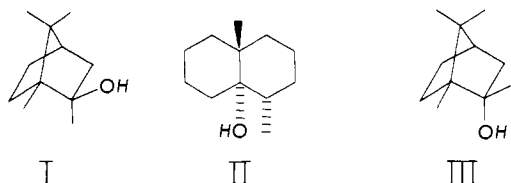


Odor Characterization of the Synthetic Stereoisomers of 2-Methylborneol

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The odor and some of the chemical and physical properties of stereospecifically synthesized (+)- and (-)-2-methylisoborneol (1,2,7,7-tetramethyl-*exo*-bicyclo[2.2.1]heptan-2-ol) are reported in this paper. Synthesis of the enantiomers of 2-methylborneol (1,2,7,7-tetramethyl-*endo*-bicyclo[2.2.1]heptan-2-ol) which are diastereoisomers of the 2-methylisoborneols are reported along with their mass spectra and odor characterization. Each of the four isomers had a camphoraceous rather than an earthy odor.

2-Methylisoborneol (1,2,7,7-tetramethyl-*exo*-bicyclo[2.2.1]heptan-2-ol (I) has been isolated from several species of microorganisms from garden soil and from water simultaneously with the earthy smelling compound geosmin (*trans*-1,10-dimethyl-*trans*-(9)-decalol) (II) (Buttery and Garibaldi, 1976; Collins et al., 1970; Gerber, 1969; Kikuchi et al., 1973; Rosen et al., 1970). Geosmin has also been identified as an odor component of table beets (Acree et al., 1976a; Murray et al., 1975) which suggests that 2-methylisoborneol may contribute to the aroma of beets. Several researchers reported that the 2-methylisoborneol which they isolated had a musty or earthy odor (Collins et al., 1970; Medsker et al., 1969; Rosen et al., 1970). Much of the literature reporting 2-methylisoborneol as having a musty odor did not distinguish between the stereoisomers of 2-methylisoborneol which could conceivably have different odors. Wood and Snoeyink (1977) determined that



the (-) enantiomer of 2-methylisoborneol was the one responsible for odorous contamination of water. Buttery and Garibaldi (1976), Kikuchi et al. (1973), Medsker et al. (1969), and Wood and Snoeyink (1977) stereospecifically synthesized (-)-2-methylisoborneol from *d*-camphor. Buttery and Garibaldi (1976) and Wood and Snoeyink (1977) described the odor of the product as earthy. Kikuchi et al. (1973) did not characterize the product's odor and Medsker et al. (1969) indicated that the odor of the product they obtained was camphoraceous. This paper describes the odor and some of the chemical and physical properties of (+)- and (-)-2-methylisoborneol. It also reports the synthesis and odor characterization of two diastereoisomers of 2-methylisoborneol, the enantiomeric 2-methylborneols (1,2,7,7-tetramethyl-*endo*-bicyclo[2.2.1]heptan-2-ol) (III).

EXPERIMENTAL SECTION

Synthesis of (+)- and (-)-2-Methylisoborneol. Samples of (+)- and (-)-2-methylisoborneol were prepared according to the procedure of Zeiss and Pease (1956). (-)-2-Methylisoborneol was prepared by reacting 30 g of *d*-(+)-camphor [$+47^{25}_D$ (*c* 10, C₂H₅OH) (Eastman Organic Chemicals) in 120 mL of ether with 39 g of previously prepared MeMgI in 115 mL of ether. The crude product was analyzed on the GC/MS system described below. At

a constant column temperature of 160 °C a peak eluted in 5.6 min with a mass spectrum corresponding to a published spectrum of camphor (Weinberg and Djerassi, 1966) and another peak eluted in 6.4 min with a mass spectrum corresponding to a published spectrum of 2-methylisoborneol (Medsker et al., 1969). The odor of the second peak was identified as it eluted from the column. (-)-2-Methylisoborneol was found to be 35% of the total crude product, calculated by measuring the relative peak heights of the two peaks present on the chromatogram. Most of the residual *d*-(+)-camphor was removed by washing the product onto a 45-g Florisil column and eluting (-)-2-methylisoborneol with 10% ether in petroleum ether. The remaining camphor contaminant was removed by washing the product onto another 45-g Florisil column and eluting (-)-2-methylisoborneol with 4% ether in petroleum ether.

