Metabolites of bird's nest fungi. Part 6.[1] The synthesis of (±)-cybullol and a new synthesis of (±)-geosmin

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The stereoselective transformation of 6,10-dimethyl-4-octal-3-one (**8**) to racemic cybullol (**1**), a metabolite of *Cyathus bulleri* Brodie, is reported. The transformation 4,10-dimethyl-4-octal-3-one to (±)-geosmin (**15**) is described. The results of the photosensitized [4 + 2] cycloaddition of oxygen to a number of 10-methyl-2,4-hexalins are discussed.

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On rapporte la transformation stéréosélective de la diméthyl-6,10 octal-4 one-3 (**8**) en cybullol racémique (**1**), un métabolite du *Cyathus bulleri* Brodie. On décrit la transformation de la diméthyl-4,10 octal-4 one-3 en (±)-géosmine (**15**). On discute des résultats obtenus lors de la cycloaddition photosensibilisée [4 + 2] de l'oxygène à un certain nombre de méthyl-10 hexalines-2,4.

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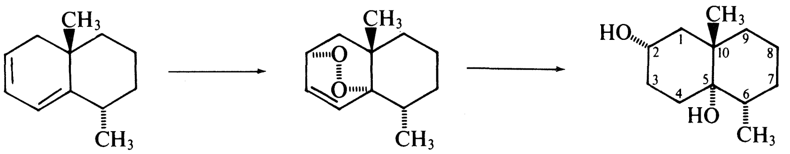
Examination of the metabolites of some of the small gastromycetous fungi known as Bird's Nest fungi (Nidulariaceae) in these laboratories has led to the isolation of a variety of terpenoid (*e.g.*, *Cyathus helenae* Brodie (1), *Cyathus bulleri* Brodie (2)) and non-terpenoid (*e.g.*, *Cyathus intermedius* (3)) constituents. We now wish to report the stereoselective synthesis of racemic cybullol (**1**), a degraded eudesmane-type sesquiterpene produced by *C. bulleri* (2). At the same time we report a new, high yield, synthesis of the related fungal metabolite, geosmin (4).

Cybullol, **1**, is a dimethyldecalindiol in which the two hydroxyl groups bear a *cis*-1,4-relationship in a *trans*-fused system. A facile synthetic approach to a *cis*-1,4-cyclohexanediol system involves the [4 + 2] cycloaddition of a 1,3-cyclohexadiene with molecular oxygen to give a cyclic peroxide, followed by reduction, as outlined in Scheme 1.

It is well documented that the photooxygenation of steroidal conjugated dienes is sensitive to steric effects (oxygen as a dienophile, ref. 5*a*; sensitized photooxygenation of olefins, ref. 5*b*) and that the *endo*-peroxide produced is usually on the side opposite to nearby angular methyl groups. However, relatively few examples of photooxygenation of hexalin dienes have been reported (6). In order to further investigate the stereochemistry of photooxygenation of hexalin systems as well as to provide a model compound for a ^{13}C nuclear magnetic resonance (cmr) study reported elsewhere (7), we examined initially the photooxygenation of 10-methyl-2,4-hexalin, **4** (Scheme 2).

The diene **4** was prepared from 10-methyl-4-octal-3-one (8) by the method of Dauben *et al.* (9). Photosensitized oxygenation (5, 6) in the presence of eosin Y yielded the *endo*-peroxide **5** and the γ-hydroxyenone **6**. Catalytic hydrogenation of the *endo*-peroxide gave a crystalline diol, which was assigned the relative stereo-



2 **3** **1**

SCHEME 1

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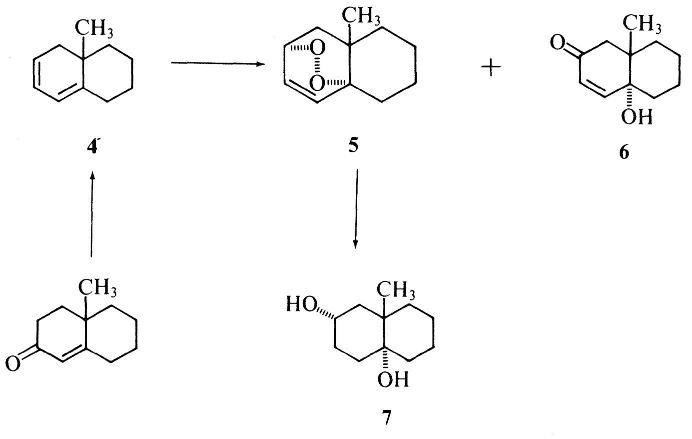
[1] For part 5 see ref. 3.

