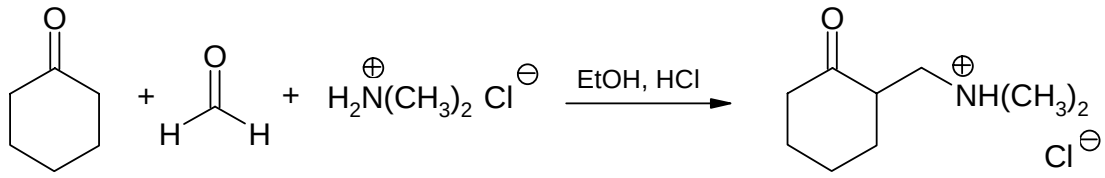
4008 Synthesis of 2-dimethylaminomethyl-cyclohexanone hydrochloride



$C_6H_{10}O$	CH_2O	C_2H_8ClN	$C_9H_{18}NOCl$
(98.2)	(30.0)	(81.6)	(191.7)

Classification

Reaction types and substance classes

reaction of the carbonyl group in aldehydes, Mannich reaction
ketone, aldehyde, amine

Work methods

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

Instruction (batch scale 10 mmol)

Equipment

25 mL round bottom flask, reflux condenser, Buechner funnel (Ø 3 cm), suction flask, heatable magnetic stirrer, magnetic stir bar, rotary evaporator, desiccator, oil bath

Substances

cyclohexanone (bp 156 °C)	0.982 g (1.03 mL, 10.0 mmol)
paraformaldehyde (mp 120-170 °C)	0.360 g (12.0 mmol)
dimethylammonium chloride	0.816 g (10.0 mmol)
hydrochloric acid (conc.)	2 drops
ethanol (bp 78 °C)	16 mL
acetone (bp 56 °C)	50 mL

Reaction

0.982 g (1.03 mL, 10.0 mmol) cyclohexanone, 0.360 g (12.0 mmol) paraformaldehyde, 0.816 g (10.0 mmol) dimethylammonium chloride and 4 mL ethanol are filled in a 25 mL round bottom flask with reflux condenser and magnetic stir bar. 2 drops of conc. hydrochloric acid are added and the mixture is heated under stirring 4 hours under reflux.

Work up
The hot solution is filtered in a round bottom flask and the solvent is evaporated at the rotary evaporator. The residue is dissolved in 2 mL ethanol under heating. At room temperature 20 mL acetone are added to the solution. For complete crystallization the solution is stored over night in the freezer compartment. The crystallized crude product is sucked off over a Buechner funnel (Ø = 3 cm) and dried in the desiccator over silica gel.
Crude yield: 1.64 g; mp 143-144 °C

For further purification the crude product is again dissolved in about 10 mL ethanol under reflux and at room temperature 30 mL acetone are added. The crystallization is completed in the freezer compartment. The product is sucked off and dried in the desiccator.
Yield: 1.45 g (7.56 mmol, 76%); mp 157-158°C

Comments
To verify a complete crystallization, the mother liquor is stored in the freezer compartment. No product should crystallize any further.

Waste management

Waste Disposal

Waste	Disposal
mother liquors	organic solvents, containing halogen

Time
4-5 hours without time for crystallization

Break
After filtration of the hot solution

Degree of difficulty
Easy

Instruction (batch scale 100 mmol)

Equipment
100 mL round bottom flask, reflux condenser, Buechner funnel (Ø 5.5 cm), suction flask, heatable magnetic stirrer, magnetic stir bar, rotary evaporator, desiccator, oil bath

Substances

cyclohexanone (bp 156 °C)	9.82 g (10.3 mL, 100 mmol)
paraformaldehyde (mp 120-170 °C)	3.60 g (120 mmol)
dimethylammonium chloride	8.16 g (100 mmol)
hydrochloric acid (conc.)	0.4 mL
ethanol (bp 78 °C)	64 mL
acetone (bp 56 °C)	180 mL

Reaction

9.82 g (10.3 mL, 100 mmol) cyclohexanone, 3.60 g (120 mmol) paraformaldehyde, 8.16 g (100 mmol) dimethylammonium chloride and 4 mL ethanol are filled in a 100 mL round bottom flask with reflux condenser and magnetic stir bar. 0.4 mL conc. hydrochloric acid are added and the mixture is heated under stirring for 4 hours under reflux.