The purified (-)-2-methylisoborneol melted in the range of 163–165 °C. (All melting points were determined on a hot stage.) Elemental analysis of the compound gave 78.35% C, 12.07% H, and 9.58% O (Galbraith Laboratories Inc., Knoxville, Tenn.). These percentages agree with the percentages 78.57% C, 11.90% H, and 9.52% O calculated for the empirical formula, C₁₁H₂₀O. The compound had a specific rotation of $[-14.8]^{25}_D$ (*c* 10, C₂H₅OH). This agrees with the specific rotation reported by Mälkönen (1964) and by Wood and Snoeyink (1977). The mass spectrum was virtually identical with the one published by Medsker et al. (1969). However, spectra reported in the literature (Kikuchi et al., 1973; Rosen et al., 1970) differed considerably from these; therefore, an additional spectrum of the pure compound was obtained from the Cornell mass spectrometry service facility. It was obtained from an AEI MS9021 CIS-2 mass spectrometer with a VG Datasystem 2040. The ionization energy was 70 eV and the direct inlet probe had a temperature of <30 °C. The ionization source was held at 100 °C. This spectrum was almost identical with Medsker's and the one reported here. The infrared spectrum of the (-)-2-methylisoborneol showed broad O-H stretching bands at 1375 and 1330 cm⁻¹ similar to the spectrum reported by Medsker et al. (1969). There was no absorption in the carbonyl region indicating the complete removal of camphor. The ¹H NMR spectrum of (-)-2-methylisoborneol showed unsplit methyl absorption peaks at δ 0.86, 0.90, 1.12, 1.25 and was virtually identical with the spectrum published by Paasivirta and Mälkönen (1971).

(+)-2-Methylisoborneol was prepared using the procedure described above except that 10 g of *l*-(+)-camphor [-38.4^{25}_D (*c* 10, C₂H₅OH) (Aldrich Chemical Co.)] in 40 mL of ether was added to 13 g of previously prepared MeMgI in 40 mL of ether. The crude product was analyzed by GC/MS in the same manner that the (-)-2-methylisoborneol product was analyzed. The odor of the (+)-2-methylisoborneol peak was noted as it was eluted.

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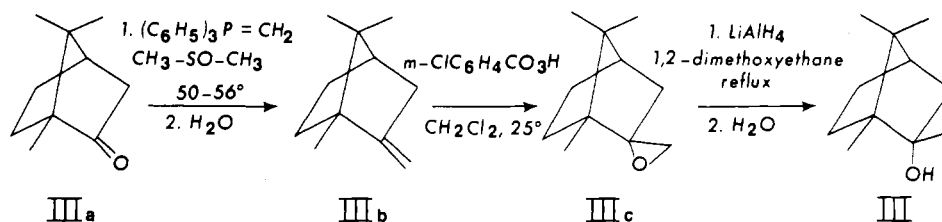


Figure 1. The synthesis of 2-methylborneol (III) from *d*-(+)-camphor (IIIa) via the intermediates 2-methylenebornane (IIIb) and 2-epoxobornane (IIIc).

The same retention times and mass spectra were obtained for *l*-(-)-camphor and (+)-2-methylisoborneol as for *d*-(+)-camphor and (-)-2-methylisoborneol. (+)-2-Methylisoborneol was found to be 37% of the total crude product which was calculated by measuring the relative peak heights of the two peaks present on the chromatogram. The (+)-2-methylisoborneol was purified in the same way as (-)-2-methylisoborneol. The purified (+)-2-methylisoborneol melted in the range of 162–165 °C. Elemental analysis of the compound showed 78.23% C, 11.94% H, and 9.83% O (Galbraith Laboratories Inc., Knoxville, Tenn.). These percentages are in agreement with the empirical formula $C_{11}H_{20}O$. It had a specific rotation of $[\alpha]_D^{25} (+12.8)$ (c 10, C_2H_5OH). The mass spectrum, 1H NMR spectrum, and infrared spectrum were essentially the same as for (-)-2-methylisoborneol.

