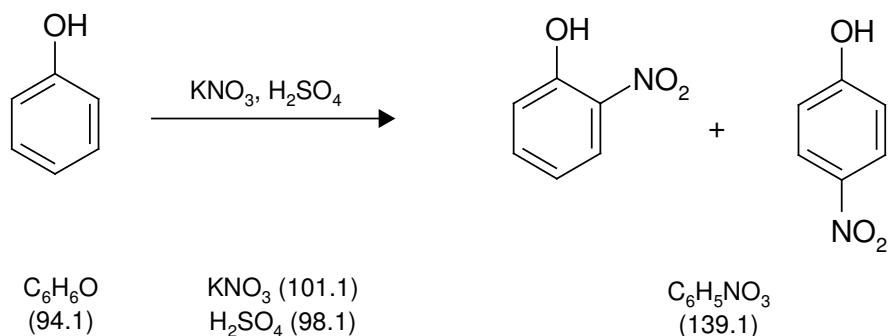


## 5001 Nitration of phenol to 2-nitrophenol and 4-nitrophenol



### Classification

#### Reaction types and substance classes

electrophilic substitution of aromatics, nitration  
 aromatics, phenol, nitroaromatics

#### Work methods

microwave-assisted reaction, stirring with magnetic stir bar, adding dropwise with an addition funnel, heating under reflux, steam distillation, extracting, shaking out, filtering, recrystallizing, draining of gases, use of an ice cooling bath

### Instruction (batch scale 270 mmol)

#### Equipment

Microwave system ETHOS 1600, glass tube (40 cm, NS 29), 500 mL Erlenmeyer flask, 500 mL three-neck flask, internal thermometer, 2 wash bottles, adapter with ground-glass joint and hose coupling, magnetic stirrer, magnetic stir bar, (cross stirrer), addition funnel with pressure balance, reflux condenser, large distillation apparatus, 250 mL round bottom flask, suction flask, Buechner funnel, desiccator, ice bath

#### Substances

phenol (mp 41 °C)	25.4 g (270 mmol)
potassium nitrate	50.0 g (495 mmol)
conc. sulphuric acid	50.6 g (27.5 mL, 495 mmol)
hydrochloric acid (0.5 M)	100 mL
aqueous sodium hydroxide solution (2 M)	250 mL
active charcoal	2 g
ice	

## Reaction

The reaction apparatus consists of a 300 mL three-neck flask with magnetic stir bar, (preferably cross stirrer), internal thermometer and addition funnel with pressure balance. To the free opening of the flask an adapter with ground-glass joint and hose coupling is attached which is connected with a draining pipe for the potentially developing nitrous fumes. The pipe is connected with an empty safety wash bottle and this with another wash bottle, containing 250 mL 2 M sodium hydroxide solution.

Initially in a 500 mL Erlenmeyer flask 25.4 g (270 mmol) phenol are dissolved as completely as possible in 100 mL water.

In the three-neck reaction flask 50.0 g (495 mmol) potassium nitrate are dissolved in 100 mL water. Under cooling in an ice bath, 50.6 g (27.5 mL, 495 mmol) conc. sulphuric acid are added. Then, at an internal temperature of 10-15 °C, the phenol-water mixture is added in small portions as follows: Each time after strong shaking of the Erlenmeyer flask, a small portion of the mixture is filled into the addition funnel and then rapidly added dropwise to the intensively stirred solution in the three-neck flask. The above indicated internal temperature (10 to 15 °C) must not be exceeded, since already at 20 °C nitrous fumes start developing.

Immediately after completion of the addition the reaction flask is taken from the ice bath, the thermometer is replaced through a temperature sensor and the apparatus is installed with a reflux condenser in the microwave system (see "Technical Instructions: Standard refluxing apparatus in the microwave system "). The gas drainage is installed on the reflux condenser. The reaction mixture is irradiated under stirring for 90 seconds with 900 W at a temperature not exceeding 60 °C and then the heated reaction mixture is stirred for further 60 seconds without microwave irradiation. Then the reaction flask is immediately cooled down to room temperature in an ice bath (about 15 minutes).

