Practical Synthesis of (9*S*,10*R*)-9,10-epoxy-(3*Z*,6*Z*)-henicosadiene: The Major Pheromone of the Saltmarsh Caterpillar moth *Estigmene acrea*

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An efficient synthesis of (3*Z*,6*Z*)-*cis*-9,10-epoxy-3,6-henicosadiene (**1**), the major component of sex pheromone of saltmarsh caterpillar moth *Estigmene acrea* (Drury), was accomplished from commercially available pentadec-3-yn-1-ol and bromoundecane. Chirality was introduced by employing Sharpless asymmetric dihydroxylation on *cis*-olefin intermediate in the synthesis of **1**, for the first time. The other key reactions include metal-dissolving coupling, Lindlar's catalyst-assisted partial hydrogenation, one-pot, three-step epoxidation from vicinal diol, and Wittig olefination. The overall yield of **1** was 24.7% in eight steps. The efficiency and simplicity of this synthesis allow the potential use of pheromone **1** in pest management programs.

Keywords: Sex pheromone, Sharpless dihydroxylation, Asymmetric synthesis, *Estigmene acrea*, Wittig olefination

Introduction

Pheromones play an important role in studying the social response among the members of same species with opposite sex, and thus are used in traps/lures to control pests. (9*S*,10*R*)-9,10-Epoxy-(3*Z*,6*Z*)-henicosadiene (**1**) is one of the major pheromone components of many Lepidopteran pests such as fall webworm moth or American white moth *Hyphantria cunea* (Drury), saltmarsh caterpillar moth *Estigmene acrea* (Drury), and Bihar hairy caterpillar moth *Diacrisia oblique* (Arctiidae).[1,2] These moths are widespread in USA, Canada, and South Asian countries such as China, Japan, and India. The larva of these pests attacks crops, oil-seed plants, fruit, and ornamental trees. The other pheromone components identified in these pests include (9*S*,10*R*)-9,10-epoxy-(3*Z*,6*Z*)-henicosatriene (**2**), (9*S*,10*R*)-9,10-epoxy-(3*Z*,6*Z*)-icosatriene (**3**), (9*Z*,12*Z*)-9,12-octadecadienal (**4**), and (9*Z*,12*Z*,15*Z*)-9,12,15-octadecatrienal (**5**) (Figure 1). According to field tests, an appropriate proportions of these pheromones **1–5** of female *H. cunea* and *D. oblique* attracted males.[2b,3] Senda *et al*. reported that a blend of **1**, **2**, and **5** was good enough to attract *H. cunea* in the field, which was then commercialized.[4] On the other hand, the optically active components **1**, **2**, and **3** are also found to be biologically active antifeedants and self-defensive substances against rice blast disease.[5] A considerable amount of research work on these insect pheromones has been performed and reported for almost three decades. Though pesticides are used to control pests all the time, organic cultivation in food industry is again demanding pheromone usage for healthy victuals, thereby enthusing synthetic chemists to focus on various practical and efficient preparation methods.

However, the stereochemical purity of synthetic pheromones also plays a vital role on their activities.[6] Hill and Roelofs suggested the absolute configuration for **1** as (9*S*,10*R*), the active pheromone component among three isolated from *E. acrea*.[1a] The first highly efficient asymmetric synthesis of **1** and its enantiomer was reported by utilizing Sharpless asymmetric epoxidation as the key step, which was an improved version of their preliminary communication.[7b] Most of the known syntheses of **1** employed the same asymmetric epoxidation, while a few followed kinetic resolution to achieve the required chirality.[2b,7] All these approaches are inefficient and furnished **1** in only 7–12% overall yields until a recent report by Du *et al*. with 31% overall yield.[7h] The limitation of this method is that the unstable epoxide will interfere with further homologation so it is difficult to synthesize the

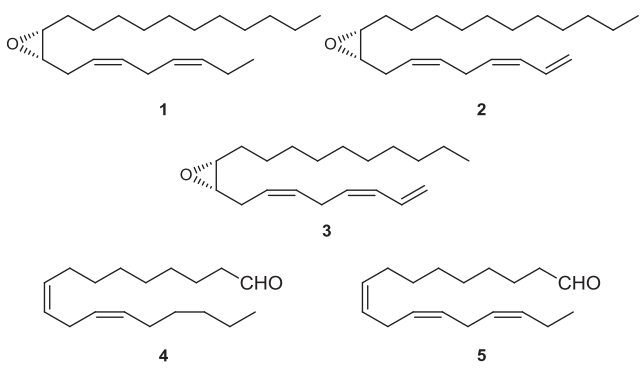


Figure 1. Pheromone components of *H. cunea* (Drury).

compound **1** on a large scale. Thus, it is still a target for chemists to achieve such pheromone components by using new and practical synthetic strategies that ensure optical purity and good overall yields.

