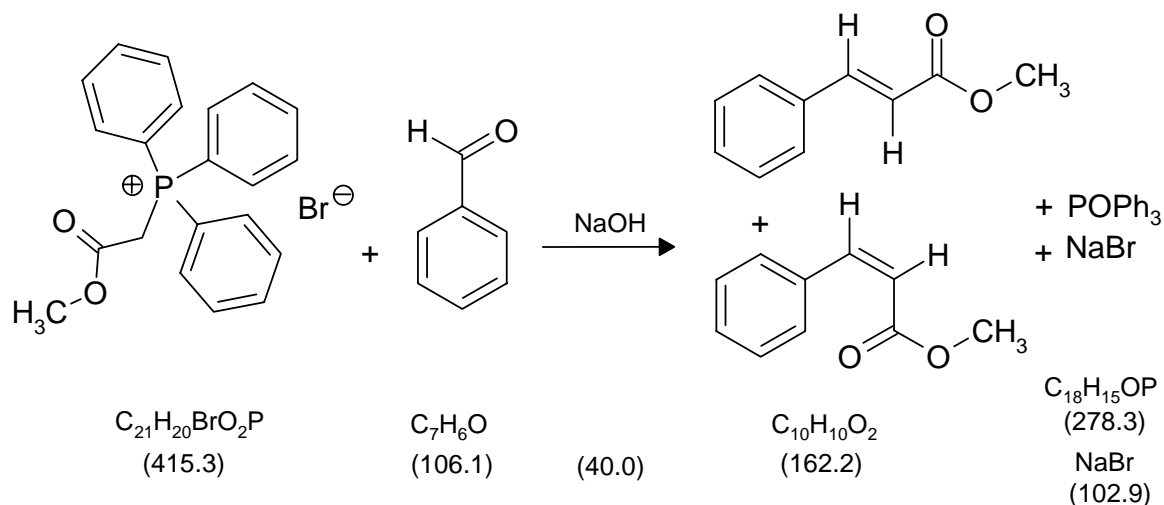


2030 Reaction of (carbomethoxymethyl)triphenylphosphonium bromide with benzaldehyde



Classification

Reaction types and substance classes

reaction of the carbonyl group in aldehydes, alkene synthesis, Wittig reaction
phosphororganic compound, phosphonium salt, aldehyde, alkene

Work methods

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

Instruction (batch scale 100 mmol)

Equipment

250 mL three-neck flask, 500 mL round bottom flask, heatable magnetic stirrer, magnetic stir bar, internal thermometer, reflux condenser, addition funnel with pressure balance, separating funnel, suction flask, glass frit (125 mL, porosity 3), 100 mL round bottom flask, distillation apparatus, rotary evaporator, vacuum pump, oil bath

Substances

benzaldehyde (freshly distilled) (bp 179 °C)	10.6 g (10.1 mL, 100 mmol)
(carbomethoxymethyl)triphenylphosphonium bromide (mp 154-157 °C, product from NOP 2029)	41.5 g (100 mmol)
NaOH	4.1 g (103 mmol)
methanol (bp 65 °C)	150 mL
<i>n</i> -heptane (bp 98 °C)	250 mL
<i>tert</i> -butyl methyl ether	100 mL

sodium disulfite ($\text{Na}_2\text{O}_5\text{S}_2$)about 65 g (for 100 mL saturated aqueous NaHSO_3 -solution)

sodium sulfate for drying

about 5 g

Reaction

Under slight heating (30-40 °C), 4.10 g (103 mmol) NaOH are dissolved in 150 mL methanol in a 250 mL three-neck flask with reflux condenser, internal thermometer and magnetic stir bar. After cooling down to room temperature 41.5 g (100 mmol) (carbomethoxymethyl)-triphenylphosphonium bromide are added, the initially light-yellow solution changes to milky-white. Under stirring, 10.6 g (10.1 mL, 100 mmol) freshly distilled benzaldehyde are added dropwise with an addition funnel (time: 20-30 minutes); the reaction mixture becomes yellow-brown and clear, the internal temperature rises to 45 °C. Then the mixture is heated for 4 hours under reflux. The solution is kept over night at room temperature.