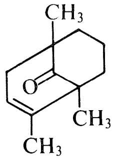


SCHEME 2

chemistry shown in **7** on the basis of pyridine induced shifts (relative to chloroform) of the methyl protons in the proton magnetic resonance (pmr) spectrum (2, 10). For diol **7**, the pyridine shift is −0.04 for the C-10 methyl. Since the equatorial secondary hydroxyl at C-2 should not influence these induced shifts (10), these data indicate that the tertiary hydroxyl is antiperiplanar to the tertiary methyl, *i.e.*, the diol obtained has the relative stereochemistry shown in **7**. It follows that the *endo*-peroxide has structure **5** and that oxygenation occurred on the side opposite to the angular methyl. Interestingly the cmr spectrum of diol **7** shows the tertiary methyl signal at low field (δ 21.0) similar to that observed in cybullol (δ 21.1) and other *trans*-10-methyl-5-decalols (2). This unusual deshielding (11) by antiperiplanar hydroxyl is discussed in detail elsewhere (7).

The octalone required for the synthesis of cybullol, **1** (Scheme 3) is *trans*-6,10-dimethyl-4-octal-3-one, **8**. Compound **8** is not readily accessible by applying the usual annelation procedures to 2,6-dimethylcyclohexanone (ref. 12, and references cited therein). In most cases low yields of **8** are obtained, or the predominant product formed is 1,2,5-trimethylbicyclo[3.3.1]-non-2-en-9-one (**9**). Several modified annelation procedures for the preparation of **8** have been reported (12, 13). In our hands, the method of Hooz and Benderley (13*a*) and that of Caine and Tuller (13*b*) were most convenient for large scale preparation. Octalone **8** was transformed to the conjugated diene **2** by treatment of the tosylhydrazone of **8** with *n*-butyllithium (9). Purification by chromatography over silica gel gave compound **2** in 50% yield. Subsequently it was found that compound **2** could be prepared in high purity and in greater than 80% yield from **8** by lithium aluminum hydride reduction to the allylic alcohol **10** followed by pyrolysis (6*b*, 14).

Photooxygenation of **2** did not yield the cyclic peroxide as readily as had been anticipated from the model studies. The products from the photooxygenation experiments varied depending on the conditions. For example, photooxygenation of a methanol–benzene solution of **2** in the presence of eosin Y at room temperature overnight gave a mixture of several compounds (thin layer chromatogram, tlc) from which *endo*-peroxide **3** could be isolated in low yield. Low temperature (−78 °C) photooxygenation of **2** in the presence of eosin Y was complete after 8 h (disappearance of diene). Chromatographic separation of the reaction mixture gave traces of *endo*-peroxide **3** along with the γ-hydroxyenone **11** (13%) and the diepoxide **12** (13%). Presumably compound **12** arises by photochemical rearrangement of **3** since it is known that this type of rearrangement occurs under both photochemical and thermal conditions (15). Low temperature photooxygenation of a methanol–ether solution of **2** in the presence of eosin Y and rose bengal was complete in 2 h. The photolysis mixture consisted mainly of compound **3** together with small amounts of compound **12** (tlc). Chromatographic separation of the components led to isolation of *endo*-peroxide **3** in 20% yield. Catalytic hydrogenation of **3** over platinum oxide provided in 49% yield, crystalline



