# Synthesis and Biological Evaluation of Candidate Nonenyl Acetates as Melon Fly Ovipositional Attractants

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(*E*)-6-Nonen-1-ol acetate is an ovipositional stimulant for the melon fly but is somewhat toxic as egg hatch is below the standard of comparison. Related compounds were obtained by synthesizing 19 7-methyl- and 8-methylnonenol acetates with cis or trans double bonds at positions 2–7. The olefins or synthons were prepared via reduction of appropriate acetylenic precursors with either hydrogen and catalyst (*Z*), LAH (*E*), or sodium–ammonia (*E*), by the Wittig condensation (*Z*), by inversion of configuration (*Z* to *E*) via epoxide and dibromide, by rearrangement of a cyclopropylmethyl carbocation (*E*), or by the ring opening with sodium of a 2-alkyl-3-chlorotetrahydropyran (*E*). On biological evaluation using a tomato juice standard, all tested olefinic acetates elicited egg laying, but 8-methyl-3-nonyn-1-ol acetate killed all eggs (zero hatch), indicating that acetylene derivatives are wholly toxic. It is tentatively suggested that 8-methylnonen-1-ol acetates stimulate oogenesis to a greater extent than do the 7-methyl analogues.

The female melon fly (*Dacus cucurbitae* Coquillett) oviposits on several valuable commerical plants; tomatoes are especially vulnerable, and the juice appears to have a quality or constituent that stimulates oviposition. A recent report (Burton and Schuster, 1981) concludes that the surface of tomato plants contains a substance that stimulates oviposition by the tomato pinworm, *Keiferia lycopersicella* (Walsingham).

In this paper we use the term "stimulant" to refer to a chemical that stimulates oogenesis, by increasing the number of eggs from an individual female. An "attractant" refers to the attraction of female flies to the chemical as an ovipositional site.

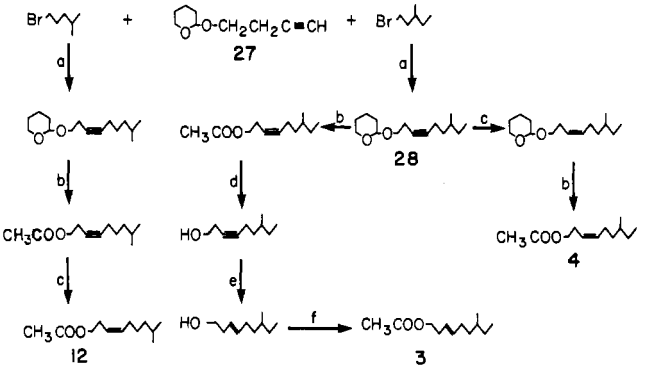
In a program designed to increase the size of the melon fly colony at the U.S. Department of Agriculture Honolulu station, we attempted to discover improved ovipositional stimulants for this insect. Nonyl (nonenyl) acetates have a chemical relationship to two components, methyl (*E*)-6-nonenoate and (*E*)-6-nonen-1-ol, of the sex pheromone of the Mediterranean fruit fly *Ceratitis capitata* (Wiedemann) (Jacobson et al., 1973). Early studies of straight-chain esters showed that the attractant (*E*)-6-nonen-1-ol acetate, **31** (Jacobson et al., 1971), was also an ovipositional attractant and stimulant for the melon fly under laboratory conditions (Keiser et al., 1973). However, this compound was toxic to the eggs and resulted in a heavy reduction in egg hatch; tests conducted in the field with this compound were not promising.

We later discovered that (*E*)-8-methyl-6-nonen-1-ol acetate, **21** prepared like **31** but using 3-chloro-2-isopropyltetrahydropyran instead of the ethyl analogue, possessed equal or greater stimulatory power and seemed somewhat less toxic. Accordingly, the synthesis of substituted nonenyl acetates was extended to cover two series of 7- and 8-methyl derivatives—**1–8**, and **9–18**, respectively—that were evaluated for ovipositional stimulation and attractancy and their effect on egg viability.

## EXPERIMENTAL SECTION

**Materials and Methods.** Chemical reagents and reagent-grade solvents were purchased commercially; acetonitrile was redistilled before use, and tetrahydrofuran (THF) was purified by distillation from lithium aluminium hydride (LAH).

Scheme I. Typical Olefin Syntheses Utilizing Acetylenic Intermediates[a]




[a] (a) BuLi-HMPTA; (b) AcOH-AcCl; (c) Pd-$CaCO_3$(Pb)-$H_2$; (d) NaOH; (e) Na-$NH_3$; (f) $Ac_2O$-$C_5H_5N$.

