# THE LOWER TERPENOIDS OF *ISOCOMA WRIGHTII*

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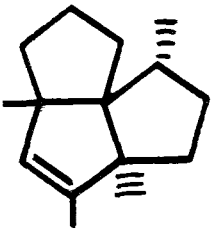
ABSTRACT.—The toxic plant "rayless goldenrod" (*Isocoma Wrightii*≡*Haplopappus heterophyllus*) has been shown to contain, in its volatile oil, three novel sesquiterpenes, isocomene (**1**), modhelphene (**2**), and the nordrimane sesquiterpene, 1,2,3,4-tetrahydro-1,1,5,6-tetramethylnaphthalene (**3**), in addition to β-caryophyllene, caryophyllene oxide and the monoterpenes limonene, borneol, bornyl acetate and carvone. The 1,1,5,8-tetramethyl (**4**) and 1,1,5,7-tetramethyl (**6**) isomers of **3** were synthesized and their nmr spectra compared.

"Milk sickness" has been described as the leading cause of death and disability in many parts of the midwest and upper South during the entire 19th Century (1). It was early established that the disease in animals ("trembles") was due to consumption of the plants white snakeroot (*Eupatorium urticaefolium*≡*E. rugosum*) east of the Mississippi and rayless goldenrod (*Haplopappus heterophyllus*≡*Isocoma wrightii*[1]) west of the Mississippi, and the toxic substance was passed on to humans ("milksickness") via the milk of the affected animal (1, 2). However, the toxin responsible for this disease has never been conclusively identified in spite of the numerous statements, even in recent times, in the literature reporting the toxin to be an unsaturated alcohol, "tremetol" ($C_{16}H_{22}O_3$) (1–4), first reported by Couch in the late 1920's (5–7). By the late 1930's, Dermer and his students (8–9) had already shown that "tremetol" was not a single pure substance but rather a complex mixture. Then, in the early 1960's Bonner (10) used Couch's procedure to reisolate "white snakeroot termetol" and further partitioned it into a sterol fraction and a ketone fraction, only the latter of which gave Couch's (5) characteristic sulfuric acid color test for "tremetol." This ketone fraction was shown to contain the benzofurans tremetone (2S-isopropenyl-5-acetyl-2,3-dihydrobenzofuran), hydroxytremetone and dehydrotremetone. At about the same time we began a reinvestigation of "rayless goldenrod tremetol" and identified toxol (2S, 3R-2-isopropenyl-3-hydroxy-5-acetyl-2,3-dihydrobenzofuran) and dehydrotremetone (11) and more recently tremetone, toxyl angelate, 2,5-diacetylbenzofuran and toxethol (2-isopropenyl-3-hydroxy-5-(1'-ethoxyethyl)-2,3-dihydrobenzofuran) (12). While none of the above-mentioned benzofurans has been implicated as the causative agent of "trembles" in higher animals, some of them have been shown to show biological activity.[2] The ethanolic plant extract of rayless goldenrod (*I. wrightii*) has been an unusually rich source of secondary plant metabolites of diverse structures. Thus, in addition to the above-mentioned benzofurans, the novel steroids 5α-androstane-3β, 16α, 17α-triol (13) and stigmasta-8(14), 22-dien-3β-ol (14) were isolated, and more recently we have identified stigmasta-5, 22-dien-3β-ol and stigmasta-8(14)-en-eβ-ol (12). The triterpenes friedelin and friedelan-3α-ol were obtained from the hexane extract (15), and now we have found squalene and phytol (12). Furthermore, the hexane extract has yielded a complex hydrocarbon fraction, and after chromatography we have isolated and identified nonacosane, hentri-

[1]*Isocoma wrightii* (Gray) Rydb. was formerly known as *Haplopappus* (*Aplopappus*) *heterophyllus*. See Cordell, D. S. and M. C. Johnston, 1970. Manual of Vascular Plants of Texas. Texas Research Foundation. Renner, Texas.

