

Synthesis, Spectra, Odor Properties, and Structural Relationship of (*Z*)-6-Nonenal and (*Z*)-5-Octen-1-ol to Fruit Fly Attractants

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A short, relatively simple synthesis is reported for (*Z*)-6-nonenal and an intermediate (*Z*)-5-octen-1-ol. Spectra and odor properties are given. Studies of melon aroma compounds and fruit fly attractants are reviewed. The structural similarities between these compounds and the possible importance of (*Z*)-6-nonenal and (*Z*)-5-octen-1-ol to aroma and insect attraction are discussed.

6-Nonenal and other closely related or similar compounds have been identified as important off-flavor or natural aroma contributors and also as insect attractants. Keppler et al. (1965) identified (*E*)- and (*Z*)-6-nonenal as the off-flavor components of hardened linseed oil, while Kemp et al. (1972a) found that (*Z*)-6-nonenal was the component characteristic of muskmelon aroma. Jacobson et al. (1973) found that methyl (*E*)-6-nonenate and (*E*)-6-nonen-1-ol are sex pheromones for the fruit fly. (*Z*)-6-Nonenal appears to be a good candidate for testing as an attractant because of its close structural relationship to the fruit fly sex pheromones. (*Z*)-6-Nonenal was synthesized at the Western Regional Research laboratory at Berkeley for testing at the U.S. Department of Agriculture Honolulu facilities. I devised a short synthesis not only for (*Z*)-6-nonenal but also for the intermediate (*Z*)-5-octen-1-ol, a compound with interesting aroma characteristics and with possible potential as an attractant. The syntheses, spectra, and odor properties of these compounds are reported with a review of previous synthetic methods and studies related to the aroma and insect attractant properties of these compounds.

EXPERIMENTAL SECTION

Materials. (*Z*)-3-Hexen-1-ol (Aldrich Chemical Co.) and ethylene oxide (Eastman Kodak Co.) were used as received. Phosphorus tribromide, PBr_3 (Eastman Kodak Co.), was distilled at 63–65 °C (20 mmHg). Pyridine (Mallinckrodt, Inc.) was dried over KOH and distilled at 115 °C. Triethyl orthoformate (Eastman Kodak Co.) was distilled at 147 °C.

Gas-Liquid Chromatography (GLC). A 0.45 cm i.d. \times 300 cm long stainless steel column packed with Chromosorb G 80–100-mesh (DMCS treated and acid washed) was coated with 2% Carbowax 20 M containing a trace of the antioxidant Ionox 330. The column was used isothermally at 140 °C with a helium flow of \sim 30 mL/min. The injector was at 190 °C and the thermal conductivity detector at 180 °C.

Spectral Information. Purified GLC samples were collected in Pyrex tubes for spectral analysis. Infrared absorption (IR) spectra were run neat on salt plates by using a Perkin-Elmer 237 instrument. The mass spectra (MS) were determined on a modified Consolidated 21-620 cycloidal-type mass spectrometer at 70-eV ionization voltage.

Odor Thresholds. Odor thresholds for (*Z*)-6-nonenal and (*Z*)-5-octen-1-ol (synthesized by the author) in water were determined by a trained panel ($N = 15$ – 20) by using the method of Guadagni et al. (1963) with odor-free Teflon squeeze bottles and tubes.

Synthesis of 1-Bromo-(*Z*)-3-hexene. (*Z*)-3-Hexen-1-ol was brominated by a modification of Hunsdicker's (1942) method. PBr_3 (65 g) and pyridine (13 g) were each separately added dropwise over 3 h to stirred (*Z*)-3-hexen-1-ol (60 g) held at -5 °C. After sitting 18 h at 25 °C, the reaction mixture was filtered, cooled, neutralized with NaHCO_3 solution, and extracted with pentane. The pentane solution was washed with cold water, dried over Na_2SO_4 , and distilled. The fraction, bp 58–62 °C (18 mmHg), yielded 1-bromo-(*Z*)-3-hexene. The reaction was repeated and redistillation of the combined products yielded 69.5 g (35.6% yield) of 1-bromo-(*Z*)-3-hexene, pure by GLC assay. The IR spectrum had no absorption at 3350 cm^{-1} , indicating replacement of $-\text{OH}$ with $-\text{Br}$.

