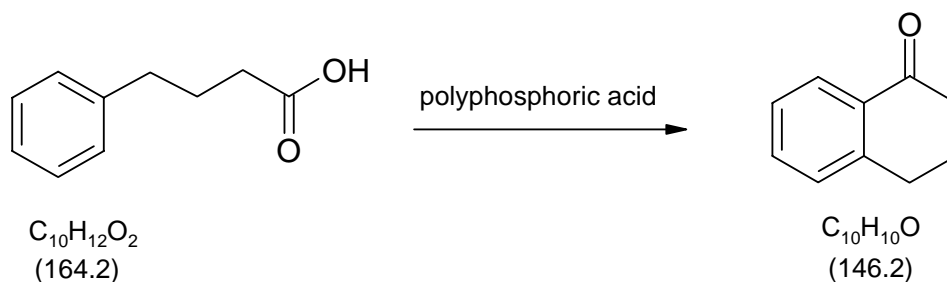


1009 Intramolecular acylation of 4-phenylbutyric acid to 1,2,3,4-tetrahydronaphthalene-1-one (alpha-tetralone)



Classification

Reaction types and substance classes

electrophilic substitution of aromatics, ring closure reaction, Friedel-Crafts acylation, reaction of the carbonyl group in carboxylic acids
 carboxylic acid, aromatics, ketone

Work methods

extracting, shaking out, evaporating with rotary evaporator, filtering, rectifying, column distillation, distilling under reduced pressure, heating with oil bath, column chromatography

For batch scale 10 mmol:

column chromatography instead of distillation

Instruction (batch scale 100 mmol)

Equipment

500 mL wide-neck Erlenmeyer flask, glass rod, internal thermometer, heating plate, 1L separating funnel, rotary evaporator, 20 cm Vigreux column, distillation apparatus or vacuum column head, vacuum pump, oil bath

Substances

4-phenylbutyric acid (mp 49-51 °C)	16.4 g (100 mmol)
polyphosphoric acid (83% P ₂ O ₅)	110 g
<i>tert</i> -butyl methyl ether (bp 55 °C)	210 mL
crunched ice	150 g
aqueous sodium hydroxide solution (5%)	30 mL
MgSO ₄ for drying	about 3 g

Reaction

A 500 mL wide-neck Erlenmeyer flask is fixed with a clamp above an oil bath which is positioned on a heating plate and an adjustable laboratory jack, so that through height adjustment of the lab jack the flask can optionally either be heated or not. In the Erlenmeyer flask 60 g polyphosphoric acid are heated in an oil bath to 90 °C (bath temperature about 100 °C), so that the polyphosphoric acid liquefies. 16.4 g (100 mmol) 4-phenylbutyric acid are liquefied in a beaker through heating to about 70 °C, then the liquid is added at once to the polyphosphoric acid under stirring with a glass rod. The oil bath level is lowered, so that the Erlenmeyer flask is no longer dipping in. The reaction mixture is stirred for further 3 minutes with the glass rod whilst its internal temperature should be kept at 90° C. Further 50 g polyphosphoric acid are added, the reaction flask is dipped again into the hot oil bath (bath temperature 100°C) and the strong stirring with the glass rod is continued for 4 minutes. The oil bath level is lowered again and the reaction mixture cooled down to 60°C, then 150 g crunched ice are added and stirring is continued until the polyphosphoric acid is completely hydrolysed and a yellow oil precipitates.

Work up

The whole mixture is transferred into a 1 L separating funnel and extracted three times with 70 mL *tert*-butyl methyl ether each. The combined organic phases are initially washed once with 50 mL water, then once with 30 mL of a 5% aqueous NaOH solution and finally with 50 mL water. If the washing water is not neutral, washing is continued with 30 mL water each until neutral reaction. The organic phase is dried over MgSO₄. After filtering off the drying agent the solvent is evaporated at a rotary evaporator. An oil remains as crude product.

