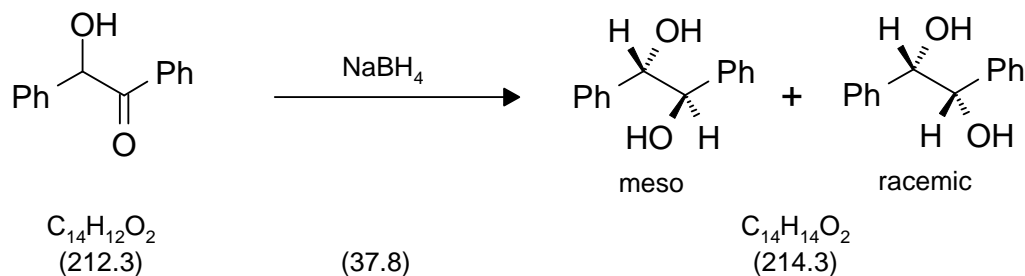


2004 Diastereoselective reduction of benzoin with sodium borohydride to 1,2-diphenyl-1,2-ethanediol



Literature

M. Yamada, T. Horie, M. Kawai, H. Yamamura, S. Araki, *Tetrahedron* **1997**, 53, 15685

Classification

Reaction types and substance classes

reaction of the carbonyl group in ketones, reduction, stereoselective addition
ketone, alcohol, complex metal hydride

Work methods

stirring with magnetic stir bar, adding dropwise with an addition funnel, evaporating with rotary evaporator, filtering, recrystallizing, heating with oil bath

Instruction (batch scale 10 mmol)

Equipment

500 mL three-neck flask, reflux condenser, addition funnel with pressure balance, internal thermometer, bubble counter, 500 mL Erlenmeyer flask, separating funnel, 500 mL round bottom flask, heatable magnetic stirrer, magnetic stir bar, rotary evaporator, suction flask, Buechner funnel, desiccator, oil bath

Substances

benzoin (mp 132-134 °C)	2.13 g (10.0 mmol)
sodium borohydride	0.756 g (20.0 mmol)
<i>tert</i> -butyl methyl ether (bp 55 °C)	300 mL
conc. hydrochloric acid (25%)	4 mL
ice	30 g
sodium sulfate for drying	
ethanol (bp 78 °C) for recrystallizing	about 3 mL

Reaction

0.756 g (20.0 mmol) sodium borohydride in 40 mL *tert*-butyl methyl ether are filled in a dry 500 mL three-neck flask with magnetic stir bar, internal thermometer, addition funnel and reflux condenser with bubble counter (filled i.e. with paraffin oil) and stirred for about 10 minutes until a fine suspension has formed. 2.13 g (10.0 mmol) benzoin are dissolved in an Erlenmeyer flask in 260 mL *tert*-butyl methyl ether under slight heating to about 30°C. The solution is cooled down to room temperature and added dropwise over an addition funnel into the reaction flask at such a rate, that the temperature of the reaction solution does not exceed 30°C (about 20 minutes). Afterwards the mixture is stirred for at least further 4 hours (or over night) at room temperature.

Work up

30 g finely crunched ice is added to the reaction mixture. Then a mixture of 4 mL conc. hydrochloric acid (25%) and 20 mL water (equivalent to about 1 M HCl) is slowly added dropwise over an addition funnel (within about 30 min). During the addition strong evolution of gas can be observed. Stirring is continued until no more gas is formed (about 10 min). Even if diluted hydrochloric acid is added dropwise, no gas evolution should be visible.

The organic phase is separated in a separating funnel and dried with sodium sulfate. After the drying agent has been filtered off, the solvent is evaporated at the rotary evaporator. The crude product remains as crystalline solid.

Crude yield: 2.14 g; mp 125-129 °C; (see analytics)

The crude product is recrystallized from an ethanol water mixture (1:1) (about 6 mL).

Yield: 1.86 g (8.69 mmol, 87%), mp 132-134 °C; colourless crystals; HPLC-purity > 99%

Comments

The stereochemistry of the product is investigated in experiment 2005.

Waste management**Recycling**

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

Waste disposal

Waste	Disposal
aqueous phase from separating funnel	solvent water mixtures, containing halogen
mother liquor from recrystallization	solvent water mixtures, halogen free
sodium sulfate	solid waste, free from mercury

Time

About 7 hours

Break

During work up after separating of the phases

Degree of difficulty

Medium

Analytics

Reaction monitoring

The reaction can be monitored with TLC and HPLC.

