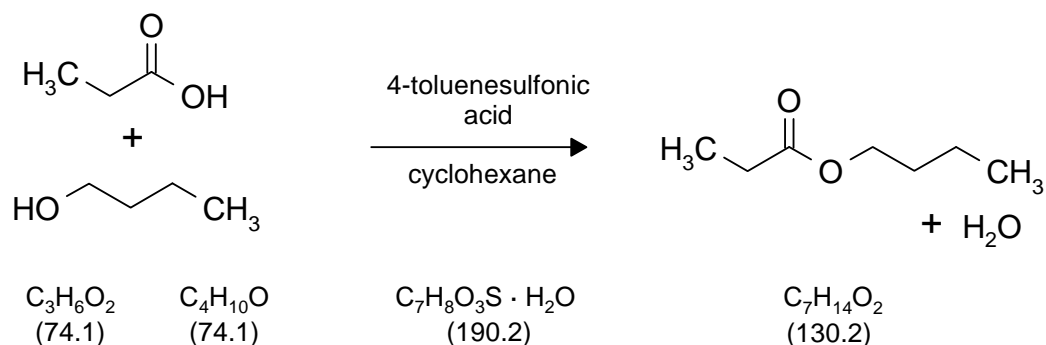


## 2008 Acid catalyzed esterification of propionic acid with 1-butanol to propionic acid 1-butyl ester



### Classification

#### Reaction types and substance classes

reaction of the carbonyl group in carboxylic acids, esterification  
 carboxylic acid, carboxylic acid ester, alcohol, acid catalyst

#### Work methods

removal of water by azeotropic distillation, shaking out, extracting, filtering, fractionating  
 column distillation, rectifying, stirring with magnetic stir bar, heating with oil bath

### Instruction (batch scale 200 mmol)

#### Equipment

500 mL round bottom flask, 50 mL round bottom flask, water separator, reflux condenser, separating funnel, heatable magnetic stirrer, magnetic stir bar, 30 cm Vigreux column with vacuum jacket (preferably NS 29/32), column head or distillation bridge, oil bath

#### Substances

propionic acid (bp 141 °C)	17.8 g (18.0 mL, 240 mmol)
1-butanol (bp 117 °C)	14.8 g (18.2 mL, 200 mmol)
4-toluenesulfonic acid monohydrate (mp 103-105 °C)	1 g (5 mmol)
cyclohexane (bp 81 °C)	180 mL
sodium hydrogen carbonate	about 10 g (für 100 mL saturated aqueous solution)
sodium chloride	etwa 7 g (für 20 mL saturated aqueous solution)
sodium sulfate for drying	about 5 g

**Reaction**

160 mL cyclohexane, 17.8 g (18.0 mL, 240 mmol) propionic acid, 14.8 g (18.2 mL, 200 mmol) 1-butanol and 1 g (5 mmol) 4-toluenesulfonic acid monohydrate are filled in a dry 500 mL round bottom flask with magnetic stir bar, water separator and reflux condenser. The mixture is heated under stirring and under reflux until no more water separates (about 1.5 hours, oil bath temperature 100-120 °C, separated volume of water 3.5 mL).

**Work up**

After cooling down the reaction solution is shaken out in a separating funnel once with 50 mL water, twice with 50 mL saturated sodium hydrogen carbonate solution each (gas development!) and once with 20 mL saturated sodium chloride solution. After drying of the organic phase over sodium sulfate the solution is filtered over a folded filter into a 500 mL round bottom flask. The drying agent is washed with 20 mL cyclohexane, which is added to the organic phase.

The solvent is distilled at normal pressure over a 30 cm Vigreux column with vacuum jacket and a column head or distillation bridge. If at a temperature of 80 C (oil bath temperature 140-160 °C) no more solvent distills over, the distillation is interrupted. In the distillation flask remains the crude product as colourless liquid.