[2]A forthcoming publication entitled "The Benzofurans of *Isocoma wrightii*" will discuss this subject in detail.

acontane and tritriacontane (12). Among the fatty acids, stearic acid was isolated. Hexanoic, octanoic, lauric, myristic, palmitic and linoleic were identified by glc of their methyl esters (16). Finally, a family of fatty alcohols has been isolated but not yet completely characterized.[3]



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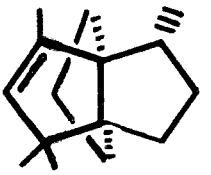

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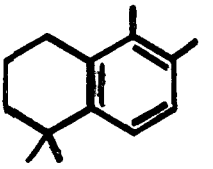

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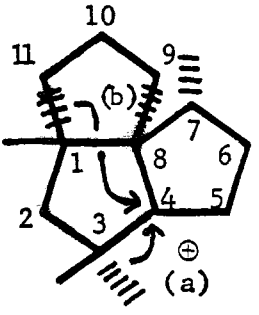
The sesquiterpenoid content of the volatile oil of *I. wrightii* has proven of particular interest from a structural point of view. Thus, in addition to the more common β-caryophyllene and its oxide we have isolated isocomene (**1**), a new sesquiterpene of novel skeletal type, the first sesquiterpenoid carbocyclic(3.3.3)-propellane, modhepene (**2**), and a novel nordrimane sesquiterpene, 1,2,3,4-tetrahydro-1,1,5,6-tetramethylnaphthalene (**3**). The structures of isocomene and modhephene were inferred from spectral analyses but only conclusively determined by single crystal X-ray analyses of the corresponding major diols derived by treatment of these tricycloalkenes with osmium tetroxide. The X-ray structures were recently presented in preliminary communications (17, 18), but full experimental details can be found in the EXPERIMENTAL of this paper.

The $^{1}H$ nmr spectra of isocomene (**1**) and modhephene (**2**) revealed that both substances possessed two quaternary methyl groups, a methyl group attached to a tertiary carbon, a methyl group attached to a trisubstituted double bond, and an olefinic hydrogen. In both of the nmr spectra of isocomene and modhephene, the two quaternary methyl groups appeared as singlets. In the case of isocomene this turned out to be misleading as will be evident. The $^{13}C$ nmr spectra of both isocomene and modhedphene verified that each contained a trisubstituted double bond and, in addition, revealed that each structure possessed three quaternary carbon atoms. The mass spectra of the two unknowns confirmed the molecular weights and elemental compositions deduced from the elemental analyses. The base peak in isocomene (*m/e* 189) seemed to correspond to the loss of propylene ($M^{+}-C_3H_6$), but in modhephene (*m/e* 162) it appeared to arise simply from the loss of a methyl group ($M^{+}-CH_3$). Thus, while the similarities in the $^{1}H$ nmr spectra suggested the two substances were skeletally related, the great differences in the $^{13}C$ nmr and mass spectra showed that isocomene and modhephene possessed different skeleta. Both substances were converted into major diols by treatment with osmium tetroxide in pyridine. The $^{1}H$ nmr spectrum of the major idol obtained from isocomene clearly showed three methyl singlets in addition to a methyl doublet, thus revealing that none of the quaternary carbons in isocomene bore a gem dimethyl group. Whereas the $^{1}H$ nmr spectrum of the major diol from modhephene showed a six proton methyl singlet analogous to that shown in modhephene, suggesting that one of the quaternary carbons in modhephene did bare a gem dimethyl group. We were only able to arrive at the unequivocal structures

[3]Unpublished work of B. Ekpo., Georgia Institute of Technology.

(**1**) and (**2**) for these two unknowns by single crystal X-ray analyses of the above mentioned diols (17, 18).

