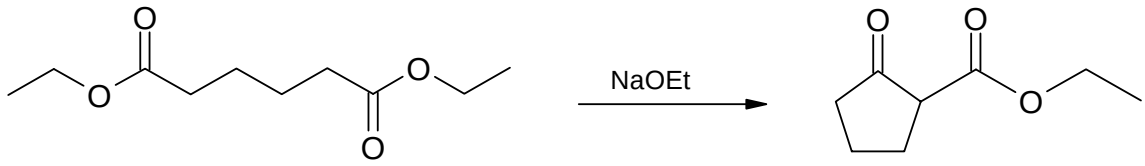
4023 Synthesis of cyclopentanone-2-carboxylic acid ethyl ester from adipic acid diethyl ester



$C_{10}H_{18}O_4$	Na	C_2H_6O	$C_8H_{12}O_3$
(202.2)	(23.0)	(46.1)	(156.2)

Classification

Reaction types and substance classes

reaction of the carbonyl group in carboxylic acid derivatives, Dieckmann condensation, ring closure reaction

carboxylic acid ester

Work methods

working with moisture exclusion, heating under reflux, stirring with KPG stirrer, stirring with magnetic stir bar, adding dropwise with an addition funnel, extracting, shaking out, filtering, evaporating with rotary evaporator, distilling under reduced pressure, heating with oil bath

With a batch scale of 10 mmol:

stirring with magnetic stirrer instead of KPG-stirrer

Instruction (batch scale 10 mmol)

Equipment

100 mL three neck flask, addition funnel with pressure balance, internal thermometer, reflux condenser (for safety reasons preferably metal reflux condenser), drying tube, separating funnel, Kugelrohr distillation apparatus or micro-distillation apparatus, heatable magnetic stirrer, magnetic stir bar, rotary evaporator, vacuum pump, oil bath

Substances

adipic acid diethyl ester (bp 245 °C)	2.02 g (2.00 mL, 10.0 mmol)
sodium	0.25 g (11 mmol)
toluene (absolute) (bp 111 °C)	40 mL
ethanol (absolute) (bp 78 °C)	0.030 g (0.038 mL, 0.65 mmol)
diethylether (bp 35 °C)	60 mL
hydrochloric acid (conc.)	5 mL
sodium sulfate for drying	about 1 g

Reaction

20 mL absolute toluene are filled in a 100 mL three neck flask with magnetic stir bar, addition funnel with pressure balance, internal thermometer and reflux condenser with drying tube. 0.25 g (11 mmol) coarsely-cut sodium without crusts are added. The mixture is heated under very strong stirring with a magnetic stirrer under reflux and until the sodium is converted into a suspension. As soon as the suspension has formed the stirrer is turned off and the suspension is cooled down to about 80 °C. Then a mixture of 2.02 g (2.00 mL, 10 mmol) adipic acid diethyl ester and 0.030 g absolute ethanol is added dropwise under intensive stirring in 10 minutes. Afterwards the reaction mixture is heated under reflux. After about 10 minutes a voluminous precipitation is formed. After addition of 20 mL absolute toluene the mixture is stirred for further 1.5 hours under reflux.

Work up

The reaction mixture is cooled down, poured into 5 g ice water and acidified with 5 mL conc. hydrochloric acid. The organic phase is separated with a separation funnel and stored. The aqueous phase is shaken out three times with 20 mL diethyl ether each. Afterwards the combined organic phases are washed twice with 10 mL water each and dried over sodium sulfate. After the drying agent has been filtered off, the solvent is evaporated at a rotary evaporator. A liquid remains as residue. Crude yield: 1.34 g

The crude product is distilled at reduced pressure in a Kugelrohr distillation apparatus or in a micro-distillation apparatus.

Yield: 1.17 g (7.49 mmol, 75%); bp 110 °C (25 hPa), colourless liquid; $n_D^{20} = 1.4520$

Comments

In experiment Number 4024 the product is used as educt.

