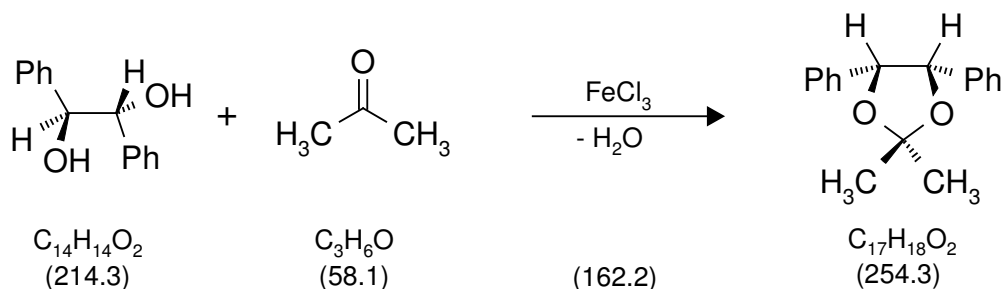


## 2005 Synthesis of the acetonide of *meso*-1,2-diphenyl-1,2-ethanediol (2,2-dimethyl-4,5-diphenyl-1,3-dioxolane)



### Classification

#### Reaction types and substance classes

reaction of the carbonyl group in ketones, acetalisation  
ketone, alcohol, acetal, protecting group, acid catalyst

#### Work methods

heating under reflux, stirring with magnetic stir bar, filtering, evaporating with rotary evaporator, shaking out, extracting, recrystallizing, working with moisture exclusion, heating with oil bath

### Instruction (batch scale 5 mmol)

#### Equipment

100 mL three-neck flask, 50 mL round bottom flask, reflux condenser, protective gas supply, adapter with ground glass joint and hose coupling, heatable magnetic stirrer, magnetic stir bar, 250 mL beaker, 250 mL separating funnel, Hirsch funnel, suction flask, rotary evaporator, vacuum pump, oil bath

#### Substances

<i>meso</i> -1,2-diphenyl-1,2-ethanediol (mp 132-134 °C, product from NOP 2004)	1.07 g (5.00 mmol)
iron(III)-chloride water free (mp 305 °C)	300 mg (1.85 mmol)
acetone (bp 56 °C) dry	23.3 g (29.4 mL, 400 mmol)
acetic acid ethyl ester (bp. 77 °C)	60 mL
petroleum ether (40–60 °C) dry, for recrystallizing	about 15 mL
potassium carbonate	about 1 g (for 50 mL of 2% aqueous solution)
magnesium sulfate for drying	about 1 g

## Reaction

Since  $\text{FeCl}_3$  is very hygroscopic, only a very short contact with air is allowed.

The reaction apparatus consists of a dry 100 mL three-neck flask, rinsed with nitrogen and equipped with a magnetic stir bar and a reflux condenser, which is connected with a nitrogen piping. In the reaction flask 1.07 g (5.0 mmol) 1,2-diphenyl-1,2-ethanediol are dissolved in 23 g (30 mL, 400 mmol) dry acetone. 300 mg (1.85 mmol) of water free iron(III)-chloride are rapidly added, whilst the reaction mixture changes its colour to yellow-brown. It is heated under stirring for 20 minutes under reflux.

## Work up

After cooling down to room temperature the reaction mixture is poured into a 250 mL beaker containing 50 mL of 2% potassium carbonate-solution. A brown fluffy precipitation is formed. The mixture is transferred into a 250 mL separating funnel and extracted three times with 20 mL acetic acid ethyl ester each. The organic phases are almost colourless. They are combined and again washed with 25 mL water and dried over water free magnesium sulfate. The mixture is filtered from the drying agent over a glass funnel with filter paper and the solvent is removed at a rotary evaporator. The light yellow oil remaining as crude product is dried for 30 minutes at about 40 °C bath temperature with a vacuum pump at 1-2 hPa.

Crude yield: 1.05 g; mp 56 °C; HPLC-purity 83%

To the crude product are added 13 mL dry and pre-heated petroleum ether (40-60 °C) in a 50 mL round bottom flask and the mixture is stirred and heated for 5 minutes under reflux. Then the still hot solution is filtered off from the insoluble residue into a 50 mL round bottom flask and the solvent is evaporated at a rotary evaporator. The remaining light yellow oily product is dried with a vacuum pump at 1-2 hPa and stored in the cooler for crystallization.

Yield: 0.918 g (3.61 mmol, 72%); mp 56-57 °C

The product can be recrystallized from 1 mL dry petroleum ether (40-60 °C), however, it is still not free from educt yet.