## Work up

In order to remove the excessive nitrating acid, the reaction mixture is diluted with 200 mL ice water and the aqueous phase is carefully decanted from the oil. The oil in the flask is washed three times with 50 mL water each, whereby the water is carefully decanted each time.

The isomers are separated by means of steam distillation: To the remaining oil in the reaction flask 300 mL water are added, the flask is equipped with a large distillation bridge and the receiving flask is cooled in an ice bath. The apparatus is again installed in the microwave system (see above). The distillation mixture is heated under stirring in 5 minutes with 800 W to boiling (target temperature 105 °C) and distilled at 500 W in 30 minutes.

The 2-nitrophenol, which accumulates as yellow solid in the distillate, is sucked off over a Buechner funnel and dried in the desiccator.

Yield: 9.80 g (70.5 mmol, 26%); mp 45 C

The distillation residue is cooled in the refrigerator over night to 4° C, then the precipitation is sucked off over a Buechner funnel. For recrystallization 100 mL 0.5 M hydrochloric acid are added to the solid in a 250 mL round bottom flask, 2 g active charcoal are added, then the

flask is installed with a reflux condenser in the microwave system and the mixture is shortly heated until reflux: Therefore the contents of the flask is heated in 3 minutes with 800 W from room temperature to 104 °C and the temperature is kept for 2 minutes with 500 W. The hot mixture is filtered by decanting the orange solution from the oily phase over a folded filter into an Erlenmeyer flask. For completion of the crystallization the filtrate is kept for some time in the refrigerator. The colourless needles of 4-nitrophenol are sucked off and dried in the desiccator.

Yield: 1.88 g (13.5 mmol, 5%); mp 114 °C

### Comments

The microwave treatment follows immediately after the addition of the phenol, without post-reaction time. Before the radiation procedure the mixture still contains 25% educt (see analytics). Through immediate ice cooling after the microwave treatment and a rapid removing of the excessive nitrating acid, a second nitration of the phenol can be avoided to a large extent.

As side products *p*-benzoquinone and 2,4-dinitrophenol could be detected (see analytics).

### Waste management

#### Waste disposal

Waste	Disposal
aqueous phase of the reaction mixture	solvent water mixtures, halogen free
aqueous phase of the steam distillation	solvent water mixtures, halogen free
mother liquor from recrystallization	solvent water mixtures, containing halogen
aqueous solution from the wash bottle	aqueous waste, alkaline
filtered active charcoal	solid waste, free from mercury

### Time

Nitration 30 minutes

Steam distillation about 1 hour

Recrystallization 30 minutes

### Break

After washing out of nitric acid, before the distillation (keeping the oil in the refrigerator)

