

A New Synthesis of the Sex Pheromone of the Indian Meal Moth *Plodia interpunctella* Hb. (Lepidoptera, Pyralidae)

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Abstract: New synthesis of (9Z,12E)-9,12-tetradecadien-1-yl acetate, the sex pheromone of the indian meal moth *Plodia interpunctella* (Lepidoptera, Pyralidae), were developed. The synthesis was based on a $C_8+C_2=C_{10}$ and $C_{10}+C_4=C_{12}$ coupling scheme. 1,8-Octanediol is the starting material used in the synthesis. The route involves, as the key step, the use of the mercury derivative of the terminal alkyne ω -functionalised as intermediate. The first coupling reaction took place between 1-tert-butoxy-8-bromo-octane and lithium acetylide-ethylendiamine complex obtaining 1-tert-butoxy-dec-9-yne, which is transformed in di[tert-butoxy-dec-9-yne]mercury. In the second coupling reaction, the mercury derivative was directly lithiated and then alkylated with (E)-1-bromo-2-butene obtaining 1-tert-butoxy-(9-yne,12E)-9,12-tetradecaenyne. After stereoselective reduction in the presence of Ni-P₂ catalyst and acetylation gave (9Z,12E)-9,12-tetradecadien-1-yl acetate with 82% isomeric purity.

Keywords: (9Z,12E)-9,12-tetradecadien-1-yl acetate, Lepidoptera, sex pheromone, *Plodia interpunctella*

Plodia interpunctella Hb. (Lepidoptera, Pyralidae) is a cosmopolitan pest, spread in Mediterranean and temperate climates, has spread a lot in the warehouses in the country, where it attacks wheat, corn, sorghum, millet, rice, soybean, sunflower germ, largely affecting germination faculty. Also, it attacks flours, dried fruits and vegetables, herbs, pastries and more. In our country, adults can be seen consistently from late May until early October. They are active at twilight and remain in the vicinity of products, even in warehouses.

The synthesis of (9Z,12E)-9,12-tetradecadiene-1-yl acetate is well known in the literature [2-10]. The pheromone has been prepared by the Wittig reaction [11], Grignard reagent reaction with allyl bromide in the presence of copper (I) salts [12], Wittig condensation between triphenyl-phosphonium (E)-3-pentenylide and 9-acetoxy-1-nonanal using either potassium in HMPT [13], cross-coupling reaction [14], coupling 2-(8-chloro-1-octyloxy)tetrahydropyran with lithium acetylide followed by reaction of lithium salt with (E)-1-bromo-2-butene [15]. A similar route was used by Su et al., beginning with 1,9-decadiyne and crotyl alcohol [16].

The aim of our work was to investigate a new synthesis of (9Z,12E)-9,12-tetradecadien-1-yl acetate, using the mercury derivative of the terminal alkyne ω -functionalized as intermediate, because *Plodia interpunctella* is a world-wide economically important pest of stored products and processed food.

Experimental part

Materials and characterization methods

All the materials used were of reagent grade and were purchased from Sigma-Aldrich and Merck.

GC-MS analysis were performed on a GC-MS spectrometer Agilent 7890A GC&5975 GC/MS Serie MSD.

¹H-NMR (300 MHz) and ¹³C-NMR (75 MHz) spectra were recorded at rt in CDCl₃ on a Brüker 300 MHz spectrometer, using TMS line as reference.

A Perkin Elmer Spectrometer Model 700 was used for IR spectra.

8-Bromo-1-octanol (3)

To a solution 73 g (0.500 moles) of 1,8-octanediol (2) solved in 300 mL benzene was added 86.17 mL hydrobromic acid 47%. The reaction mixture was refluxed for 2.5 h. The organic layer was separated and washed with brine, saturated NaHCO₃ solution and dried over anhydrous MgSO₄. After removal of the solvent the product was purified by liquid-liquid distribution (petroleum ether:aqueous methanol), 62.7 g of 8-bromo-1-octanol (3) was obtained. $n_D^{18} = 1.478$, Yield = 60%, GC purity: 97%.

Mass spectrum (m/z, %): 190(<1), 178(<1), 164(<1), 151(<1), 111(<1), 109(<1), 148(34.80), 97(26.47), 83(43.13), 69(87.25), 55(100), 41(74.01), 31(29.41).