Sample preparation:

Using a Pasteur pipette, 5 mL from the reaction solution are taken for each sample and filled in a small Erlenmeyer flask containing 1g crunched ice. 5 mL 0.1 M HCl are added slowly and the mixture is shaken until no more gas is formed. The pH-value of the aqueous phase should be in the slightly acidic range, otherwise some drops of hydrochloric acid are added. The phases are separated in a small separating funnel. Samples for TLC can be taken directly from the organic phase. For HPLC the organic phase is dried with sodium sulfate, filtered and the solvent is evaporated. 0.5 mg of the residue are dissolved in 2 mL acetonitrile.

TLC

TLC-conditions:

adsorbant: TLC-alufoil silica gel 60 F₂₅₄
eluent: petroleum ether/acetic acid ethyl ester 7:3

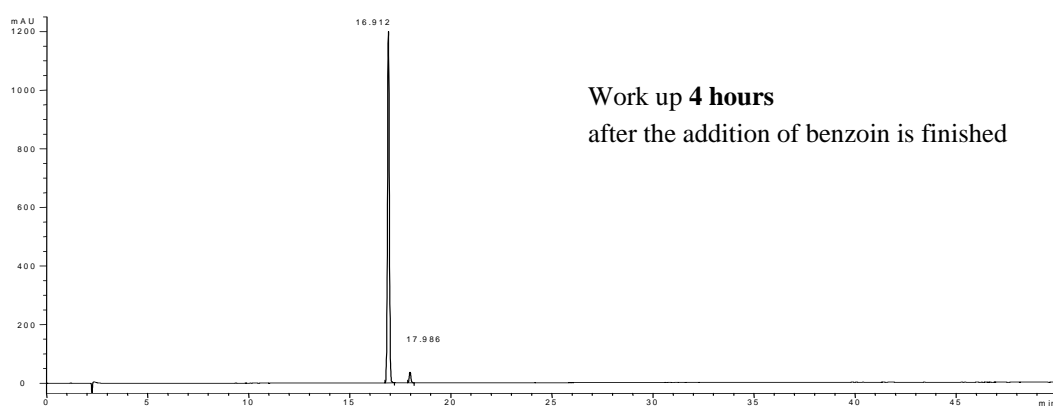
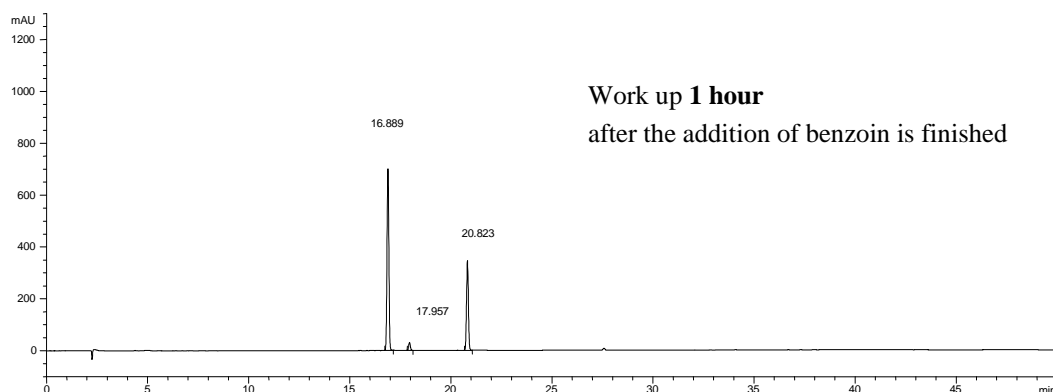
R_f (benzoin) 0.4
R_f (product) 0.2

HPLC

HPLC-conditions:

column: Phenomenex Luna C18; particle size 3 µm, length 150 mm, internal diameter 4.6 mm
column temperature: 25 °C
injection volume: 10 µL
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

