prepared from (6*E*)-neroridol via the Claisen rearrangement.[20]

The transformation of **5** to **10** not only presents the first example of the unprecedented tandem sequence in which *the oxy-Cope triggers the Cope rearrangement* but also furnishes the overall sequence depicted by eq 3 in Scheme I. Furthermore, the new sequence provides a novel, versatile method for the synthesis of functionalized 1,5-diene derivatives which are commonly found in many terpenoid natural products. In particular, farnesylacetaldehyde obtained above is a promising precursor of geranyl farnesylacetate (so-called Gefarnate), a commercial antiulser agent.[21]

Further stereochemical studies of the three new sigmatropic sequences outlined in this study and their applications to natural product synthesis are in progress.

Registry No. *erythro*-**2a**, 79705-03-6; *threo*-**2a**, 79705-02-5; *erythro*-**2b**, 79803-44-4; *threo*-**2b**, 79803-45-5; *erythro*-**3a**, 79803-46-6; *threo*-**3a**, 79803-47-7; (*E*)-**4a**, 21662-19-1; (*Z*)-**4a**, 21661-98-3; (*E*)-**4b**, 41547-29-9; (*Z*)-**4b**, 41547-22-2; *erythro*-**5a**, 79803-48-8; *threo*-**5a**, 79803-49-9; *erythro*-**5b**, 79803-50-2; *threo*-**5b**, 79803-51-3; *erythro*-**5c**, 79803-52-4; *threo* **5c**, 79803-53-5; **5d**, 79803-54-6; **5e**, 79803-55-7; **5f**, 79803-56-8; **6a**, 79803-57-9; **6b**, 79761-79-8; (*E*)-**6c**, 79803-58-0; **6d**, 79772-67-1; **7** (R = CH_3; R′ = H), 79803-59-1; **7** (R = H; R′ = $(CH_2)_2CH{=}CH_2$, 79803-60-4; **8e**, 79803-61-5; **8f**, 79803-62-6; **9e**, 79803-63-7; **9f**, 79803-64-8; (*E*)-**10e**, 18445-88-0; (*Z*)-**10e**, 18445-81-3; (*Z*,*E*)-**10f**, 79803-65-9; (*E*,*E*)-**10f**, 67858-78-0; (*Z*,*Z*)-**10f**, 79803-66-0; (*E*,*Z*)-**10f**, 79803-67-1; 3,4-dimethyl-1,5-hexadien-3-ol, 30884-86-7; (*E*)-oct-6-en-2-one, 51193-76-1; (*Z*)-oct-6-en-2-one, 74810-53-0; (*E*)-2,7-octadienol, 62179-18-4; geraniol, 106-24-1; nerol, 106-25-2; (*E*)-nerolidol, 40716-66-3; (*Z*)-nerolidol, 3790-78-1.

Supplementary Material Available: Tables containing experimental results of the oxy-Cope rearrangement and spectral data for new compounds (6 pages). Ordering information is given on any current masthead page.

(20) In a similar manner, another authentic mixture (4*E*/4*Z*, 2:1) of (8*Z*)-**10f** was prepared from (6*Z*)-neroridol.

(21) Activity: Adami, E. *Experimentia* **1962**, *18*, 461. Takagi, K.; Okabe, S. *Jpn. J. Pharmacol.* **1968**, *18*, 9. Synthesis: Pala, G; Mantegani, A.; Bruzzese, T.; Sekules, G. *Helv. Chim. Acta* **1970**, *53*, 1827. Fujita, Y.; Ohmura, Y.; Nishida, T.; Itoi, K. U.S. Patent 3 928 403.

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Lasidiol Angelate: Ant Repellent Sesquiterpenoid from *Lasiantheae fruticosa*

Summary: Lasidiol angelate, a new sesquiterpenoid containing a carotane skeleton, has been isolated from *Lasiantheae fruticosa* (Compositae). A structure was proposed on the basis of spectral evidence and confirmed by a synthesis which achieves oxidation α to the less substituted terminus of a trisubstituted double bond by a double-reverse strategy. The natural products and several of the synthetic compounds are potent ant repellents.

