

Synthesis of the Monounsaturated Sex Pheromones of Some Lepidoptera Involving Mercury Derivatives

IRINA CIOTLAUS*, LUCIA GANSCA, ADRIANA ANDREICA, SANDA MAXIM, IOAN OPREAN

Babe^o-Bolyai University, Raluca Ripan Institute for Research in Chemistry, Natural Products Laboratory, 30 Fantanele Str., 400294, Cluj-Napoca, Romania

New and practical synthesis of (E)-5-decen-1-yl acetate and (Z)-5-tetradecen-1-yl acetate were developed. The synthesis were based on a $C_6 + C_4 = C_{10}$, and $C_6 + C_8 = C_{14}$ coupling scheme. The routes involve, as the key step, the use of the same mercury derivative of the terminal-alkyne w-functionalised as intermediate. The first coupling reaction took place between 1-tert-butoxy-4-bromo-butan and lithium acetylide-ethylendiamine complex obtaining 1-tert-butoxy-hex-5-yne, which is transformed in di[tert-butoxy-hex-5-yne]mercury, the common intermediate in the synthesis of the two pheromones. In order to obtain (E)-5-decen-1-yl acetate, the mercury derivative was directly lithiated and then alkylated with 1-bromo-butan obtaining 1-tert-butoxy-dec-5-yne. After reduction with lithium aluminium hydride of 1-tert-butoxy-dec-5-yne and acetylation gave (E)-5-decen-1-yl acetate with 85 % isomeric purity. In order to obtain (Z)-5-tetradecen-1-yl acetate, the mercury derivative was directly lithiated and then alkylated with 1-bromo-octan obtaining 1-tert-butoxy-tetradec-5-yne. After acetylation of 1-tert-butoxy-tetradec-5-yne and stereoselective reduction in the presence of NiP-2 catalyst gave (Z)-5-tetradecen-1-yl acetate with 96 % isomeric purity.

Keywords: (E)-5-decen-1-yl acetate, (Z)-5-tetradecen-1-yl acetate, Lepidoptera, sex pheromone

(E)-5-decen-1-yl acetate and (Z)-5-tetradecen-1-yl acetate are components for a lot of *Lepidoptera* insect sex pheromones [1]. Some important economic pest insects are: *Anarsia lineatella* (peach twig borer), *Cossus cossus* (goat moth), *Agrotis exclamationis* (heart and dart moth) and *Amathes c-nigrum* (spotted cutworm).

The synthesis of (E)-5-decen-1-yl acetate and (Z)-5-tetradecen-1-yl acetate are well known in the literature [2-7].

The paper describes new and practical synthesis of (E)-5-decen-1-yl acetate and (Z)-5-tetradecen-1-yl acetate based on the C-alkylation reaction, using the same mercury derivative of the terminal alkyne w-functionalized.

Experimental part

GS-MS analysis were performed on a GS-MS spectrometer Agilent 7890A GC& 5975 GS/MS Serie MSD. ¹H-NMR (300 MHz) and ¹³C-NMR (75 MHz) spectra were recorded at *rt* in CDCl₃ on a Bruker 300 MHz spectrometer, using TMS line as reference. A Perkin Elmer Spectrometer Model 700 was used for IR spectra.

4-Bromo-butan-1-yl acetate (3)

To a mixture of 72g (1000 mmoles) THF and 0.5g (400 mmoles) ZnCl₂ anhydrous was added in dropwise 123 g (1000 mmoles) CH₃COBr in about 1.5-2 h. The reaction mixture was perfected at reflux 1h. The compounds **3** was distilled from the reaction mixture at 85-86°C / 8 mm Hg. After distillation was obtained 166 g (846 mmoli) 4-bromo-butane -10-yl acetate (**3**). Yield: 85%, GC purity: 99%. Mass spectrum (m/z, %): 281(<1), 207 (<1), 193(<1), 176(<1), 164(<1), 151(<1), 134(22.92), 115(4.39), 101(<1), 87(3.41), 73(8.78), 55(57.56), 43(100).

