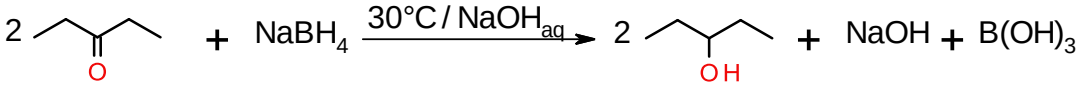
Reduction of 3-Pentanone

1. Introductory Remarks

Reductions of carbonyls like ketons are widely used in organic chemistry. The reduction with $NaBH_4$ allows a selective reaction giving the alcohol only. According the principles of green chemistry after Anatas and Warner organic chemical reactions should be of high yield, easy to supervise and of non-toxic reactants. This is a fitting example.

The product is purified by a short path distillation and checked by gas chromatography. Due to the non-absorbance of UV and to the low boiling point thin layer chromatography is barely possible. A GC analysis is by far a better alternative.

2. Reaction Scheme



Calculate the amount of the educt, of the reagents and the theoretical yield. Before starting the work note the results in your protocol and show it to your expert.

3. Reagents Synthesis

Reagent	Amount	Information	Safety advice
3-Pentanone	0.2*mol*		H: 225-335-336 P: 210
Sodium borohydride	0.105*mol*		H: 260-301-311-314 P: 280-301+330+331-302+352-305+351+338-402+404
Sodium hydroxide $\beta_{(NaOH)}$ ≈ 10*g/L*	67*mL*	diluted pellets	H: 290-314 P: 280-301-+330+331+351+338-308+310
Hydrochloric acid $w_{(HCl)}$ = 0.32*g/g*	about 7.5*mL*		H:290-314-335 P: 234-260-304+340-303+361+353-305+351+338-309+311-501
Sodium thiosulfate pentahydrate	1.5*g*		none
Diethyl ether	3*50*mL*		H: 224-302-336 P:210-240-403+235
NaCl	as required		none
Na_2SO_4 anhydrous	as required		none

Acetone	as reqiured	for GC use	H: 225-319-336 P: 210-233-305+351+338
DMSO-d_6	0.7*mL*	for NMR use	none
3-Pentanole		as yielded	H: 226-332-335-315 P: 210-241-302+352-303+361+353-405-501

4. Equipment Synthesis

Preparation		*Isolation*	
lab balance	1 4all	Spatula for adding NaCl	1
Spatula for weighing $NaBH_4$ and NaOH	2	Funnel 120*mm* with folded filter	1
Pergamin paper	1	Separatory funnel 250*mL* and stopper	2
Measuring cylinder 100*mL*	1	Erlenmeyer flask 500mL	1
Erlenmeyer flask 200 - 300*mL*	1	Pergamin paper for weighing $Na_2S_2O_3$	1
Lab jack	1	Rotary evaporator	2 4all
Magnetic stirring motor	1	Round-bottomed flask 500*mL* with NS 29	1
Magnetic stirring bar	1	pH-stripes	4all
PE bowl for warm and icy water	1	Measuring cylinder 100*mL for diethyl ether*	1
Three necked round bottomed flask 250*mL*	1	Buchner funnel ø 4.5*cm (or similar diamet)*	1
Dropping funnel 25*mL*	1	Reaction tube for peroxide testing	2
Stopper for dropping funnel	1	KI – starch stripes	2 4all
Thermometer and Rd-14 holder	1		
Bubble counter (with PEG - Oil)	1		
Rd-14 joint for latex tubing	1		
Latex tubing about 0.5*m* (into waste air)	1		
Measuring cylinder for hydrochloric acid			
Funnel for filling hydrochloric acid			
Clamp and clampholder	2		
Plastic bowl for warm and icy water	2		
Purification		***Characterization***	
Round bottomed flask with NS 14.5 25*mL*	3	Crimp vial with cap	1
Vigreux column ≈ 10*cm* NS 14.5	1	Crimp vial tongue	1 4all
Distillation bridge with Liebig condenser	1	Piston stroke pipet 100*µL*	1 4all
Thermometer with adapter NS 14.5	1	Piston stroke pipet 1000*µL*	1 4all
Tubing for cooling water	1	NMR tube	1
“Spider” with three exits	1	Syringe and cannula for adding DMSO-d_6	1 4all
Oil bath with regulation	1	Rack for vials	1
Round bottomed flasks with NS 14.5 10*mL*	2		
Boiling stones	≈3		
additional clamp and clamphoder	1		
Pasteur pipettes as required.			

