

10-Undecenoic Acid, an Inexpensive Source for the Synthesis of the Pheromones of Cotton Pests, Peach Tree Borer and Cherry Tree Borer

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Abstract: The aldehyde **7**, derived from 10-undecenoic acid (**5**) on *cis*-selective Wittig reaction with pentylidenetriphenylphosphorane, subsequent deprotection and oxidation gave the pheromone (11*Z*)-hexadecenal (**1**). Wittig-Horner olefination of **1** with the phosphonate **9** furnished the conjugated ester **10** which on base catalyzed isomerization to the (3*Z*)-ester **11** followed by LAH reduction and acetylation gave (3*Z*,13*Z*)-octadecadien-1-yl acetate (**2**). Compound **10** on the other hand was chemoselectively reduced and acetylated to furnish the pheromone (2*E*,13*Z*)-octadecadien-1-yl acetate (**4**). For the synthesis of (3*E*,13*Z*)-octadecadien-1-yl acetate (**3**), **1** was condensed with malonic acid under modified condition to afford the acid **13** which was converted to **3** by standard reaction protocol.

Keywords: Insect pheromones, cotton bollworm, peach tree borer, cherry tree borer, 10-undecenoic acid.

Introduction

In the quest for practical syntheses of agriculturally important insect pheromones, 10-undecenoic acid (**5**) seems to be an ideal starting material. Besides its easy availability from castor oil, the terminal bifunctionality of **5** is amenable to synthetic maneuvers to different target long chain olefinic compounds. Earlier we have used [1-4] it extensively for the syntheses of some plant growth regulators, insect pheromones, marine demospongiac acids, prostaglandin synthon, *etc.* Herein, we report a divergent synthetic strategy for some other pheromones of destructive pests of cash crops and fruits *viz.* (11*Z*)-hexadecenal (**1**), (3*Z*,13*Z*)-octadecadienyl acetate (**2**) and its 3*E*-isomer (**3**) and (2*E*,13*Z*)-octadecadienyl acetate (**4**). While compound **1** is a pheromone component [5] of the cotton bollworm, *Heliothis armigera*, **2-4** have been isolated as the pheromones of various orchard pests in the genera,

Synanthedon [6], *Sanninoidea* [6], *Melittia* and *Vitacea* [7]. In view of their importance, several individual synthesis of **1** [8a], **2-4** [8b-e] have been reported. However, to the best of our knowledge, this is the first divergent synthesis (Scheme 1) of all of these from a single commercially available precursor involving extremely simple stereoselective methodologies and hence seems suitable as a practical route.

