SYNTHESIS OF (8*E*,10*Z*)-TETRADECA-8,10-DIENAL, SEX PHEROMONE OF HORSE CHESTNUT LEAFMINER (*Cameraria ohridella*), AND ALL ITS GEOMETRICAL ISOMERS

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Dedicated to Professor Otakar Červinka on the occasion of his 75th birthday in recognition of his outstanding contribution to the stereochemistry of organic compounds.

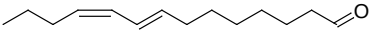
(8*E*,10*Z*)-Tetradeca-8,10-dienal (**1a**), sex pheromone of the horse chestnut leafminer (*Cameraria ohridella*; Lepidoptera, Gracillariidae), and its geometrical isomers (**1b**–**1d**) were efficiently synthesized using tetrakis(triphenylphosphine)palladium catalyzed cross-coupling reactions of alk-1-ynes or alkenyl alanes with corresponding vinyl iodides. The stereoisomeric purity of obtained tetradecadienals **1a**–**1d** was higher than 95% (GC). Relative electroantennographic (EAG) activities of the prepared compounds **1a**–**1d** elicited on male antennae supported the previously published identification of the *C. ohridella* sex pheromone.

Key words: Conjugated dienals; Stereoselective synthesis; Negishi reaction; Sex pheromones; *Cameraria ohridella*; Cross-coupling reactions; Alkenes; Dienes.

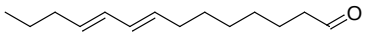
During the last 10 years, the horse chestnut leafminer[1], *Cameraria ohridella* Deschka and Dimić, 1986 (Lepidoptera, Gracillariidae), a moth of yet unknown origin, spread over vast areas of Central and Eastern Europe[2]. The larvae of this species develop inside the horse chestnut (*Aesculus hippocastanum* L.) leaves where they consume the parenchyma. As a consequence, leaves die soon, and defoliation of trees starts in early summer. Availability of a synthetic sex pheromone of this species could lead to environmentally-safe pest management.

Recently the sex pheromone of *C. ohridella* was identified in our laboratory[3,4]. The convergent identification of the pheromone using electroantennographic (EAG) recordings employed high sensitivity and selectivity of male antennae to the sex pheromone and their structure analogs. Conse-

quently, after determination of the functional group (aldehyde), the chain length (linear, 14 carbon atoms) and tentative assignment of the positions of double bonds (8,10) we needed to prepare stereoisomers of the corresponding conjugated tetradecadienals. Here we are presenting the preparation of (8*E*,10*Z*)-tetradeca-8,10-dienal (**1a**), the identified sex pheromone of *C. ohridella* and its geometric isomers (**1b**–**1d**). EAG recordings of the isomers are also reported.

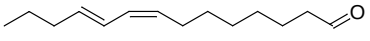


1a



1b

1c



1d

The key step of the synthesis of the target compounds **1a**–**1d**, a construction of the conjugated diene moiety, is based on tetrakis(triphenylphosphine)palladium catalyzed C(sp)–C(sp^2) and C(sp^2)–C(sp^2) cross-coupling reactions of alk-1-ynes or vinyl organometallics with vinyl halogenides[5–7]. This "vinyl" cross-coupling approach offers high isomeric purity of products and reasonable yields in comparison with other synthetic paths[8] (for example Wittig reaction). Another advantage is using the same intermediates (pent-1-yne, **4**, **13**) and chemical transformations in the synthesis (Scheme 1) of all four tetradecadienal isomers **1a**–**1d**.

EXPERIMENTAL

Chemical Synthesis

Spectral methods: NMR spectra were determined in $CDCl_3$ solutions on a Varian UNITY-500 spectrometer operating at 499.5 MHz for ^1H and at 125.7 MHz for ^{13}C NMR, respectively. Chemical shifts are expressed in δ (ppm) scale relative to tetramethylsilane for ^1H and relative to $CDCl_3$ signal (77.00 ppm) for ^{13}C NMR, respectively. Coupling constants are reported in Hz. Electron impact (70 eV) mass spectra were obtained on Fisons MD 800 GC/MS instrument.

Chromatography: GC analyses were performed on a Hewlett–Packard HP 6890 gas chromatograph equipped with FID detector (275 °C), split/splitless injection port (230 °C), electronic pressure control (EPC), and HP 6890 automatic injector. A Hewlett–Packard HP-5 capillary column (30 m × 0.32 mm; film thickness 0.25 μm) and helium gas (constant pressure 66 kPa) were used for separations. The temperature program started at 100 °C, then the temperature of the oven was increased to 220 °C (rate 5 °C min^{-1}; 10 min delay at 220 °C). Preparative medium-pressure liquid chromatography (PMPLC) separations were made on Merck 60 silica gel (0.040–0.063 mm) using a Büchi B-680 Prep LC System with ethyl acetate

or benzene in hexane. The mobile phase for chromatography of the sensitive final products, conjugated dienic aldehydes **1a**–**1d**, was spiked with triethylamine (0.3% v/v).

Chemicals: All chemical reactions were run in oven-dried glassware under argon. Tetrahydrofuran (THF), hexane and benzene were distilled from sodium benzophenone ketyl in argon atmosphere. Dichloromethane was distilled from calcium hydride and stored over molecular sieves. All other chemicals were used as purchased. NMR spectra (^{13}C NMR spectra of dienals **1a**–**1d** are presented separately in Table I) and elemental analyses of all synthesized compounds were fully consistent with the proposed structures.

1-Bromo-7-(*tert*-butoxy)heptane (**2**)

The compound **2** was prepared by a standard manner[9] from 7-bromoheptan-1-ol (39.0 g, 0.20 mol), 2-methylpropene (200 ml) and Amberlyst H-15 (5.0 g). Yield 98% (49.2 g). ^{1}H NMR ($CDCl_3$): 1.18 s, 9 H (3 × CH_3); 1.26–1.49 m, 8 H (4 × CH_2); 1.50 m, 2 H (–C**H**$_2$CH$_2$OR); 3.33 t, 2 H, *J* = 6.9 (–C**H**$_2$OR); 3.40 t, 2 H, *J* = 2 × 6.8 (–CH_2Br). For $C_{11}H_{23}BrO$ (251.2) calculated: 52.59% C, 9.23% H, 31.81% Br; found: 52.66% C, 9.17% H, 31.68% Br.