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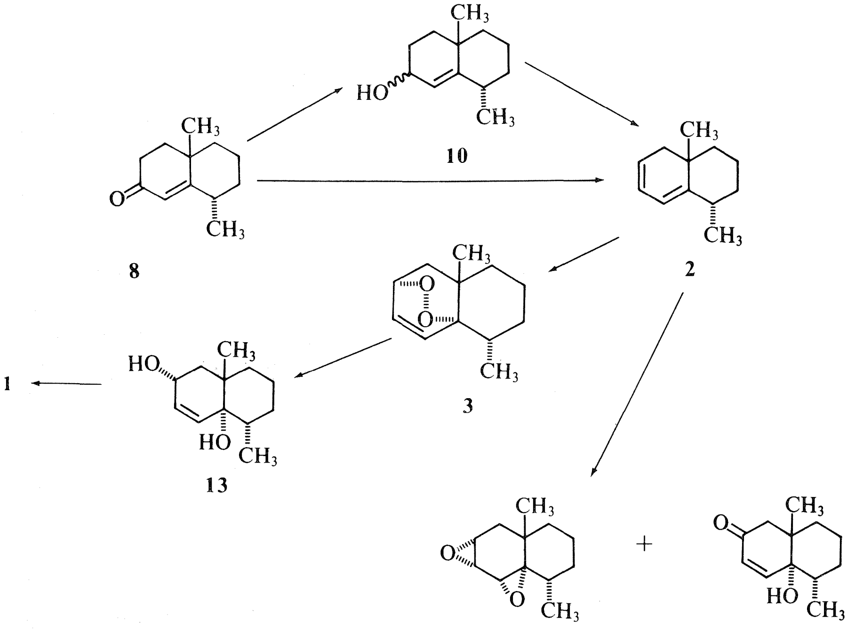
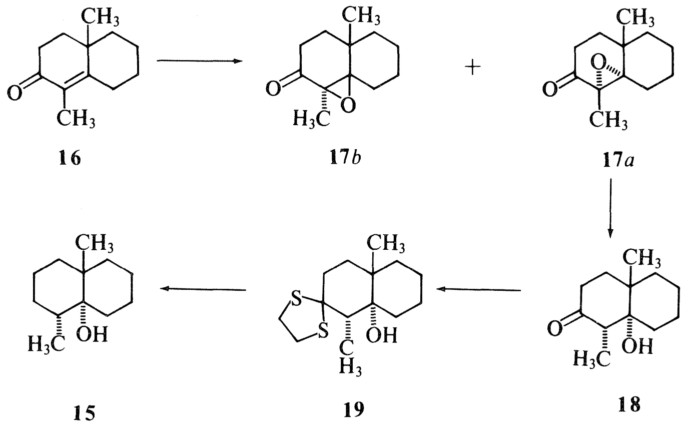


SCHEME 3

(±)-cybullol, identical with an authentic sample (2).

In an effort to improve the overall yield in the sequence **2** to **1**, several other synthetic routes were explored. Two chemical methods (16, 17) for generating the reactive oxygen species were investigated but neither method led to improved yields of compound **3**. Attempted transformation of diene **2** to *endo*-peroxide **3** by treatment with a large excess of sodium hypochlorite – hydrogen peroxide (16) gave unreacted starting material. Treatment of **2** with the triphenylphosphite–ozone complex (17) gave *endo*-peroxide **3** in only 15% yield. Attempted conversion of the initially formed cyclic peroxide *in situ* to the more stable allylic diol **13** by photooxygenation in the presence of thiourea (18) was unsuccessful. The crude photolysis product contained the same mixture of compounds (tlc) as the product obtained in the absence of thiourea. We also explored the use of **11** and **12** as precursors to cybullol. Lithium aluminum hydride reduction of γ-hydroxyenone **11** gave a 1:2 mixture of allylic diol **13** and its C-2 epimer, whereas lithium aluminum hydride reduction of diepoxide **12** gave a 1:3 mixture of cybullol and an unidentified compound. An improved overall yield of **1** was obtained when it was found that a change of solvent (ether–methanol (1:1) to methylene chloride) in the photooxygenation reaction gave increased yields of compound **3**. Thus low temperature photooxygenation of a methylene chloride solution of **2** in the presence of rose bengal led to *endo*-peroxide **3** in 46% overall yield from **10**. It was also found that a two step transformation of **3** to **1** proceeded



SCHEME 4

more efficiently than direct catalytic hydrogenation. Treatment of **3** with aluminum amalgam (19) yielded the crystalline allylic diol **13** in 77% yield. Catalytic hydrogenation of **13** then gave cybullol (**1**) in quantitative yield.

Geosmin, **15**, a degradation product of cybullol, is the fungal metabolite responsible for the 'earthy' aroma of freshly plowed soil (20) and beetroot (21), and the muddy taste in surface water supplies (22) and trout (23). The constitution of geosmin was first suggested by Gerber (24) and the structure and relative stereochemistry proven by Marshall's stereoselective synthesis (4) of the racemic form. Herein we report another stereoselective synthesis of racemic geosmin in 24% overall yield from the dimethyloctalone **16** (Scheme 4).