Crude yield 21.8 g; GC-purity 90% (see analytics)

The crude product is transferred into a 50 mL round bottom flask and the fractional distillation over the column at normal pressure is continued.

Distillation protocol (example):

<b>Fraction</b>	<b>Head temperature (°C)</b>	<b>Oil bath temperature (°C)</b>	<b>Mass (g)</b>	<b>GC-purity (%)<sup>*)</sup></b>
1	Until 115	188	1.373	22.0
2	140-141	188	0.978	75.1
3	141-142	188	2.166	93.0
4	141-142	188	6.252	98.5
5	142	188	5.158	99.5
6	142-143	188	0.800	99.8
7	143	190-200	1.471	99.8

\*) Here percent product for each fraction are listed, the rest is cyclohexane.

Yield (fractions 4 - 7): 13.7 g (105 mmol, 53%); colourless liquid

Distillation residue: 2.24 g; light brown liquid

From this residue without column but over a small distillation bridge further 1.20 g (9.22 mmol, 5% ) pure product can be distilled over.

Total yield: 14.9 g (114 mmol, 57%)

**Comments**

In order to remove the excessive propionic acid the reaction solution must be thoroughly shaken out with sodium hydrogen carbonate solution during work up. Ester and acid have practically the same boiling point and can therefore not be separated through distillation.

It is important to distil the solvent carefully over a column as aforementioned, since otherwise too much product distills over together with the solvent resulting in significant losses in yield. In the first third of the cyclohexane, which is distilled over the column, 0.3% propionic acid butyl ester can be proved with GC, in the second third 0.8% and in the last third 1.3%.

**Waste management****Recycling**

The distilled cyclohexane can not be recycled since it contains even after a rectification variable amounts of propionic acid butyl ester.

**Waste disposal**

Waste	Disposal
aqueous phase from water separator	solvent water mixtures, halogen free
aqueous phase from shaking out without addition of NaCl	solvent water mixtures, halogen free
aqueous phase with addition of NaCl	solvent water mixtures, containing halogen
cyclohexane	organic solvents, halogen free
distillation residue	organic solvents, halogen free
sodium sulfate	solid waste, free from mercury

**Time**

8 hours

**Break**

After shaking out of the reaction mixture and after distillation of the solvent

**Degree of difficulty**

Easy

**Instruction (batch scale 1 mol)****Equipment**

1 L round bottom flask, 250 mL round bottom flask, water separator, reflux condenser, separating funnel, heatable magnetic stirrer, magnetic stir bar, 30 cm Vigreux column with vacuum jacket (preferably NS 29/32), column head or distillation bridge, oil bath

**Substances**

propionic acid (bp 141 °C)

88.9 g (89.8 mL, 1.20 mol)

1-butanol (bp 117 °C)	74.1 g (91.5 mL, 1.00 mol)
4-toluenesulfonic acid monohydrate (mp 103-105 °C)	5 g (26 mmol)
cyclohexane (bp 81 °C)	640 mL
sodium hydrogen carbonate	about 25 g (for 150 mL saturated aqueous solution)
sodium chloride	about 20 g (for 50 mL saturated aqueous solution)
sodium sulfate for drying	about 20 g

### Reaction

600 mL cyclohexane, 88.9 g (89.8 mL, 1.20 mol) propionic acid, 74.1 g (91.5 mL, 1.00 mol) 1-Butanol and 5 g (26 mmol) 4-Toluenesulfonic acid-mono-hydrate are filled in a dry 1 L round bottom flask with magnetic stir bar, water separator and reflux condenser. The mixture is heated under strong stirring and under reflux until no more water separates (about 3 hours, oil bath temperature 100-120 °C, separated water volume 18.8 mL).

### Work up

After cooling down the reaction solution is shaken out in a separating funnel twice with 50 mL water each, three times with 50 mL saturated sodium hydrogen carbonate solution each (gas development!) and once with 50 mL saturated sodium chloride solution. After drying of the organic phase over sodium sulfate the solution is filtered over a folded filter into a 1 L round bottom flask. The drying agent is washed with 40 mL cyclohexane, which is added to the organic phase.