Our previous work toward the total synthesis of various pheramones[8] encouraged us to take up a different approach to synthesize **1;** also it is a part of our research on the synthesis of biologically and pharmacologically[9] important chemical entities. Here we report a practical synthesis of the sex pheromone **1** in eight steps by utilizing Sharpless asymmetric dihydroxylation as the key step.

Experimental

All glassware was dried thoroughly in a hot oven and streamed with nitrogen before use. Solvents were dried and purified by conventional methods prior to use. All the chemicals were purchased from Sigma-Aldrich (St. Louis, MO, USA). IR measurements were performed on an FTIR-6300 spectrometer (JASCO, Tokyo, Japan). ^{1}H NMR (at 400 MHz) and ^{13}C NMR (at 100 MHz) spectroscopic data were recorded on an Avance 400 MHz spectrometer (Bruker, Rheinstetten, Germany). Gas chromatography-mass spectrometry (GC-MS) analyses were carried out with Hewlett-Packard 6890 and 5973 system (Agilent, Santa Clara, USA).

Pentadec-3-yn-1-ol (7). Catalytic $Fe(NO_3)_3{\cdot}9H_2O$ was added to an ammonia solution (100 mL) (appearing in an ammonia condenser) and stirred for 30 min. Lithium metal (1.48 g, 212.8 mmol, 4.0 equiv) was added slowly to the reaction mixture, and brown color turned into white-gray after 30 min. Then, butyn-1-ol **9** (4.8 mL, 63.8 mmol, 1.2 equiv) in dry tetrahydrofuran (THF) was added dropwise and stirred for 1 h, compound **8** (12.5 g, 53 mmol, 1.0 equiv) in THF (16 mL) was added slowly, and stirring was continued for 16 h at −45 °C. Thin Layer Chromatography (TLC) was used to monitor the complete consumption of the starting alcohol. Saturated NH_4Cl (150 mL) was added to the reaction mixture and then extracted with ethyl ether (2 × 100 mL). The combined organic layers were washed with water and dried over anhydrous Na_2SO_4. The crude compound was purified by column chromatography to get the pure alcohol compound **7** (8.44 g, 76%) as a white solid. M.p. 42–43 °C; IR (KBr) ν_{max} 3327, 2918, 2850, 2106, 1629, 1471, 1048, 1018, 885 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 6.8 Hz, 3H), 1.22–1.38 (m, 16H), 1.44–1.53 (m, 2H), 2.13–2.20 (m, 2H), 2.41–2.47 (m, 2H), 3.69 (q, J = 6.0 and 12.3, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 82.8, 76.2, 61.3, 31.9, 29.6, 29.5, 29.1, 29.0, 28.9, 23.2, 22.7, 18.7, 14.1 ppm; GC-MS (*m/z*): 224 [M]$^+$; Anal. calcd for $C_{15}H_{28}O$: C, 73.36; H, 11.17. Found: C, 73.07; H, 10.87.

(*Z*)-Pentadec-3-en-1-ol (10). To a suspension of compound **7** (8.0 g, 35 mmol, 1.0 equiv) in ethyl acetate (100 mL) was added a catalytic amount of Lindlar's catalyst in a Parr reaction bottle and quinoline (70 mg) was added. The reaction mixture was shaken under H_2 atmosphere (40 psi, 6 h) using a Parr hydrogenation apparatus. After completion of the reaction, it was filtered through Celite and washed with ethyl acetate (2 × 150 mL). The combined organic layer was dried over anhydrous Na_2SO_4. The crude compound was purified by flash column chromatography to get the pure alkene compound **10** (7.52 g, 94%) as a light yellowish oil. IR (neat) ν_{max} 3327, 2955, 2918, 2850, 1629, 1471, 1372, 1048, 885 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 6.8 Hz, 3H), 1.22–1.35 (m, 18H), 1.95–2.12 (m, 2H), 2.23–2.37 (m, 2H), 3.59–3.67 (m, 2H), 5.32–5.44 (m, 1H), 5.50–5.61 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.6, 124.9, 62.3, 31.9, 30.8, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.3, 27.9, 22.7, 14.2 ppm; GC-MS (*m/z*): 226 [M]$^+$; Anal. calcd for $C_{15}H_{30}O$: C, 79.58; H, 13.36. Found: C, 79.27; H, 13.07.