Synthesis of the Enantiomers of 2-Methylborneol. 2-Methylenebornane (Figure 1) (IIIb) was formed from *d*-(+)-camphor $[\alpha]_D^{25} (+47)$ (c, 10, CH_2H_5OH) (IIIa) using the Wittig reaction procedure of Greenwald et al. (1963). Eight grams of *d*-(+)-camphor in 27 mL of dimethyl sulfoxide reacted with a solution of 0.06 mol of previously prepared methylenetriphenylphosphorane. A 45-g Florisil column was used to purify the crude product in place of an alumina column. The crude product weighed 2 g. This product was analyzed by GC/MS. At a constant column temperature of 150 °C, a peak eluted in 2.7 min, with a mass spectrum which had a significant abundance at mass 150, the molecular weight of 2-methylenebornane, and showed a base peak of 107 which is typical of many borneol compounds (Dimmel and Wolinsky, 1967). This compound constituted 22% of the total product as determined by relative peak height measurement. Another peak, eluted in 10.1 min, had a mass spectrum corresponding to a published spectrum of camphor (Weinberg and Djerassi, 1966). This peak composed approximately 70% of the total product. Three unidentified peaks constituted the remaining product. The crude 2-methylenebornane was purified once more on a Florisil column using tetranitromethane to detect its presence (Greenwald et al., 1963). This product was analyzed on the GC/MS system as before and found to be 77% methylenebornane. The pentane solvent was evaporated leaving 1.5 g of product mp 63–67 °C. The epoxide of 2-methylenebornane was formed using the procedure of Valente and Wolfhagen (1966) (Figure 1) (IIIc). The purified 2-methylenebornane (1.5 g) was reacted with 1.1 g of *m*-chloroperbenzoic acid in 35 mL of CH_2Cl_2 . The crude product was analyzed by GC/MS. The column temperature was held at 150 °C for the first 9 min and then changed to a 180 °C isothermal setting for the remainder of the chromatogram. A peak, eluted in 14.2 min, had a mass spectrum with a significant *m/e* at mass 166, the expected molecular weight of 2-epoxobornane. The mass spectrum showed a base peak at mass 105. This compound composed about 20% of the total product as measured by relative peak heights. Another peak, eluted in 10.8 min, had a spectrum corresponding to the published spectrum of camphor

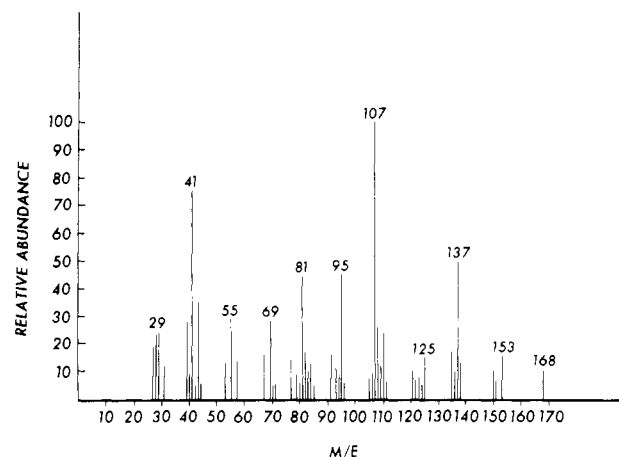


Figure 2. Mass spectrum of 2-methylborneol.

(Weinberg and Djerassi, 1966). This compound constituted about 30% of the product as measured by peak height. The remaining peaks were unidentified. The crude 2-epoxobornane product was reduced with lithium aluminum hydride using the procedure of Lyle and Krueger (1967) (Figure 1). Crude 2-epoxobornane (1.35 g) in 50 mL of anhydrous 1,2-dimethoxyethane was reacted with 0.8 g of lithium aluminum hydride in 0.90 mL of anhydrous 1,2-dimethoxyethane. The resultant crude product weighed 0.46 g and was analyzed by GC/MS. A peak eluting in 27 min at a constant column temperature of 150 °C had the mass spectrum shown in Figure 2. This compound showed a significant *m/e* at the expected molecular weight of 168. None of the other compounds in the mixture showed significant *m/e* at mass 168. The odor of the peak was sniffed as it eluted. The compound presumed to be 2-methylborneol (III) constituted about 15% of the total product as determined by peak height measurement. The 2-methylborneol was purified by trapping from the GC and re trapping as described below. This method of purification was used because the complex product mixture appeared to contain several other borneols and compounds of similar polarities which would make purification by other methods extremely difficult. The purified 2-methylborneol showed only one gas chromatographic peak and melted in the range of 82–85 °C. The following percentages were obtained from an elemental analysis: 77.4% C, 12.3% H, and 10.3% O (Galbraith Laboratories Inc., Knoxville, Tenn.). The sample size was too small to give an accurate analysis; however, it indicated a formula of $C_{11}H_{20}O$. The only other possible formula is that of borneol, $C_{10}H_{18}O$. This compound could not be borneol because the mass spectrum obtained for it is very different from that of borneol. The enantiomer of the 2-methylborneol described above was synthesized according to the same procedure using 10 g of *l*-(-)-camphor $[\alpha]_D^{25} (-38.4)$ (c 10, C_2H_5OH) as a starting material. The identity of the synthetic intermediates and the final product were confirmed by GC/MS as before. A compound comprising about 10% of the final product mixture

