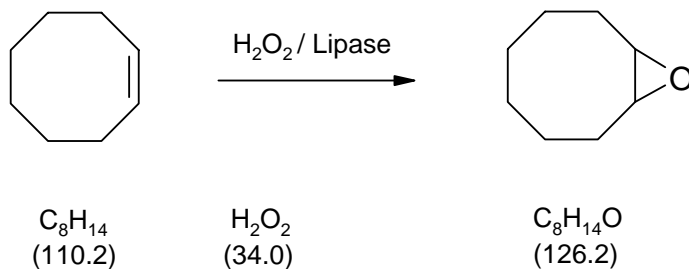


3035 Synthesis of cis-1,2-epoxycyclooctane from cyclooctene**Literature**

S. Warwel, M. Rüschen gen. Klaas, *J. Mol. Catalysis B: Enzym. 1* **1995**, 29-35

M. Rüschen gen. Klaas und S. Warwel, *Organic Lett.* **1999**, 1, 1025-6.

Classification**Reaction types and substance classes**

addition to alkenes, oxidation

alkene, epoxide, peroxide, enzyme, natural product

Work methods

stirring with magnetic stir bar, distilling under reduced pressure, shaking out, extracting, filtering, evaporating with rotary evaporator, heating with oil bath

Instruction (batch scale 10 mmol)**Equipment**

100 mL round bottom flask, 250 mL Erlenmeyer flask, magnetic stirrer, magnetic stir bar, rotary evaporator, separating funnel, short-path still or micro-distillation apparatus, vacuum pump, oil bath

Substances

<i>cis</i> -cyclooctene (bp 145-146 °C)	1.10 g (1.31 mL, 10.0 mmol)
hydrogen peroxide (33%)	5.7 g (5.1 mL, 55 mmol)
Chirazyme L2-cf (Roche Biochemicals 1 865 439)	0.5 g
acetic acid ethyl ester (bp 77 °C)	50 mL
peroxide test strips or potassium iodide starch solution	
sodium sulfite solution (saturated)	
sodium hydrogen carbonate solution (saturated)	
sodium sulfate, for drying	
water free	

Reaction

When working with hydrogen peroxide all equipment must be free from heavy metals, especially one should look after the intact plastic cover of the magnetic stir bars.

In a 100 mL round bottom flask with magnetic stir bar 1.10 g (10.0 mmol) *cis*-cyclooctene are dissolved in 50 mL acetic acid ethyl ester and 0.5 g of the Lipase are added. Within 3 hours and at intervals of 15 minutes 425 μ L at a time hydrogen peroxide (total 5.1 mL) are added under stirring. Afterwards the mixture is stirred for 24 hours at room temperature.

Work up

The reaction solution is filtered over a folded filter into a 250 mL Erlenmeyer flask. The Lipase in the filter is stored in acetic acid ethyl ester. Sodium sulfite solution is added dropwise under stirring to the filtrate until the peroxide test strips or the potassium iodide starch solution do not indicate any further peroxide. Then the solution is shaken out with a saturated NaHCO₃-solution until no further gas evolution can be observed. The phases are separated and the organic phase is dried over sodium sulfate. The drying agent is filtered off, and washed with little solvent. The solvent is evaporated at the rotary evaporator at a pressure not below 200 hPa. The remaining cyclooctene oxide should have a melting point of at least 52 °C.

For further purification the crude product can be distilled with a short path still or a micro-distillation apparatus under reduced pressure.

Yield: 950 mg (7.53 mmol, 75%); colourless waxlike solid, bp 69 °C (13 hPa), mp 52°

Comments

The enzyme can be used several times. If so, it should not be dried, but stored in the relevant solvent.

Waste management**Recycling**

The evaporated acetic acid ethyl ester is collected and redistilled.

Waste disposal

Waste	Disposal
aqueous phases	solvent water mixtures, halogen free
distillation residue	organic solvents, halogen free
sodium sulfate	solid waste, free from mercury

Time

4 hours, additionally 24 hours for stirring

Break

After addition of hydrogen peroxide

Degree of difficulty

Easy

Analytics**GC**

Sample preparation:

About 100 mg of the substance are dissolved in 1 mL *tert*-butyl methyl ether, of which 1 μ L is injected.

