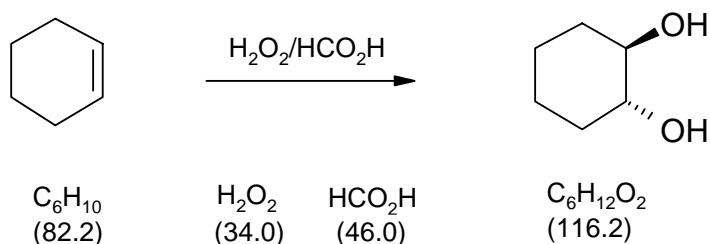


3034 Synthesis of trans-1,2-cyclohexanediol from cyclohexene



Classification

Reaction types and substance classes

addition to alkenes, stereoselective addition, oxidation
alkene, peroxy acid, alcohol

Work methods

stirring with magnetic stir bar, adding dropwise with an addition funnel, evaporating with rotary evaporator, distilling under reduced pressure, use of an ice cooling bath, heating with oil bath, heating with water bath

Instruction (batch scale 100 mmol)

Equipment

250 mL three-neck flask, reflux condenser, addition funnel with pressure balance, heatable magnetic stirrer, magnetic stir bar, internal thermometer, rotary evaporator, short path distillation apparatus or distillation bridge with air cooler, hot air dryer, ice bath, vacuum pump, water bath,

Substances

cyclohexene (bp 83 °C)	8.22 g (10.2 mL, 100 mmol)
formic acid (99%) (bp 101 °C)	37 g (30 mL, 800 mmol)
hydrogen peroxide (30%) (bp 107 °C)	14 g (13 mL, 130 mmol)
sodium hydroxide	6.0 g (150 mmol)
hydrochloric acid (conc.)	about 2 mL
potassium iodide starch test strips	
sodium disulfite or sodium sulfite	

Reaction

Under cooling in an ice bath, a solution of 30 mL (37 g, 0.80 mol) formic acid (99%) and 13 mL (14 g, 0.13 mol) hydrogen peroxide (30%) is prepared in a 250 mL three-neck flask with reflux condenser, addition funnel, internal thermometer and magnetic stir bar. It is cooled to 0 °C, and without further cooling 10.2 mL (8.22 g, 100 mmol) cyclohexene are

slowly added dropwise under stirring. During the addition the internal temperature should not exceed 80 °C ; if necessary the reaction flask is cooled in an ice bath. The reaction should be finished after 35 minutes. It is tested with potassium iodide starch test strips for peroxide. In case of a positive peroxide test, the reaction mixture must be heated in a water bath to 60-70 °C, until the test is negative. If the test result is still positive after one hour, the remaining peroxide is destroyed through addition of sodium disulfite.

The acid and the water are removed at the rotary evaporator at about 12 hPa. The remaining viscous residue is cooled and for hydrolysis of the intermediately formed formic acid ester a solution of 6.0 g (150 mmol) NaOH in 30 mL water is added, thereby the internal temperature must not exceed 60 °C. Then it is neutralized with about 2 mL conc. hydrochloric acid (check the pH !).

Work up

The solvent is completely removed at the rotary evaporator at about 12 hPa and at a water bath temperature of 50 °C. The solid residue is distilled under reduced pressure in a short path distillation apparatus or over a distillation bridge with air cooler. The product crystallizes during distillation, therefore it must be occasionally heated with a hot air dryer.

Yield: 9.48 g (81.6 mmol, 82%); bp 123 °C (13 hPa), mp 105 °C; colourless crystals

Comments

Compared with other procedures based on an extraction with acetic acid ethyl ester, the aforementioned work up produces considerably increased yields.

Waste management

Waste disposal

Waste	Disposal
aqueous distillate with formic acid	neutralize with sodium hydroxide solution, then: solvent water mixtures, halogen free
aqueous distillate after neutralization	waste water
distillation residue	solid waste, free from mercury

Time

About 3 hours

Break

After evaporation of the formic acid

After neutralization

Before distillation

Degree of difficulty

Medium

Instruction (batch scale 10 mmol)

Equipment

50 mL three-neck flask, reflux condenser, addition funnel with pressure balance, heatable magnetic stirrer, magnetic stir bar, internal thermometer, rotary evaporator, short path distillation apparatus or distillation bridge with air cooler, hot air dryer, ice bath, vacuum pump, water bath, oil bath