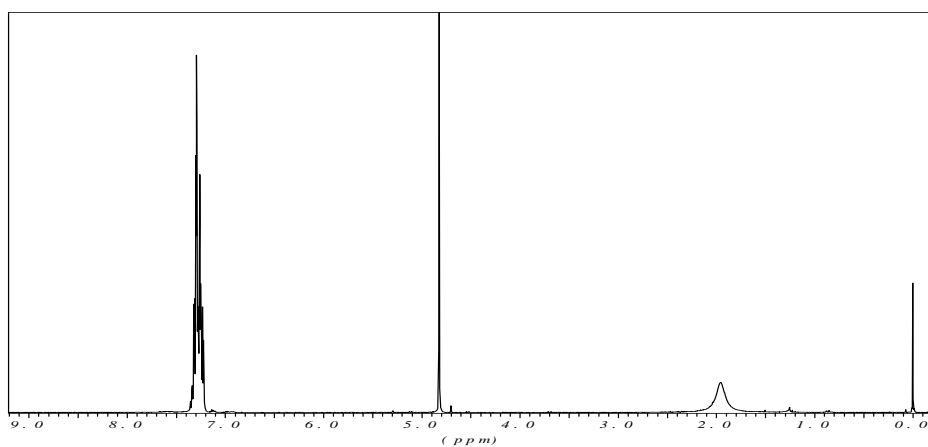
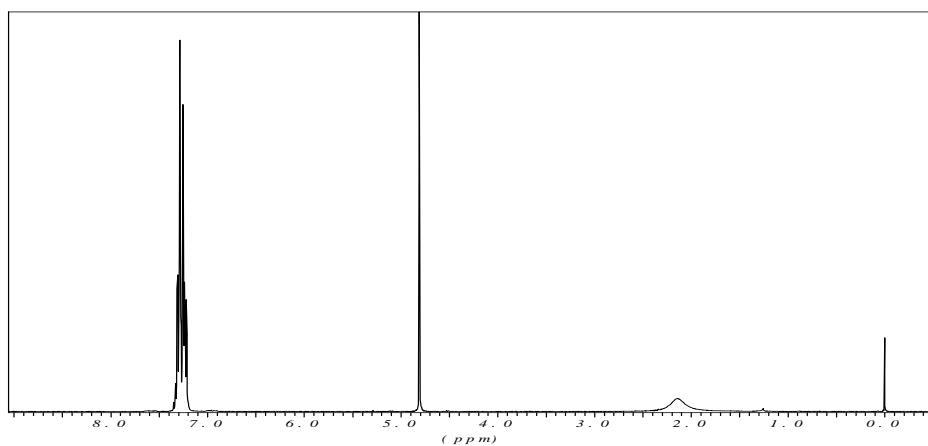
Percent concentration was calculated from peak areas.

HPLC of the crude product

Retention time (min)	Substances	Peak area %	
		after 1h	after 4 h
16.9	<i>meso</i> -product	64.6	97.3
18.0	racemic product	2.7	2.7
20.8	benzoin	31.9	–
others	not identified	0.7	–

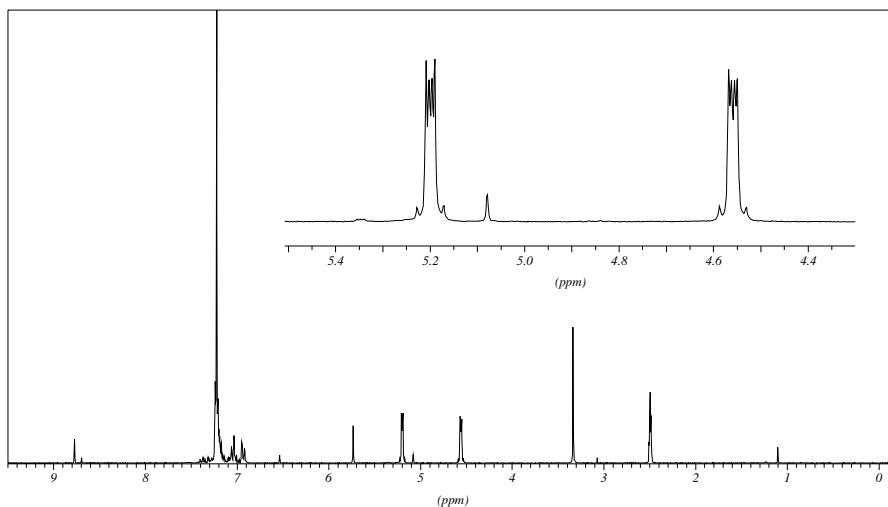
A quantitative analysis of the diol in the crude product with HPLC and internal standard resulted in a purity of > 99% (mixture of diastereomers).

With HPLC no racemic compound can be identified in the recrystallized product.

