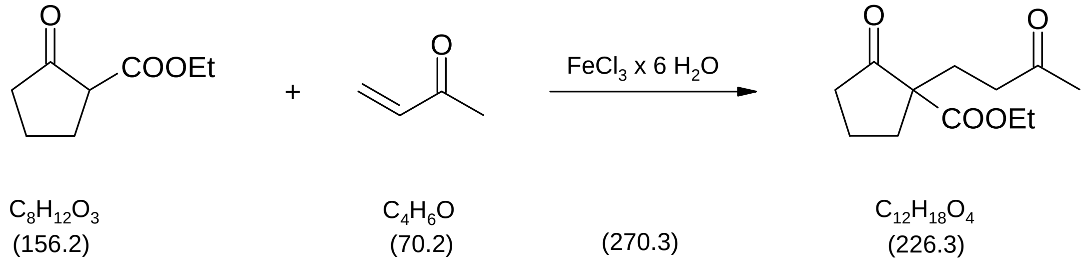
4006 Synthesis of 2-(3-oxobutyl)cyclopentanone-2-carboxylic acid ethyl ester



Classification

Reaction types and substance classes

addition to alkenes, Michael addition
carboxylic acid ester, ketone, acid catalyst

Work methods

working with protective gas, stirring with magnetic stir bar, adding dropwise with an addition funnel, extracting, shaking out, evaporating with rotary evaporator, distilling under reduced pressure, heating with oil bath

Instruction (batch scale 10 mmol)

Equipment

10 mL two-neck flask, protective gas supply, addition funnel with pressure balance, heatable magnetic stirrer, magnetic stir bar, micro distillation apparatus, water bath, vacuum pump, oil bath

Substances

cyclopentanone-2-carboxylic acid ethyl ester (bp 224-228 °C)	1.56 g (1.45 mL, 10.0 mmol)
methyl vinyl ketone (distilled) (bp 80-81 °C)	0.981 g (1.15 mL, 14.0 mmol)
iron(III) chloride hexahydrate	54 mg (0.20 mmol)

Reaction

1.56 g (1.45 mL, 10.0 mmol) cyclopentanone-2-carboxiylic acid ethyl ester and 54 mg (0.20 mmol) iron(III) chloride hexahydrate are filled in a 10 mL two-neck flask, for reasons of temperature constance fixed in a spacious water bath at room temperature and equipped with an additon funnel with pressure balance, a magnetic stir bar and a nitrogen connection. The apparatus is rinsed thoroughly with nitrogen. 0.981 g (1.15 mL, 14.0 mmol) methyl vinyl ketone are added under stirring within one hour. Afterwards the reaction mixture is stirred for further 4 hours at room temperature. The reaction can be monitored either by thin layer chromatography or gas chromatography (see analytics).

Work up

Addition funnel and nitrogen connection are removed, a micro distillation bridge is installed and the product is distilled under reduced pressure.

Yield: 1.73 g (7.64 mmol, 76%); head temperature 86°C ($5 \cdot 10^{-3}$ hPa, oil bath temperature 135 C), colourless liquid; $n_D^{20} = 1.4656$

Waste management

Waste disposal

Waste	Disposal
distillation residue	dissolve in little acetone, then: organic solvents, containing halogen

Time

8-9 hours

Break

Before distillation

Degree of difficulty

Easy

Instruction (batch scale 100 mmol)

Equipment

50 mL two-neck flask, protective gas supply, addition funnel with pressure balance, heatable magnetic stirrer, magnetic stir bar, separating funnel, rotary evaporator, distillation apparatus, water bath, vacuum pump, oil bath,

Substances

cyclopentanone-2-carboxylic acid ethyl ester, (bp 224-228 °C)	15.6 g (14.5 mL, 100 mmol)
methyl vinyl ketone (distilled) (bp 80-81 °C)	9.81 g (11.5 mL, 140 mmol)
iron(III) chloride hexahydrate	0.54 g (2.0 mmol)
tert-butyl methyl ether (bp 55 °C)	40 mL
sodium sulfate for drying	

Reaction

15.6 g (14.5 mL, 100 mmol) cyclopentanone-2-carboxylic acid ethyl ester and 0.54 g (2.0 mmol) iron(III) chloride hexahydrate are filled in a 50 mL two-neck flask, for reasons of temperature constance fixed in a spacious water bath at room temperature and equipped with an addition funnel with pressure balance, a magnetic stir bar and a nitrogen connection. The apparatus is thoroughly rinsed with nitrogen. 9.81 g (11.5 mL, 140 mmol) methyl vinyl ketone are added under stirring within one hour. Afterwards the reaction mixture is stirred for further 4 hours at room temperature. The reaction can be monitored either by thin layer chromatography or gas chromatography (see analytics).

