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δ-Patchoulene, an Acid-Catalyzed Transformation Product of Patchouli Alcohol

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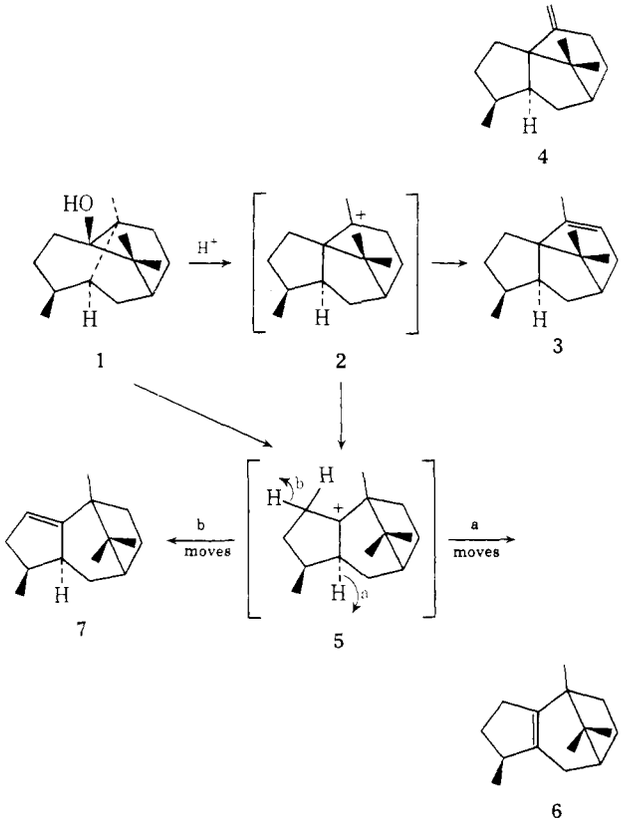
Treatment of patchouli alcohol with a strong cation exchange resin yielded a new sesquiterpene, δ-patchoulene. Its structure was determined on the basis of spectral data and by conversion to a ketone which was derived from β-patchoulene.

It is known that patchouli alcohol **1** dehydrates and rearranges, mostly to β-patchoulene **6**, when treated with boric acid, sulfuric acid (Treibs, 1949; Büchi *et al.*, 1961), and iodine (Büchi and Erickson, 1956). In the presence of phosphorus oxychloride (Büchi *et al.*, 1961), patchouli alcohol **1** gives mainly α-patchoulene **3** together with β-patchoulene **6** and ν-patchoulene **4**. This transformation involves a series of Wagner–Meerwin shifts as proposed by Santhanakrishnan (1965). If this mechanism is correct, the intermediate carbonium ion **5** could also produce another new sesquiterpene **7**. Compound **7** has neither been isolated nor synthesized before. The present paper reports the formation of this new compound **7** from patchouli alcohol **1** by treatment with a strong exchange resin. We propose to name the new sesquiterpene **7** "δ-patchoulene."

Scheme I. Mechanism of Formation of δ-Patchoulene 7



International Flavors & Fragrances (IFF-R&D), Union Beach, New Jersey 07735.