9-(*tert*-Butoxy)non-1-yne[10] (**3**)

To a stirred and cooled (0 °C) suspension of lithium acetylide–ethylenediamine complex (20.0 g, 0.20 mol) in anhydrous dimethyl sulfoxide (100 ml) was slowly (60 min) added compound **2** (25.1 g, 0.10 mol). The reaction mixture was stirred at room temperature for 6 h, then it was poured into ice water and extracted with hexane (4 × 100 ml). The combined hexane extracts were washed with water (3 × 100 ml), brine (2 × 100 ml) and dried over K_2CO_3. Solvents were evaporated, and the oily residue (22.3 g) was distilled *in vacuo*. The distillation gave alkyne **3** (18.0 g, 92%; b.p. 130–135 °C/1.33 kPa). ^{1}H NMR ($CDCl_3$): 1.18 s, 9 H (3 × CH_3); 1.28–1.44 m, 8 H (4 × CH_2); 1.52 m, 2 H (–C**H**$_2$CH$_2$OR); 1.93 t, 1 H, *J* = 2.7 (HC≡C–); 2.18 dt, 2 H, *J* = 2.7, 2 × 7.2 (HC≡C–C**H**$_2$–); 3.32 t, 2 H, *J* = 6.7 (–C**H**$_2$OR). For $C_{13}H_{24}O$ (196.3) calculated: 79.53% C, 12.32% H; found: 79.38% C, 12.50% H.

(*E*)-9-(*tert*-Butoxy)-1-iodonon-1-ene[11] (**4**)

A solution of alkyne **3** (9.82 g, 50 mmol) in hexane (30 ml) was treated with diisobutylaluminium hydride (DIBAH; 1 M solution in hexanes, 55 ml) at 55 °C for 5 h, cooled to –45 °C, and a solution of iodine (12.94 g, 51 mmol) in THF (30 ml) was added dropwise. After the addition, the mixture was stirred overnight at room temperature. The reaction mixture was poured into 200 ml of 6 M NaOH and stirred until the brown color had disappeared. Organic layer was separated and the aqueous one was extracted with hexane (3 × 100 ml). The organic layers were collected, washed with water (3 × 75 ml) and dried over anhydrous K_2CO_3. The crude product, obtained after evaporation of solvents was purified by PMPLC (0.5% ethyl acetate in hexane) affording vinyl iodide **4** (11.6 g, 72%). ^{1}H NMR ($CDCl_3$): 1.18 s, 9 H (3 × CH_3); 1.26–1.42 m, 8 H (4 × CH_2); 1.51 m, 2 H (–C**H**$_2$CH$_2$OR); 2.14 dq, 2 H, *J* = 1.5, 3 × 7.2 (I–CH=CH–C**H**$_2$–); 3.32 t, 2 H, *J* = 6.7 (–C**H**$_2$OR); 5.96 dt, 1 H, *J* = 2 × 1.5, 14.4 (I–C**H**=CH–); 6.50 dt, 1 H, *J* = 2 × 7.2, 14.4 (I–CH=C**H**–). For $C_{13}H_{25}IO$ (324.2) calculated: 48.16% C, 7.77% H; 39.14% I; found: 48.12% C, 7.92% H; 39.33% I.

(*E*)-14-(*tert*-Butoxy)tetradec-6-en-4-yne (**5**)

Tetrakis(triphenylphosphine)palladium (0.60 g, 0.5 mmol) was added at 20 °C to a solution of iodide **4** (3.24 g, 10.0 mmol) in benzene (25 ml). The mixture was stirred for additional 60 min. A solution of pent-1-yne (1.66 g, 15.0 mmol) in anhydrous butylamine (7.34 g, 100 mmol) and cuprous iodide (0.37 g, 2.0 mmol) was added. After 2 h at room temperature, the mixture was diluted with ether (150 ml) and subsequently poured into saturated aqueous ammonium chloride (100 ml). The organic layer was washed with 20% aqueous ammonia (3 × 100 ml), brine (2 × 100 ml), water (2 × 100 ml), and dried over anhydrous $MgSO_4$. Removal of the solvents *in vacuo* and purification of the residue by PMPLC (0.5–1.5% of ethyl acetate in hexane) gave 2.38 g (90%) of enyne **5**. ^{1}H NMR ($CDCl_3$): 0.98 t, 3 H, J = 7.5 (CH_3CH_2–); 1.18 s, 9 H (3 × CH_3); 1.25–1.39 m, 8 H (4 × CH_2); 1.50 m, 2 H (CH_3CH_2–); 1.52 m, 2 H (–CH_2CH_2OR); 2.07 dq, 2 H, J = 1.5, 3 × 7.1 (–CH=CHCH_2–); 2.26 dt, 2 H, J = 1.2, 2 × 1.7 (–CH_2C≡C–); 3.32 t, 2 H, J = 6.7 (–CH_2OR); 5.45 m, 1 H, J = 4 × 1.7, 15.8 (–CH=C**H**–); 6.03 m, 1 H, J = 4 × 1.7, 15.8 (–C**H**=CH–). For $C_{18}H_{32}O$ (264.5) calculated: 81.75% C, 12.20% H; found: 81.95% C, 12.08% H.

TABLE I
^{13}C NMR data (δ in ppm) for 8,10-tetradecadienals **1a**–**1d**

Carbon	**1a**(*E*,*Z*)	**1b**(*Z*,*Z*)	**1c**(*E*,*E*)	**1d**(*Z*,*E*)
1	202.77	202.81	202.83	202.80
2	43.90	43,88	43.87	43.87
3	22.00	21.99	22.02	22.02
4	29.29	29.25	29.16	29.52
5	28.58	29.19	29.00	27.33
6	29.05	27.42	28.86	28.92
7	32.80	29.52	32.45	29.00
8	134.50	123.73	132.04	131.69
9	125.71	123.68	130.52	123.82
10	128.75	131.88	130.41	123.67
11	129.90	132.93	132.34	132.01
12	29.74	29.54	34.69	29.37
13	22.88	22.80	22.56	22.80
14	13.77	13.77	13.71	13.78

(4*Z*,6*E*)-14-(*tert*-Butoxy)tetradeca-4,6-diene (**6**)