Oxidation of dimethyloctalone **16** (25) with alkaline hydrogen peroxide gave an 85% yield of a 6:5 mixture of α- and β-epoxy ketones, **17***a* and **17***b* (26). The epimeric mixture **17** was not separated but was reduced directly with lithium in ammonia. The product obtained was a viscous oil which partially solidified on standing. Isolation of the solid material by crystallization gave in 53% yield a single crystalline ketol; the mother liquors contained mainly unreacted epoxy ketone **17***b*. The ketol so obtained was assigned the relative stereochemistry shown in **18** on the basis of pyridine induced shifts of the C-10 methyl ($\Delta\delta$ +0.04) in the pmr spectrum (2, 10, 27). Removal of the carbonyl in **18** was effected in over 95% yield by thio ketal formation followed by desulfurization with Raney nickel. The crystalline product obtained was identical in ir, pmr, mass spectrum, and tlc behavior with (−)-geosmin (2, 28). Geosmin has not previously been obtained in crystalline form. It is interesting to note that the crystalline material has the characteristic penetrating odor of natural geosmin.

Experimental

Mass spectra were recorded on an A.E.I. model MS-9 or MS-12 mass spectrometer and are reported as *m/e* (relative intensity). Unless diagnostically significant only peaks at least 20% as intense as the base peak are reported. Infrared spectra were recorded on a Unicam SP1000 or a Perkin Elmer Model 421 dual grating spectrophotometer. Proton magnetic resonance spectra were measured using a Varian HA-100 spectrophotometer with tetramethylsilane as internal standard. Melting points were recorded on a Fisher–Johns melting point apparatus and are uncorrected.

Silica gel tlc plates were 0.5 mm silica gel G (E. Merck, Darmstadt) containing 1% electronic phosphor (General Electric, Cleveland); materials were detected by spraying with 30% sulfuric acid and charring. Silica gel (Woelm, less than 0.08 mm) was used for elution chromatography.

General Procedure for Photooxygenation

A solution of diene and sensitizer was irradiated through a pyrex filter with a Hanovia 250 W medium pressure mercury dispersion lamp while oxygen was bubbled through the reaction mixture. The reaction was monitored by the disappearance of diene (tlc). When all diene had been consumed, the photolysis mixture was concentrated and either separated or used as such in subsequent reactions as described below.

10β-Methyl-2α,5α-epidioxy-3-octalin, **5**

Photooxygenation of 10-methyl-2,4-hexalin (**4**) (8) (0.58 g) was carried out in benzene–methanol (1:1, 200 ml) containing eosin Y (5 mg) for 12 h. Thin layer chromatography (pentane–ether, 4:1) showed the presence of two components (R_f 0.41, 0.12). Elution chromatography with pentane–ether (9:1) gave *endo*-peroxide **5** as an oil (0.30 g, 43%, R_f 0.41); pmr ($CDCl_3$) δ 0.96 (s, 3, C-10 CH_3), 1.32 (d of d, 1, J = 2.2, 13 Hz, H-1α), 1.86 (d of d, 1, J = 4, 13 Hz, H-1β), 4.53 (octet, 1, J = 1.5, 2.2, 4, 5.7 Hz, H-2β), 6.23 (d of d, 1, J = 1.5, 8 Hz, H-3), 6.54 (d of d, 1, J = 5.7, 8 Hz, H-4); double irradiation at 4.53 collapses 1.32, 1.86, 6.23, 6.54 to doublets; ms m/e calcd. for $C_{11}H_{16}O_2$: 180.1150, found: 180.1157 (6), 148(52), 133(27), 105(29), 97(23), 95(54), 93(25), 91(34), 83(30), 82(55), 81(38), 79(26), 69(33), 67(58), 56(25), 55(99), 53(27), 43(36), 41(100). Further elution gave 5α-hydroxy-10β-methyl-3-octal-2-one, **6** (R_f 0.12); ir ($CHCl_3$) 1660 (C=O), 1620 (C=C) cm^{-1}; pmr ($CDCl_3$) δ 1.24 (s, 3, C-10 CH_3), 6.10 (br s, 1, OH), 6.20 (d of d, 1, J = 2, 10 Hz, H-4), 6.77 (d, 1, J = 10 Hz, H-3); ms m/e calcd. for $C_{11}H_{16}O_2$: 180.1151, found: 180.1158 (2), 162(100), 147(28), 134(25), 119(48), 106(33), 105(37), 91(78).

