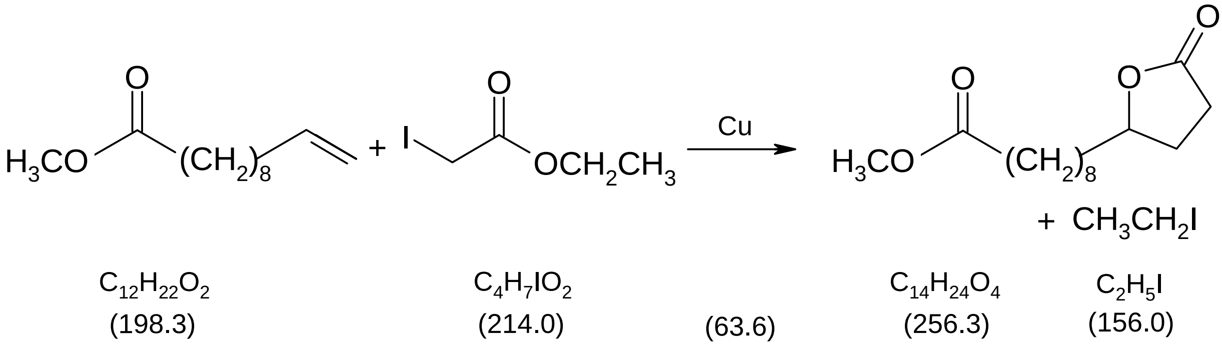
# 4005 Synthesis of 9-(5-oxotetrahydrofuran-2-yl)nonanoic acid methyl ester



## Classification

### Reaction types and substance classes

addition to alkenes, radical reaction, ring closure reaction
alkene, halogencarboxylic acid ester, lactone

### Work methods

working with protective gas, stirring with magnetic stir bar, heating under reflux, evaporating with rotary evaporator, filtering, recrystallizing, heating with oil bath

## Instruction (batch scale 10 mmol)

### Equipment

50 mL two-neck flask, protective gas supply, reflux condenser, heatable magnetic stirrer, magnetic stir bar, rotary evaporator, Buechner funnel, suction flask, desiccator, oil bath

### Substances

| | |
|---|---|
| undecenoic acid methyl ester (bp 248 °C) | 1.98 g (2.23 mL, 10.0 mmol) |
| iodoacetic acid ethyl ester (bp 73-74 °C/ 21 hPa) | 2.78 g (1.54 mL, 13.0 mmol) |
| copper powder (finely powdered, >230 mesh ASTM) | 3.05 g (48.0 mmol) |
| *tert*-butyl methyl ether (bp 55 °C) | 50 mL |
| petroleum ether (bp 60-80 °C) | 150 mL |

### Reaction

In a 50 mL two-neck flask with magnetic stir bar and a reflux condenser connected with a protective gas piping 1.98 g (2.23 mL, 10.0 mmol) undecenoic acid methyl ester and 2.78 g (1.54 mL, 13.0 mmol) iodoacetic acid ethyl ester are mixed with 3.05 g (48.0 mmol) copper powder under a protective gas atmosphere. Afterwards the reaction mixture is stirred at 130 °C oil bath temperature under protective gas for 4 hours. (Reaction monitoring see Analytics.)

### Work up

The reaction mixture is cooled down to room temperature, 20 mL *tert*-butyl methyl ether are added, the mixture is stirred for 5 minutes and filtered off. The copper powder on the filter is washed 3 times with 10 mL *tert*-butyl methyl ether each. Filtrate and wash solutions are combined, the solvent is evaporated at the rotary evaporator. A yellow oil remains as crude product.
Crude yield: 2.5 g.

The crude product is dissolved in 150 mL petroleum ether under reflux. The solution is allowed to cool down to room temperature, then it is stored in the refrigerator over night for complete crystallization. The crystalline product is sucked off over a Buechner funnel and dried in the vacuum desiccator. The mother liquor is stored again in the refrigerator for a check of complete crystallization.
Yield: 1.84 g (7.20 mmol, 72%); white solid, mp 33-34 °C

### Comments

In order to achieve a quantitative reaction within 4 hours, a fivefold excess of copper is used.

### Waste management

### Recycling

The copper powder can be used three times.