A dicyclohexylborane suspension was prepared in THF (30 ml) from borane–dimethyl sulfide complex (10 mol l^{-1}, 0.97 ml) and cyclohexene (1.59 g, 19.4 mmol). The obtained white suspension was treated at 0 °C with a solution of enyne **5** (2.33 g, 8.8 mmol) in THF (10 ml). The mixture was warmed to room temperature, and stirred for 4 h. The formed vinylborane was hydrolyzed with glacial acetic acid (10 ml) at 20 °C for 12 h, the reaction mixture was neutralized with NaOH (20%, 20 ml), and carefully treated with aqueous H_2O_2 (30%, 10 ml). The product was extracted with hexane (4 × 75 ml). Chromatography (PMPLC) in hexane yielded protected dienol **6** (1.61 g, 69%) in 97.8% isomeric purity (GC). ^{1}H NMR ($CDCl_3$): 0.92 t, 3 H, *J* = 7.4 (C**H**$_3$CH$_2$–); 1.18 s, 9 H (3 × CH_3); 1.24–1.36 m, 8 H (4 × CH_2); 1.40 m, 2 H, *J* = 5 × 7.4 (CH_3C**H**$_2$–); 1.51 m, 2 H (–C**H**$_2$CH$_2$OR); 2.09 bdq, 2 H, *J* = 1.5, 3 × 7.5 (–CH=CHC**H**$_2$–); 2.14 dq, 2 H, *J* = 1.5, 3 × 7.5 (–C**H**$_2$CH=CH–); 3.32 t, 2 H, *J* = 6.7 (–C**H**$_2$OR); 5.30 bdt, 1 H, *J* = 2 × 7.5, 10.8 (–C**H**=CH–CH=CH–); 5.65 bdt, 1 H, *J* = 3 × 7.3, 15.0 (–CH=CH–CH=C**H**–); 5.95 dtt, 1 H, *J* = 0.8, 2 × 1.5, 2 × 10.9 (–CH=C**H**–CH=CH–); 6.29 ddq, 1 H, *J* = 3 × 1.5, 11.0, 15.0 (–CH=CH–C**H**=CH–). For $C_{18}H_{34}O$ (266.5) calculated: 81.12% C, 12.86% H; found: 81.31% C, 13.12% H.

(8*E*,10*Z*)-Tetradeca-8,10-dien-1-ol (**7**)

To a solution of protected dienol **6** (1.07 g, 4.0 mmol) in ether (20 ml) was added acetic anhydride (2 ml), and then anhydrous $FeCl_3$ (65 mg, 0.40 mmol). The dark brown solution was stirred for 20 h at room temperature. A saturated aqueous solution of Na_2HPO_4 (15 ml) was added, and the mixture was stirred for 2 h. The solid $FePO_4$ was filtered off, and the aqueous layer was extracted with ether (3 × 40 ml). The collected organic phases were dried over anhydrous $MgSO_4$, and then concentrated. The red oily residue (1.03 g) was dissolved in methanol (10 ml) and an aqueous solution of NaOH (0.60 g in 4 ml of water) was added. The mixture was stirred at 20 °C for 16 h, poured into water (75 ml), and extracted with hexane–ether (3 : 2, 4 × 25 ml). The combined extracts were dried (anhydrous K_2CO_3), evaporated, and the dark residue (0.98 g) was purified by PMPLC. Chromatography (10% ethyl acetate in hexane) gave 0.69 g (82%) of *E,Z*–dienol **7**. ^{1}H NMR ($CDCl_3$): 0.92 t, 3 H, *J* = 7.4 (C**H**$_3$CH$_2$–); 1.25–1.39 m, 8 H (4 × CH_2); 1.41 m, 2 H (CH_3C**H**$_2$–); 1.57 m, 2 H (–C**H**$_2$CH$_2$OR); 2.09 bdq, 2 H, *J* = 1.5, 3 × 7.1 (–CH=CHC**H**$_2$–); 2.14 dq, 2 H, *J* = 1.6, 3 × 7.5 (–C**H**$_2$CH=CH–); 3.65 t, 2 H, *J* = 6.6 (–C**H**$_2$OH); 5.31 dtt, 1 H, *J* = 2 × 0.7, 2 × 7.5, 10.8 (–C**H**=CH–CH=CH–); 5.65 dtt, 1 H, *J* = 2 × 0.8, 2 × 7.1, 15.1 (–CH=CH–CH=C**H**–); 5.96 dtt, 1 H, *J* = 0.9, 2 × 1.6, 2 × 10.9 (–CH=C**H**–CH=CH–); 6.30 ddq, 1 H, *J* = 3 × 1.5, 11.0, 15.1 (–CH=CH–C**H**=CH–). For $C_{14}H_{26}O$ (210.4) calculated: 79.94% C, 12.46% H; found: 80.22% C, 12.50% H.

(8*E*,10*Z*)-Tetradeca-8,10-dienal (**1a**)

Dienol **7** (210 mg, 1 mmol) was injected into a stirred suspension of pyridinium chlorochromate (PCC; 258 mg, 1.2 mmol) and anhydrous sodium acetate (20 mg) in dichloromethane (2 ml). The mixture was stirred at room temperature for 90 min, then poured into 50 ml of ether and filtered through a combined layer of neutral alumina/charcoal/Celite. A subsequent evaporation of the solvents and PMPLC (0.3% triethylamine in benzene–hexane, 1 : 1) afforded 151 mg (72%) of the pure (96%, GC) target compound, dienal **1a**. ^{1}H NMR ($CDCl_3$): 0.92 t, 3 H, *J* = 7.4 (C**H**$_3$CH$_2$–); 1.27–1.38 m, 6 H (3 × CH_2); 1.40 m, 2 H, *J* = 5 × 7.4 (CH_3C**H**$_2$–); 1.63 m, 2 H (–C**H**$_2$CH$_2$CHO); 2.09 bdq, 2 H, *J* = 1.5, 3 × 7.1

(–CH=CHC**H**$_2$–); 2.14 dq, 2 H, *J* = 1.6, 3 × 7.5 (–C**H**$_2$CH=CH–); 2.42 dt, 2 H, *J* = 2 × 6.5 (–C**H**$_2$CHO); 5.31 dtt, 1 H, *J* = 2 × 0.7, 2 × 7.5, 10.8 (–C**H**=CH–CH=CH–); 5.65 dtt, 1 H, *J* = 2 × 0.8, 2 × 7.0, 15.1 (–CH=CH–CH=C**H**–); 5.95 dtt, 1 H, *J* = 0.9, 2 × 1.6, 2 × 10.9 (–CH=C**H**–CH=CH–); 6.30 ddq, 1 H, *J* = 3 × 1.5, 11.0, 15.1 (–CH=CH–C**H**=CH–); 9.76 t, 1 H, *J* = 1.8 (–CHO). EI-MS, *m/z* (rel.%): 39 (11), 41 (33), 54 (23), 55 (27), 67 (100), 68 (18), 79 (33), 80 (13), 81 (50), 82 (21), 91 (16), 93 (14), 95 (26), 96 (18), 98 (19), 109 (14), 208 (9, $M^{+\bullet}$). For $C_{14}H_{24}O$ (208.3) calculated: 80.71% C, 11.61% H; found: 80.37% C, 11.44% H.