The solvent is distilled at normal pressure over a 30 cm Vigreux column with vacuum jacket and a column head or distillation bridge. If at a temperature of 80 °C (oil bath temperature 140-160 °C) no more solvent distills over, the distillation is interrupted. In the distillation flask remains the crude product as colourless liquid.

Crude yield 120 g; GC-purity 90% (see analytics)

The crude product is transferred into a 250 mL round-bottom flask and the fractional distillation over the column at normal pressure is continued.

Example for distillation protocol see next page.

Yield (fractions 4 - 10): 99.0 g (760 mmol, 76%); colourless liquid

Distillation residue: 2.81 g; light brown liquid

From this residue without column but over a small distillation bridge further 1.50 g (11.5 mmol, 1.2% ) pure product can be distilled over.

Total yield: 101 g (776 mmol, 78%)

Distillation protocol (example):

Fraction	Head temperature (°C)	Oil bath temperature(°C)	Mass (g)	GC purity (%) <sup>*)</sup>
1	Until 117	160-180	6.29	66.4
2	125-135	182	5.16	67.1
3	138-142	182	6.70	94.2
4	142-143	182-185	19.25	99.5
5	143	185	16.77	99.5
6	143	185	16.49	99.6
7	143	185	17.50	99.8
8	143	185	18.48	99.9
9	143	185	7.11	99.9
10	140-143	185-200	3.40	99.9

\*) Here percent product for each fraction are listed, the rest is cyclohexane.

### Comments

In order to remove the excessive propionic acid the reaction solution must be thoroughly shaken out with sodium hydrogen carbonate solution during work up. Ester and acid have practically the same boiling point and can therefore not be separated through distillation.

It is important to distil the solvent carefully over a column as aforementioned, since otherwise too much product distills over together with the solvent resulting in significant losses in yield. In the first third of the cyclohexane, which is distilled over the column, 0.3% propionic acid butyl ester can be proved with GC, in the second third 0.8% and in the last third 1.3%.

### Waste management

#### Recycling

The distilled cyclohexane can not be recycled since it contains even after a rectification variable amounts of propionic acid butyl ester.

#### Waste disposal

Waste	Disposal
aqueous phase from water separator	solvent water mixtures, halogen free
aqueous phase from shaking out without addition of NaCl	solvent water mixtures, halogen free
aqueous phase with addition of NaCl	solvent water mixtures, containing halogen
cyclohexane	organic solvents, halogen free
distillation residue	organic solvents, halogen free
sodium sulfate	solid waste, free from mercury