Synthesis of (*Z*)-5-Octen-1-ol. The method described by Vogel (1962) was used with lower reaction temperatures and different separation procedures. 1-Bromo-(*Z*)-3-hexene (69.5 g) in ether (100 mL) was reacted with magnesium (11 g) in ether (50 mL) to form the Grignard compound. Ethylene oxide (26.4 g) in ether (40 mL) was added dropwise to the -5 °C Grignard solution and then refluxed 0.5 h. Benzene (200 mL) was added and the mixture was distilled until the distillate temperature reached 65 °C. The remaining solid was cooled to 0 °C and decomposed with cold 10% H_2SO_4 , extracted with ether, washed with NaHCO_3 solution and then water, and dried over CaSO_4 . (*Z*)-5-Octen-1-ol (29.7 g), yield 54%, distilled at 90–100 °C (\sim 18 mmHg) and was 95% pure by GLC. The IR and MS spectra data were consistent with that published by Ohloff et al. (1977).

Synthesis of 1-Bromo-(*Z*)-5-octene. (*Z*)-5-Octen-1-ol (28.4 g) was brominated with PBr_3 (25 g) and pyridine (7 g) as previously described for the synthesis of 1-bromo-(*Z*)-3-hexene. A 43% yield was obtained for 1-bromo-(*Z*)-5-octene (17.5 g), bp 88–98 °C (18–20 mmHg). The IR spectrum had no absorption at 3350 cm^{-1} , indicating replacement of $-\text{OH}$ with $-\text{Br}$.

Synthesis of (*Z*)-6-Nonenal. Some modifications were made in the method described by Vogel (1962) for hexanal. 1-Bromo-(*Z*)-5-octene (17.5 g) in ether (40 mL) was reacted with magnesium (2.3 g) in ether (20 mL) to form the Grignard compound. Triethyl orthoformate (11.4 g) in ether (25 mL) was added to 0 °C Grignard solution. The solution was refluxed for 4 h and then left at 25 °C for 18 h. After removal of ether, the cold solution was treated with cold 6% HCl and the diacetal extracted with ether. The diacetal, after removal of ether, was hydrolyzed with 12% cold H_2SO_4 to yield the aldehyde. The freed aldehyde was steam distilled and collected in NaHSO_3 solution. The NaHSO_3 solution was steam distilled to remove any impurities and then was cooled and treated with NaHCO_3 to free the (*Z*)-6-nonenal. (*Z*)-6-Nonenal was extracted with ether. The ether extract was washed with water, dried over Na_2SO_4 , and then distilled, yielding 80% pure (*Z*)-6-nonenal (2.2 g) in 16.7% yield, bp 87 °C (19 mmHg). The IR and MS spectral data were consistent with the

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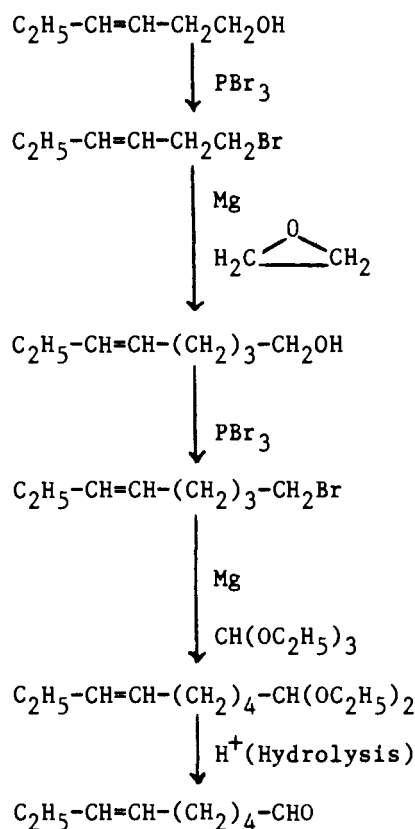


Figure 1. Synthesis of (*Z*)-5-octen-1-ol and (*Z*)-6-nonenal.

published data of Kemp (1972a).

RESULTS AND DISCUSSION

Synthesis. The reaction sequence (Figure 1) starting from (*Z*)-3-hexen-1-ol yielded both (*Z*)-5-octen-1-ol, as an intermediate, and (*Z*)-6-nonenal. The modest 35% and 43% yields for both bromination of (*Z*)-3-hexen-1-ol and (*Z*)-5-octen-1-ol probably resulted from bromination of the double bond, thus lowering yields of the desired product. Unreacted starting material accounted for ~10% of the final crude mixture. Variations from the bromination method described, including reverse addition, varied temperatures and reaction times, neutralization with pyridine, and direct distillation of the crude product, all resulted in lower or negligible improvement in the yield. The synthesis of (*Z*)-5-octen-1-ol with 54% yield was in the expected range as described by Vogel (1962) for hexanal synthesis. However, Nakamura et al. (1979) reported a 90% yield for (*Z*)-5-octen-1-ol from reacting the Grignard reagent of (*Z*)-3-hexenyl chloride with ethylene oxide in THF (no other conditions were reported in the abstract). The 16% yield of (*Z*)-6-nonenal from 1-bromo-(*Z*)-5-octene via the ethyl orthoformate procedure described by Vogel (1962) was unexpectedly low. The bisulfite addition of the aldehyde was apparently complete because no aldehyde was found (1) in ether extractions of the pot residue after steam distillation of the freed aldehyde or (2) in the steam distillate from the bisulfite complex. Product loss may have occurred during acid hydrolysis of the diacetal although this was not investigated.

