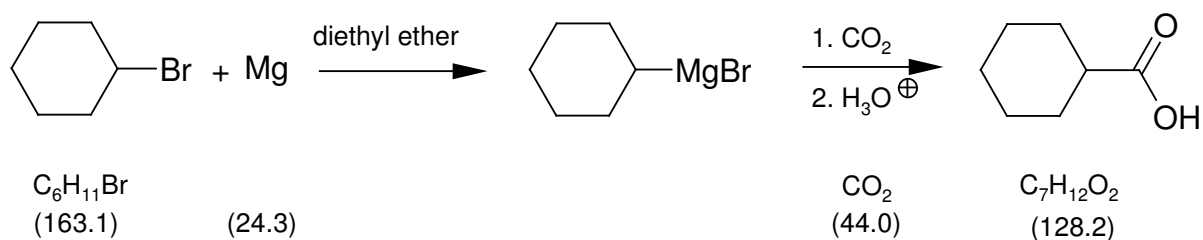


2028 Reaction of cyclohexyl magnesium bromide with carbon dioxide to cyclohexanecarboxylic acid



Classification

Reaction types and substance classes

Grignard reaction, reaction of the carbonyl group in carbon dioxide
metal-organic compound, bromoalkane, carboxylic acid

Work methods

working with moisture exclusion, adding dropwise with an addition funnel, heating under reflux, stirring with magnetic stir bar, heating with oil bath, heating with water bath, use of an ice cooling bath, working with dry ice, shaking out, extracting, filtering, evaporating with rotary evaporator, distilling under reduced pressure

Instruction (batch scale 100 mmol)

Equipment

500 mL three-neck flask (with NS 29 opening on a side neck), reflux condenser with drying tube, heatable magnetic stirrer, magnetic stir bar, hot-air gun, addition funnel with pressure balance, separating funnel, powder funnel, distillation apparatus, ice bath, oil bath, vacuum pump

Substances

bromocyclohexane (bp 163-165 °C)	16.3 g (10.3 mL, 100 mmol)
diethyl ether (bp 35 °C) dry	70 mL
diethyl ether (bp 35 °C)	500 mL
magnesium turnings	2.67 g (110 mmol)
iodine	40-50 mg
dry ice	44 g (1.0 mol)
aqueous NaOH-solution (20%)	50 mL
conc. hydrochloric acid (32%)	about 60 mL
ice	
sodium sulfate	about 5 g

Reaction

40-50 mg crystals of iodine are filled in a 500 mL three neck flask with a 100 mL addition funnel with pressure balance and a reflux condenser with drying tube. 2.67 g (110 mmol) magnesium turnings are superposed on the iodine crystals and the flask is heated with a hot-air gun at the place, where the iodine is located, until violet fumes are formed. After the flask is cooled down again to room temperature, so much dry ether is added, that the magnesium turnings are just covered (about 6 mL).

Without stirring, 0.6 mL of the 10.3 mL bromocyclohexane are added at once over the addition funnel. If the reaction does not start within a few minutes (visible at the boiling of the ether and a grey clouding), the mixture is shortly heated – still without stirring – with a hot air fan until boiling continues without heating. Then immediately under stirring, the remaining bromocyclohexane dissolved in 64 mL dry diethylether is added over the addition funnel at such a rate as to maintain gentle reflux. By any means, the reaction must be prevented from “falling asleep” (addition time about 30 minutes). After the addition is finished, the colourless solution is still heated for one hour in the water bath under reflux until the magnesium has dissolved almost entirely. The mixture is cooled with an ice bath.

Under stirring (as long as possible) about 44 g (1.0 mol) dry ice in small pieces (of a size, that they are quite fitting through the NS 29 neck of the flask) now are added to the reaction solution through the flask opening, each piece of it must be dried with a paper towel before the addition. The mixture is kept for about one hour, until all dry ice has evaporated and the contents of the flask has a temperature of about 0 C. If necessary, the defrosting is accelerated by using a cold water bath.

Work up

To the reaction mixture 100 ml diethyl ether are added and the contents of the flask is thoroughly mixed with a glass rod. Under stirring with a magnetic stirrer a mixture of 15 mL conc. hydrochloric acid (32%) and 100 g ice are slowly added over a powder funnel. The pH-value of the mixture is checked, and if necessary, more hydrochloric acid is added until clear acidic reaction. The mixture is stirred until all remaining magnesium has dissolved and the contents of the flask is completely clear (about 1 hour).

