A NEW ROUTE FOR THE SYNTHESIS OF 10-HYDROXYDEC-2E-ENOIC AND DEC-2E-ENEDIOIC ACIDS

V. N. Odinokov, G. Yu. Ishmuratov,
and G. A. Tolstikov

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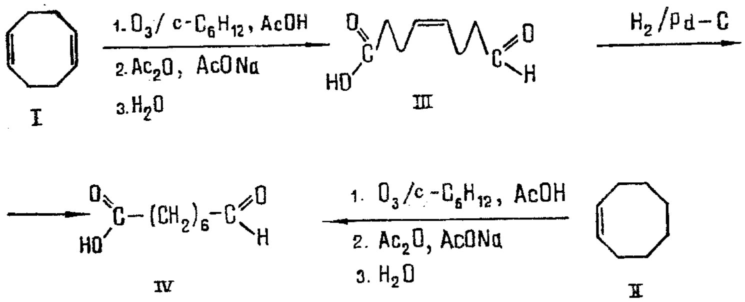
A new simple route for the synthesis of 10-hydroxydec-2E-enoic and dec-2E-enedioic acids from cycloocta-1Z,5Z-diene has been developed.

Known methods for the synthesis of 10-hydroxydec-2E-enoic and dec-2E-enedioic acids (components of the secretion of the mandibular gland of the honey bee *Apis mellifera* L.) [1, 2] are based on the selective oxidation of one of the hydroxy groups in octan-1,8-diol, which takes place insufficiently selectively [3, 4]. The oxidation of the difficultly accessible 8-halodecan-1-ols or the α,β-dehydration of undecylenic acid ester with the subsequent selective ozonolysis of the terminal double bond [5] cannot be considered as convenient preparative methods, either.

We have developed a new route for the synthesis of 10-hydroxydec-2E-enoic acid (VIII) and dec-2E-enedioic acid (IX) from the readily available cycloocta-1Z,5Z-diene (I) or the product of its hydrogenation — cyclooctene (II). The ozonolysis of the latter by a method described previously [6] gave an 80% yield of 8-oxooctanoic acid (IV), which can also be obtained by the selective ozonolysis of the diene (I) as described in [7] with the subsequent palladium-catalyzed hydrogenation of the 8-oxooct-4Z-enoic acid (III) formed. The yield of the acid (IV) calculated on the initial butadiene dimer (I) amounted to 90%.

Obviously, the variant of the ozonolysis of the diene (I) is preferable, since it eliminates the necessity for its selective hydrogenation to the monoene (II).



Esterification with methanol in the presence of p-toluenesulfonic acid (TsOH) converted the formyl carboxylic acid (IV) into methyl 8,8-dimethoxyoctanoate (V), the reduction of which with the aid of diisobutylaluminum hydride (DIBAH) in tetrahydrofuran (THF) solution gave 8,8-dimethyoxyoctan-1-ol (VI) with a yield of 97%. After the acetyl protection had been removed by hydrolysis in an acid medium, the resulting 8-hydroxyoctan-1-al (VII) was condensed with malonic acid by the Knoevenagel reaction, which gave a 49% yield of the required hydroxy carboxylic acid (VIII). An analogous condensation of the formyl carboxylic acid (IV) and malonic acid led to the Δ^{2E}-unsaturated dicarboxylic acid (IX). The overall yields of compounds (VIII) and (IX), calculated on the initial diene (I) amounted to 38% and 50%, respectively.

The E configuration of the double bonds in compounds (VIII) and (IX) was confirmed unambiguously by the magnitude of spin–spin coupling constant of the vinyl protons (J = 16 Hz), which is characteristic for E-olefins [8].

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EXPERIMENTAL

The PMR spectra of the substances were obtained on a Tesla BS-487B spectrometer with a working frequency of 80 MHz using as solvents $CDCl_3$ and CD_3OD (for the diacid (IX)), and the chemical shifts are given in the δ scale relative to the signal of HMDS (internal standard). IR spectra were taken on a UR-20 spectrometer in a thin layer or in Nujol. GLC was performed on a Chrom-41 instrument with SE-30 (5%) as the stationary phase on Chromaton N-AW-DMCS (0.2-0.25 mm) at a working temperature of 50-300°C (14 deg/min) with a feed of the carrier gas, helium, at the rate of 50 ml/min.