4-bromo-butan-1-ol (4)

A homogeneous mixture consisting of 140g (714.14 mmoles) 4-bromo-butane -1-yl acetate (**3**), 1953 mL

methanole and 6.4 mL HCl conc. was allowed overnight at room temperature. The reaction was checked by TLC on silica gel G (benzene: ether 9:1, developed with methyl red). At the end of reaction the methanol is concentrated by rotavapory and the residue was diluted with double amount of water. The organic phase was extracted with diethyl ether, washed with brine and with aqueous NaHCO₃ till neutral pH of the washings. The organic layer was drying over MgSO₄. After the removal of the solvent, 80.6 g (526 mmoli) 4-bromo-butan-1-ol (**4**) were obtained. Yield: 73%, GC purity: 97%. Mass spectrum (m/z, %): 281(<1), 207(<1), 150(<1), 134(35.12), 121(<1), 106(10.73), 93(2.92), 71(12.19), 55(100), 42(43.9), 31(37.07).

1-tert-Butoxy-4-bromo-butan (5)

To a solution 80.6 g (520 mmoles) of 4-bromo-butan-1-ol (**4**) and 574.16 mL *tert*-butyl-methyl-ether was added dropwise 34.66 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 Na₂SO₄. After the removal of the solvent, 66 g of 1-*tert*-Butoxy-4-bromo-butan (**5**) were obtained. Yield: 60%, GC purity: 95%. Mass spectrum (m/z, %): 281(<1), 207 (<1), 193(13.1), 177(<1), 165(<1), 153(<1), 135(100), 120(<1), 107(2.42), 57(81.55), 41(26.1).

1-tert-Butoxy-hex-5-yne (6)

To a stirred and cooled (0°) suspension of 20 g (200 mmoles) lithium acetylide-ethylendiamine complex in 100 mL anhydrous dimethyl sulfoxide was slowly added (60 min) 20.9 g (100 mmoles) compound **5**. The reaction

* email: irina_ciotlaus@yahoo.com; Tel: 0744831620

mixture was stirred at room temperature for 6h, then it was poured into ice water and extracted with hexane. The combined hexane extracts were washed with water, brine and dried over Na_2SO_4 . After removal of the solvent, 13.86 g (90 mmoles) of 1-*tert*-Butoxy-hex-5-yne (**6**) were obtained. Yield: 90 %, GC purity: 92 %. Mass spectrum (m/z, %): 139(13.59), 126 (<1), 121(<1), 110(<1), 98(10.3), 93(<1), 81(95.14), 70(11.65), 57(100), 53(33), 41(72.81), 29 (24.27).

Di[1-tert-Butoxy-hex-5-yne]mercury (7)

To 61.12 g of potassium iodide dissolved in 61.12 mL water were added 24.75 g mercury (II) chloride and the mixture was stirred till the mercury salt was dissolved. To the mixture were added 33.12 mL of 10% sodium hydroxide solution. After external cooling of reaction mixture with ice, were added dropwise 9.42 g (61 mmoles) of 1-*tert*-butoxy-hex-5-yne (**5**) dissolved in 262 mL cooling ethyl alcohol. The obtained precipitate was filtrated and washed on the filter with cooling aqueous ethylic alcohol 50%. After drying were obtained, 21.7 g (42.8 mmoles) of di(*tert*-Butoxy-hex-5-yne) mercury (**7**). Yield: 70%, m.p.=105° C.

1-tert-Butoxy-dec-5-yne (8)

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

7 g (12 mmoles) of compound **7** in 33 mL diglyme was treated with 0.19 g lithium (27.14 mmoles) at 110° C for 3 hours. 4.72 g (34 mmoles) of butyl bromide dissolved in 10 mL diglyme was added dropwise at 90° C then the temperature was raised to 120-125° C under stirring for 4.5 h. The mixture was poured out over the 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 MgSO_4 , the solvent was removed and 1.73 g (8.2 mmoles) of 1-*tert*-Butoxy-dec-5-yne (**8**) was obtained. Yield: 60%, GC purity: 78%. Mass spectrum (m/z, %): 251(23.90), 237(≤ 1), 211(≤ 1), 210(≤ 1), 181(≤ 1), 163(≤ 1), 151(≤ 1); 123(13.65); 109(41.95); 95(40.97); 81(47.80); 57(100); 41(80); 29(21.95).

