SYNTHESIS OF THE RACEMIC ANALOG OF A HONEYBEE (*Apis mellifera*) BREEDING PHEROMONE COMPONENT

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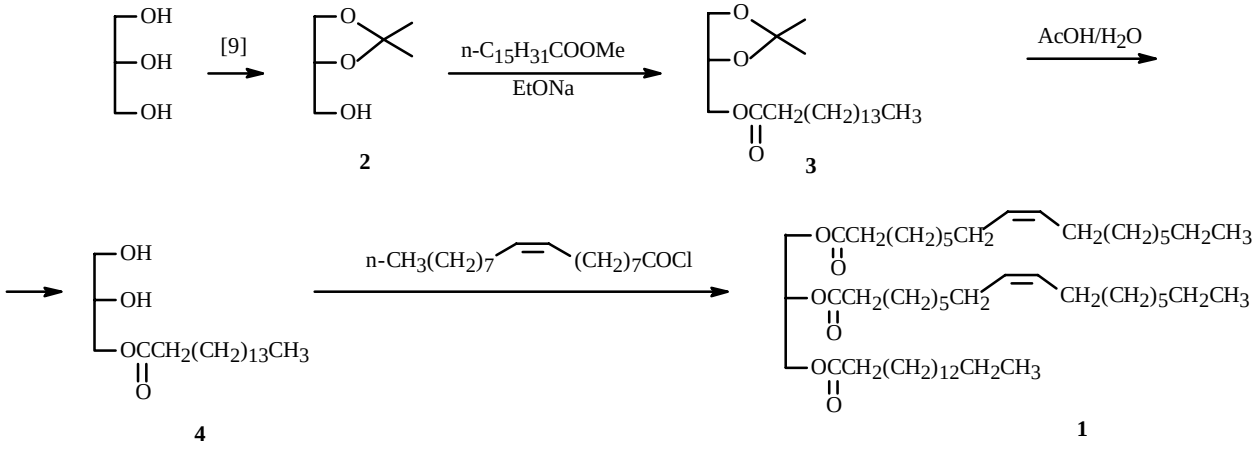
The synthesis of 1-palmitoyl-2,3-dioleoylglycerine, the racemic analog of a honeybee breeding pheromone component, from 1,2-O-isopropylideneglycerine was proposed.

Key words: 1,2-O-isopropylideneglycerine, 1,2-O-isopropylidene-3-O-palmitoylglycerine, 1-monopalmitoylglycerine, 1-palmitoyl-2,3-dioleoylglycerine, pheromone, racemic analog.

Phermones that are emitted during breeding and control the activity of bees near the hive play an important role in chemical communication within the bee colony [1-6].

1,2-Dioleoyl-3-palmitoylglycerine was isolated and identified in 1984 as a component of the honeybee (*Apis mellifera* L.) breeding pheromone that can cause them to mass on artificial maternal cells of honeycombs [7].

Syntheses of this compound that include mutual transesterification of trioleoyl- and tripalmitoylglycerines are known [8]. We propose a synthesis of the title compound that is based on chemoselective transformations of DL-1,2-isopropylideneglycerine, which is readily accessible from glycerine [9]. The synthetic scheme consists of transesterification in the presence of sodium ethoxide of the methyl ester of palmitic acid by diprotected triol **2**, acid hydrolysis of intermediate **3** to α-monoglyceride **4**, and exhaustive acylation of it by oleoylchloride. The overall yield of **1** calculated per starting **2** was 20%.



EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument as thin layers. NMR spectra were recorded on a Bruker AM-300 spectrometer (working frequency 300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C) in $CDCl_3$ using as an internal standard the

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impurity protons in the deuterated solvent (PMR, δ 7.27 ppm) and the average $CDCl_3$ signal (^{13}C NMR, δ 77.00 ppm). GC was carried out on Chrom-5 instruments [column length 1.2 m, silicone SE-30 (5%) on Chromaton N-AW-DMCS (0.16-0.20 mm) stationary phase, working temperature 50-300°C] with He carrier gas. Column chromatography was performed on silica gel L (Czech Rep.) of particle size 40-100 μm; TLC, on Silufol UV-254 plates (Czech Rep.). Elemental analyses of all compounds agreed with those calculated. Petroleum ether (40-70°C, PE) was used for the reactions.