Results and Discussion

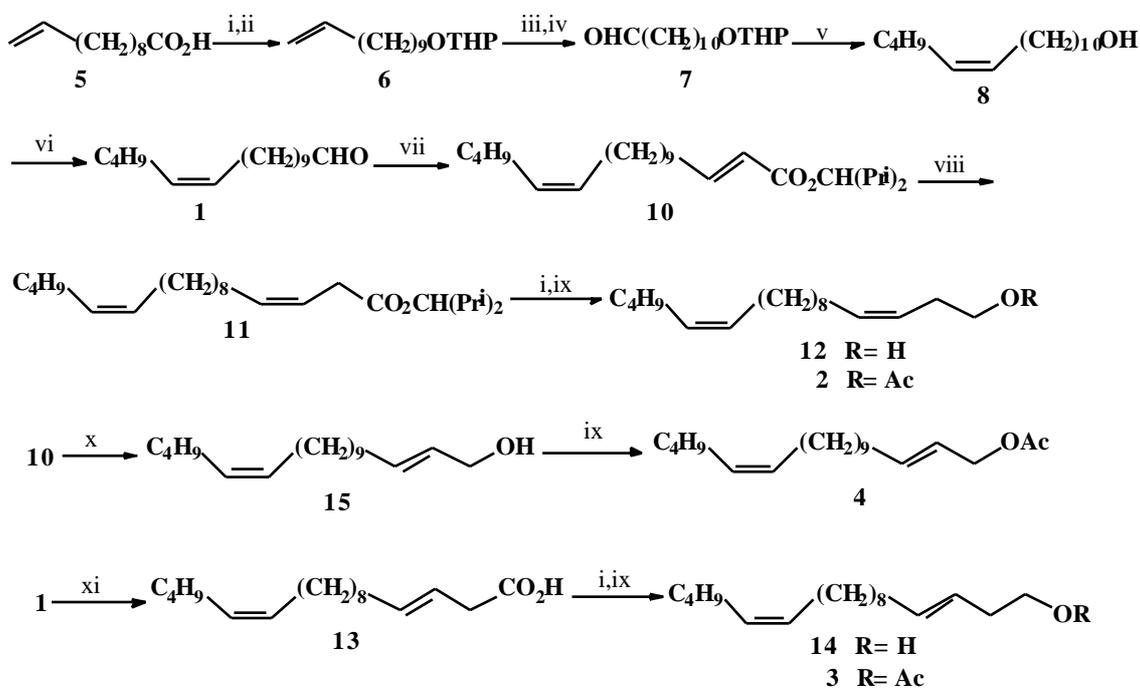
The acid **5** on LAH reduction followed by tetrahydropyranylation gave **6**. Its hydroboration-oxidation furnished the known aldehyde **7** [9] which on *Z*-selective Wittig olefination with *n*-pentylidenetriphenylphosphorane and subsequent deprotection gave the alcohol **8**. This was oxidized with PCC to furnish the title pheromone **1**.

Compound **1** thus obtained, on Wittig-Horner reaction

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with the hindered phosphonoacetate **9** [10] furnished the (2*E*)-C₁₈ ester **10**. Its base catalyzed deconjugation [10] with potassium hexamethyldisilazide afforded the (3*Z*)-ester **11** exclusively. This on LAH reduction gave the alcohol **12** which was acetylated to furnish the pheromone **2**. On the other hand, compound **1** when subjected to modified Doebner condensation [11] gave the (3*E*)-acid **13** in excellent yield. Its LAH reduction followed by acetylation

provided the pheromone **3**. Likewise, chemoselective reduction of the ester functionality in **10** with AlH₃ [12] gave the alcohol **15** which on acetylation afforded the title pheromone **4**. The spectral and physical data of the pheromones **1-4** were in good agreement with those reported [8a-e] in literature. The olefinic stereochemistry of the pheromones were assigned [4] based on the ¹³C allylic carbon signals of individual compounds.



i) LAH/ether, ii) DHP/PPTS/CH₂Cl₂, iii) BH₃.THF; H₂O₂/NaOH, iv) PCC/NaOAc/CH₂Cl₂, v) Dimethyl ion/C₅H₁₁PPh₃Br/DMSO/THF; MeOH/HCl, vi) PCC/CH₂Cl₂, vii) NaH/(EtO)₂P(O)CH₂CO₂CH(Prⁱ)₂ (**9**), viii) Pot. Hexamethylsilazide, ix) Ac₂O/Py, x) AlH₃/THF, xi) Malonic acid/piperidine/xylene/ .

Scheme 1.

Experimental

General

All bp's are uncorrected. The IR spectra were scanned with a Perkin-Elmer spectrophotometer model 783. The ¹H and ¹³C NMR spectra were recorded in CDCl₃ with a Bruker AC-200 (200 MHz) spectrometer. All solvents were dried prior to use employing standard procedures. The organic extracts were dried over anhydrous Na₂SO₄.