10β-Methyl-2α,5α-decalin Diol, 7

A solution of *endo*-peroxide **5** (0.13 g) in ether (20 ml) was hydrogenated over palladium–charcoal (5%; 10 mg) at 40 psi hydrogen for 1 h. The product was filtered, concentrated, and purified by preparative tlc (ether) to give crystalline diol **7** (0.07 g, 49%); mp 167–169 °C; ir ($CHCl_3$) 3600, 3450 (OH) cm^{-1}; pmr ($CDCl_3$) δ 1.02 (s, 3, C-10 CH_3), 3.98 (septet, 1, J = 5 Hz, H-2a); pmr (pyridine-d_5) δ 1.06 (s, 3, C-10 CH_3); ms m/e calcd. for $C_{11}H_{20}O_2$: 184.1463, found: 184.1466 (46), 176(73), 151(61), 148(28), 138(35), 137(41), 128(39), 127(76), 123(26), 122(26), 112(100), 111(43), 110(28), 109(63), 108(48), 97(35), 95(39), 93(30), 85(73), 84(35), 83(50), 82(68), 81(46), 73(52), 71(33), 69(40), 68(41), 67(46), 57(39), 55(63), 43(65), 41(65). *Anal.* calcd. for $C_{11}H_{20}O_2$: C 71.70, H 10.94; found: C 71.21, 71.09, H 10.86, 10.90.

6α,10β-Dimethyl-2,4-hexalin, 2

(a) Via Tosylhydrazone of 8

6α,10β-Dimethyl-4-octal-3-one, **8** (12*a*, *b*) (1.0 g), tosylhydrazine (1.1 g), and acetyl chloride (20 μl) in anhydrous tetrahydrofuran (30 ml) were heated under reflux for 3.5 h. Anhydrous benzene (50 ml) was added and the solvents removed by distillation until a boiling point of 80 °C was reached. The reaction flask was cooled (5 °C) and *n*-butyllithium (8 ml, 1.9 *M*) was added. After stirring overnight, the reaction mixture was diluted with water and sodium chloride added to saturate the solution which was then extracted with ether. The ether extract was dried ($MgSO_4$) and concentrated. Elution chromatography of the product (pentane) gave diene **2** (0.45 g, 50%) as a yellow oil.

(b) Via Pyrolysis of Allylic Alcohol 10

A solution of octalone **8** (3.7 g) in ether (70 ml) was added dropwise to a cooled (0 °C) solution of lithium aluminum hydride in ether (70 ml, 0.5 *M*). The reaction mixture was allowed to stir at room temperature for 1 h, then excess hydride was destroyed and the product isolated in the usual way. 6α,10β-Dimethyl-4-octal-3-ol (3.6 g, 97%) was isolated as an oil; ir (neat) 3350 (OH), 1655 (C=C) cm^{-1}; pmr ($CDCl_3$) 0.99 (d, 3, J = 7 Hz, C-6 CH_3), 1.11 (s, 3, C-10 CH_3), 4.2 (br s, 1, H-3), 5.4 (br s, 1, H-4); ms m/e calcd. for $C_{12}H_{20}O$: 180.15142, found: 180.15149 (1), 162(60), 147(100), 119(27), 105(45), 91(51).

Allylic alcohol **10** (0.5 g) was impregnated on pyridine treated alumina (5 g, Woelm neutral grade activity I, mixed with 2% w/v anhydrous pyridine) and loosely packed in a glass gas chromatography column (5 ft × $\frac{1}{4}$ in.). The column was placed in a gas chromatograph oven with one end connected to the injector and the other connected directly to the collector. The flow rate of carrier gas was set ~150 ml/min, then the oven was heated to 250 °C, and maintained at that temperature for 2 h. The pyrolysis product (collected in a U-shaped tube immersed in a dry ice – acetone bath) was obtained as a colorless oil (0.36 g, 80%); λ_{max} (EtOH) 248, 254, 266, 274 nm; ir (neat) 3020, 1640, 1585 (C=C) cm^{-1}; pmr ($CDCl_3$) δ 0.98 (s, 3, C-10 CH_3), 1.17 (d, 3, J = 8 Hz, C-6 CH_3), 5.58 (m, 3, H-2, H-3, H-4); ms m/e calcd. for $C_{12}H_{18}$: 162.14085, found: 162.14071 (63), 147(83), 119(34), 106(35), 105(75), 93(22), 91(100), 79(24), 77(25), 55(24), 41(46).

Diene **2** was characterized further as its Diels–Alder adduct with 4-phenyl-1,2,4-triazoline-3,5-dione (27); mp 128–130 °C (from ether). *Anal.* calcd. for $C_{20}H_{23}N_3O_2$: C 71.19, H 6.87, N 12.45; found: C 71.23, 71.17, H 6.78 6.76, N 12.67 12.72.