Waste management

Waste disposal

Waste	Disposal
aqueous phase	solvent water mixtures, containing halogen
evaporated organic solvent mixture	organic solvents, halogen free
distillation residue	dissolve in a small amount of acetone, then: organic solvents, halogen free
sodium sulfate	solid waste, free from mercury

Time

5-6 hours

Break

After shaking out

Degree of difficulty

Medium

Instruction (batch scale 100 mmol)

Equipment

500 mL three neck flask, addition funnel with pressure balance, internal thermometer, reflux condenser (for safety reasons preferably metal reflux condenser), drying tube, separating funnel, distillation apparatus, stirring motor with KPG-stirrer, heatable magnetic stirrer, magnetic stir bar, rotary evaporator, vacuum pump, oil bath

Substances

adipic acid diethyl ester (bp 245 °C)	20.2 g (20.0 mL, 100 mmol)
sodium	2.5 g (110 mmol)
toluene (absolute) (bp 111 °C)	300 mL
ethanol (absolute) (bp 78 °C)	0.30 g (0.38 mL, 6.5 mmol)
diethyl ether (bp 35 °C)	210 mL
hydrochloric acid (conc.)	15 mL
sodium sulfate for drying	about 5 g

Reaction

150 mL absolute toluene are filled in a 500 mL three neck flask with KPG-stirrer, addition funnel with pressure balance and reflux condenser with drying tube. 2.5 g (110 mmol) coarsely-cut sodium without crusts are added. The mixture is heated under strong stirring under reflux and until the sodium is converted into a suspension. As soon as the suspension has formed the stirrer is turned off and the suspension is cooled down to about 80°C. A mixture of 20.2 g (20.0 mL, 100 mmol) adipic acid diethyl ester and 0.30 mL absolute ethanol is added dropwise under intensive stirring within 10 minutes. Afterwards the reaction mixture is heated under reflux. After about 10 minutes a voluminous precipitation is formed. After adding of 150 mL absolute toluene the mixture is stirred for further 2.5 hours under reflux.

Work up

The reaction mixture is cooled down, poured into 40 g ice water and acidified with 15 mL conc. hydrochloric acid. The organic phase is separated over a separating funnel and stored. The aqueous phase is shaken out three times with 70 mL diethyl ether each. Afterwards the combined organic phases are washed twice with 50 mL water each and dried over sodium sulfate. After the drying agent has been filtered off, the solvent is evaporated at a rotary evaporator. A liquid remains as residue. Crude yield: 14.2 g

The crude product is distilled at reduced pressure without a column.

Yield: 11.8 g (75.5 mmol, 75%); bp 113 °C (36 hPa, oil bath 130 °C), colourless liquid; n_D^{20} = 1.4524

Comments

In experiment Number 4024 the product is used as educt.

Waste management

Waste disposal

Waste	Disposal
aqueous phase	solvent water mixtures, containing halogen
evaporated organic solvent mixture	organic solvents, halogen free
distillation residue	dissolve in a small amount of acetone, then: organic solvents, halogen free
Sodium sulfate	solid waste, free from mercury

Time
6 hours

Break
After shaking out

Degree of difficulty
Medium

Analytics

Reaction monitoring with GC

Sample preparation from the reaction solution:
Using a Pasteur pipette, 5 drops are taken from the reaction solution, diluted with 10 mL dichloromethane and shaken out with 3 drops of water. The aqueous phase is separated and the organic phase is dried over sodium sulfate. 0.2 µl of the solution are injected.

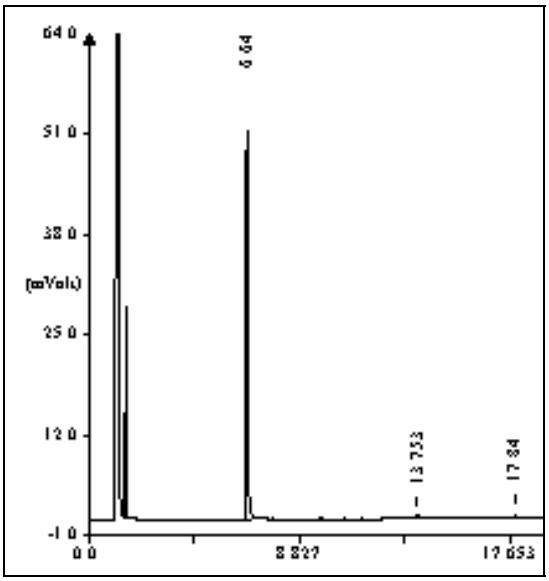
Sample preparation from the isolated product:
1 drop of the product is dissolved in 10 mL dichlormethane. 0.2 µl of the solution are injected.