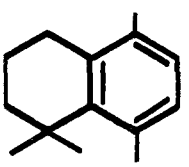
In the preparation of the *cis* diols of isocomene and modhephene, respectively, which were used for the above mentioned X-ray analyses, *cis* hydroxylation from one side predominated in each case. Thus, in the case of isocomene (**1**), the predominant isomer was formed by *cis* hydroxylation from the $\alpha$ side of (**1**) (*cis* to the two *cis* methyl groups), while in the case of modhephene (**2**), the predominant isomer was formed by $\alpha$ hydroxylation of (**2**) (*cis* to the unsubstituted bridge). A cursory examination of models of (**1**) and (**2**) fails to reveal any apparent steric or conformational preference for either face of the double bonds in these highly symmetrical tricycloalkenes. This remains an intriguing question. Another interesting observation is the difference in the magnitudes of the plain negative ord curves with the molecular rotation curve of isocomene being about ten times greater than that of modhephene. An examination of models of the two molecules clearly reveals that modhephene (**2**) is the more symmetrical of the two, and removal of the secondary methyl group would convert it into a non-chiral substance with a plane of symmetry running through the three carbon bridge bearing the gem dimethyl group and double bond. Since caryophyllene is by far the major sesquiterpenoid component of this plant, it is tempting to suggest it as a precursor to isocomene (**1**) and modhephene (**2**). It seems very likely that both these sesquiterpenes arise from the common intermediate carbonium ion indicated (scheme 1) via methyl migration (path a) to give isocomene (**1**) or migration of bond C(1)–C(11) to give modhephene (path b). The relative configurations of these two sesquiterpenes are consistent with this postulation.




Steam distillation of the hexane extract of the entire aboveground portion of the plant yielded a yellow essential oil which, upon distillation, gave a low boiling fraction containing (+) limonene, (−) borneol, (−) carvone, and bornyl acetate, which were isolated by chromatography on alumina. Chromatography of the higher boiling residue on silica gel yielded in some of the hexane eluents a homogeneous (glc) colorless liquid in 2% yield based on steam volatile oil. The analytical and spectral data suggested that this unknown possessed one of the structures **3**–**5**.

A synthesis of the more symmetrical isomer **4** was undertaken beginning with *p*-xylene by Friedel-Crafts acylation with succinic anhydride to give 4(2,5-dimethylphenyl)-4-oxo-butanoic acid, followed by Huang-Minlon reduction to 4(2,5-dimethylphenyl)butanoic acid, then esterification with diazomethane, followed by addition of the Grignard reagent methylmagnesium iodide to give 5(2,5-dimethylphenyl)-2-methyl-2-pentanol, and finally Friedel-Crafts alkylation

with polyphosphoric acid to give 1,1,5,8-tetramethyl-1,2,3,4-tetrahydronaphthalene (**4**). The *p*-xylene used in the synthesis contained a small amount of *m*-xylene, which reacted in a parallel series of reactions to give ultimately 1,1,5,7-tetramethyl-1,2,3,4-tetrahydronaphthalene (**6**). The two tetrahydronaphthalenes **4** and **6** were separated by chromatography on silica gel impregnated with silver nitrate, with **6** being eluted first. Tetralin **6** was identified by comparison of its ir and nmr spectra with those of an authentic sample prepared in a similar manner (19).[4] While the ir and mass spectra of synthetic **4** were similar to those of the unknown, the two differed in glc retention time, and the differences in their nmr spectra were particularly instructive. A comparison of the nmr spectra of **6** with that of **4** and the unknown suggested that the correct structure of the unknown was, in fact, **3** and not **5** because in both the unknown and in **6** the gem dimethyl group and the two aromatic methyl groups had almost identical chemical shifts respectively. Whereas, in **4** both the gem dimethyl group and the aromatic methyl group at C–8 showed rather considerable deshielding, as would be expected if the correct structure of the unknown were **5**.