Preparations were by routes appropriate to the positional and geometrical isomers required. Eleven of the olefinic esters were made by reducing acetylenes with the same carbon skeletons—six of them (**2, 4, 10, 12, 14, 16**) with cis stereochemistry by hydrogenation using Lindlar catalyst, three trans isomers (**3, 13, 15**) by sodium–ammonia reduction, and two (**1, 9**), which are acetates of 2-propen-1-ols, by LAH reduction of propynyl precursors (Chanley and Sobotka, 1949). The application of such methods in the syntheses of **3, 4, 12**, and precursors is shown in Scheme I. (*Z*)-8-Methyl-3-nonen-1-ol, the alcohol base of **12**, has been reported in the patent literature (Watson et al., 1975).

The Wittig olefin synthesis was used to prepare compounds **6, 8, 17**, and **18**, starting from tetra-, penta-, hexa- and heptamethylene halohydrins and condensing the derived ylids with appropriate aldehydes or with acetone (for **18**). A preparation of 8-methyl-7-nonen-1-ol, the alcohol corresponding to **18**, has been reported (Min'kovskiĭ and Cherkaev, 1973).

The geometry of two cis olefins (**6, 8**) was inverted by conversion to *vic*-dibromides and elimination of the halogen with zinc. With erythro dibromides this is stereospecifically trans (Sonnet and Oliver, 1976), and hence **6** and **8** (*Z*) gave **5** and **7** (*E*), respectively.

The rearrangement with ring opening of a cyclopropylmethyl carbocation gives a trans olefin (Julia et al., 1960; Schwarz and Wakabayashi, 1977). By converting

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α-(4-methylpentyl)cyclopropanemethanol to (*E*)-1-bromo-8-methyl-3-nonene, the carbon skeleton of 11 was obtained.

New compounds were identified through method of synthesis, elemental analysis (Galbraith Laboratories, Inc.), and infrared (IR) or proton nuclear magnetic resonance ($^1$H NMR) spectra. The IR spectra were obtained from thin films of samples between NaCl or AgCl plates with a Perkin-Elmer 283 spectrophotometer. NMR spectra were made in carbon tetrachloride solution with tetramethylsilane as the zero reference on a Varian T-60 spectrometer. Analysis by gas–liquid chromatography was on packed (e.g., 6 ft × $^1/_8$ in. DEGS) or capillary (50 ft × 0.02 in. DEGS–SCOT or 60 m × 0.25 mm SP-1000 WAL-COT) columns.

**Acetylenic Intermediates.** Substitution reactions between acetylide anions and organic halides gave **22**, **24**, **28**, and **29** (Schwarz and Waters, 1972); **25** and **27** were prepared by acid-catalyzed addition of dihydropyran to the alcohols.

*Tetrahydro-2-[(8-methyl-5-nonynyl)oxy]-2H-pyran* (**22**). 4-Methylpentyne (9 g, 100 mmol) in THF (60 mL) under $N_2$ at −30 °C was treated with 1.6 M *n*-butyllithium in hexane (70 mL) followed by 2-[(4-chlorobutyl)oxy]tetrahydro-2H-pyran (23.9 g, 124 mmol) in HMPTA (30 mL). The mixture was stirred 4 h and poured into ice–water, and the product was extracted with hexane and distilled to give **22** (19.8 g, 75%): bp 90°C (0.025 mmHg).

*Tetrahydro-2-[(8-methyl-4-nonynyl)oxy]-2H-pyran* (**24**). Similar condensation of 5-methylhexyne (5.7 g, 60 mmol) and 2-[(3-bromopropyl)oxy]tetrahydro-2*H*-pyran (13.3 g, 64 mmol) gave **24** (10.5 g, 69%): bp 90 °C (0.1 mmHg).

*Tetrahydro-2-(2-propynyloxy)-2H-pyran* (**25**). The interaction of 2- propynol and 2,3-dihydropyran in presence of hydrochloric acid (Green et al., 1967) or *p*-toluenesulfonic acid (Corey and Terashima, 1972) gave **25**: bp 73–75 °C (18 mmHg); $^1$H NMR δ 1.62 (s, 6 H), 2.24 t, 1 H), 3.47 (m, 2 H), 4.08 (d, 2 H), 4.68 (s, 1 H).

*2-(3-Butynyloxy)tetrahydro-2H-pyran* (**27**). 3-Butyn-1-ol (21 g, 0.3 mol) and hydrochloric acid (2 drops), stirred at 0 °C, was treated with 2,3-dihydropyran (26 g, 0.31 mol). After 1 h sodium bicarbonate (0.75 g) was added, and the mixture was stirred 2 h, filtered, and distilled to give **27**: bp 92–93.5 °C (20 mmHg); $n^{25}_D$ 1.4558; IR 3289 (s), 2128 (w) cm$^{-1}$; MS *m/z* (rel intensity) 153 (M − 1), 85 (100).

*Tetrahydro-2-[(7-methyl-3-nonynyl)oxy]-2H-pyran* (**28**). The coupling (BuLi, HMPTA) of 1-bromo-3-methylpentane (14 g, 85 mmol) and the acetylene **27** (12.35 g, 80 mmol) gave **28** (13.75 g, 72%): bp 109–110 °C (0.5 mmHg).