GC-conditions:

column:	DB-1, 28 m, internal diameter 0.32 mm, Film 0.25 µm
inlet:	on-column-injection
carriergas:	hydrogen (40 cm/sec)
oven:	90 °C (5 min), 10 °C/min at 240 °C (30 min)
detector:	FID, 270 °C

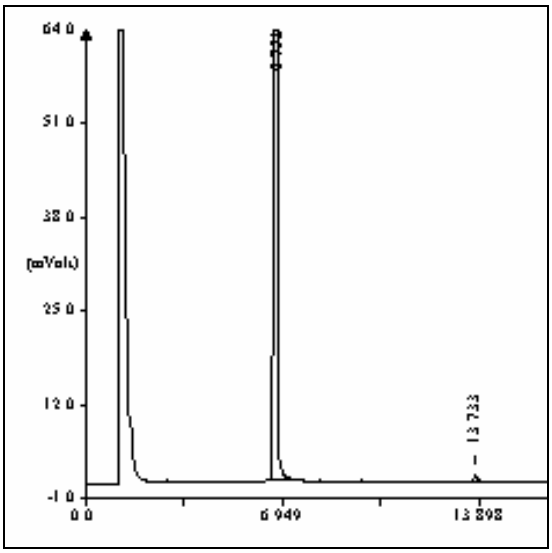
Percent concentration was calculated from the peak areas.

GC of the crude product



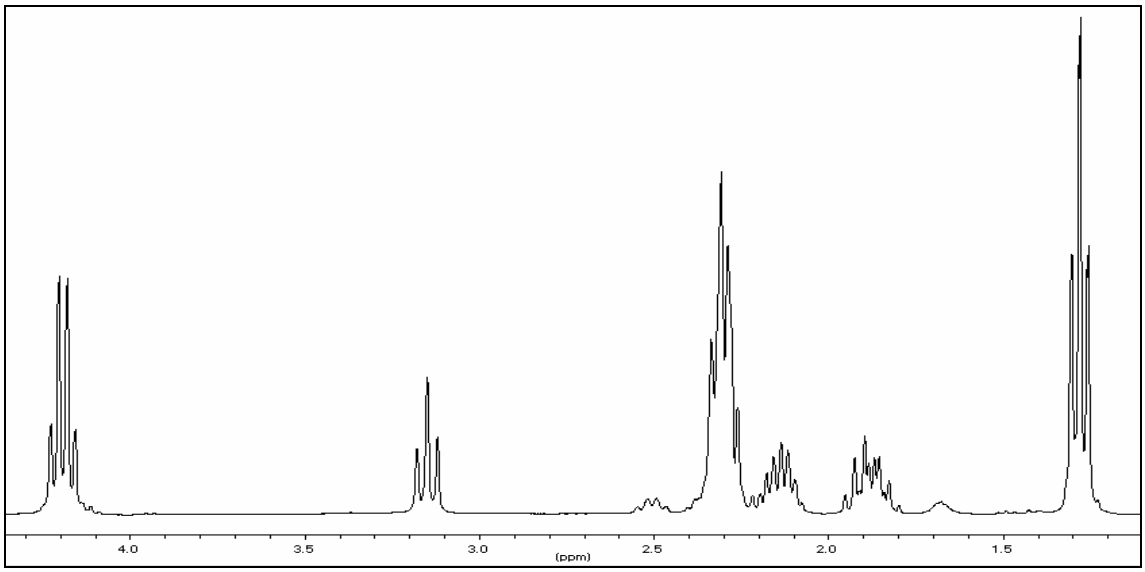
Retention time (min)	Substance	Peak area%
6.4	product (cyclopentanone-2-carboxylic acid ethyl ester)	98.7
others	unknown impurities	< 0.7 per peak