Work up

The reaction solution is transferred into a 500 mL round bottom flask and the methanol is completely evaporated at a rotary evaporator. 55.8 g of a brown solid remain as residue, it contains cinnamic acid methyl ester, triphenylphosphane oxide, benzaldehyde and sodium bromide (see analytics).

The residue is repeatedly digested with 50 mL *n*-heptane each:

Hereby, a glass frit (125 mL, porosity 3) with suction flask is used, which is initially not connected with a vacuum pump. The solid is suspended in the glass frit in 50 mL *n*-heptane and the suspension is stirred with a glass rod as long as the *n*-heptane drops slowly into the suction flask (about 5 minutes). The finally remaining solvent is sucked off using vacuum. The *n*-heptane solution is transferred into a 100 mL round bottom flask, the solvent is evaporated at the rotary evaporator and the amount of residue is determined. The solid in the frit is again digested with 50 mL *n*-heptane and the procedure is repeated four to five times.

Example:

Solution charge	Amount of residue (g) from <i>n</i> -heptane-solution	Property
1	13.40	colourless liquid
2	3.17	colourless liquid
3	0.508	colourless liquid
4	0.180	colourless liquid, partial solid
5	0.125	colourless solid

The liquid residues consist to about 90% of cinnamic acid methyl ester, the solid residue consists to more than 90% of triphenylphosphane oxide (see analytics).

The residues from the charges 1 to 4 are combined and processed as crude product of the reaction.

Crude yield 17.3 g; GC-purity 87%, mixture of *cis*- and *trans*-cinnamic acid methyl ester in a ratio of 32 to 68, about 5% benzaldehyde

To remove the still contained benzaldehyde, the crude product is dissolved in 100 mL *tert*-butyl methyl ether. (If thereby a small amount of a colourless crystalline substance does not dissolve, it is triphenylphosphane oxide. It is filtered off over a small glass funnel with a filter paper, washed with little *tert*-butyl methyl ether and combined with the main amount of the formed triphenylphosphane oxide). The *tert*-butyl methyl ether solution of the crude product is at least four times strongly and persistently shaken out in a separating funnel with 20 mL of a saturated sodium hydrogensulfite solution each and washed once with 20 mL water. After drying with sodium sulfate and filtering off the drying agent, the *tert*-butyl methyl ether is evaporated at the rotary evaporator. As residue remains a colourless liquid.

Yield: 14.0 g; GC-purity 97%, less than 1% benzaldehyde

This extracted crude product is fractional distilled under reduced pressure.

Distillation protocol (example):

Fraction	Yield	Bp (3.7 hPa)	GC-purity	Ratio <i>cis</i> : <i>trans</i>
1	1.00 g (6.17 mmol, 6%)	until 101 °C	95%	50 : 50
2	8.96 g (55.2 mmol, 55%);	101 °C	> 99%	35 : 65
3	1.41 g (8.69 mmol, 9%)	101-105 °C	> 99%	19 : 81

(Literature values for the boiling points of cinnamic acid methyl ester: *cis* 230-232 °C, *trans* 260 °C)

Distillation residue: 1.83 g light-yellow solid, mainly triphenylphosphane oxide (see analytics)

During the aforementioned digesting of the solvent free reaction mixture with *n*-heptane remains a brown solid residue. This consists of the couple products triphenylphosphane oxide and sodium bromide.

Total amount: 36.1 g (95% of the theoretical amount to be expected)

If the triphenylphosphane oxide is to be isolated from the mixture, the sodium bromide is extracted with water: To the solid are added 120 mL water in a beaker, the mixture is stirred for 15 minutes with a magnetic stirrer, the solid is sucked off, washed twice with 20 mL water each and sucked off until it is as dry as possible. The triphenylphosphane oxide is dried in the vacuum desiccator for some days until weight constancy.

Yield: 27.5 g (98.8 mmol, 99%); colourless solid, mp 150-153 °C (Lit. 155-158 °C)

Comments

Before distillation of the crude product the benzaldehyde contained in the crude product should be removed as completely as possible through shaking out with sodium hydrogen sulfite solution, since it otherwise is carried along in all fractions. However, it can be removed only through repeated very intensive shaking with saturated sodium hydrogen sulfite solution.