### Waste disposal

| **Waste** | **Disposal** |
|---|---|
| evaporated *tert*-butyl methyl ether (might contain iodoethane) | organic solvents, containing halogen |
| mother liquor from recrystallization | organic solvents, containing halogen |
| copper powder | solid waste, free from mercury, containing heavy metals |

### Time

6-7 hours

### Break

After heating and before recrystallizing

### Degree of difficulty

Easy

## Instruction (batch scale 100 mmol)

### Equipment

250 mL two-neck flask, protective gas supply, reflux condenser, heatable magnetic stirrer, magnetic stir bar, rotary evaporator, Buechner funnel, suction flask, desiccator, oil bath

### Substances

| | |
|---|---|
| undecenoic acid methyl ester (bp 248 °C) | 19.8 g (22.3 mL, 100 mmol) |
| iodoacetic acid ethyl ester (bp 73-74 °C/ 21 hPa) | 27.8 g (15.4 mL, 130 mmol) |
| copper powder (finely powdered, >230 mesh ASTM) | 30.5 g (480 mmol) |
| *tert*-butyl methyl ether (bp 55 °C) | 130 mL |
| petroleum ether (bp 60-80 °C) | 300 mL |

### Reaction

In a 250 mL two-neck flask with magnetic stir bar and a reflux condenser connected with a protective gas piping 19.8 g (22.3 mL, 100 mmol) undecenoic acid methyl ester and 27.8 g (15.4 mL, 130 mmol) iodoacetic acid ethyl ester are mixed with 30.5 g (480 mmol) copper powder under a protective gas atmosphere. Afterwards the reaction mixture is stirred at 130 °C oil bath temperature under protective gas for 4 hours. (Reaction monitoring see Analytics.)

### Work up

The reaction mixture is cooled down to room temperature, 30 mL *tert*-butyl methyl ether are added, the mixture is stirred for 5 minutes and filtered off. The copper powder on the filter is washed four times with 25 mL *tert*-butyl methyl ether each. Filtrates and wash solutions are combined, the solvent is evaporated at the rotary evaporator. A yellow oil remains as crude product.
Crude yield: 25.4 g.

The crude product is dissolved in 300 mL petroleum ether under reflux. The solution is allowed to cool down to room temperature, then it is stored in the refrigerator over night for complete crystallization. The crystalline product is sucked off over a Buechner funnel and dried in the vacuum desiccator. The mother liquor is stored again in the refrigerator for a check of complete crystallization.
Yield: 19.5 g (76.1 mmol, 76%); white solid, mp 34 °C

### Comments

In order to achieve a quantitative reaction within 4 hours, a fivefold excess of copper is used.

### Waste management

### Recycling

The copper powder can be used three times.

### Waste disposal

| Waste | Disposal |
|---|---|
| evaporated *tert*-butyl methyl ether<br>(might contain iodoethane) | organic solvents, containing halogen |
| mother liquor from recrystallization | organic solvents, containing halogen |
| copper powder | solid waste, free from mercury,<br>containing heavy metals |

### Time

6-7 hours

### Break

After heating and before recrystallizing

### Degree of difficulty

Easy

## Analytics

### Reaction monitoring with TLC

Sample preparation:

Using a Pasteur pipette, two drops of the reaction mixture are taken and diluted with 0.5 mL diethyl ether.

TLC-conditions:

| | |
|---|---|
| adsorbant: | TLC-aluminium foil (silica gel 60) |
| eluent: | petroleum ether (60/80) : acetic acid ethyl ester = 7 : 3 |
| visualisation: | The TLC-aluminium foil is dipped in 2 N $H_2SO_4$ and then dried with a hot air dryer. |

### Reaction monitoring with GC

Sample preparation:

Using a Pasteur pipette, one drop of the reaction mixture is taken and diluted with 10 mL dichloromethane. From this solution, 0.2 µL are injected.

10 mg from the solid product are dissolved in 10 mL dichloromethane. From this solution, 0.2 µL are injected.

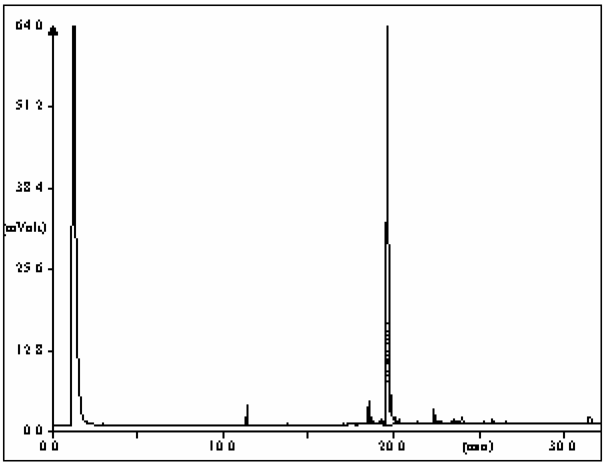
GC-conditions:

| | |
|---|---|
| column: | DB-1, 28 m, internal diameter 0.32 mm, film 0.25 µm |
| inlet: | on-column-injection |
| carrier gas: | hydrogen (40 cm/s) |
| oven: | 90 °C (5 min), 10 °C/min to 240 °C (40 min) |
| detector: | FID, 270 °C |

Percent concentration was calculated from peak areas.