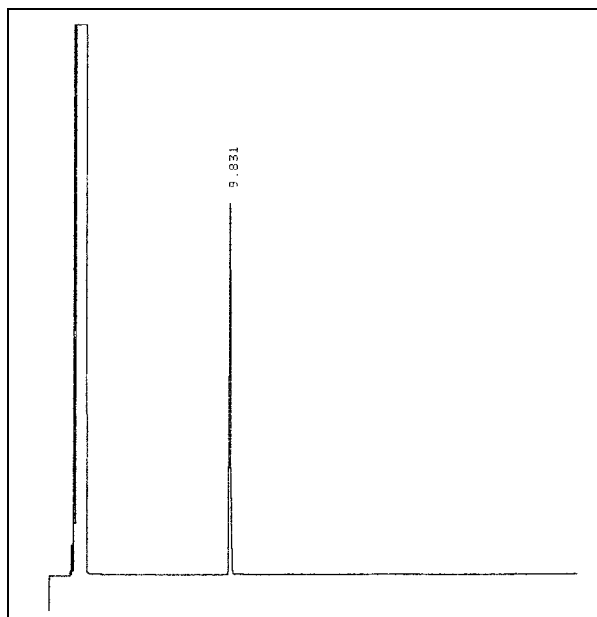
GC-conditions:

column: Macherey and Nagel, SE-54, 326-MN-30705-9, length 25 m, ID 0.32 mm, DF 0.25 μ minlet: Gerstel KAS with control unit, injector temperature 250 $^{\circ}$ C;split injection 1:20, injected volume 1 μ L

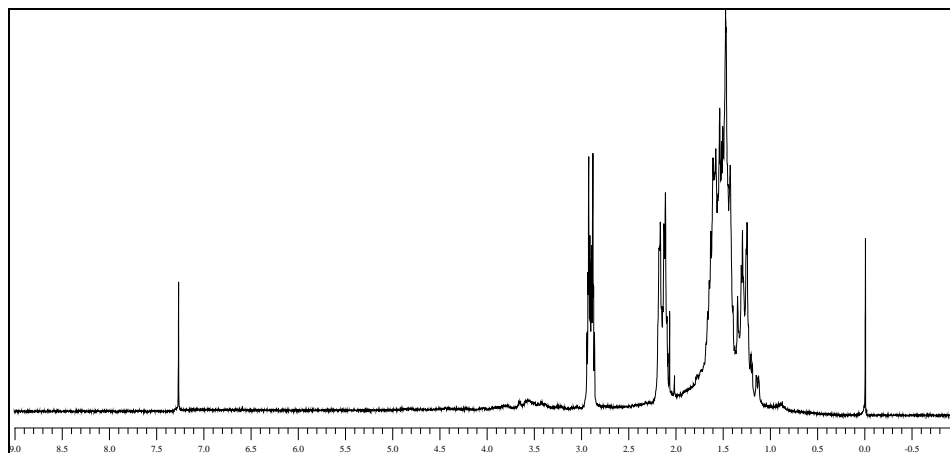
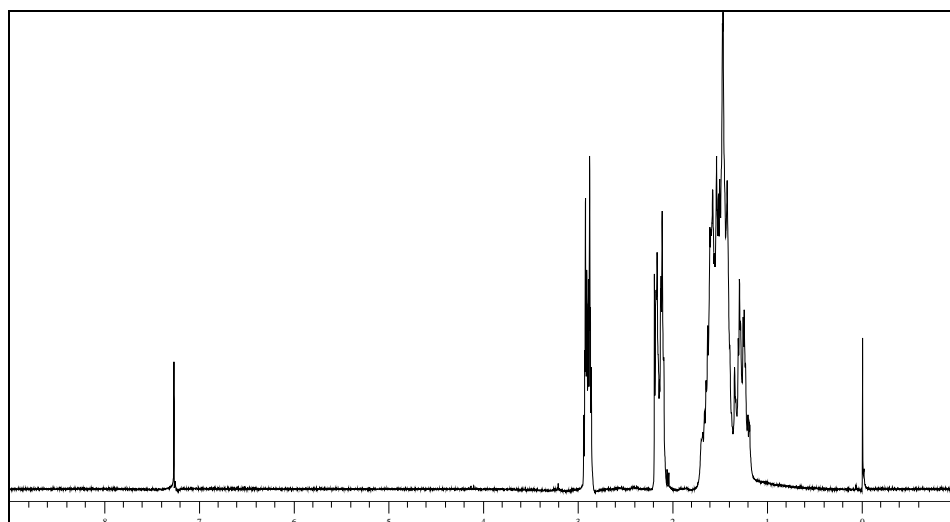
carrier gas: nitrogen, pre-column pressure 62 kPa, 1.04 mL/min

oven: start temperature 80 $^{\circ}$ C, 1 min, heating rate 5 $^{\circ}$ C/min, 250 $^{\circ}$ C, 30 mindetector: FID, 275 $^{\circ}$ C