Substances

cyclohexene (bp 83 °C)	822 mg (1.0 mL, 10 mmol)
formic acid (99%ig) (bp 101 °C)	6.2 g (5.0 mL, 130 mmol)
hydrogen peroxide (30 %) (bp 107 °C)	1.4 g (1.3 mL, 13 mmol)
sodium hydroxide	600 mg (15 mmol)
hydrochloric acid (conc.)	
potassium iodide starch test strips	
sodium disulfite or sodium sulfite	

Reaction

Under cooling in an ice bath, a solution of 5 mL (6.2 g, 134 mmol) formic acid (99%) and 1.3 mL (1.4 g, 13 mmol) hydrogen peroxide (30%) is prepared in a 50 mL three-neck flask with reflux condenser, addition funnel, internal thermometer and magnetic stir bar. It is cooled to 0 °C, and without further cooling 1.0 mL (822 mg, 10 mmol) cyclohexene are slowly added dropwise under stirring. During the addition the internal temperature should not exceed 80 °C ; if necessary, the reaction flask is cooled in an ice bath. The reaction should be finished after 35 minutes. It is tested with potassium iodide starch test strips for peroxide. In case of a positive peroxide test, the reaction mixture must be heated in a water bath to 60-70 °C, until the test is negative. If the test result is still positive after one hour, the remaining peroxide is destroyed through addition of sodium disulfite.

The acid and the water are removed at the rotary evaporator at about 12 hPa. The remaining viscous residue is cooled and for hydrolysis of the intermediately formed formic acid esters a solution of 600 mg (15 mmol) NaOH in 3 mL water is added, thereby the internal temperature must not exceed 60 °C. Then it is neutralized with about 2 mL conc. hydrochloric acid (check the pH !).

Work up

The solvent is completely removed at the rotary evaporator at about 12 hPa and at a water bath temperature of 50 °C. The solid residue is distilled under reduced pressure in a short path distillation apparatus or over a distillation bridge with air cooler. The product crystallizes during distillation, therefore it must be occasionally heated with a hot air dryer.

Yield: 930 mg (8.02 mmol, 80%); bp 123 °C (13 hPa), mp 105 °C; colourless crystals

Comments

Compared with other procedures based on an extraction with acetic acid ethyl ester, the aforementioned work up produces considerably increased yields.

Waste management**Waste disposal**

Waste	Disposal
aqueous distillate with formic acid	neutralize with sodium hydroxide solution, then: solvent water mixtures, halogen free
aqueous distillate after neutralization	waste water
distillation residue	solid waste, free from mercury

Time

About 3 hours

Break

After evaporation of the formic acid

After neutralization

Before distillation

Degree of difficulty

Medium

Analytcs**Reaction monitoring with GC**

After the complete addition of cyclohexene, for each sample a few drops of the reaction mixture are taken and shaken with 1 mL diethyl ether in a small stoppered glass or a GC-Vial. The organic phase is analyzed by means of gas chromatography.

GC

GC-conditions:

column: Macherey and Nagel, SE-54, 326-MN-30705-9, length 25 m, ID 0.32 mm, DF 0.25 μm

inlet: Gerstel KAS with control unit, injector temperature 250 $^{\circ}\text{C}$;