Waste management**Recycling**

Methanol, evaporated at the rotary evaporator from the reaction solution,
n-heptane, evaporated after digesting
 and *tert*-butyl methyl ether, evaporated after shaking out with NaHSO₃-solution
 are collected and redistilled.

Waste disposal

Waste	Disposal
aqueous sodium hydrogen sulfite phase from shaking out-procedures	solvent water mixtures, halogen free
aqueous NaBr containing filtrate	solvent water mixtures, containing halogen
distillation residue	solid waste, free from mercury
triphenylphosphane oxide with or without NaBr	solid waste, free from mercury
sodium sulfate	solid waste, free from mercury

Time

10 hours total; 5 hours for reaction, 5 hours for work up

Break

After heating under reflux and between all following steps

Degree of difficulty

Easy

Analytcs**GC-measurements**

GC-conditions:

column: Zebron ZB-1, length 15 m, internal diameter 0.25 mm, film 0.25 μm
 (Phenomenex, Torrance, CA, USA)
 inlet: injector temperature 280 °C; split injection; injected volume 0.1 μL
 carrier gas: H₂, pre-column pressure 150 kPa
 oven: start temperature 30 °C (2 min), 8 °C/min at 250 °C (2 min)
 detector: FID, 300 °C, H₂ 25.1 mL/min; synth. air 393 mL/min
 integration: integrator 4290 (Thermo Separation Products)

Sample preparation:

About 25 mg substance are dissolved in 0.5 mL dichloromethane.

Percent concentration was calculated from peak areas.

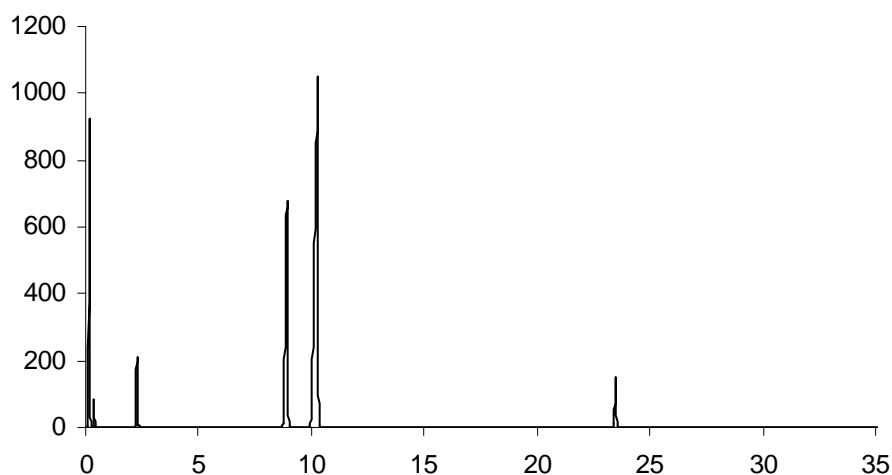
Reaction monitoring with GC

Sample preparation:

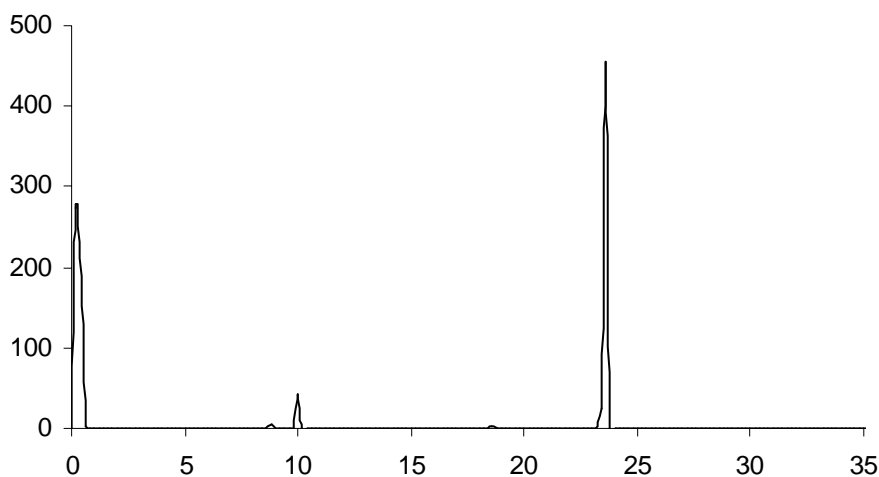
Using a Pasteur pipette, a small sample is taken from the reaction solution and stored at -15 °C until measuring. 0.1 µL from the solutions are injected.

