Russian Journal of Organic Chemistry, Vol. 37, No. 6, 2001, pp. 781–783. Translated from Zhurnal Organicheskoi Khimii, Vol. 37, No. 6, 2001, pp. 829–831.

Isomerization of Methyl (9*Z*)-12-Oxooctadec-9-enoate

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Received July 19, 2000

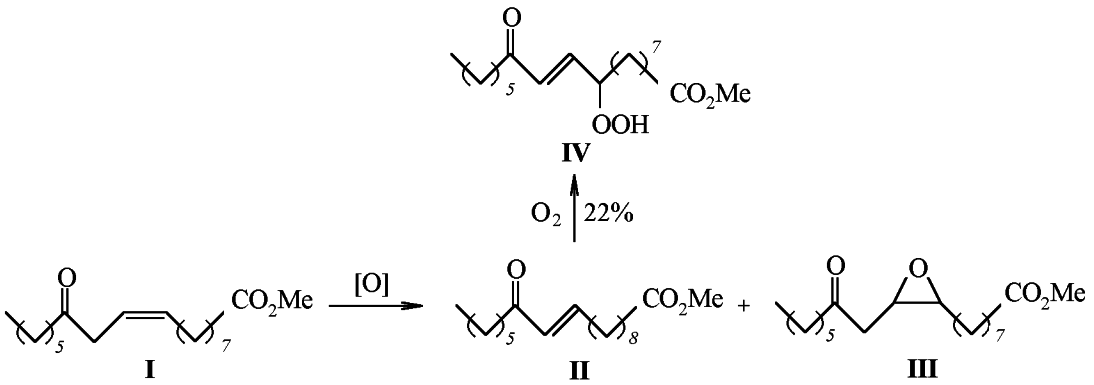
Abstract—Methyl (9*Z*)-12-oxooctadec-9-enoate isomerizes stereoselectively in 86% yield into methyl (10*E*)-12-octadec-10-enoate in the presence of a complex H_2O_2–BF_3–Et_2O.

The interest to chemical transformations of ricinoleic [(9*Z*), (12R)-12-hydroxyoctadec-9-enoic) acid has grown recently [1, 2]. Its derivatives possess antiviral, antiphlogistic, and antiallergic properties [3, 4]. It was shown formerly that the reaction of methyl (9Z)-12-oxooctadec-9-enoate (**I**) with peroxyacids resulted in epoxydation of the C=C bond [1, 3, 5].

In the present study during preparation of new derivatives of ricinoleic acid by oxydation of methyl (9*Z*)-12-oxooctadec-9-enoate (**I**) according to Bayer–Williger procedure we found that the compound suffered a stereoselective isomerization. Treating of ethereal solution of enone **I** with the reagent for ketone oxidation, a complex of 90% hydrogen peroxide and boron trifluoride etherate [6] [molar ratio ketone **I**–H_2O_2–BF_3–Et_20 1 : 1 : 2], afforded methyl (10*E*)-12-octadec-10-enoate (**II**) in 86% yield. In the reaction under study alongside the displacement of the C=C bond from C^9 to C^{10} occurred its selective *cis-trans* isomerization as showed the coupling constant of the vicinal protons attached to the C^{10}=C^{11} bond of enone **II** (~16 Hz). Under similar conditions in the presence of only boron trifluoride etherate the ketoester **I** yielded just 58% of ester **II**.

The structure of compound **II** was confirmed by a known isomerization procedure for ketoester **I** isomerization [7]: refluxing of ether **I** in ethanol in the presence of oxalic acid under argon atmosphere.

A detailed investigation of ketoester **I** oxidation with a 5-foid excess of monoperoxyphthalic or *meta*-chloroperoxybenzoic acids revealed that alongside methyl 12-oxo-9,10-epoxyoctadecanoate **III** formed also ketoester **II**. The yields of compounds **III** and **II** amount respectively to 79 and 14% or 75 and 17%. No products resulting from oxidation of ketone **I** along Bayer–Williger reaction was detected.