*Tetrahydro-2-[(8-methyl-2-nonynyl)oxy]-2H-pyran* (**29**). 5-Methylhexan-1-ol, bp 70 °C (40 mmHg), was prepared from 3-methylbutylmagnesium bromide and ethylene oxide (Dreger, 1941). It was converted by dibromotriphenylphosphorane to 1-bromo-5-methylhexane, bp 90–93 °C (60 mmHg). This halide with the acetylene **25** in HMPTA gave **29**: bp 105–110 °C (0.1 mmHg).

**Synthesis of Candidate Esters.** *(E)-7-Methyl-2-nonen-1-ol Acetate* (**1**). 7-Methyl-2-nonyn-1-ol (2 g, 13 mmol) in THF (10 mL) was added slowly to LAH (2 g, assay 90+%) in $N_2$-protected THF (30 mL) at −78°C, stirred 1 h, heated 2.5 h under reflux, and treated *cautiously* with water (7 mL). Solid was removed by filtration; workup of the filtrate gave (*E*)-7-methyl-2-nonen-1-ol (IR 971 cm$^{-1}$), which was dissolved in pyridine (3 mL) and acetic anhydride (2.5 mL). The mixture was heated 0.5 h at 80 °C, left overnight, diluted with water, and extracted with hexane to give **1**: bp 121–122 °C (18 mmHg); $n^{25}_D$ 1.6389; IR 1740, 1665, 1378/1361, 1230, 1022, 966 cm$^{-1}$.

*(Z)-7-Methyl-2-nonen-1-ol Acetate* (**2**). 7-Methyl-2-nonyn-1-ol acetate (**26**) (from the acetylene **25** and 4-bromohexane; 3.41 g, 17.4 mmol) in hexane (60 mL) was hydrogenated at 18 °C with Lindlar catalyst (0.34 g, 5% Pd on $CaCO_3$, Pb poisoned; Strem Chemicals, Inc.). Filtration and workup gave **2** (2.9 g, 85%): bp 120–121 °C (18 mmHg); $n^{25}_D$ 1.4387; IR 1743, 1234 cm$^{-1}$.

Alternatively, a suspension of nickelous acetate tetrahydrate in ethanol under $H_2$ was treated with methanolic $NaBH_4$ and then ethylenediamine in ethanol and **26** was added. When hydrogen uptake was complete **2** was isolated, identical in properties with the preceding sample.

*(E)-7-Methyl-3-nonen-1-ol Acetate* (**3**). The THP ether **28** (10.7 g, 45 mmol) was stirred 2 h at 57 °C with acetyl chloride (12 mL) and acetic acid (50 mL), and the mixture was cooled and neutralized (ice, $NaHCO_3$). Workup gave 7-methyl-3-nonyn-1-ol acetate (8 g, 91%): bp 87–88 °C (1.1 mmHg); IR 2228 (w), 1743, 1382, 1366, 1239, 1041 cm$^{-1}$. Hydrolysis of the ester (5.9 g) with 10% aqueous NaOH (15 mL) and methanol (15 mL) gave 7-methyl-3-nonyn-1-ol (4.1 g, 88%): bp 117–119 °C (17 mmHg); IR 3340, 2220 (w); 1044 (v s), 846 cm$^{-1}$.

A 250-mL flask with Nichrome Hershberg stirrer and reflux condenser (dry ice) was charged with liquefied ammonia (100 mL) at −33 °C and a solution of 7-methyl-3-nonyn-1-ol (4 g) in THF (25 mL). Small pieces of sodium were added until the blue color persisted for 3 h, with GLC monitoring to follow the reduction. Careful addition of saturated aqueous $NH_4Cl$ solution (15 mL), evaporation of ammonia, and hexane extraction gave crude (*E*)-7-methyl-3-nonen-1-ol (3.8 g; IR 3324, 1046, 966 cm$^{-1}$), which was directly converted to **3** by solution in acetic anhydride (5 mL) and pyridine (5 mL): bp 119–120 °C (17 mmHg), $n^{25}_D$ 1.4375; purity by GLC 98.3%; IR 1740, 1380/1363, 1043, 967 cm$^{-1}$.

*(Z)-7-Methyl-3-nonen-1-ol Acetate* (**4**). The acetylene **28** (2.38 g, 10 mmol) was hydrogenated in hexane with Lindlar catalyst with GLC monitoring. The cis olefin obtained by evaporating the solvent was dissolved at 0 °C in acetyl chloride and acetic acid, which was left overnight, quenched with ice–water, and extracted with hexane. Distillation gave **4** (1.47 g, 74%): bp 140–145 °C (bath temperature; 17 mmHg); $n^{25}_D$ 1.4386; IR 1743, 1380/1363, 1240, 1036 cm$^{-1}$.