MS Spectra. The mass spectra obtained for (*Z*)-5-octen-1-ol and for (*Z*)-6-nonenal are listed below (the two most intense ions every 14 mass units above m/e 34; intensities in parentheses; the molecular ion in boldface). The spectrum for (*Z*)-5-octen-1-ol is as follows: 39 (60), 41 (100); 55 (75), 57 (42); 67 (90), 68 (56); 81 (72), 82 (52); 95 (24), 96 (2); 110 (14), 111 (2); 128 (1). The spectrum for (*Z*)-6-nonenal is as follows: 39 (41), 41 (100); 54 (45),

55 (75); 67 (42), 69 (27); 81 (34), 83 (17); 93 (17), 96 (16); 107 (5), 111 (5); 122 (11), 123 (2); 140 (no molecular ion). The spectrum for (*Z*)-6-nonenal was consistent with that published by Kemp et al. (1972a) except that Kemp's spectrum contained the molecular ion 140 with an intensity of 2. The spectrum for (*Z*)-5-octen-1-ol was consistent with that published by Ohloff et al. (1977) except for higher intensities for the 55, 81, and 95 ions (~25% higher).

IR Spectra. The complete IR spectra from 700 to 2000 cm^{-1} for (*Z*)-5-octen-1-ol and (*Z*)-6-nonenal have not been reported before. The absorption intensities are denoted VS for very strong, S for strong, M for moderate, W for weak, and VW for weak. The spectrum for (*Z*)-6-nonenal is as follows: (VS) 1725; (M) 1460; (W) 1410, 1390, 1065, 970, 710; (VW) 1305, 1020, 880, 795. The spectrum for (*Z*)-5-octen-1-ol is as follows: (VS) 1060; (S) 1455; (M) 710, 1650; (W) 1440, 1400, 1375, 1305, 1165, 1120, 985, 965, 935, 790; (VW) 1280, 1250, 1200, 900, 880, 855, 825, 820.

Odor Properties. (*Z*)-6-Nonenal and its *E* isomer are important potent aroma compounds found in natural products and off-flavors and aromas of oils. However, only sparse and sometimes undocumented odor threshold and descriptive data have been published. Keppler et al. (1965) stated that both (*Z*)- and (*E*)-6-nonenal have "typical flavor reminiscent of green melon" with the *E* form 10 times as potent as the *Z* form in a paraffin solution. Keppler et al. (1967) reported the threshold value for odor of (*E*)-6-nonenal as 5 ppb in paraffin oil. However, the method of determining these descriptions and thresholds was not reported. Kemp et al. (1972b) reported the flavor threshold to be 0.02 part of (*Z*)-6-nonenal in 10^9 parts of water with a 0.9-ppb solution described as strong melon by panel members. Parks et al. (1969) found (*E*)-6-nonenal to be less than 0.07 ppb in fresh milk. No published threshold or descriptive data were found by the author for (*Z*)-5-octen-1-ol.

In the present study the odor threshold of (*Z*)-5-octen-1-ol was 6 parts in 10^9 parts of water (95% confidence level). The odor threshold of (*Z*)-6-nonenal was 0.005 parts in 10^9 parts of water (95% confidence level). The most frequently used description by the panel ($N = 16$) for (*Z*)-5-octen-1-ol at 1 part in 10^6 parts of water was "cucumber"- or "melon"-like with no significant difference between the two descriptions. The description for (*Z*)-6-nonenal as "green melon", informally arrived at, was in agreement with the description used by other investigators (Keppler et al., 1965, 1967; Kemp et al., 1972b; Parks et al., 1969). Although (*Z*)-5-octen-1-ol has an aroma associated with cucumbers or melons, this compound has not been found (to the author's knowledge) in a natural product.

Comparison of Natural Aroma Compounds with Fruit Fly Attractants. Compounds important to the aroma of several members of the melon family and compounds identified as fruit fly attractants have common structural features. The following studies of these compounds show those structural similarities which could be used as a basis for choosing compounds for fruit fly testing.