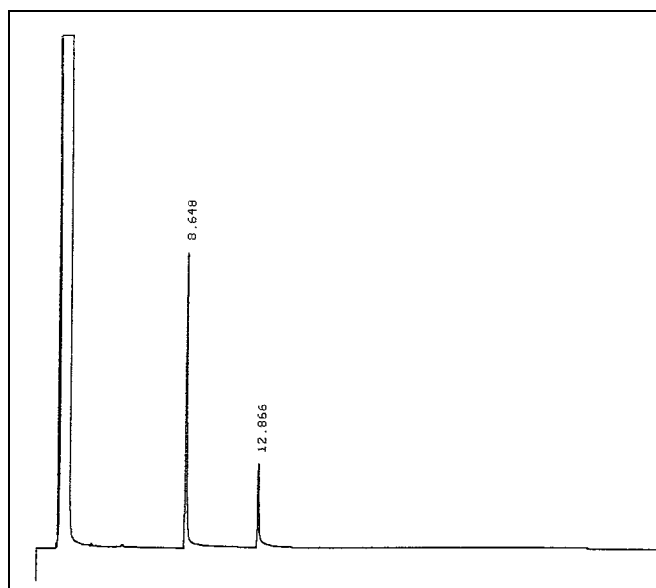
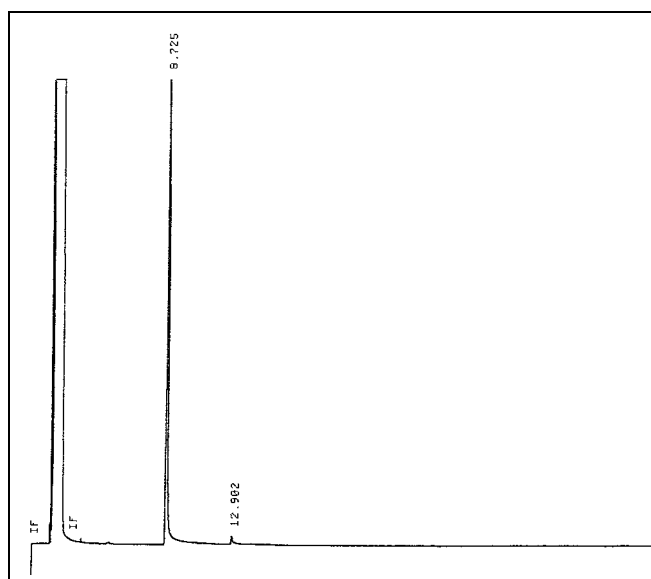
split injection 1:20, injected volume 1 μL

carrier gas: nitrogen, pre-column pressure 62 kPa, flow rate 1.04 mL/min

oven: start temperature 80 $^{\circ}\text{C}$ (1 min), 5 $^{\circ}\text{C}/\text{min}$, final temperature 250 $^{\circ}\text{C}$ (30 min)

detector: FID, 275 $^{\circ}\text{C}$

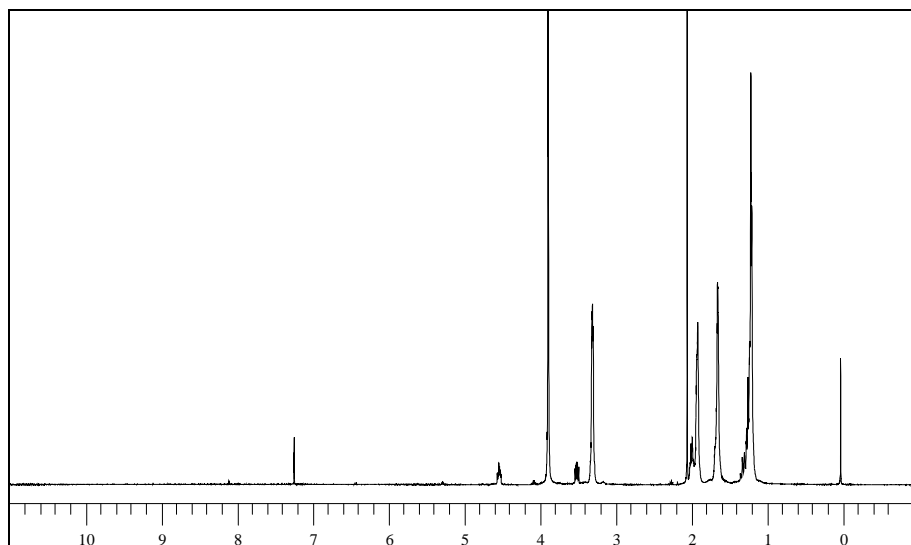
Percent concentration was calculated from peak areas.

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

Retention time (min)	Substance	Peak area %	
		crude product	pure product
8.7	product (1,2-cyclohexanediol)	74	98
12.9	intermediate product (formic acid 2-hydroxy-cyclohexyl ester, assigned with GC/MS)	26	2