Photooxygenation of Diene 2

Photooxygenation of diene **2** (0.35 g) in methanol–benzene (4:1) containing eosin Y (5 mg) overnight gave a crude reaction mixture which contained at least six components (tlc silica gel, pentane–ether, 1:1). Separation of the mixture by preparative tlc (pentane–ether, 1:1) led to the isolation of *endo*-peroxide **3** (0.05 g, 13%) as an oil.

Photooxygenation of diene **2** (0.47 g) in methanol–ether (1:1) containing eosin Y (~10 mg) at −78 °C for 8 h gave a crude reaction mixture which contained at least six components (tlc). Elution chromatography of a portion of the product (pentane–ether, 4:1) led to the isolation of traces of *endo*-peroxide **3**, (0.009 g, 4%) γ-hydroxyenone **11** (0.03 g, 13%) and diepoxide **12** (0.03 g, 13%).

Photooxygenation of diene **2** (0.55 g) in ether–methanol (1:1) containing eosin Y (0.005 g) and rose bengal (0.005 g) at −78 °C was complete in 2 h. The concentrated photolysis mixture was divided into two equal portions. One portion was purified by elution chromatography (pentane–ether, 9:1) to yield *endo*-peroxide **3** (0.06 g, 20%) as an oil. The remaining portion was dissolved in ether–methanol (1:1, 20 ml) and hydrogenated over platinum oxide at 40 psi hydrogen for 1 h. The solution was filtered and concentrated. Elution chromatography gave cybullol, **1** (0.06 g, 20%).

Photooxygenation of diene **2** (obtained by pyrolysis of allylic alcohol **10** (0.50 g)) in methylene chloride at −78 °C containing rose bengal (0.01 g) was complete in 2 h. The crude extract showed the presence of mainly 2 components (tlc). Elution chromatography (pentane–ether 9:1) yielded *endo*-peroxide **3** (0.26 g, 46% overall from **10**) as an oil.

6α,10β-Dimethyl-2α,5α-epidioxy-3-octalin, 3

Endo-peroxide **3** was isolated as an oil (R_f 0.8, pentane–ether 1:1); ir (neat) 3140, 1455, 1440, 1370, 1010, 970, 960, 920, 885, 870, 765, 690, 670 cm^{-1}; pmr ($CDCl_3$) δ 0.94 (s, 3, C-10 CH_3), 1.00 (d, 3, J = 7 Hz, C-6 CH_3), 1.32 (d of d, 1, J = 3, 13 Hz, H-1α), 1.88 (d of d, 1, J = 4, 13 Hz, H-1β), 4.52 (octet, 1, J = 1.5, 3, 4, 6 Hz, H-2β), 6.44 (d of d, 1, J = 1.5, 8 Hz, H-4), 6.58 (d of d, 1, J = 6, 8 Hz, H-3); ms *m*/e calcd. for $C_{12}H_{18}O_2$: 194.1307, found: 194.1313 (2), 162(100), 147(36), 119(20), 106(38), 105(48), 92(20), 91(68), 79(20).

6α,10β-Dimethyl-2α,3α,4α,5α-diepoxydecalin, ***12***

Diepoxide **12** was isolated as an oil. (R_f 0.5, pentane–ether 1:1); ir (neat) 1460, 1375, 960, 950, 930, 900, 870, 815, 740, 720 cm^{-1}; nmr ($CDCl_3$) δ 0.72 (d, 3, J = 7 Hz, C-6 CH_3), 1.06 (s, 3, C-10 CH_3), 2.92 (q, 1, J = 5 Hz, H-2β), 3.20 (d of t, 1, J = 3, 5 Hz, H-3β), 3.31 (d, 1, J = 3 Hz, H-4β); ms *m/e* calcd. for $C_{12}H_{18}O_2$: 194.1306, found: 194.1302 (5), 161(23), 126(92), 123(22), 109(52), 107(36), 105(46), 97(28), 96(32), 95(100), 93(60), 91(53). 84(45), 81(80), 80(25), 79(46), 77(33), 73(26).