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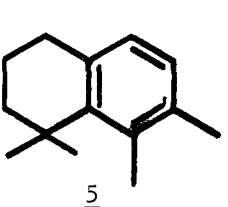

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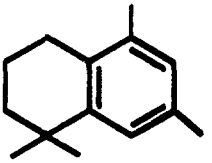

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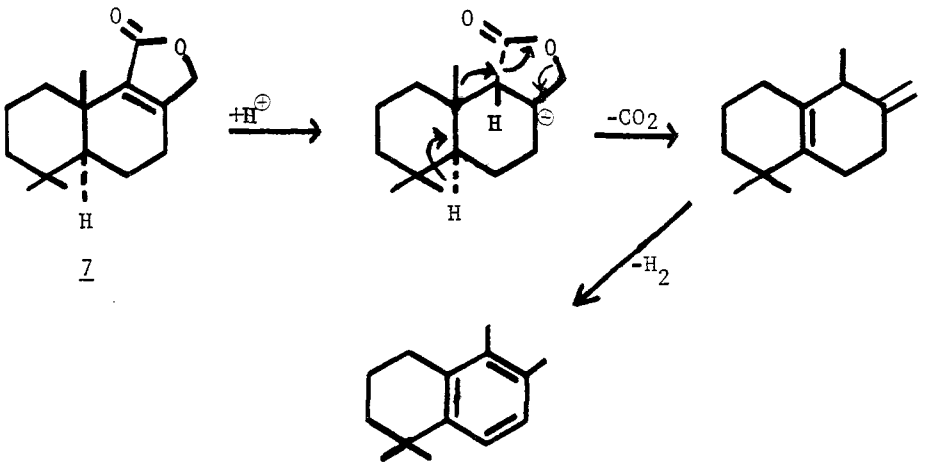
A search of the literature revealed that 1,2,3,4-tetrahydro-1,1,5,6-tetramethylnaphthalene (**3**) had recently been reported as a rearranged degradation product of the sesquiterpene avarol formed on dehydrogenation with 10% Pd-C at 270° (20). Indeed, the reported spectral properties and a copy of the nmr spectrum verified that our unknown was identical to the above degradation product.[5] An examination of the carbon skeleton of 1,2,3,4-tetrahydro-1,1,5,6-tetramethylnapthalene (**3**) indicates that it is a nordrimane sesquiterpene with the bridgehead methyl group missing. Indeed, a mechanistically feasible pathway for its biogenesis can be visualized from the known sesquiterpene isodremenin (**7**) as outlined. The extremely mild isolation procedure used involving hexane extraction, steam distillation, fractional distillation, and finally chromatography on alumina make it highly unlikely that **3** is an artefact. Indeed, we know of no precursors, including isodremenin (**7**) which would lead to **3** under these conditions.

Saponification of the methanolic plant extract gave an ether soluble dark red oil (1% based on dried plant) which on steam distillation gave an essential oil which upon further fractional distillation gave (−) carvone, (−) borneol and (−) caryophyllene. Chromatography of the fraction bp 75–95°/0.05 mm on alumina (act III) gave (−) caryophyllene oxide. Each of these terpenes was identical, within experimental error, by ir, nmr and $[\alpha]_D$ with authentic samples. When the methanolic plant extract was diluted with an equal volume of water then extracted with pentane, (+) limonene was obtained, identical by ir, nmr and $[\alpha]_D$ with an authentic sample.

[4]We are grateful to Professor Nasipuri, Department of Chemistry, Indian Institute of technology, Kharagur, India for the ir and nmr spectra of **6**.

[5]We thank: Professor Minale, Consiglio Nazionale Delle Richerche, Laboratorio per la Chimica di Molecole Interesse Biologio, Napoli, Italy, for a copy of the nmr spectrum of **3**.




