Tetrahedron Letters, Vol.31, No.39, pp 5559-5562, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

LASIOL, A NEW ACYCLIC MONOTERPENOL IN THE MANDIBULAR GLAND SECRETION OF *Lasius meridionalis*

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Summary: A new, biogenetically anomalous, acyclic monoterpenol has been found in the mandibular glands of the formicine ant *Lasius meridionalis*, and identified as *erythro*-1, 2,3,6-trimethyl-5-heptenol (lasiol) on the basis of spectroscopic evidence and total synthesis.

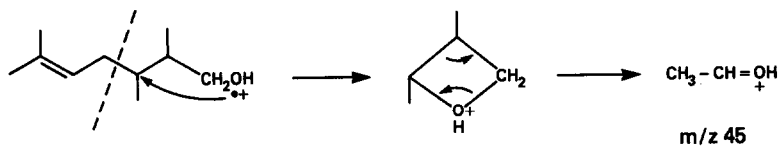
Citronellol, 3,7-dimethyl-6-octenol, is widely distributed in insects, and has been found in the secretions of a number of species of ants in the genus *Lasius*, either as a major volatile component (*L. umbratus*) or as a relatively minor one (*L. alienus, L. speculiventris, L. neoniger*).[1] We have examined the mandibular gland secretion of *L. meridionalis* and report a novel acyclic monoterpenol, structurally isomeric with citronellol, as the major volatile constituent.

Examination of the CH_2Cl_2 extracts of excized mandibular glands from male *L. meridionalis* collected in Oland, Sweden, revealed the presence of five volatile components, and larger amounts of this mixture could be obtained from the extracts of whole heads. The major component (85% of the mixture) had a molecular ion at m/z =156 as did two of the minor components, one of which had GC/MS behavior identical to that of citronellol. The other minor components were probably homologues of these compounds, having molecular ions at m/z=170.

The two largest fragments in the mass spectrum of the major component, m/z = 41 and 69, suggested a terminal isopentenyl group similar to that of citronellol, while an intense ion at m/z =45 initially suggested a secondary alcohol. All of the components of the natural mixture took up one equivalent of hydrogen (H_2; Pd/C), and silylation (BSTFA) of the reduction mixture provided five trimethylsilyl ethers, all having an intense

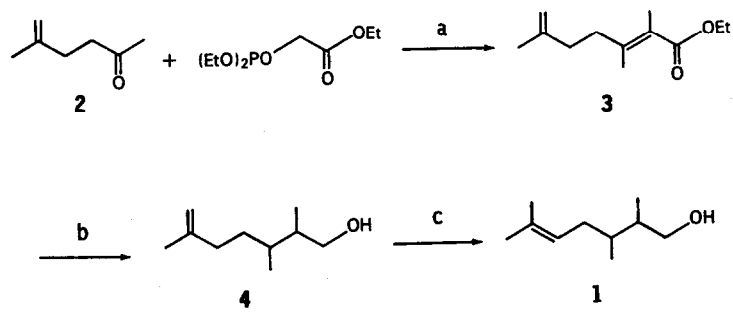
fragment ion at m/z=103, $[CH_2=O-SiMe_3]^+$, indicating that they were derived from primary alcohols.[2]

Since the amount of the natural mixture available was limited and the one unknown constituted so much of the mixture, ^1H and ^{13}C nmr spectra were obtained directly.[3] A broad triplet (1H) at 5.1ppm and two broad singlets (3H) at 1.59 and 1.69 ppm were consistent with two gem methyl groups on a trisubstituted double bond and a multiplet (2H) at 3.5ppm represented the methylene protons of a primary alcohol. Two doublets, 0.86ppm (3H, J=6.7Hz) and 0.92ppm (3H, J=6.6Hz) showed that the unknown must have two vicinal tertiary methyl groups. Only one structure, 2,3,6-trimethyl-6-heptenol (1) satisfies all these requirements, and the compound, which we have named lasiol, is therefore a biogenetically anomalous terpene possessing the lavandulyl skeleton. The unusually intense fragment ion at m/z=45 in the mass spectrum of lasiol can be explained by the following fragmentation scheme:



A rapid confirmation of the overall structure of lasiol was obtained from a non-stereoselective synthesis beginning with 5-methyl-5-hexen-2-one (2)[4] (SCHEME I). The diunsaturated ester **3** was formed in 66% yield and reduced to **4** in two steps in 70% yield. The isomerization of **4** to **1** was carried out with NaH in ethylenediamine/TMEDA, conditions that were operationally more convenient than those described previously.[5] This procedure provided 80% of a product with GC/MS behavior identical to lasiol. It was an inseparable (GC) 2:1 mixture of the stereoisomers in which the ^1H and ^{13}C nmr signals of the major isomer matched those of natural lasiol.