6α,10β-Dimethyl-5α-hydroxy-3-octal-2-one, ***11***

γ-Hydroxyoctalone **11** was crystalline, mp 99–102 °C (R_f 0.48 pentane–ether 4:1); ir ($CHCl_3$) 3600, 3500 (OH), 1680 (C=O), 1620 (sh, w, C=C) cm^{-1}; nmr ($CDCl_3$) δ 0.99 (d, 3, J = 6 Hz, C-6 CH_3), 1.06 (s, 3, C-10 CH_3), 2.00 (d of d, 1, J = 1, 16 Hz, H-1α), 2.67 (d of d, 1, J = 1, 16 Hz, H-1β), 5.95 (d of d, 1, J = 2, 10 Hz, H-3), 6.96 (d, 1, J = 10 Hz, H-4); ms *m/e* calcd. for $C_{12}H_{18}O_2$: 194.1307, found: 194.1305 (33), 111(72), 110(31), 93(47), 91(29), 82(26), 81(24), 79(23), 77(23), 69(24), 67(26), 55(44), 53(23), 51(100).

Oxygenation using Triphenylphosphite–Ozone (15)

Methylene chloride (35 ml) was added to a 100 ml 3-necked flask equipped with a dropping funnel, a gas inlet tube, and a drying tube. This was cooled to −78 °C and ozone (generated from oxygen using a Welsbach Laboratory ozonator) was bubbled through the solution. Triphenylphosphite (2.8 g) in methylene chloride (20 ml) was added dropwise at such a rate that the solution remained blue at all times (~1.5 h). When addition was complete, the blue solution was flushed with dry oxygen-free nitrogen to remove the remaining ozone.

Diene **8** (prepared by pyrolysis of allylic alcohol **10** (0.5 g)) in cold methylene chloride (10 ml) was added to the cold (−78 °C) triphenylphosphite–ozone solution. The reaction mixture was allowed to warm to room temperature, then concentrated. Elution chromatography led to the isolation of *endo*-peroxide **3** (0.08 g, 15% from **10**).

6α,10β-Dimethyl-3-octal-2α,5α-diol. ***13***

endo-Peroxide **3** (0.032 g) in ether (5 ml) was added to freshly prepared aluminum amalgam (0.2 g) (19). After 0.5 h, the reaction mixture was filtered, the aluminum turnings washed with ether, and the combined ether extracts concentrated. Allylic diol **13** (0.026 g, 77%) was obtained as colorless crystals, mp 109–111 °C; ir ($CHCl_3$) 3600, 3440 (OH) cm^{-1}; pmr ($CDCl_3$) δ 0.91 (d, 3, J = 6 Hz, C-6 CH_3), 0.98 (s, 3, C-10 CH_3), 4.31 (t of t, 1, J = 1.5, 2.5, 7 Hz, H-2β), 5.78 (t of d, 1, J = 1.5, 2.5, 10 Hz, H-3), 6.00 (d of d, 1, J = 1.5, 10 Hz, H-4); pmr (pyridine-d_5) δ 1.06 (d, 3, J = 6 Hz, C-6 CH_3), 1.10 (s, 3, C-10 CH_3); ms *m*/e calcd. for $C_{12}H_{20}O_2$: 196.1463, found: 196.1460 (7), 178(100), 163(63), 136(35), 135(37), 126(45), 122(22), 121(37), 109(39), 108(26), 107(72), 105(21), 97(28), 95(44), 94(75), 91(36), 84(20), 82(33), 81(85), 80(68), 79(60), 77(35), 71(33), 69(40), 67(50), 57(26), 55(85), 53(33).

6α,10β-Dimethyldecalin-2α,5α-diol, ((±)-Cybullol), ***1***

Allylic diol **13** (0.020 g) in ether (20 ml) was hydrogenated over platinum oxide at 40 psi hydrogen for 1 h. The solution was filtered and concentrated to give (±)-cybullol, **1** (0.021 g, quantitative) which was recrystallized from ether, mp 145–147 °C (mp for (−)-cybullol (2) 125–126 °C). The ir, pmr, and mass spectra were identical with authentic cybullol (2). *Anal.* calcd. for $C_{12}H_{22}O_2$: C 72.68, H 11.18; found: C 72.61, H 11.15.