(*E*)-9-Iodonon-8-en-1-ol (**8**)

The iodoalkenol **8** (2.50 g, 93%) was prepared from *tert*-butyl ether **4** (3.23 g, 10.0 mmol) following the above described standard deprotection procedure. ^{1}H NMR ($CDCl_3$): 1.28–1.44 m, 8 H (4 × CH_2); 1.56 m, 2 H (–C**H**$_2$CH$_2$OH); 2.05 m, 2 H, *J* = 1.5, 3 × 7.3 (I–CH=CHC**H**$_2$–); 3.64 t, 2 H, *J* = 6.5 (–C**H**$_2$OH); 5.97 dt, 1 H, *J* = 2 × 1.5, 14.4 (I–C**H**=CH–); 6.50 dt, 1 H, *J* = 2 × 7.2, 14.4 (I–CH=C**H**–). For $C_9H_{17I}O$ (268.13) calculated: 40.31% C, 6.39% H, 47.33% I; found: 40.40% C, 6.11% H, 47.09% I.

1-(*tert*-Butyldimethylsilyloxy)-(*E*)-9-iodonon-8-ene (**9**)

A mixture of the iodoalkenol **8** (2.40 g, 9.0 mmol), *tert*-butyl(chloro)dimethylsilane (1.42 g, 9.5 mmol), anhydrous pyridine (0.77 ml, 9.5 mmol) and 4-(dimethylamino)pyridine (DAP; 10 mg) in dichloromethane (50 ml) was stirred at room temperature for 20 h. The reaction mixture was then diluted with ether (200 ml), washed with saturated $NaHCO_3$ solution (3 × 75 ml), brine (2 × 75 ml), and dried over anhydrous K_2CO_3. Evaporation of the solvents and subsequent chromatography (hexane) afforded 2.98 g (87%) of vinyl iodide **9**. ^{1}H NMR ($CDCl_3$): 0.05 s, 6 H (2 × CH_3); 0.89 s, 9 H (3 × CH_3); 1.27–1.40 m, 8 H (4 × CH_2); 1.50 m, 2 H (–C**H**$_2$CH$_2$OR); 2.04 dq, 2 H, *J* = 1.5, 3 × 7.3 (I–CH=CHC**H**$_2$); 3.59 t, 2 H, *J* = 6.6 (–C**H**$_2$OR); 5.97 dt, 1 H, *J* = 2 × 1.5, 14.4 (I–C**H**=CH–); 6.50 dt, 1 H, *J* = 2 × 7.2, 14.4 (I–CH=C**H**–). For $C_{15}H_{31}IOSi$ (382.4) calculated: 47.11% C, 8.17% H, 33.19% I, 7.34% Si; found: 46.95% C, 7.90% H, 33.22% I, 7.26% Si.

(4*E*,6*E*)-14-[*tert*-Butyl(dimethyl)silyloxy]tetradeca-4,6-diene (**10**)

To a stirred hexane (5 ml) solution of pent-1-yne (0.44 ml, 4.0 mmol) DIBAH (1 M solution in hexanes; 3.0 ml) was added at –50 °C. After the addition was completed, the reaction mixture was slowly warmed to 50 °C and then stirred at the same temperature for 5 h. The solution was transferred with a PTFE cannula to a mixture of vinyl iodide **9** (1.00 g, 2.6 mmol), zinc chloride (1 M solution in THF; 3.0 ml), and $[Pd(Ph_3P)_4]$ (300 mg, 0.26 mmol) in THF (10 ml) at room temperature. After 18 h stirring, the mixture was decomposed by the addition of 10% NaOH solution (at 20 °C). Extraction with pentane (3 × 20 ml), drying (anhydrous K_2CO_3) of the collected extracts and evaporation produced a dark oily residue (1.01 g). PMPLC gave silyl ether **10** (650 mg) as a colorless oil in 76% yield. ^{1}H NMR ($CDCl_3$): 0.05 s, 6 H (2 × CH_3); 0.89 s, 9 H (3 × CH_3); 0.90 t, 3 H, *J* = 7.0 (C**H**$_3$CH$_2$–); 1.28–1.40 m, 8 H (4 × CH_2); 1.41 m, 2 H (CH_3C**H**$_2$–); 1.57 m, 2 H (–C**H**$_2$CH$_2$OR); 2.04 m, 4 H (2 × –CH=CHC**H**$_2$–); 3.57 t, 2 H, *J* = 6.6 (–C**H**$_2$OR); 5.51–5.59 m, 2 H (–C**H**=CH–CH=C**H**–); 5.97–6.02 m, 2 H (–CH=C**H**–C**H**=CH–). For $C_{20}H_{40}OSi$ (324.6) calculated: 74.00% C, 12.42% H, 8.65% Si; found: 73.79% C, 12.22% H, 8.46% Si.

(8*E*,10*E*)-Tetradeca-8,10-dien-1-ol[12,13] (**11**)

A mixture of tetrabutylammonium fluoride (1 M solution in THF; 2 ml) and silyl ether **10** (600 mg, 1.85 mmol) was stirred at room temperature for 24 h. The reaction mixture was poured into water (30 ml) and extracted with hexane–ether (3 : 2). Collected extracts were washed with brine (2 × 25 ml), dried over anhydrous $MgSO_4$ and evaporated. Purification of the residual by PMPLC (10% ethyl acetate in hexane) afforded 328 mg (84%) of dienol **11**. ^{1}H NMR ($CDCl_3$): 0.90 t, 3 H, *J* = 7.1 (CH_3CH_2–); 1.28–1.41 m, 8 H (4 × CH_2); 1.41 m, 2 H (CH_3CH_2–); 1.57 m, 2 H (–CH_2CH_2OH); 2.04 m, 4 H (2 × –CH=CHCH_2–); 3.64 t, 2 H, *J* = 6.6 (–CH_2OH); 5.52–5.61 m, 2 H (–CH=CH–CH=CH–); 5.97–6.03 m, 2 H (–CH=CH–CH=CH–). For $C_{14}H_{26}O$ (210.4) calculated: 79.94% C, 12.46% H; found: 79.63% C, 12.55% H.