(3*S*,4*R*)-Pentadecane-1,3,4-triol (11). Into a round-bottomed flask was added ^{t}BuOH (85 mL) and H_2O (85 mL), AD-mix-β (43 g), and methane sulfonamide (2.99 g, 31.4 mmol, 1.0 equiv). The mixture was stirred at room temperature (RT) until the solution became clear, and then the reaction mixture was cooled to 0 °C. To this cooled solution was added compound **10** (6.68 g, 31.4 mmol, 1.0 equiv) and stirred at 0 °C for 2 days. The reaction was quenched with saturated sodium sulfite solution and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated. On silica gel column chromatography with 1:9 (methanol/ethyl acetate) gave pure diol **11** (7.88 g, 96%, 86.5% ee [checked by chiral HPLC, Chiral Pak AD-H, 250 × 4.6 × 5 m, 0.01 M NH_4OAc in water:ACN (1:9), 1 mL/min with mono *p*-nitro benzoate derivative of **12**]) as a white solid. M.p. 79–81 °C. $[\alpha]_D^{25}$ = +6.9 (*c* 1.0, methanol); IR (KBr) ν_{max} 3313, 3270, 3214, 2917, 2850, 1632, 1467, 1314, 1143, 1062, 884, 778, 688 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (t, J = 6.8 Hz, 3H), 1.24–1.38 (m, 18H), 1.49–1.88 (m, 4H), 3.29–3.33 (m, 2H), 3.36–3.42 (m, 1H), 3.51–3.61 (m, 1H), 3.65–3.78 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.0, 73.3, 60.4, 36.0, 33.7, 33.1, 30.9, 30.8, 30.5, 27.0, 23.7, 14.2 ppm; GC-MS (*m/z*): 260 [M]$^+$; Anal. calcd for $C_{15}H_{32}O_3$: C, 69.18; H, 12.39. Found: C, 69.39; H, 12.00.

2-(4*S*,5*R*)-2,2-Dimethyl-5-undecyl-1,3-dioxolan-4-yl)ethanol (12). A mixture of compound **11** (7.00 g, 26.8 mmol, 1.0 equiv) and *p*TsOH·H_2O (1.02 g, 5.37 mmol, 0.2 equiv) in acetone (250 mL) was stirred at RT for 24 h. The reaction was quenched with $NaHCO_3$. After filtration, the solvent was concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc, 1:1) to give the acetonide-protected compound **12** (7.43 g, 92%) as a colorless oil. $[\alpha]_D^{25}$ = +44.5 (*c* 1.0, methanol); IR (neat) ν_{max} 3440, 2927, 1418, 1375, 1074, 909, 796, 674, 448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 6.8 Hz, 3H), 1.21–1.32 (m, 16H), 1.34 (d, J = 8.3 Hz, 6 H), 1.47–1.64 (m, 4H), 1.66–1.88 (m, 2H), 3.61–3.89 (m, 2H), 4.04–4.13 (m, 1H), 4.21–4.30 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 107.8, 81.0, 80.9, 61.3, 38.8, 32.1, 31.9, 29.8, 29.7, 29.6, 29.6, 29.3, 29.3, 28.4, 27.2, 26.3, 22.7, 14.1 ppm; GC-MS (*m/z*): 300 [M]$^+$; Anal. calcd for $C_{18}H_{36}O_3$: C, 71.95; H, 12.08. Found: C, 72.25; H, 12.38.