Crude yield: 13.8 g

The crude product is fractional distilled under reduced pressure over a 20 cm Vigreux column. Yield: 12.6 g (86.2 mmol, 86%); bp 135-137 °C (20 hPa) or 105-107 °C (1.7 hPa); colourless liquid; $n_D^{20} = 1.5685$

Waste management**Recycling**

The evaporated *tert*-butyl methyl ether is collected and redistilled.

Waste disposal

Waste	Disposal
aqueous phases	neutralize, then: solvent water mixtures, halogen free
distillation residue	organic solvents, halogen free
magnesium sulfate	solid waste, free from mercury

Time

3 hours

Break

Before evaporation of the solvent and before distillation

Degree of difficulty

Easy

Instruction (batch scale 10 mmol)**Equipment**

250 mL wide-neck Erlenmeyer flask, glass rod, internal thermometer, heating plate, 250 mL separating funnel, rotary evaporator, chromatography column (length 60 cm, diameter 4 cm), oil bath

Substances

4-phenylbutyric acid (mp 49-51 °C)	1.64 g (10 mmol)
polyphosphoric acid (83% P ₂ O ₅)	11 g
<i>tert</i> -butyl methyl ether (bp 55 °C)	30 mL
crunched ice	30 g
aqueous sodium hydroxide solution (5%)	5 mL
MgSO ₄ for drying	about 1g
silica gel 60 for column chromatography	
<i>n</i> -heptane: acetic acid ethyl ester = 9:1 (elution solvent)	about 4 L

Reaction

A 250 mL wide-neck Erlenmeyer flask is fixed with a clamp above an oil bath which is positioned on a heating plate and an adjustable laboratory jack, so that through height adjustment of the lab jack the flask can optionally either be heated or not. In the Erlenmeyer flask 6.0 g polyphosphoric acid are heated in an oil bath to 90 °C (bath temperature about 100 °C), so that the polyphosphoric acid liquefies. 1.64 g (10.0 mmol) 4-phenylbutyric acid are liquefied in a beaker through heating to about 70 °C, then the liquid is added at once to the polyphosphoric acid under stirring with a glass rod. The oil bath level is lowered, so that the Erlenmeyer flask is no longer dipping in. The reaction mixture is stirred for further 3 minutes with the glass rod whilst its internal temperature should be kept at 90° C. Further 5.0 g polyphosphoric acid are added, the reaction flask is dipped again into the hot oil bath (bath temperature 100°C) and the strong stirring with the glass rod is continued for 4 minutes. The oil bath level is lowered again and the reaction mixture cooled down to 60°C, then 30 g crunched ice are added and stirring is continued until the polyphosphoric acid is completely hydrolysed and a yellow oil precipitates.

Work up

The whole mixture is transferred into a 250 mL separating funnel and extracted three times with 10 mL *tert*-butyl methyl ether each. The combined organic phases are initially washed once with 30 mL water, then once with 5 mL of a 5% aqueous NaOH solution and finally with 20 mL water. If the washing water is not neutral, washing is continued with 20 mL water each until neutral reaction. The organic phase is dried over MgSO₄. After filtering off the drying agent the solvent is evaporated at a rotary evaporator. An oil remains as crude product. Crude yield: 1.21 g

The crude product is purified through column chromatography:

The column is filled with silica gel. The substance is added on the column and eluted with about 4 L elution solvent (*n*-heptane: acetic acid ethyl ester = 9 : 1). The fractions are examined by thin-layer chromatography, the R_f -value of the product is 0.5. The product fractions are combined, the solvent is evaporated at a rotary evaporator. The product remains as colourless liquid.

Yield: 1.14 g (7.80 mmol, 78%); $n_D^{20} = 1.5685$.

Waste management

Recycling

The evaporated *tert*-butyl methyl ether is collected and redistilled.

The evaporated elution solvent is collected and redistilled; it can be used - after GC-control - for further chromatographic separations in the lab course.

Waste disposal

Waste	Disposal
aqueous phases	neutralize, then: solvent water mixtures, halogen free
magnesium sulfate	solid waste, free from mercury
silica gel from the column	solid waste, free from mercury

Time

1 day

Break

Before evaporation of the solvent and before chromatographic.