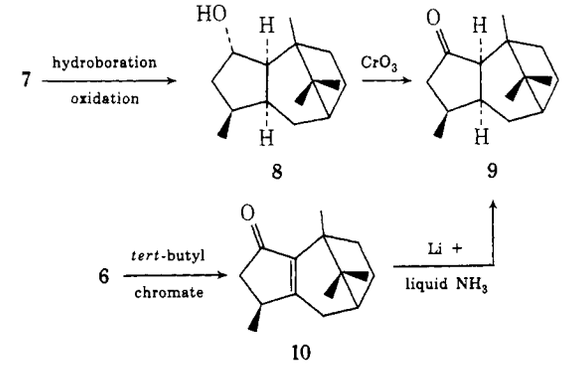
DISCUSSION

Treatment of patchouli alcohol **1** with Amberlite IR-120H in refluxing hexane yielded a mixture of sesquiterpenes (77%) whose glc analysis showed two major peaks and a minor peak. The minor peak (5%) was not investigated. The first major peak (40%) was isolated and analyzed by ir, nmr, and mass spectrometry. Infrared absorptions at 3.31, 5.09, 12.32, and 12.74 μ indicated that the molecule contained a trisubstituted double bond (C=CH). The sharp and strong absorption band at 3.2 μ suggested that this unsaturation might be in a five-membered ring. Doublet absorptions at 7.24 and 7.32 μ were due to a geminate dimethyl group (CH_3CCH_3). The nmr singlets at δ 0.78, 0.88, and 1.05 were ascribed to three tertiary methyl groups (CH_3C). The shoulder band at δ 0.95 was attributed to a secondary methyl group (CH_3CH). The broad signal at δ 5.0 was due to an olefinic proton (CH=C). The mass spectrum showed the molecular ion peak at *m/e* 204 with an empirical formula of $C_{15}H_{24}$, which suggested that if the compound has one double bond, it must possess a tricyclic structure. All of this evidence led us to assign the structure **7** to the new sesquiterpene. There is a great structural similarity between δ-patchoulene **7** and β-patchoulene **6**. The only difference is that δ-patchoulene contains a trisubstituted double bond, whereas β-patchoulene contains a tetrasubstituted double bond. The structure of δ-patchoulene **7** was confirmed in the following way.

Hydroboration–oxidation (Brown and Zwiefel, 1959) of this new sesquiterpene **7** gave a secondary alcohol **8** whose ir showed an absorption band at 3.0 μ due to a hydroxyl group. The presence of a secondary hydroxyl group was supported by a broad nmr signal at δ 4.1 (1 H, C*H*OH). The mass spectrum showed the expected molecular ion peak at *m/e* 222. The assigned "cis" stereochemistry of this alcohol was based on the prediction that diborane would preferentially attack from the least hindered side. Oxidation of **8** with chromium trioxide gave the ketone **9**. The ir spectrum of this ketone showed a band at 5.75 μ consistent with a five-membered ring ketone. The band at 7.08 μ was due to the active methylene group (CH_2C=O); the 7.18- and 7.32-μ bands were due to a geminate dimethyl group (CH_3CCH_3) whose correct assignment was confirmed by nmr singlets at δ 0.73 and 0.81. The downfield singlet at δ 1.2 was due to a tertiary methyl group (CH_3C) in the vicinity of an electronegative group, *i.e.*, a C=O group. The multiplet at δ 1.07 was due to a secondary methyl group (CH_3CH; J=6 Hz). The mass spectrum showed the expected molecular ion peak at *m/e* 220 ($C_{15}H_{24}O$). These spectral data firmly support the structure **9** which was further confirmed by synthesis.

tert-Butyl chromate oxidation of β-patchoulene **6** according to the procedure of Hunter and Brogden (1965) afforded an α,β-unsaturated ketone **10**, together with other minor ketones as described in a patent by Mookherjee (1972). Lithium–liquid ammonia reduction of **10**, using ammonium chloride as the proton donor (Cheity *et al.*, 1966), gave the desired saturated ketone **9** together with two unknown isomers. It is known that lithium–ammonia reduction of an α,β-saturated ketone can produce both cis and trans isomers depending upon transition states of the enolate ions (Stork and Darling, 1960, 1964). No attempts were made to determine the stereochemistry of the unknown isomers.

Scheme II. Degradation of 7



EXPERIMENTAL PROCEDURE

Instrumental Methods. Gas–liquid chromatographic (glc) analyses were performed on an F&M 810 instrument using a 5% Carbowax 20M coated on Anakrom ABS (80–100 mesh) packed in a stainless steel column (20 ft × 0.25 in. o.d.) with an inlet pressure of 50 psi and helium flow of 60 ml/min. Preparative glc work was done on the same substrate packed in a stainless steel column (25 ft × 0.37 in. o.d.). The following spectrometers were used: infrared (ir), Beckman IR-5A; nuclear magnetic resonance (nmr), Varian A-60 (TMS as internal standard); mass spectrometer, CEC Model 21-103 and AEI-MS 9 for high-resolution spectra. Mass spectra major fragmentation peaks are recorded in decreasing order of intensity except for the molecular ion peak which is listed first. Five per cent deactivated silicic acid (Grace, 100–200 mesh), made by adding 5 ml of water to 95 g of silicic acid, was used for column chromatography. Anhydrous magnesium sulfate was used as a drying agent.

