SIMPLE SYNTHESIS FOR METHYL ESTERS OF 7-OXOHEPTANOIC AND 9-OXANONANOIC ACIDS

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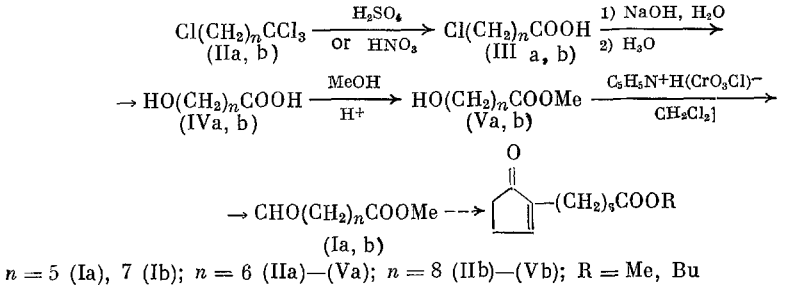
The condensation of the methyl ester of 7-oxoheptanoic acid (Ia) with 1-morphilino-1-cyclopentene readily gives 2-(6-butoxycarbonylhexyl)-2-cyclopentene-1-one [1], which is a synthetic precursor for a series of prostaglandins, while the methyl ester of 9-oxononanoic acid (Ib) may be readily converted according to Novak [2] and Reuter [3] to 2-(6-methoxycarbonylhexyl)-2-cyclopenten-1-one. Several methods have been reported for the preparation of esters (Ia) and (Ib) [4-8]. We have carried out a simple synthesis of (Ia) and (Ib) from 1,1,1,7-tetrachloroheptane (IIa) and 1,1,1,9-tetrachlorononane (IIb) which are products of the telomerization of ethylene with CCl_4 [9-10].



$n = 5$ (Ia), 7 (Ib); $n = 6$ (IIa)—(Va); $n = 8$ (IIb)—(Vb); R = Me, Bu

The hydrolysis of (IIa) and (IIb) by H_2SO_4 [11] or HNO_3 [12] gives virtually quantitative yields of 7-chloroheptanoic (IIIa) and 9-chlorononanoic acids (IIIb). Heating (IIIa) and (IIIb) in aqueous NaOH at 105-108°C smoothly gives 7-hydroxyheptanoic (IVa) and 9-hydroxynonanoic acids (IVb), which react with methanol in the presence or sulfuric acid to give the methyl esters of 7-hydroxyheptanoic (Va) and 9-hydroxynonanoic acids (Vb) and with ethanol to give the ethyl esters of 7-hydroxyheptanoic and 9-hydroxynonanoic acids. Oxidation of the hydroxy group in (Va) and (Vb) by pyridinium chlorochromate according to Bosone [8] and Corey [13] readily leads to (Ia) and (Ib).

EXPERIMENTAL

The purity of the compounds studied was determined by gas—liquid chromatography on an LKhM-8 MD chromatograph with katharometer detector using helium as the gas carrier and a 200 × 0.3-cm column packed with 15% SE-30 on Chromatone N-AW. A sample of 7-chloroheptanoic acid (IIIa) was obtained by the hydrolysis of (IIa) by 93% H_2SO_4 in 95% yield according to our previous work [11].

Methyl Ester of 7-Hydroxyheptanoic Acid (Va). A solution of 50 g (IIIa) in 180 g 20% aq. NaOH was heated at reflux for 6 h, cooled, acidified with hydrochloric acid, and thoroughly extracted with ether. The ethereal extract was dried with $MgSO_4$. The ether was distilled off to give 39.4 g (IVa) as a thick oil, which was dissolved in 120 ml methanol, 3 ml conc. H_2SO_4 was added, and the solution was heated at reflux for 12 h. Then, the solution was cooled and a small excess of anhydrous $NaHCO_3$ was carefully added to neutralize the sulfuric acid and most of the methanol was distilled off. The residue was diluted with water, extracted with ether, and dried over $MgSO_4$. After removal of the ether, the residue was distilled in vacuum to yield 39 g (81%) (Va), bp 102-103°C (2 mm), n_D^{20} 1.4412 [4].

The ethyl ester of 7-hydroxyheptanoic acid, bp 113-114°C (3 mm), n_D^{20} 1.4392, was obtained by analogy in 83% yield. Found: C 62.21; H 10.42%. $C_9H_{18}O_2$. Calculated: C 62.065; H 10.34%.

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Methyl Ester of 7-Oxoheptanoic Acid (Ia). A solution of 22 g (Va) in 20 ml CH_2Cl_2 was added dropwise with stirring to a suspension of 79 g pyridinium chlorochromate [13] in 240 ml CH_2Cl_2. The mixture was stirred for 2 h at 20°C and then 120 ml ether was added and the reaction mixture was filtered through neutral alumina. The solvents were removed in vacuum. Distillation of the residue in vacuum gave 14.9 g (69%) (Ia), bp 75-76°C (2 mm) [4].

9-Chlorononanoic Acid (IIIb). A mixture of 50 g (IIb) and 100 g 93% H_2SO_4 was heated with vigorous stirring on a steam bath. The liberation of HCl was complete after 1.5 h and the mixture became homogeneous. After cooling, the sulfuric acid solution was poured into ice water and extracted with chloroform. The extract was washed with water and dried over $CaCl_2$. Vacuum distillation gave 33 g (91%) (IIIb), bp 141-142°C (3 mm), mp 26-27°C (from pentane) [9].

9-Hydroxynonanoic Acid (IVb). A solution of 25 g (IIIb) in 80 g 20% aq. NaOH was heated at reflux for 7 h, cooled, and acidified with hydrochloric acid. The oil which separated upon cooling was recrystallized and then extracted with ether. The extract was dried over $MgSO_4$. Distilling off the ether gave 21.5 g (96%) (IVb), mp 50-51°C (from water). Found: C 62.25; H 10.25%. $C_9H_{18}O_3$. Calculated: C 62.06; H 10.34%.

Methyl Ester of 9-Hydroxynonanoic Acid (Vb) was obtained in 93% yield by heating (IVb) with methanol in the presence of H_2SO_4, bp 117-118°C (2 mm), n_D^{20} 1.4476. Found: C 63.25; H 10.49%. $C_{10}H_{20}O_3$. Calculated: C 63.38; H 10.63%.

The ethyl ester of 9-hydroxynonanoic acid was obtained by analogy in 94% yield, bp 128-129°C (2 mm), n_D^{20} 1.4459. Found: C 64.74; H 11.78%. $C_{11}H_{24}O_3$. Calculated: C 64.70; H 11.76%.

Methyl ester of 9-oxononanoic acid (Ib) was obtained by analogy with the methyl ester of 7-oxoheptanoic acid in 71% yield, bp 93-94% (1 mm), n_D^{20} 1.4352 [3].

CONCLUSIONS

A simple method was proposed for the synthesis of the methyl esters of 7-oxoheptanoic and 9-oxononanoic acids from 1,1,1,7-tetrachloroheptane and 1,1,1,9-tetrachlorononane, which are products of the telomerization of ethylene with CCl_4.

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