Example measurement: Samples were taken after heating under reflux and 20 hours later (24 hours after start of the reaction). The peak areas of cinnamic acid methyl ester (mixture of isomers), triphenylphosphane oxide and benzaldehyde were identical for both measurings within the expected precision.

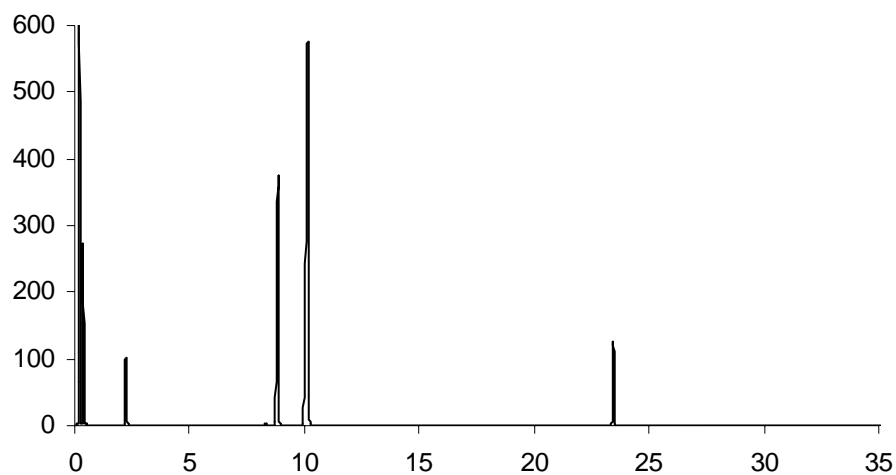
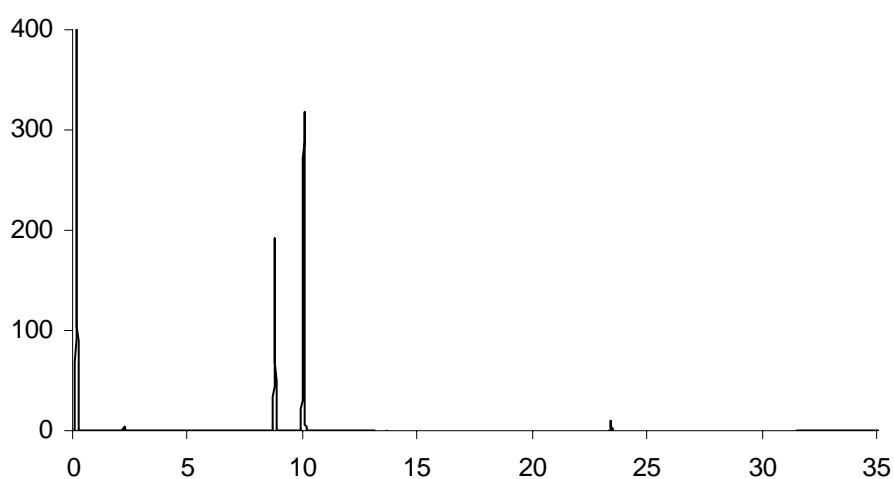
GC of the residue of the *n*-heptane solution, charge 1 (from digesting)