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1-tert-Butoxy-8-bromo-octan (4)

To a solution 65 g (311 mmoles) of 8-bromo-1-octanol (3) and 344.5 mL *tert*-butyl-methyl-ether was added dropwise 20.5 mL concentrated sulfuric acid under cooling. The reaction mixture was maintained at 40°C. The reaction was checked by TLC on silica gel G (benzene : ether = 2 : 1, detection with H₂SO₄ d=1.25). The reaction mixture was diluted with water. After removal of the *tert*-butyl-methyl-ether under reduced pressure, the mixture was extracted with ethyl ether (3x50 mL). The combined ethereal extracts were washed with saturated NaHCO₃ solution up to basic and dried over anhydrous Na₂SO₄. After the removal of the solvent, 53.56 g of *1-tert*-butoxy-8-bromo-octan (4) were obtained. b.p. = 102⁰-104⁰C/3 mmHg, n_D¹⁸ = 1.456, Yield = 90%, GC purity: 97%.

Mass spectrum (m/z, %): 277(<1), 236(<1), 219(<1), 177(<1), 163(<1), 137(<1), 121(<1), 97(<1), 83.29(<1), 59(100), 41(21.56).

1-tert-Butoxy-dec-9-yne (6)

All operations were performed in an inert gas atmosphere and under stirring.

To a stirred and cooled (0°C) suspension of 3.8 g (41.30 mmoles) lithium acetylide-ethylendiamine complex (5) in 20.65 mL anhydrous dimethyl sulfoxide was added 5.47 g (20.64 mmoles) of *1-tert*-butoxy-8-bromo-octan (4). The reaction mixture was stirred at room temperature for 6h. It was poured into ice water and extracted with hexane. The combined hexane extracts were washed with water, brine and dried over anhydrous MgSO₄. After removal of the solvent, 4.04 g of *1-tert*-butoxy-dec-9-yne (6) were obtained. b.p. = 94⁰-100⁰C/4mmHg, n_D¹⁸ = 1.441, Yield = 84.52%, GC purity: 90.62%.

Mass spectrum (m/z, %): 195(24.50), 177(<1), 154(<1), 153(<1), 135(<1), 121(<1), 107(<1), 95(28.43), 81(35.78), 67(6.37), 59(100), 57(89.21), 55(26.96), 41(46.07), 29(17.64).

Di[1-tert-butoxy-dec-9-yne]mercury (7)

To 6.53 g of potassium iodide dissolved in 6.53 mL water was added 2.64 g mercury (II) chloride and the mixture was stirred till the mercury salt was dissolved. To the mixture were added 5 mL of 10% sodium hydroxide solution. After external cooling of reaction mixture with ice, were added dropwise 1.89 g (9 mmoles) of *1-tert*-butoxy-dec-9-yne (6) dissolved in 28 mL cooling ethyl alcohol. The reaction mixture was perfected 1 hour under stirring. The obtained precipitate was filtrated and washed on the filter with cooling aqueous ethylic alcohol 50%. After drying were obtained 3.15 g of di(*1-tert*-butoxy-dec-9-yne) mercury (7). Yield: 57%, m.p. = 102⁰C.

1-tert-Butoxy-(9-yne,12E)-9,12-tetradecaenyne (9)

All operations were performed in an inert gas atmosphere and under stirring.

7 g (11.3 mmoles) of di[*1-tert*-butoxy-dec-9-yne]mercury (7) in 29 mL diglyme was treated with 0.15 g lithium (25.42 mmoles) at 100⁰-115⁰C for 1 hour. 3.5 g (25.92 mmoles) of (E)-1-bromo-2-butene (8) dissolved in 7 mL diglyme was added dropwise at 78⁰-80⁰C then the temperature was raised to 85⁰-86⁰C under stirring for 5 hours. The mixture was poured out over 100 g of break ice. The reaction mixture was extracted with petroleum ether. The ethereal solution was washed successively with 10% HCl, water and brine till neutral pH of the washings. After drying over anhydrous MgSO₄, the solvent was removed and 4 g of *1-tert*-butoxy-(9-yne,12E)-9,12-tetradecaenyne (9) was obtained. Yield: 71%, GC purity: 80%.

Mass spectrum (m/z, %): 249(<1), 235(<1), 208(<1), 207(<1), 179(<1), 161(<1), 150(8.74), 135(13.59), 121(9.7), 107(15.53), 94(42.72), 79(45.63), 57(100), 41(47.57), 29(19.42).