### Time

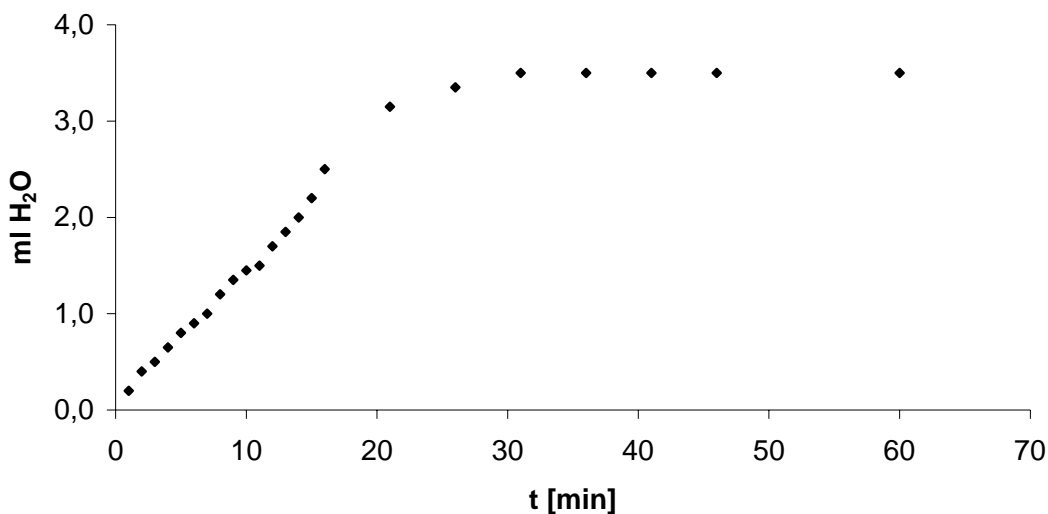
10 hours

**Break**

After shaking out of the reaction mixture and after distillation of the solvent

**Degree of difficulty**

Easy

**Analytics****Reaction monitoring through the volume of water separated during reaction****Reaction monitoring with GC**

Sample preparation:

For each sample the lab jack with the oil bath is lowered. When the reaction mixture has stopped boiling, the stirrer is switched off. Using a pipette one takes 2 mL from the reaction solution and fills it into a cooled test tube, which contains 2 mL dichloromethane. The test tube is closed immediately and cooled in an ice bath. Until measuring it is stored in the freezer. 0.1  $\mu\text{L}$  from this solution are injected

GC-conditions:

column: CP-Wax 57 CB, length 50 m, internal diameter 0.31 mm, film 1.2  $\mu\text{m}$

inlet: injector temperature 250  $^{\circ}\text{C}$ ; split injection

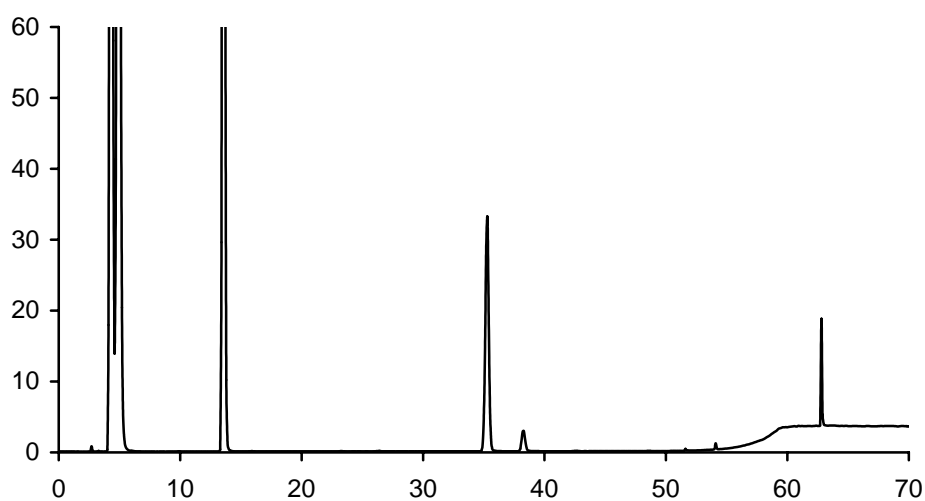
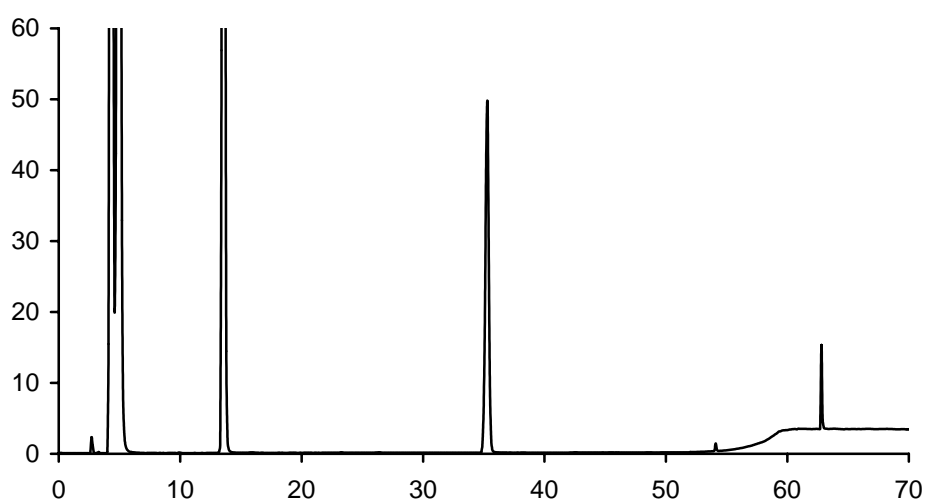
carrier gas: He, pre-column pressure 50 kPa

