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Fe-Catalyzed Synthesis of (4*E*)-Tridec-4-en-1-yl Acetate, Sex Pheromone of Tomato Pinworm (*Keiferia lycopersicella*)

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Abstract—Starting with industrially available 1,3-dichloropropene a stereoselective process was developed for the preparation of (4*E*)-tridec-4-en-1-yl acetate, sex pheromone of tomato pinworm (*Keiferia lycopersicella*) using in the key stage the Fe-catalyzed cross-coupling of ethyl (4*E*)-5-chloropent-4-enoate with octylmagnesium bromide.

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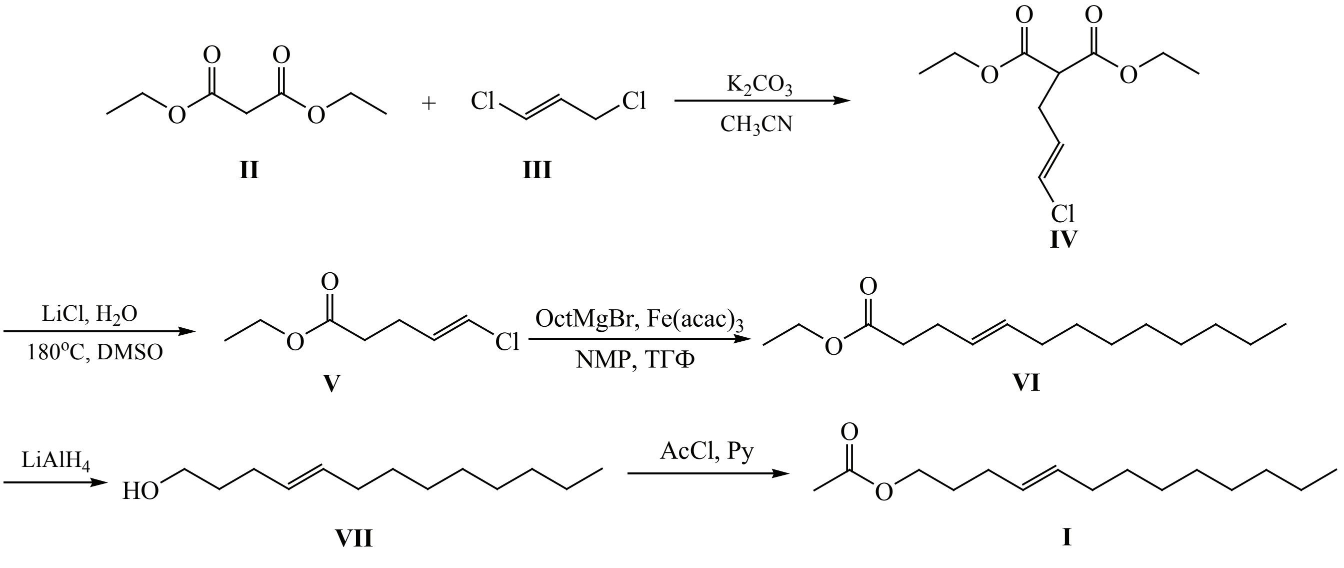
(4*E*)-Tridec-4-en-1-yl acetate (**I**) was identified as the sex pheromone of tomato pinwarm [1], a dangerous pest of the nightshade vegetables growing in the Russian Federation. Several methods of synthesis are known where the transoid configuration of a double bond is built up using acetylene intermediates [2–4], Knoevenagel condensation [5], Claisen rearrangement [6], the opening of a cyclopropane [7] or dihydropyran ring [8], the isomerization of a *cis*-alkenol in a *trans*-isomer [9].

We examined the possibility to obtain the tomato pinwarm pheromone proceeding from the industrially available 1,3-dichloropropene, a toxic side product of propylene chlorination.