Sir: The leafcutter ants, which are abundant from Texas to Argentina, are polyphagous herbivores. Among their preferred host plants are many of commercial value, including citrus, banana, and coffee.[1] This has led to the classification of leafcutter ants as serious agricultural pests in most of the New World, including the United States.

While the leafcutter ants are broadly polyphagous, many native plants do escape their attack. Plant defenses against their herbivory might take many forms, but it is reasonable to postulate that some plants have evolved chemical defenses.[2] We have developed bioassays to measure the relative acceptability of various species and the palatability of plant extracts to leafcutter ants.[3] Using these bioassays to direct an isolation sequence, we have isolated an ant repellent sesquiterpenoid from *Lasiantheae fruticosa* (Compositae), a plant common within the range of *Atta cephalotes* Hymenoptera, Formicidae, Attini) but not attacked by this ant.

The active compound (ca. 35 mg) was isolated from the chloroform extract of *L. fruticosa* leaves (2.3 kg) by a sequence of column and preparative layer chromatography. The electron impact (EI) mass spectrum of this compound does not show a molecular ion, but the chemical ionization (CI) mass spectrum revealed a molecular weight of 320. Because the ^{13}C NMR spectrum shows 20 carbons, including an ester group and a hydroxylic carbon (δ 167.3, 83.2, 77.3), a molecular formula of $C_{20}H_{32}O_3$ could be deduced. The delayed decoupled[4] ^{13}C NMR spectrum allowed recognition of two trisubstituted double bonds (δ 142.3, 122.2, 138.4, 127.8) and six methyl groups (δ 25.7, 24.3, 22.7, 21.3, 20.9, 15.7). Therefore, this compound, with a total of five degrees of unsaturation, must be bicyclic. The upfield portion of the ^1H NMR spectrum revealed three methyl groups attached to double bonds, a methyl singlet, and an isopropyl group. In the downfield region of the spectrum a quartet (δ 6.04, 1 H, J = 6 Hz) and two doublets (δ 5.16, 1 H, J = 6 Hz; δ 5.42, 1 H, J = 6 Hz) are visible. Homonuclear decoupling experiments confirmed spin–spin coupling between the two doublets and also established coupling between the quartet and an upfield methyl group (δ 1.9, 3 H, J = 6 Hz). The ^1H and ^{13}C NMR data indicate that this compound is a sesquiterpenoid containing a tertiary hydroxyl group and bearing a secondary angelate ester.[5,6]

To further characterize this sesquiterpenoid, a small portion of our sample (6 mg) was reduced with $LiAlH_4$ to afford a C_{15} diol. The CI mass spectrum confirmed the expected molecular weight of 238. As predicted, in the ^{13}C NMR spectrum the carbon bonded to the newly formed hydroxyl group shifted upfield by ca. 2 ppm (to δ 75.4). Because the carbons of the double bond and a quaternary carbon also shifted, it appeared as though this secondary hydroxylic carbon was flanked by these two groups. The ^1H NMR spectrum also is consistent with these conclusions. One methyl signal had shifted slightly upfield, while the two methyl signals of the angelate were absent. The signal for the proton geminal to the newly formed hydroxyl group was observed at δ 4.0 vs. a chemical shift of δ 5.4 in the ester. These facts are summarized by part structure 1.

For completion of a structure assignment, the diol (all 3 mg) was oxidized with pyridinium chlorochromate (PCC) to afford a keto alcohol. The EI mass spectrum showed

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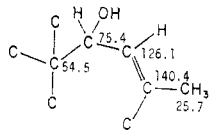

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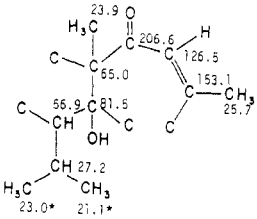
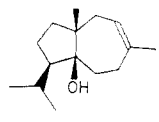


2

Figure 1. Partial structures with ^{13}C NMR assignments.

the expected molecular ion of m/z 236 (8%), while a carbonyl carbon (δ 206.6) was apparent in the ^{13}C NMR spectrum. The carbon resonance for one quaternary carbon shifted ca. 10 ppm downfield while the resonance for the β sp^2 carbon also shifted downfield (ca. 13 ppm). Smaller shifts were observed for other carbons; the most informative was the upfield shift of the remaining quaternary (hydroxylic) carbon, which suggested that this carbon was β to the carbonyl group. In the ^1H NMR spectrum, one methyl singlet shifted slightly downfield (from δ 0.99 in the diol to δ 1.2 in the ketone), suggesting a methyl group β to the carbonyl group. After comparison with ^{13}C NMR data for known monoterpenoids,[7] the relative position of the isopropyl group could be assigned. To best account for the observed chemical shifts, a carbon β to the isopropyl group should bear a hydroxyl substituent. These observations are summarized in partial structure **2** (see Figure 1).