1-tert-Butoxy-(9Z,12E)-9,12-tetradecadiene (10)

1-tert-Butoxy-(9-yne,12E)-9,12-tetradecaenyne (9) was hydrogenated at *1-tert*-butoxy-(9Z,12E)-9,12-tetradecadiene (10) in the presence of the Ni-P₂/EDA catalyst, prepared in situ according to the standard procedure [20]. *1-tert*-Butoxy-(9Z,12E)-9,12-tetradecadiene (10) was obtained in yield of 78%, GC purity: 82%.

Mass spectrum (m/z, %): 266(<1), 251(<1), 210(<1), 192(<1), 166(<1), 149(<1), 135(<1), 121(<1), 109(13.72), 95(33.3), 81(42.16), 67(40.2), 57(100), 41(51.96), 29(19.61).

¹H-RMN (CDCl₃, 300 MHz): 1.13 (9H, s, 3CH₃), 1.23 (10H, s, 5CH₂), 1.43-1.50 (2H, m, CH₂), 1.58-1.60 (3H, m, CH₃), 1.93-2.00 (2H, m, CH₂), 2.64-2.68 (2H, m, CH₂), 3.27 (2H, t, J = 6 Hz, OCH₂), 5.29-5.40 (4H, m, 2HC=CH).

¹³C-RMN (CDCl₃, 75 Hz): 18.0 (CH₃), 26.3 (CH₂), 27.1 (CH₂), 27.6 (CH₂), 29.3 (CH₂), 29.5 (CH₂), 29.6 (CH₂), 29.7 (CH₂), 30.5 (CH₂), 30.7 (CH₂), 61.7 (OCH₂), 72.5 (tertiary carbon), 125.1 (CH=), 127.6 (CH=), 129.7 (CH=), 130.5 (CH=).

(9Z,12E)-9,12-tetradecadien-1-yl acetate (1)

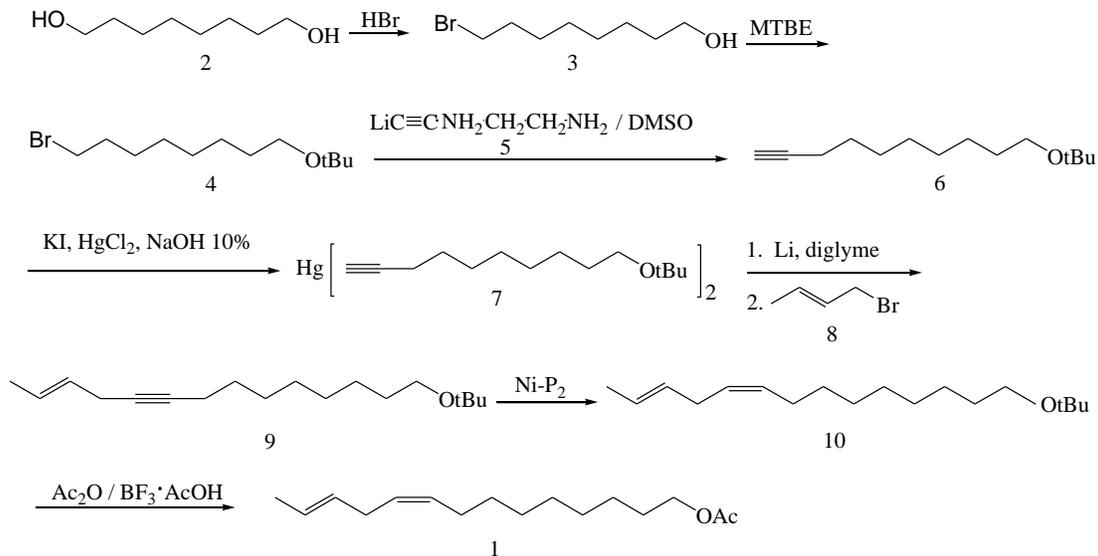
All operations were performed in an inert gas atmosphere and under stirring.

At 2.5 g (9.3 mmoles) of *1-tert*-butoxy-(9Z,12E)-9,12-tetradecadiene (10) was added 3 mL of acetic anhydride and 1 mL BF₃/AcOH complex. The reaction mixture was kept at room temperature. The reaction development was checked up by TLC on silica gel G (benzene : ether = 10 : 2, detection with H₂SO₄ d=1.25). The solution was poured on crushed ice, extracted with petroleum ether, washed with aqueous NaHCO₃ and brine. After drying over anhydrous MgSO₄ and removal of the solvent was obtained 1.6 g of (9Z,12E)-9,12-tetradecadien-1-yl acetate (1). Yield: 70%, GC purity: 82%.

