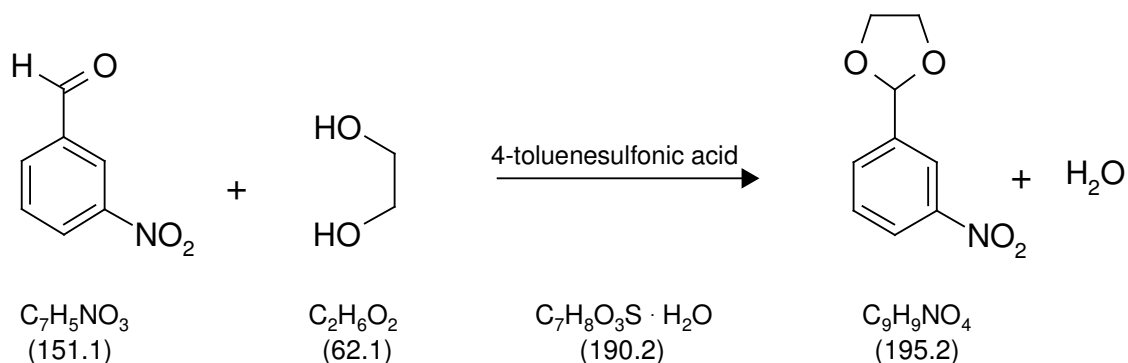


## 5004 Acid catalyzed acetalisation of 3-nitrobenzaldehyde with ethanediol to the correspondent 1,3-dioxolane



### Classification

#### Reaction types and substance classes

reaction of the carbonyl group in aldehydes, acetalisation  
aldehyde, acetal, alcohol, protecting group, acid catalyst

#### Work methods

microwave-assisted reaction, stirring with magnetic stir bar, heating under reflux, distillation, introduction of gas, shaking out, extracting, evaporating with rotary evaporator, filtering, recrystallizing

### Instruction (batch scale 100 mmol)

#### Equipment

microwave heating system ETHOS 1600, 100 mL three-neck flask, distillation apparatus, 100 mL round-bottom flask, bubble counter, adapter with ground-glass joint and hose coupling, 250 mL two-neck flask, reflux condenser, 250 mL round-bottom flask, magnetic stirrer with magnetic stir bar, rotary evaporator, suction flask, suction filter, separating funnel, desiccator, glass connecting pipe (NS 29, 40 cm),

#### Substances

3-nitrobenzaldehyde (mp 58 °C; product from NOP-Nr. 1003)	15.1 g (100 mmol)
ethanediol (bp 198 °C)	9.32 g (8.4 mL, 150 mmol)
4-toluenesulfonic acid monohydrate (mp 103-105 °C)	1.0 g (5.3 mmol)
<i>tert</i> -butyl methyl ether (bp 55 °C)	240 mL
petroleum ether (bp 40-60 °C)	70 mL
sodium sulfate for drying	etwa 15 g
sodium disulfite	about 13 g (for 20 mL saturated aqueous NaHSO <sub>3</sub> -solution)

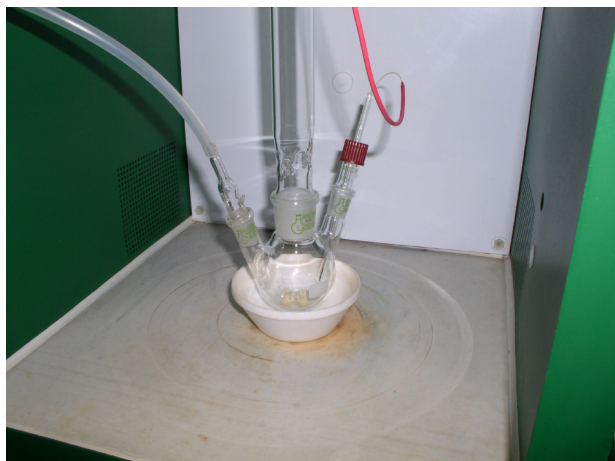
## Reaction

For the set up of the reaction apparatus in the microwave see:

“Technical instructions. Standard refluxing apparatus for microwave systems”.