The developed protocol of the pheromone synthesis is based on the alkylation of malonic ester **II** with (*E*)-1,3-dichloropropene (**III**) [10] to obtain diethyl [(2*E*)-3-chloroprop-2-en-1-yl]propanedioate (**IV**). Its subsequent decarboxylation by Krapcho procedure [11] leads to the formation of ethyl (4*E*)-5-chloropent-4-enoate (**V**). The Fe-catalyzed cross-coupling of ester **V** with octylmagnesium bromide in the presence of *N*-methylpyrrolidone (NMP) furnishes in a high yield ethyl (4*E*)-



tridec-4-enoate (**VI**). The subsequent reduction of ester **VI** with lithium aluminum hydride and the acetylation of the formed alcohol **VII** affords the target pheromone **I** containing over 99% of the (*E*)-isomer.

The stereochemical homogeneity and the configuration of the substituents at the double bond of the obtained pheromone were proved by GLC on a capillary column and by NMR spectra. In the ^{13}C NMR spectrum of the synthesized (4*E*)-tridec-4-en-1-yl acetate (**I**) the allyl carbon atoms give rise to the signals at δ 28.79 (C^3) and 32.51 (C^6), whereas in the spectrum of its *cis*-analog they are shifted upfield by 5 ppm. Similar characteristic shift of the allyl carbon signals has been observed several times [12], and it may serve as a proof of the spatial arrangement of unsaturated compounds.

EXPERIMENTAL

IR spectra were recorded on a Fourier spectrophotometer IRPrestige-21 Shimadzu from thin films. ^1H and ^{13}C NMR spectra were registered in $CDCl_3$ on a spectrometer Bruker AM-300 (operating frequencies 300 and 75.47 MHz), internal reference TMS. GC-MS measurements were carried out on an instrument GCMS-QP2010S Shimadzu (EI, 70 eV, range of detected masses 33–500 Da), capillary column HP-1MS (30 m × 0.25 mm Ч 0.25 μm), vaporizer temperature 280°C, ion source temperature 200°C., ramp from 50 to 280°C at a rate 10 deg/min, carrier gas helium (1.1 ml/min).

Diethyl [(2*E*)-3-chloroprop-2-en-1-yl]propanedioate (IV). A mixture of 10.00 g (0.062 mol) of malonic ester, 8.31 g (0.075 mol) of (*E*)-1,3-dichloropropene, 0.33 g (1.25 mmol) of 18-crown-6, 15.27 g (0.11 mol) of K_2CO_3, and 25 ml of acetonitrile was stirred at boiling for 4 h. Then it was diluted with 50 ml of water and 50 ml of hexane, the organic layer was separated, the water layer was extracted with hexane (2 × 50 ml). The combined organic solutions were washed with water and dried with Na_2SO_4. The reaction product was isolated from the mixture by vacuum distillation, bp 90–92°C (2 mm Hg). Yield 10.08 g (69%), oily substance. IR spectrum, cm^{-1}: 2982, 2938, 2907, 1748, 1732, 1699, 1634, 1464, 1445, 1393, 1369, 1337, 1281, 1221, 1153, 1096, 1032, 978, 937. ^1H NMR spectrum, δ, ppm: 1.27 t (6H, $2CH_3$, *J* 7 Hz), 2.63 t.d (2H, $=CH\underline{CH_2}$, *J* 7.3, 1.2 Hz), 3.40 t (1H, CHC=O, *J* 7.3 Hz), 4.21 q (4H, $2CH_2O$, *J* 7 Hz), 5.88 d.t (1H, $=C\underline{H}CH_2$, J_{trans} 13.2, 7.3 Hz), 6.09 d.t (1H, =CHCl, J_{trans} 13.2, 1.2 Hz). ^{13}C NMR spectrum, δ, ppm: 13.89 ($2CH_3$), 29.84 ($=CH\underline{C}H_2$), 51.15 ($\underline{C}HC=O$), 61.44 ($2CH_2O$), 120.04 (=CHCl), 129.06 ($=\underline{C}HCH_2$), 168.25 (2C=O). Mass spectrum, *m/z* (I_{rel}, %): 199 (17), 161 (13), 160 (16), 143 (18), 133 (14), 125 (100), 115 (15), 97 (88), 81 (19), 77 (11), 75(29), 69 (11), 55 (12), 53 (24), 51 (12).