Degree of difficulty

Easy

Analytcs

TLC

TLC-conditions:

adsorbant:

Macherey and Nagel Polygram SilG/UV foils, 0.2 mm

eluent:

n-heptane : acetic acid ethyl ester 9 : 1

R_f (4-phenylbutyric acid) 0.20

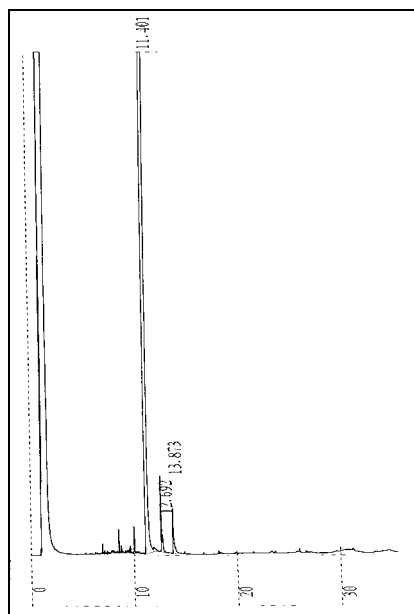
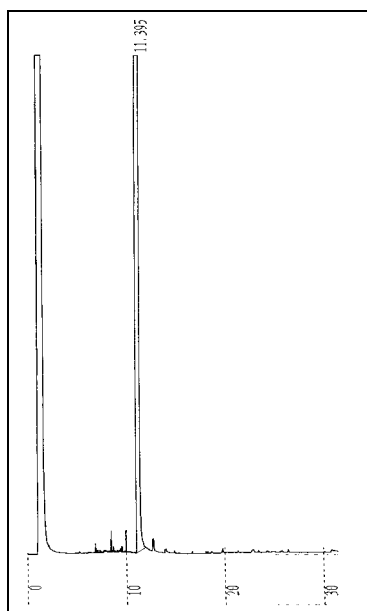
R_f (α -tetralone) 0.53

GC

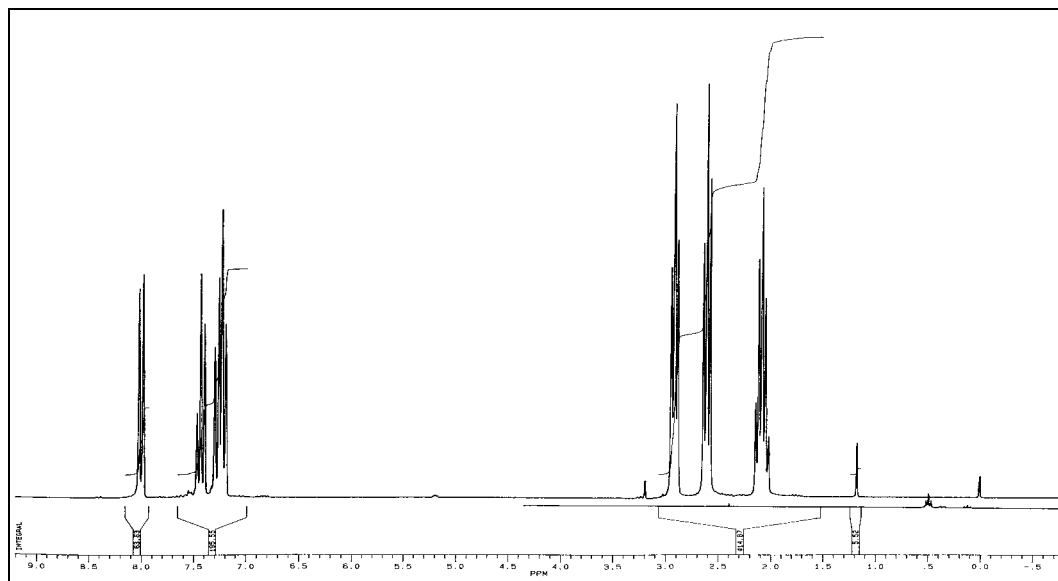
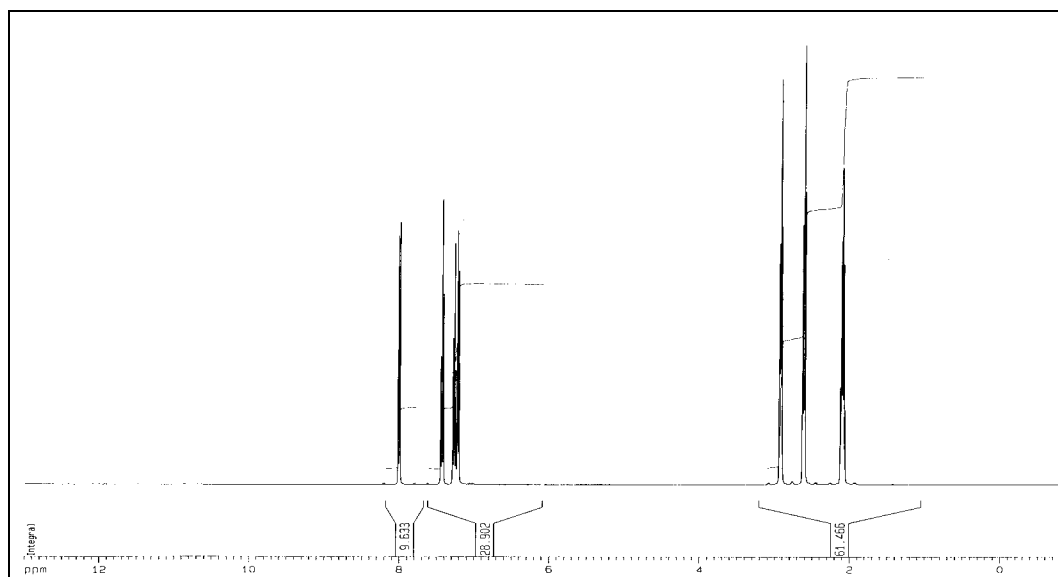
GC-conditions:

column: 5CB Low Blend/MS, length 30 m, internal diameter 0.32 mm, film 0.25 μm
 inlet: injector temperature 210 $^{\circ}\text{C}$, split injection, injected volume 1 μL
 carrier gas: H_2 , pre-column pressure 50 kPa
 oven: 60 $^{\circ}\text{C}$ (2 min), heating rate 10 $^{\circ}\text{C}/\text{min}$, isotherme 240 $^{\circ}\text{C}$ (30 min)
 detector: FID, 310 $^{\circ}\text{C}$
 integrator: Shimadzu

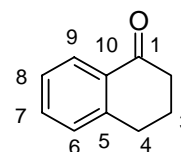
Percent concentration was calculated from peak areas.

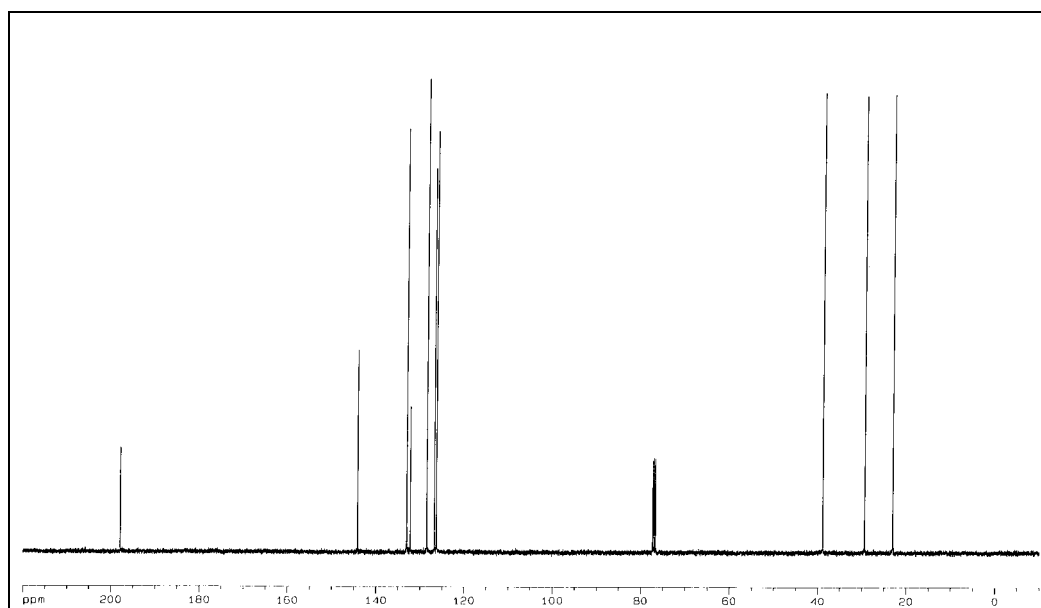
GC of the crude product**GC of the pure product**