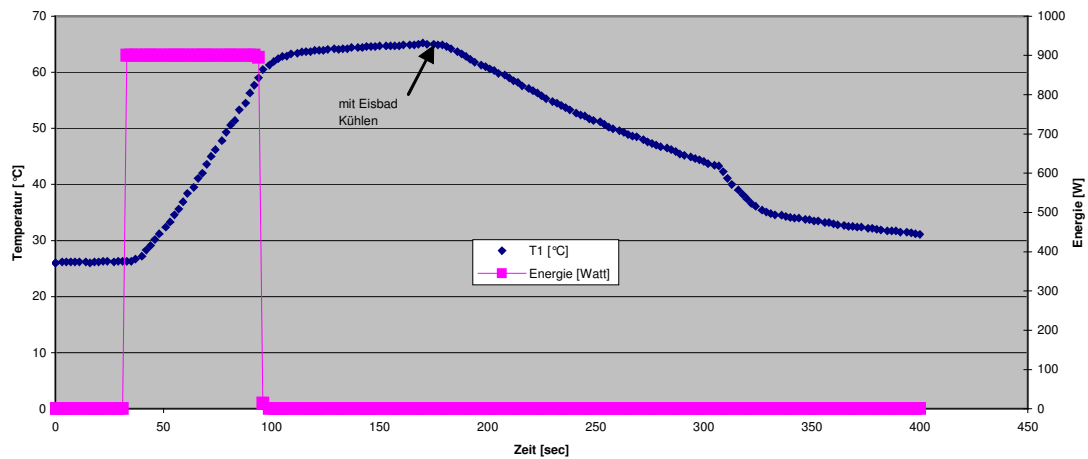
### Degree of difficulty

Medium

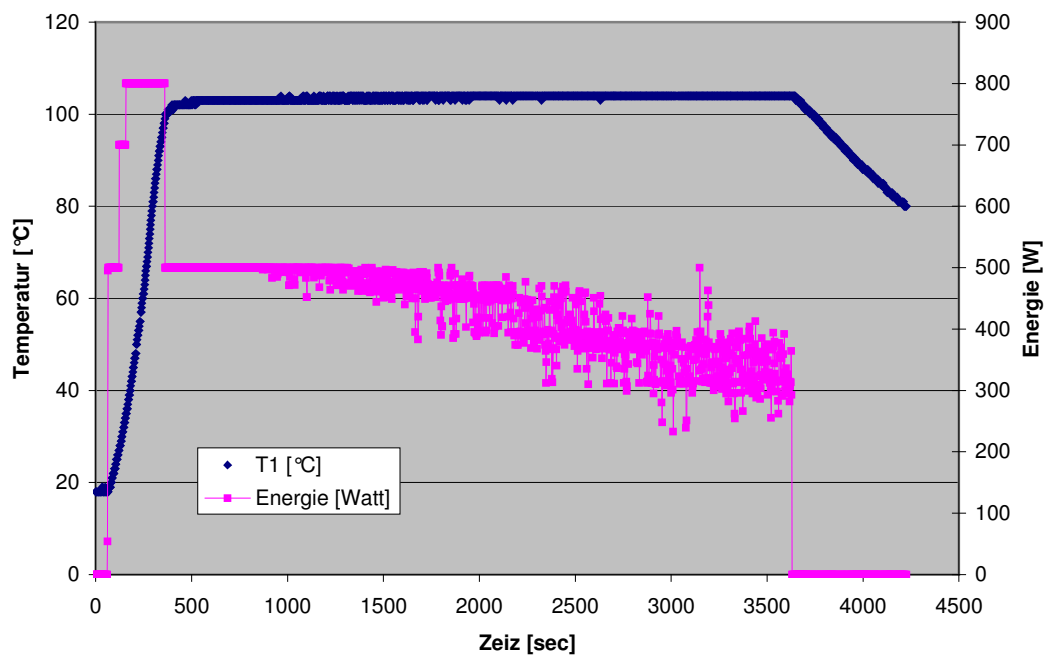
## Analytics

### Temperature-time-dependence of the working steps in the microwave field

phenol nitration in the microwave field



steam distillation of o-nitrophenol in the microwave field



### Reaction monitoring with GC

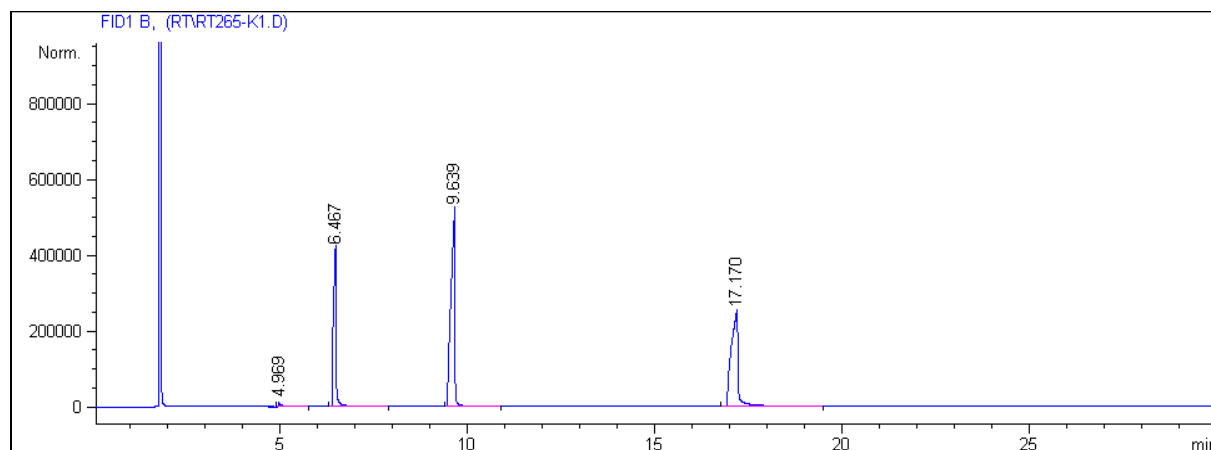
Sample preparation: Before and after the microwave treatment, a sample is taken from the oil phase and 50 mg of the sample are dissolved in 1 mL dichloromethane. 3  $\mu$ L from this solution are injected.