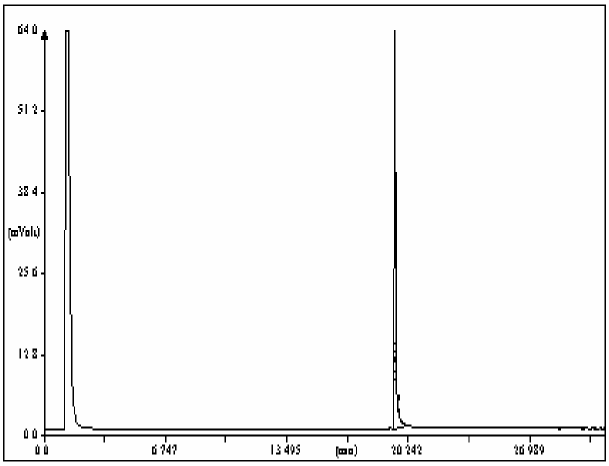
## GC of the crude product

GC-conditions are the same as for the reaction monitoring



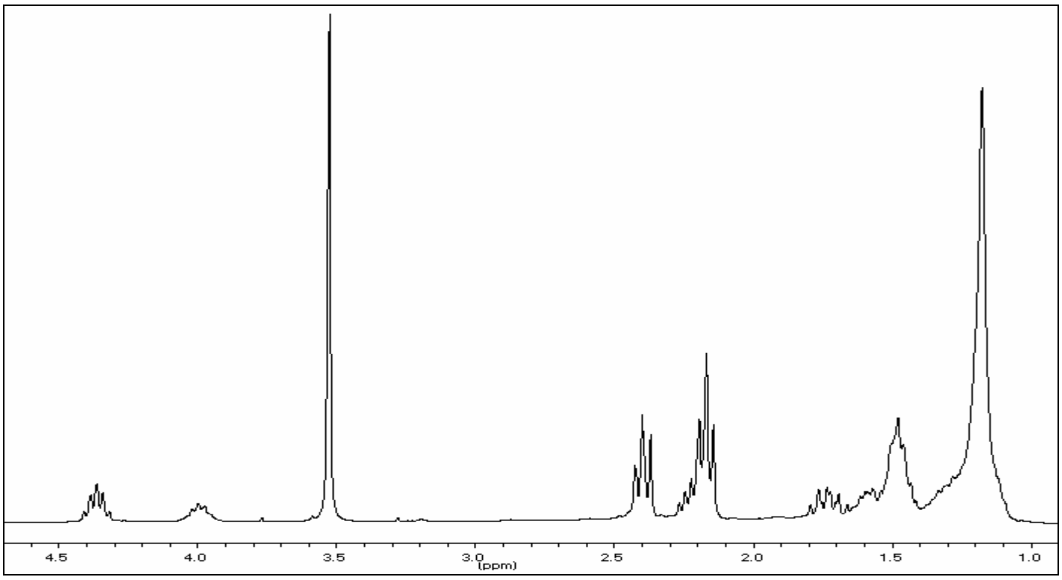
| Retention time (min) | Substance | Peak area % |
|---|---|---|
| 19.63 | product | 86.1 |
| | impurities | each < 2 |