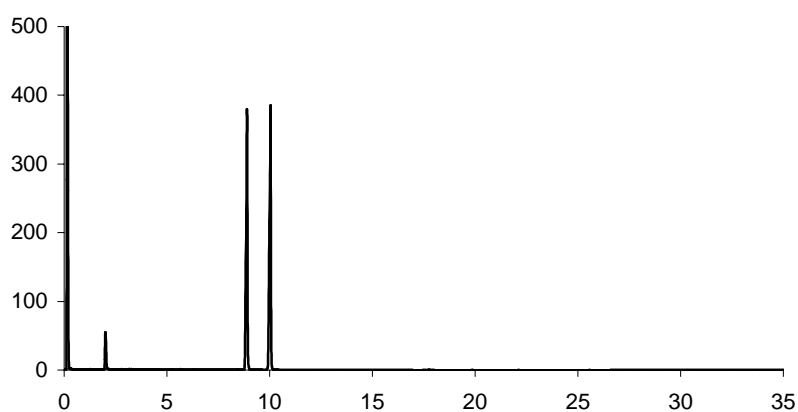
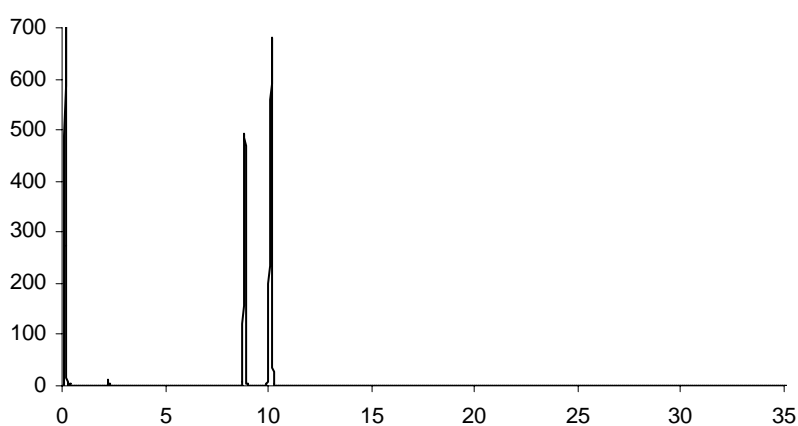
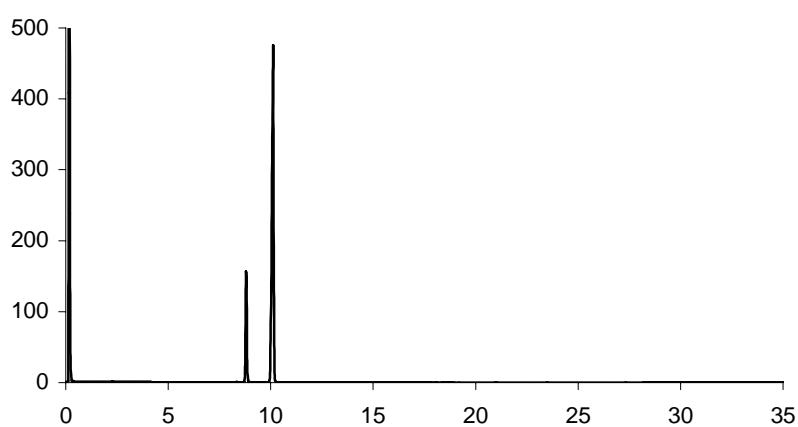
GC of the residue of the *n*-heptane solution, charge 5 (from digesting)



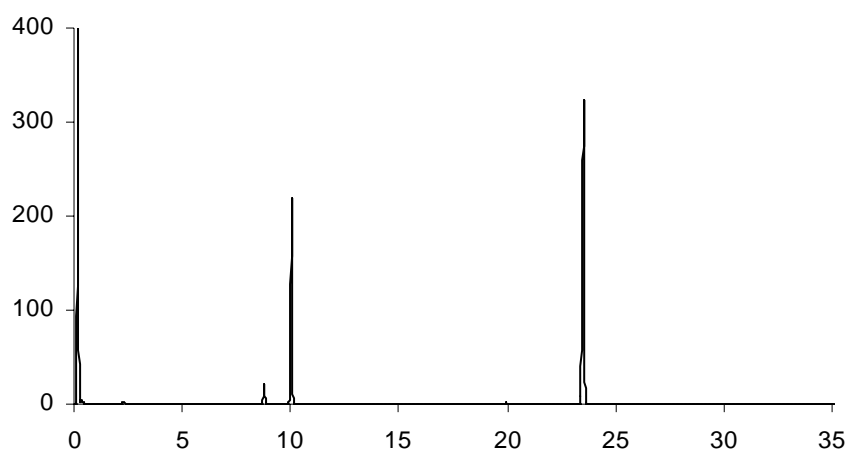
Retention time (min)	Substance	Peak area %	
		solution charge 1	solution charge 5
2.2	benzaldehyde	4.4	0.2
8.9	<i>cis</i> -cinnamic acid methyl ester	27.5	1.1
10.2	<i>trans</i> -cinnamic acid methyl ester	61.9	4.5
23.5	triphenylphosphane oxide	5.9	94.2