Yield: 0.52 g (2.05 mmol, 41%); mp 58-60 °C

The residue (120 mg) which is insoluble in the hot petroleum ether consists predominantly of not reacted 1,2-diphenylethanediol.

## Comments

The product in solid state is stable under moisture exclusion at room temperature. A solution of the product in  $\text{CDCl}_3$  shows already after one day partly cleavage into the educts, probably due to traces of acid (detection with  $^1\text{H}$  NMR).

**Waste management****Recycling**

The evaporated petroleum ether is collected and redistilled.

**Waste disposal**

Waste	Disposal
aqueous phase from shaking out	solvent water mixtures, containing halogen
evaporated acetic acid ethyl ester (might contain acetone)	organic solvents, halogen free

**Time**

3 hours

**Break**

After evaporation of the acetic ester

**Degree of difficulty**

Easy

**Analytics****Reaction monitoring with HPLC**

Sample preparation for a batch scale of 5 mmol:

For taking of each sample the oil bath is lowered. As soon as the reaction solution stops boiling, 5 mL are taken using a pipette and the sample is added to 10 mL of 2% potassium carbonate solution in a separating funnel. The solution is shaken out three times with 5 mL acetic acid ethyl ester each. The organic phases are combined and dried over water free magnesium sulfate. After filtering off the drying agent the solvent is evaporated at a rotary evaporator. 0.5 mg from the residue are dissolved in 2 mL acetonitrile. 5  $\mu$ L from this solution are injected.

HPLC-conditions:

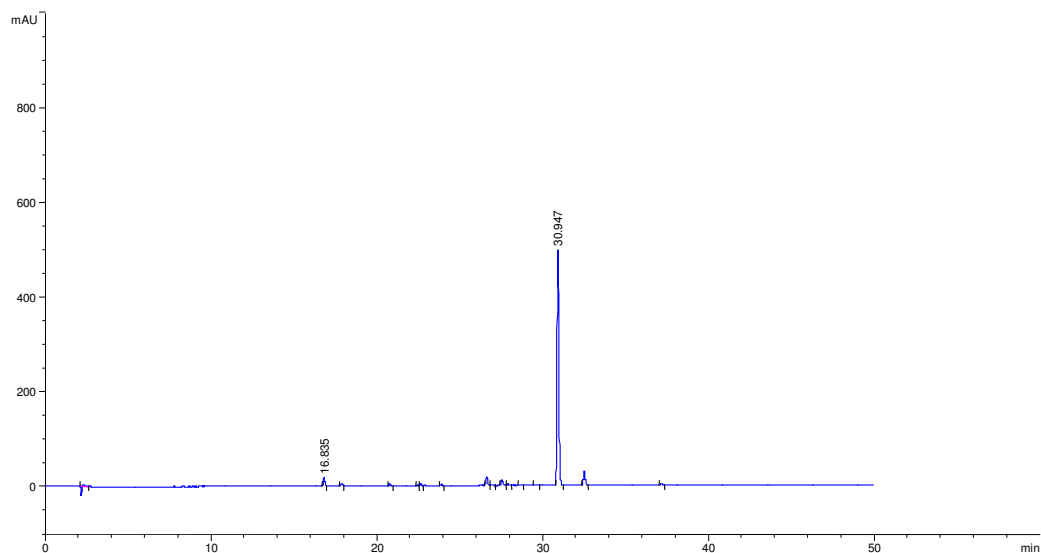
colum: Phenomenex Luna C18; particle size 3  $\mu$ m, length 150 mm, internal diameter 4.6 mm  
 column temperature: 25 °C  
 injection volume: 5  $\mu$ L  
 gradient: 0 min 5% acetonitrile + 95% water  
 40 min 95% acetonitrile + 5% water  
 50 min 95% acetonitrile + 5% water  
 flow: 1.0 mL/min  
 wave length: 220 nm

Samples taken after 10, 20, 30, 40 and 60 minutes reaction time showed in the HPLC all the same ratio of product to educt: 95% acetonide and 5% 1,2-diphenylethanediol.