5. Synthesis of 3-Pentanole

Preparation

In a ≈300*mL* Erlenmeyer flask, about 70 to 100*mL* sodium hydroxide solution $\beta_{(NaOH)}$ ≈ 10*g*/*L* (Note 1) is prepared, swiveled by hand until a clear solution is present and cooled to ambient temperature.

In a 250*mL* three necked flask, fitted with a thermometer, a magnetic stirring bar, a 25*mL* dropping funnel and a bubble counter (filled with PEG oil) which is connected to the waste air stream. 67*mL* sodium hydroxide solution $\beta_{(NaOH)}$ ≈ 10*g*/*L* followed by 0.105*mol* $NaBH_4$ (Note 1) are placed into the flask and stirred gently. The flask is now stoppered in order to lead the possibly built hydrogen gas through the bubble counter. To the slightly turbid, greyish solution 0.2*mol* 3-Pentanone are added dropwise at such a rate, that 30°*C* is not exceeded. The reaction mass is additionally stirred at about 30°*C* for 45 to 60 minutes with a warm-water bath and is then cooled down to ambient temperature with an icy-water bath. About 6.5*mL* – 9*mL* hydrochloric acid $w_{(HCl)}$ = 0.32*g*/*g* are added dropwise through the earlier used dropping funnel until a pH of 7-9 is reached (Note 2).

Isolation

1.5*g* solid $Na_2S_2SO_3$*$5H_2O$ are added in one lot under powerful stirring. The reaction mass is then saturated with solid NaCl (Note 3). 50*mL* peroxide free diethyl ether is added. After a while, the emulsion or suspension is filtrated through a folded filter into a separation funnel. The aqueous phase is removed and extracted two times with 50*mL* diethyl ether (Note 4). The combined organic layers are dried with anhydrous sodium sulfate, filled in a 500*mL* round bottomed flask, tested for peroxide again (Note 4) and evaporated not higher than 40°*C* and not lower than 300*mbar* in a rotary evaporator. Take the mass of the raw product.

Purification

The liquid crude product is distillated through a short path distillation apparatus (Note 5) at ambient pressure taking a first fraction with the residues of solvent and a second fraction with the pure product. According to the GESTIS database the boiling point at ambient pressure is 116°*C*.

Characterization

The characterization and the purity of the product are determined by means of GC and NMR.

GC (Gas Chromatography)

50*µL* sample are mixed together with 1000*µL* acetone in a crimp vial. The crimp vial is tightly capped and clearly marked with a marker pen and handed over to the GC operator. The chromatogram is taken by a GC operator with a prepared and tested method. You have to add it to the protocol as an appendix.

Stationary Phase:	0.25*µm* RTX coating; 30*m**0.32*mm* (given)
Mobile Phase:	Hydrogen 2.4*mL*/*min* (given)
Concentration:	50*µL* pure product are diluted with 1000*µL* acetone in a marked crimp vial
Detection:	FID

Note the calculated GC area percentage in your protocol.

NMR

50μL of the sample are mixed together with 0.7mL DMSO-d_6 in a NMR tube. The tube is clearly marked with a marker pen and given to the NMR operator. You have to add the spectrum to the protocol as an appendix.

6. Notes and Safety Advices Synthesis

Note1

Sodium hydroxide and Sodium borohydride are harmful in contact with skin and eyes. Avoid any contact and always wear clean gloves.

The addition of 3-pentanone is exothermic. During addition the round bottomed flask can be cooled by means of an icy-water bath.

Note 2

During this step gas evolution can be observed. With the aid of latex tubing, the emerging hydrogen gas is led directly into the hood's waste air flow.

Note 3

The saturation is visible by a white salt precipitation. Not more than 2g NaCl are required.

If there is already a suspension present, no NaCl is added.

Note 4

Peroxide testing: In an reaction tube a ≈ 100μL ether sample is placed together with three to five drops hydrochloric acid $w_{(HCl)}$ = 0.32g/g. The tube is capped and well agitated. A drop of the aqueous phase is placed on KI/starch indicator paper. If peroxide is present in the sample, the indicator will show a blueish-black color immediately. Caused by the oxygen in the atmosphere moist KI/starch indicator paper grows blueish-black after a delay.

Note 5

The short path apparatus consists of a short Vigreux column, a distillation bridge, a "spider" with three exits and three collecting flasks.

General Note

After use, rinse all glassware with demineralized (WBI) water. If there are chemicals visible, rinse it with ethanol first and with demineralized (WBI) water. If this procedure is insufficient, clean it with soap water and a test tube brush, and then rinse it well with tap water followed by demineralized (WBI) water.