*(E)-7-Methyl-4-nonen-1-ol Acetate* (**5**). The isomeric *Z* olefin **6** with *m*-chloroperbenzoic acid gave 4,5-epoxy-7-methylnonan-1-ol acetate (92%): bp 80 °C (0.01 mmHg). The epoxide (2.3 g) was treated with dibromotriphenylphosphorane as for **7** to give crude dibromide. The reduction with Zn powder then gave **5**: bp 140 °C (bath temperature; 18 mmHg); IR 1736, 1245, 1045, 971 cm$^{-1}$.

*(Z)-7-Methyl-4-nonen-1-ol Acetate* (**6**). [4-[(Tetrahydropyran-2-yl)oxy]butyl]triphenylphosphonium iodide (24.5 g, 45 mmol) in HMPTA (250 mL) was treated at 5 °C with 90% *n*-butyllithium in hexane (9 g), stirred 0.5 h, and treated with 3-methylpentanal (4.5 g, 45 mmol). After 2.5 h it was diluted with ice–water (1.5 L) and extracted with hexane (500 mL), which was washed with 9:1 $Me_2SO$–water (2 × 30 mL). Removal of solvent gave the protected olefinic alcohol, which was added to acetyl chloride (10 mL) and acetic acid (40 mL) and after 24 h worked up to give **6** (6.9 g, 77%): bp 125–130 °C (18 mmHg; bath temperature); IR 1740, 1238, 1037 cm$^{-1}$.

*(E)-7-Methyl-5-nonen-1-ol Acetate* (**7**). The isomeric *Z*-olefinic ester **8** (2.98 g, 15 mmol) was added to dichloromethane (60 mL) at 0 °C containing 85% *m*-chloroperbenzoic acid (3.2 g) and stirred 16 h with GLC monitoring; 24 h later the solution was decanted from

chlorobenzoic acid and worked up to give 5,6-epoxy-7-methylnonan-1-ol acetate (2.95 %, 91%; purity 98% by GLC).

The epoxide was added to dibromotriphenylphosphorane (15 mmol) in benzene (55 mL) and stirred 18 h. The resultant 5,6-dibromo-7-methylnonan-1-ol acetate (3.3 g) was stirred 1 h with Zn dust (3 g) in acetic acid (30 mL). Dilution with water, hexane extraction, and distillation (130–160 °C, bath temperature; 17 mmHg) and molecular still treatment gave colorless **7** (1.2 g, 63%): $n^{25}_D$ 1.4378; IR 1739, 1240, 1040, 970 $cm^{-1}$.

*(Z)-7-Methyl-5-nonen-1-ol Acetate* (**8**). 2-[(Chloropentyl)oxy]tetrahydro-2*H*-pyran (from Mid-West Research Institute) was converted to tetrahydro-2-[(5-iodopentyl)oxy]-2*H*-pyran by heating with sodium iodide in 2-butanone. This was heated 36 h with triphenylphosphine in acetonitrile to give [5-[(tetrahydropyran-2-yl)oxy]-pentyl]triphenylphosphonium iodide, a very stiff gum.

The iodide in HMPTA was treated with 90% *n*-butyllithium in hexane followed after 20 min by 2-methylbutanal. After stirring for 16 h, treatment with ice–water and cleanup gave (*Z*)-tetrahydro-2-[(7-methyl-5-nonenyl)oxy]-2*H*-pyran (80%). This was heated 1 h at 50 °C with acetyl chloride and acetic acid to give **8** (79%): bp 70–71 °C (0.5 mmHg); $n^{25}_D$ 1.4365; IR 1744, 1650 (w), 1240, 1036, 730 $cm^{-1}$. Analysis by GLC on 50-ft DEGS and 60-m SP-1000 WALCOT columns showed purity >98.6%; the minor component was presumably the *E* isomer.

*(E)-8-Methyl-2-nonen-1-ol Acetate* (**9**). The THP ether **29** was converted to 8-methyl-2-nonyn-1-ol acetate by heating for 2.5 h at reflux in acetic acid and acetyl chloride (9:1). Reduction of this acetate was carried out with LAH in the manner of **1**. The resultant (*E*)-8-methyl-2-nonen-1-ol was reacetylated with acetic anhydride–pyridine to give **9**: bp 75 °C (bath temperature; 0.01 mmHg).

*(Z)-8-Methyl-2-nonen-1-ol Acetate* (**10**). The acetylene **29** (1 g) in hexane (25 mL) was hydrogenated with Lindlar catalyst (0.2 g). After filtration and removal of the solvent, the residue was kept 18 h at 40 °C in 1 mL of acetyl chloride and 10 mL of acetic acid to give **10**: bp 80 °C (0.1 mmHg); $n^{25}_D$ 1.4392; IR 1739, 1230, 1023 $cm^{-1}$.