## EXPERIMENTAL[6]

ISOLATION OF 1,2,3,4-TETRAHYDRO-1,1,5,6-TETRAMETHYLNAPHTHALENE (3).—The aboveground parts of rayless goldenrod (*I. Wrightii*) were collected in the vicinity of Artesia, New Mexico, in October 1968, air dried, ground, and stored in sealed bags until extracted in 1974. Ten kilograms of the plant material was extracted with 16 liters of hexane in a Soxhlet for 2 days. Removal of the hexane with a rotary evaporator gave 170 g of extract. Steam distillation and ether extraction of 350 g of this extract gave 6.8 g of yellow oil after drying and removal of the ether with a rotary evaporator. Distillation of this oil yielded a lower boiling fraction (b.p. 26–36°C/0.15 mm) from which (+) limonene, (−) borneol, (−) carvone, and bornyl acetate were isolated by chromatography on Brochman alumina (act. II) and a residue (2.1 g) which was chromatographed on 72 g of silica gel. Among the hexane eluents, there was obtained a homogeneous (glc) oil in about 2% yield based on steam volatile oil. Bp 75–80°/0.2 mm (air bath); $\nu$ max (film) 800 $cm^{-1}$; $\lambda$ max (MeOH) 269, 277 nm; nmr ($CCl_4$) $\delta$ 1.26 (6H, s), 2.10 (3H, 3), 2.24 (3H, s), 2.66 (2H, t, $J$=6 Hz), 6.92 (2H, q, $J$=8 Hz); mass spectrum $m/e$ 188 ($M^+$, 18%), 173 $M^+$-$CH_3$, 100%). Anal. Calcd. for $C_{14}H_{20}$: C, 89.30; H, 10.70. Found: C, 89.37; H, 10.61.

SYNTHESIS OF 1,1,5,8-TETRAMETHYL-1,2,3,4-TETRAHYDRONAPHTHALENE (4) AND 1,1,5,7-TETRAMETHYL-1,2,3,4-TETRAHYDRONAPHTHALENE (6).—To an ice-cooled solution prepared by adding 14.3 g of succinic anhydride to 130 ml of commercial *p*-xylene was added 50 g of anhydrous $AlCl_3$ with stirring. After warming to room temperature, the solution was heated on the steam bath for 20 min; then 75 ml of $H_2O$ was added dropwise while the reaction mixture was cooling in an ice bath. Excess xylene was removed by steam distillation; and, on cooling in an ice bath, the crude 4(2,5-dimethylphenyl)-4-oxobutanoic acid separated as an oil on top of the solution and soon solidfied. The solid was removed by filtration, washed successively with ice cold 2N HCl and ice water, then dissolved in 15% $Na_2CO_3$. The solution was filtered and decolorized with charcoal. Acidification with conc. HCl precipated the acid, which was collected by filtration, dried, and recrystallized from EtOH-$H_2O$ to give mp 66–68°, yield 46% (lit. ref. 21, mp 86°). $\nu$ max ($CHCl_3$) 3500–2500 br, 1701, 1680 $cm^{-1}$; nmr ($CCl_4$) $\delta$ 2.36 (3H, s), 2.43 (3H, s), 2.73 (2H, t, $J$=6 Hz), 3.13 (2H, t, $J$=6 Hz). The low mp and complex aromatic region in the nmr spectrum was due to the presence of a small amount of 4(2,4-dimethylphenyl)-4-oxobutanoic acid arising from m-xylene contaminant in the p-xylene. It was more convenient to separate isomers at a later stage.

To 10 g of KOH dissolved in 57 ml of diethylene glycol at 80–100° was added 10.4 g of the above ketoacid mixture and 7.3 ml of 85% hydrazine hydrate. The solution was refluxed for 1 hr. Then the low boiling materials were distilled out until the pot temperature reached 205°, when the solution was again allowed to reflux for 1 hr. After cooling, the solution was poured into $H_2O$ and acidified with conc. HCl, whereupon crude 4(2,5-dimethylphenyl)butanoic acid