(11*Z*)-Hexadecenol (**8**)

To a solution of dimethyl anion [prepared from NaH (0.86 g, 50% suspension in oil, 0.018 mol) in DMSO (30

mL)] was added *n*-pentyltriphenylphosphonium bromide (7.44 g, 0.018 mol) at room temperature. After 1 h, THF (20 mL) was introduced in the flask, the reaction mixture cooled to -20 °C and the aldehyde **7** [9] (4.32 g, 0.016 mol) in THF (40 mL) added in dropwise fashion. Stirring was continued for 2 h at -20 °C and 1 h at room temperature. The mixture was poured in large excess of water and extracted with hexane. The hexane layer was washed with water, brine and dried. The crude product obtained on concentration, was reextracted with cold hexane. Removal of solvent gave a residue which was dissolved in MeOH (50 mL) containing dil. HCl (50%, 2-3 drops) and heated to reflux for 6 h. Most of the solvent was removed under vacuum, the residue dissolved in ether and washed with aqueous 10% NaHCO₃, water and brine. After drying, the

solvent was removed in vacuo and the crude compound purified by column chromatography over silica gel (0-15% EtOAc/hexane) to furnish pure **8** (2.7 g, 70%): bp 100-102 °C/ 0.1 mm; IR: 3340, 3075, 1060 cm⁻¹; ¹H NMR: 0.90 (dist. t, 3H), 1.30 (br. s, 20H), 1.8-2.0 (m, 4H), 2.2 (s, D₂O exchangeable, 1H), 3.48 (t, *J* = 7 Hz, 2H), 5.4-5.6 (m, 2H). Anal. Calcd. for C₁₆H₃₂O: C, 79.93; H, 13.42. Found: C, 80.14; H, 13.33.

(11Z)-Hexadecenal (1)

To a stirred suspension of pyridinium chlorochromate (PCC) (5.39 g, 0.025 mol) in CH₂Cl₂ (50 mL) was added the compound **8** (4.0 g, 0.017 mol) in one lot. After completion of the reaction (~ 3 h), the mixture was diluted with 50 mL of ether and the supernatant passed through a 2" pad of silica gel which was thoroughly eluted with ether. The eluent on concentration furnished pure **1** (3.48 g, 86%): IR: 3075, 2700, 1730 cm⁻¹; ¹H NMR: 0.90 (dist. t, 3H), 1.32 (br. s, 18H), 1.9-2.2 (m, 4H), 2.3-2.4 (m, 2H), 5.4-5.6 (m, 2H), 9.8 (t, *J* = 1.5 Hz, 1H); ¹³C NMR: 22.5, 23.0, 25.2, 25.9, 62.5, 130.2, 132.6, 174. Anal. Calcd. for C₁₆H₃₀O: C, 80.60; H, 12.68. Found: C, 80.39; H, 12.77.

2',4'-Dimethyl-3'-pentyl (2E,13Z)-octadecadienoate (10)

To a stirred suspension of NaH (0.77 g, 50% dispersion in oil, 0.016 mol) in THF (20 mL) at 0 °C was added the phosphonoacetate **9** [10] (4.7 g, 0.016 mol) in THF (10 mL). When the solution became clear (0.5 h), compound **1** (3.0 g, 0.013 mol) in THF (20 mL) was injected into it. Stirring was continued for 2 h at the same temperature and for 2 h at room temperature. The mixture was poured into water and extracted with ether. The ether layer was washed with water, brine and dried. Removal of solvent and subsequent column chromatography (silica gel, 0-5% EtOAc/hexane) of the product afforded pure **10** (3.88 g, 79%): IR: 1710, 1640, 980 cm⁻¹; ¹H NMR: 0.8-1.1 (m, 15H), 1.28 (br. s, 18H), 1.9-2.2 (m, 8H), 4.61 (t, *J* = 7 Hz, 1H), 5.2-5.3 (m, 2H), 5.84 (d, *J* = 15.6 Hz, 1H), 6.91 (dt, *J* = 15.6 Hz, 5.7 Hz, 1H); ¹³C NMR: 13.86, 17.13, 19.41, 22.22, 22.56, 26.80, 27.07, 27.99, 29.07, 29.39, 29.62, 31.84, 32.10, 82.01, 121.23, 129.70, 149.04, 166.74. Anal. Calcd. for C₂₅H₄₈O₂: C, 79.30; H, 12.25. Found: C, 79.52; H, 12.40.