had a mass spectrum identical with that shown in Figure 2. The odor of compound was evaluated as it eluted from the gas chromatograph. The retention times of the two 2-methylborneol isomers on a glass capillary column were measured in succession and were both found to be 7.3 min under identical conditions described in the gas chromatography section. Although the amount of each of the 2-methylborneols was too small to obtain specific rotations, it was assumed that they retained the chirality of their respective camphor starting materials because none of the reagents used in the synthesis would be expected to affect this chirality. The compound was not purified further because it was present in an amount too minute for additional analytical tests and because its camphoraceous odor was not of interest.

GC/MS System. The GC/MS system consisted of a Varian 1440 gas chromatograph coupled to a time-of-flight mass spectrometer with a source temperature of 25 °C (Bendix Model 12 modified with a CVC Mark IV) through a methyl silicone helium separator (Black et al., 1969). The GC/MS system was equipped with a sniffer to detect the odors of compounds as they were eluted from the gas chromatographic column (Acree et al., 1976b). A 4 m × 3 mm stainless steel column packed with 5% SP-1000 (Carbowax 20 m modified with nitroterephthalic acid, Supelco Inc., State College, Penn.) on Chromosorb W was used. The relative retention times for (+)- and (-)-2-methylisoborneol, the purified 2-methylborneol made from *d*-(+)-camphor, and geosmin were all measured on the GC/MS system. The column temperature was programmed from 100 to 210 °C at 4 °C/min. The relative retention times of (+)- and (-)-2-methylisoborneol, geosmin, and the purified 2-methylborneol were 16.5, 23.6, and 25 min, respectively.

Gas Chromatographic Trapping. The synthetic product, 2-methylborneol made from *d*-(+)-camphor, was trapped from the effluent of a Packard Model 800 gas chromatograph. The effluent was split; one part to the flame ionization detector, ten parts to an exit port. The peak of interest was trapped in a glass capillary tube bent into a "U" shape which was suspended in a methanol-dry ice bath and attached to an exit port tube of the gas chromatograph with a small Teflon sleeve. The column used was the same as the one described in the GC/MS section. The column temperature was held at 100 °C for 3 min and was then temperature programmed to 210 °C at 4 °C/min. The trapped effluent was washed from the tube with Freon 113 (1,1,2-trichloro-1,2,2-trifluoroethane) and reinjected into the GC. The resultant chromatogram showed that the synthetic 2-methylborneol still contained several small contaminants. The synthetic mixture was trapped again and a chromatogram of the product showed only one peak. The twice-trapped product was washed from the tube onto a small watch glass and it was crystallized as the solvent slowly evaporated to yield approximately 200 µg of material.

Gas Chromatography. A 50 m × 0.3 mm glass column coated with Carbowax 20M was used in a Packard Model 800 gas chromatograph to measure the relative retention times of the enantiomeric 2-methylborneols. The effluent was split in the ratio of one part to the flame ionization detector, 60 parts to the sniffer (Acree et al., 1976b). The

column was operated isothermally at 170 °C with a helium flow rate of 2.2 mL/min.

Infrared Spectroscopy. (+)- and (-)-2-methylisoborneol were analyzed as 1% solutions in chloroform in a 1-mm pathlength NaCl cell on a Beckman IR-7 spectrophotometer.

Stereochemistry. The specific rotations for (+)- and (-)-2-methylisoborneol were obtained in a 1-dm pathlength cell using a Rudolph Model No. 80 photoelectric polarimeter. The compounds were analyzed as 0.01 g/mL solutions in absolute ethanol at 25 °C.

¹H NMR Spectroscopy. (+)- and (-)-2-methylisoborneol were dissolved in CDCl₃ and analyzed on a 100-MHz Varian HA-100 instrument.

RESULTS AND DISCUSSION

(+)-2-Methylisoborneol, (-)-2-methylisoborneol, and both 2-methylborneols had camphoraceous type odors when they were sniffed in the GC effluent. Both 2-methylborneols had rubbery overtones to their camphoraceous characters. The odor character of (+)-2-methylisoborneol and (-)-2-methylisoborneol did not change when they were sniffed as 1 part per thousand and 1 part per million dilutions in distilled water. The relative retention data for geosmin and the borneol compounds were useful in looking for the appearance of these compounds in vegetable flavor extracts. However, since none of the borneol-type compounds studied had musty or earthy odors which are important characteristic vegetable odors, their analytical characterization was not pursued further.

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