[6]MP's were taken on a Kofler hot stage and are uncorrected. Ir spectra were recorded with a Perkin Elmer 237 B spectrophotometer. $^1H$ nmr spectra were obtained with a Varian A-60D or T60 spectrometer with $Me_4Si$ as an internal standard ($\delta$ 0); $^{13}C$ nmr spectra were run on a JOEL-PFT-100 FT spectrometer. Mass spectra were run on a Hitachi RMV-7 spectrometer; gas chromatography was done with a F&M Biomedical Gas Chromatograph, model 402; and ord spectra were recorded using a Jasco ORD/UV-5 instrument.

oiled out and then solidfied. After purification as described above, the product was recrystallized from pentane to give mp 57–59°, yield 97% (lit. ref. 22, m.p. 70–72°); $\nu$ max ($CHCl_3$) 3500–2500 br, 1705 $cm^{-1}$. The acid mixture (8.4 g) was treated with excess ethereal diazomethane and allowed to stand at room temperature overnight. Water was added, the ether layer was removed and washed successively with water, ice cold 5% NaOH, then saturated brine and finally dried over $MgSO_4$ to give the crude methyl ester mixture ($\nu$ max (film) 1740 $cm^{-1}$) in 48% yield. Gas chromatography on an OV-17 column at 140° clearly showed the presence of the two esters methyl-4(2,5-dimethylphenyl)butanoate and methyl-4(2,4-dimethylphenyl)butanoate in a ratio of 2:1. A 60 MHz nmr spectrum did not distinguish between the two isomers: $\delta$ 2.33 (6H, s), 3.70 (3H, s).

A solution of 4.6 g of the above ester mixture dissolved in 44 ml of anhyd. ether was dropped slowly into an ethereal solution containing a large excess of methylmagnesium iodide prepared in situ. The solution was refluxed for one hr. then cooled in an ice bath and hydrolyzed by the slow addition of 40 ml of 20% ammonium chloride. The usual workup gave a 93% yield of the mixture of alcohols 5-(2,5-dimethylphenyl)-2-methyl-2-pentanol and 5(2,4-dimethylphenyl)-2-methyl-2-pentanol in a ratio of 2:1 respectively (glc, same column as above). Bp 103–105°/0.35 mm; $\nu$ max (film) 3200–3500 br; $\delta$ 1.20 (6H, s), 2.30 (6H, s), isomers not distinguishable; *m/e* 132 (100%).

A solution prepared by dissolving 1 g of the above alcohol mixture in 17 g of polyphosphoric acid was heated at 160° for 3 hrs. It was then cooled, poured onto crushed ice in water, and the latter was extracted with hexane. The combined hexane extracts were washed successively with 5% NaOH and saturated brine and finally dried over $MgSO_4$. Removal of the solvent gave 0.63 g of oil, bp 68–69°/0.15 mm, and nmr indicated that this oil was a mixture of **4** and **6** in ° ratio of 2:1, and, therefore, it was chromatographed on silica gel impregnated with 20% $AgNO_3$. Elution with hexane-$CH_2Cl_2$ (85:15) gave first the minor component **6** and then the major component **4**. 1,1,5,7-tetramethyl-1,2,3,4-tetrahydronaphthalene (**6**) was identical by ir and nmr spectra with those of an authentic sample (19). $\nu$ max (film) 855 $cm^{-1}$; $\delta$ ($CCl_4$): 1.25 (6H, s), 2.13 (3H, s), 2.23 (3H, s), 6.70 (1H, s), 6.92 (1H, s). 1,1,5,8-Tetramethyl-1,2,3,4-tetrahydronaphthalene (**4**) was isolated as a colorless oil. Bp ~80°/0.2 mm (air bath); $\nu$ max (film) 807 $cm^{-1}$; $\delta$ ($CCl_4$) 1.38 (6H, s), 2.10 (3H, s), 2.43 (3H, s), 6.73 (2H, s); mass spectrum *m/e* 188 ($M^+$, 48%), 173 (100%). Anal Calcd. for $C_{14}H_{20}$: C, 89.30; H, 10.70. Found: C, 89.18; H, 10.81.