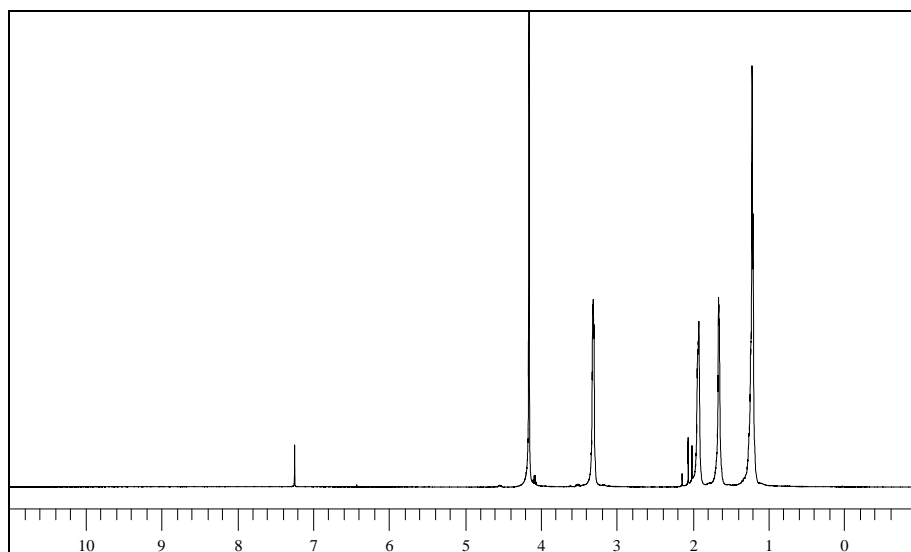
The intermediate product can be detected only if the hydrolysis was finished too early.

^1H NMR spectrum of the reaction product after incomplete hydrolysis
(500 MHz, CDCl_3)

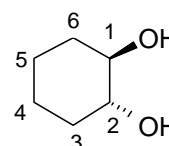


With an incomplete hydrolysis the signals of the ester, which is formed as intermediate product, are visible in the reaction product.

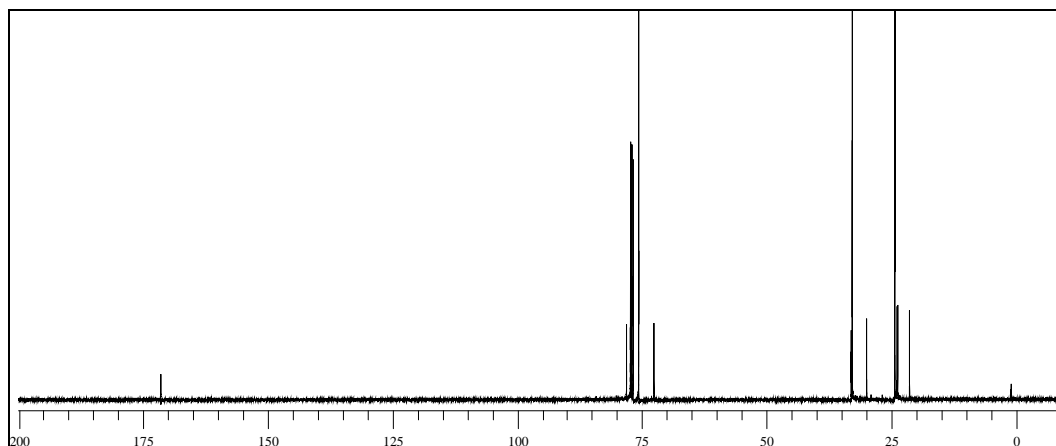
^1H NMR spectrum of the pure product (500 MHz, CDCl_3)



δ (ppm)	Multiplicity	Number of H	Assignment
1.21	m	4	4-H, 5-H
1.65	m	2	3-H, 6-H (axial)
1.92	m	2	3-H, 6-H (equatorial)
3.30	m	2	1-H, 2-H
4.15	s	2	OH
7.26			solvent



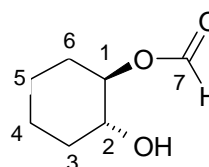
^{13}C NMR spectrum of the reaction product after incomplete hydrolysis
(125 MHz, CDCl_3)



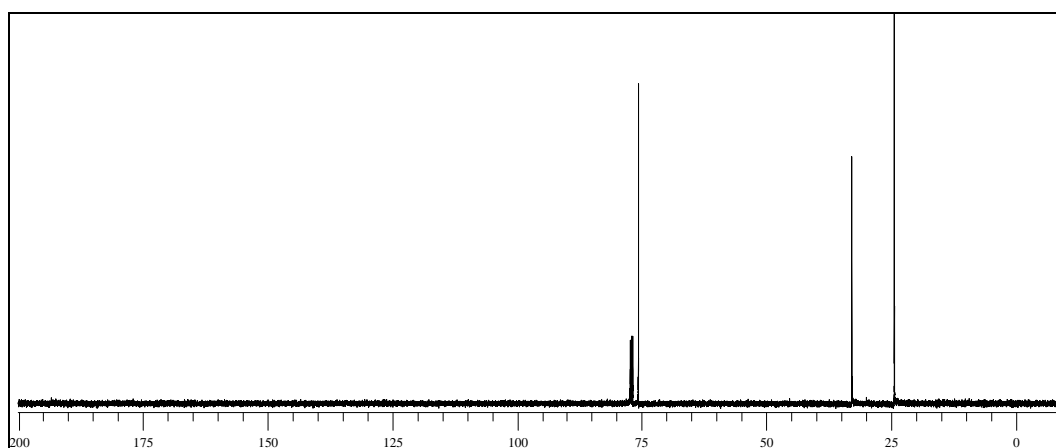
With an incomplete hydrolysis the signals of the ester which is formed as intermediate product, are visible in the reaction product.

