8-3 Reduction of some carbonyl compounds (1) (2) (3) (4)

Type of reaction:

Reduction with complex hydrides, Reaction acc. to Wolf-Kishner, reduction with zinc / sodium hydroxide

Techniques and methods:

Standard methods, part 3: ball tube distillation

Equipment:

Standard equipment, part 3: ball tube apparatus, part 4: mortar

Chemicals:

- Part 1: Lithium aluminium hydride (1,0 g), abs. diethyl ether (60 ml), stearic acid (3 g), ethyl acetate (2,5 ml), sodium hydroxide, sodium sulfate, half concentrated sulfuric acid (when necessary), diethyl ether
- *Part 2:* 4-Methyl-4'-nitro-benzophenone (2 g), toluene (20 ml), sodium borohydride (1 g), ethanol (20 ml), diethyl ether (120 ml), sodium sulfate
- *Part 3:* Diethylene glycol (30 ml), potassium hydroxide (6 g), hydrazine hydrate (80 %, 5 ml), benzophenone (4,5 g), hexane, sodium sulfate
- Part 4: Zinc dust (18 g), copper(II)-sulfate (0,1 g), sodium hydroxide (8 g), phthalimide (14,7 g), hydrochloric acid (25 %, ca. 22 ml)

Hint:

For part 2 use 4-Methyl-4'-nitro-benzophenone prepared in reaction 6-6! Ask your assistant if you did not prepare this compound yourself.

Warning hints:

Lithium aluminium hydride is highly inflammable. It reacts extremely violent with water and alcohols by forming easily inflammable hydrogen gas. With some other solvents too (which?) it can react so violently that self inflammation occurs. Above 120 °C vigorous degradation occurs. Grinding in a mortar may cause spontaneous ignition. Lithium aluminium hydride is often supplied in small sealed plastic-bags covered with a small soldered can. Only open these bags after getting advice of your assistant! Especially do not leave the opened bag lying around! To pour out the hydride work under a completely dry and empty fume hood! (*Caution! Inhalation of the dust causes strong coughing!*) Empty the bag as completely as possible to a tightly lockable and completely dry bottle! The best way to do this is to pour the substance onto a weighing paper and then fill it into the bottle. See further instructions found at: http://userpage.chemie.fu-berlin.de/~tlehmann/gp/laborpraxis/ba/lahabfuellen.html.

• Don't put the plastic-bag and weighing paper in the waste bin before deactivating the remaining lithium aluminium hydride on all surfaces! - Hazard of fire!

By the way, this is also valid for all materials (e.g. filtration paper) which came in contact

Freie Universität Berlin - Institut für Chemie und Biochemie - Organisch-chemische Praktika

with the substance during the experiment! If there are only traces present the deactivation could be done by completely dipping into water. Dust residues that occurred during work with the substance, especially on the operating desk or bottles (*storage bottle!*), have to be wiped away with a moist piece of blotting paper. Label the storage bottle completely including the recommended warning advices, date and your name! Keep the storage bottle tightly sealed and away from easily inflammable solvents at any time!

For controlled deactivation of the substance it is best covered first with an inert solvent. (*In part 1 of this experiment this is the distillation residue.*) Then ethanol is slowly added. (*Which reaction takes place?*) To deactivate the dry powder sometimes it is recommended to add the substance in portions to a saturated sodium sulfate solution. That reaction is accompanied by vigorous evolution of hydrogen but it has the advantage that the used solvent is not inflammable.

If you find the lithium aluminium hydride in a bottle, you should be distrustful, because the substance may have been decomposed by air moisture when treated improperly. Active lithium aluminium hydride is a grey powder, the decomposed compound is often colorless or contains colorless pigments. Unfortunately this is no reliable criterion. The vigorous reaction with water is not hazardous if only a few milligrams are used. This reaction is therefore suitable to test the reactivity. (Take care that the spatula immersed into the bottle is clean and completely dry!) If you are not sure ask your assistant! Active lithium aluminium ignites when one drop of conc. nitric acid is added. This reaction may also be used on a small scale experiment (only a few milligrams!) to test the activity. See your assistant for advice first!

Lithium aluminium hydride may also be distributed as pressed pills. This has two advantages:

- 1. No hazardous dust is formed.
- 2. Material found inside the pill is a little better protected against decomposition.

Whenever possible prefer to use the pills!

To get a better reactivity crush the pills using a spatula when they have been filled into the reaction flask.