8-Oxooctanoic Acid (IV). A. A mixture of ozone and oxygen (5.5 mass-% of O_3) was passed at 5°C through a solution of 11.9 g (110 mmole) of the diene (I) and 15.4 ml of glacial acetic acid in 110 ml of redistilled cyclohexane until 100 mmole of ozone had been absorbed, and the mixture was then worked up as described previously [7]. This gave 14.4 g (92%) of the unsaturated acid (III), bp 123-127°C (0.05 mm), n_D^{20} 1.4725 [7], which was dissolved in 40 ml of glacial acetic acid, treated with 2 g of catalyst (5% Pd/C) and kept in an autoclave in hydrogen (20 atm, 20°C) for 15 h, after which the mixture was filtered and the filtrate was evaporated (argon, vacuum). This gave 14.2 g (98%) of the oxoacid (IV) with bp 131-134°C (0.1 mm) [6].

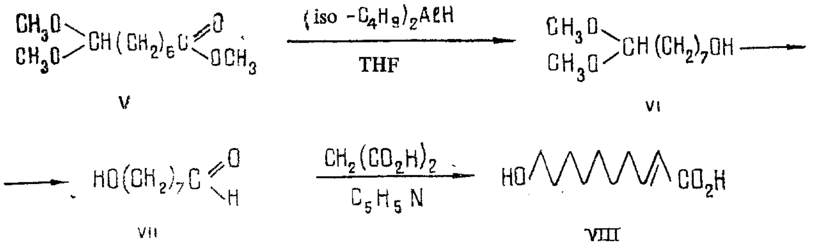
B. A mixture of ozone and oxygen (5.5 mass-% of O_3) was passed at 5°C through a solution of 11.0 g (10 mmole) of the monoene (II) and 15.4 ml of glacial acetic acid in 120 ml of redistilled cyclohexane until ozone was detected in the issuing gas (by the liberation of iodine from an aqueous solution of potassium iodide), and the mixture was then worked up as described previously [6]. This led to 12.8 g (81%) of the oxo acid (IV), bp 130-133°C (0.1 mm), identical with that obtained in the preceding experiment.

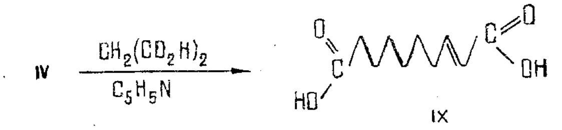
Methyl 8,8-Dimethoxyoctanoate (V). A mixture of 1.58 g (10 mmole) of the formyl carboxylic acid (IV), 0.15 g of TsOH, and 20 ml of absolute methanol was kept at 20°C for 16 h, and then 1 g of $NaHCO_3$ was added and the mixture was evaporated (argon, vacuum). The residue was dissolved in diethyl ether and the solution was washed with 10% $NaHCO_3$ and then with saturated NaCl (pH ~7), dried over Na_2SO_4, and evaporated. After chromatography of the residue [SiO_2, hexane—ether (8:2)], 1.96 g (90%) of compound (V) was obtained with n_D^{20} 1.4308 [9]. IR spectrum (ν, cm^{-1}): 1065 m, 1090 infl., 1135 m, 1180 m, 1203 m, 1260 m, 1740 s. PMR spectrum (ppm): m 1.28 (10 H, CH_2), t 2.22 (2 H, CH_2CO_2, J = 7 Hz), s 3.22 (6 H, OCH_3), s 3.57 (3 H, CO_2CH_3), t 4.25 (1 H, OCHO, J = 5 Hz).

8,8-Dimethoxyoctan-1-ol (VI). At —15°C, 12.7 ml (56 mmole) of a 73% solution of DIBAH in toluene was added (argon) to a solution of 4.36 g (20 mmole) of compound (V) in 150 ml of a mixture (1:1) of absolute toluene and THF, the reaction mixture was then kept at —10°C for 1.5 h, and 12 ml of water was added at —2°C, after which the temperature was raised to 20°C, and the mixture was stirred for 2 h. Then 200 ml of diethyl ether was added and filtration was carried out. The filtrate was washed with saturated NaCl, dried over Na_2SO_4, and evaporated. After chromatography of the residue [SiO_2, hexane—ether (7:3)], 3.7 g (97%) of compound (VI) was obtained with n_D^{20} 1.4441. IR spectrum (ν, cm^{-1}): 1065 s, 1080 infl., 1135 s, 1370 m, 1390 m, 3420 br.s. PMR spectrum (ppm): m 1.28 (12 H, CH_2), s 3.22 (6 H, OCH_3), s 3.4 (1 H, OH), t 3.5 (2 H, CH_2O, J = 6 Hz), t 4.28 (1 H, OCHO, J = 5 Hz).