(*Z*)-6-Nonenal was first identified by Kemp et al. (1971, 1972a) as the aroma component characteristic of muskmelon (*Cucumis melo* L.). Kemp et al. (1972a) identified (*Z*)-6-nonen-1-ol from muskmelon and described its odor as reminiscent of cucumbers. Kemp et al. (1974a) found (*Z*)-6-nonenal and (*ZZ*)-3,6-nonadien-1-ol in the botanically related cucumber along with the major components (*EZ*)-2,6-nonadienal and (*E*)-2-nonenal previously determined by Forss et al. (1962). Kemp et al. (1974b) isolated (*ZZ*)-3,6-nonadien-1-ol as the watermelon aroma com-

pound from the genus related watermelon (*Citrullus vulgaris*) and muskmelon (*Cucumis melo* L.). All of these melon aroma compounds are C₉ aliphatic alcohols and aldehydes predominantly unsaturated in the 6 position. Precursors of these type compounds have been studied in hydrogenated oils.

Keppler et al. (1965) identified (*E*)-6-nonenal as the principal contributor and (*Z*)-6-nonenal as a lesser contributor to off-flavor in "hardened" linseed oil and advanced the theory that isolinoleic acids present could be oxidized according to the theory of Farmer and Sutton (1946) to 6-nonenal. The model oxidation experiments of Keppler et al. (1967) showed (*Z*)-6-nonenal was formed from (*ZZ*)-8,15- and (*ZZ*)-9,15-octadecadienoic acids; however, the important (*E*)-6-nonenal could come only from *EE* or *ZE* isomers which had not yet been found in hydrogenated oils. Kawada et al. (1966) identified a number of compounds which are formed immediately upon hydrogenation but before oxidation of the oil can occur; no nonenal was found under these conditions. Parks et al. (1969) reported that (*E*)-6-nonenal is the off-flavor component in spray dried milk. Yasuda et al. (1975) reported a spectrum of compounds including (*E*)- and (*Z*)-6-nonenals in deodorized soybean oil. The above investigators presumed that both nonenals are oxidation products of isolinoleic acids although the required C₁₈ isomers have not been identified in the materials containing the nonenals.

The pattern of C₉ compounds in the melon family also extends to several related C₉ compounds found as fruit fly attractants. Jacobson et al. (1971) found that (*E*)-6-nonen-1-ol acetate was a strong attractant for the female melon fly, *Dacus cucurbitae* Coquillett. Jacobson et al. (1973) isolated, identified, and synthesized methyl (*E*)-6-nonenate and (*E*)-6-nonen-1-ol as sex pheromones for the Mediterranean fruit fly, *Ceratitis capitata* Wiedemann. Ohinata et al. (1977, 1979) through field testing and research found that these C₉ compounds were potent attractants for several species of fruit flies. Rossi et al. (1978) found that (*Z*)-6-nonen-1-ol was the most potent attractant of a series of C₉ enols tested on the olive fruit fly, *Dacus oleae* (Gmelin). (*Z*)-6-Nonenal is currently being tested at the U.S. Department of Agriculture Honolulu laboratory.

Several synthesis with varying approaches have been published for C₉ enols and enals which should be useful in obtaining compounds for testing. Keppler et al. (1965) published two long reaction sequences for (*E*)- and (*Z*)-6-nonenals. Jacobson et al. (1971) synthesized (*E*)-6-nonen-1-ol using a modification of the synthesis of Keppler et al. (1965). Both Jones et al. (1975) and Rossi et al. (1978) reported synthesis for the 6-nonenals and other enals. Recently there has been interest in other alkenols, including 5-octen-1-ol, as potential fruit fly attractants and also for flavoring purposes. Ohloff et al. (1977), Brown et al. (1979), and Svirskaya et al. (1979) applied various synthetic methods to synthesize 5-octen-1-ol and other alkenols. Nakamura et al. (1979) patented a synthesis for (*Z*)- and (*E*)-5-octen-1-ols and claimed various esters were useful as food flavors.

Conclusions. A comparison of known fruit fly attractants shows that the most potent are aliphatic C₉ compounds unsaturated in the 6 position containing various terminal functional groups and are thus closely related to the C₉ compounds important to the characteristic aromas of the melon family and off-aromas in linoleic acid containing oils. Other closely related compounds may have

attractant potential. Svirskaya et al. (1979) synthesized (*Z*)-5-octen-1-ol and other (*E*)-alkenols as candidates for testing. The author's short reaction sequence leading to (*Z*)-5-octen-1-ol and to (*Z*)-6-nonenal should be useful in obtaining these two compounds for investigation and testing as attractant and aroma constituents.

Preliminary screening of small amount of (*Z*)-6-nonenal as an attractant indicated the need for further testing. No quantitative results are available at this time. There has been no testing of (*Z*)-5-octen-1-ol.

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