2-((4*S*,5*R*)-2,2-Dimethyl-5-undecyl-1,3-dioxolan-4-yl)acetaldehyde (13). 2-Iodoxybenzoic acid (IBX) (12.68 g, 45.2 mmol, 2.0 equiv) was dissolved in a minimum amount of dry Dimethyl sulfoxide (DMSO) and stirred for 15 min. Then the starting material **12** (6.80 g, 22.6 mmol, 1.0 equiv) dissolved in THF (80 mL) was added. Then reaction was stirred for 3 h at RT and filtered through a Celite pad. The reaction mixture was dissolved in ethyl acetate and washed with aqueous sodium bicarbonate solution. The organic layer was dried over Na_2SO_4 and concentrated, followed by column chromatography purification to get the pure aldehyde compound **13** (6.01 g, 89%) as a colorless oil. $[\alpha]_D^{25} = -10.1$ (*c* 1.0, methanol); IR (Neat) ν_{max} 3404, 2924, 2847, 1398, 1085, 910, 789, 674 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.16–1.50 (m, 26H), 2.44–2.77 (m, 2H), 4.14–4.21 (m, 1H), 4.54–4.63 (m, 1H), 9.82–9.84 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.9, 108.1, 77.4, 72.8, 44.7, 31.9, 29.6, 29.6, 29.6, 29.6, 29.5, 29.5, 28.3, 26.3, 25.7, 22.7, 14.1 ppm; GC-MS (*m/z*): 299 $[M]^+$; Anal. calcd for $C_{18}H_{34}O_3$: C, 72.44; H, 11.48. Found: C, 72.02; H, 11.04.

(*Z*)-Hex-3-en-1-yltriphenylphosphonium iodide (14). Into a round-bottomed flask was added (*Z*)-1-iodohex-3-ene (14.0 g, 66.4 mmol, 1.0 equiv), triphenyl phosphine (19.20 g, 73.5 mmol, 1.1 equiv), and toluene (100 mL). The mixture was stirred at reflux condition for 24 h and then monitored by TLC. The reaction mixture was then cooled to RT and filtered, and washed with hexane (300 mL) to get the pure Wittig salt (30 g, 95%) as a white solid. M.p. 120–122 °C. IR (KBr) ν_{max} 3429, 3016, 2963, 2865, 1627, 1578, 1486, 1438, 1336, 1163,1111, 996, 808, 743, 720 cm^{-1}; ^1H NMR (400 MHz, CD_3COCD_3): δ 0.92 (t, *J* = 7.5 Hz, 3H), 1.88–2.04 (m, 2H), 2.35–2.50 (m, 2H), 3.47–3.60 (m, 2H), 5.34–5.57 (m, 2H), 7.77–7.94 (m, 15H) ppm; ^{13}C NMR (100 MHz, CD_3OCD_3): δ 136.4, 136.3, 136.3, 136.3, 135.4, 135.4, 135.0, 134.9, 134.9, 134.9, 134.8, 131.6, 131.5, 126.5, 119.5, 119.5, 30.8, 21.5, 14.1; ESI-MS (*m/z*): 473 $[M + H]^+$. Anal. calcd for $C_{24}H_{26}IP$: C, 61.03; H, 5.55. Found: C, 61.32; H, 5.26.