*(E)-8-Methyl-3-nonen-1-ol Acetate* (**11**). The Grignard solution prepared from 1-bromo-4-methylpentane (33 g, 200 mmol) and magnesium (5.35 g, 0.22 g-atom) in ether (200 mL) was treated with cyclopropyl cyanide (13.4 g, 200 mmol) in ether (50 mL), stirred 16 h under reflux, treated with saturated ammonium chloride solution (40 mL) and 12 N hydrochloric acid (45 mL), and extracted with hexane after removal of ether, giving cyclopropyl 4-methylpentyl ketone (**30**) (24.2 g, 78%): bp 90–92 °C (18 mmHg); IR 1700 $cm^{-1}$. It had a powerful fruity odor.

Reduction of **30** (7.7 g, 50 mmol) was effected by adding, with stirring, the solution in 30 mL of ethanol to a solution of sodium borohydride (3.5 g) and sodium hydroxide (0.3 g) in ethanol (100 mL) at 0 °C. On the following day, 25 mL of ice–water was added and ethanol removed; extraction with hexane gave α-(4-methylpentyl)cyclopropanemethanol (6.3 g, 80%): bp 120 °C (20 mmHg). Treatment of the carbinol (5.4 g, 34 mmol) in ether (30 mL) at 0 °C with chilled 48% hydrogen bromide (18 mL) during 0.5 h, followed by stirring 0.5 h, addition of 30 mL of ice–water, and workup, gave (*E*)-1-bromo-8-methyl-3-nonene (6.8 g, 90%): bp 120 °C (18 mmHg); IR 3084, 3050, 1386, 1370, 1155, 1024, 966, 829, 740, 678 $cm^{-1}$.

The bromide (5.4 g, 27 mmol) was heated at 140 °C (oil bath) with potassium acetate (8.1 g) in acetic acid (19 mL) for 36 h, giving **11** (4 g, 82%): bp 63–65 °C (0.5 mmHg); IR 1737, 1635 (w), 1240, 1039, 966 $cm^{-1}$.

*(Z)-8-Methyl-3-nonen-1-ol Acetate* (**12**). The acetylene **27** (10.8 g, 70 mmol) in THF (100 mL) was treated under $N_2$ at −50 °C with 1.6 M *n*-butyllithium in hexane (48 mL), followed by 1-bromo-4-methylpentane (12.3 g, 75 mmol) in HMPTA (20 mL), keeping the mixture at −30 °C. The solution, at 15 °C after overnight stirring, was poured onto crushed ice (200 g). Extraction with hexane (140 mL) gave tetrahydro-2-[(8-methyl-3-nonynyl)oxy]-2*H*-pyran (13 g, 80%): bp 105–107 °C (0.5 mmHg). Anal. Required for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.18; H, 10.58.

This nonynyl ether was heated 1 h at 55 °C in acetyl chloride (18 mL) and acetic acid (70 mL) to give 8-methyl-3-nonyn-1-ol acetate (**20**) (12.1 g, 92%): bp 80–82 °C (0.8 mmHg); $n^{25}_D$ 1.4420; purity by GLC (DEGS columns) was >99.7%.

Compound **20** (5.9 g, 30 mmol) in hexane (70 mL) was hydrogenated in presence of Lindlar catalyst (0.6 g) with GLC monitoring until reduction to the cis olefin was complete. Workup gave **12** (4.8 g, 81%): bp 63.5–64.5 °C (0.5 mmHg); $n^{25}_D$ 1.4360; GLC purity >99.7%; IR 1740, 1654 (w), 1382/1364, 1239, 1034 $cm^{-1}$.

*(E)-8-Methyl-4-nonen-1-ol Acetate* (**13**). The acetylene **24** (5 g) in THF (25 mL) in liquid ammonia (25 mL, −33 °C) was treated with Na (1.2 g) until the blue color persisted. Evaporation of the $NH_3$ and workup (cf. **3**) gave the trans olefin. This was treated with acetyl chloride–acetic acid to give **13** (3 g, 72%): bp 70–75 °C (bath temperature; 0.01 mmHg); $n^{25}_D$ 1.4388; IR 1743, 1388/1370, 1244, 1040, 970 (trans CH=CH) $cm^{-1}$.

*(Z)-8-Methyl-4-nonen-1-ol Acetate* (**14**). The action of 2 mL of acetyl chloride and 20 mL of acetic acid on the THP ether **24** (5 g) for 18 h at 40 °C gave 8-methyl-4-nonyn-1-ol acetate: bp 80–85 °C (0.01 mmHg). Hydrogenation with Lindlar catalyst gave **14**: bp 75 °C (0.01 mmHg); $n^{25}_D$ 1.4384; IR 1741, 1389/1369, 1246, 1041 $cm^{-1}$.

*(E)-8-Methyl-5-nonen-1-ol Acetate* (**15**). The acetylene **22** was reduced with sodium in liquid ammonia to (*E*)-tetrahydro-2-[(8-methyl-5-nonenyl)oxy]-2*H*-pyran. This protected alcohol (8.41 g, 35 mmol) was heated 1.5 h with acetyl chloride (11 g) and acetic acid (45 mL). Workup gave **15** : bp 55–57 °C (0.1 mmHg); IR 1745, 1646 (w), 1389/1369, 1242, 1042, 970 $cm^{-1}$; $^1H$ NMR δ 0.88 (d, 6 H), 1.96 (s, 6 H), 4.0 (t, 2 H), 5.37 (t, 2 H).

