaosu, have been isolated from the aerial parts of *Artemisia lancea*. The two new monoterpene peroxides were identified as (3*R*,4*S*)-1,5-dimethyl-4-vinyl-3-hydroperoxy-1,5-hexadiene, or (3*R*,4*S*)-isolyratyl hydroperoxide A [**1**] and (3*R*,4*R*)-1,5-dimethyl-4-vinyl-3-hydroperoxy-1,5-hexadiene, or (3*R*,4*R*)-isolyratyl hydroperoxide B [**2**].

Artemisia lancea Van (Compositae), distributed in Yunnan, China, has an unpleasant odor. Its chemical composition has not been reported. We have isolated two novel peroxides: (3*R*,4*S*)-isolyratyl hydroperoxide A [**1**] and (3*R*,4*R*)-isolyratyl hydroperoxide B [**2**], which have unpleasant odors, and one known sesquiterpene peroxide, qinghaosu, from the aerial parts of *A. lancea* by repeated cc and hplc. Both new peroxides are very unstable, highly volatile, colorless, viscous oils, which decompose above 70°, crystallize below 0°, and give positive reactions with NHSCN-FeSO reagent.

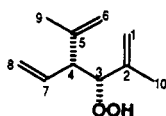
Compound **1** has a molecular ion at m/z 168, consistent with a composition $C_{10}H_{16}O_2$. Its ^{13}C -nmr (DEPT) spectra at 113.4 ppm (CH_2), 116.3 ppm (CH_2), 115.8 ppm (CH_2), 137.0 ppm (CH), 142.3 ppm (C), and 143.8 ppm (C) shows the presence of three double bonds. Two of the double bonds are ω -vinylidene groups, and one is an ω -vinyl group; the absence of any uv absorption above 210 nm indicates that all double bonds are unconjugated.

Its 1H -nmr spectrum, with signals at

1.72 ppm (3H, s, -Me) and 1.78 ppm (3H, s, -Me) and its ^{13}C -nmr spectrum, with signals at 17.8 ppm (Me) and 19.8 ppm (Me), coupled with the absence of other quaternary carbons, indicate that two methyl groups are attached to the two vinylidene groups. Compound **1** thus has two isopropenyl groups. The sharp OH stretching vibration at 3420 cm^{-1} in the ir spectrum and the signals of one proton in the 1H -nmr spectrum at 8.40 ppm, which can be exchanged by D_2O , indicate the presence of a hydroperoxy group. The 1H -nmr signal at 4.44 ppm (1H) and ^{13}C -nmr signal at 90.3 ppm (CH) show that **1** has one -CH-OOH group. The 1H -nmr signals at 4.44 ppm (1H, d, $J = 9.7$ Hz), 2.92 ppm (1H, dd, $J_1 = 9.7$ Hz, $J_2 = 7.8$ Hz), and 5.90 ppm (1H, ddd, $J_1 = 9.7$ Hz, $J_2 = 7.8$ Hz, $J_3 = 17$ Hz) and the ABX system of the vinyl group (see Experimental) indicate that **1** has a CH=CH-CH-CH-OOH group. Compound **1** is thus 2,5-dimethyl-4-vinyl-3-hydroperoxy-1,5-hexadiene. The 1H -nmr spectra of **1** is very similar to that of isolyratol, previously reported from *Artemisia arbuscula* var. *arbuscula* (1), except that the chemical shift of the H-3 of **1** is 0.32 ppm downfield from its value in isolyratol. This confirms that **1** is the hydroperoxy analogue of isolyratol, and this assignment is supported by the mass spectrum of **1** with peaks at m/z 81 [C_6H_9] $^+$ (100), 135 [$M - OOH$] $^+$, 87



1



2

$[\text{C}_4\text{H}_7\text{O}_2]^+$, 41 $[\text{C}_3\text{H}_5]^+$, and 93 $[\text{C}_7\text{H}_9]^+$.

Compound **2**, which was assigned the formula $\text{C}_{10}\text{H}_{16}\text{O}_2$ ($[\text{M}]^+$ at m/z 168), is similar to **1** in uv, ir, and mass spectra. The coupling constants of the ^1H nmr and the ^{13}C nmr (DEPT) of **2** also suggest that compound **2** has the same planar structure as **1**. However, the obvious differences of chemical shifts of corresponding protons and carbons between **1** and **2** require that **2** is an epimer of **1**.

In 2,5-dimethyl-4-vinyl-3-hydroperoxy-1,5-hexadiene, C-3 and C-4 are asymmetric carbon atoms. The $J_{3,4}$ (9.7 Hz) of **1** and the $J_{3,4}$ (11.8 Hz) of **2** suggest that the dihedral angle between H-3 and H-4 is about 180° in both compounds (**2**, **3**). The values of H-7 and H-1_b of compound **1** are shifted downfield by 0.22 ppm and 0.21 ppm with respect to compound **2**, while the value of H-9 of compound **2** is shifted downfield by 0.1 ppm with respect to compound **1** (see Experimental). This indicates that the hydroperoxy group in compound **1** is near C-7 and C-1 in space, while in compound **2** the hydroperoxy group is near C-9, because the high electronegativity of the oxygen atoms in the hydroperoxy group cause a decrease of electron density around H-7, H-1_b, and H-9. Compounds **1** and **2** are thus in the configurations shown.