Formation of δ-Patchoulene 7. A solution of patchouli alcohol **1** (3.7 g) in hexane (3.5 ml) was refluxed with Amberlite-IR-120H (1 g) for 5 hr. The resin was filtered off and the reaction mixture was chromatographed on deactivated silicic acid (30 g); hexane eluted a mixture of sesquiterpenes (2.6 g, 77%) whose glc showed three peaks due to β-patchoulene **6** (55%, peak I, R_t 18 min.), δ-patchoulene **7** (40%, peak II, R_t 22 min), and an unknown peak III (5%, R_t 24 min). Pure **7** was isolated by preparative glc: $[\alpha]^{25}D$ −61.7° (EtOH); ir (neat) 3.31 (sharp and strong), 3.41, 3.45, 3.51, 3.55, 5.09, 6.8 (shoulder), 6.9 (very strong), 7.24 and 7.32 (strong and of almost equal intensity), 7.45, 7.52, 7.71, 7.78, 7.94, 8.08, 8.23, 8.31, 8.55, 8.72, 8.82, 9.1, 9.3, 9.48, 9.62, 9.8, 9.92, 10.13, 10.2, 10.42, 10.61, 10.75, 10.89, 10.95, 11.32, 11.6, 11.8, 12.32, 12.74, and 13.42 (the latter two bands are strong and of equal intensity) μ; nmr (CCl_4) δ 0.78 (s, 3 H, CH_3C), 0.88 with a shoulder band at 0.9 (s, 6 H, CH_3C and CH_3CH), 1.0 (s, 3 H, $CH_3CC{=}C$), 5.0 (br, 1 H, $CH{=}C$); mass spectrum *m/e* 204 (molecular ion), 29, 41, 121, 161, 93, 91, 106. *Anal.* Calcd for $C_{15}H_{24}$: *m/e* 204.18799. Found: *m/e* 204.18783.

Hydroboration–Oxidation of 7 to Alcohol 8. To a solution of **7** (0.123 g) in anhydrous ether (5 ml) containing a trace of zinc chloride was added sodium borohydride (1 g) at −5°; the mixture was stirred for 1 hr and then to it was slowly added a solution of boron trifloride etherate (10 ml) in ether (10 ml). After an additional hour of stirring at −5°, water (2 ml), 3 *N* aqueous sodium hydroxide (5 ml), and 30% hydrogen peroxide (7 ml) were added consecutively and the mixture was stirred for 2 hr at −5°. The ether layer was separated and the aqueous layer was extracted with ether. The combined ether extracts were washed with water, dried, and on removal of the solvent yielded crude product which was chromatographed on deactivated silicic acid (3 g); hexane eluted a mixture of unreacted **6** and **7** (0.06 g), and ether eluted alcohol **8** (0.05 g). Glc of **8** showed one peak: ir (neat) 3.0 (OH), 3.4, 6.85, 7.05, 7.19, 7.24, 7.3, 7.35, 7.63, 7.9, 8.1, 8.29, 8.48, 8.6, 8.9, 8.99, 9.14, 9.3, 9.69, 9.8, 10.12, 10.37, 10.5, 10.6, 10.8, 11.01, 11.38, 11.55, 12.0, 12.45, 12.6, 13.45, 13.75 μ; nmr (CCl_4) δ 0.83 (s, 6 H, CH_3CCH_3), 0.95 (d, other half buried in 0.83 band, CH_3CH), 0.99 (s, 3 H, CH_3C), 4.1 (br, 1 H, CHO); mass spectrum *m/e* 222 (molecular ion), 41, 95, 55, 81, 29, 151, 39. *Anal.* Calcd for $C_{15}H_{26}O$: *m/e* 222.19835. Found: *m/e* 222.19839.