*(Z)-8-Methyl-5-nonen-1-ol Acetate* (**16**). (a) The acetylene **22** (6 g, 25.4 mmol) was hydrogenated in hexane with palladium catalyst (5% in $BaSO_4$; Strem Chemicals, Inc.) with GLC monitoring, and the resultant cis olefin was heated 1 h at 50 °C with acetyl chloride (8 g) and acetic acid (30 mL) to give **16**: bp 46 °C (0.075 mmHg); IR 1744, 1650 (w), 1386/1369 *gem*-$Me_2$, 1244, 1037 $cm^{-1}$; $^1H$ NMR δ 0.89 (d, 6 H), 1.96 (s, 3 H), 4.0 (t, 2 H), 5.37 (t, 2 H).

(b) Treatment of **22** (7.14 g, 30 mmol) with acetyl chloride–acetic acid gave 8-methyl-5-nonyn-1-ol acetate (**23**) (5.62 g, 95%): bp 63.5 °C (0.05 mmHg). Reduction of **23** with Lindlar catalyst gave material identical with **16**.

*(Z)-8-Methyl-6-nonen-1-ol Acetate* (**17**). (6-Hydroxyhexyl)triphenylphosphonium iodide in HMPTA was treated at 10 °C with 90% *n*-butyllithium in hexane; the dark red solution of the ylid was stirred 2 h at 15 °C and 2-methyl-1-propanal added. After 18 h, workup (ice–water, solvent extraction) gave 8-methyl-(*Z*)-6-nonen-1-ol, bp 100–115 °C (30 mmHg), which was purified by chromatography on alumina (final elution with pure ether). The alkenol in acetic anhydride with pyridine, left overnight and worked up in the usual manner, gave **17**: bp 120 °C (18 mmHg; bath temperature); IR 1740, 1236, 1046 $cm^{-1}$.

*8-Methyl-7-nonen-1-ol Acetate* (**18**). (7-Hydroxyheptyl)triphenylphosphonium bromide in HMPTA was

treated at 0 °C under $N_2$ with 1.6 M *n*-butyllithium solution; after 5 min acetone was added. The mixture was heated 1 h at 85 °C, left overnight, chilled to 0 °C, and directly acetylated with pyridine and acetyl chloride. The suspension was filtered and washed with hexane, and the organic liquid was added to ice, separated, washed, and dried, to give 18: bp 76–77 °C (0.65 mmHg); $n^{25}_D$ 1.4441; IR 1740, 1238 $cm^{-1}$; purity by GLC (Carbowax 20M-TPA column) was 99.4%.

*(E)-8-Methyl-6-nonen-1-ol Acetate* (21). Ether (450 mL) containing 2-propylmagnesium bromide (3.28 mol) was treated with 2,3-dichlorotetrahydropyran (343 g) in ether (280 mL). The resultant 3-chloro-2-isopropyltetrahydropyran [bp 75 °C (20 mmHg); $n^{25}_D$ 1.4578] was added in ether (250 mL) to powdered sodium (61.3 g) under ether (350 mL), and the mixture was refluxed 1 h. Quenching (water, aqueous HCl) and extraction gave (*E*)-6-methyl-4-hepten-1-ol: bp 85–100 °C (10 mmHg); $n^{25}_D$ 1.4420. Treatment with phosphorus tribromide (94 g) and pyridine (15 mL) in ether and refluxing for 3 h after the slow addition gave (*E*)-bromo-6-methyl-4-heptene: bp 85–93 °C (17 mmHg); $n^{25}_D$ 1.4627.

The ethanolic solution of ethyl sodiomalonate prepared from Na (11.6 g) and the ester (80 g) was treated at 45 °C with the (*E*)-bromo-6-methyl-4-heptene, refluxed for 6 h, and worked up to give diethyl (*E*)-(6-methyl-4-heptenyl)malonate (70.4 g): bp 105–115 °C (0.3 mmHg); $n^{25}_D$ 1.4403. On saponification this gave (*E*)-(6-methyl-4-heptenyl)malonic acid (63.6 g), which was decarboxylated by heating 3 h at 175–180 °C. Distillation of the residue gave (*E*)-8-methyl-6-nonenoic acid (28.7 g): bp 110 °C (0.5 mmHg); $n^{25}_D$ 1.4452.

Dry ether (175 mL) containing the methylnonenoic acid was added dropwise to LAH (10.3 g) in ether (300 mL). After 0.5 h, treatment with ice and $H_2SO_4$ gave (*E*)-8-methyl-6-nonen-1-ol (18.3 g): bp 75–78 °C (0.3 mmHg); $n_D^{25}$ 1.4468.