Compound **3**.—The mp, mmp, ir, mass spectra and the R_f value on tlc of compound **3** are entirely compatible with those for qinghaosu.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Thomas-Kofler hot stage equipped with microscope and are uncorrected. Ir spectra were recorded on a Perkin-Elmer 557 ir spectrometer. ^1H -nmr and ^{13}C -nmr spectra were observed in CDCl_3 with TMS as internal standard on a Bruker WH-400 spectrometer. Chemical shifts are in ppm, coupling constants are in Hz. Mass spectra were recorded on a Finnigan-4510 mass spectrometer at an ionizing voltage of 70 eV. Hplc was carried on

QC-prep HPLC System with C_{18} Ultrasphere Semiprep 5μ 10×250 mm column.

PLANT MATERIALS.—The plant material was collected during blooming from the garden of Kunming Institute of Botany, Yunnan province, in September 1989. It was authenticated by Prof. He Jilian, Department of Biology, Yunnan University. A voucher specimen has been deposited in our laboratory.

EXTRACTION AND ISOLATION.—Air-dried, powdered aerial parts of *A. lancea* (1500 g) were macerated with petroleum ether (bp $30\text{--}60^\circ$) for 2 days. Evaporation of petroleum ether at reduced pressure supplied 22 g dark green extract. This extract was fractioned on a Si gel column (Si gel 200–300 mesh) and eluted with petroleum ether- Et_2O (100:1, 50:1, 25:1, 5:1). Peroxide-containing fractions were collected when the R_f [Si gel G, petroleum ether- EtOAc (5:1)] of the eluate is 0.70–0.76 (fraction A) and 0.22–0.24 (fraction B).

Fraction A (0.15 g) containing compounds **1** (75%) and **2** (25%) was isolated by hplc with petroleum ether (bp $30\text{--}60^\circ$)- EtOAc (20:1 to 10:1) as eluting solvent. Compound **1** (ca. 100 mg) and compound **2** (ca. 30 mg) were obtained. They were colorless, highly volatile, and unstable viscous oils.

The EtOH solution of fraction B gave compound **3** (ca. 300 mg) as crystals.

(3R,4S)-1,5-dimethyl-4-vinyl-3-hydroperoxy-1,5-hexadiene [**1**].—Ir ν max 3420, 3065, 2920, 1655, 1645, 1634, 1450, 1435, 1375, 991, 900 cm^{-1} ; gc-ms m/z 135, 93, 87, 81, 41; ^1H nmr 5.10 (d, $J_{1a,1b} = 1.8$, H-1a), 5.07 (d, $J_{1a,1b} = 1.8$, H-1b), 4.44 (d, $J_{3,4} = 9.7$, H-3), 2.92 (dd, $J_{4,7} = 7.8$, H-4), 5.13 (d, $J_{6a,6b} = 1.0$, H-6a), 5.04 (d, $J_{6a,6b} = 1.0$, H-6b), 5.90 (ddd, $J_{7,8a} = 17$, $J_{7,8a} = 9.8$, H-7), 4.8 (dd, $J_{8a,8b} = 1.5$, H-8a), 5.06 (dd, $J_{8a,8b} = 1.5$, H-8b), 1.72 (s, H-9), 1.78 (s, H-10), 8.40 (s, -OOH); ^{13}C nmr 116.3 (C-1), 142.3 (C-2), 90.3 (C-3), 52.8 (C-4), 143.8 (C-5), 115.8 (C-6), 137.0 (C-7), 113.4 (C-8), 19.8 (C-9), 17.2 (C-10).

(3R,4R)-1,5-dimethyl-4-vinyl-3-hydroperoxy-1,5-hexadiene [**2**].—Ir and ms data are the same as those of compound **1**; ^1H nmr 5.06 (d, $J_{1a,1b} = 1.7$, H-1a), 4.86 (d, $J_{1a,1b} = 1.7$, H-1b), 4.43 (d, $J_{3,4} = 11.8$, H-3), 2.91 (dd, $J_{4,7} = 7.8$, H-4), 5.09 (d, $J_{6a,6b} = 1.0$, H-6a), 5.08 (d, $J_{6a,6b} = 1.0$, H-6b), 5.68 (ddd, $J_{7,8a} = 17$, $J_{7,8b} = 9.8$, H-7), 4.80 (dd, $J_{8a,8b} = 1.5$, H-8a), 5.06 (dd, $J_{8a,8b} = 1.5$, H-8b), 1.81 (s, H-9), 1.76 (s, H-10), 8.38 (s, -OOH); ^{13}C nmr 116.2 (C-1), 142.3 (C-2), 89.8 (C-3), 52.3 (C-4), 144.6 (C-5), 117.6 (C-6), 135.9 (C-7), 112.5 (C-8), 14.1 (C-9), 17.1 (C-10).

Compound 3.—Colorless needles, mp 156–157°; $[\alpha]_D^{17} +66.3$ ($c = 1.64$, CHCl_3); R_f 0.45 [Si gel G, petroleum ether-EtOAc (5:1)]; ν_{max} 2992, 2960, 2880, 1745, 1375, 1345, 1250, 1115, 881, 831 cm^{-1} ; m/z $[M]^+$ 282, 267, $[M - O_2]^+$ 250. Compound **3** gave a positive reaction with KI-starch reagent.

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