1-tert-Butoxy-E-5-decen (9)

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

1.4 g (37 mmoles) of LiAlH_4 was placed in a solution of 2 mL of anhydrous THF and 40 mL of diglyme. The mixture was heated at 140° C. The solvent was partially removed. After cooling at 0° C, the suspension was treated with 1.73g (8.23 mmoles) of compounds **8** in 6 mL diglyme maintaing the temperature below 10° C. The mixture was heated at 145-150° C which was maintained for 20 h. The reaction was checked by TLC on silicagel G (benzene ether 5:1, detection with H_2SO_4 d=1.28). After cooling, the solution was treated with 15 mL of H_2SO_4 dil. (d=1.28). The reaction mixture was extracted with diethyl ether, washed with brine and dried over MgSO_4 . After removal of the solvent and distillation (79-80° C/1mmHg) to give 1.39 g (6.5 mmol), 1-*tert*-butoxy-E-5-decen (**9**). GC purity: 98 %. Yield 80%. Mass spectrum (m/z, %): 212(<1), 197(5.2), 155(<1), 139(4.9), 111(10), 97(21.56), 69(29.4), 57(100), 41(73.5), 29 (29.4).

(E)-5-Decen-1-yl acetate (1)

1.39 g (6.5 mmoles) of 1-*tert*-butoxy-dec-5-ene (**9**) was dissolved in 6.5 mL of 1:10 mixture of acetyl chloride: acetic acid and was refluxed for 4-5 h. The reaction

development was checked up by TLC on silica gel G (hexane: ether, 15:1, detection with H_2SO_4 d=1.25). The solution was poured on crushed ice, extracted with petroleum ether, washed with brine and with aqueous NaHCO_3 till neutral pH of the washings. After drying over MgSO_4 and removal of the solvent the product was purified by distillation (79 - 80° C/1mmHg) obtaining 1.03 g (5.2 mmoles) of E-5-decen-1-yl acetate (**1**). Yield: 65%, GC purity: 85%. Mass spectrum (m/z, %): 281(<1), 207(<1), 155(<1), 138(31.55), 123(<1), 110(51.45), 95(63.1), 81(100), 67(81.06), 55(65.04), 43(85.92).

(¹H, NMR, 300Mz, CDCl_3 , δ , ppm): 0.85(H_{10} , t, J=7.5 Hz, - CH_3 , 3H); 1.28-1.30(H_8, H_9 , m, -(CH_2)₂-, 4H), 1.38(H_3 , m, - CH_2 -, 2H), 1.94-1.98 (H_7, H_6 , m, -(CH_2)₂-, 4H), 5.36 (H_5, H_6 , m, J=15.3Hz, - $\text{CH}=\text{CH}$ -, 2H), 1.59(H_2 , m, - CH_2 -, 2H) 4.02(H_1 , t, J=6.6Hz, - CH_2 -O-, 2H), 2.01 (H_1 , s, - OCOCH_3 , 3H)

(¹³C, NMR, 75Mz, CDCl_3 , δ , ppm): 13.8(C_{10}), 22.2 (C_9), 32.2(C_8), 32.1 (C_7), 129.7(C_6 , $\text{CH}=\text{CH}$ -), 131.1(C_5 , - $\text{CH}=\text{CH}$ -), 31.9(C_4), 25.4(C_3), 27.7(C_2), 64.1(C_1 , - CH_2 O-), 171.2(C_2 , - OCOCH_3), 20.9(C_1 , - OCOCH_3)

1-tert-Butoxy-tetradec-5-yne (10)

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

9 g (17.7 mmoles) of compound **7** in 50 mL diglyme was treated with 0.24 g lithium (35.4 mmoles) at 110° C for 3 h. 6.83 g (35.4 mmoles) of octyl bromide dissolved in 15 mL diglyme was added dropwise at 90° then the temperature was raised to 120-125° C under stirring for 4.5 h. The mixture was poured out over the 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 MgSO_4 , the solvent was removed and 2.59 g (9.73 mmoles) of 1-*tert*-Butoxy-tetradec-5-yne (**10**) was obtained. Yield: 55%, GC purity: 80%. Mass spectrum (m/z, %): 251(≤ 1), 235(≤ 1), 222(≤ 1), 210(1.45), 194(≤ 1), 182(≤ 1), 166(2.42), 154(2.91), 137(2.42), 123(6.31), 111(24.27), 95 (44.66), 79 (25.24), 57 (100), 41(26.21).