Mass spectrum (m/z, %): 252(<1), 209(<1), 192(9.46), 177(<1), 163(<1), 149(6.76), 135(10.81), 121(18.92), 110(13.51), 95(41.89), 79(70.27), 67(81.08), 55(52.7), 43(100), 29(13.51).

Results and discussions

For the synthesis of (9Z,12E)-9,12-tetradecadiene-1-yl acetate (1) we explored the pathway outlined in scheme 1. The synthesis were based on $C_8+C_2=C_{10}$ and $C_{10}+C_4=C_{14}$ coupling schemes, starting from 1,8-octane-diol, the route involving the use of the mercury derivative of the terminal alkyne ω -functionalised as intermediate.



Scheme 1

Use has been made of methyl-*t*-butyl-ether [17] in acid catalysis in order to protect the -OH function of the 8-bromo-1-octanol (3). The first coupling reaction [18] was performed by adding 1-*tert*-butoxy-8-bromo-octan (4) to lithium acetylide-ethylenediamine complex in dimethyl sulfoxide. 1-*tert*-Butoxy-dec-9-yne (6) was checked by means of IR spectrum (film, cm^{-1} : 895 m, 1110 vs, 1220 vs, 2160 w $\text{-C}\equiv\text{C-}$, 3280 s $\equiv\text{CH}$), which presents the vibration of terminal triple bond.

1-*tert*-Butoxy-dec-9-yne (6) with mercuric chloride in an aqueous solution containing potassium iodide and sodium hydroxide (Nessler's reagent) [19] was precipitated as di[1-*tert*-butoxy-dec-9-yne]mercury (7).

The key step in our acetylenic route consisted in transmetalation of compound 7, which was directly lithiated by treating with metal lithium in diglyme and then alkylated with (E)-1-bromo-2-butene (8), obtaining 1-*tert*-butoxy-(9-yne,12E)-9,12-tetradecaenyne (9).

The molecular peak of 1-*tert*-butoxy-(9-yne,12E)-9,12-tetradecaenyne (9) was not identified, the mass spectrum presenting only characteristic fragmentations shown in figure 1: the base peak in the spectrum ($m/z = 59$), the peak $m/z = 57$ generated by the very stable carbocation $+\text{C}(\text{CH}_3)_3$, the peaks of medium intensity at $m/z = 79$ and $m/z = 55$ corresponds to vinylic cleavages, the peaks of medium intensity at $m/z = 94$ and $m/z = 41$ corresponds to propargylic cleavages.

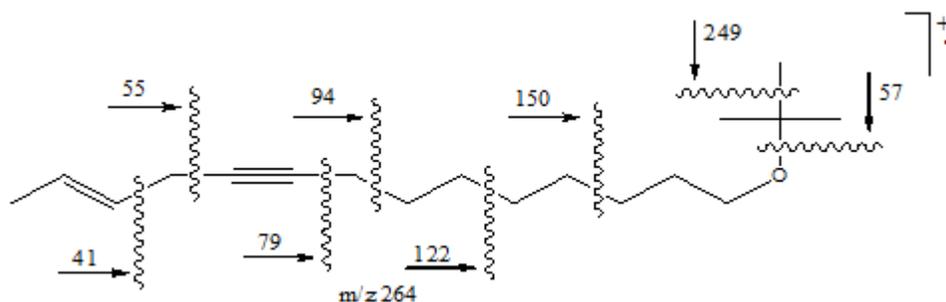


Figure 1

Compound 9 was hydrogenated using Ni-P₂/EDA catalyst [20], obtaining 1-*tert*-butoxy-(9Z,12E)-9,12-tetradecadiene (10). Mass spectrum and ¹³C-NMR spectrum of compound 10 are shown in figure 2 and figure 3.