ISOLATION OF ISOCOMENE (**1**), MODHEPHENE (**2**), CARYOPHYLENE, CARYOPHYLENE OXIDE AND MONOTERPENES.—The aboveground parts of rayless goldenrod (10 kg) were extracted with 10 liters of methanol to give 300 g of extract, which was saponified with 5% methanolic KOH and extracted with ether to give 30 g of red oil ("tremetol"). Steam distillation of the latter gave in 11% yield the essential oil. When some of the original methanol extract was diluted one to one with water, it became cloudy. On extraction with ligroin, drying, and evaporation, a colorless oil was obtained which by glc showed one major (60%) component. This component was isolated by fractional distillation and identified by its physical and spectral properties as (−) limonene.

The essential oil from above was distilled to give fractions of the following boiling points at 0.05 mm: A, 40–55°; B, 55–65°; C, 65–75°, and D, 75–95°. Refractionation of fraction A gave a fraction of bp 65–73°/1 mm which was chromatographed on alumina to yield (−) carvone in the benzene-chloroform (1:1) eluent, and (−) borneol in the chloroform eluent. The fraction of bp 75–80°/1 mm (from fraction A) gave $\beta$-caryophyllene, which was also isolated directly from "tremetol" by partition chromatography on florisil (stationary phase 95% methanol saturated with ligroin). Fraction C was chromatographed on silica gel impregnated with silver nitrate (20%) to give $\beta$-caryophyllene, isocomene (**1**) (17), and modhephene (**2**) (18) in the pentane-methylene chloride eluents.

Pentane-methylene chloride (95:5) eluted first isocomene, then modhephene, and finally caryophyllene. Of this mixture of sesquiterpenes, caryophyllene comprised about 64%; isocomene, 26%; and modhephene, 10%. All were distinguishable by glc on a 6′ x ¼″ 5% SE 30 column. Isocomene (**1**) was obtained as a colorless oil (single peak by glc) which crystallized after standing at room temperature for several months. Bp 65–70°/0.35 mm (air bath); mp 60–62°; $\nu$ max ($CCl_4$) 3020, 1670 and 840 $cm^{-1}$; $^1H$ nmr $\delta$($CCl_4$) 0.87 (3H, d, *J* 7 Hz), 1.02 (6H, s), 1.67 (3H, d, *J* 1.5 Hz), 4.83 (1H, m); $^{13}C$ nmr 142.1(s), 132.1(d), 63.6(s), 59.7(s), 56.4(s), 42.5(t), 39.8(d), 37.2(t), 33.6(t), 31.9 (t), 24.0 (t), 23.7(q), 23.1(q), 17.3(q), 13.0(q) ppm; *m/e* 204($M^+$, 15%), 189(19%), 162 (100%), 147(42%), 119(35%); ord (C, 1.18; $CHCl_3$): $[\phi]_{600}$ −129.7, $[\phi]_{589}$ −138.3, $[\phi]_{550}$ −155.7, $[\phi]_{500}$ −172.8, $[\phi]_{450}$ −259.3, $[\phi]_{400}$ −363.1, $[\phi]_{350}$ −535.9, $[\phi]_{300}$ −881.7, $[\phi]_{260}$ −1694.2°. Anal. Calcd. for $C_{15}H_{24}$: C, 88.16: H, 11.84, Found: C, 88.11; H, 11.88. On treatment of isocomene with osmium tetroxide in pyridine (for conditions, see modhelphene diol preparation), a mixture of cis diols was obtained in an approximate ratio of 3:2 as determined by $^1H$ nmr (isomers were not distinguishable on several glc columns). The major isomer was obtained pure by chromatography on silica gel and crystallization from pentane-ether. Mp 134–136°; $\nu$ max ($CDCl_3$) 3540, 3590 $cm^{-1}$; $^1H$ nmr $\delta$ ($CDCl_3$) 0.91 (3H, d, *J* 6.51 Hz), 0.94 (3H, s), 1.03 (3H, s), 1.15 (3H, s), 3.50 (1H, d, *J* 8 Hz); *m/e* 238 ($M^+$, 2%), 220 ($M^+-H_2O$, 29%), 134(30%), 122(90%), 109(100%); ord (C, 1.18; $CHCl_3$) $[\phi]_{589}$ −46.6°. Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.54; H, 11.04. This diol was used for a single crystal X-ray analysis (17).