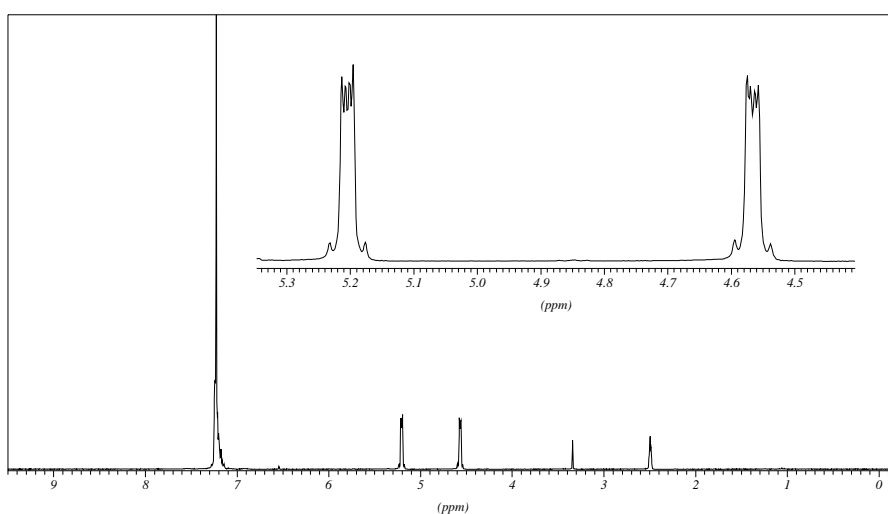
^1H NMR spectrum of the crude product (250 MHz, CDCl_3) **^1H NMR spectrum of the pure product (250 MHz, CDCl_3)**

δ (ppm)	Multiplicity	Number of H	Assignment
2.14	Wide s	2	CH – OH
4.81	S	2	CH – OH (<i>meso</i> -Isomer)
7.21 - 7.31	M	10	CH arene

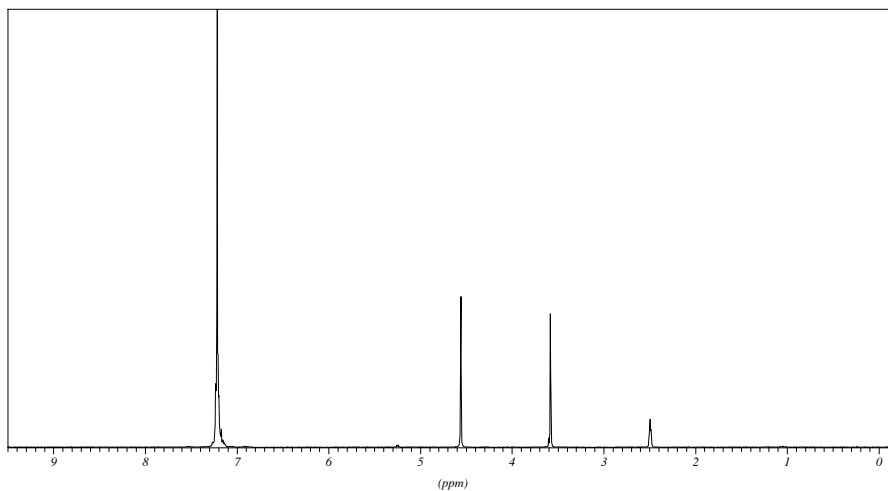
The weak signal at $\delta = 4.72$ ppm in the spectrum of the crude product corresponds to proton $\text{R}_1\text{R}_2\text{CH} - \text{OH}$ in the racemat, resulting in a relation of the *meso*-product to the racemic product of **98:2**.

^1H NMR spectrum of the crude product (250 MHz, DMSO- D_6)

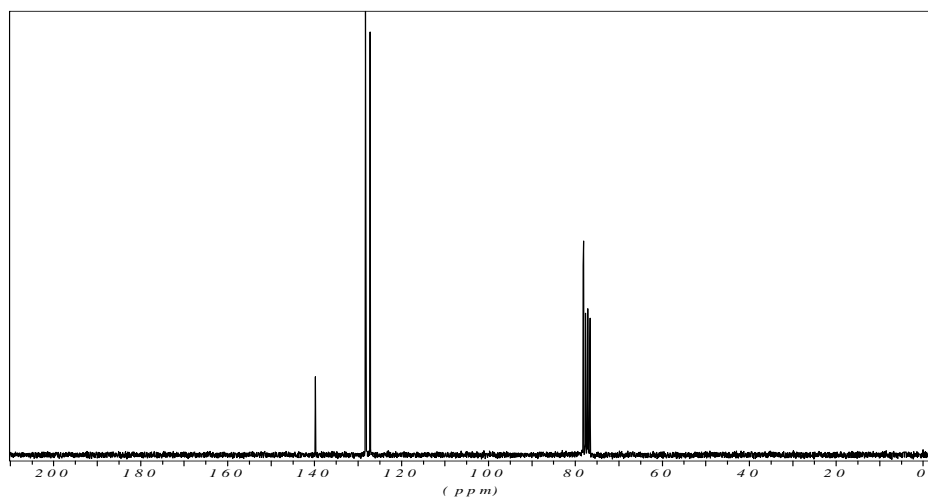
In contrast to the spectrum in CDCl_3 , the spectrum of the crude product in DMSO shows still some foreign signals, for the racemic isomer no separate signal can be detected.