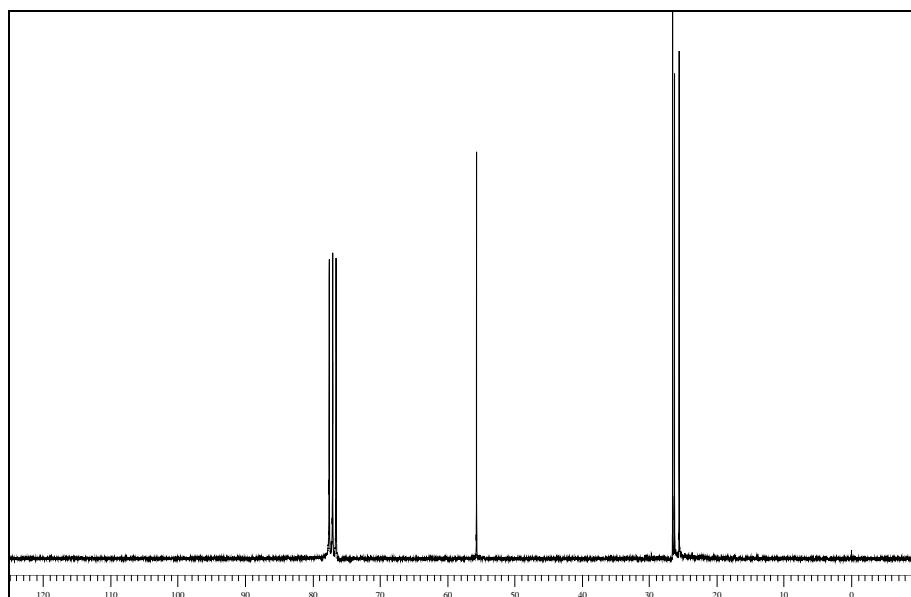
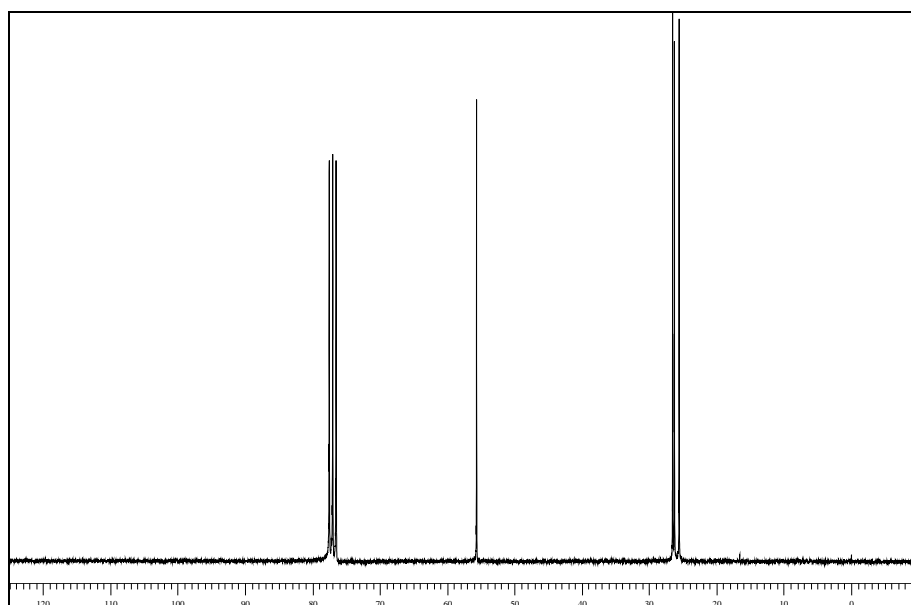
Percent concentration was calculated from peak areas.

GC of the pure product

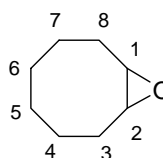
Retention time(min)	Substance	Peak area%
9.8	product (epoxycyclooctane, determined with GC/MS) m/e: 111, 98, 97, 93, 84, 83, 82, 79, 67, 57, 55, 42, 41, 39	100