GC of the crude product before shaking out with NaHSO₃-solution**GC of the crude product after shaking out with NaHSO₃-solution**

Retention time(min)	Substance	Peak area %	
		before shaking out	after shaking out
2.2	benzaldehyde	5.3	0.8
8.9	<i>cis</i> -cinnamic acid methyl ester	28.0	33.0
10.2	<i>trans</i> -cinnamic acid methyl ester	58.8	64.2
23.5	triphenyl phosphane oxide	7.9	2.0

GC of the distillate (1. fraction)**GC of the distillate (2. fraction)****GC of the distillate (3. fraction)**

Retention time (min)	Substance	Peak area %		
		1. fraction	2. fraction	3. fraction
2.2	benzaldehyde	4.9	0.5	0.1
8.9	<i>cis</i> -cinnamic acid methyl ester	49.7	35.0	19.3
10.2	<i>trans</i> -cinnamic acid methyl ester	50.3	64.5	80.6

GC of the distillation residue

Retention time (min)	Substance	Peak area %
2.2	benzaldehyde	0.1
8.9	<i>cis</i> -cinnamic acid methyl ester	3.1
10.2	<i>trans</i> -cinnamic acid methyl ester	32.8
23.5	triphenylphosphane oxide	64.0

Monitoring of digesting with *n*-heptane with TLC

TLC-conditions:

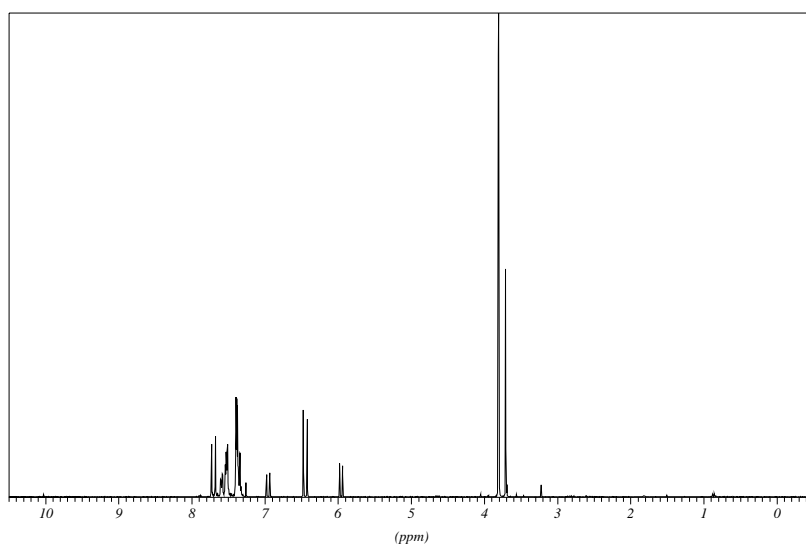
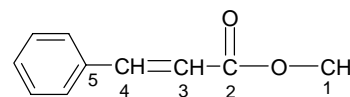
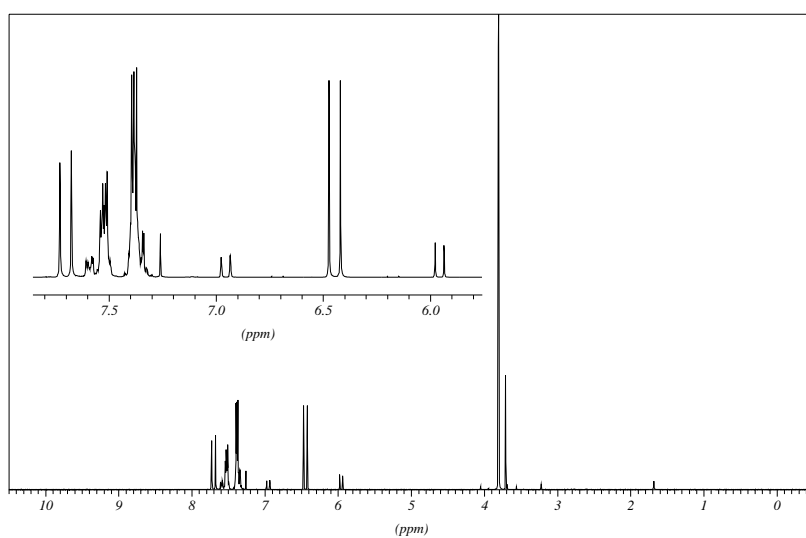
adsorbant: TLC-aluminium foil (silica gel 60), F₂₅₄eluent: acetic acid ethyl ester/*n*-heptane 1 : 9