Work up

The hot solution is filtered in a round-bottom flask and the solvent is evaporated at the rotary evaporator. The residue is dissolved in 20 mL ethanol under heating. At room temperature 70 mL acetone are added to the solution. For complete crystallization the solution is stored over night in the freezer compartment. The crystallized crude product is sucked off over a Buechner funnel (Ø = 5.5 cm) and dried in the desiccator over silica gel.
Crude yield: 15.6 g; mp 149-150 °C

For further purification the crude product is again dissolved in about 40 mL ethanol under reflux and at room temperature 110 mL acetone are added. The crystallization is completed in the freezer compartment. The product is sucked off and dried in the desiccator.
Yield: 14.7 g (76.7 mmol, 77%,); mp 156-157 °C

Comments

To verify a complete crystallization, the mother liquor is stored in the freezer compartment. No product should crystallize any further.

Waste management

Waste disposal

Waste	Disposal
mother liquors	organic solvents, containing halogen

Time

4-5 hours without time for crystallization

Break

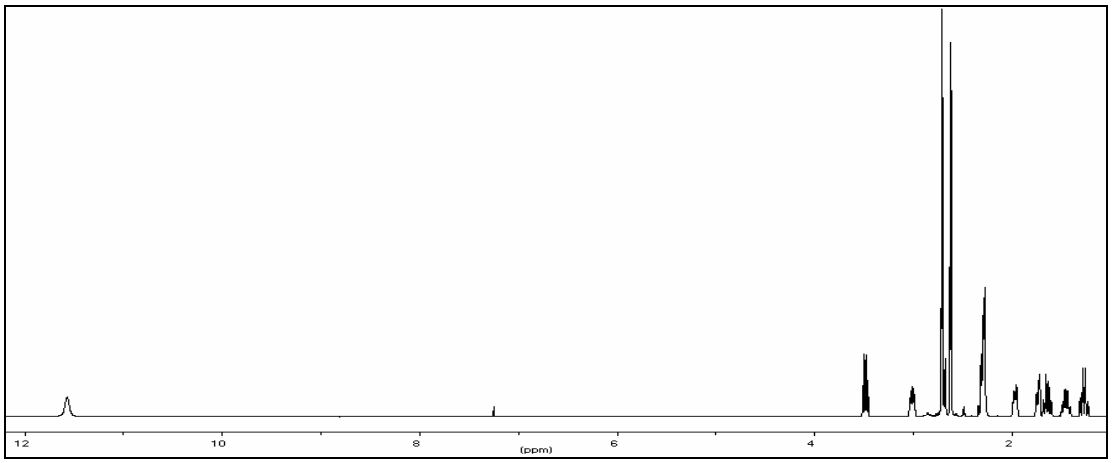
After filtration of the hot solution

Degree of difficulty

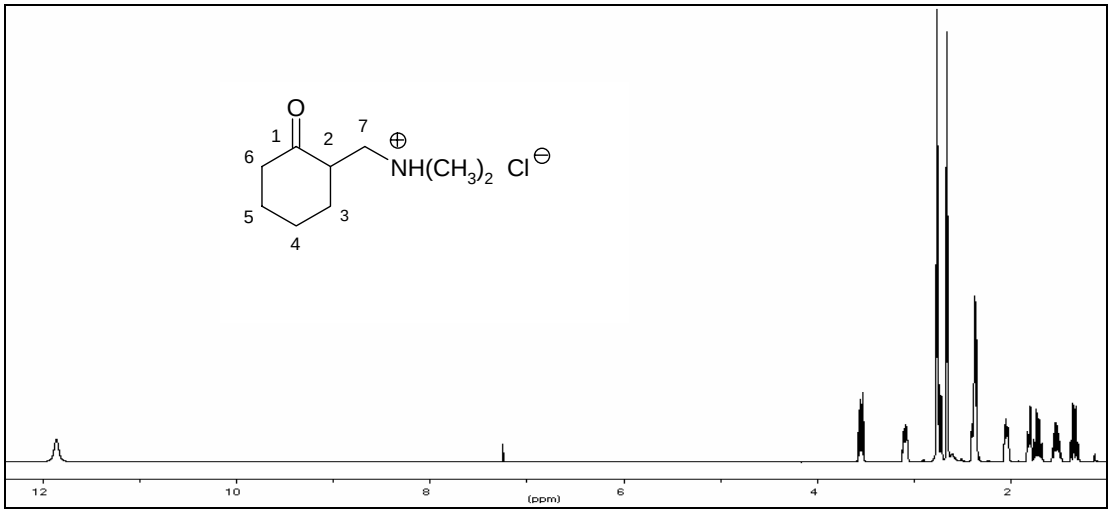
Easy

Analytics

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

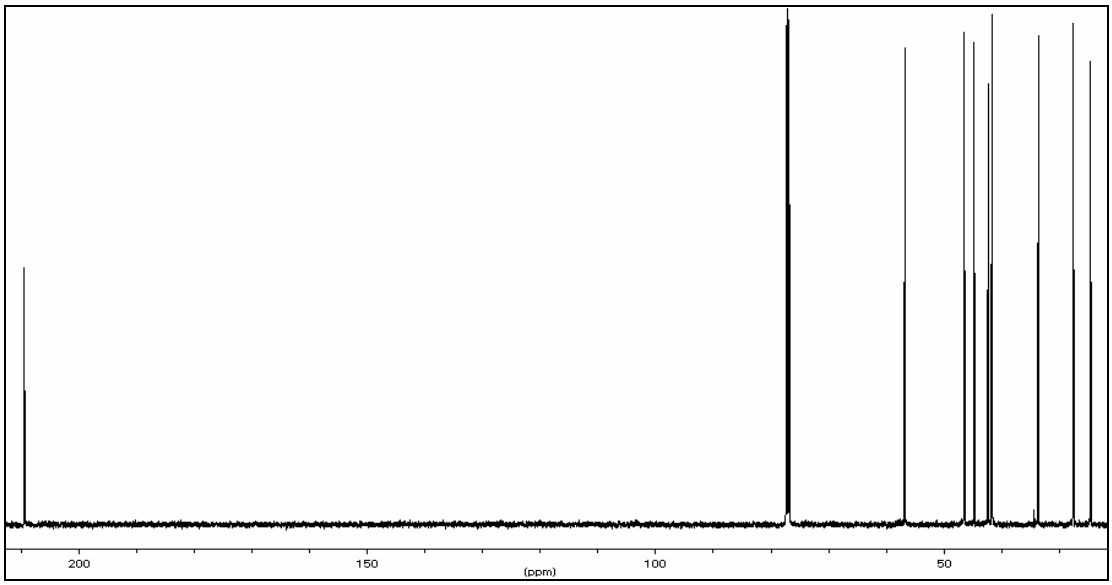


^{1}H NMR spectrum of the pure product (500 MHz, $CDCl_3$)