## HPLC of the crude product

Sample preparation:

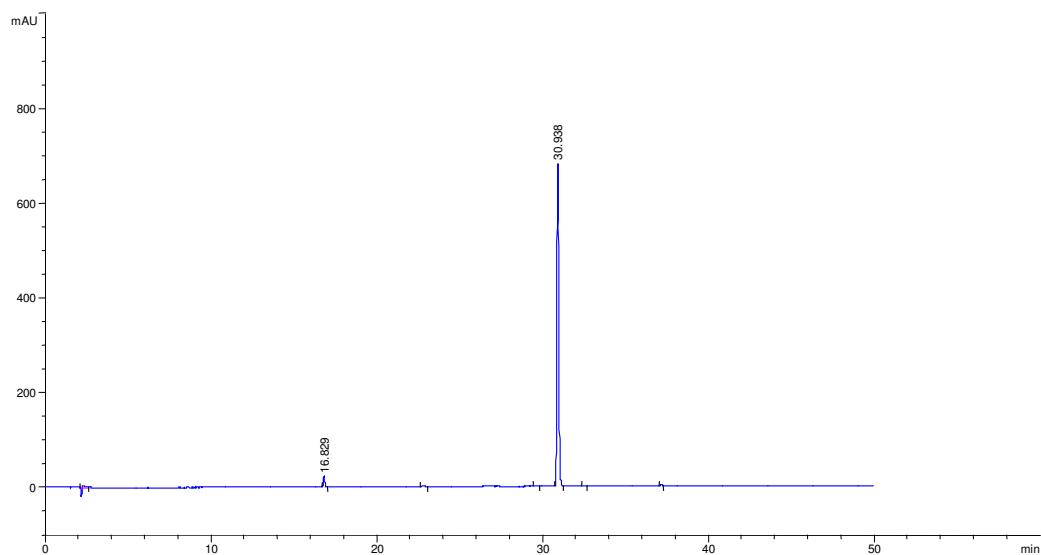
0.5 mg substance are dissolved in 2 mL acetonitrile, from this solution 5  $\mu$ L are injected.



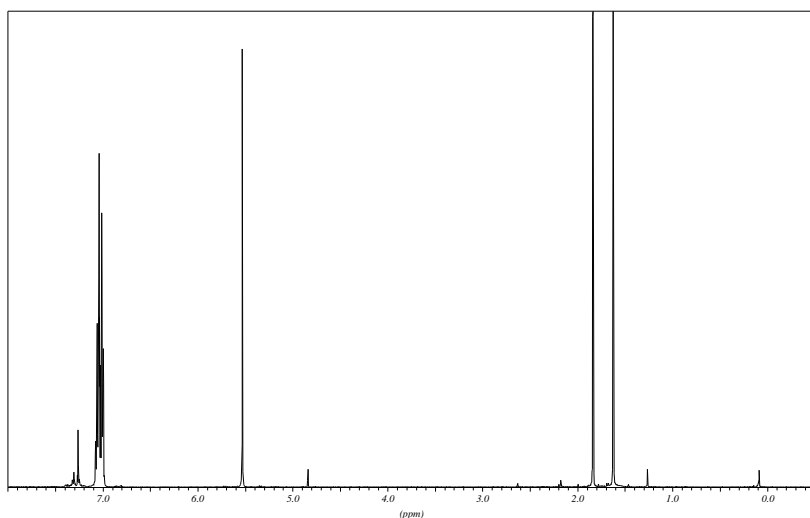
## HPLC of the pure product

(After recrystallization)

Sample preparation as described for the crude product



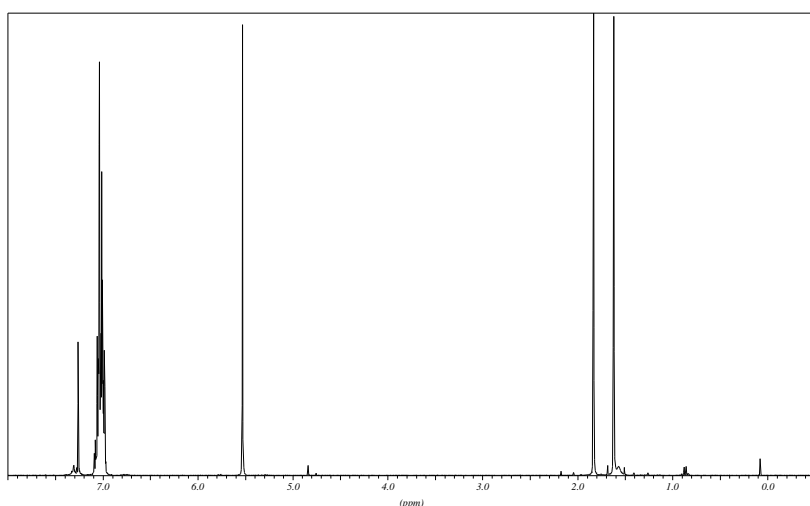
Retention time (min)	Substance	Peak area %	
		Crude product	Pure product
16.8	1,2-diphenyl-1,2-ethanediol (educt)	2.5	2.8
30.9	acetone (product)	82.9	96.1
others	not identified	14.4	1.1

**<sup>1</sup>H NMR spectrum of the crude product (400 MHz, CDCl<sub>3</sub>)**

From the intensities of the two singulets at 5.53 and 4.83 ppm results a ratio acetone to diphenylethanediol 96 : 4. The fact, that the methyl groups show clearly different chemical shifts, proves the stereochemistry of the used diol: The acetone of the *meso*-isomer has both phenyl groups at the same side of the five membered ring, so that the two methyl groups have a very different environment.