## GC-conditions:

column: HP-5; length 30 m, internal diameter 0.32 mm, film 0.25  $\mu\text{m}$   
 inlet: split injection 194:1  
 carriergas: H<sub>2</sub>, pre-column pressure 31 kPa  
 oven: 3 min isotherme at 50 °C, then with 8 °C/min to 320 °C  
 detector: 300 °C

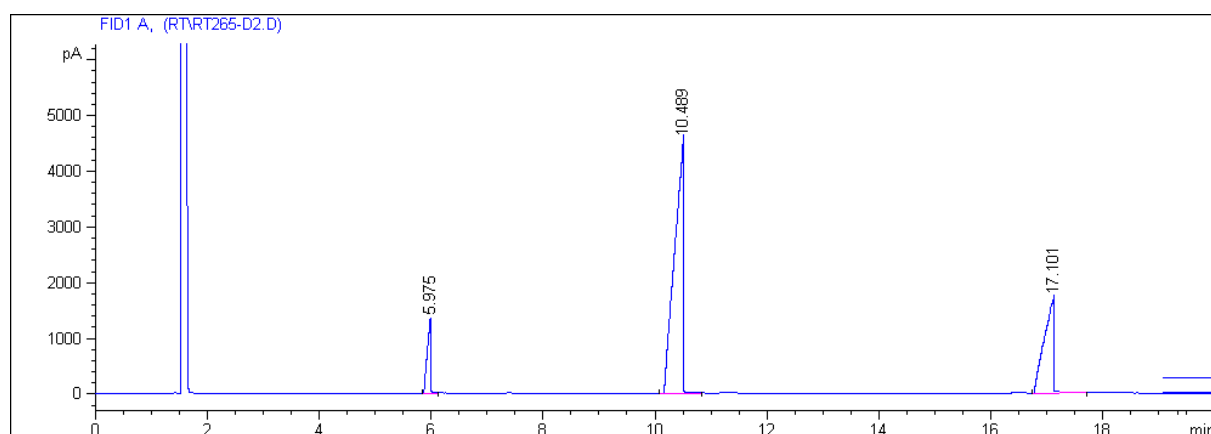
Percent concentration was calculated from peak areas.

