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SYNTHESIS OF DEHYDROCINEOLE, A NEW MONOTERPENE FROM THE ACARID MITE, *Caloglyphus rodriguezi* (ARACHNIDA: ACARI)

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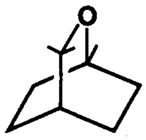
Abstract: Dehydrocineole, a new monoterpene ether, 6-methylsalicylaldehyde, undecane and tridecane are reported from the opisthonotal gland secretion of the mite, *Caloglyphus rodriguezi*. A synthesis of dehydrocineole is described.

The opisthonotal gland[1] secretions of acarid mites representing six genera have been shown to contain a variety of low molecular weight organic compounds including: neryl formate, geranial, neral, 6-methylsalicylaldehyde, perillen and several saturated and unsaturated hydrocarbons ranging from C_{10} to C_{15}.[2,3] We report here the chemistry of the opisthonotal gland secretions of *Caloglyphgus rodriguezi*.

Gas chromatographic-mass spectroscopic analysis[4] of methylene chloride extracts of whole bodies of *Caloglyphus rodriguezi*[5] showed four major peaks in a ratio of 2:6:9:4. Peak 1 eluting from the column exhibited a mass spectrum with a molecular ion at m/z 152(5), with additional fragment ions at 137(2), 124(17), 109(100), 94(15), 79(61), 77(22), and 43(73). Peak 2 and peak 3 gave molecular ions at m/z 156 and 184 respectively. Their fragmentation patterns and retention times matched those of undecane and tridecane. Peak 4 showed a molecular ion at m/z 136(90) with additional fragment ions at 135(100), 118(15), 107(17), 105(4), 90(30), 89(20), 79(30), 77(50), 63(15), 55(5), 53(20) and 51(30). Peak 4 thus appeared to be 6-methylsalicylaldehyde.[3,6] It was isolated from the mixture by preparative gas chromatography and gave a proton NMR[7] spectrum consistent with the structure of 6-methylsalicylaldehyde. It was synthesized from 2-nitro-6-methylbenzoic acid[8] in four steps giving material identical to the natural product.

The compound corresponding to peak 1 was also isolated by preparative gas chromatography. Reduction of the unknown with hydrogen (Pt) gave 1,8-cineole (1), identified by its retention time and mass spectrum using an authentic sample.[9] The unknown had a molecular weight of 152.1199 indicating a molecular formula of $C_{10}H_{16}O$.[10] The base peak had a molecular formula of $C_8H_{11}O$ corresponding to loss of C_3H_7 from the molecular ion. This ion (m/z 109) appears to be formed by a retro-Diels-Alder reaction followed by loss of methyl from the gem-dimethyl group leaving a dimethylsubstitruted pyran ion. The ion at m/z 94 (C_7H_{10}) is in accord with this rationalization, it being the alternate retro-Diels-Alder with loss of acetone. A proton NMR[7] spectrum showed δ 6.34, apparent triplet, J=7.3Hz,1H; 5.98,d,J=7.6Hz,1H; 2.44, apparent quartet,J=7.3Hz,1H; 1.53-2.23,m,4H; 1.21,s,3H; 1.16,s,3H; 0.87,s,3H. ^{13}C NMR showed the following δ 135.3 and 135.1,C=C; 74.2 and 71.0,C-O; 39.5,C-H; 29.1 and 20.5,CH_2; 28.1, 27.5 and 24.8,CH_3.[11] These data are consistent only with dehydrocineole (2).



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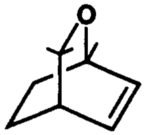
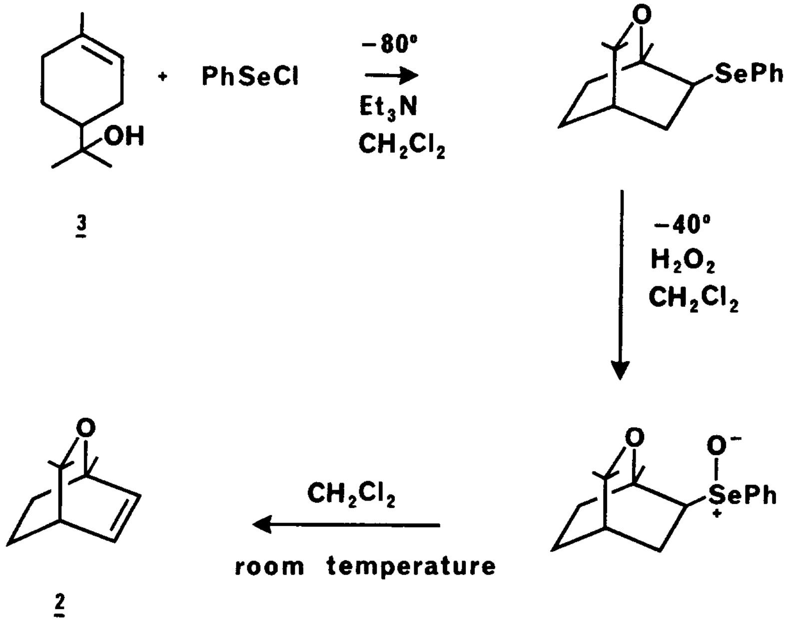