The used apparatus, compared to the standard refluxing apparatus, is slightly modified: A three-neck round-bottom flask is used instead of a two-neck round-bottom flask, and the reflux condenser is exchanged with a distillation bridge with a collection round-bottom flask. A temperature sensor is placed into one of the side openings in the three-neck round-bottom flask. In the second side opening a PTFE tube is connected via a ground glass joint adapter. This tube passes through an opening in the microwave system and is connected to a bubble counter and a stop-cock that is connected to the air pressure or nitrogen line. The flow rate of the cooling water in the distillation bridge can be reduced to a minimum during the course of the experiment. The stop-cock is closed to begin with.

**Picture 1:** Three-neck round-bottom flask with gas inlet and fibre optic temperature sensor



**Picture 2:** Distillation bridge as add on to the glass connecting tube



15.1 g (100 mmol) 3-nitrobenzaldehyde, 9.32 g (8.4 mL, 150 mmol) ethanediol and 1.0 g (5.3 mmol) *p*-toluenesulfonic acid monohydrate are placed in a 100 mL three-neck round-bottom flask fitted with a stir bar or a cross stirrer. The reaction mixture is irradiated for 50 minutes with 900 W at a set temperature of 130 °C.

The stop-cock remains closed during the first 25 minutes. Thereby a weak reflux is established in the glass connecting tube. The volatile components of the reaction mixture are mainly water and ethanediol. As the absorption of the microwaves in the gas phase is much less than in the liquid phase, neither water nor ethanediol is distilled over.

After 25 minutes reaction time under reflux whilst the microwave program continues to run, an air or nitrogen flow is introduced with such a flow rate that no single gas bubbles are visible in the bubble counter (if a flow rate meter is present, 5 L/h). A mixture (3-8 mL) of water, ethanediol and small amounts of product are collected in the collection round-bottom flask.

### Work up

Once the program is completed, the reaction flask is placed in a water bath and the oily contents, which tends to crystallization, is allowed to stir for 5 minutes. One then adds 80 mL water and allows to stir intensively for a further 15 minutes. The water is separated from the ivory coloured solid product with a folded filter paper. The crystallized product traces in the condenser and in the collection round-bottom flask are also rinsed out with water and filtered. Yield of crude product: 18.6 g; mp 50-52 °C; purity according to GC 98%

In order to remove the not converted aldehyde with sodium hydrogensulfite, the crude product (which can still be wet) is dissolved in 200 mL *tert*-butyl methyl ether and extracted with 20 mL saturated aqueous sodium hydrogen sulfite solution. The organic phase is dried over sodium sulfate. Once the drying agent has been filtered off, the solvent is completely evaporated on the rotary evaporator with a bath temperature of 40 °C. The bath temperature should not be higher due to the low melting point of the product. A pale yellow, fine crystalline solid remains.

Yield: 17.7 g (90.7 mmol, 91%); mp 52-54 °C; purity according to GC 99.8%

The product can be recrystallized from a solvent mixture of *tert*-butyl methyl ether/petroleum ether: The product is placed into a 250 mL two-neck round-bottom flask containing a magnetic stir bar. A solvent mixture of 40 mL *tert*-butyl methyl ether and 50 mL petroleum ether (40-60 °C) is added. The flask is set up in the microwave, as described for the standard reflux apparatus, and allowed to stir under reflux for 2 minutes at 500 W and 55 °C. The clear solution is cooled in a water bath during the 5 minute ventilation period in the microwave. The semi-solid crystalline slurry is then allowed to stand for at least a further 15 minutes at room temperature and then a further 1 hour in the refrigerator. The crystals are filtered off using a suction filter. The crystallization flask is washed 2 times with 10 mL petroleum ether, thereby washing the residue onto the filter. The recrystallized product is dried in the desiccator at reduced pressure.