Work up

The reaction mixture is transferred with 25 mL *tert*-butyl methyl ether into a separation funnel and shaken out four times with 15 mL water each. The combined aqueous phases are again shaken out with 15 mL *tert*-butyl methyl ether. The organic phases are combined, dried with sodium sulfate, filtered and the solvent is evaporated at a rotary evaporator.
Crude yield: 22.2g

The crude product is distilled under reduced pressure over a short distillation bridge.
Yield: 18.0 g (79.5 mmol, 80%); head temperature 90°C ($3{\cdot}10^{-3}$ hPa, oil bath temperature 120 C), colourless liquid; n_D^{20} = 1.4658

Comments

The extraction steps during work-up serve the removal of iron salts from the product solution. If one goes without, decomposition products are formed during distillation.

Waste management

Recycling

tert-Butyl methyl ether is collected and redistilled

Waste disposal

Waste	Disposal
distillation residue	dissolve in little acetone, then: organic solvents, containing halogen
sodium sulfate	solid waste, free from mercury,

Time

10-11 hours

Break

Before shaking out and before distillation

Degree of difficulty

Easy

Analytics

Reaction monitoring with TLC

Sample preparation:

Using a Pasteur pipette, one drop of the reaction mixture is diluted with 1 mL dichloromethane.

TLC-conditions:

adsorbant:	TLC-aluminium foil (silica gel 60)
eluent:	petroleum ether (60-80 °C) : *tert*-butyl methyl ether = 6 : 4
visualizing agent:	the TLC-aluminium foil is dipped in 2N H_2SO_4 and then dried with a hot-air dryer
R_f (product)	0.21
R_f (educt).	0.50

Reaction monitoring with GC

Sample preparation:

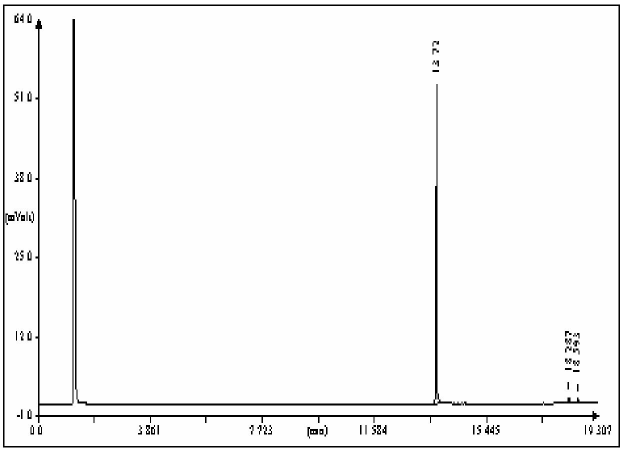
Using a Pasteur pipette, one drop from either the crude product or the pure product is diluted with 10 mL dichloromethane and shaken out with 2 mL water. The aqueous phase is separated and the organic phases dried with sodium sulfate. After filtering off the drying agent, 0.2 µL of this solution are injected.

GC - conditions:

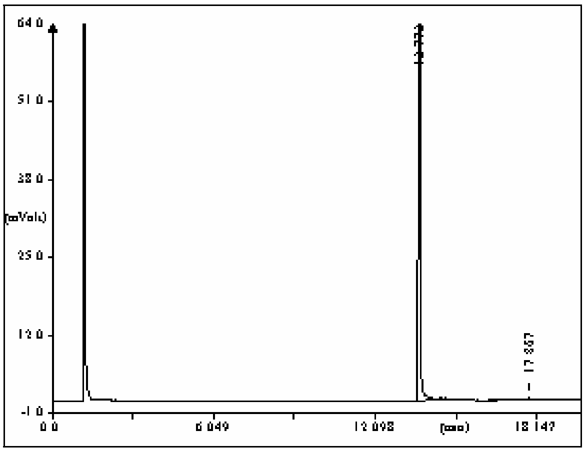
colum:	DB-1, 28 m, internal diameter 0.32 mm, film 0.25 µm
inlet:	on-column-injection
carrier gas:	hydrogen (40 cm/s)
oven:	90 °C (5 min), 10 °C/min to 240 °C (30 min)
detector:	FID, 270 °C

Percent concentration was calculated from peak areas.