GC of the pure product

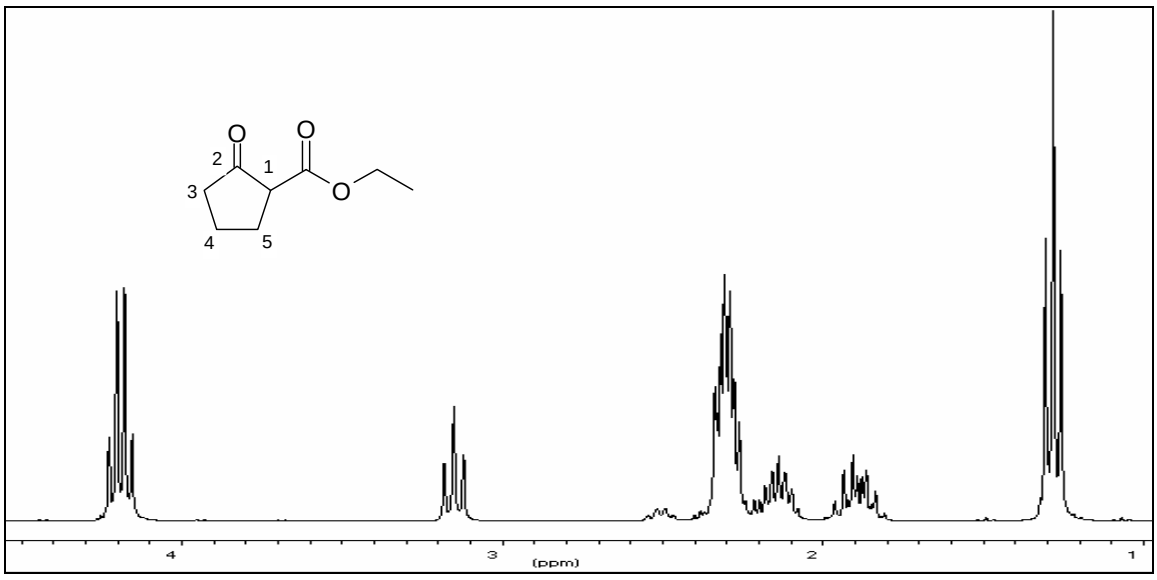


Retention time (min)	Substance	Peak area %
6.6	product (cyclopentanone-2-carboxylic acid ethyl ester)	99.7

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

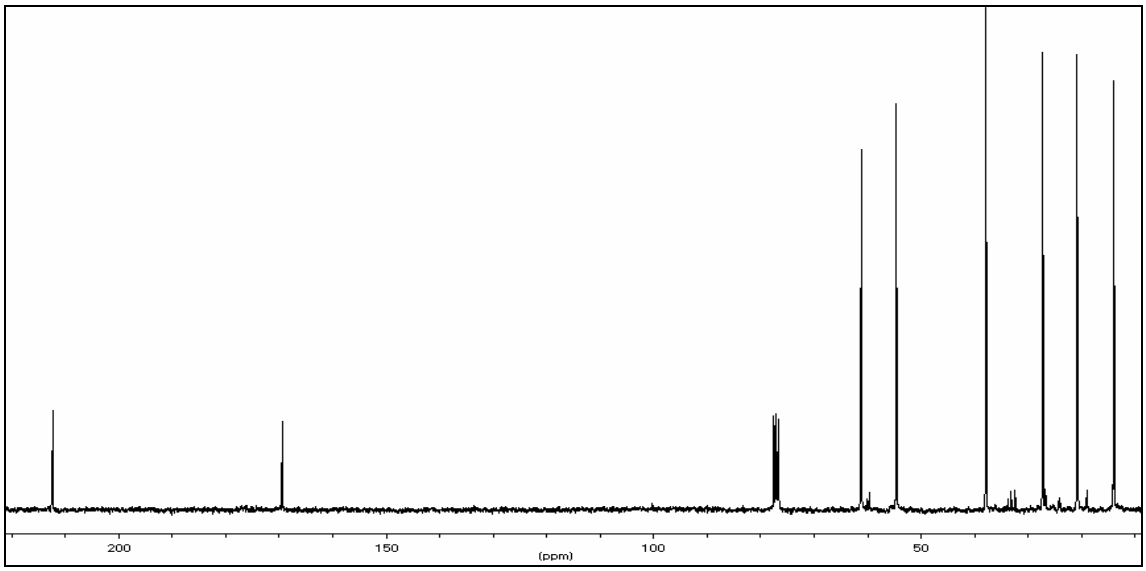


^{1}H NMR Spectrum of the pure product (300 MHz, $CDCl_3$)