Oxidation of Alcohol 8 to Ketone 9. A solution of chromium trioxide (0.05 g) in glacial acetic acid (1.5 ml) containing water (two drops) was added to a solution of alcohol **8** (0.04 g) in glacial acetic (2 ml) at 0°, and the mixture was left at room temperature for 1 hr with occasional shaking. Water (10 ml) was added and the mixture was extracted with ether. The combined ether extracts were washed with 10% aqueous sodium carbonate and water and dried, and on removal of the solvent crude ketone was obtained (0.03 g). Glc analysis showed one major peak due to **9**: ir (neat) 3.39, 5.75 (five-membered ring ketone), 6.75, 7.08 ($CH_2C{=}O$), 7.18, and 7.23 (CH_3CCH_3), 7.39, 7.45, 7.55, 7.65, 7.78, 7.92, 8.02, 8.11, 8.22, 8.32, 8.42, 8.59, 8.65, 8.91, 9.05, 9.25, 9.72, 12.45 μ; nmr (CCl_4) δ 0.73 and 0.81 (two s, 6 H, CH_3CCH_3), 1.07 (m, 3 H, CH_3CH), 1.2 (s, 3 H, $CH_3CC{=}O$), 2.13 (m, 3 H, CH_2CCH); mass spectrum *m/e* 220 (molecular ion), 41, 39, 109, 110, 107, 69. *Anal.* Calcd for $C_{15}H_{24}O$: *m/e* 220.18270. Found: *m/e* 220.18278.

β-Patchoulenone 10. Oxidation of β-patchoulene **6** (2.5 g) with *tert*-butyl chromate reagent according to the procedure of Hunter and Brogden (1965) yielded crude ketones (1.5 g). Pure **10** was isolated by glc: ir (neat) 3.4, 5.89 (α,β-unsaturated five-membered ring C=O), 6.15 (C=C conjugated to C=O), 6.9, 7.0, 7.23, 7.53, 8.1, 9.02, 10.15 (strong) μ; nmr (CCl_4) δ 0.83 and 0.91 (two s, 6 H, CH_3CCH_3), 1.1 (d, 3 H, $CH_3CHC{=}C$), 1.25 (s, 3 H, $CH_3CC{=}O$); mass spectrum *m/e* 218 (molecular ion), 175, 41, 133, 69. *Anal.* Calcd for $C_{15}H_{22}$: *m/e* 218.16705. Found: *m/e* 218.16709.

Dihydro-β-patchoulenone 9. A solution of ketone **10** (1.9 g) in dry ether (70 ml) was added to a stirred solution of lithium (0.5 g) in liquid ammonia (500 ml). Stirring was continued for 0.5 hr, after which solid ammonium chloride (8 g) was added and the ammonia allowed to evaporate. The reaction mixture was diluted with water and then extracted with ether. The combined ether extracts were washed with dilute (3.7%) hydrochloric acid and water, dried, and evaporated to obtain 1.6 g of crude material which was chromatographed on deactivated silicic acid (30 g); 2.5% ether in pentane eluted 0.73 g of material whose glc showed three peaks in the ratio of 3:4:3. Peak I (one of the isomers of **9**) had the following characteristics: ir (neat) 3.45, 5.77 (saturated five-membered ring C=O), 6.87, 7.1 ($CH_2C{=}O$), 7.2 and 7.25 (CH_3CCH_3), 7.85, 7.99, 9.45, and 9.55 (equal intensity), 8.95, 9.15, 9.4, 9.54, 9.75, 10.75, 10.9, 11.3, 11.75, 12.32, 14.15 μ; nmr (CCl_4) δ 0.78 and 0.82 (two s, 6 H, CH_3CCH_3), 1.04 (d, 3 H, CH_3CH), 1.22 (s, 3 H, $CH_3CC{=}O$), 1.92 (m, 3 H,

CH_2CCH); mass spectrum m/e 220 (molecular ion), 41, 97, 39, 109, 107.