1,2-O-Isopropylideneglycerine (2) was prepared from glycerine as before [9]. The IR and PMR spectra were practically identical to those previously described [10]. ^{13}C NMR spectrum ($CDCl_3$): 25.01 and 26.42 (q, $\underline{C}H_3$-C), 62.73 (t, CH_2OH), 65.66 (t, CH_2O), 76.03 (d, CHO), 109.16 (s, $CH_3\underline{C}$).

1,2-O-Isopropylidene-3-O-palmitoylglycerine (3). A solution of sodium ethoxide that was prepared from Na (0.09 g, 3.8 mg-at) in absolute EtOH (10 mL) was treated with protected triol (**2**, 5.00 g, 37.9 mmol) and methylpalmitate (10.00 g, 37.9 mmol) and heated to 100°C until the alcohol had distilled. The dry solid was extracted with PE (3 × 50 mL) and evaporated to afford **3** (8.02 g, 57%), mp 31-32°C. IR spectrum (KBr, ν, cm^{-1}): 1735 (C=O), 1050 (C–O).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 0.88 (3H, t, J = 3, $C\underline{H}_3CH_2$), 1.24 (26H, br.s, CH_2), 1.32, 1.40 (6H, both s, CH_3–C), 2.30 (2H, t, J = 7, CH_2COO), 3.52-3.59 (1H, m, CHO), 3.92-4.32 (4H, m, CH_2O). ^{13}C NMR ($CDCl_3$): 14.02 (q, $\underline{C}H_3CH_2$), 25.27, 26.59 (both q, $\underline{C}H_3$–C), 22.60, 22.70, 24.80, 25.15, 29.02, 29.17, 29.28, 29.37, 29.59, 31.83, 34.00 (all t, CH_2), 34.57 (t, $\underline{C}H_2COO$), 64.41 (t, $\underline{C}H_2OOC$), 66.23 (t, CH_2O), 73.56 (d, CHO), 109.71 (s, CH_3–$\underline{C}$), 173.57 (COO).

1-Monopalmitoylglycerine (4). A solution of **3** (5.00 g, 13.5 mmol) in PE (40 mL) was treated with CH_3COOH (13 mL, 60%), stirred for 24 h at room temperature, diluted with PE (50 mL), washed successively with saturated $NaHCO_3$ and NaCl solutions, dried over $MgSO_4$, and evaporated to afford **4** (2.64 g, 60%), mp 71-72°C (cf. [10]). IR and PMR spectra were identical to those reported previously [11]. ^{13}C NMR spectrum ($CDCl_3$): 13.97 (q, CH_3), 22.49, 24.70, 28.93, 29.08, 29.17, 29.26, 29.47, 31.74 (all t, CH_2), 33.91 (t, $\underline{C}H_2COO$), 66.13 (t, CH_2OH), 69.96 (d, CHOH), 73.46 (t, $\underline{C}H_2OOC$), 173.96 (s, COO).

1-Palmitoyl-2,3-dioleoylglycerine (1). Oleic acid chloride (5.48 g, 19.2 mmol) was added to **4** (2.00 g, 6.0 mmol) in dry pyridine (30 mL). The mixture was stirred for 10 h, treated with water (8 mL), extracted with PE (3 × 50 mL), washed successively with HCl (10%) and saturated $NaHCO_3$ and NaCl solutions, dried over $MgSO_4$, and evaporated. The solid was chromatographed over SiO_2 (PE:ethylacetate, 9:1) to afford **1** (2.73 g, 52%). PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 0.88 (9H, t, ^3J = 6.7, $C\underline{H}_3CH_2$), 1.20-1.40 (64H, br.s, CH_2), 1.90-2.10 (8H, m, CH_2C=), 2.30 (6H, t, J = 7.2, CH_2COO), 4.15 (4H, dd, ^3J = 8.2, ^4J = 1.7, CH_2OOC), 4.28 (1H, m, CHOOC), 5.36 (4H, t, CH=). ^{13}C NMR spectrum ($CDCl_3$): 14.12 (q, $\underline{C}H_3CH_2$), 22.67 (t, $CH_3\underline{C}H_2$), 24.11-24.68 (t, CH_2), 27.20 (t, $\underline{C}H_2C$), 34.05, 34.19 (both t, CH_2COO), 62.07 (t, $\underline{C}H_2OOC$), 68.83 (d, $\underline{C}HOOC$), 130.01 (d, CH=), 173.58, 175.31 (s, COO).

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