Ethyl (4*E*)-5-chloropent-4-enoate (V). A mixture of 10.08 g (0.0429 mol) of compound **IV**, 1.54 g (0.0856 mol) of H_2O, 3.64 g (0.0856 mol) of LiCl, and 16 ml of DMSO was stirred at boiling for 18 h. Then it was diluted with 30 ml of water and 30 ml of hexane, the organic layer was separated, the water layer was extracted with hexane (2 × 30 ml). The combined organic solutions were washed with water, dried with Na_2SO_4, and concentrated. The reaction product was isolated by column chromatography. Yield 5.32 g (76%), oily substance. IR spectrum, cm^{-1}: 2982, 2932, 1732, 1634, 1445, 1373, 1350, 1300, 1240, 1192, 1161, 1096, 1036, 935, 856. ^1H NMR spectrum, δ, ppm: 1.26 t (3H, CH_3, *J* 7 Hz), 2.34–2.44 m (4H, $2CH_2$), 4.11 q (2H, CH_2O, *J* 7.1 Hz), 5.86–5.95 m (1H, $=C^4H$), 6.03 d (1H, $=C^5H$, J_{trans} 13.3 Hz). ^{13}C NMR spectrum, δ, ppm: 14.04 (CH_3), 26.07 (C^3), 33.34 (C^2), 60.39 (CH_2O), 118.30 (C^5), 131.67 (C^4), 172.27 (C^1). Mass spectrum, *m/z* (I_{rel}, %): 127 (86), 117 (27), 99 (100), 91 (24), 89 (40), 88 (31), 75 (27), 53 (46), 43 (15).

Ethyl (4*E*)-tridec-4-enoate (VI). To a solution of 0.507 g (3.12 mmol) of compound **V,** 1.5% (14.5 mg) of $Fe(acac)_3$ in a mixture of 3 ml of THF and 3 ml of *N*-methylpyrrolidone in an argon atmosphere was added dropwise within 5 min at 0 °C 3.6 ml (3.6 mmol) of 1 M solution of octylmagnesium bromide in THF. The mixture was stirred for 30 min at room temperature, then it was diluted with 10 ml of 5% aqueous HCl and 10 ml of hexane, the organic layer was separated, the water layer was extracted with hexane (2 × 10 ml). The combined organic solutions were washed with saturated solution of $NaHCO_3$, dried with Na_2SO_4, and concentrated. The reaction product was isolated by column chromatography. Yield 0.540 g (72%), oily substance. IR spectrum, cm^{-1}: 2924, 2853, 1735, 1470, 1371, 1344, 1300, 1248, 1177, 1161, 1040, 968. ^1H NMR spectrum, δ, ppm: 0.88 t (3H, $C^{13}H_3$, ^{J} 7 Hz), 1 .23–1.36 m (15H, $\underline{CH_3}CH_2O$, 6 CH_2), 1.96 q (2H, C^3H_2, *J* 6.7 Hz), 2.27–2.39 m (4H, C^2H_2, C^6H_2), 4.13 q (2H, CH_2O, *J* 7 Hz), 5.34–5.51 m (2H, $=C^4H$, $=C^5H$). ^{13}C NMR spectrum, δ, ppm: 14.03 (C^{13}), 14.18 ($\underline{C}H_3CH_2O$), 22.63 (C^{12}), 27.90 (C^3), 29.10 (CH_2), 29.25 (CH_2), 29.43 (CH_2), 29.67 (CH_2), 31.85 (C^{11}), 32.45 (C^6), 34.47 (C^2), 60.13 (CH_2O), 127.87 (C^5), 131.79 (C^4), 173.22 (C^1). Mass spectrum, *m/z* (I_{rel}, %):

152 (44), 110 (41), 109 (21), 101 (29), 98 (28), 97 (46), 95 (38), 88 (83), 84 (46), 83 (38), 82 (32), 81 (47), 71 (38), 70 (46), 69 (51), 68 (36), 67 (69), 61 (25), 60 (20), 57 (30), 55 (85), 54 (35), 43 (73), 41 (100).