5-Tetradecyne-1-yl acetate (11)

2.59 g (9.73 mmoles) of 1-*tert*-Butoxy-tetradec-5-yne (**10**) was dissolved in 9.73 mL of 1:10 mixture of acetyl chloride : acetic acid and was refluxed for 4-5 hours. The reaction development was checked up by TLC on silica gel G (hexane: ether, 15:1, detection with H_2SO_4 d=1.25). The solution was poured on crushed ice, extracted with petroleum ether, washed with brine and with aqueous NaHCO_3 till neutral pH of the washings.

After drying over MgSO_4 and removal of the solvent the product was purified by distillation (80-85° C/1mmHg) obtaining 1.96 g (7.77 mmoles) of 5-tetradecyne-1-yl acetate (**11**). Yield: 80%, GC purity: 85%. Mass spectrum (m/z, %): 252(<1), 237(1.46), 222(≤1), 209 (<1), 193(<1), 181(<1), 166(1.95), 153(3.41), 135(9.75), 121(13.17), 107(15.6), 94(85.8), 79(100), 67(30.24), 55(24.39), 43(61.25).

(Z)-5-Tetradecen-1-yl acetate (2)

5-Tetradecyne-1-yl acetate (**11**) was hydrogenated at (Z)-5-tetradecene-1-yl acetate (**2**) in the presence of the NiP-2/EDA catalyst, prepared in situ according to the standard procedure [12]. (Z)-5-Tetradecene-1-yl acetate (**2**) was obtained in yield of 70%, GC purity: 96%. Mass spectrum (m/z, %): 254(<1), 211(<1), 194(19.04), 179(<1), 166(11.42), 152(1.9), 138(15.23), 124(14.28), 110(19.04), 109(22.85), 96(63.8), 95(64.76), 82(100), 81(70.47), 68(57.14), 67(82.85), 55(42.85), 54(40.95), 43(72.38), 41(36.19), 32(1.9).

(¹H, NMR, 500 Mhz, CDCl₃, δ, ppm): 0.87 (H₁₄, t, J=6 Hz, -CH₃, 3H); 1.26 (H₉, H₁₀, H₁₁, H₁₂, s, -(CH₂)₄-, 8H), 1.37-1.43 (H₃, H₈, H₁₃, m, -(CH₂)₂-, 6H), 1.60-1.66 (H₅, m, -(CH₂)₂-, 2H), 1.98-2.05 (H₇, H₁₀, t, -(CH₂)₂-, 4H), 4.06 (H₁, t, J=6,5 Hz, -CH₂-O-, 2H), 5.33 (H₅, H₆, m, J=10 Hz, -CH=CH-, 2H), 2.05 (H₁, s, -OCOCH₃, 3H)

Results and discussions

For the synthesis of (E)-5-decen-1-yl acetate (**1**) and (Z)-5-tetradecen-1-yl acetate (**2**), we explored the pathway outlined in scheme 1. The synthesis were based on C₆+C₄=C₁₀ and C₆+C₈=C₁₄ coupling schemes, the routes involving the use of the same mercury derivative of the terminal alkyne w-functionalised as intermediate.

4-Bromo-butan-1-yl acetate (**3**), which was prepared by opening the tetrahydrofuran ring with acetyl bromide and zinc chloride [8] was hydrolyzed with acidulated methanol to yield 4-bromo-butan-1-ol (**4**).

Use has been made of methyl-*t*-butyl-ether [9] in acid catalysis in order to protect the -OH function of the 4-bromo-butan-1-ol (**3**). The first coupling reaction [10] was effected by adding 1-*tert*-Butoxy-4-bromo-butan (**5**) to lithium acetylide-ethylendiamine complex in DMSO. 1-*tert*-Butoxy-hex-5-yne (**6**) was checked by means of IR spectrum (film, cm⁻¹: 895 m, 1110 vs, 1220 vs, 2160 w - C≡C-, 3280 s ≡ CH), which presents the vibration of terminal triple bond and the mass spectrum characteristic to a *tert*-butyl ether, (fig. 1).