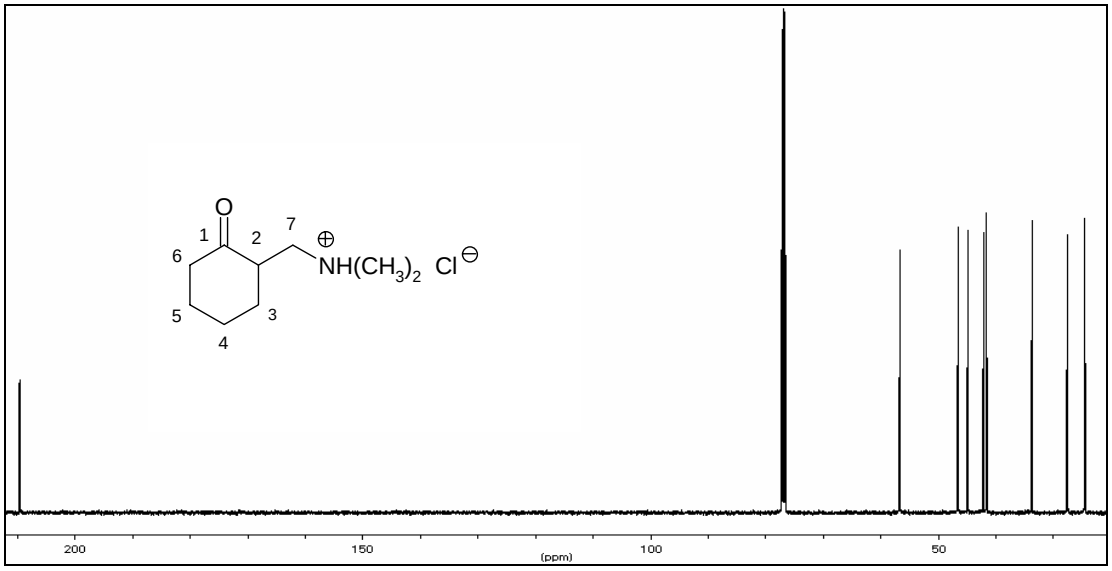


δ (ppm)	Multiplicity	Number of H	Assignment
1.35	m	1	
1.54	m	1	
1.73	m	1	
1.82	m	1	
2.05	m	1	
2.37	m	2	6-H
2.41	m	1	
2.67	d	3	NH-C**H$_3$**
2.74	m	1	
2.77	d	3	NH-C**H$_3$**
3.09	m	1	7-H
3.57		1	7-H
11.88	m	1	NH
7.26			solvent

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

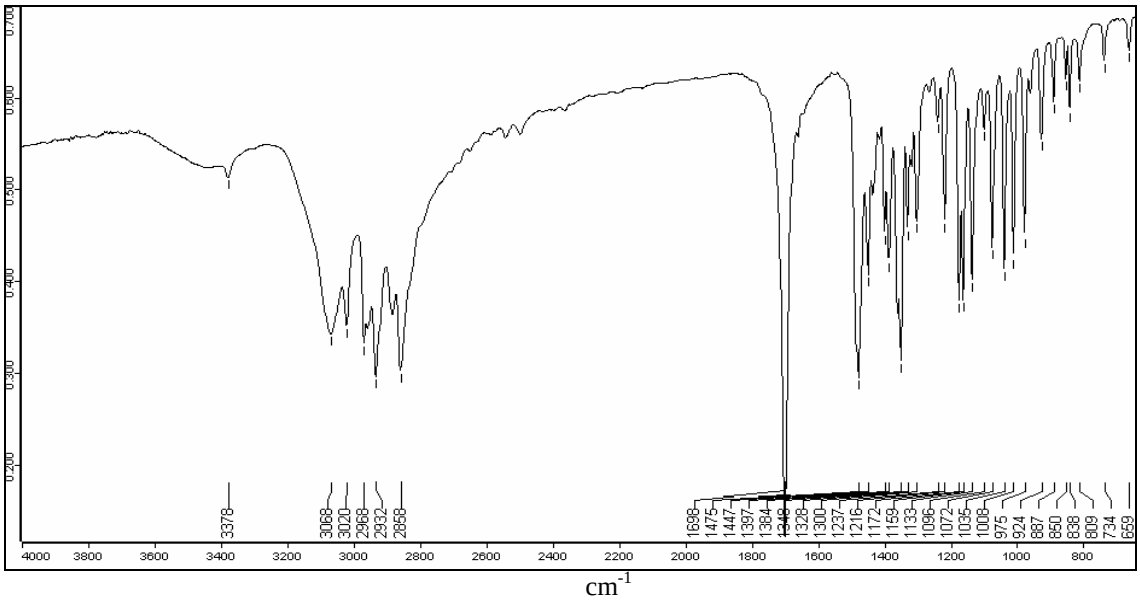


^{13}C NMR spectrum of the pure product (125 MHz, $CDCl_3$)



δ (ppm)	Assignment
209.58	C-1
56.80	C-7
46.69	C-2
44.99	C-6
42.26	CH_3
41.75	CH_3
33.88	C-4
27.70	C-3
24.70	C-5
76.5-77.5	solvent

IR spectrum of the pure product (film)



(cm^{-1})	**Assignment**
3068,	N-H-valence
3020	N-H-valence
2932	C-H-valence, alkane
2858	C-H-valence, alkane
1698	C=O-valence, ketone