Yield of recrystallized product: 16.4 g (84.0 mmol, 84%); mp 53-55 °C

After evaporating the solvent of the mother liquor from the recrystallization, a residue of 1.2 g, consisting of 95 % product, is obtained.

### Comments

If the reaction is performed only under reflux, but without distilling off the volatile substances, less than 90 % of the 3-nitrobenzaldehyde is converted to the acetal. Together with condensing water also some ethanediol is distilled off as an azeotrope.

By stirring the reaction mixture with water possible residues of ethanediol and *p*-toluene-sulfonic acid are removed.

During recrystallization the cooling water bath prevents the release of hot solvent vapors from the product solution, when the flask is removed from the microwave oven.

### **Waste management**

#### **Recycling**

The *tert*-butyl methyl ether evaporated during the work up of the crude product can be used for the recrystallization. The leftover ether is collected and redistilled.

#### **Waste disposal**

<b>Waste</b>	<b>Disposal</b>
aqueous phases	solvent water mixtures, halogen free
mother liquor from recrystallization	organic solvents, halogen free
sodium sulfate	solid waste, free from mercury

#### **Time**

Isolation of the crude product 2 hours

Work up to the pure product 1 hour

Recrystallization with drying about 2 hours

#### **Break**

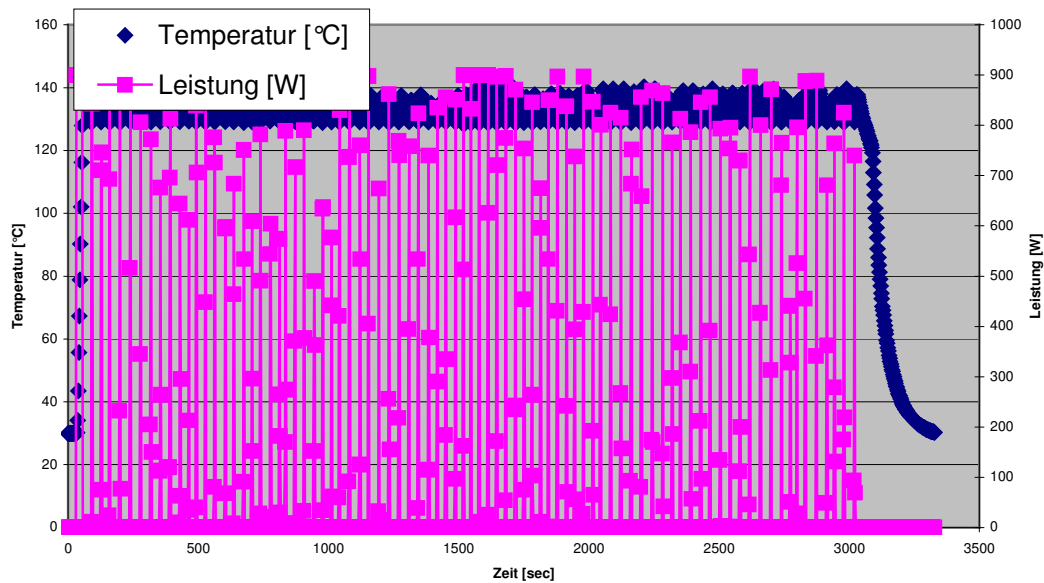
After stirring the reaction mixture with water