(8*E*,10*E*)-Tetradeca-8,10-dienal (**1b**)

The dienal **1b** (161 mg, 77%) was prepared from dienol **11** (210 mg, 1.0 mmol) and PCC (258 mg, 1.2 mmol) following the above described procedure for the preparation of compound **1a**. Isomeric purity 97.5% (GC). ^{1}H NMR ($CDCl_3$): 0.90 t, 3 H, *J* = 7.0 (CH_3CH_2–); 1.29–1.38 m, 6 H (3 × CH_2); 1.41 m, 2 H (CH_3CH_2–); 1.63 m, 2 H (–CH_2CH_2CHO); 2.04 m, 4 H (2 × –CH=CHCH_2–); 2.42 dt, 2 H, *J* = 1.8, 2 × 7.3 (–CH_2CHO); 5.52–5.59 m, 2 H (–CH=CH–CH=CH–); 5.96–6.02 m, 2 H (–CH=CH–CH=CH–); 9.76 t, 1 H, *J* = 1.8 (–CHO). EI-MS, *m*/*z* (rel.%): 39 (13), 41 (38), 54 (20), 55 (25), 67 (100), 68 (16), 79 (31), 80 (13), 81 (45), 82 (17), 91 (14), 93 (12), 95 (20), 96 (14), 98 (19), 109 (11), 208 (5, $M^{+\bullet}$). For $C_{14}H_{24}O$ (208.3) calculated: 80.71% C, 11.61% H; found: 80.57% C, 11.80% H.

9-(*tert*-Butoxy)-1-iodonon-1-yne (**12**)

A 9-(*tert*-butoxy)non-1-yne (**3**; 4.2 g, 21.4 mmol) solution in THF (30 ml) was metallated at –50 to 0 °C with butyllithium (1.6 M solution in hexanes; 13.4 ml) for 20 min. The formed solution was cooled to –60 °C, a solution of iodine (5.43 g, 21.4 mmol) in THF (20 ml) was added slowly, and the reaction mixture was allowed to warm up to 20 °C. The obtained white suspension was diluted with ether (50 ml) and then quenched with saturated aqueous ammonium chloride (50 ml). The organic layer was separated and the aqueous layer extracted with pentane (2 × 50 ml). The combined organic phases were successively washed with saturated aqueous $Na_2S_2O_3$ (2 × 50 ml), brine (2 × 50 ml), and dried over anhydrous $MgSO_4$. The mixture was passed through a short silica gel column (50 g) and solvents were then evaporated. The obtained iodide **12** (6.69 g, 97%) was used in the next hydroboration step without further purification.

(*Z*)-9-(*tert*-Butoxy)-1-iodonon-1-ene (**13**)

The vinyl iodide **12** (4.66 g, 72%) was prepared from alkyne **12** (6.44 g, 20.0 mmol), borane–dimethyl sulfide complex (10 mol l^{-1}, 2.0 ml) and cyclohexene (3.29 g, 40.0 mmol) following the procedure for the reduction of compound **5**. ^{1}H NMR ($CDCl_3$): 1.18 s, 9 H (3 × CH_3); 1.21–1.56 m, 8 H (4 × CH_2); 1.51 m, 2 H (–CH_2CH_2OR); 2.13 m, 2 H (I–CH=CH–CH_2–); 3.32 t, 2 H, *J* = 6.8 (–CH_2OR); 6.13–6.18 m, 2 H (I–CH=CH–). For $C_{13}H_{25}IO$ (324.2) calculated: 48.16% C, 7.77% H, 39.14% I; found: 47.87% C, 7.99% H, 38.91% I.

(*Z*)-14-(*tert*-Butoxy)tetradec-6-en-4-yne (**14**)

The enyne **14** (1.75 g, 86%) was prepared from vinyl iodide **13** (3.24 g, 10.0 mmol), $[Pd(Ph_3P)_4]$ (600 mg, 0.5 mmol), Cu_2I_2 (370 mg, 2.0 mmol), and pent-1-yne (1.66 g, 15.0 mmol) following the procedure for preparation of compound **5**. ^{1}H NMR ($CDCl_3$): 1.01 t, 3 H, *J* = 7.4 (C**H**$_3$CH$_2$–); 1.18 s, 9 H (3 × CH_3); 1.28–1.48 m, 8 H (4 × CH_2); 1.52 m, 2 H (CH_3C**H**$_2$–); 1.57 m, 2 H (–C**H**$_2$CH$_2$OR); 2.28 dq, 2 H, *J* = 1.4, 3 × 7.3 (–CH=CHC**H**$_2$–); 2.32 dt, 2 H, *J* = 0.5, 2 × 7.1 (–C**H**$_2$C≡C–); 3.32 t, 2 H, *J* = 6.9 (–C**H**$_2$OR); 5.43 dtt, 1 H, *J* = 2 × 1.4, 2 × 2.2, 10.7 (–CH=C**H**–); 5.81 dtt, 1 H, *J* = 1 × 1.4, 2 × 2.2, 10.7 (–C**H**=CH–). For $C_{18}H_{32}O$ (264.5) calculated: 81.75% C, 12.20% H; found: 81.52% C, 12.33% H.

(4*Z*,6*Z*)-14-(*tert*-Butoxy)tetradeca-4,6-diene (**15**)

The protected *Z*,*Z*-dienol **15** (1.15 g, 80%) was prepared from enyne **14** (1.45 g, 5.5 mmol), borane–dimethyl sulfide complex (10 mol l^{-1}, 0.55 ml) and cyclohexene (0.90 g, 11.0 mmol) following the procedure for the preparation of compound **6**. ^{1}H NMR ($CDCl_3$): 0.91 t, 3 H, *J* = 7.3 (C**H**$_3$CH$_2$–); 1.18 s, 9 H (3 × CH_3); 1.24–1.42 m, 8 H (4 × CH_2); 1.41 m, 2 H (CH_3C**H**$_2$–); 1.51 m, 2 H (–C**H**$_2$CH$_2$OR); 2.16 m, 4 H (2 × –CH=CHC**H**$_2$–); 3.32 t, 2 H, *J* = 6.7 (–C**H**$_2$OR); 5.39–5.48 m, 2 H (–C**H**=CH–CH=C**H**–); 6.22–6.29 m, 2 H (–CH=C**H**–C**H**=CH–). For $C_{18}H_{34}O$ (266.5) calculated: 81.12% C, 12.86% H; found: 81.01% C, 13.07% H.