8-Hydroxyoctanal (VII). A solution of 3.7 g (19.4 mmole) of compound (VI) in 40 ml of THF was treated with 15 ml of 10% HCl and the mixture was kept at 20°C for 16 h (argon), and then 300 ml of diethyl ether was added and the resulting solution was washed with 10% $NaHCO_3$ (to pH ~8) and then with saturated NaCl (to pH ~7) and was dried over Na_2SO_4 and evaporated (argon, finally in vacuum). After chromatography of the residue [SiO_2, hexane—ether (7:3)], 2.7 g (97%) of the hydroxy aldehyde (VII) was obtained with mp 62-65°C [3]. IR spectrum (ν, cm^{-1}): 1065 s, 1075 infl., 1130 s, 1370 m, 1390 m, 1725 s, 2730 w, 3420 br.s. PMR spectrum (ppm): m 1.27 (10 H, CH_2), t 2.3 (2 H, CH_2CO, J = 5.5 Hz), s 3.4 (1 H, OH), t 3.5 (2 H, CH_2O, J = 6 Hz), s 9.7 (1 H, CHO).

10-Hydroxydec-2E-enoic Acid (VIII). A solution of 1.44 g (10 mmole) of the hydroxy aldehyde (VII), 1.56 g (15 mmole) of malonic acid, and 0.5 ml of piperidine in 10 ml of anhydrous pyridine was kept at 20°C for 16 h and was then heated at 110-115°C for 1 h, after which it was poured into a mixture of 25 ml of concentrated HCl and 20 g of ice and was extracted with diethyl ether (3 × 100 ml). After the drying ($MgSO_4$) and evaporation of the solution (vacuum), a residue was obtained which was treated with 10% $NaHCO_3$ (to pH ~8-9), and the alkaline solution was washed with diethyl ether (2 × 100 ml) and was then acidified with 10% HCl (to pH ~4) and was again extracted with diethyl ether (3 × 150 ml), and the extract was dried with Na_2SO_4 and evaporated (finally in vacuum). This gave 0.91 g (49%) of the hydroxy acid (VIII), mp 64-65°C [ether–hexane (2:1)] [3]. IR spectrum (ν, cm^{-1}), 990 m, 1135 w, 1660 m, 1700 s, 2600 br.s., 3420 s. PMR spectrum (ppm): m 1.26 (10 H, CH_2), s 2.0 (1 H, OH), m 2.1 (2 H, $CH_2C{=}C$), t 3.57 (2 H, CH_2O, J = 6 Hz), d 5.75 (1 H, $C^2H{=}C$, J = 16 Hz), dt 7.03 (1 H, $C^3H{=}C$, J_1 = 16 Hz, J_2 = 7 Hz), s 7.9 (1 H, CO_2H).





Dec-2E-enedioic Acid (IX). A solution of 1.58 g (10 mmole) of the formyl carboxylic acid (IV), 1.56 g (15 mmole) of malonic acid, and 0.5 ml of piperidine in 10 ml anhydrous pyridine was kept at 20°C for 30 h; it was then heated at 110-115°C for 2 h, poured into a mixture of 40 ml of concentrated HCl and 30 g of ice, and extracted with diethyl ether (3 × 150 ml). The subsequent working up, identical with that described in the preceding experiment, gave 1.1 g (55%) of the dicarboxylic acid (IX), mp 168-170°C [ethanol–water (3:2)] [10]. IR spectrum (ν, cm^{-1}): 955 s, 995 m, 1655 m, 1700 s, 2700 br.s. PMR spectrum (ppm): m 1.25 (8 H, CH_2), m 2.1 (2 H, $CH_2C{=}C$), m 2.2 (2 H, CH_2CO), s 4.9 (2 H, CO_2H), d 5.7 (1 H, $C^2H{=}C$, J = 16 Hz), dt 6.9 (1 H, $C^3H{=}C$, J_1 = 16 Hz, J_2 = 7 Hz).

SUMMARY

A new route for the synthesis of 10-hydroxydec-2E-enoic and dec-2E-enedioic acids — components of the "queen jelly" of the honey bee *Apis mellifera* L. — has been developed which is based on the selective ozonolysis of the cyclic dimer of butadiene.

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