#### **Degree of difficulty**

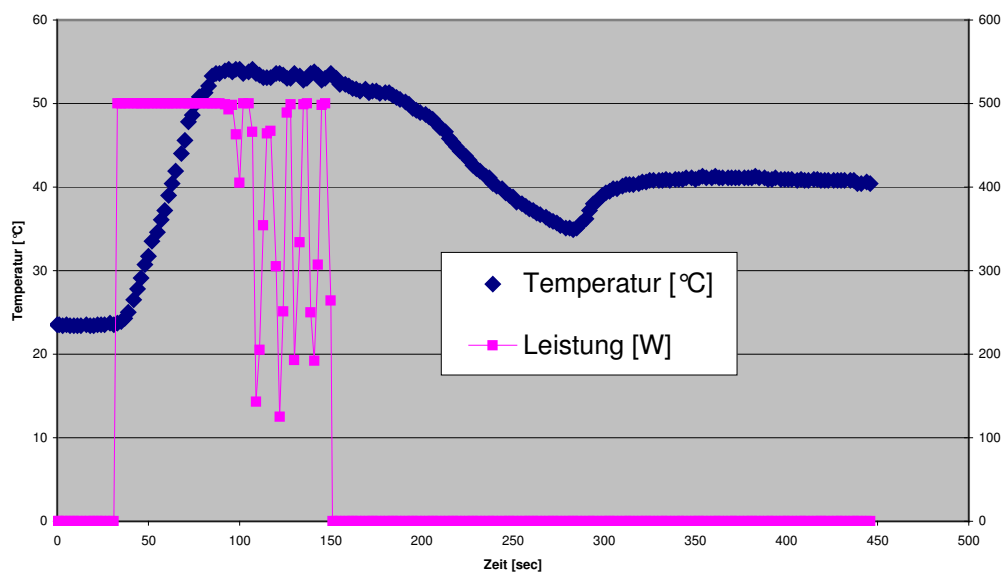
Medium

## Analytics

### Temperature-time-dependence of the synthesis in the microwave



### Temperature-time-dependence of the recrystallization in the microwave



## Reaction monitoring by GC

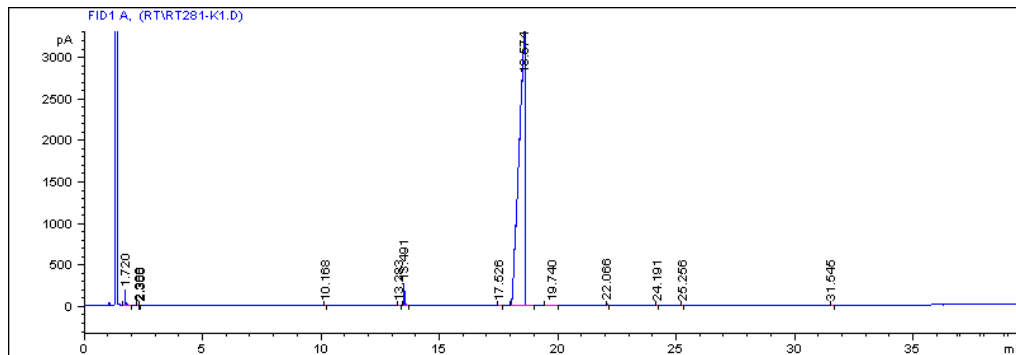
Sample preparation: Of each sample, 20 mg are dissolved in 0.5 mL ethyl acetate. 3  $\mu$ L of the solution is injected.  
For the analysis of the extracted product, 3  $\mu$ L *tert*-butyl methyl ether solution can be injected.

GC conditions:

column: HP-5; L=30 m, d=0.32 mm, film=0.25  $\mu$ m (Phenomenex)  
inlet: split injection 194:1  
carrier gas: H<sub>2</sub>, precolumn pressure 31 kPa  
oven: 50 °C, 8 °C/min 320 °C  
detector: 300 °C

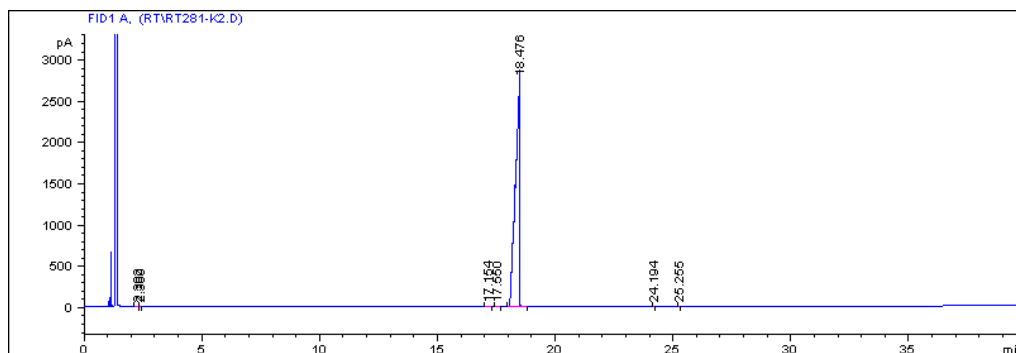
Percent concentration was calculated from peak areas