GC of the crude product

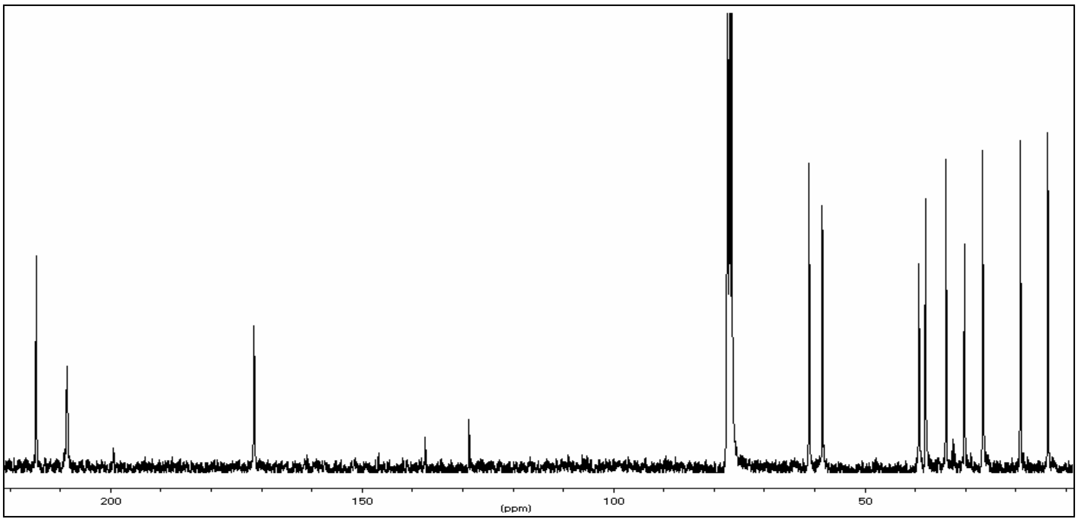


GC of the pure product

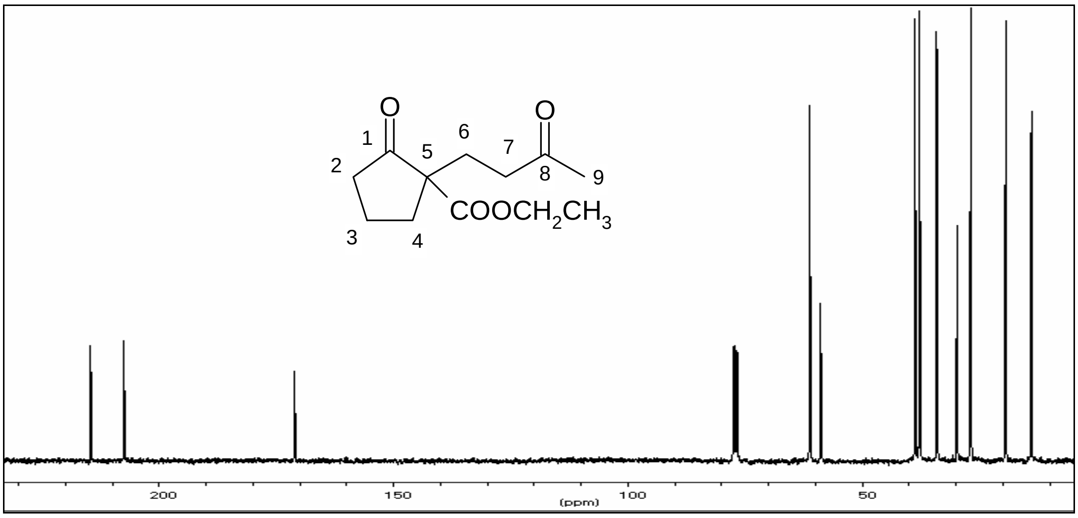


Retention time (min)	Substances	Peak area %	
		crude product	**pure product**
13.7	product	94.6	99.8
18.3	other impurities	2.4	
18.6	other impurities	3.0	

^{13}C NMR spectrum of the pure product (75.5 MHz, $CDCl_3$)