(8*Z*,10*Z*)-Tetradeca-8,10-dien-1-ol (**16**)

The dienol **16** (0.662 g, 79%) was obtained from compound **15** (1.07 g, 4.0 mmol) following the procedure for the deprotection of dienol **6**. ^{1}H NMR ($CDCl_3$): 0.92 t, 3 H, *J* = 7.3 (C**H**$_3$CH$_2$–); 1.27–1.40 m, 8 H (4 × CH_2); 1.41 m, 2 H (CH_3C**H**$_2$–); 1.56 m, 2 H (C**H**$_2$CH$_2$OH); 2.16 m, 4 H (2 × –CH=CHC**H**$_2$–); 3.64 t, 2 H, *J* = 6.6 (–C**H**$_2$OH); 5.39–5.48 m, 2 H (–C**H**=CH–CH=C**H**–); 6.22–6.29 m, 2 H (–CH=C**H**–C**H**=CH–). For $C_{14}H_{26}O$ (210.4) calculated: 79.94% C, 12.46% H; found: 79.79% C, 12.31% H.

(8*Z*,10*Z*)-Tetradeca-8,10-dienal (**1c**)

The aldehyde **1c** (155 mg, 74%) was prepared from dienol **16** (210 mg, 1.0 mmol) and PCC (258 mg, 1.2 mmol) following the above described procedure for the oxidation of dienol **7** to dienal **1a**. Isomeric purity 97% (GC). ^{1}H NMR ($CDCl_3$): 0.92 t, 3 H, *J* = 7.3 (C**H**$_3$CH$_2$–); 1.27–1.38 m, 6 H (3 × CH_2); 1.41 m, 2 H (CH_3C**H**$_2$–); 1.63 m, 2 H (–C**H**$_2$CH$_2$CHO); 2.16 m, 4 H (2 × –CH=CHC**H**$_2$–); 2.43 dt, 2 H, *J* = 1.8, 2 × 6.4 (–C**H**$_2$CHO); 5.39–5.48 m, 2 H (–C**H**=CH–CH=C**H**–); 6.22–6.28 m, 2 H (–CH=C**H**–C**H**=CH–); 9.75 t, 1 H, *J* = 1.8 (–CHO). EI-MS, *m/z* (rel.%): 39 (12), 41 (37), 54 (27), 55 (28), 67 (100), 68 (18), 79 (34), 80 (13), 81 (56), 82 (22), 91 (15), 93 (13), 95 (23), 96 (18), 98 (19), 109 (11), 208 (5, $M^{+\cdot}$). For $C_{14}H_{24}O$ (208.3) calculated: 80.71% C, 11.61% H; found: 80.88% C, 11.62% H.

(*Z*)-9-Iodonon-8-en-1-ol (**17**)

The iodoalkenol **17** (1.31 g, 88%) was prepared from *tert*-butyl ether **9** (1.80 g, 5.55 mmol) following the above described standard deprotection procedure. ^{1}H NMR ($CDCl_3$): 1.29– 1.47 m, 8 H (4 × CH_2); 1.57 m, 2 H (–C**H**$_2$CH$_2$OH); 2.14 bdq, 2 H, *J* = 1.5, 3 × 7.5 (I–CH=CHC**H**$_2$–); 3.64 t, 2 H, *J* = 6.6 (–C**H**$_2$OH); 6.15–6.18 m, 2 H (I–C**H**=C**H**–). For $C_9H_{17}IO$ (268.1) calculated: 40.31% C, 6.39% H, 47.33% I; found: 40.40% C, 6.11% H, 47.09% I.

(*Z*)-1-[*tert*-Butyl(dimethyl)silyloxy]-9-iodonon-8-ene (**18**)

The silyl ether **18** (1.54 g, 98%) was obtained from the iodoalkenol **17** (1.10 g, 4.1 mmol) and *tert*-butyl(chloro)dimethylsilane (650 mg, 4.3 mmol) following the above described standard silylation procedure. ^{1}H NMR ($CDCl_3$): 0.05 s, 6 H (2 × CH_3); 0.89 s, 9 H (3 × CH_3); 1.27–1.46 m, 8 H (4 × CH_2); 1.51 m, 2 H (–C**H**$_2$CH$_2$OR); 2.13 bdq, 2 H, *J* = 1.5, 3 × 7.1 (I–CH=CHC**H**$_2$); 3.60 t, 2 H, *J* = 6.6 (–C**H**$_2$OR); 6.14–6.18 m, 2 H (I–C**H**=C**H**–). For $C_{15}H_{31}IOSi$ (382.4) calculated: 47.11% C, 8.17% H, 33.19% I, 7.34% Si; found: 47.29% C, 8.28% H, 33.02% I, 7.46% Si.

(4*E*,6*Z*)-14-[*tert*-Butyl(dimethyl)silyloxy]-tetradeca-4,6-diene (**19**)