Recrystallization

7. Introductory Remarks

Recrystallization is an effective cleaning process in technical organic chemistry. In the following task, an impure sample is cleaned by this method.

8. Reagents Recrystallization

Reagent	Amount	Information	Safety advice
RC-Sample	5.0*g*	heterogeneous	See cinnamic acid and alcohol
Cinnamic alcohol	Pollutant	as reference	H: 302-317 P: 262-280-302+352
***(E)* Cinnamic acid**	Bulk	as reference	H: 319 P: 280-264-305+351+338-337+313
Ethanol/Water 3:7	40*mL*	solvent	For Ethanol H: 225; P: 210
Acetone		for TLC	H: 225-319-336 P: 210-233-305+351+338
Toluene		for TLC	H: 225-361d-304-373-315-336 P: 210-301+310-331-302+352
Acetic acid		for TLC	H: 226-314 P: 280-301+330+331-307+310-305+351+338

Equipment Recrystallization

Recrystallization		*Characterization*	
Measuring cylinder 100*mL*	1	Reaction tubes for TLC sample	4
Erlenmeyer flask 200*mL*	1	Pastettes for TLC sample	4
Round bottomed flask 100*mL*		Spatula	2
Oil bath with regulation	1	Analytical balance	1 4all
Magnetic stirring motor	1	2*µL* TLC capillary	as needed
Magnetic stirring bar	1	UV cabinet	1 4all
Reflux condenser	1	Measuring cylinder 10*mL* for mobile phase	1
Tubing for cooling water	1	TLC tank	1
Lab balance	1 4all	Clamp	2
Suction filtration device (Buchner)	1	Clamp holder	2
Spatula	1	Melting point tube	1
Stopper for pressing the filter cake	1	Melting point apparatus	1 4all
Crystallizing dish	1	Potsherd	1
Drying oven	1 4all	Plastic bowl for icy water (from synthesis)	

9. Recrystallization

In an Erlenmeyer flask 30mL ethanol and 70mL water are mixed together and well agitated.

The 5*g* sample of (*E*) cinnamic acid is contaminated with cinnamic alcohol. In a 100*mL* round bottomed flask, which is fitted with a reflux condenser and a magnetic stirring bar, the sample is suspended in 80*mL* ethanol/water mixture 3:7. The suspension is heated with an oil bath and if necessary refluxed until a clear solution is present (Note 1). Then, the oil bath is removed. Under gentle stirring, the solution is cooled down to ambient temperature slowly while the suspension reappears (Note 2). At about ambient temperature the suspension is filtrated through a Buchner funnel under vacuum. With the aid of the mother liquor, the remaining crystals are rinsed onto the filter. Then the filter cake is washed two times with 5*mL* ice-cold pure ethanol/water mixture 3:7, filtered off sharply and filled in a tared crystallizing dish (Note 3). The purified (*E*) cinnamic acid is dried over night at 50°*C* under reduced pressure.

10. Characterization

TLC

Samples for TLC are taken from: Purified sample, pure cinnamic alcohol and pure cinnamic acid as references

plate	Polygram SIL G/UV_{254}
mobile phase	toluene / acetic acid 1:10 (v/v)
expansion	≈ 5*cm*
concentration	$\beta_{(Samples)}$ ≈ 20*mg*/*mL* in acetone
spot volume	2*µL*
visualization	UV 254*nm*

Melting Point

A small sample of the purified (*E*) cinnamic acid is dried on a potsherd, filled in a melting point tube and the melting point is taken with the Büchi B 540. According to the GESTIS database the melting point is 134°*C*.

11. Notes and Safety Advices Recrystallization

Note1

If there is a slightly turbid solution present, you can continue after two minutes refluxing.

Note2

If there are no crystals reappearing, 1*mL* solution can be transferred into a test tube. The solution is scratched with a glass rod on the tube wall in order to provoke crystallization. These crystals are placed into the flask giving the impulse of crystallization.
If the suspension reaches less than about 35°*C*, the cooling process can be accelerated by means of a water bath with some ice cubes.

Note3

At this point, a melting point sample can be taken and dried on a potsherd.

General note

After use, rinse all glassware well with tap water. If there are chemicals present, rinse it with ethanol and then with demineralized (WBI) water. If this procedure is insufficient, clean it with soap water and a test tube brush, and then rinse it well with demineralized (WBI) water.

12. Protocols

You have to write a protocol in handwriting on a blank sheet. Write separate protocols for the synthesis and the recrystallizing work. Note your yields and the characterizations.

Early in the morning the next day, the protocol of your recrystallizing work is finished after the dried (*E*) cinnamic acid is weighed and the yield is calculated.