The contents of the flask is transferred into a separating funnel, thoroughly shaken and the two phases are separated. The aqueous phase is shaken out two times with 50 mL diethyl ether each, the three ether phases are combined. The aqueous phase is disposed.

The combined ether phases are thoroughly shaken with 50 mL of a 20% aqueous NaOH-solution. The ether phase is disposed.

The alkaline aqueous phase, which contains besides the salt of the cyclohexanecarboxylic acid also parts of the side product cyclohexanol, is shaken out three times with 30 mL diethyl ether each, in order to remove this side product to a large extent. The three ether phases are combined and are disposed (see comments).

Then the alkaline aqueous phase is acidified with 65 mL half-concentrated hydrochloric acid (check the pH – value!) and shaken out first with 100 mL diethyl ether once, then twice with 50 mL diethyl ether each. The aqueous phase is disposed.

The ether extracts are combined and dried over sodium sulfate. After filtering off the drying agent and washing with 10 mL ether, the ether is evaporated at a rotary evaporator at normal pressure. As crude product remains a colourless liquid. Crude yield: 8.70 g; GC-purity > 99.5% (see analytics)

The crude product is fractional distilled under reduced pressure.

Yield: 7.77 g (60.6 mmol, 61%); bp 99-100 °C (2.9-3.1 hPa); colourless liquid. All fractions have the same boiling point and a GC-purity of > 99.5%

Distillation residue: 930 mg

Comments

If the start of the Grignard-reaction causes problems, the reaction mixture can be dipped for a about 5 minutes in an ultrasound-bath instead of being heated using a fan.

Among others, the size of the dry ice pieces is important for the product yield. If the dry ice is thoroughly crunched, more moisture condensates at the correspondingly larger surface and more Grignard-reagent is deleted through hydrolysis.

After the acidic hydrolysis of the reaction mixture, the GC of the ether phase shows some substances, which correspondent to the side products, which are commonly described for Grignard-reactions (see analytics).

The side product cyclohexanol dissolves both in diethyl ether and in water. During the shaking out of the ether phase with aqueous NaOH-solution it therefore moves partly together with the salt of the cyclohexanecarboxylic acid into the aqueous phase. It is advisable to remove the cyclohexanol to a large extent from the aqueous phase (as aforementioned under „work up“) through repeated shaking out of the alkaline aqueous phase with diethyl ether. Otherwise the cyclohexanol can reach during the further work up the crude product and is carried along into the first fractions of the distillation.

Waste management

Recycling

The diethyl ether from shaking out of the alkaline aqueous phase is collected and redistilled; it contains only some cyclohexanol (bp 161 °C) as impurity.

The diethyl ether which is evaporated from the crude product is also collected and redistilled.

Waste disposal

Waste	Disposal
aqueous phase after shaking out with diethyl ether of the acidified reaction solution	solvent water mixtures, containing halogen
aqueous phase after shaking out with diethyl ether of the acidified aqueous phase	solvent water mixtures, containing halogen
diethyl ether phase after shaking out with aqueous NaOH-solution (contains also other volatile substances)	organic solvents, halogen free
distillation residue	solid waste, free from mercury
sodium sulfate	solid waste, free from mercury

Time

Altogether about 8 hours

Break

After the acidifying of the reaction solution (5 hours), then between the single working steps

Degree of difficulty

Medium

Analytics

GC-measurement

GC-conditions:

column: Zebtron ZB-1, length 15 m, internal diameter 0.25 mm, film 0.25 μm
(Phenomenex, Torrance, CA, USA)

inlet: injector temperature 250 $^{\circ}\text{C}$; split injection; injected volume 0.1 μL

carrier gas: H_2 , pre-column pressure 25 kPa (necessary for cyclohexane/cyclohexene-separation)

oven: start temperature 30 $^{\circ}\text{C}$ (3.5 min), 4 $^{\circ}\text{C}/\text{min}$ to 180 $^{\circ}\text{C}$ (5 min)

detector: FID, 300 $^{\circ}\text{C}$, H_2 25.1 mL/min; synth air 393 mL/min

integration: integrator 4290 (Thermo Separation Products)

