A New Synthesis of (E)-10-Dodecenyl Acetate the Major Sex Pheromonal Component of Phyllonorycter blancardella

IULIANA VASIAN*, STEFANIA TÓRTOS, IOAN OPREAN

* Babes-Bolyai University, “Raluca Ripan” Institute for Research in Chemistry, 30 Fantanele, Cluj-Napoca 400294, Romania

A new synthesis of (E)-10-dodecenyl acetate and the corresponding alcohol, which are the sex pheromone components of many species of Lepidoptera order as spotted tentiform leafminer Phyllonorycter blancardella has been developed starting from 1,9-nonandiol using classical, modern and original organic methods.

Keywords: (E)-10-dodecenyl acetate, (E)-10-dodecen-1-ol, Phyllonorycter blancardella, sex pheromone, trans-reduction

Phyllonorycter blancardella, the spotted tentiform leafminer moth is a damaging insect of apple and pear. The synonym is Lithocolletis blancardella and other common name of this insect is Blotch miner. The major sex pheromone component of Phyllonorycter blancardella (F.) (Lepidoptera: Gracillariidae), from Ontario, Canada was identified as (E)-10-dodecen-1-yl acetate (E10-12:Ac) using chemical analysis and field trapping experiments [1]. The minor components (E)-10-dodecen-1-ol (E10-12:OH) (4.6%), dodecan-1-ol (12:OH) (2.3%), and Z-(10)-dodecen-1-yl acetate (Z10-12:Ac) 1.6% were also identified [1]. The species is commonly distributed also in Poland, Romania, Hungary, Bulgaria, Russia, France, England and Wales, Scotland, Ireland and other parts of Europe. The leaf miner’s impact on production and quality of fruit depends on the time of infestation, apple variety, tree vigor, number of mines, and additional stresses such as water stress or damage by other pests [1-3]. The tests made for monitoring and control of Phyllonorycter blancardella on apple in Romania, since 1987, with standard adhesive traps containing atrac-twice the BLANC specific synthetic pheromone baits synthesized in our laboratory were successfully used to monitor adult flight for correct timing of applications of insecticide [4]. Because only a severe infestation with Phyllonorycter blancardella is dangerous on orchards, a preventive ecological monitoring with pheromonal synthetic traps is very important.

Experimental part

Electron impact (70 eV) mass spectra were obtained on Hewlett-Packard MD 5072 GC-MSimstrument. GC analyses were performed on a Hewlett-Packard HP 5890 gas chromatograph. A HP-5MS capillary column (30 m x 0.25 mm x 0.33 μm) and helium gas were used for separations. 1H-NMR (300 MHz) and 13C-NMR (75 MHz) spectra were recorded at room temperature in CDCl3 on Bruker 300 MHz spectrometer, using the solvent line as reference. Thin layer chromatography (TLC) was conducted on silica gel 60 F254 TLC plates purchased from Merck. Chemicals were purchased from Aldrich, Merck or Acros and were used without further purification. All crude products were purification by column chromatography on silica gel (Merck). All chemical reactions took place in argon stream.

9-Bromononan-1-ol (3)