Modhephene (**2**) was isolated as a colorless oil from the chromatography and showed a single peak by glc. Bp 65–70°/0.25 mm (air bath); $\nu$ max ($CCl_4$) 3010, 1650, 1380, 840 $cm^{-1}$; $^1H$ nmr $\delta$ ($CCl_4$) 0.97 (6H, s), 0.99 (3H, d, $J$ 5.5 Hz), 1.58 (3H, d, $J$ 1.5 Hz), 4.80 (1H, m); $^{13}C$ nmr 140.2(s), 134.8(d), 71.9 (s), 65.9(s), 45.7(s), 43.8, 38.7, 35.7, 34.2, 29.9, 29.2, 27.1, 26.4, 15.7, 13.7 ppm; *m/e* 204 ($M^+$, 19%), 189 (100%), 161(29%), 149(36%), 147(30%), 133(26%), 119(32%); ord (C, 1.50; $CHCl_3$): $[\phi]_{600}$ −8.2°, $[\phi]_{589}$ −8.6°, $[\phi]_{550}$ −13.7°, $[\phi]_{500}$ −16.3°, $[\phi]_{450}$ −19.0°, $[\phi]_{400}$ −30.0°, $[\phi]_{350}$ −46.0°, $[\phi]_{300}$ −84.3°, $[\phi]_{260}$ −182.2°. Anal. Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.01; H, 11.89.

Modhephene (61 mg) was added to a solution containing 250 mg osmium tetroxide in 5 ml of dry pyridine. After stirring in the dark at room temperature for 10 days, a solution of 1 g $NaHSO_3$ dissolved in 10 ml water was added. After stirring for an additional 0.5 hr, 10 ml of half saturated brine solution was added, and the entire stirred solution was finally extracted with $CHCl_3$. The $CHCl_3$ extract was washed with 3M aq HCl then saturated brine solution and finally dried over $MgSO_4$. Evaporation under reduced pressure gave 66 mg of a light brown oil which solidified on standing at room temperature overnight. Glc analysid (5% SE–30 column) showed one major component and three minor ones. The minor component of shortest retention time was unreacted modhephene; whereas the minor component of retention time closest to the major component is presumably the isomeric cis diol. The apparent ratio of the major and minor diols is 4:1. Chromatography of the crude product on Merck acid washed alumina, act III, gave 41 mg of the diol mixture in the hexane-benzene (1:1) eluent as a crystalline material. Fractional crystallization by vapor diffusion with ether as the solvent and pentane as the external liquid gave colorless prisms of the major diol with properties listed below. A small piece of one of these crystals was cut off and used for the X-ray analysis (18). Mp 145–145.5°; $\nu$ max (KBr) 3500, 3375, 1070 $cm^{-1}$; $^1H$ nmr $\delta$ ($CDCl_3$) 0.98 (3H, d, $J$ 6 Hz), 1.00 (6H, s), 1.25 (3H, s), 3.38 (1H, br d, $J$ 6 Hz); *m/e* 238 ($M^+$, 8%), 220 ($M^+$–$H_2O$, 40%), 192(73%), 164(90%), 136(100%), 124(77%), 110(75%), 96(77%). Anal. Calcd. for $C_{15}H_{26}O$: C, 75.58; H, 10.99. Found: C, 75.54; H, 10.98. Fraction D was chromatographed on neutral alumina (act III) to give caryophyllene oxide in the benzene-hexane (1:3). All of the known terpenes isolated from the essential oil were identified by comparison of their physical and spectral properties with those of authentic samples.

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