oven: start temperature 30  $^{\circ}\text{C}$  (8 min isotherm), 4  $^{\circ}\text{C}/\text{min}$  at 50  $^{\circ}\text{C}$  (0 min), 0.5  $^{\circ}\text{C}/\text{min}$  at 68  $^{\circ}\text{C}$  (0 min), 10  $^{\circ}\text{C}/\text{min}$  at 170  $^{\circ}\text{C}$  (up to 20 min)

detector: FID, 300  $^{\circ}\text{C}$ , gas H<sub>2</sub> 93 mL/min; synth. air 300 mL/min

integration: integrator 4290 (Thermo Separation Products)

Percent concentration was calculated from peak areas.

**GC of the reaction solution (20 minutes after beginning of the water separation)****GC of the reaction solution (90 minutes after beginning of the water separation)**

Retention time (min)	Substance	Peak area %	
		Sample after 20 min	Sample after 90 min
35.3	propionic acid butyl ester	81.3	93.5
38.3	1-butanol	7.4	0.0
62.8	propionic acid	11.3	6.5

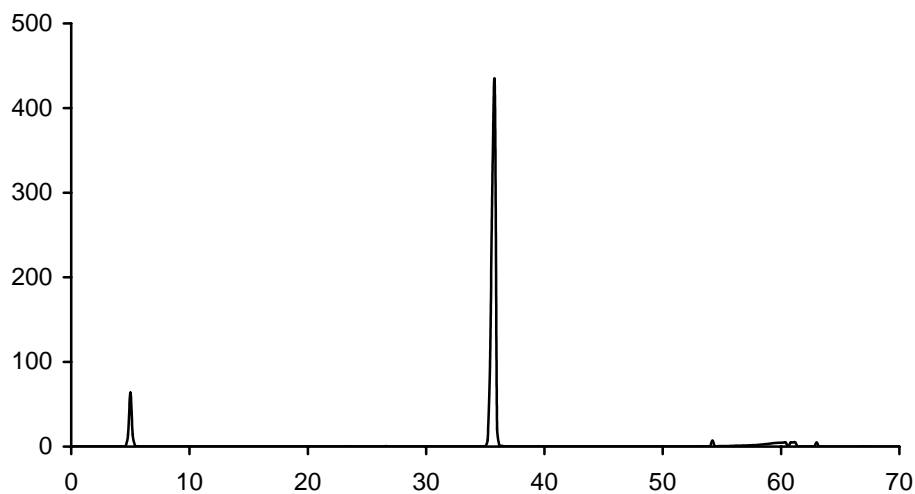
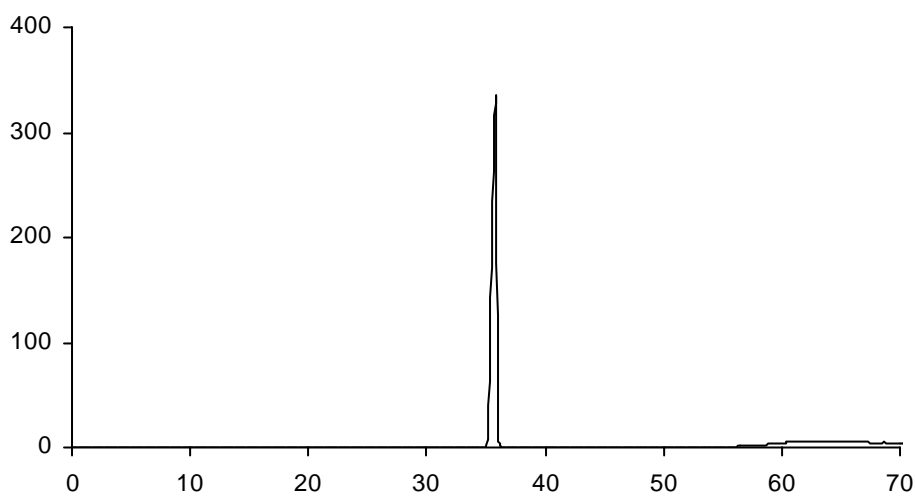
For calculation of peak area percent only the three reaction components are taken in account, not the solvent peaks in the left half of the chromatograms