The methylnonenol in benzene (80 mL) and pyridine (11.5 mL) was treated at 0 °C with acetyl chloride (11.2 g), refluxed 4 h, left overnight, chilled, and treated with 5% aqueous HCl. The organic layer yielded **21** (20.7 g): bp 78 °C (0.2 mmHg); $n^{25}_D$ 1.4349; IR 1764, 1397/1374, 1242, 1053, 975 $cm^{-1}$.

**Biological Methods.** In all studies canned tomato juice diluted 1:1 with water (v/v) was used as the standard of comparison with the synthetic substances. This is the formulation used to treat sponges placed in egging receptacles for mass rearing in Hawaii.

Receptacles were the pin-pierced 1-oz plastic creamers, containing synthetic sponge treated with the candidate chemical or diluted tomato juice, in cages as previously described (Keiser et al., 1973). Each glass-fronted cage contained 500 adult melon flies—250 males and 250 females ca. 20–30 days old of the same emergence hatch for any particular test. After each period of exposure, the receptacles were removed and the number of eggs determined. When this number was too large for convenient counting, a calibration method suitable for small eggs was used. The eggs were washed into a small beaker with water and transferred to a small funnel, which had a stem of constant diameter closed at the end with a cotton cloth for straining. The height of the drained egg column could be compared with that from a known count of eggs. An aliquot of these eggs was retained to determine the percent hatch.

In the first series of tests, one egging receptacle containing the sponge with tomato juice and one egging receptacle containing a sponge saturated with the test chemical were placed in the same cage. Suitable controls with water-only sponges were included in the earliest studies but elicited little or no oviposition.

**Table I. Fecundity and Egg Viability with Synthetic Unsaturated Acetates**[a]

| compound no. | no. of eggs collected | % hatch |
|---|---|---|
| | Candidate Chemical | |
| 5 | 935 | 5 |
| 6 | 550 | 6 |
| 7 | 233 | 4 |
| 8 | 2805 | 53 |
| 9 | 1760 | 11 |
| 10 | 1540 | 7 |
| 11 | 1210 | 18 |
| 12 | 1925 | 16 |
| 13 | 1815 | 13 |
| 14 | 1595 | 10 |
| 15 | 1760 | 16 |
| 16 | 1815 | 19 |
| 17 | 4345 | 17 |
| 18 | 3850 | 22 |
| 20 | 170 | 0 |
| 21 | 3190 | 7 |
| 31 | 3740 | 4 |
| | Tomato Juice[b] | |
| | 5555 | 80 |
| | 3025 | 81 |
| | 2530 | 85 |
| | 6545 | 88 |
| | 3410 | 83 |
| | 2365 | 84 |
| | 2255 | 83 |

[a] Four or more replicates of the standard of comparison, each in separate cages. [b] Mean = 3669 and SD = 1698 for number of eggs collected; mean = 83.4 and SD = 2.6 for percent hatch.

Preliminary tests with several of the compounds evaluated in the above manner showed that they were more powerful ovipositional attractants of female melon flies that the tomato juice standard of comparison when both egging receptacles were placed in the same cage. However, the egg hatch for tomato juice was lower (median 51%) than that for the control (median 83% when cage contained only a receptacle with tomato juice), indicating that when both receptacles were in one cage the vapors from the chemical-containing receptacle adversely affected the eggs laid in the one with the tomato juice. Accordingly, in the later series of studies (Table I), the egging receptacles with chemicals and tomato juice were kept in separate cages. To make best use of the comparatively small quantities of synthesized chemicals and to prevent drying out of the sponges, 10 drops of 1.0% ethanol solution of the chemical plus 10 drops of water were placed on each treated sponge.

## RESULTS AND DISCUSSION

Melon fly egg hatch in the tomato juice standard ranged from 80 to 88% (median 83%) while the hatch with the compounds reported here (Table I) ranged from 0 to 53% (median 11%). Hence, the methylnonenyl acetates, like the original unbranched ester **31**, are toxic to the eggs, as evidenced by the reduced hatch. Nevertheless, all are ovipositional attractants for melon flies, with compounds **8**, **17**, **18** and **21** better than the other test compounds in this respect. Compound **8**, with 53% egg hatch, was least toxic to the eggs, and compound **7** (also **31** in this set of tests) was the most toxic olefin, with 4% egg hatch. Compound **20** was tested as it was an intermediate in the preparation of **12** and was seen to be most toxic of all (no hatch), but because of this high toxicity and because analogues corresponding to each olefin could not be

available from all synthetic routes, no other acetylenic compounds were tested.

Hence, all of the compounds gave a significantly lower egg hatch than that obtained with tomato juice, the standard of comparison. We are researching the possibility of using metal fruit-shaped "decoys" baited with these ovipositional lures in the field to "drain" the eggs of melon flies prior to their undesirable deposition on actual ripening fruit such as tomato, squash, and cucumber.