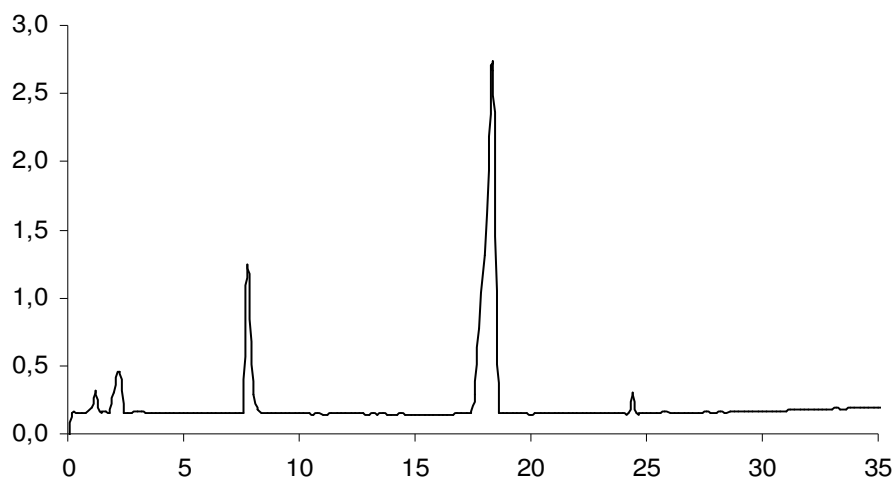
Sample preparation:

About 25 mg substance are dissolved in 0.5 mL dichloromethane.

The analyzed ether solutions are injected undiluted.

Percent concentration was calculated from peak areas.

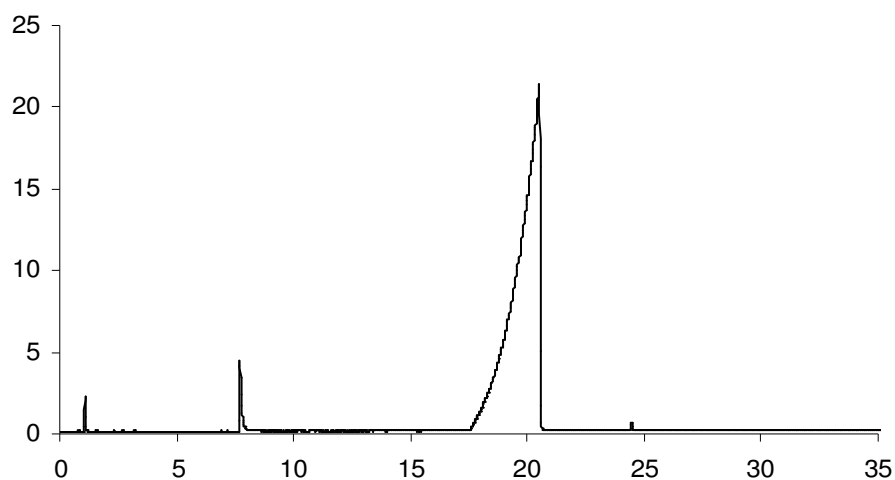
GC of the ether phase of the acidified reaction mixture



Retention time(min)	Substance	Peak area %
2.0	cyclohexane	6.4
2.2	cyclohexene	4.6
7.8	cyclohexanol	9.4
18.4	cyclohexanecarboxylic acid	68.2
24.5	bicyclohexyl	11.4

GC of the crude product

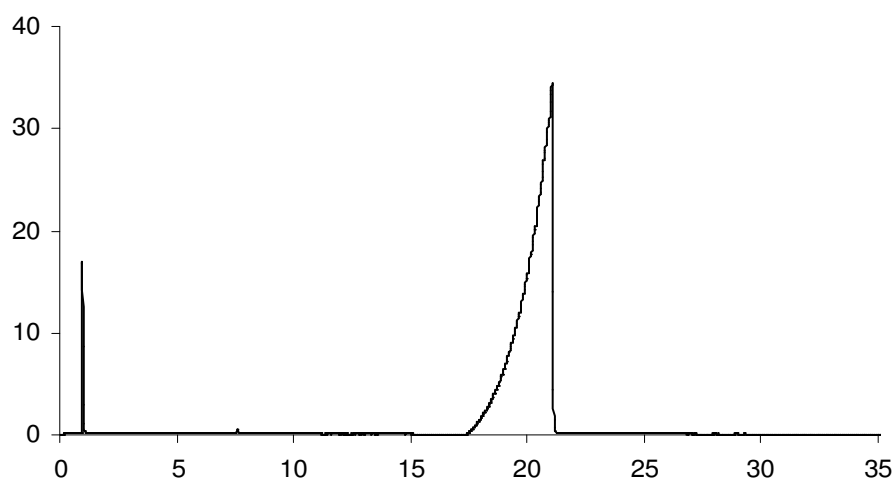
In this case the alkaline aqueous phase was **not shaken out with ether** before acidification.