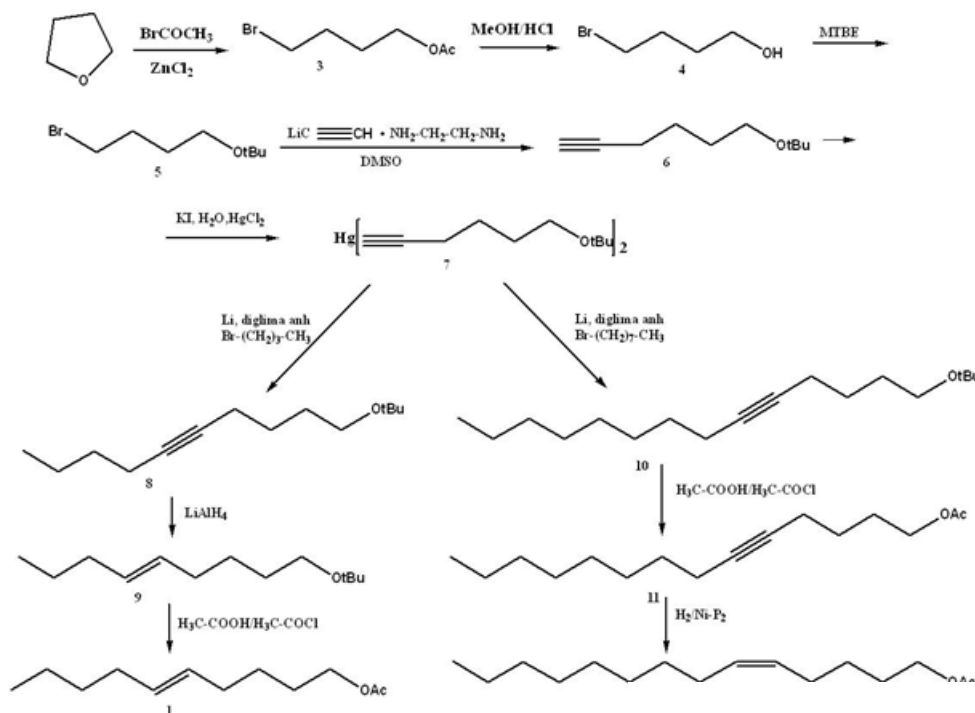
The molecular peak of 1-*tert*-Butoxy-hex-5-yne (**6**) was not identified, the mass spectrum presenting only characteristic fragmentations. It is necessary to mention the base peak in the spectrum (m/z=59), the peak m/z 57 which is generated by the very stable tertiary carbocation +C(CH₃)₃, the peak corresponding to the cleavage of a methyl group from the branch part (m/z=139) and of a neutral molecule of isobutylene (m/z=98), (scheme 2).

1-*tert*-Butoxy-5-hex-yne (**6**) with mercuric chloride in an aqueous solution containing potassium iodide and sodium hydroxide (Nessler's reagent) [11] was precipitated as di[1-*tert*-butoxy-hex-5-yne]mercury (**7**), the common intermediate in the synthesis of the two sex pheromones.

The key step in our acetylenic route consisted in transmetalation of compound **7**, which was directly lithiated by treating with lithium metal in diglyme and then alkylated.

In order to obtain (E)-5-decen-1-yl acetate (**1**), compound **7** was alkylated with 1-bromo-butan, obtaining 1-*tert*-butoxy-dec-5-yne (**8**), which was reduced with lithium aluminium hydride and then acetylated.