Retention time(min)	Substance	Peak area %
11.4	product	99 (in the pure product)
others	unknown	1 (in the pure product)

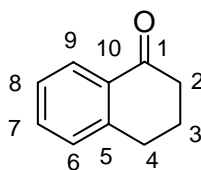
^1H NMR spectrum of the crude product (200 MHz, CDCl_3) **^1H NMR spectrum of the pure product (400 MHz, CDCl_3)**

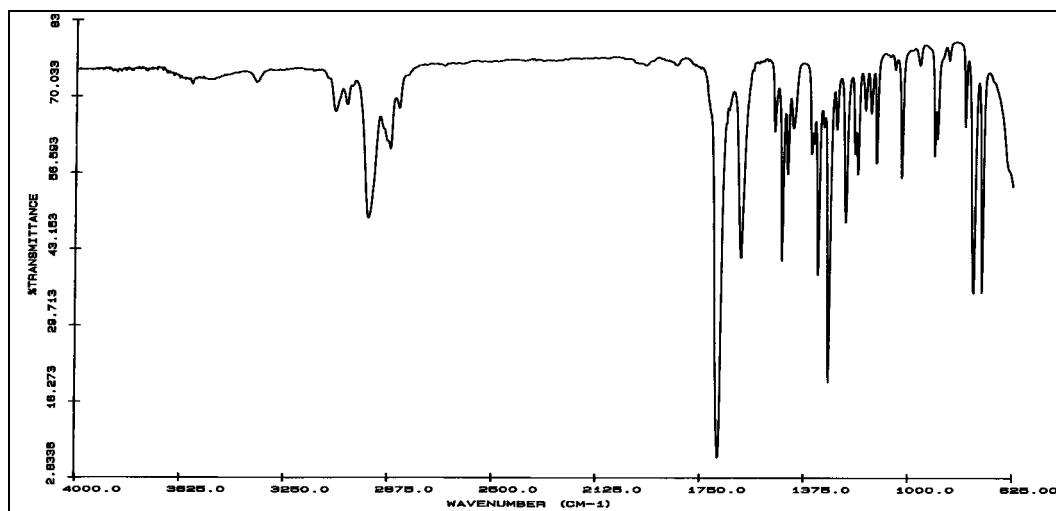
δ (ppm)	Multiplicity	Number of H	Assignment
2.06 - 2.13	m	2	3-H
2.60 - 2.63	m	2	2-H
2.91 - 2.94	m	2	4-H
7.21 - 7.28	m	1	6-H
7.41 - 7.45	m	2	7-H, 8-H
7.99 - 8.01	m	1	9-H



^{13}C NMR spectrum of the pure product (100 MHz, CDCl_3)

δ (ppm)	Assignment
23.00	C-3
29.38	C-4
38.85	C-2
126.29	C-8
126.78	C-6
128.51	C-9
132.30	C-10
133.08	C-7
144.20	C-5
197.91	C-1
76.5-77.5	solvent



IR spectrum of the pure product (KBr)

(cm ⁻¹)	Assignment
3025, 3070	-CH-valence, arene
2945, 2870, 2860	C-H-valence, alkane
1685	C=O-valence, ketone
1600	C=C-valence, arene