### GC of the crude product



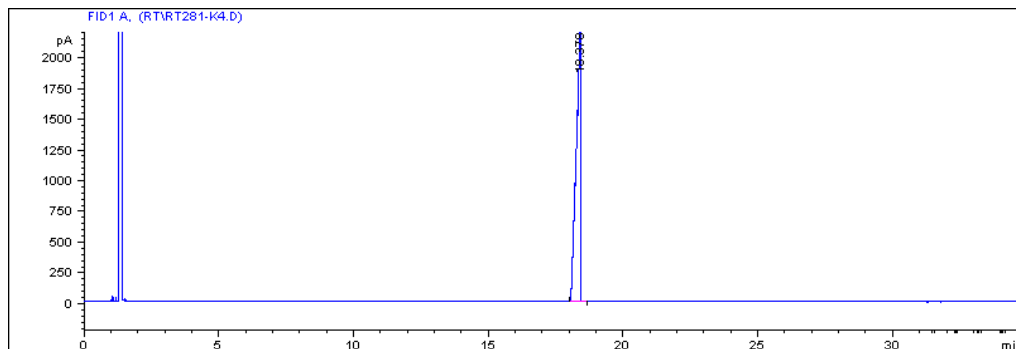
Retention time (min)	Substance	Peak area %
1.7	educt (ethanediol)	0.7
13.5	educt (3-nitrobenzaldehyde)	1.0
18.5	product (1,3-dioxolane)	98.3

### GC of the product (after extraction with sodium hydrogensulfite solution)



Peak area %: 99.8 % product

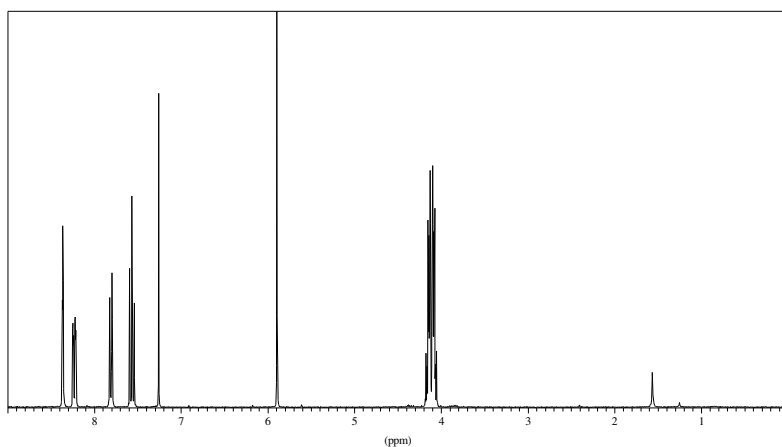
### GC of the pure product (after recrystallization)



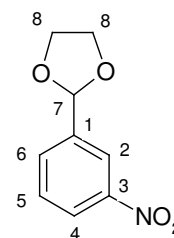
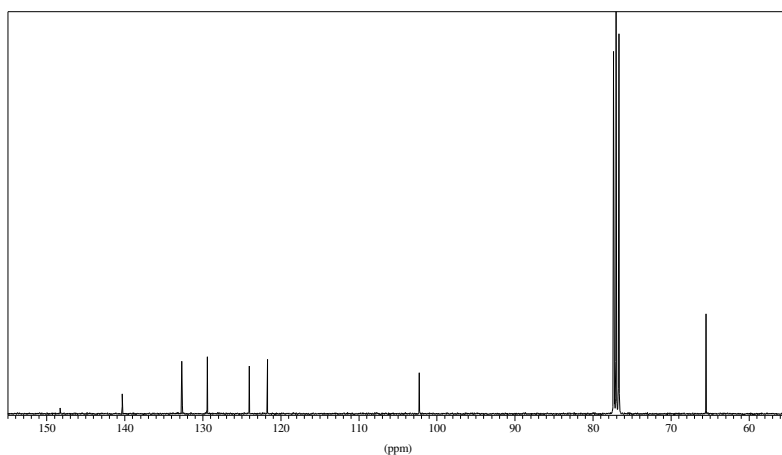
Peak area %: 100 % product