Peak II (one of the isomers of **9**) had the following characteristics: ir (neat) 3.4, 5.76 (saturated five-membered ring C=O), 6.75, 6.85, 7.09 (CH_2C=O), 7.19, and 7.25 (CH_3CCH_3), 7.6, 7.7, 7.8, 7.99, 8.08, 8.35 (strong), 8.59, 8.75, 8.9, 9.05, 9.25, 9.7, 9.85, 9.95, 10.15, 10.75, 11.25, 11.6, 12.2 μ; nmr (CCl_4) δ 0.84 and 0.86 (two s, 6 H, CH_3CCH_3), 1.08, (a shoulder due to CH_3CH) of a singlet at 1.1 (total 6 H, CH_3CC=O), 1.93 (m, 3 H, CH_2CCH); mass spectrum m/e 220 (molecular ion), 41, 97, 109, 110, 39.

Peak III (dihydro-β-patchoulenone **9**) had the following characteristics: ir, nmr, and mass spectral data were superimposable with those of the saturated ketone **9** obtained by the oxidation of alcohol **8**.

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California Bay Oil. I. Constituents, Odor Properties

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The steam volatile oil of the leaves of the California "bay" tree (*Umbellularia californica*) was analyzed by capillary and packed column gas chromatography separation with characterization by mass and infrared spectrometry. The characterizations of the major components umbellulone (39%), 1,8-cineole (19%), α-terpineol (7.6%), terpinen-4-ol (6.2%), sabinene (6%), α-pinene (4.7%), and 3,4-dimethoxyallylbenzene (5.4%) were confirmed and 26 additional compounds also characterized. Odor threshold studies indicated that 1,8-cineole was by far the major contributor to the odor of dilute water solutions of the oil. Comparison of the composition and odor properties was made with other well-known "bay" oils from the leaves of Mediterranean bay (*Laurus nobilis*) and West Indian bay (*Pimenta racemosa*).

Deer in certain areas of California are numerous and protected by law. They do significant damage to certain crops. There are some plants that deer generally avoid. One of these is the leaves of the California bay tree (*Umbellularia californica*). It seems likely that the volatile oil of the leaves of California bay contain components responsible for repelling deer.

An increased knowledge of the constituents of the oil of the leaves of *Umbellularia californica* is also of importance for other reasons. The leaves of the tree are used by many Californians as a spice. One major California spice company sells the dried leaves on the retail market.

Toxicity studies of California bay oil and components were carried out in connection with the present work and are reported elsewhere in this journal (MacGregor *et al.*, 1974).

Umbellularia californica leaf oil was analyzed remarkably thoroughly for the time using classical methods early in this century (Powers and Lee, 1904; Semmller, 1908). The structure of the main component umbellulone was elucidated at that time. Other components also characterized were α-pinene, 1,8-cineole, eugenol, safrole, and methyleugenol. Additional studies on the chemical properties of umbellulone were made later by Kiyohiro (1938). In the present study the modern, more thorough methods of capillary gas liquid chromatography (glc)–mass spectrometry and infrared spectrometry were used to give a more comprehensive analysis.

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EXPERIMENTAL SECTION

Materials. Authentic samples of compounds were obtained from reliable commercial sources or synthesized by well-established methods. They were purified by gas chromatography before use. δ-Terpineol was obtained from commercial α-terpineol using the method described by Mitzner and Lemberg (1966).

California bay oil was obtained from three principal sources. (1) The first source was from the Konocti Bay Corporation, Kelseyville, Calif. This involved direct steam distillation of the chopped, mature leaves in a pilot plant type operation. The leaves were in general at least partly dry and had been picked several days before the steam distillation. The oil was separated from the water layer and then dried over sodium sulfate and filtered. (2) A second method involved using steam distillation–continuous extraction in the laboratory with mature leaves that had been picked fresh (near Hopland, Calif.) and stored at −20°F in polyethylene bags. This was carried out using a 12-l. flask equipped with a steam distillation continuous extraction head of the type described by Nickerson and Likens (1966) at atmospheric pressure and using hexane as solvent. (3) A final source was from fresh mature leaves picked locally (El Cerrito, Calif., hills) using the same procedure as the second source.

The major analyses were carried out with the whole oil but, for a more complete study, the oil was divided up into three main fractions by chromatography on activated alumina in the following way. California bay oil (10 ml) in hexane (50 ml) was placed on a hexane-prepared column