To a solution of 1,9-nonadiol 2 (6.2 g, 38.7 mmol) in benzene (300 cm3), hydrobromic acid (48%: 7.8 cm3, 69 mmol) was added and the mixture was stirred for 40 h under reflux, the mixture was decanted and the residue was again heated to reflux for three times with 150 cm3 fresh benzene and decanted. This organic mixture was poured into water and extracted for three times with 150 cm3 n-hexan. The extracts was washed successively with water, saturated aq. NaHCO3, and brine, dried (MgSO4 anh.) and concentrated under reduced pressure. The residue was chromatographed over silica gel (n-Hexan:EtO1=1:1) to give the bromo alcohol 3 as colorless oil 7.6 g, 89% yield. Mass spectrum (EI, 70 eV), m/z (I rel, %): 223 (M+, 0), 176, 178(2.4), 162, 164(6.8), 148, 150(12.25), 135, 137(20.5), 123(<1), 107, 109(3.9), 97(32.8), 83(29.4), 69(61.3), 55(100), 43(25.5), 41(91.6), 29(30.4), H-NMR spectrum (300 MHz, CDCl3, δ ppm, J/Hz): 1,29-1,31 (m, 10H, 5 -CH2-), 1.59-1,61 (m, 2H, -C(CH3)2), 1.84-1.88 (m, 2H, -CH2O), 2.0 (s, 1H, -OH); 3.4 (t, 2H, CH2-Br, J = 6.8Hz); 3.64 (t, 2H, J=6.7 Hz, -CH2Br). 3.35 (t, 2H, J=6.7 Hz, -CH2Br). 3.78 (t, 1H, J=6.3 Hz, -CHBr) 3.35 (t, 2H, J=6.7 Hz, -CH2-Br). 2.25 (s, 3H, -CH3).

1-Bromo-9-(tert-butoxy)nonanone (4)

A mixture of 9-bromononanol 3 (5g, 22.4 mmol), 66 cm3 methyl tert-butyl ether (MTBE) and 1 cm3 H2SO4 conc. was refluxed for 16 h when was added another 1 cm3 of H2SO4 and was refluxed another 12 h. The reaction mixture was diluted with diethyl ether and washed successively with water, saturated aq. NaHCO3, and brine, dried over MgSO4 anh. and concentrated under reduced pressure. The residue was purified over silica gel (n-Hexan:EtO=1:1=10:1) to give 4.52g protected compound 4 with 73% yield. Mass spectrum (EI, 70 eV), m/z (I rel, %): 279 (M+, 0), 263, 265(8.3), 223, 205, 202, 167(<1), 149(1), 135(1), 123(1), 107, 109(1), 83(8.8), 59(100), 41(41.6), 29(15.7). H-NMR spectrum (300 MHz, CDCl3, δ ppm, J/Hz): 1.19 (s, 9H, -CH3), 1.24-1,26 (m, 10H, -CH2-), 1.43-1.46 (m, 2H, CH2O), 1.76-178 (m, 2H, CH2CH2Br). 2.37 (t, 2H, J=6.3 Hz, -CH2Br), 3.35 (t, 2H, J=6.7 Hz, -CH2O). 6.5 Hz, -CH2O).

11-Tert-Butoxyundec-1-yne (5)

To a stirred and cooled (0-5°C) suspension of lithium acetylide-ethylenediamine complex (2.95g, 32 mmol) in anhydrous dimethyl sulfoxide (DMSO) (25 cm3) was slowly added (15 min.) 1-bromo-9-(tert-butoxynonylanol 4 (4.5g, 16 mmol). The reaction mixture was stirred at room temperature for 6 h, and then it was poured in ice water and extracted with n-hexane (3X100 cm3). The combined n-hexane extracts were washed with water, aq. dill. HCl and brine and dried over MgSO4 anh. Solvent was evaporated and the oily residue was purified over silica gel
Butoxydodec-2-ene (70 eV), m/z (Irel, %): 240 (M+, <1); 225 (5.2); 183, 184 (1%); oily residue was purified over silica gel. The reaction mixture was heated to max 30°C and stirred for 2h when all methyl iodide was consumed and then was diluted with n-hexane, poured in water and extracted with n-hexane (3X100 cm³). The organic extracts was washed with water, aq. HCl dil. solution and CH₃CN (43 cm³) was heating at 70°C for 15 h after cooling the reaction mixture was diluted with diethyl ether 100 cm³ and poured in water. The aqueous layer was extracted with another 2X100 cm³ ether and the organic extracts was washed successively with water, NaHCO₃ saturated solution and brine, and dried over MgSO₄ anh. The residue was purified by silica gel (n-Hexane: Acetone=5:1) to give 650 mg 10-dodecenyl acetate (first way) with 92% yield (>90% purity). Mass spectrum (EI, 70 eV), m/z (Irel, %): 226 (M+, 0), 183(<1), 168(1.5), 166(11.7), 151(<1), 137(3.43), 124(6.4), 109(17.7), 110(11.7), 96(26.5), 82(56), 68(75.5), 55(80.4), 43(100), 29(20.6). h-NMR spectrum (300 MHz, CDCl₃, δ, ppm, J/Hz): 1.28 (m, 10H, CH₂), 1.51-1.65 (m, 4H, CH₂), 1.77 (m, 3H, CH₃), 1.97 (m, 2H, CH₂-CH=), 2.05 (s, 3H, CH₃CO), 4.05 (t, 2H, J=6.8 Hz, CH₂O).