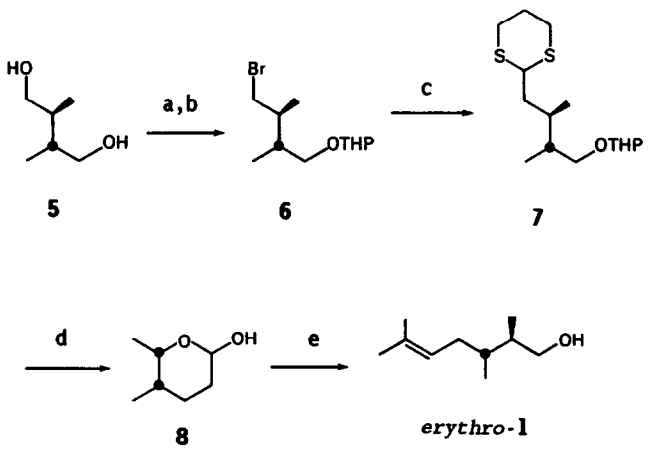
SCHEME I



Reagents: a) NaH; b) Mg/MeOH, then $LiAlH_4$; c) NaH, 1:1 TMEDA, $(H_2NCH_2)_2$, reflux 20 min.

To establish the C-2, C-3 stereochemistry of lasiol, *erythro*-1 was prepared from *meso*-2,3-dimethyl-1,4-butanediol (5)[6] (SCHEME II). Continuous extraction of a mixture of 5 and 9N HBr with hexane[7] provided a 30% yield of 4-bromo-2,3-dimethyl-1-butanol which was converted nearly quantitatively to its tetrahydropyranyl ether 6. Lithio-1,3-dithiane was alkylated with 6, and both protecting groups of the thioacetal 7 were removed to form hemiacetal 8 in 60% yield from 6. Treatment of 8 with an excess of sodium triphenylphosphoniumisopropylid provided 80% of *erythro*-1 whose ^{1}H and ^{13}C spectra were identical to those of natural lasiol and those of the major stereoisomer of the mixture of 1 formed in SCHEME I.

SCHEME II



Reagents: a) 9N HBr, 60°, hexane extract, 7 days; b) DHP, ptsa; c) lithio-1,3-dithiane; d) $HgCl_2/CaCO_3$; e) Na $Ph_3PCH(CH_3)_2$.

The lavandulane (2,3,6-trimethylheptane) monoterpenes are relatively rare natural products. Lavandulol, 2-isopropenyl-5-methyl-4-hexen-1-ol, the only major naturally occurring member of this class of compounds, is a component of lavender oil (*Lavendula vera*) along with several minor bifunctional lavandulyl compounds. These compounds all bear an oxygen function on the C-3 methyl in contrast to the C-1 alcohol of lasiol.[8]

The superficial similarity of the mass spectra of lasiol and citronellol raises the possibility that lasiol may have been misidentified in cursory GC/MS examinations of other insect exocrine secretions. Indeed, the unidentified monoterpenol we reported from mandibular glands of two species of ants in the genus *Myrmecocystus* (*M. colei* and *M. wheeleri*) has a mass spectrum identical to that of lasiol.[9] The role of lasiol in the mandibular secretions of male *L. meridionalis* has not yet been established. It is conceivable that this new terpenol is a sex attractant since it is not found in extracts

of females and workers of this species, and the behavioral role of volatile compounds from the male mandibular glands of other ant species has been known for some time.[10]

References and Notes

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3. The following spectral data were obtained for natural lasiol: ^{1}H nmr δ=5.12(1H, br t), 3.4-3.6(2H, m), 2.1-1.6(4H, m), 1.7(3H, br s), 1.6(3H, br s), 0.92(3H, d, J=6.6Hz), 0.87(3H, d, J=6.7Hz); ^{13}C nmr δ=131.98, 123.54, 66.06, 40.23, 35.50, 31.39, 25.77(2C), 16.94, and 13.76; MS m/z(rel. intensity) 156(13, M+), 138(6), 123(19), 109(12), 97(15), 96(20), 95(17), 85(22), 82(21), 81(15), 71(13), 70(52), 69(100), 68(12), 67(15), 57(17), 56(18), 55(49), 45(59), 43(35), 42(16), 41(82), and 31(15). The minor, *threo* isomer had the following readily observable differences in its nmr spectra: ^{1}H nmr δ=0.83(3H, d, J=6.8Hz), 0.78(3H, d, J=6.7Hz); ^{13}C nmr δ=131.98, 123.54, 66.83, 39.05, 34.16, 33.35, 25.77(2C), 17.64, and 14.40.

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(Received in USA 22 June 1990)