Compound **19** (390 mg, 65%) was prepared from vinyl iodide **18** (700 mg, 1.83 mmol), pent-1-yne (440 µl, 4.00 mmol), DIBAH (1 M solution in hexanes; 2.0 ml), zinc chloride (1 M solution in THF; 2.0 ml), and [Pd(Ph$_3$P)$_4$] (300 mg, 0.26 mmol) following the above described procedure for the preparation of the dienic silyl ether **15**. ^{1}H NMR ($CDCl_3$): 0.05 s, 6 H (2 × CH_3); 0.89 s, 9 H (3 × CH_3); 0.90 t, 3 H, *J* = 7.2 (C**H**$_3$CH$_2$–); 1.29–1.41 m, 8 H (4 × CH_2); 1.42 m, 2 H (CH_3C**H**$_2$–); 1.57 m, 2 H (–C**H**$_2$CH$_2$OR); 2.09 dq, 2 H, *J* = 1.6, 3 × 7.3 (–CH=CHC**H**$_2$–); 2.16 dq, 2 H, *J* = 1.6, 3 × 7.3 (–C**H**$_2$CH=CH–); 3.57 t, 2 H, *J* = 6.6 (–C**H**$_2$OR); 5.29 bdt, 1 H, *J* = 2 × 7.3, 11.0 (–CH=CH–CH=C**H**–); 5.65 bdt, 1 H, *J* = 2 × 7.0, 15.0 (–C**H**=CH–CH=CH–); 5.95 ddt, 1 H, *J* = 0.8, 2 × 1.5, 11.0 (–CH=CH–C**H**=CH–); 6.30 ddq, 1 H, *J* = 3 × 1.5, 11, 15.0 (–CH=C**H**–CH=CH–). For $C_{20}H_{40}OSi$ (324.6) calculated: 74.00% C, 12.42% H, 8.65% Si; found: 74.11% C, 12.18% H, 8.50% Si.

(8*Z*,10*E*)-Tetradeca-8,10-dien-1-ol (**20**)

The *Z*,*E*-dienol **20** (171 mg, 69%) was prepared from compound **19** (380 mg, 1.17 mmol) following the above described standard deprotection procedure. ^{1}H NMR ($CDCl_3$): 0.91 t, 3 H, *J* = 7.0 (C**H**$_3$CH$_2$–); 1.29–1.43 m, 8 H (4 × CH_2); 1.42 m, 2 H (CH_3C**H**$_2$–); 1.57 m, 2 H (–C**H**$_2$CH$_2$OH); 2.09 dq, 2 H, *J* = 1.6, 3 × 7.3 (–CH=CHC**H**$_2$–); 2.16 dq, 2 H, *J* = 1.6, 3 × 7.3 (–C**H**$_2$CH=CH–); 3.64 t, 2 H, *J* = 6.6 (–C**H**$_2$OH); 5.29 bdt, 1 H, *J* = 2 × 7.3, 11.0 (–CH=CH–CH=C**H**–); 5.66 bdt, 1 H, *J* = 2 × 7.1, 14.9 (–C**H**=CH–CH=CH–); 5.95 ddt, 1 H, *J* = 0.8, 2 × 1.5, 11.0 (–CH=CH–C**H**=CH–); 6.30 ddq, 1 H, *J* = 3 × 1.5, 11.0, 15.0 (–CH=C**H**–CH=CH–). For $C_{14}H_{26}O$ (210.4) calculated: 79.94% C, 12.46% H; found: 80.14% C, 12.64% H.

(8*Z*,10*E*)-Tetradeca-8,10-dienal (**1d**)

The dienal **1d** (67 mg, 64%) was obtained from dienol **20** (105 mg, 0.50 mmol) and PCC (130 mg, 0.6 mmol) following the above described procedure for the preparation of compound **1a**. Isomeric purity 96.5% (GC). ^{1}H NMR ($CDCl_3$): 0.91 t, 3 H, *J* = 7.0 (C**H**$_3$CH$_2$–); 1.26–1.38 m, 6 H (3 × CH_2); 1.41 m, 2 H (CH_3C**H**$_2$–); 1.63 m, 2 H (–C**H**$_2$CH$_2$CHO); 2.42 dt, 2 H, *J* = 1.8, 2 × 7.3 (–C**H**$_2$CHO); 2.16 dq, 4 H, *J* = 1.6, 3 × 7.3 (2 × –C**H**$_2$CH=CH–); 5.40– 5.48 m, 2 H (–C**H**=CH–CH=C**H**–); 6.22–6.28 m, 2 H (–CH=C**H**–C**H**=CH–); 9.76 t, 1 H, *J* = 1.8 (–CHO). EI-MS, *m*/*z* (rel.%): 39 (11), 41 (34), 54 (25), 55 (28), 67 (100), 68 (18), 79 (34), 80 (13), 81 (51), 82 (21), 91 (16), 93 (14), 95 (25), 96 (19), 98 (18), 109 (14), 208 (9, $M^{+\bullet}$). For $C_{14}H_{24}O$ (208.3) calculated: 80.71% C, 11.61% H; found: 80.90% C, 11.50% H.

Insects and Bioassays

Cameraria ohridella adults were reared from pupae collected in Prague parks during autumn 1999. Emerged adults were sexed, and two days old males[14] were used for EAG experiments[15] with standard 1 ng doses of synthesized compounds **1a**–**1d**.