10-Dodeceny-1-ol (8)

A solution formed by tert-butyl ether 6 (1g, 4.3 mmol), NaOH (0.645g, 4.3 mmol), CeCl₃•7H₂O (1.6 g, 4.3 mmol) and CH₃CN (43 cm³) was heating at 70°C for 15 h after cooling the reaction mixture was diluted with diethyl ether 100 cm³ and poured in water. The aqueous layer was extracted with another 2X100 cm³ ether and the organic extracts was washed successively with water, NaOH 20%, water and brine, dried over MgSO₄ anh. and concentrated. The residue was purified by silica gel (n-Hexane: Acetone=5:1) to give 650 mg 10-dodeceny-1-ol (8) with 83% yield. Mass spectrum (EI, 70 eV), m/z (Irel, %): 182 (M+, 0), 135(7.8); 121(8.8); 111(2.9); 100, 107, 109(13.7); 95(52.9); 91(12.7); 79(60.7); 67(100); 55(66.7); 41(90.2), 31(62.7).

(E)-10-Dodecen-1-ol (1')

A solution of 8 (650 mg, 3.57 mmol) in dry diglyme [bis-(2-methoxyethyl) ether] (2 cm³) was added to a stirred suspension of LiAlH₄ (1.29 g, 34 mmol) and LiI (g, 8.4 mmol) (E)-12-tert-Butoxydodec-2-yne (7.43 g, 29 mmol) in dry diglyme (20 cm³) under argon atmosphere was added compound 1 (2 g, 8.4 mmol) in dry diglyme (20 cm³) under argon at room temperature. The mixture was heated at 160-170°C for 24 h while being stirred. After cooling, the suspension was treated with 10 cm³ of aq. HCl dil. solution 10% to decompose the excess of the hydride under argon and diluted with ether. The aqueous layer was extracted with another 2X75 cm³ ether and the organic extracts was washed successively with water, NaHCO₃ saturated solution and brine, and dried over MgSO₄ anh. Solvent was evaporated, the residue was purified over silica gel (n-Hexane:Acetone=5:1) to give 525 mg (E)-10-dodecen-1-ol (1') with 80% yield (90% purity). Mass spectrum (EI, 70 eV), m/z (Irel, %): 184 (M+, 0), 166(2.9), 138(2.9), 123(4.4), 109(9.3), 95(24.5), 82(42.1), 67(50.5), 55(100), 41(77.4), 31(40.2), 29(31.4). h-NMR spectrum (300 MHz, CDCl₃, δ, ppm, J/Hz): 0.75 (t, 3H, CH₃), 1.2-1.9 (m, 8H, CH₂, C=O), 2.07 (m, 1H, OH), 3.5 (s, 2H, CH₂OH), 5.45-5.5 (m, 2H, C=O).