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

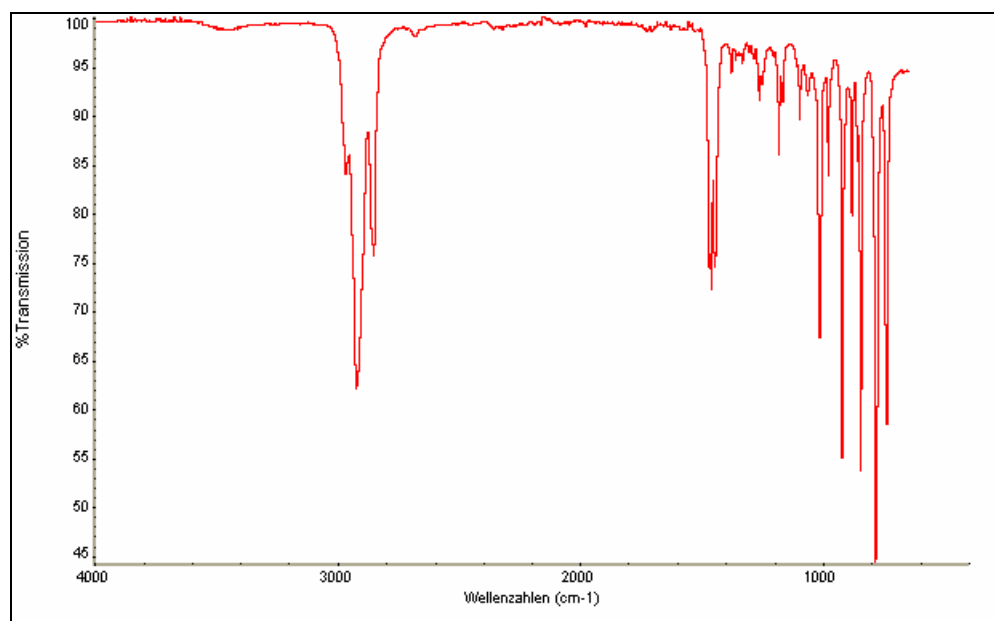
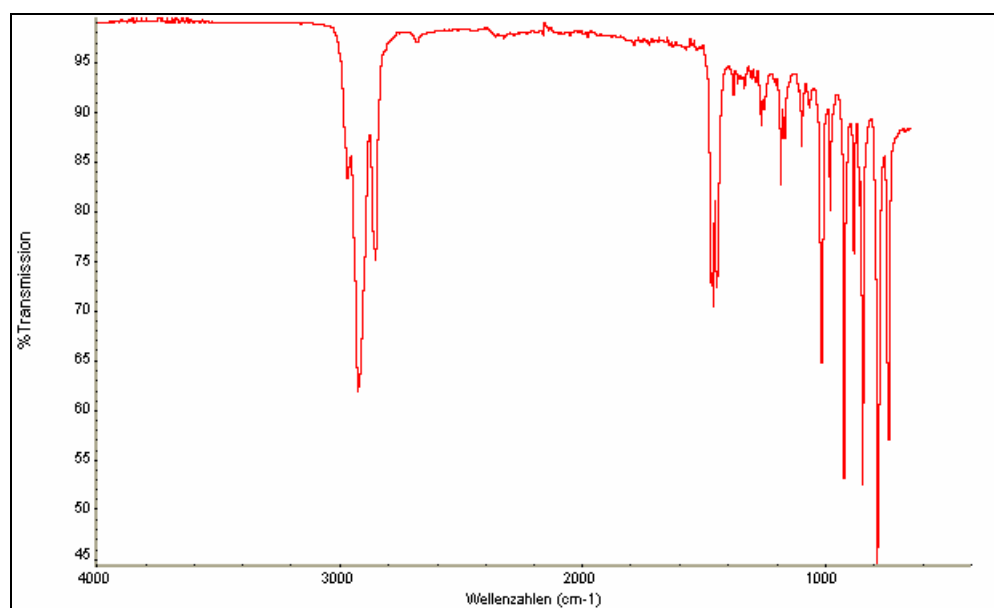
δ (ppm)	Multiplicity	Number of H	Assignment
1.10-1.79	m	10	
2.14	m	2	
2.90	m	2	CH-O-CH
7.26			solvent

^{13}C NMR spectrum of the crude product (62.5 MHz, CDCl_3) **^{13}C NMR spectrum of the pure product (62.5 MHz, CDCl_3)**

δ (ppm)	Assignment ¹
25.5	C-5, C-6
26.2	C-4, C-7
26.5	C-3, C-8
55.6	C-1, C-2
76.5-77.5	solvent



¹ N. R. Easton, Jr., F. A. L. Anet, P. A. Burns and C. S. Foote, *J. Am. Chem. Soc.* **1974**, *96*, 3945.

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

(cm ⁻¹)	Assignment
2969	C-H-valence, alkane
2924	
2853	