For completion of the structure determination, it was necessary to construct a bicyclic compound while accounting for the four remaining resonances in the ^{13}C NMR spectrum of the keto alcohol (δ 39.4, 32.7, 31.0, 24.5, all CH_2's). From the IR absorbance of the ketone carbonyl group (1670 cm^{-1}), it was clear that the enone could not be part of a five-membered ring. Of the remaining possibilities, a structure (e.g., **6**) based on a carotane skeleton would be most compatible with our data. Compounds containing this hydroazulene skeleton have been observed although they are not common.[8] Perhaps the best known compounds of this type are carotol **3**[9] and laserol **4**.[10]



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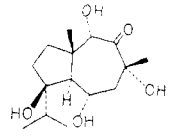
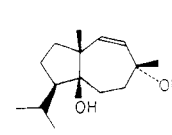


4

To confirm our proposed structure (**6**) and to determine the stereochemistry of the natural product, we decided to synthesize this compound. Because the structure and absolute stereochemistry of carotol had been established, both by X-ray crystallography[11] and by total synthesis,[9] it is an ideal starting material. Preparation of the ketone **6** could be achieved by oxidation of carotol α to the less substituted end of the double bond. To obtain the necessary regioselectivity, we employed a "double reverse" strategy. As expected,[12] the allylic alcohol **5** was the major product of the photooxidation of carotol (ca. 20% yield following isolation by column chromatography). Oxidation of this allylic alcohol with PCC[13] gave the desired ketone **6** (80% yield). This synthetic ketone, prepared by a new strategy complementary to SeO_2 oxidation, is identical in all respects[14] with the ketone prepared from the natural ester. This finding confirmed our earlier structure assignments and established the absolute stereochemistry.

Reduction of ketone **6** with 9-borabicyclo[3.3.1]nonane gave a mixture of diols. The major product, identical with the diol prepared earlier from the natural ester, was assigned structure **7a** by assuming predominant reduction



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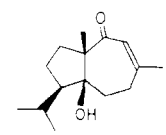
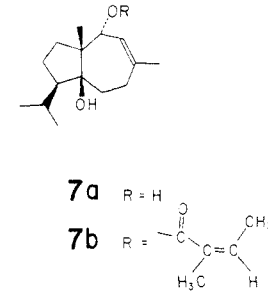


6



7a R = H

7b R =

from the less hindered face of the ketone. Thus structure **7b**, including the indicated absolute stereochemistry, represents the natural ester we have named lasidiol angelate.[15]

Both lasidiol angelate and the synthetic ketone **6** are potent ant repellents in our bioassays;[16] the natural ester may well be an important component of *L. fruticosa*'s defenses against leafcutter ants. Further work to establish the mechanism(s) responsible for this biological activity and to characterize other plant defenses against the leafcutter ants is in progress.

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Registry No. **3**, 465-28-1; **5**, 79803-25-1; **6**, 79803-26-2; **7a**, 79803-27-3; **7b**, 79803-28-4.

Supplementary Material Available: Details on isolation and properties of lasidiol angelate (**7b**), preparation of **7a**, and **6**, and photooxidation of carotol (3 pages). Ordering information is given on any current masthead page.

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(14) Identity was established by gas and thin-layer chromatography and ^1H (90 MHz) and ^{13}C NMR spectroscopy, and mass spectrometry.
(15) The IUPAC name for this compound is (1*R*,3a*R*,4*R*,8a*S*)-1,2,3,3a,4,7,8,8a-octahydro-8a-hydroxy-1-isopropyl-3a,6-dimethyl-4-azulenyl (*Z*)-2-methylcrotonate.
(16) A concentration of 33 μg/rye flake causes significant rejection of this potential food. Hubbell, S. P., personal communication, 1981.

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