(4*E*)-Tridec-4-en-1-ol (VII). To a solution of 0.54 g (2.2 mmol) of compound **VI** in 20 ml of anhydrous ether was added 0.08 g (1.5 mmol) of $LiAlH_4$ at 0°C in an argon atmosphere. The mixture was stirred at room temperature for 3 h till the complete conversion of ester **VI** (GLC monitoring**).** Then the mixture was diluted with 10 ml of 5% aqueous HCl and 10 ml of hexane, the organic layer was separated, the water layer was extracted with hexane (2 × 10 ml). The combined organic solutions were washed with saturated solution of $NaHCO_3$, dried with Na_2SO_4, and concentrated. The reaction product was isolated by column chromatography. Yield 0.385 g (88%), oily substance. IR spectrum, cm^{-1}: 3339 br (OH), 2955, 2926, 2853, 1466, 1454, 1059, 966, 909. ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, $C^{13}H_3$, *J* 7 Hz), 1.23–1.34 m (12H, $6CH_2$), 1.62 quintet (2H, C^2H_2, *J* 6.9 Hz), 1.90 br.s (1H, $CH_2O\underline{H}$), 1.97 q (2H, C^3H_2, *J* 6.8 Hz), 2.07 q (2H, C^6H_2, *J* 7 Hz), 3.63 t (2H, C^1H_2, *J* 6.7 Hz), 5.37–5.48 m (2H, $=C^4H$, $=C^5H$). ^{13}C NMR spectrum, δ, ppm: 14.03 (C^{13}), 22.60 (C^{12}), 28.83 (C^3), 29.13 (CH_2), 29.25 (CH_2), 29.43 (CH_2), 29.52 (CH_2), 31.83 (C^{11}), 32.40 (CH_2), 32.52 (C^6), 62.38 (C^1), 129.30 (C^5), 131.16 (C^4). Mass spectrum, *m/z* (I_{rel}, %): 97 (16), 96 (31), 95 (30), 83 (23), 82 (63), 81 (73), 79 (30), 71 (23), 69 (34), 68 (84), 67 (81), 57 (36), 56 (18), 44 (14), 43 (57), 42 (15), 41 (100).

(4*E*)-Tridec-4-en-1-yl acetate (I). To a solution of 0.24 g (1.21 mmol) of compound **VII** in 3 ml of anhydrous diethyl ether was added 0.115 g (1.45 mmol) of pyridine and 0.114 g (1.45 mmol) of acetyl chloride at 0°C. The mixture was stirred at room temperature for 1 h. Then the mixture was diluted with 5 ml of water and 10 ml of hexane, the organic layer was separated, the water layer was extracted with hexane (2 × 10 ml). The combined organic solutions were washed with saturated solution of $NaHCO_3$, dried with Na_2SO_4. The solvent was distilled off, the reaction product was isolated by column chromatography. Yield 0.270 g (93%), oily substance. IR spectrum, cm^{-1}: 3020, 2924, 2850, 1743, 1450, 1375, 1240, 1051, 965. ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, $C^{13}H_3$, *J* 7 Hz), 1.24–1.34 m (12H, $6CH_2$), 1.68 quintet (2H, C^2H_2, *J* 7 Hz), 1.97 q (2H, C^6H_2, *J* 6.9 Hz), 2.03–2.07 m (5H, C^3H_2, $CH_3C=O$), 4.06 t (2H, C^1H_2, *J* 6.7 Hz), 5.34–5.47 m (2H, $=C^4H$, $=C^5H$). ^{13}C NMR spectrum, δ, ppm: 14.05 (C^{13}), 20.95 ($\underline{C}H_3C=O$), 22.62 (C^{12}), 28.44 (C^2), 28.79 (C^3), 29.12 (CH_2), 29.24 (CH_2), 29.42 (CH_2), 29.48 (CH_2), 31.85 (C^{11}), 32.51 (C^6), 63.97 (C^1), 128.56 (C^5), 131.59 (C^4), 171.16 ($CH_3\underline{C}=O$). Mass spectrum, *m/z* (I_{rel}, %): 96 (20), 95 (17), 82 (39), 81 (48), 79 (16), 69 (19), 68 (87), 67 (63), 55 (37), 54 (32), 43 (100), 41 (49).

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