## GC of the reaction mixture before the microwave treatment

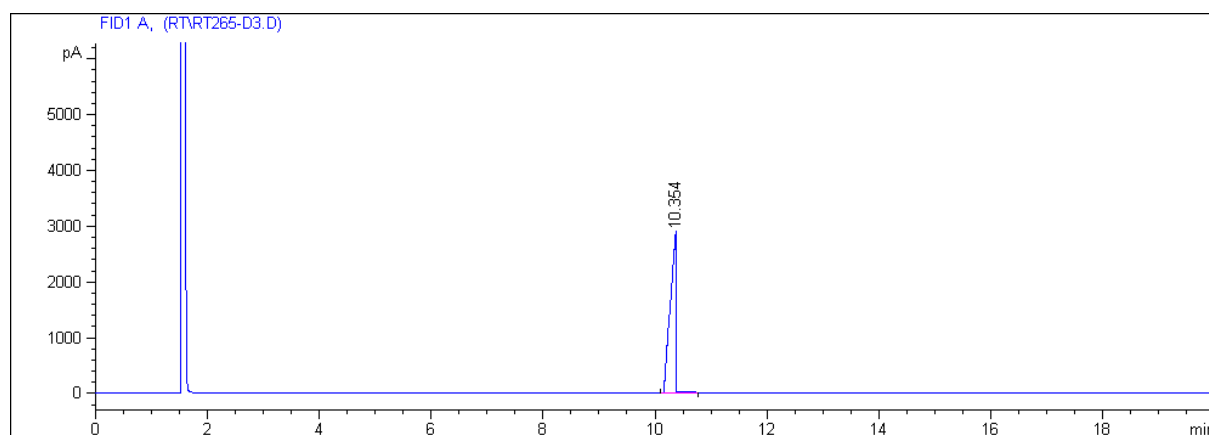


Retention time (min)	Substance	Peak area %
5.0	<i>p</i> -benzoquinone	1
6.5	phenol	25
9.6	2-nitrophenol	34
17.2	4-nitrophenol	40

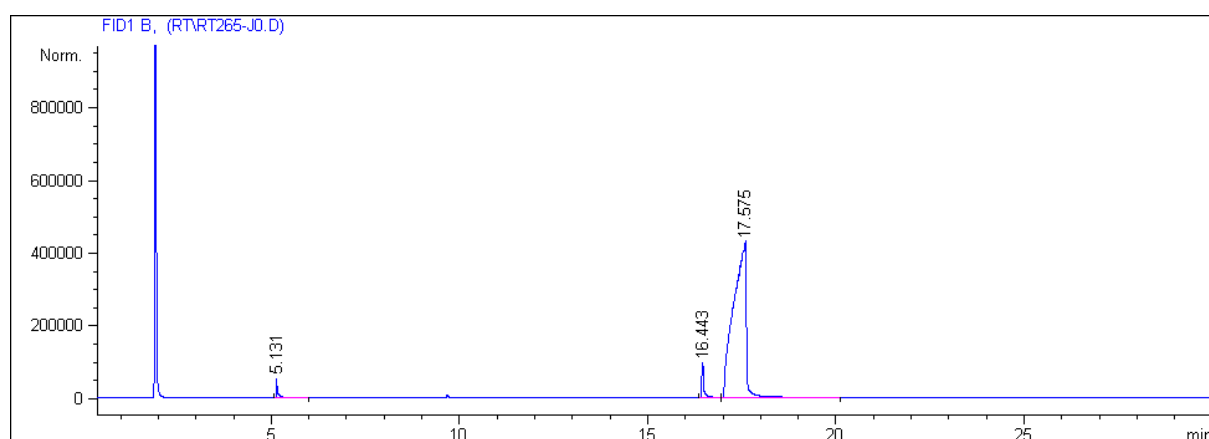
## GC of the reaction mixture after the microwave treatment



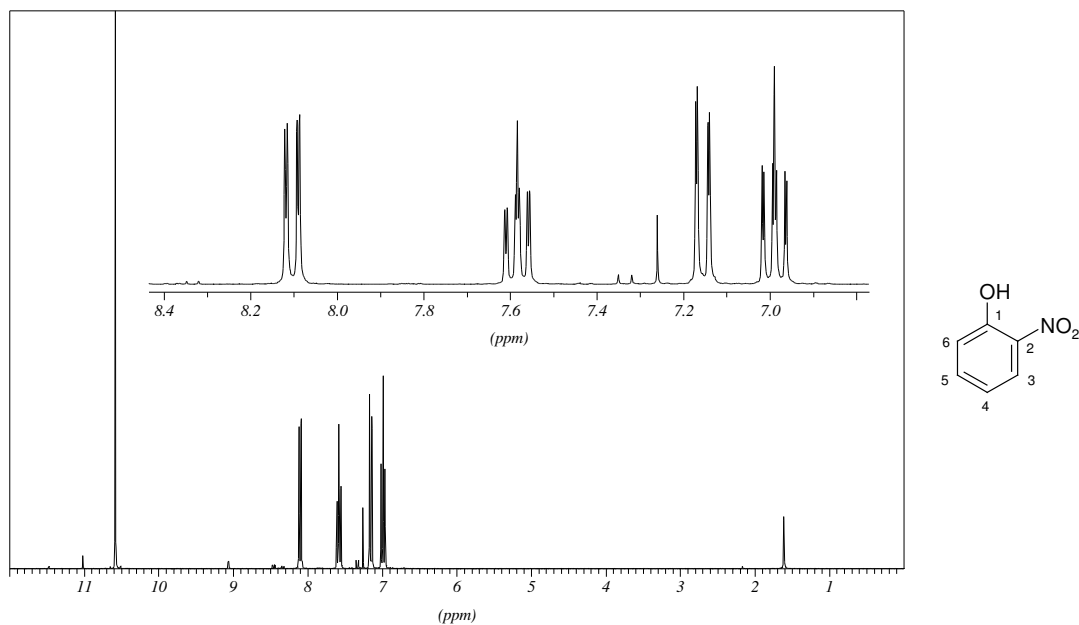
Retention time (min)	Substance	Peak area %
6.0	<i>p</i> -benzoquinone	4
10.4	2-nitrophenol	40
17.0	4-nitrophenol	56