### GC of the residue of the mother liquor (from recrystallization)

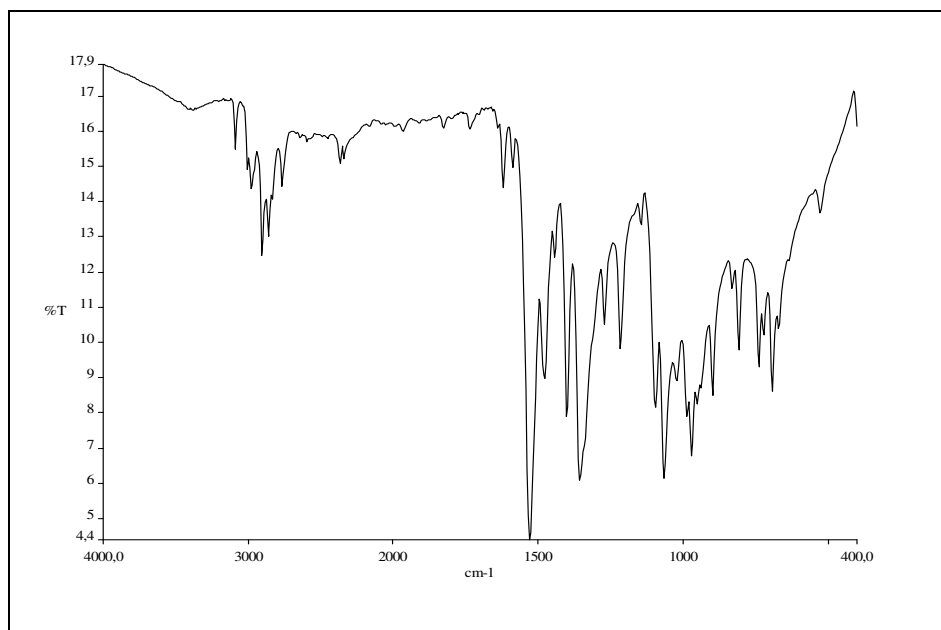
Peak area %: 95 % product, 5 % not identified

**$^1\text{H}$  NMR spectrum of the product (200 MHz,  $\text{CDCl}_3$ )**

$\delta$ (ppm)	Multiplicity	Number of H	Assignment
8.37 - 8.35	m	1	2-H
8.25 - 8.20	m	1	4-H
7.83 - 7.79	m	1	6-H
7.60 - 7.54	m	1	5-H
5.90	s	1	7-H
4.18 - 4.05	m	4	8-H
1.55			water
7.26			solvent

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

$\delta$ (ppm)	Assignment
65.5	- O - $\text{CH}_2$ - $\text{CH}_2$ - O -
102.3	- O - CH - O -
121.7	CH arene
124.0	CH arene
129.4	CH arene
132.7	CH arene
140.4	C - CH(dioxolane) arene
148.3	C - $\text{NO}_2$ arene
76.5-77.5	solvent

**IR spectrum of the product (KBr)**

(cm <sup>-1</sup> )	Assignment
3093	C – H – valence, arene
2978, 2905, 2862	C – H – valence, alkane
2769	C – H – valence, O – CH – O
1621, 1588	C = C – valence, arene
1532, 1359	N = O – valence, asymm. and symm.