## GC of the pure product

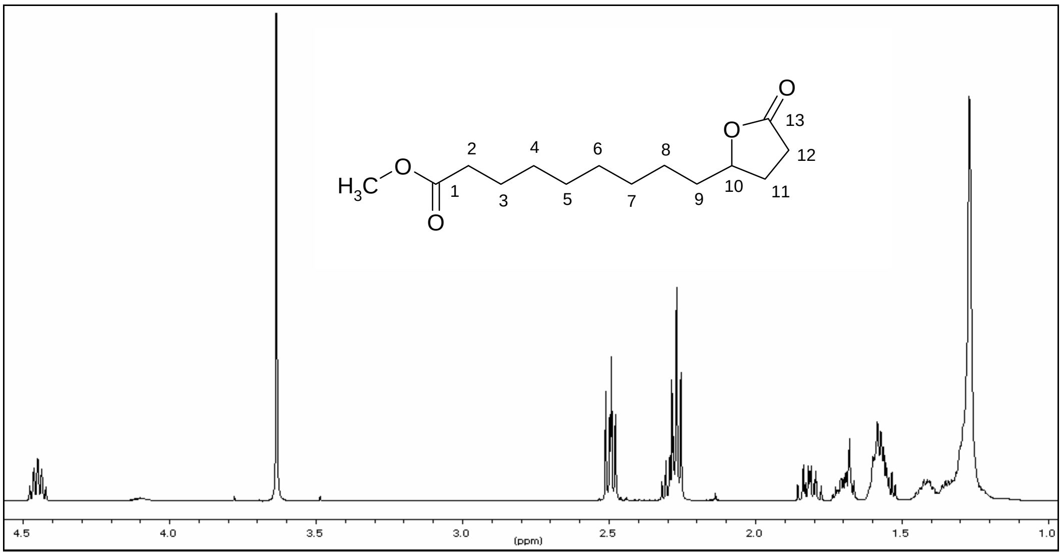


| Retention time (min) | Substance | Peak area % |
|---|---|---|
| 19.54 | product | 99.7 |