2

Dehydrocineole was synthesized from α-terpineol (3) by Scheme I. It takes advantage of a recently developed intramolecular etherification via selenylation, followed by peroxide oxidation with subsequent syn elimination of the selenoxide.[12]

Dehydrocineole is a new natural product. These "wet grain mites" are thus quite distinct from the "cheese mite", Tyrophagus putrescentieae, which contains the common geranial and neral. 6-Methylsalicylaldehyde has been identified in a longhorned beetle (Cerambycidae)[6] as well as in the opisthonotal gland secretions of several genera of acarid mites.[3]

Experimental: Methylene chloride (400ml) containing 7.0g (0.037 mol) phenylselenyl chloride was added to a 1 L three-neck flask equipped with a thermometer, magnetic stirrer and a dropping funnel. The dark brown solution was cooled to -80°C, turning orange. α-Terpineol (3) (5.0 g, 0.032 mol) in 50 ml of methylene chloride was added dropwise, keeping the temperature between -80 and -75°C. After 30 min. of stirring, 5.0 g (0.049 mol) triethylamine in 50 ml methylene chloride was added dropwise giving a light yellow solution. After stirring one hour at -80°C, the solution was warmed to -40°C. After 6 ml of 30% hydrogen peroxide was added, the reaction mixture was warmed to room temperature. The organic layer was removed, dried over anhydrous sodium sulfate, and evaporated on a rotary evaporator at room temperature. The dark crude mixture was vacuum distilled (1mm/Hg) at 27°C using a cooled receiver. The resultant light yellow oil was fractionally distilled (1mm/Hg) at room temperature giving 2.0 g (40%) of (2), a minty-smelling colorless oil as well as 2.2 g of α-terpineol(3).[13]



SCHEME 1

REFERENCES AND NOTES

1. The paired opisthonotal glands are located dorsal-laterally on the opisthosoma (body) of the mites. Its presence is primarily restricted to species belonging to the families which comprise the Acaroidea.

2. Y. Kuwahara, S. Ishii and F. Fukami, Experientia, 31, 1115 (1975); Y. Kuwahara, Proc. Sym. Insect Pheromones and Their Application, Agr. Forestry Fish Res. Res. Council, Tokyo, 65, 1976.

3. R. F. Curtis, A. Hobson-Frohock, G. R. Fenwick and J. M. Berreen, J. Stored Prod. Res., 17, 197 (1981).

4. A computerized Finnigan 3200 E gas chromatograph-mass spectrometer utilizing a 1.6 m 3% OV-17 on Supelcoport 60/80 column was used.

5. *Caloglyphus rodriquezi* cultures were reared on finely ground Purina dog food at 27°C. 70% relative humidity and a normal daylight cycle. The presence of specimens on the top surfaces of the lids of the rearing vials indicated mature cultures. Specimens were removed from them with a camel's hair brush onto glassine paper, poured into 2 dram vials, and extracted with a minimal amount of methylene chloride. Approximately 10 ml of mites (males, females and immatures) were extracted for chemical analysis. Treatment of whole mites with potassium permanganate solution and aqueous bromine solution indicated that the opisthonotal glands contained unsaturated compound(s). Due to the small size of individual mites, it was not possible to dissect glands to confirm that these glands contained 2.

6. B. P. Moore and W. V. Brown, *Aust. J. Chem.*, 25, 591 (1972).

7. Proton NMR spectra were taken on a Nicolet NT-200 superconducting NMR using deuterochloroform and TMS as an internal standard. We thank Mr. A. Carty for these spectra. δ 10.33,s,1H; 9.45,s,1H; 6.73,d,J=8Hz,1H; 6.80,d,J=8Hz,1H; 7.38,t,1H; 2.62,s,3H for 6-methylsalicylaldehyde.

8. F. O. Ayorinde, Ph.D. Thesis, Howard University, 1980.

9. An authentic sample of 1,8-cineole was generously supplied by Berje Chemical Co., Inc., New York.

10. We thank Mr. Noel Whittaker of the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases (NIH) for high resolution mass spectra. A V.G. Micromass Ltd. 7070F was used.

11. We thank Dr. Robert J. Highet, National Heart, Lung and Blood Institute (NIH) for ^{13}C spectra which were taken on a Joelco FX-60 spectrometer.

12. K. B. Sharpless, M. W. Young and R. F. Lauer, *Tetrahedron Lett.*, 1979 (1973); K. C. Nicolaou and Z. Lysenko, *Tetrahedron Lett.*, 1257 (1977); and D. Liotta and G. Zima, *Tetrahedron Lett.*, 4977 (1978).

13. We thank Dr. J. G. Rodriguez, Department of Entomology, University of Kentucky for the initial cultures of *Caloglyphus rodriguezi* Samsinak. We also thank the United States Department of Agriculture Competitive Research Grants Program (59-2117-9-1-433-0) for support of this work and Dr. Caspa Harris for his continued interest in this research program.

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