Reagent	Yield of compound **II**	Yield of compound **III**
90% H_2O_2, $BF_3 \cdot Et_2O$	86	–
$BF_3 \cdot Et_2O$	58	–
$H_2C_2O_4$	41	–
2-$(HO_2C)C_6H_4CO_3H$	14	79
3-$ClC_6H_4CO_3H$	17	75

1070-4280/01/3706-0781$25.00

Note that ketoester **II** stored in air readily undergoes autooxidation by air oxygen affording methyl (10*E*)-9-hydroperoxy-12-oxodec-10-enoate (**IV**) in 22% yield.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on Bruker AM-300 spectrometer in $CDCl_3$. IR spectra were measured on Specord M-80 instrument from samples as thin films. Mass spectra were taken on spectrometer MKh-1300, injection source temperature 100°C, electron ionization energy 70 and 12 eV. The reaction products were analysed by GLC on Chrom-5 chromatograph, flame-ionization detector, column 1200×5 mm packed with 5% SE-30 on Inerton NAW DMCS carrier (0.125–0.165 μ), carrier gas helium.

Methyl (9*Z*)-12-oxooctadec-9-enoate (I) was prepared by oxidation of methyl (9*Z*),(12R)-12-hydroxyoctadec-9-enoate with the Collins reagent [3].

Oxidation of ketone I with H_2O_2–BF_3–Et_2O complex. To a solution of 0.85 g (2.74 mmol) of ketone **I** in 0.24 ml of Et_2O was added dropwise under argon at stirring while cooling to 0°C 0.11 g (2.88 mmol) of 90% H_2O_2 solution and 0.77 g (5.48 mmol) of BF_3–Et_20. The reaction mixture was maintained at 0°C for 2.5 h, then diluted with 5 ml of Et_2O, washed with saturated solutions of Na_2SO_3 (3×3 ml) and K_2CO_3 (3×3 ml), and dried with $MgSO_4$.

The solvent was removed in vacuo, and the residue was subjected to column chromatography on silica gel (L 100/250, eluent petroleum ether–Et_2O, 20:1). Ketone **II** was separated in 0.73 g amount (86%). IR spectrum (cm^{-1}): 1000 (*trans*-C=C), 1190 (C=O), 1650 (*trans*-C=C), 1690 (C=O), 3030 (*trans*-C=C), 1745 (CO_2). ^{1}H NMR spectrum (δ, ppm, *J*, Hz): 0.80 t (3H, $C^{18}H_3$, 6.5), 1.13–1.42 m (16H, CH_2), 1.45–1.61 m (4H, C^3H_2, $C^{14}H_2$), 2.12 q (2H, C^9H_2, 7.2), 2.22 t (2 H, C^2H_2, 7.6), 2.45 t (2H, $C^{13}H_2$, 7.6), 3.60 s (3H, CO_2CH_3), 6.02 d (1H, $C^{11}H$, 16.2), 6.25 d.t (1H, $C^{10}H$, 15.9 and 6.9). ^{13}C NMR spectrum (δ_C, ppm): 14.06 (C^{18}), 22.54 (C^{17}), 24.33 (C^3), 24.91 (C^{15}), 28.11 (C^{14}), 29.01 (C^4), 29.12 (C^5, C^6, C^7), 29.72 (C^8), 31.66 (C^{16}), 32.44 (C^9), 34.08 (C^2), 40.13 (C^{13}), 51.48 (OCH_3), 130.36 (C^{11}), 147.34 (C^{10}), 173.33 (C^1), 201.12 (C^{12}). Mass spectrum, *m/z*: 310 $[M]^+$.

Isomerization of ketone I. (a) In the presence of BF_3–Et_20. From 0.3 g (0.97 mmol) of ketone **I** and 0.275 g (1.94 mmol) of BF_3–Et_20 along procedure described above was obtained 0.17 g (58%) of ketone **II**.

(b) In the presence of oxalic acid. A solution of 0.5 g (1.55 mmol) of ketone **I** and 0.05 g (0.55 mmol) of anhydrous oxalic acid in 20 ml of 95% ethanol was heated under argon for 2 h, then cooled to 20°C, and the solvent was evaporated in vacuo. The residue was diluted with 8 ml of Et_2O and treated with saturated solution of Na_2CO_3 (3×5 ml)the reaction product was extracted with Et_2O, and extract was drid on $MgSO_4$. The solvent was evaporated in vacuo. We obtained 0.21 g (41%) of ketone **II**.