(E)-10-Dodeceny acetate (1) (first way)

To a solution of FeCl₃ (148 mg, 0.949 mmol) and Ac₂O (177 mg, 1.74 mmol) in methylene chloride (50 cm³) under argon atmosphere was added compound 7 (380 mg, 1.58 mmol) and refluxed for 15 h. The reaction was quenched by the addition of 10% aqueous sodium hydroxide solution (50 cm³). The organic product was extracted with diethyl ether, washed with brine, dried over MgSO₄ anh. and concentrated. The residue was purified by silica gel column chromatography (n-Hexane:EtOAc=2:1) to give 285 mg (E)-10-dodeceny acetate 1 with 80% yield. Mass spectrum (EI, 70 eV), m/z (Irel, %): 226 (M+, 0), 183(<1), 168(1.5), 166(11.7), 151(<1), 137(3.43), 124(6.4), 109(17.7), 110(11.7), 96(26.5), 82(56), 68(75.5), 55(80.4), 43(100), 29(20.6). h-NMR spectrum (300 MHz, CDCl₃, δ, ppm, J/Hz): 1.28 (m, 10H, CH₂), 1.51-1.65 (m, 4H, CH₂), 1.77 (m, 3H, CH₃), 1.97 (m, 2H, CH₂-CH=), 2.05 (s, 3H, CH₃CO), 4.05 (t, 2H, J=6.8 Hz, CH₂O).

(E)-10-Dodeceny acetate (1) (second way)

A mixture of (E)-10-dodeceny-1-ol (525 mg, 2.85 mmol), acetic anhydride (320mg, 3.1 mmol) and pyridine (245 mg, 3.1 mmol) was heated at 90°C by 2 h. The reaction was quenched by addition of water (10 cm³) followed by addition of ether. The aqueous layer was extracted with another 2X250 cm³ ether and the organic extracts was washed successively with water, solution HCl dil. and brine, dried over MgSO₄ anh.. Solvent was evaporated, purified over silica gel (n-Hex:EtO=10:1) to give 592 mg (E)-10-dodeceny acetate 1 with 92% yield (>90% purity). Mass spectrum (EI, 70 eV), m/z (Irel, %): 226 (M+, 0), 183(<1), 168(1.5), 166(11.7), 151(<1), 137(3.43), 124(6.4), 109(17.7), 110(11.7), 96(26.5), 82(56), 68(75.5), 55(80.4), 43(100), 29(20.6). h-NMR spectrum (300 MHz, CDCl₃, δ, ppm, J/Hz): 1.28 (m, 10H, CH₂), 1.51-1.65 (m, 4H, CH₂), 1.77 (m, 3H, CH₃), 1.97 (m, 2H, CH₂-CH=), 2.05 (s, 3H, CH₃CO), 4.05 (t, 2H, J=6.8 Hz, CH₂O), 5.39-5.43 (m, 2H, CH₂-CH=).
Results and discussions

In the literature are known few synthesis of (E)-10-dodecenyl acetate and the major component of *Phylonorycter blancardella* with good results [5-8], our synthesis is based on original and known organic modern methods [9-13] and thus obtained significant results. We try whit success to obtain stereoselectively low pheromonal compounds (E)-10-dodecenyl acetate (1) and (E)-10-dodecen-1-ol (1') through the key compound 6 synthesized starting from commercially 1,9-nonandiol in a good overall yield. First, 1,9-nonandiol (2) was converted into the corresponding bromohydrin 3 with 89% yield. The hydroxyl group was then protected with MTBE (Methyl tert-butyl ether) in the presence of H2SO4 conc. obtained protected compound 4 with 73% yield. This was coupled with lithium acetylacetonate in diglyme [13] at 160°C obtained (E)-10-Dodecen-1-ol (1') with a phenomol component of many species of insect as *Phylonorycter blancardella* from Lepidoptera species. Acletylation of (E)-10-Dodecen-1-ol (1') with acetic anhydride in the presence of pyridine gives (E)-10-dodecenyl (1) acetate in 89% overall yield from starting material (1,9-nonandiol) (scheme 2).

These two methods of synthesis are easily reproducible and follow with very good yields.

Conclusions

Our synthesis of (E)-10-dodecenyl acetate and the corresponding alcohol (E)-10-dodecen-1-ol is a very simple and facile stereoselective synthesis.

We managed to reduce alkenes with a hydroxyl group protected directly to trans olefin without requiring their deprotection, which is an original method of trans reduction.

References