**GC of the product**

Sample preparation:

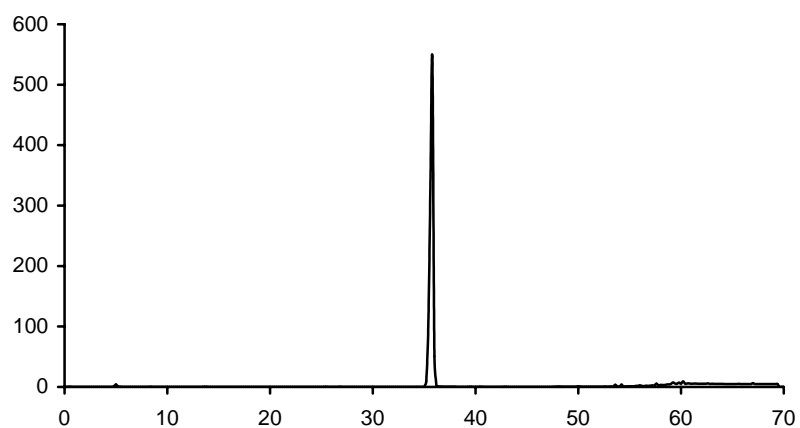
The product samples are injected without addition of solvent. Injected volume: 0.05  $\mu\text{L}$ .

GC-conditions as described for the reaction monitoring.

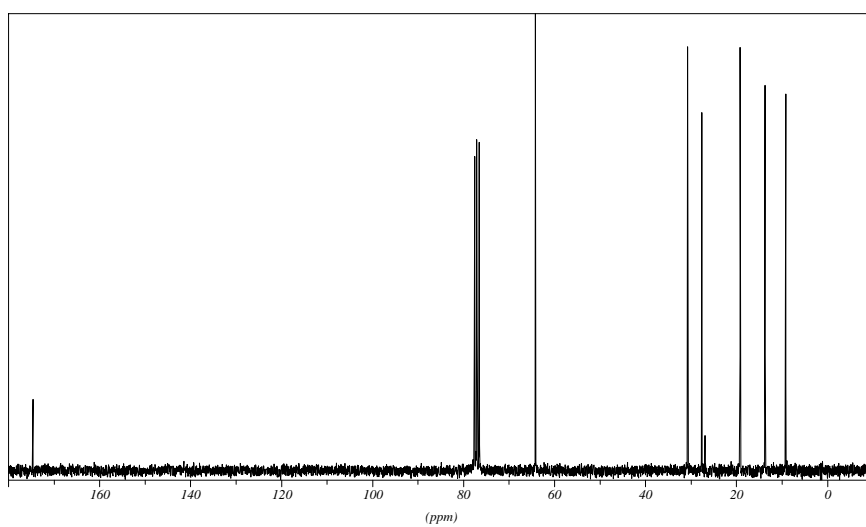
**GC of the crude product****GC of the pure product**

Retention time(min)	Substance	Peak area %	
		Crude product	Pure product
4.99	cyclohexane	9.9	0.0
35.8	propionic acid butyl ester	90.1	99.9