RESULTS AND DISCUSSION

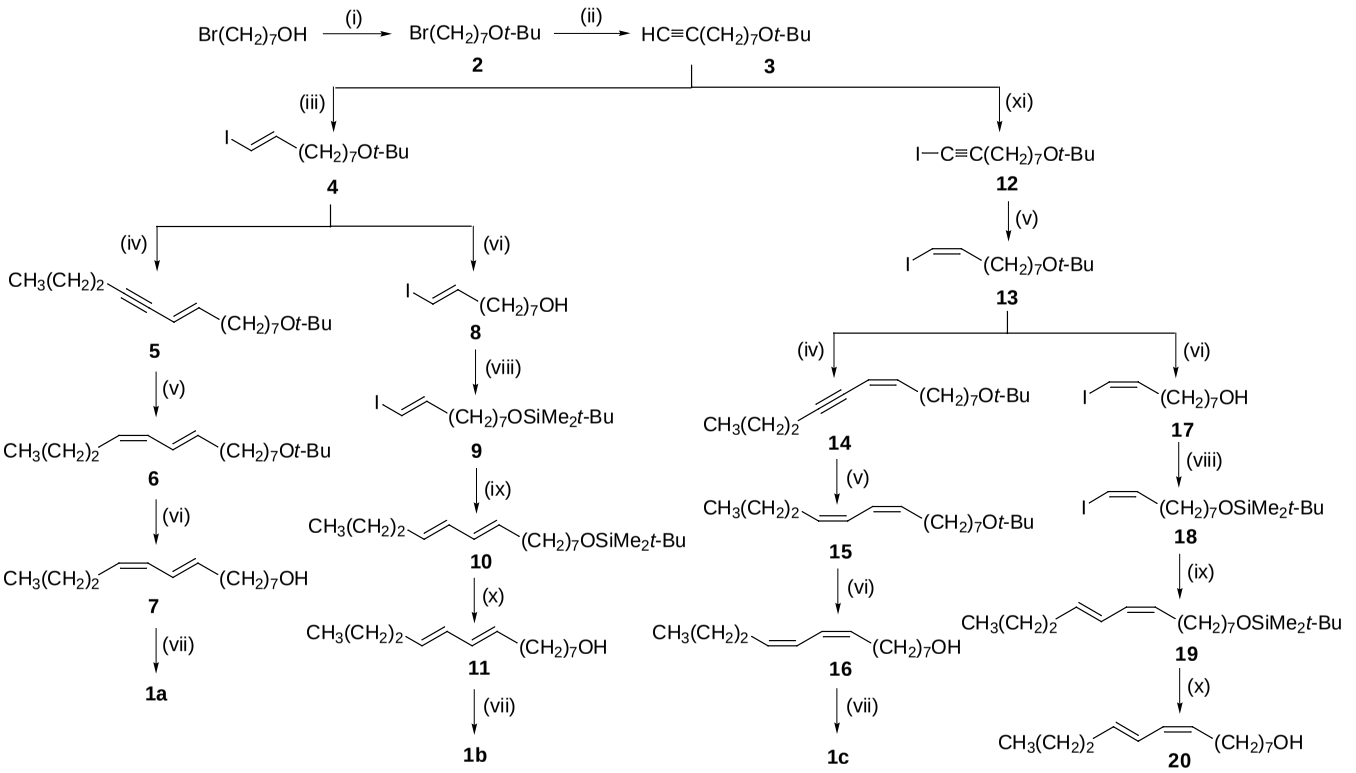
Chemical Synthesis

The dienals **1a**–**1d** were prepared using the strategy shown in Scheme 1. The key intermediates for the synthesis, (*E*)-9-*tert*-butoxy-1-iodonon-1-ene (**4**) and (*Z*)-9-*tert*-butoxy-1-iodonon-1-ene (**13**), were prepared from 9-*tert*-butoxynon-1-yne[9] (**3**). The (*E*)-vinyl iodide **4** was synthesized in high stereoisomeric purity (98.2%, GC) using hydroalumination[16] with diisobutylaluminium hydride (DIBAH) in hexane followed by iodination of the formed alkenyl diisobutylalane. For the preparation of the (*Z*)-vinyl iodide **13**, hydroboration of iodoalkyne **12** with dicyclohexylborane[17] was used.

The method for the construction of the required carbon chain with a conjugated diene moiety was different for the 10*Z* and 10*E* branch of the synthetic scheme. In the first case, the palladium-catalyzed cross-coupling of the key intermediate **4** (or **13**) with pent-1-yne[5,6] followed by *cis*-hydroboration with dicyclohexylborane[17] was used. In the second one, the palladium-catalyzed cross-coupling reaction of the vinyl iodide **4** (or **13**) with (*E*)-penten-1-yl diisobutylalane[7] (prepared by hydroalumination of pent-1-yne) directly providing the desired 8*E*,10*E* (or 8*Z*,10*E*) diene system.

The simplicity of the designed synthetic strategy was hampered by problems with hydroxy-protective groups. The *tert*-butyl group, which was used for protection of the hydroxy group of the starting material **2**, is generally suitable as a protective group[9] for the majority of proposed synthetic steps. The *tert*-butyl group is also stable under conditions of hydroalumination. Unfortunately, the *tert*-butyl group showed to be unsuitable for cross-coupling reactions in the presence of zinc chloride (the modified Negishi reaction[7]). This strong Lewis acid destroyed the protected vinyl iodides **4** and **13**, which resulted in virtually zero yields in the above cross-coupling reaction. Therefore, the *tert*-butyl group was replaced with the resistant *tert*-butyl(dimethyl)silyl group (TBDMS) in the vinyl iodides **9** and **18**.

In the last steps of the synthesis, the protected dienols were deprotected and oxidized with pyridinium chlorochromate[18] (PCC) to the target compounds **1a**–**1d**. Stereoisomeric purity of obtained dienals **1a**–**1d** was higher



Reagents and catalysts: (i) 2-methylpropene, Amberlist; (ii) LiC≡CH·EDA; (iii) 1. DIBAH, 2. I_2; (iv) pent-1-yne/[$Pd(Ph_3P)_4$], Cu_2I_2, butylamine; (v) 1. dicyclohexylborane, 2. AcOH, 3. NaOH, 4. H_2O_2; (vi) 1. $Ac_2O/FeCl_3$, 2. NaOH/MeOH;(vii) PCC/NaOAc; (viii) *t*-$BuMe_2SiCl$/pyridine, DAP; (ix) (*E*)-penten-1-yl di(isobutyl)alane/[$Pd(Ph_3P)_4$], $ZnCl_2$; (x) Bu_4NF; (xi) 1. BuLi, 2. I_2

SCHEME 1

than 95% (GC). Overall yields of compounds **1a**–**1d** were between 16 and 26% based on the starting 7-bromoheptan-1-ol.

EAG responses of **1a** and its geometrical isomers **1b**–**1d** (Fig. 1) clearly showed high selectivity of the pheromone receptors on male antenna for **1a**, which was previously independently disclosed to be the sex pheromone[3,4] of *Cameraria ohridella*. A slightly higher response of the **1d** isomer is most likely due to the similarity of the *Z*,*E* system to *E*,*Z* double bonds in **1a**. Complete dose-response curves of all the isomers will be published elsewhere.

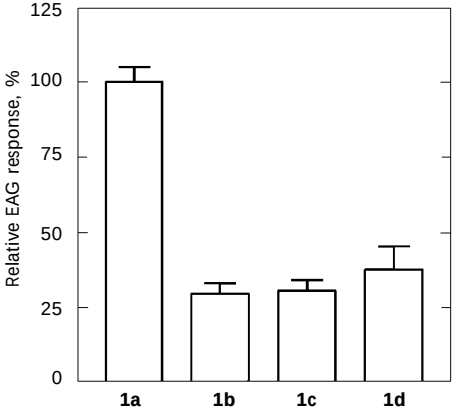


FIG. 1
Relative EAG responses of *C. ohridella* males to 1 ng doses of (8*E*,10*Z*)-tetradeca-8,10-dienal (**1a**) and its isomers (**1b**–**1d**) expressed as percentages of the EAG response to **1a**. Each bar is the mean of 3 replications. Error bars represent standard deviation of the mean

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