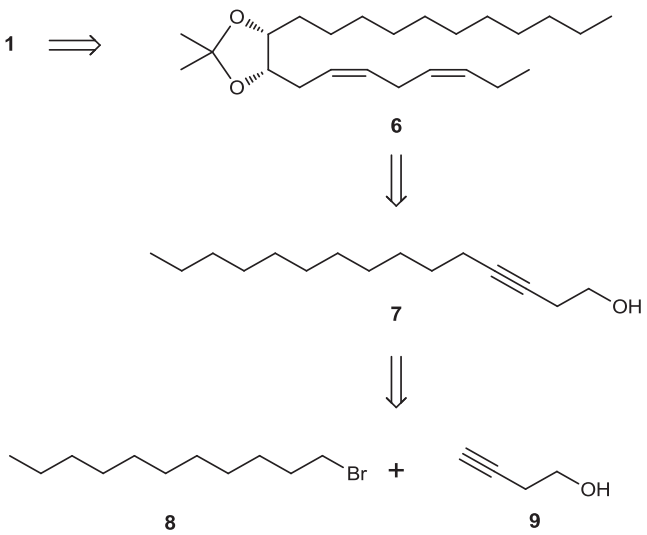
(4*S*,5*R*)-2,2-Dimethyl-4-((2*Z*,5*Z*)-octa-2,5-dien-1-yl)-5-undecyl-1,3-dioxolane (6). A solution of the Wittig salt **14** (17.4 g, 36.9 mmol, 2.0 equiv) in THF (60 mL) at −78 °C was treated dropwise with *n*-BuLi (18.4 mL, 1.6 M solution in THF, 29.5 mmol, 1.6 equiv). The bright orange-red reaction mixture was warmed to 25 °C and stirred for 10 min. The reaction mixture was recooled to −78 °C, treated with compound **13** (5.5 g, 18.4 mmol, 1.0 equiv), and brought to 25 °C. After stirring at 25 °C for 30 min, the reaction mixture was treated with saturated aqueous NH_4Cl solution and partitioned between EtOAc (100 mL) and H_2O (100 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure and purified by column chromatography afford pure **6** (5.20 g, 78%) as a colorless oil. $[\alpha]_D^{25} = +10.9$ (*c* 1.0, methanol); IR (Neat) ν_{max} 3009, 2925, 2858, 1743, 1645, 1466, 1375, 1244, 1220, 1171, 1069, 1033, 865,721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.8 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H), 1.20–1.31 (m, 18H), 1.36 (d, J = 19.7Hz, 6H), 1.48–1.58 (m, 2H), 2.02–2.38 (m, 4H), 2.71–2.86 (m, 2H), 3.55–3.71 (m, 1H), 4.04–4.12 (m, 1H), 5.26–5.56 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.8, 132.3, 132.1, 126.6, 125.3, 73.973.8, 31.9,31.6, 30.9, 29.6, 29.6, 29.6, 29.6, 29.3, 29.0, 26.0, 25.6, 22.7, 20.6, 20.5, 14.2, 14.1 ppm; GC-MS (*m/z*): 365 $[M]^+$; Anal. calcd for $C_{24}H_{44}O_2$: C, 79.06; H, 12.16. Found: C, 79.41; H, 12.42.

(3*Z*,6*Z*,9*S*,10*R*)-Henicosa-3,6-diene-9,10-diol (15). Compound **6** (4.2 g, 11.5 mmol, 1.0 equiv) was dissolved in methanol, and a catalytic amount of *p*-Toluenesulfonic acid (PTSA) was added. The reaction mixture was stirred for 24 h at RT and passed through silica gel with CH_2Cl_2 solvent to get the diol product **15** (3.25 g, 87%) as a colorless oil. $[\alpha]_D^{25} = +41.5$ (*c* 1.0, methanol); IR (Neat) ν_{max} 3422, 3290, 3013, 2958, 2925, 2872, 2850, 1632, 1464, 1060, 1044, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.8 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H), 1.23–1.29 (m, 18H), 1.45–1.54 (m, 2H), 2.04–2.12 (m, 2H), 2.19–2.25 (m, 1H), 2.35–2.45 (m, 1H), 2.76–2.91 (m, 2H), 3.58–3.68 (m, 1H), 3.79–3.87 (m, 1H), 5.19–5.54 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.10, 132.27, 132.1, 126.83, 125.52, 77.97, 77.77, 33.05, 32.99, 31.93, 30.9, 29.72, 29.67, 29.61, 29.57, 25.81, 25.71, 22.71, 20.58, 14.28, 14.15 ppm; GC-MS (*m/z*): 324 $[M]^+$; Anal. calcd for $C_{21}H_{40}O_2$: C, 77.72; H, 12.42. Found: C, 78.12; H, 12.10.