**GC of the product 2-nitrophenol after the steam distillation**

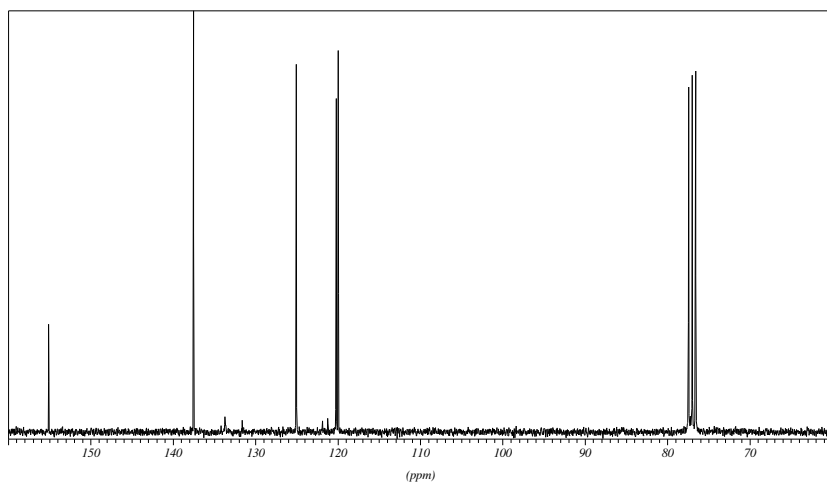
Retention time(min)	Substance	Peak area %
10.4	2-nitrophenol	> 99.5

**GC of the product 4-nitrophenol**

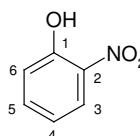
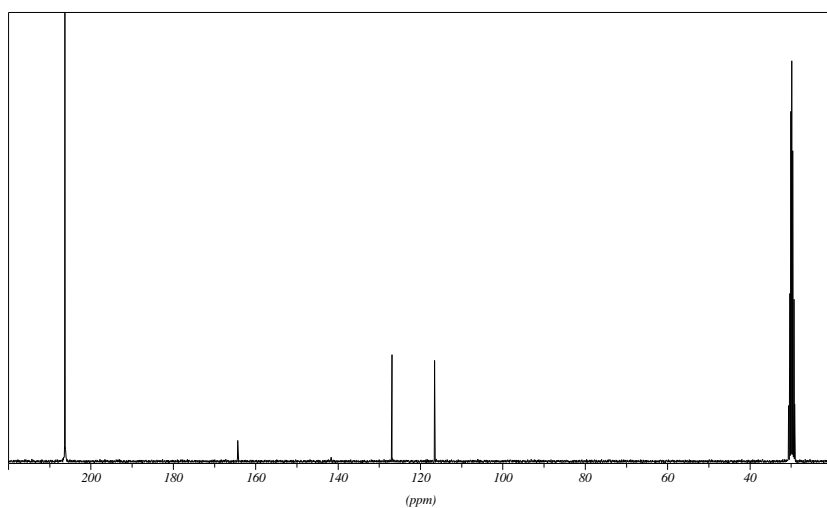
Retention time (min)	Substance	Peak area %
5.1	<i>p</i> -benzoquinone	0.3
16.4	2,4-dinitrophenol	1.1
17.6	4-nitrophenol	98.6