In order to obtain (Z)-5-tetradecen-1-yl acetate, compound **7** was alkylated with 1-bromo-octan, obtaining 1-*tert*-butoxy-tetradec-5-yne (**10**). The conversion of the *tert*-butyl ether **10** into the acetate **11** was effected with acetyl chloride. 5-Tetradecyn-1-yl acetate (**11**) was



Scheme 1

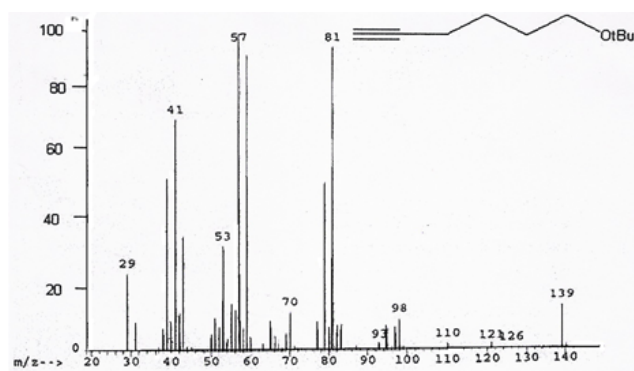
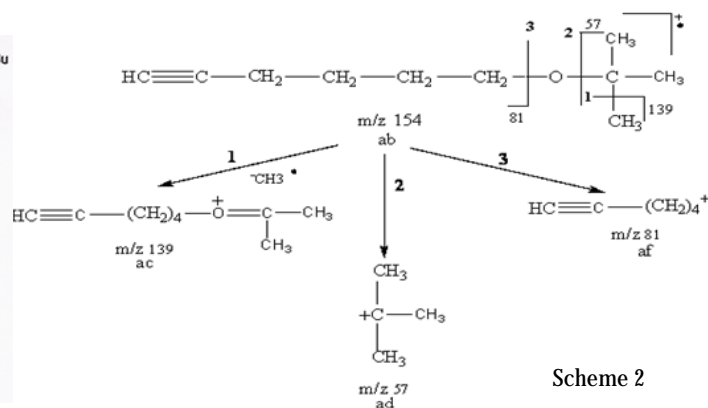


Fig. 1 Mass spectrum of 1-*tert*-Butoxy-hex-5-yne



Scheme 2

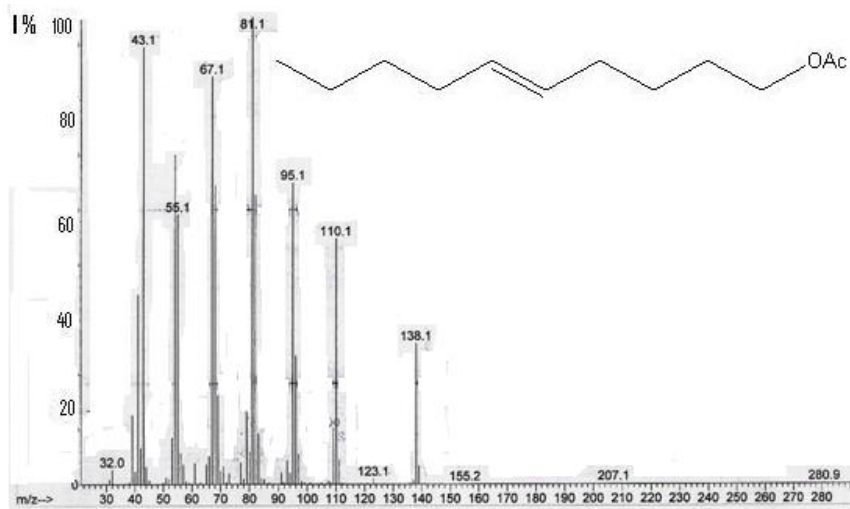


Fig. 2 Mass spectrum of (E)-5-decen-1-yl acetate (**1**)