 ^1H NMR spectrum of the pure product (250 MHz, DMSO- D_6)

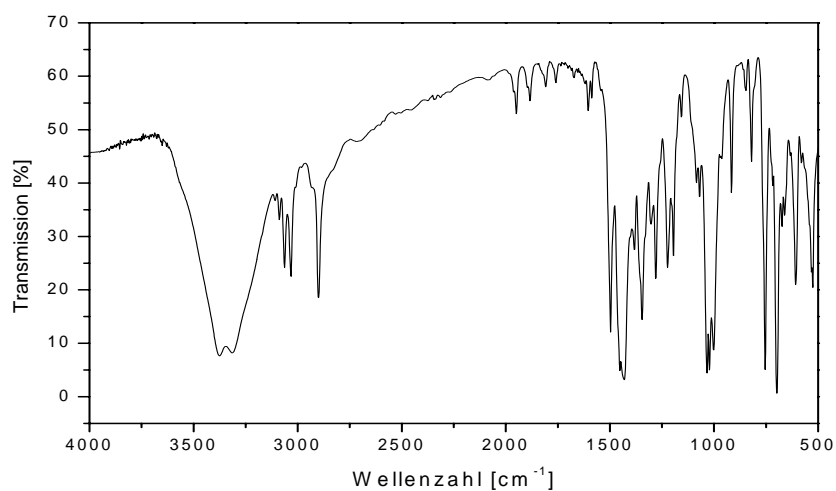
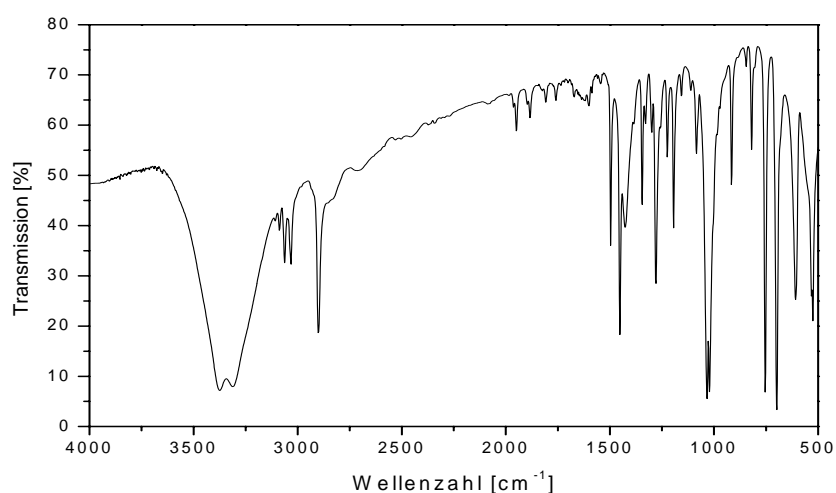
δ (ppm)	Multiplicity	Number of H	Assignment
2.49	m		DMSO
3.33	s		H_2O
4.53 – 4.59	m	2	$\text{CH} - \text{OH}$
5.17 – 5.23	m	2	$\text{CH} - \text{OH}$
7.22	m	10	CH arene

¹H NMR spectrum of the pure product (250 MHz, DMSO-D₆) with D₂O-exchange

δ (ppm)	Multiplicity	Number of H	Assignment
2.49	m		DMSO
3.58	s		H ₂ O
4.56	m	2	CH – OH
7.22	m	10	CH arene

¹³C NMR spectrum of the pure product (250 MHz, CDCl₃)

δ (ppm)	Assignment
78.1	CH – OH
127.1	CH arene
128.1	CH arene
128.2	CH arene
139.8	C _{quart} arene
76.5 - 77.5	solvent

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

(cm ⁻¹)	Assignment
3380	O – H – valence
3300	O – H – valence
3080	C – H – valence, arene
3050	C – H – valence, arene
2896	C – H – valence, alkane
1500	C = C – valence, arene