visualizing: UV-lamp

R _f	Substance
0.44	cinnamic acid methyl ester
0.44	benzaldehyde
0.70	triphenylphosphane (is not expected to be present in these solutions)
0.09	triphenylphosphane oxide

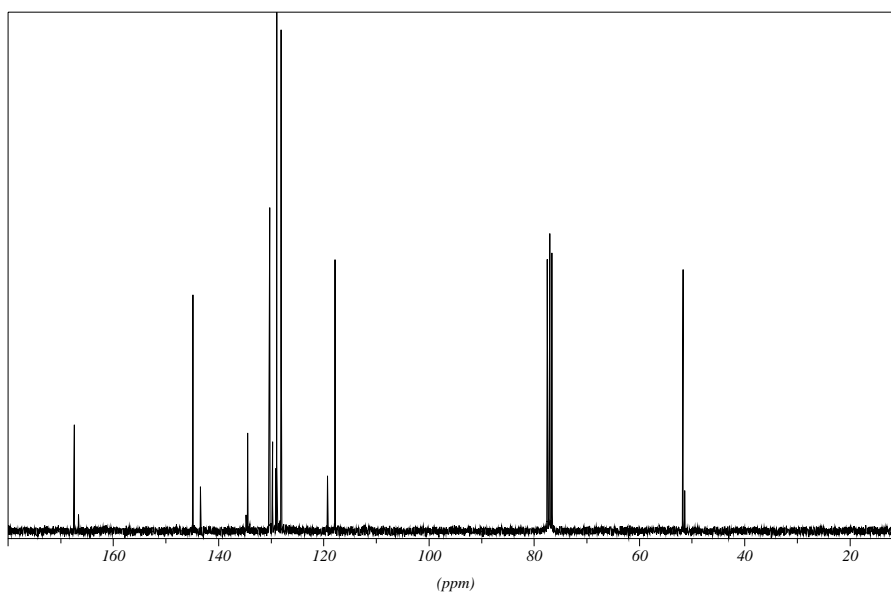
Sample preparation:

The *n*-heptane solutions obtained during digesting can be used directly for TLC

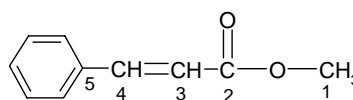
¹H NMR spectrum of the crude product (300 MHz, CDCl₃)**¹H NMR spectrum of the pure product (3. fraction of the distillation) (300 MHz, CDCl₃)**