Signal assignment for formic acid-2-hydroxy-cyclohexylester

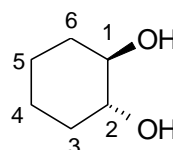
δ (ppm)	Assignment
21.3	C-4
23.8	C-5
29.9	C-6
33.0	C-3
72.6	C-2
78.1	C-1
171.5	C-7
76.5-77.5	solvent

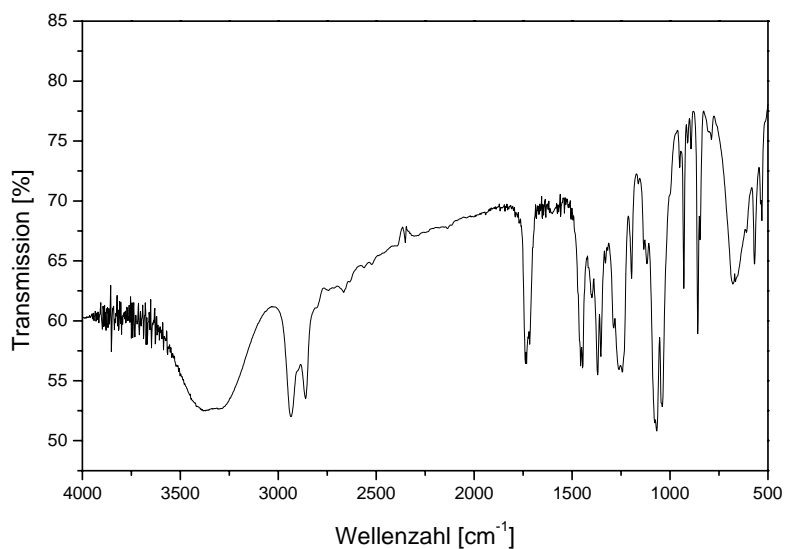
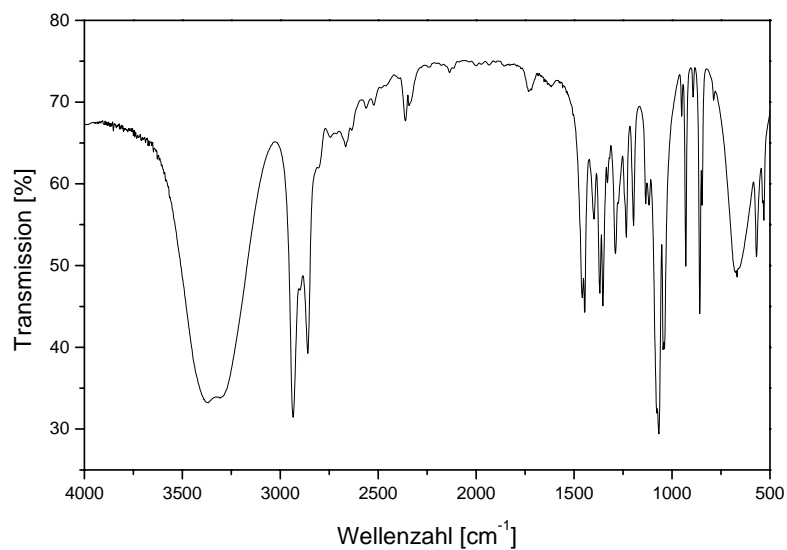


^{13}C NMR spectrum of the pure product (125 MHz, CDCl_3)



δ (ppm)	Assignment
24.3	C-4, C-5
32.8	C-3, C-6
75.6	C-1, C-2
76.5-77.5	solvent



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

(cm ⁻¹)	Assignment
3340	O-H-valence
2939, 2862	C-H-valence, alkane