(9*S*,10*R*)-9,10-Epoxy-(3*Z*,6*Z*)-henicosa-3,6-diene (1). To a solution of **15** (2.60 g, 8.0 mmol, 1.0 equiv) in freshly distilled CH_2Cl_2 was added trimethyl orthoacetate (5.1 mL, 40.1 mmol, 5.0 equiv) and PPTS (0.20 g, 0.80 mmol, 0.1 equiv) at RT for 10 h; most of the volatile components were removed by rotary evaporation. The residue was dissolved in freshly distilled CH_2Cl_2 and cooled to 0 °C. Trimethylsilyl chloride (5.0 mL, 40.1 mmol, 5.0 equiv) was added via a syringe, and the mixture was allowed to warm to room temperature and stirred for 1.5 h. Most of the volatiles were removed *in vacuo*, and the resulting residue was dissolved in methanol. K_2CO_3 (3.30 g, 24.0 mmol, 3.0 equiv) was added in one portion, and the mixture was stirred at room temperature for 1 h. The reaction mixture was poured into saturated ammonium chloride, extracted with ethyl acetate, dried, concentrated, and chromatographed to get the final epoxide product **1** (1.59 g, 65% yield for three steps) as a colorless oil. $[\alpha]_D^{25} = +3.9$ (*c* 1.7, CCl_4) [Refs 7g and 7h $[\alpha]_D^{28} = +3.9$ (*c* 1.8, CCl_4), $[\alpha]_D^{22} = +3.99$ (*c* 1.65, CCl_4)]; IR (Neat) ν_{max} 3012, 2960, 2925, 2854, 1650, 1464, 1382, 1076, 1025 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.8 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H), 1.22–1.32 (m, 18 H),1.50–1.56 (m, 2H), 2.03–2.12 (m, 2H), 2.18–2.27 (m, 1H), 2.35–2.46 (m, 1H), 2.73–2.84 (m, 2H), 2.90–2.97 (m, 2H), 5.26–5.56 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.2, 130.7, 126.7, 124. 2, 57.2, 56.4, 31.9, 29.6, 29.6, 29.5, 29.3, 27.7, 26.6, 26.2, 25.7, 22.7, 20.5, 14.2, 14.1 ppm; GC-MS (*m/z*): 306 $[M]^+$; Anal. calcd. for $C_{21}H_{38}O$: C, 82.28; H, 12.50. Found: C, 82.59; H, 12.11.

Results and Discussion

Our synthetic strategy involves Sharpless asymmetric dihydroxylation on *cis*-olefin as the key step, for the first time, to achieve chirality in **1**.