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

(After recrystallization)

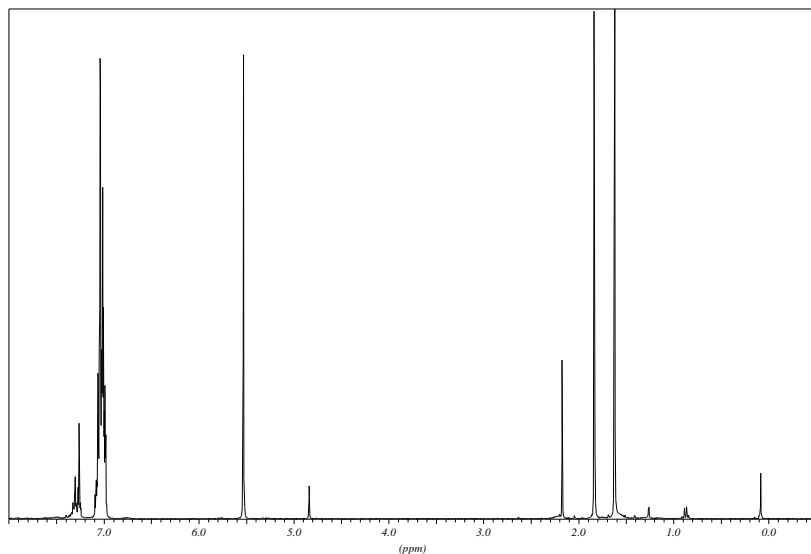


→ ratio  
acetone : diol:  
98 : 2

$\delta$ (ppm)	Multiplicity	Number of H	Assignment
7.4-7.2	M		CH arene (educt)
7.2-6.8	M	10	CH arene (product)
5.53	S	2	CH – O – (product)
4.84	s		CH – O – (educt)
1.84	s	3	CH <sub>3</sub>
1.62	s	3	CH <sub>3</sub>
7.26	s		solvent

**$^1\text{H}$  NMR spectrum of the crude product (300 MHz,  $\text{CDCl}_3$ )**

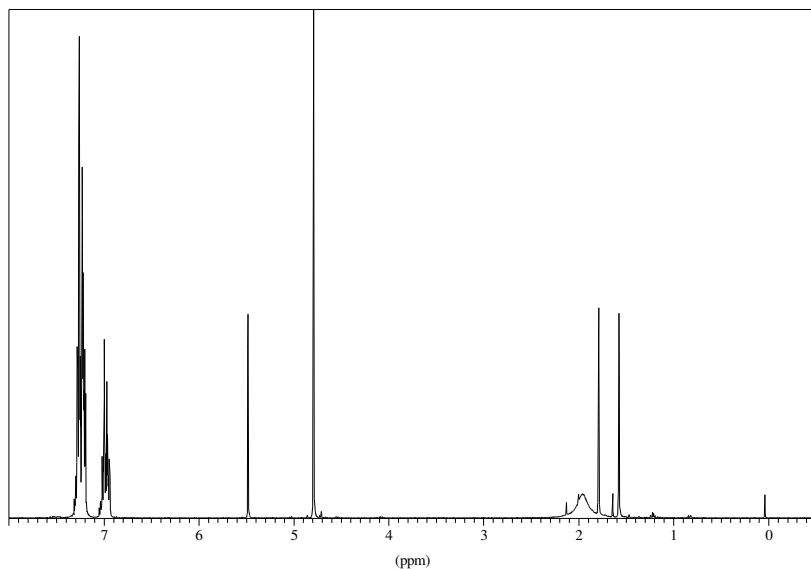
(After the solution was stored for 2 days)