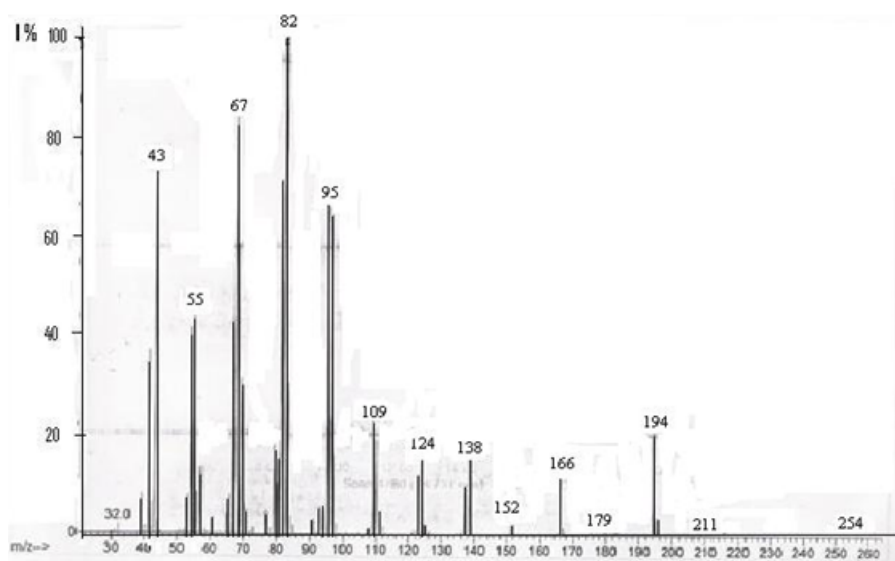


Fig. 3 Mass spectrum of (Z)-5-tetradecen-1-yl acetate (**2**)

hydrogenated using Ni-P2/EDA catalyst [12], obtaining (Z)-5-tetradecen-1-yl acetate (**2**) with 96% isomeric purity.

The mass spectrum of (E)-5-decen-1-yl acetate (**1**) and (Z)-5-tetradecen-1-yl acetate (**2**) are characteristic to alcohol acetates figure 2,3.

Are present: m/z 138 (fig.2) and m/z 194 (fig.3) resulted from the cleavage of acetic acid from the molecular ion, m/z 61 as ion of double transposition ($\text{CH}_3\text{COOH}_2^+$) and m/z 43 (CH_3CO^+).

Conclusions

It was presented new synthesis of (E)-5-decen-1-yl acetate and (Z)-5-tetradecen-1-yl acetate, components of Lepidoptera insects sex pheromones, using the same intermediate, di[*tert*-butoxy-hex-5-yne] mercury, which is directly lithiated and then alkylated with 1-bromo-butan, respectively 1-bromo-octan.

References

- 1.ASHRAF M. EL-SAZED, <http://www.pherobase.com>
- 2.ZAKHARKIN, L.I., PETRUSKINA, E.A., Russian Chemical Bulletin, **1/34**, 1985, p. 193

- 3.ODINOKOV, V. N., BALEZINA, ISHMURATOV, G. Yu., VAKHITOV, R. Sh., TOLSTIKOV, G. A., Chemistry of Natural Compounds, **21/3**, 1985, p 369
- 4.PEDERSON, R. L., GRUBBS, R., US Patent, 6215019, April 10, 2001
- 5.SCHEFFLOLD, R., ABRECHT, S., ORLINSCHI, R., RUF, H. R. , STAMOULI, P., TINEMBART, O., WALDER, L., WEYMUTH, C., Pure & Appl. 59/3, 1987, p. 363
- 6.KELKER, S.V., REDDY, G.B., KUKARNI G.H., Indian Journal of Chemistry section B Organic Chemistry including Medicinal Chemistry, **28/11**, 1989. p. 980
- 7.BESTMANN,H.J., BROSCHE, T., KOSCHATZKY K. H., MICHAELIS, K., PLATZ, H., VOSTROWSKY.O., Knauff.W., Tetrahedron Lett, **21**, 1980, p. 747
- 8.SMORGONSKII, L. M., GOLDFARB, Y. L., Chem. Abstr., **35**, 1941, 4011
- 9.GOCAN, A. V. M., POP, L. M., CIUPE, H., OPREAN, I., HODOSAN, P., Rom. Pat., 93050, Nov.28, 1985
- 10.HOSKOVEC, M., SAMAN, D., SVATOS, A., Collect. Czech. Chem. Commun., **65**, 2000, p.511
- 11.MULLER, E., JOHNSON, J. K., MC EWEN, W. L., J. Amer. Chem. Soc. **48, 1928**, p.469
- 12.BROWN, C.A., AHNYA, V. K., Chem.Commun. 1973, p. 553

Manuscript received: 3.12.2105