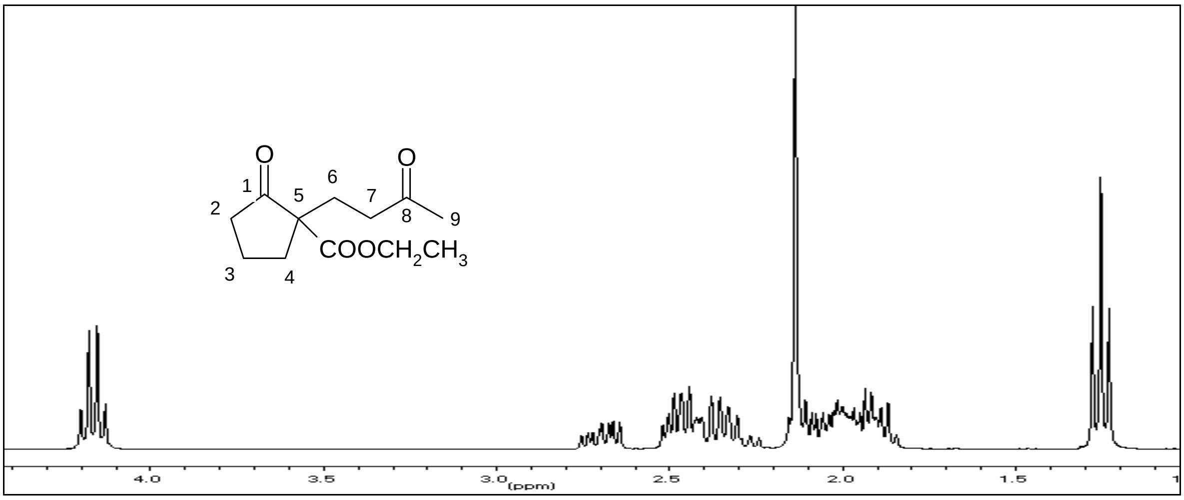


^{13}C NMR spectrum of the pure product (75.5 MHz, $CDCl_3$)



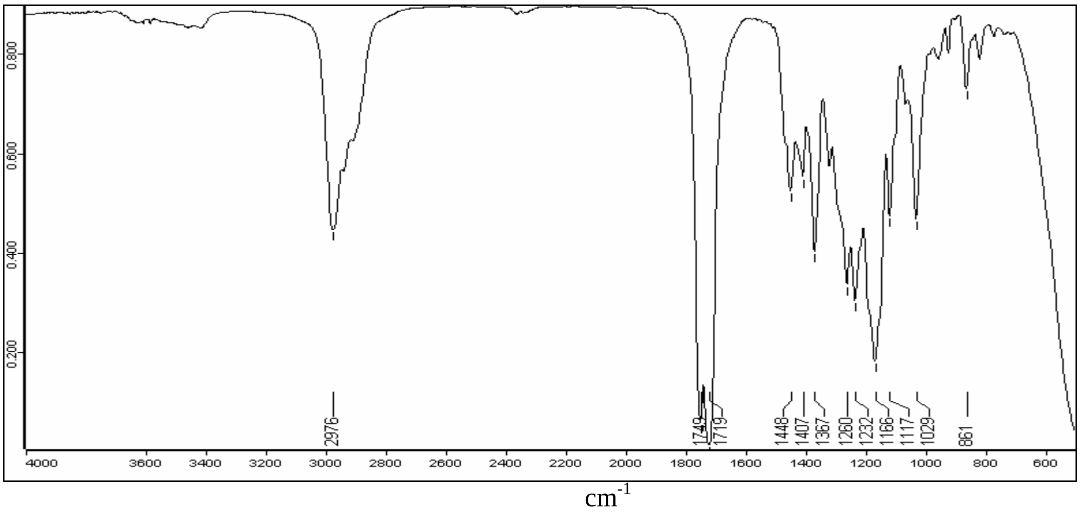
δ (ppm)	Assignment
214.46	C-1
207.37	C-8
171.07	**C**OOCH_2CH_3
61.10	**C**H_2CH_3
58.70	C-5
38.58	C-2
37.66	C-7
33.97	C-6
29.59	C-9
26.74	C-4
19.29	C-3
13.79	CH_2**C**H_3
76.5-77.5	solvent

^{1}H NMR spectrum of the pure product (300 MHz, $CDCl_3$)



δ (ppm)	Multiplicity	Number of H	Assignment
1.23	t	3	CH_2-$\mathbf{CH_3}$
1.82-2.13	m	5	2-H, 3-H, 6-H_a
2.12	s	3	9-H
2.24-2.52	m	4	7-H, 4-H
2.69	ddd	1	6-H_b
4.14	q	2	$\mathbf{CH_2}$-CH_3

IR spectrum of the pure product (film)



(cm^{-1})	**Assignment**
2976	C-H-valence, alkane
1749	C=O-valence, ester
1719	C=O-valence, ketone