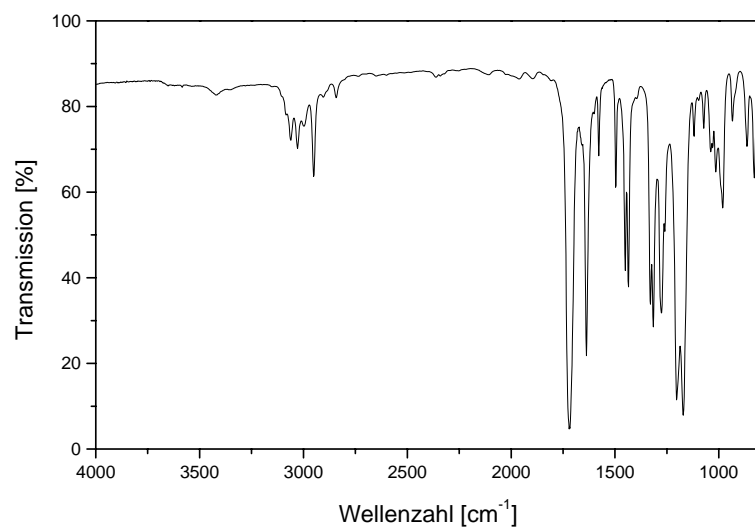
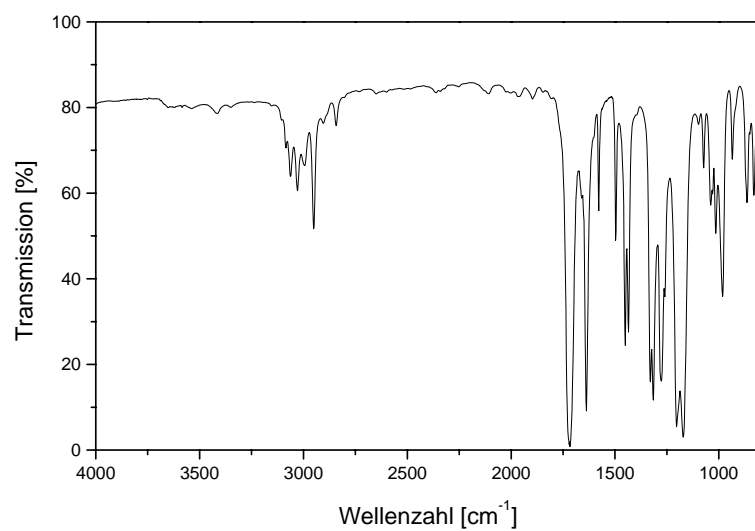
δ (ppm)	Multiplicity	Number of H	Assignment
3.71	S	3	1-H (<i>cis</i>)
3.81	S		1-H (<i>trans</i>)
5.96 ($J = 12.6$)	D	1	3-H (<i>cis</i>)
6.45 ($J = 16.0$)	d		3-H (<i>trans</i>)
6.96 ($J = 12.6$)	d	1	4-H (<i>cis</i>)
7.71 ($J = 16.0$)	d		4-H (<i>trans</i>)
7.30-7.60	m	5	arene-H
7.26			solvent

The integration of the signals leads to an isomer ratio *cis* : *trans* of 17 : 83.

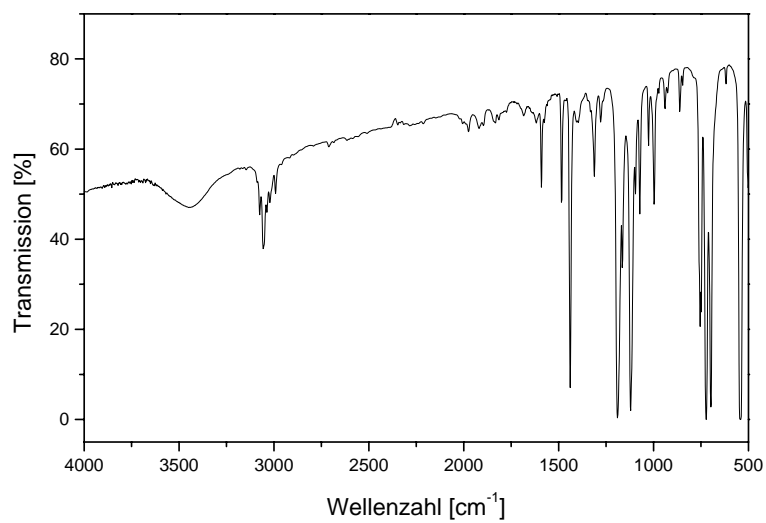
^{13}C NMR spectrum of the pure product (3. fraction of the distillation) (300 MHz, CDCl_3)

δ (ppm)	Assignment (<i>cis + trans</i>)
51.36 51.69	C-1
117.80 119.28	C-3
128.03 128.07 128.88 129.08 129.71 130.29	C arene, others than C-5
134.39 134.76	C-5
143.39 144.86	C-4
166.48 167.41	C-2
76.5-77.5	solvent



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

(cm ⁻¹)	Assignment
3050, 3030	C – H – valence, arene and alkane
2950, 2850	C – H – valence, alkane
1720	C = O – valence, ester
1640	C = C – valence, alkene
1580, 1495	C = C – valence, arene

IR-spectrum of the isolated triphenylphosphane oxide (KBr)

(cm ⁻¹)	Assignment
3055	C – H – valence, arene
1585, 1485	C = C – valence, arene
1440	P – phenyl