Retention time(min)	Substance	Peak area %
< 2	solvent	
7.8	cyclohexanol	1.8
20.5	cyclohexanecarboxylic acid	97.8
24.5	bicyclohexyl	0.2

GC of the crude product

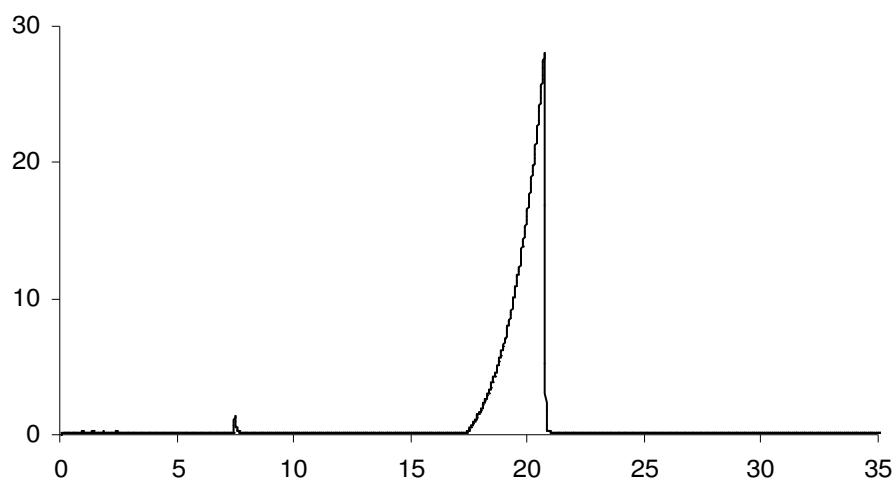
In this case the alkaline aqueous phase was **shaken out with ether** before acidification.



Retention time(min)	Substance	Peak area %
< 2	solvent	
7.8	cyclohexanol	0.1
21.1	cyclohexanecarboxylic acid	99.9

GC of the crude product, fore-run of the distillation (10% of the total product volume)

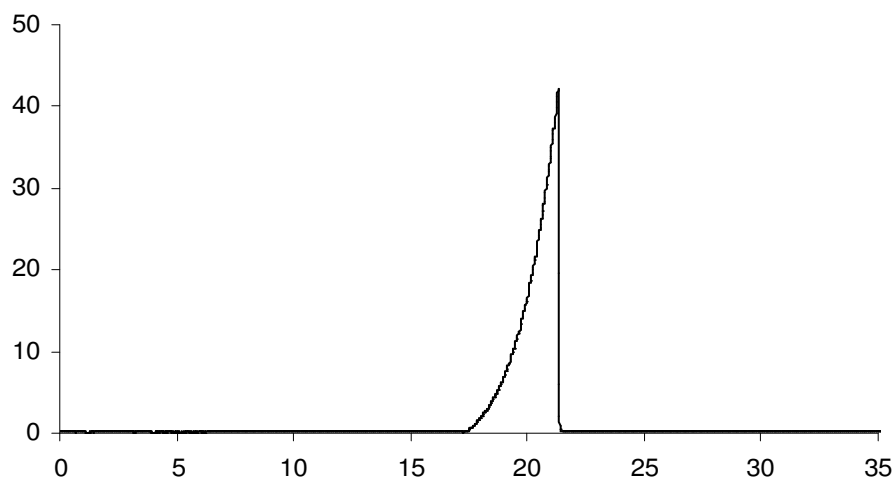
In this case the alkaline aqueous phase was **shaken out with ether** before acidification.



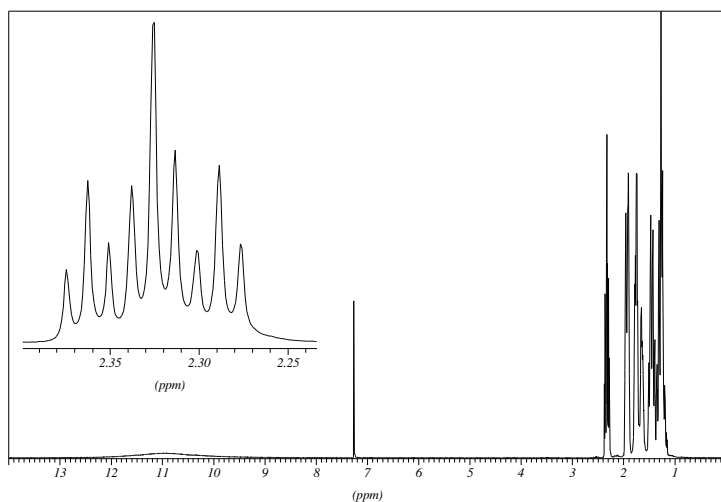
Retention time (min)	Substance	Peak area %
7.4	cyclohexanol	0.4
20.8	cyclohexanecarboxylic acid	99.6