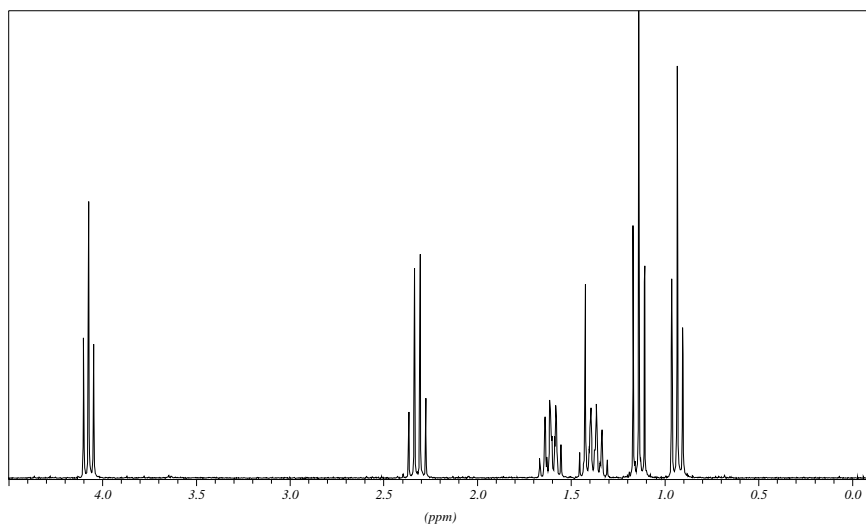
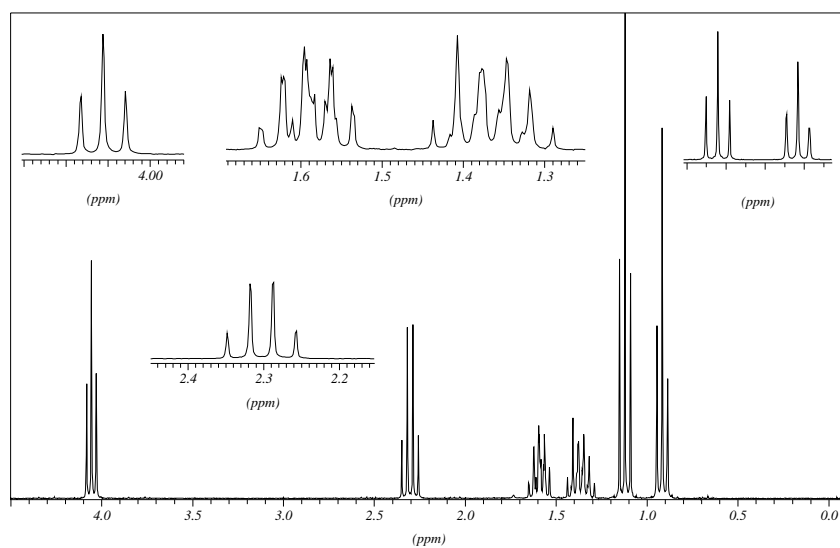


**GC of the distillation residue**

Retention time (min)	Substance	Peak area %
35.8	propionic acid butyl ester	96.4
	not identified	3.6