4,10β-Dimethyl-4,5-epoxyoctal-3-one, ***17*** *(26)*

Hydrogen peroxide (30%, 24.0 ml) and sodium hydroxide (4 *N*, 11.6 ml) were added dropwise, and simultaneously to a cooled (0 °C), rapidly stirred solution of dimethyloctalone **16** (25) (13.3 g) in methanol (300 ml). The reaction mixture was allowed to stand at 0 °C for 1 day, then at room temperature for 3 days. The mixture was diluted with water and extracted with ether. The ether extract was washed with water, dried ($MgSO_4$), and concentrated to give **17** (12.3 g, 85%) as an oil which was purified by distillation (bp 90–93 °C/0.1 torr): ir (neat): 1720 cm^{-1}; pmr ($CDCl_3$) δ 1.06 (3, s), 1.20 (3, s), 1.37 (3, s), 1.42 (3, s); ms *m/e* calcd. for $C_{12}H_{18}O_2$: 194.1307, found: 194.1306 (7), 176(18), 151(20), 109(100), 81(25), 67(37), 55(27), 43(57), 41(35). *Anal.* calcd. for $C_{12}H_{18}O_2$: C 74.19, H 9.34; found: C 73.87, H 9.15.

4α,10β-Dimethyl-5-hydroxydecal-3-one, ***18***

Liquid ammonia (70 ml) was distilled through a tube containing sodium hydroxide into a dry flask containing epoxy ketones **17** (1.14 g). Lithium (0.2 g) was added in small pieces to the stirred solution. After 6 h excess ammonium chloride was added and the ammonia allowed to evaporate. Water was added to the residue and the resulting mixture was extracted with ether. The ether extract was washed with water, dried ($MgSO_4$), and concentrated to a viscous oil (1.06 g) which partially solidified on standing. The crude solid was crystallized from Skellysolve B to give ketol **18** (0.33 g, 53% from **17***a*), mp 109–110 °C; ir ($CHCl_3$) 3600, 1720 cm^{-1}; pmr ($CDCl_3$) δ 0.99 (d, 3, J = 6 Hz, C-4 CH_3), 1.28 (s, 3, C-10 CH_3); pmr (pyridine-d_5) 1.26 (d, 3, J = 6 Hz, C-4 CH_3), 1.24 (s, 3, C-10 CH_3); ms *m/e* 196(19), 112(100), 97(22), 55(27), 41(20). *Anal.* calcd. for $C_{12}H_{20}O_2$: C 73.43, H 10.27; found: C 73.72, H 10.44.

(±)-Geosmin, ***15***

Ketol **18** (0.215 g) in glacial acetic acid (15 ml) was treated with ethanedithiol (1 ml) and boron trifluoride etherate (0.1 ml). The resulting solution was allowed to stand at room temperature for 15 min then quickly worked-up by dilution with brine and extraction with ether. The ether extract was washed with 4 *N* sodium hydroxide, then water, then dried ($MgSO_4$) and concentrated to give thio ketal **19** (0.287 g, 96%). An analytical sample was obtained by recrystallization from Skellysolve B, mp 95–96 °C; ir ($CHCl_3$) 3600 cm^{-1}; pmr ($CDCl_3$) δ 1.07 (s, 3, C-10 CH_3), 1.12 (d, 3, J = 6 Hz, C-4 CH_3), 3.17 (m, 4); ms *m/e* calcd. for $C_{14}H_{24}OS_2$: 272.1268, found: 272.1268 (59), 254(56), 225(49), 133(39), 132(58), 112(100), 55(45). *Anal.* calcd. for $C_{14}H_{24}OS_2$: C 61.71, H 8.88; found: C 61.71, H 8.78.

Thio ketal **19** (0.92 g), Raney nickel (W-2, 2 g), and absolute ethanol (10 ml) were stirred at room temperature for 1.5 h then heated under reflux for 2 h. Additional

Raney nickel (1 g) was added and heating continued an additional 2 h. The mixture was cooled, filtered, diluted with water, and extracted with pentane. The pentane extract was washed with brine, dried ($MgSO_4$), and solvents removed by distillation to give (±)-geosmin **15** (0.62 g, quantitative) as a colorless oil. On standing at 0 °C liquid geosmin crystallized, mp 78–82 °C. The spectroscopic data obtained for synthetic geosmin is identical in all respects with an authentic sample (2); ir (CCl_4) 3630 (OH) cm^{-1}; pmr ($CDCl_3$) δ 0.77 (d, 3, J = 6 Hz, C-4 CH_3), 1.03 (s, 3, C-10 CH_3); pmr (pyridine-d_5) 0.93 (d, 3, J = 6 Hz, C-4 CH_3), 1.04 (s, 3, C-10 CH_3); ms m/e calcd. for $C_{12}H_{22}O$: 182.1670, found: 182.1677 (10), 149(18), 112(100).

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