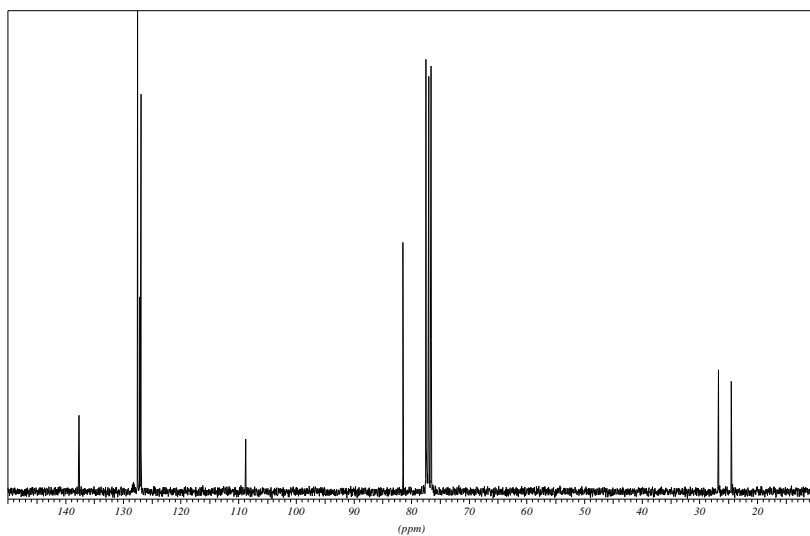
Obviously the signals from 1,2-diphenylethanediol increased a bit, furthermore there is an additional singlet at 2.17 ppm from acetone.

 **$^1\text{H}$  NMR spectrum of the flask residue (300 MHz,  $\text{CDCl}_3$ )**

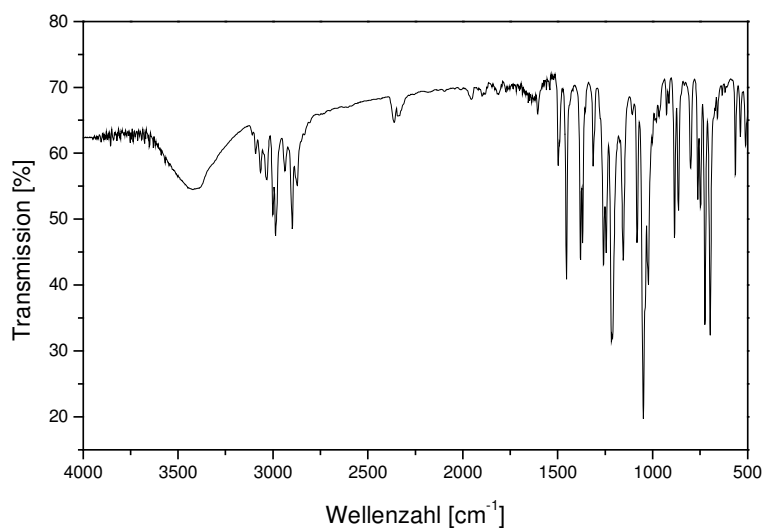
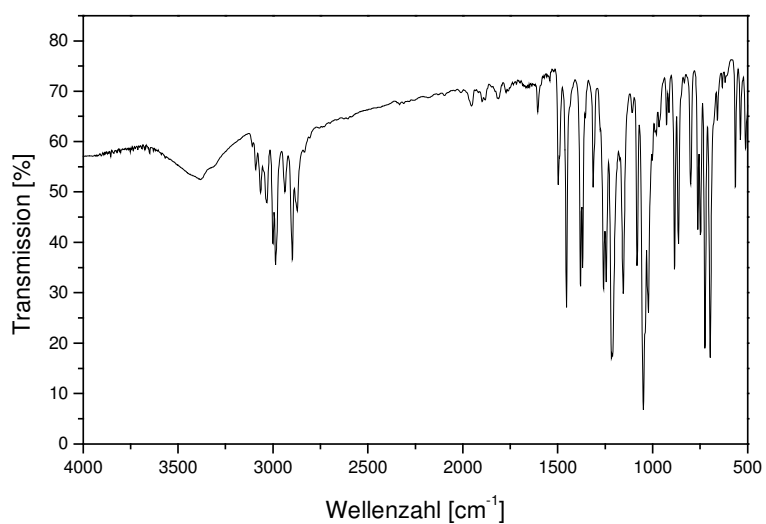
(After the hot filtration)



Here the signals from 1,2-diphenylethanediol are significantly stronger than those from the product. (The broad singlet at 1.95 ppm originates from the OH-protons of the diol.)

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

$\delta$ (ppm)	Assignment
137.7	$\text{C}_{\text{quart}}$ arene
128.3 - 126.9	CH arene
108.8	– O – C – O –
81.5	CH – O –
26.8	$\text{CH}_3$
24.5	$\text{CH}_3$
76.5-77.5	solvent

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

(cm <sup>-1</sup> )	Assignment
3095-3000	C – H – valence, arene
2990-2880	C – H – valence, alkane
1490, 1454	C = C – valence, arene