2',4'-Dimethyl-3'-pentyl (3Z,13Z)-octadecadienoate (11)

Potassium metal (0.39 g, 0.01 mol) was added to a stirred solution of naphthalene (1.28 g, 0.01 mol) in THF (20 mL) under Ar atmosphere. After the dissolution of the metal, HMDS (2.2 mL, 0.01 mol) was introduced into the resultant green solution at 0 °C. The pink solution was then quickly transferred into a stirred and cooled (-78 °C)

solution of **10** (2.65 g, 7 mmol) in THF (15 mL). After stirring for 4 h at the same temperature, it was quenched with saturated NH₄Cl solution and brought to room temperature. Water was added and the mixture extracted with ether. The ether layer was washed with water and brine and dried. Removal of solvent *in vacuo* followed by column chromatography (silica gel, 0-5% EtOAc/hexane) of the residue furnished pure **11** (1.98 g, 75%): IR: 3010, 1740 cm⁻¹; ¹H NMR: 0.8-1.1 (m, 15H), 1.26 (br. s, 16H), 2.0-2.4 (m, 8H), 2.97 (d, *J* = 5 Hz, 2H), 4.57 (t, *J* = 7 Hz, 1H), 5.2-5.6 (m, 4H). Anal. Calcd. for C₂₅H₄₆O₂: C, 79.30; H, 12.25. Found: C, 79.25; H, 12.18.

(3Z,13Z)-Octadecadienyl acetate (2)

The above ester **11** (1.9 g, 5.0 mmol) was reduced with LAH (0.300 g, 8.0 mmol) in ether (30 mL) to furnish the alcohol **12** (1.1 g, 80%): bp: 138-140 °C/ 0.1 mm; IR: 3380, 3010, 1053 cm⁻¹; ¹H NMR: 0.90 (dist. t, 3H), 1.3 (br. s, 16H), 2.0-2.3 (m, 8H), 2.44 (br. s, 1H, D₂O exchangeable), 3.63 (t, *J* = 6 Hz, 2H), 5.3-5.6 (m, 4H); Anal. Calcd. for C₁₈H₃₄O: C, 81.13; H, 12.86. Found: C, 80.98; H, 13.05.

A mixture of **12** (1.1 g, 4.1 mmol), acetic anhydride (2 mL) and pyridine (2 mL) was stirred for 18 h. Ice-water was added into it and the mixture stirred for 1 h. It was then extracted with ether, the ether layer washed with water and brine and dried. Removal of solvent *in vacuo* gave **2** (1.02 g, 81%). IR: 1730, 1230 cm⁻¹; ¹H NMR: 0.88 (dist. t, 3H), 1.28 (br. s, 16H), 2.0-2.4 (m containing a s at 2.04, 11H), 4.08 (t, *J* = 7 Hz, 2H), 5.3-5.7 (m, 4H); ¹³C NMR: 13.62, 20.88, 22.14, 22.86, 26.04, 26.32, 28.10, 28.88, 29.12, 29.32, 64.44, 124.34, 129.34, 132.54, 133.08, 170.12. Anal. Calcd. for C₂₀H₃₆O₂: C, 77.86; H, 11.76. Found: C, 77.72; H, 11.61.

(2E,13Z)-Octadecadienyl acetate (4)

To a stirred suspension of AlH₃ [12] (9.0 mmol) in THF (20 mL) was added **10** (2.46 g, 6.5 mmol) in THF (20 mL) and stirring continued till the completion of the reaction (*cf.* tlc). The reaction mixture was worked up by first adding saturated aqueous Na₂SO₄ solution followed by dil. HCl (2 N) and extraction with ether. The ether layer was washed with water and dried. After concentration, the residue was purified by careful chromatography over silica gel (0-15% EtOAc/hexane) to give the alcohol **15** (1.35 g, 78%): bp 122-124 °C/ 0.1 mm; IR: 3340, 1060 cm⁻¹; ¹H NMR: 0.86 (dist. t, 3H), 1.26 (m, 18H), 2.0-2.3 (m, partially D₂O exchangeable, 7H), 4.03 (d, *J* = 6 Hz, 2H), 5.3-5.4 (m, 2H), 5.5-5.6 (m, 2H); ¹³C-NMR: 13.93, 22.28, 25.70, 26.89, 27.13, 29.23, 29.60, 32.26, 64.88, 128.81, 129.79, 133.32. Anal. Calcd. for C₁₈H₃₄O: C, 81.13; H, 12.86. Found: C, 80.92; H, 12.66.