GC of the pure product, main fraction (90% of the total product volume)

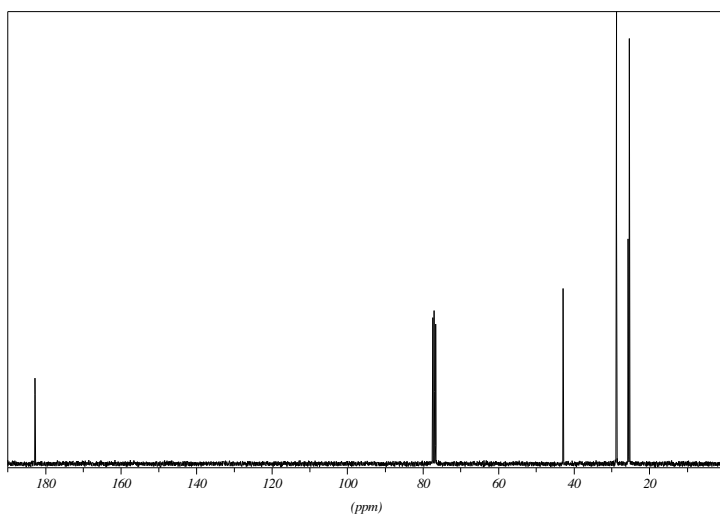
In this case the alkaline aqueous phase was **shaken out with ether** before acidification.



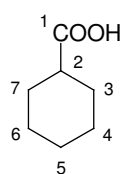
Retention time (min)	Substance	Peak area %
7.4	cyclohexanol	0.04
21.3	cyclohexanecarboxylic acid	99.9

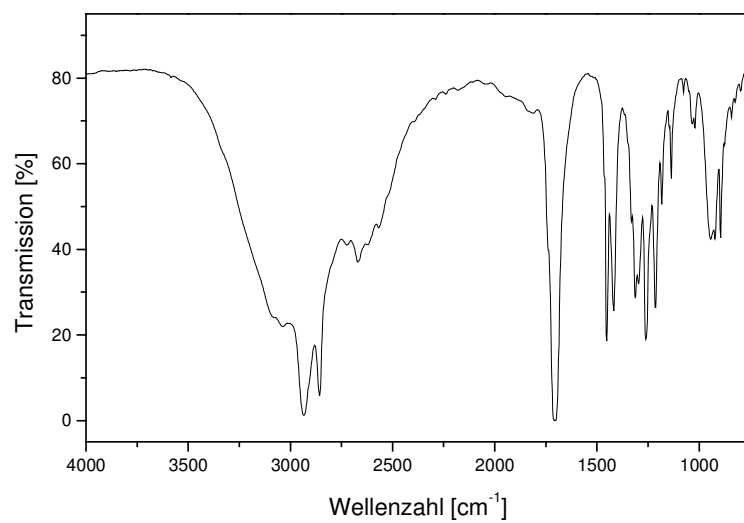
^1H NMR spectrum of the pure product (300 MHz, CDCl_3)

δ (ppm)	Multiplicity	Number of H	Assignment
1.1-2.0	M	10	CH_2
2.33	m (tt)	1	$\text{CH} - \text{COOH}$
11.0	wide s	1	OH
7.26			solvent

 ^{13}C NMR spectrum of the pure product (300 MHz, CDCl_3)

δ (ppm)	Assignment
25.31	C-4, C-6
25.67	C-5
28.53	C-3, C-7
42.92	C-2
182.77	C-1
76.5-77.5	solvent



IR spectrum of the pure product (film)

(cm ⁻¹)	Assignment
3300-2500	O – H – valence, carboxylic acids
2935, 2855	C – H – valence, alkane, superimposed by O-H
1705	C = O – valence, carboxylic acid

IR, ¹H NMR and ¹³C NMR spectra of the crude product are identical with those of the pure product.