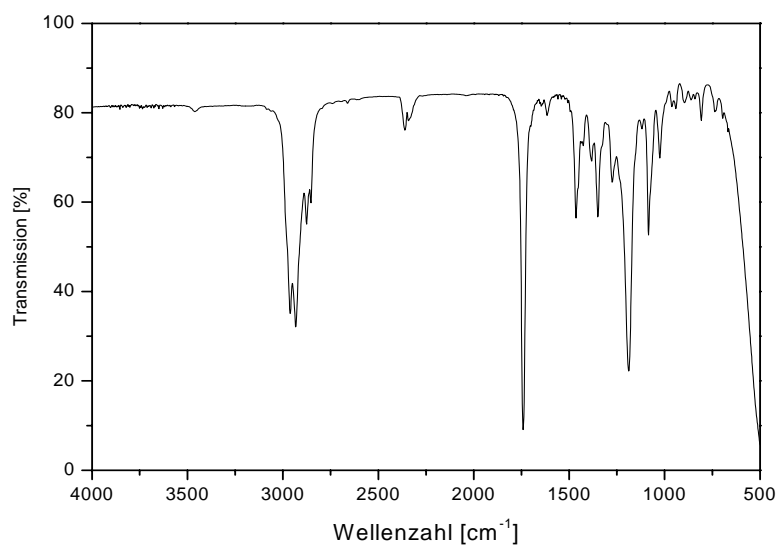
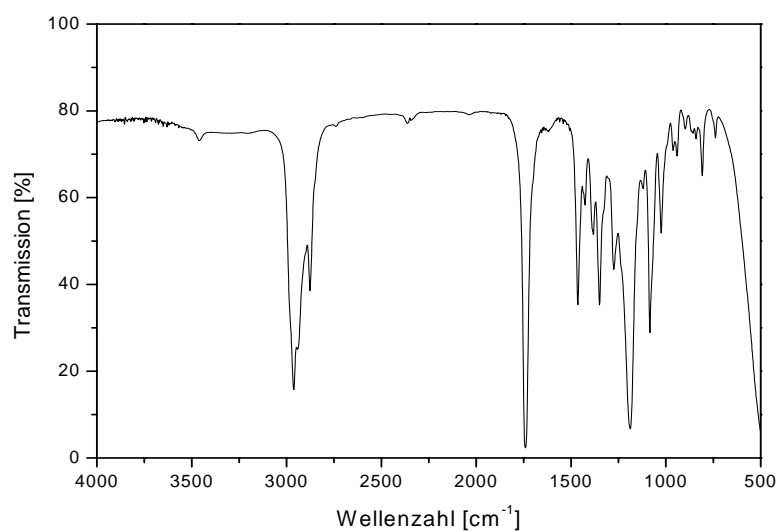
**<sup>13</sup>C NMR spectrum of the pure product (250 MHz, CDCl<sub>3</sub>)**

$\delta$ (ppm)	Assignment
9.2	CH <sub>3</sub> – CH <sub>2</sub> – CO – O –
13.7	CH <sub>3</sub> – CH <sub>2</sub> – CH <sub>2</sub> – CH <sub>2</sub> – O –
19.1	CH <sub>3</sub> – CH <sub>2</sub> – CH <sub>2</sub> – CH <sub>2</sub> – O –
27.6	– CH <sub>2</sub> – CO – O –
30.7	– CH <sub>2</sub> – CH <sub>2</sub> – O – CO –
64.2	– CH <sub>2</sub> – O – CO – CH <sub>2</sub>
174.6	– CO – O – CH <sub>2</sub> –
26.9	CH <sub>2</sub> cyclohexane
76.5-77.5	solvent

**$^1\text{H}$  NMR spectrum of the crude product (250 MHz,  $\text{CDCl}_3$ )** **$^1\text{H}$  NMR spectrum of the pure product (250 MHz,  $\text{CDCl}_3$ )**

$\delta$ (ppm)	Multiplicity	Number of H	Assignment
0.99	t	3	$\text{CH}_3 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 -$
1.13	t	3	$\text{CH}_3 - \text{CH}_2 - \text{CO} -$
1.38	m	2	$\text{CH}_3 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 -$
1.60	m	2	$\text{CH}_3 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 -$
2.31	q	2	$\text{CH}_3 - \text{CH}_2 - \text{CO} -$
4.06	t	2	$-\text{CH}_2 - \text{O} -$

The signal at 1.42 ppm in the crude product comes from cyclohexane.

**IR spectrum of the crude product (film)****IR-spectrum of the pure product (film)**

(cm <sup>-1</sup> )	Assignment
2962, 2876	C - H - valence, alkane
1741	C = O - valence, ester