Oxidation of ketone I with peroxyacids. (a) To a solution of 0.46 g (1.5 mmol) of ketone **I** in 2 ml of Et_2O at 0°C under argon while stirring was added dropwise a solution of 1.37 g (7.5 mmol) of monoperoxyphthalic acid in 7 ml of Et_2O, the mixture was maintained at 0°C for 4–5 h and left standing overnight at room temperature. The reaction mixture was filtered, washed with saturated solutions of Na_2SO_3 (3×5 ml) and Na_2CO_3 (3×5 ml), and dried with $MgSO_4$. The solvent was evaporated in vacuo. The residue was subjected to column chromatography on silica gel (L 100/250, eluent petroleum ether–Et_2O, 15:1). We separated 0.04 g (14%) of ketone **II** and 0.22 g (79%) of epoxide **III**.

(b) In a similar way 0.5 g (1.6 mmol) of ketone **I** dissolved in 2 ml of CH_2Cl_2 was oxidized with a solution of 1.4 g (8.1 mmol) of *meta*-chloroperoxybenzoic acid in 7 ml of CH_2Cl_2. Yield of ketone **II** 0.07 g (17%), of epoxide **III** 0.29 g (75%). IR and ^{1}H NMR spectra are consistent with the published data [1, 3, 5]. ^{13}C NMR spectrum (δ_C, ppm): 14.06 (C^{18}), 22.51 (C^{17}), 23.58 (C^3), 24.91 (C^{15}), 26.43 (C^8), 28.00 (C^{14}), 28.84 (C^4), 29.04 (C^5), 29.17 (C^6), 29.29 (C^7), 31.61 (C^{16}), 34.06 (C^2), 41.63 (C^{13}), 43.36 (C^{11}), 51.51 (CO_2CH_3), 52.37 (C^{10}), 56.36 (C^9), 174.29 (C^1), 208.52 (C^{12}). Mass spectrum, *m/z*: 326 $[M]^+$.

Methyl (10*E*)-9-hydroperoxy-12-oxooctadec-10-enoate (IV). 4 g (1.3 mmol) of ketone **II** was stored in air at room temperature for 1 month. The resulting mixture was subjected to column chromatography on silica gel (L 100/250, eluent petroleum ether–Et_2O, 15:1). We separated 0.09 g (22%) of hydroperoxide **IV**. IR spectrum (cm^{-1}): 855 (C–O–O–H), 1050 (*trans*-C=C), 1190 (CO_2), 1645 (*trans*-C=C), 1690 (C=O), 1745 (CO_2), 3030 (*trans*-C=C), 3425 (C–O–O–H). ^{1}H NMR spectrum (δ, ppm, *J*, Hz): 0.83 t (3H, $C^{18}H_3$, 6.6), 1.15–1.41 m (16H, CH_2), 1.42–1.65 m (4H, C^3H_2, $C^{14}H_2$), 2.23 t (2H, C^2H_2, 7.5),

2.52 t (2H, $C^{13}H_2$, 7.4), 3.6 s (3H, CO_2CH_3), 3.7 m (1H, OH), 4.43 m (1H, C^9H), 6.22 d (1H, $C^{11}H$, 16.2), 6.70 d.d (1H, $C^{10}H$, 15.9 and 6.6). ^{13}C NMR spectrum (δ_C, ppm): 13.96 (C^{18}), 22.44 (C^{17}), 23.72 (C^3), 24.45 (C^7), 24.72 (C^{14}), 27.42 (C^{15}), 28.81 (C^4, C^6), 29.18 (C^5), 31.43 (C^{16}), 33.98 (C^2), 35.20 (C^8), 40.35 (C^{13}), 51.39 (OCH_3), 84.58 (C^9), 130.72 (S^{11}), 144.57 (S^{10}), 174.29 (S^1), 200.50 (S^{12}).

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