Acetylation of **15** (1.1 g, 4.1 mmol) with acetic anhydride (2 mL) and pyridine (2 mL) gave **4** (1.0 g, 81%): IR: 1730, 1230 cm^{-1} ; ^1H NMR: 0.88 (dist. t, 3H), 1.24 (br. s, 18H), 2.0-2.2 (m containing a s at 2.1, 9H), 4.26 (d, $J=7$ Hz, 2H), 5.3-5.7 (m, 4H). ^{13}C -NMR: 13.63, 21.28, 25.68, 26.48, 28.13, 29.30, 29.44, 32.56, 70.38, 124.84, 129.77, 132.93, 181.12. Anal. Calcd. for $\text{C}_{20}\text{H}_{36}\text{O}_2$: C, 77.86; H, 11.76. Found: C, 77.81; H, 11.52.

(3E,13Z)-Octadecadienoic acid (**13**)

To a gently refluxing mixture of malonic acid (4.68 g, 0.45 mol) and piperidine (0.1 mL) in xylene (60 mL) was added **1** (2.38 g, 0.01 mol). Refluxing was continued for 18 h, most of the solvent was removed under reduced pressure and the residue extracted with ether. The ether layer was thoroughly extracted with 20% aqueous Na_2CO_3 solution, the organic layer discarded and the aqueous portion acidified to pH 2. It was then reextracted with ether, the ether layer washed with water and brine and finally dried. Removal of solvent furnished the acid **13** (2.18 g, 78%): IR: 3700-3500, 1710, 980 cm^{-1} ; ^1H NMR: 0.86 (dist. t, 3H), 1.28 (br. s, 16H), 2.0-2.5 (m, 6H), 3.1 (d, $J=6$ Hz, 2H), 5.3-5.7 (m, 4H), 8.4 (br. s, D_2O exchangeable, 1H). Anal. Calcd. for $\text{C}_{18}\text{H}_{32}\text{O}_2$: C, 77.09; H, 11.50. Found: C, 77.44; H, 11.78.

(3E,13Z)-Octadecadienyl acetate (**3**)

The above acid (2.50 g, 8.9 mmol) was reduced with LAH (0.51 g, 13.4 mmol) in ether (50 mL) to furnish the alcohol **14** (1.86 g, 78%): bp: 140-144°C/0.1 mm; IR: 3340, 3010, 1060, 980 cm^{-1} ; ^1H NMR: 0.90 (dist. t, 3H), 1.32 (br. s, 16H), 2.0-2.5 (m, 8H), 2.72 (br. s, 1H, D_2O exchangeable), 3.68 (t, $J=6$ Hz, 2H), 5.3-5.7 (m, 4H); Anal. Calcd. for $\text{C}_{18}\text{H}_{34}\text{O}$: C, 81.13; H, 13.05. Found: C, 81.30; H, 13.19.

As done for **2**, the alcohol **14** (1.33 g, 5.0 mmol) was converted to the title pheromone **3** (1.25 g, 81%): IR: 1730, 1230, 980 cm^{-1} ; ^1H NMR: 0.86 (dist. t, 3H), 1.28 (br. s, 16H), 1.9-2.4 (m containing a s at 2.1, 11H), 4.12 (t, $J=7$ Hz, 2H), 5.2-5.6 (m, 4H). ^{13}C NMR: 13.22, 21.14, 22.44, 22.90, 26.22, 28.34, 28.86, 29.42, 32.21, 32.57, 64.12, 123.72, 124.33, 129.19, 132.24, 132.98, 170.28. Anal. Calcd. for $\text{C}_{20}\text{H}_{36}\text{O}_2$: C, 77.86; H,

11.76. Found: C, 77.64; H, 11.78.

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Sample Availability: Samples available from the authors.