A structure–activity relationship in these substances (16 olefinic esters, as it was not possible at the time to test 1–4) is not readily apparent. Hatching is low in all, and even **8** is quite toxic. Compounds **8**, **17**, **18**, **21** and **31** have better oogenesis qualities, and in these the highest toxicity is possessed by **21** and **31**, both of which have the trans configuration. Three of the four 7-methyl derivatives (**5**, **6**, **7**) strongly reduce egg production and are also highly toxic.

**Registry No.** **1**, 90368-73-3; **2**, 90368-74-4; **3**, 90368-75-5; **4**, 90368-76-6; **5**, 90368-77-7; **6**, 90368-78-8; **7**, 90368-79-9; **8**, 90368-80-2; **9**, 90368-81-3; **10**, 90368-82-4; **11**, 90368-83-5; **12**, 90368-84-6; **13**, 90368-85-7; **14**, 90368-86-8; **15**, 90368-87-9; **16**, 90368-88-0; **17**, 90368-89-1; **18**, 90368-90-4; **20**, 90368-91-5; **21**, 90368-92-6; **22**, 90368-93-7; **23**, 90368-94-8; **24**, 90368-95-9; **25**, 6089-04-9; **26**, 90368-96-0; **27**, 40365-61-5; **28**, 90368-97-1; **29**, 62088-66-8; **30**, 90368-98-2; **31**, 30412-53-4; 4-methylpentyne, 7154-75-8; 2-[(4-chlorobutyl)oxy]tetrahydro-2*H*-pyran, 41302-05-0; 5-methylhexyne, 2203-80-7; 2-[(3-bromopropyl)oxy]tetrahydro-2*H*-pyran, 33821-94-2; 2-propynol, 107-19-7; 2,3-dihydropyran, 110-87-2; *p*-toluenesulfonic acid, 104-15-4; 3-butyn-1-ol, 927-74-2; 1-bromo-3-methylpentane, 51116-73-5; 5-methylhexan-1-ol, 627-98-5; 1-bromo-5-methylhexane, 35354-37-1; 7-methyl-2-nonyn-1-ol, 90368-99-3; (*E*)-7-methyl-2-nonen-1-ol, 90369-00-9; 7-methyl-3-nonyn-1-ol acetate, 90369-01-0; 7-methyl-3-nonyn-1-ol, 90369-02-1; (*E*)-7-methyl-3-nonen-1-ol, 90369-03-2; 4,5-epoxy-7-methylnonan-1-ol acetate, 90369-04-3; 4,5-dibromo-7-methylnonan-1-ol acetate, 90369-05-4; [4-[(tetrahydropyran-2-yl)oxy]butyl]triphenylphosphonium iodide, 90369-06-5; 3-methylpentanal, 15877-57-3; 5,6-epoxy-7-methylnonan-1-ol acetate, 90369-07-6; 5,6-dibromo-7-methylnonan-1-ol acetate, 90369-08-7; 2-[(5-chloropentyl)oxy]tetrahydro-2*H*-pyran, 13129-60-7; tetrahydro-2-[(5-iodopentyl)oxy]-2*H*-pyran, 55305-32-3; [5-[(tetrahydropyran-2-yl)oxy]pentyl]triphenylphosphonium iodide, 90369-09-8; 2-methylbutanol, 96-17-3; (*Z*)-tetrahydro-2-[(7-methyl-5-nonenyl)oxy]-2*H*-pyran, 90369-10-1; 8-methyl-2-nonyn-1-ol acetate, 90369-11-2; (*E*)-8-methyl-2-nonen-1-ol, 90369-12-3; α-(4-methylpentyl)cyclopropanemethanol, 90369-13-4; (*E*)-1-bromo-8-methyl-3-nonene, 90369-14-5; 1-bromo-4-methylpentane, 626-88-0; tetrahydro-2-[(8-methyl-3-nonynyl)oxy]-2*H*-pyran, 90369-15-6; 8-methyl-4-nonyn-1-ol acetate, 90369-16-7; (*E*)-tetrahydro-2-[(8-methyl-5-nonenyl)oxy]-2*H*-pyran, 90369-17-8; (6-hydroxyhexyl)triphenylphosphonium iodide, 19100-91-5; 2-methyl-1-propanol, 78-84-2; 8-methyl-(*Z*)-6-nonen-1-ol, 90369-18-9; (7-hydroxyheptyl)triphenylphosphonium bromide, 76771-95-4; 3-chloro-2-isopropyltetrahydropyran, 59721-81-2; (*E*)-6-methyl-4-hepten-1-ol, 59721-82-3; (*E*)-1-bromo-6-methyl-4-heptane, 59721-83-4; ethyl sodiomalonate, 996-82-7; diethyl (*E*)-(6-methyl-4-heptenyl)malonate, 59721-84-5; (*E*)-(6-methyl-4-heptenyl)malonic acid, 90369-19-0; (*E*)-8-methyl-6-nonenoic acid, 59320-77-3; (*E*)-8-methyl-6-nonen-1-ol, 90369-20-3.

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