**<sup>1</sup>H NMR spectrum of the product 2-nitrophenol (300 MHz, CDCl<sub>3</sub>)**

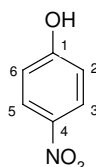
$\delta$ (ppm)	Multiplicity	Number of H	Assignment
10.58	S	1	O-H
8.10	dd, $^3J_{3,4} = 8.4$ Hz $^4J_{3,5} = 1.7$ Hz	1	3-H
7.58	dt, $^3J_{5,6} = 8.5$ Hz $^3J_{5,4} = 8.5$ Hz $^4J_{5,3} = 1.7$ Hz	1	5-H
7.15	ddd, $^3J_{6,5} = 8.5$ Hz $^4J_{6,4} = 1.5$ Hz $^5J_{6,3} = 0.4$ Hz	1	6-H
6.99	dt, $^3J_{4,3} = 8.4$ Hz $^3J_{4,5} = 8.5$ Hz $^4J_{4,6} = 1.5$ Hz	1	4-H
7.26			solvent

**$^{13}\text{C}$  NMR spectrum of the product 2-nitrophenol (300 MHz,  $\text{CDCl}_3$ )**

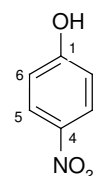
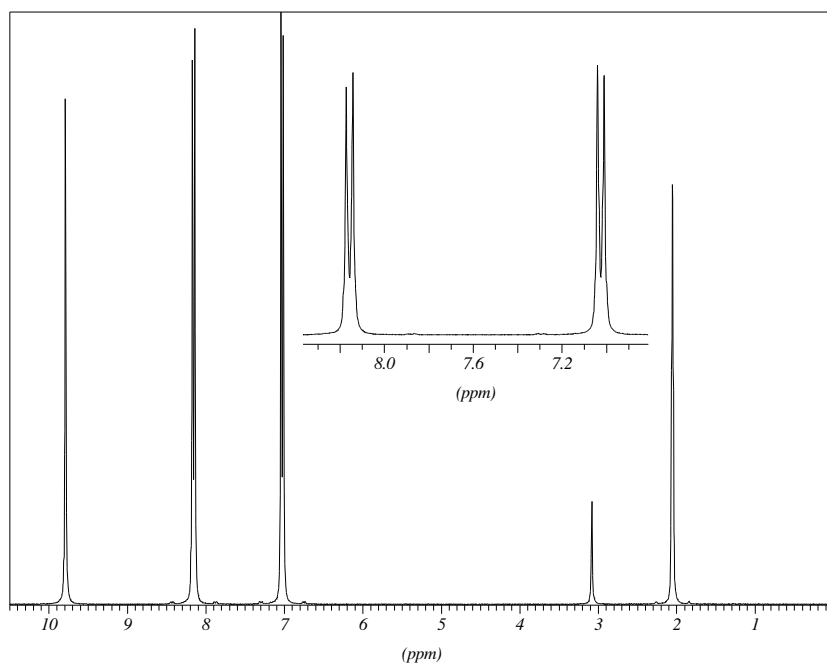
$\delta$ (ppm)	Assignment
155.1	C-1
137.5	C-5
133.7	C-2
125.1	C-3
120.2	C-4
119.9	C-6
76.5-77.5	solvent