**$^1$H NMR spectrum of the crude product** (500 MHz, $CDCl_3$)

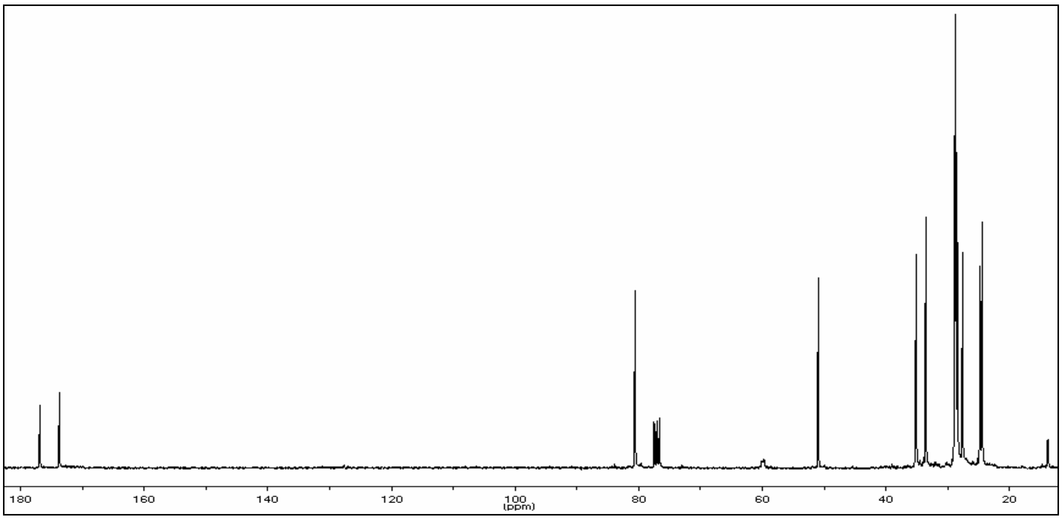


**$^1$H NMR spectrum of the pure product** (500 MHz, $CDCl_3$)

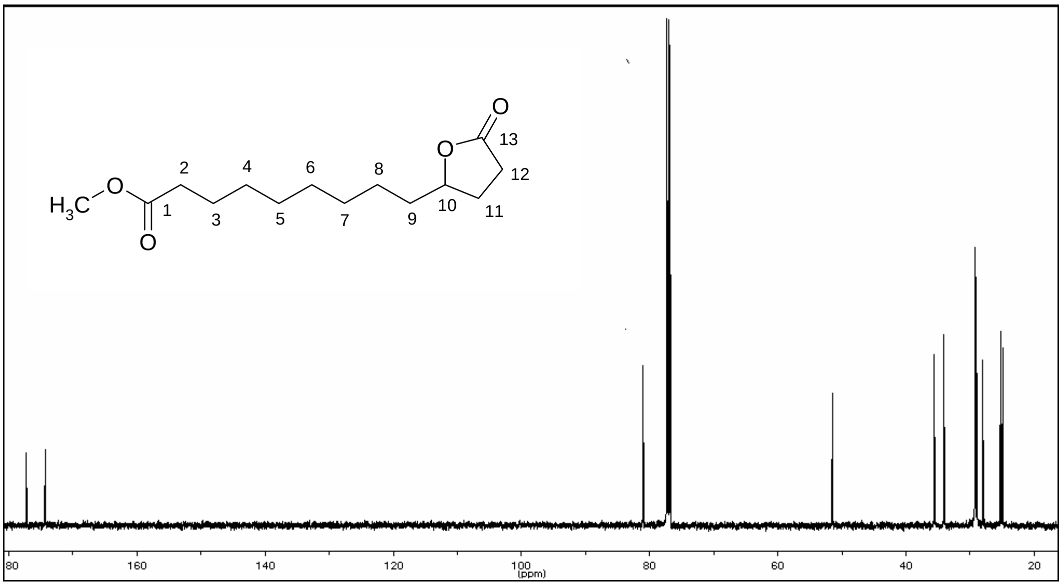


| δ (ppm) | Multiplicity | Number of H | Assignment |
|---|---|---|---|
| 4.48 | M | 1 | 10-H |
| 3.67 | S | 3 | O-$CH_3$ |
| 2.50 | M | 2 | 12-H |
| 2.30 | M | 2 | 11-H |
| 2.27 | T | 2 | 2-H |
| 1.82 | M | 1 | 9-H |
| 1.70 | M | 1 | 9-H |
| 1.57 | M | 2 | 3-H |
| 1.24-1.45 | M | 10 | 4-H to 8-H |

**$^{13}$C NMR spectrum of the crude product** (125.7 MHz, $CDCl_3$)

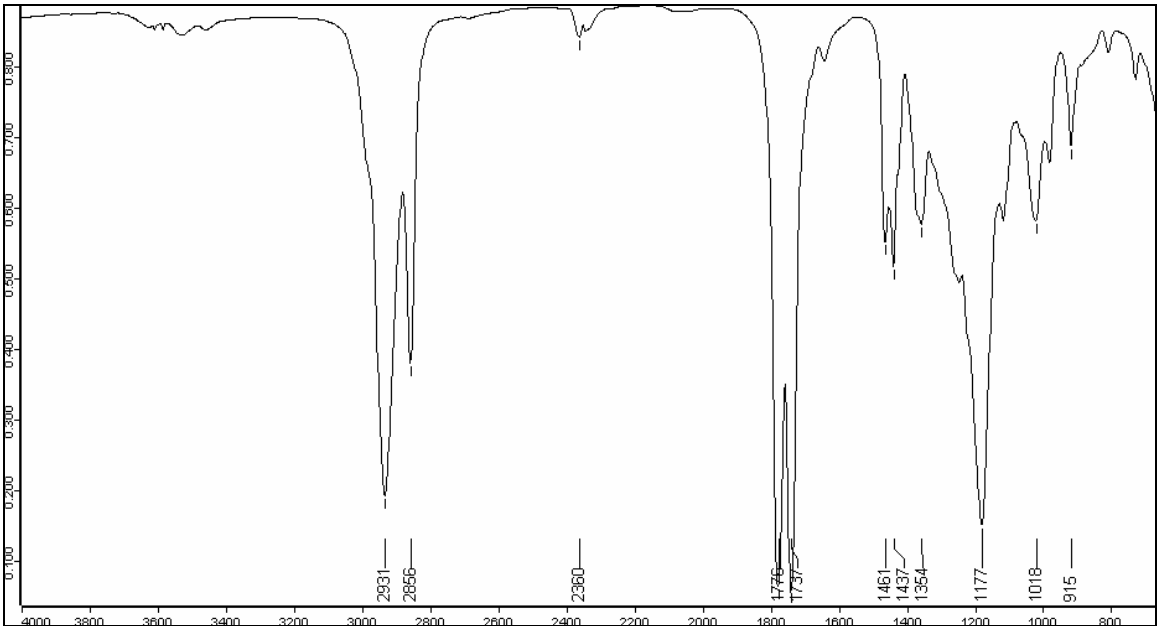


**$^{13}$C NMR spectrum of the pure product** (125.7 MHz, $CDCl_3$)



| δ (ppm) | Assignment |
|---|---|
| 177.2 | C-13 |
| 174.2 | C-1 |
| 81.0 | C-10 |
| 51.4 | O-$CH_3$ |
| 35.5 | C-12 |
| 34.0 | C-2 |
| 28.0-29.2 | C-4 to C-8, C-11 |
| 25.2 | C-9 |
| 24.9 | C-3 |
| 76.5-77.5 | solvent |

## IR spectrum of the pure product (film)



| **(cm$^{-1}$)** | **Assignment** |
|---|---|
| 2931 | C-H-valence, alkane |
| 2856 | C-H-valence, alkane |
| 1776 | C=O-valence, lactone |
| 1737 | C=O-valence, ester |