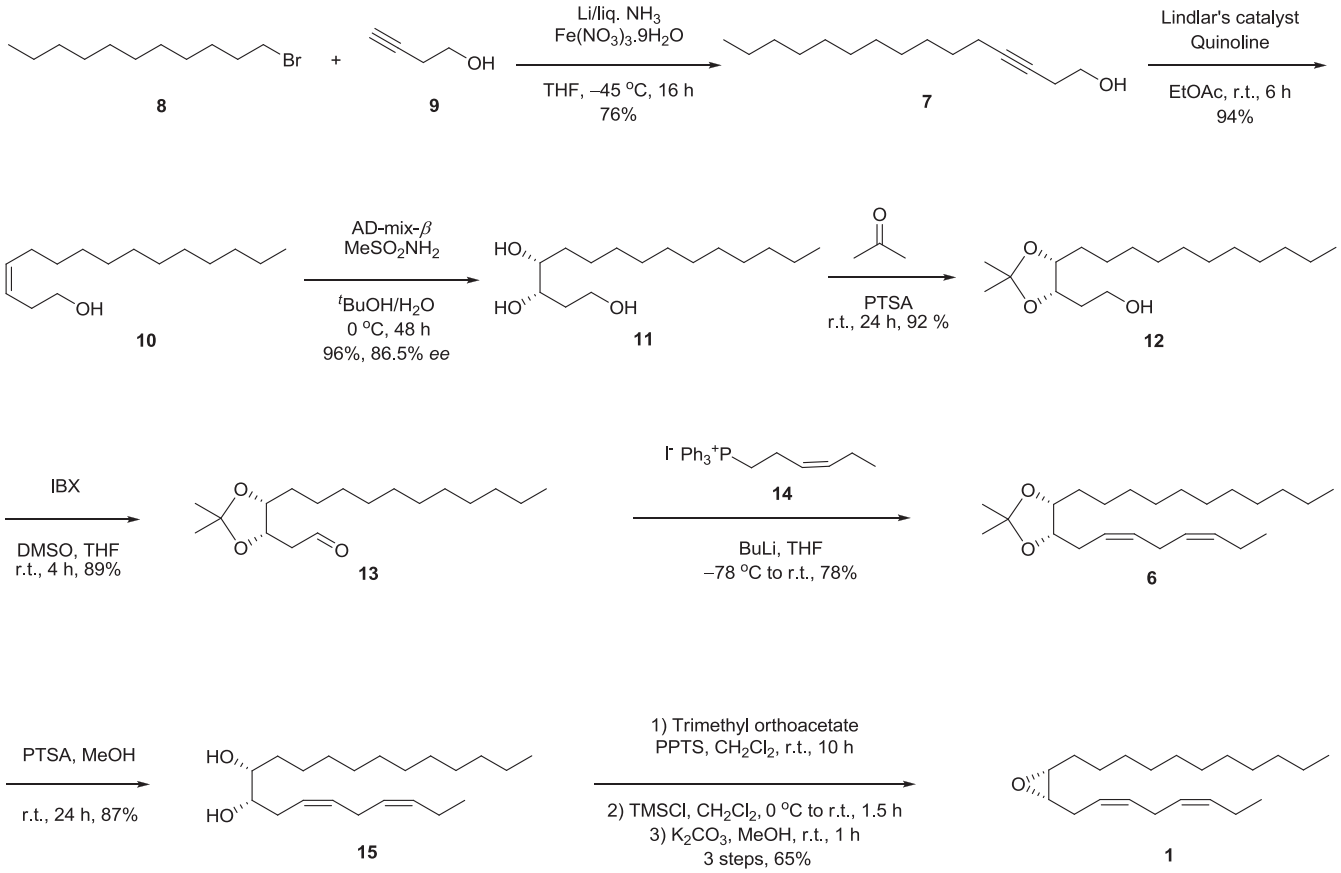


Scheme 1. Retrosynthetic analysis of pheromone **1**.

The retrosynthetic analysis of pheromone **1** starting from commercially available 1-bromoundecane (**8**) and 3-butyn-1-ol (**9**) is shown in Scheme 1. The target pheromone **1** can be achieved from the intermediate **6** in four synthetic steps.

Compound **6** can be obtained from **7** by partial hydrogenation, Sharpless asymmetric hydroxylation, and Wittig olefination as key steps. The intermediate **7** can be synthesized by metal-based coupling reaction in liquid ammonia between **8** and **9**.

The asymmetric synthesis of pheromone **1** is outlined in Scheme 2. Here, we have carried out a metal dissolving coupling reaction between **8** and **9**, which generates lithium amide in liquid ammonia at −45 °C in the presence of catalytic $Fe(NO_3)_3{\cdot}9H_2O$ in 76% yield. This reaction successfully afforded pentadec-3-yn-1-ol (**7**) and was further preceded for hydrogenation using Lindlar's catalyst (5% Pd on $CaCO_3$ poisoned with lead) in presence of catalytic quinoline under 1 atm H_2 gas. Partial hydrogenation of **7** afforded the *cis*-olefin **10** in 94% yield, which was confirmed by IR absorption bands at 1048 cm^{-1} (═C─H bending) for *cis*-olefin. Carbons appearing at δ 125.6 and 124.9 in ^{13}C NMR spectrum also confirmed the same. This *cis*-olefin **10** was subjected to Sharpless asymmetric dihydroxylation using AD-mix-β to afford triol **11** in 96% yield with 86.5% ee. The vicinal diol of **11** was protected by acetone in presence of catalytic PTSA to achieve acetonide



Scheme 2. Synthesis of pheromone **1**.

12 in 92% yield. The primary alcohol of **12** was oxidized in presence of IBX in DMSO/THF to obtain the key intermediate aldehyde **13** in 89% yield. This aldehyde can be used for Wittig olefination to achieve different pheromone components depending on the appropriate Wittig counterpart. We have taken the known Wittig salt **14**[10] to make phosphonium ylide in presence of *n*-BuLi, which was then used for the Wittig olefination in THF at −78 °C to obtain **6** in 78% yield. The Wittig olefin **6** was treated with PTSA to afford diol **15** in 87% yield. Finally, the epoxide was then obtained in a one-pot, three-step synthesis from diol **15**. At first, **15** was treated with trimethyl orthoacetate in presence of PPTS to achieve the corresponding cyclic orthoacetate, which was directly treated with TMSCl for 1 h and then with K_2CO_3 in MeOH affording the target pheromone **1** in 65% yield (three steps).

This product was confirmed by ^1H, ^{13}C NMR, IR, and MS analyses, which were in accordance with the reported ones. All the intermediates prepared in this approach are convenient enough to be used in the syntheses of other pheromones of *E. acrea*, *H. cunea*, *D. oblique* and others.

Conclusion

In summary, we have accomplished concise and practical synthesis of (3Z,6Z)-*cis*-9,10-epoxy-3,6-henicosadiene (**1**), the major sex pheromone of *E. acrea* (Drury) starting from commercially available but-3-yn-1-ol and 1-bromoundecane in 24.7% overall yield in eight steps. The simplicity of the method and purity of the products in this synthetic approach allow the potential and practical use of pheromone **1** in field studies to understand the responses of pest management programs.

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