 **$^{13}\text{C}$  NMR spectrum of the product 4-nitrophenol (300 MHz, acetone- $\text{D}_6$ )**

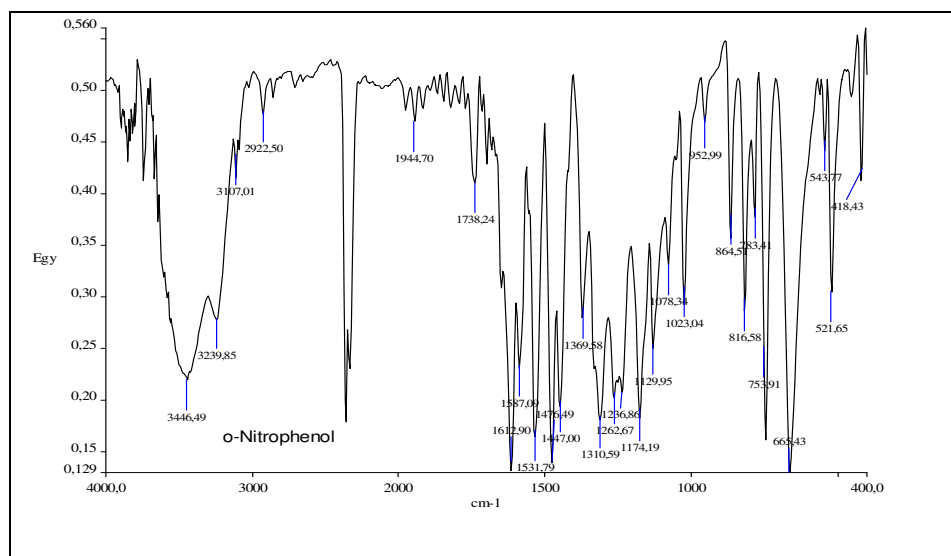
$\delta$ (ppm)	Assignment
164.3	C-1
141.7	C-4
126.9	C-3, C-5
116.5	C-2, C-6
206, 30	solvent



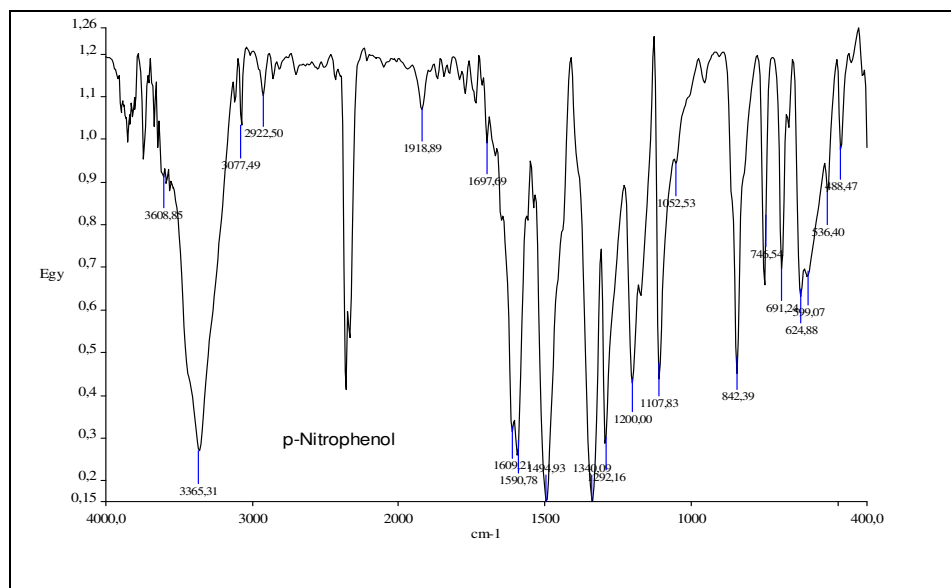


**<sup>1</sup>H NMR spectrum of the product 4-nitrophenol (300 MHz, acetone-D<sub>6</sub>)**

$\delta$ (ppm)	Multiplicity	Number of H	Assignment
9.80	s	1	O-H
8.15	d (AA')	2	3-H, 5-H
7.02	d (XX')	2	2-H, 6-H
2.04			acetone
3.1			water

**IR spectrum of the product 2-nitrophenol (KBr)**

( $\text{cm}^{-1}$ )	Assignment
3445, 3240	O-H-valence, superimposed by C-H-valence, arene
1610, 1590	C=C-valence, arene
1530, 1310	N=O-valence, asymm. and. symm.

**IR spectrum of the product 4-nitrophenol (KBr)**

( $\text{cm}^{-1}$ )	Assignment
3365	O-H-valence, superimposed by C-H-valence, arene
1610, 1590	C=C-valence, arene
1495, 1340	N=O-valence, asymm. and. symm.