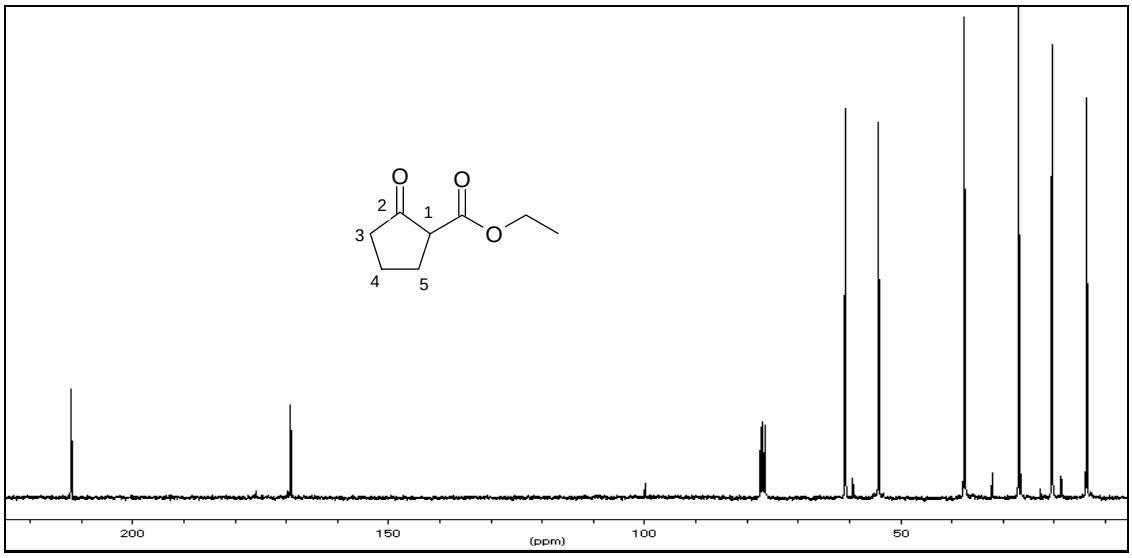


δ (ppm)	Multiplicity	Number of H	Assignment
1.28	t	3	O-$CH_2C\mathbf{H_3}$
1.84	m	1	5-H_a
2.14	m	1	5-H_b
2.25	m	4	3-H, 4-H
3.15	dd	1	1-H
4.19	q	2	O-$C\mathbf{H_2}CH_3$

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

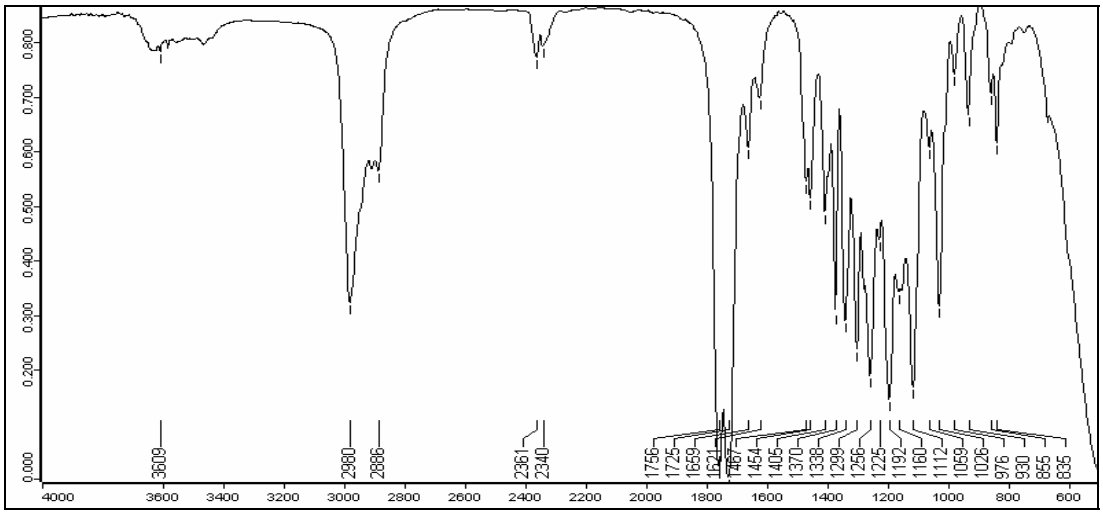


^{13}C NMR spectrum of the pure product (75.5 MHz, $CDCl_3$)



δ (ppm)	Assignment
13.8	**C**H_3
20.6	C-4
27.1	C-5
37.7	C-3
54.4	C-1
60.9	O-**C**$H_2$$CH_3$
169.1	CO-O
211.9	C-2
76.5-77.5	solvent

IR spectrum of the pure product (film)



cm^{-1}

(cm^{-1})	**Assignment**
2980, 2886	C-H-valence, alkane
1756	C=O-valence, ester
1725	C=O-valence, ketone