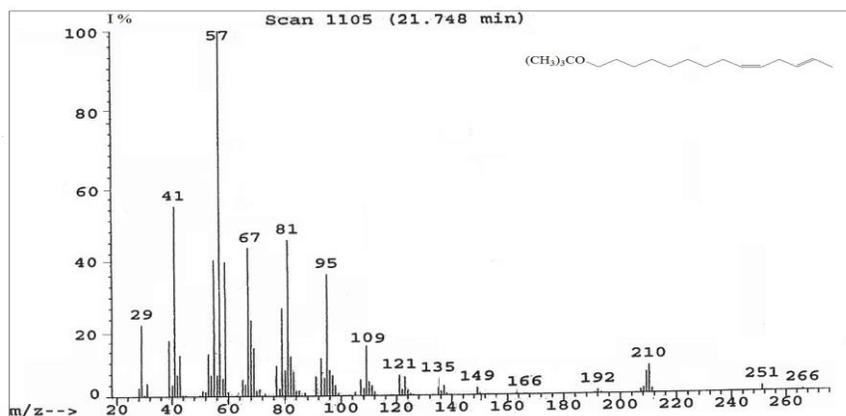


Figure 2. Mass spectrum of 1-*tert*-butoxy-(9*Z*,12*E*)-9,12-tetradecadiene

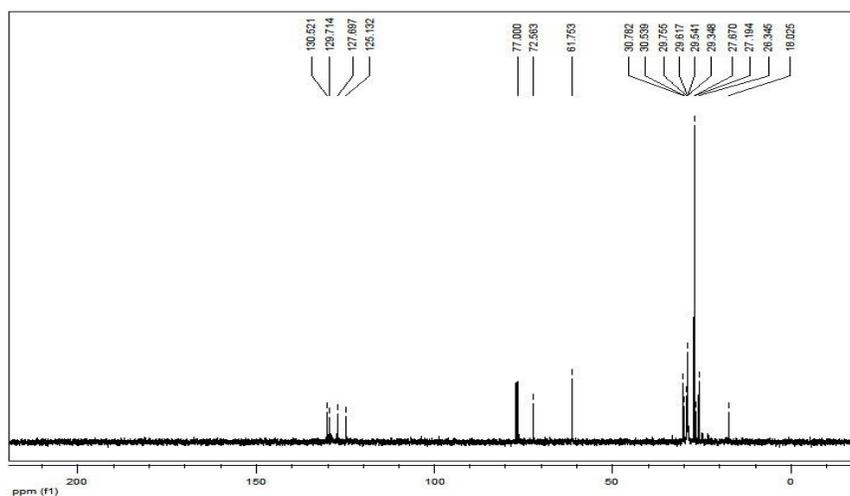


Figure 3. Spectrum ^{13}C -RMN of 1-*tert*-butoxy-(9*Z*,12*E*)-9,12-tetradecadiene

The conversion of the *tert*-butyl ether 10 into acetate 1 was performed with acetic anhydride and boron trifluoride acetic acid complex, obtaining (9*Z*,12*E*)-9,12-tetradecadien-1-yl acetate (1) with 82% isomeric purity.

The mass spectrum of (9*Z*,12*E*)-9,12-tetradecadien-1-yl acetate (1) is shown in figure 4 and are characteristic to acetates: $m/z = 43$ (CH_3CO^+) the base peak, $m/z = 192$ resulted from the cleavage of acetic acid from molecular ion, $m/z = 61$ ion of double transposition ($\text{CH}_3\text{COOH}_2^+$).

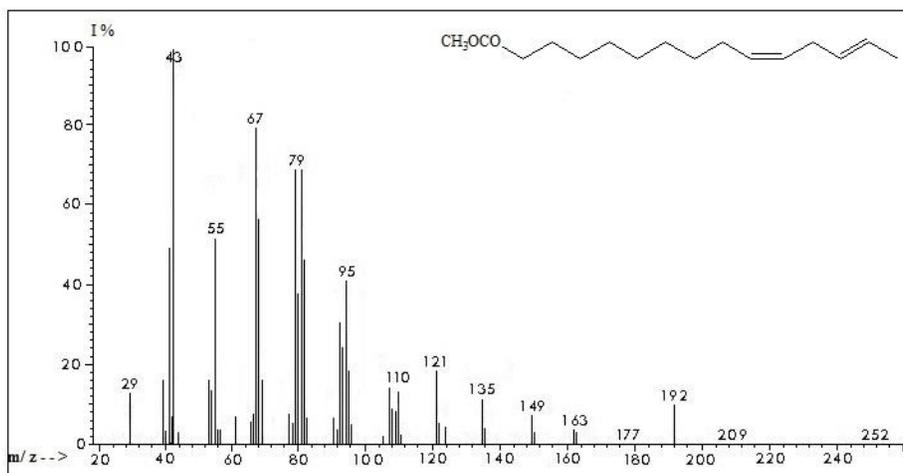


Figure 4. Mass spectrum of (9*Z*,12*E*)-9,12-tetradecadien-1-yl acetate

Conclusions

It was presented new synthesis of (9Z,12E)-9,12-tetradecadien-1-yl acetate with 82% isomeric purity. The key step is the transmetallation of the mercury derivative with metal lithium and then alkylated with (E)-1-bromo-2-butene, followed by stereoselective hydrogenation in the presence of Ni-P₂ and acetylation.

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