Sodium borhydride is easily inflammable and toxic. In contrast to lithium aluminium hydride there is only gentle reaction with water. Nevertheless it is also an unstable reagent and therefore the same is true as for lithium aluminium hydride. Unfortunately the deactivated material does not give any change in color.

Hydrazine is toxic, allergenic and has a low potential to cause cancer. The greatest danger is the skin resorption, which goes along with local skin irritation and burning. Latex gloves are not decomposed by hydrazine and are therefore well suitable for skin protection. Because of the low vapor pressure the danger of inhalation is normally relatively low. (*The substance has a pungent smell, similar to ammonia. The smell has a strong warning effect.*) Since hydrazine reacts extremely violent with many substances, especially with oxidizing agents, forming of aerosols in this case should be anticipated.

The decay of hydrazine to ammonia and nitrogen normally occurs only at higher temperatures, but then explosively. This decay can strongly be accelerated by catalysts, e.g. porous materials, so that spontaneous inflammation can even happen at room temperature. Often the substance decays slowly in the sealed storage bottle, which therefore may get under distinct pressure.

Work under a clean fume hood on a <u>completely</u> dry operating desk without any waste lying around, in order to notice any spilled substance immediately. For deactivation the substance is diluted with water and <u>carefully</u> oxidized with hydrogen peroxide until the evolution of gas

- 2 -

Freie Universität Berlin - Institut für Chemie und Biochemie - Organisch-chemische Praktika

comes to an end. **Caution**: Dilute the solution, if the reaction is too violent! A vigorous reaction means that aerosols may occur! Use a big beaker with a plastic bowl as a secure device. If the solution gets to hot adding of ice is advisable. The obtained solution can be flushed to the drain with plenty of water. If hydrazine is spilled you may either flush it to the drain using plenty of water or - if this is not possible - you have to take it up. In this case first decompose the hydrazine using diluted hydrogen peroxide solution. Again take care, that the reaction is not too vigorous! If hydrazine is spilled outside the fume hood, all persons have to leave the room at once! In this case see your assistant for advice and use a gas mask when decontaminating the room.

Experimental:

1. Reduction of stearic acid with lithium aluminium hydride:

Hints:

- To prepare abs. diethyl ether use the special apparatus found in room 31.05. Make yourself familiar in time how to operate this apparatus. To add more ether to the apparatus only use flash dried diethyl ether which is either available as a commodity or has to be previously prepared by yourself by column chromatography on basic alumina.
- All glass ware you need for this reaction has to be freshly heated in an oven. Use a calcium chloride filled drying tube to exclude air moisture.
- Strictly follow the instructions given for the hydrolysation procedure. Otherwise you will get a voluminous and slimy precipitate which hardly can be separated.

In a 100 ml-3-neck-round bottom flask with reflux condenser and a septum lithium aluminium hydride (1,0 g) is suspended in abs. diethyl ether (20 ml). Carefully crush the pill with a spatula. In a second 100-ml-flask prepare a solution of stearic acid (3,0 g) in abs. diethyl ether (40 ml) (*Gentle warming helps to dissolve the acid.*) Fill a syringe with this solution, grease the cannula a little and then drop the solution through the septum into the flask while stirring that way that the mixture is gently boiling. The mixture is refluxed for an additional hour, then cooled down and ethyl acetate (2,5 ml) is added while stirring. (*Why?*) Then with stirring and cooling in an ice bath water (1/2 - 1 pasteur pipette) is added. Stirring and cooling is continued for 20 minutes. If there is no precipitate, which can be filtered off, a few drops of a saturated aqueous potassium-sodium-tartrate solution (*available in room 31.05*) are added and stirred until the precipitate occurs. The precipitate is filtered off and washed with a little diethyl ether.

Disposal advice:

The precipitate is stirred with a little water to ensure that there is no more active lithium aluminium hydride present. Then the solvent is evaporated in the fume hood and the residue is transferred into the disposal bottle designed for this purpose.

The filtrate normally contains no water layer. If it is present it is separated. The etheric solution is dried with sodium sulfate, filtered into a small tarred flask and then evaporated. Calculate the raw yield in your lab journal. Recrystallise in a suitable solvent and determine yield and melting point.

Freie Universität Berlin - Institut für Chemie und Biochemie - Organisch-chemische Praktika

2. Reduction of 4-methyl-4'-nitro-benzophenone with sodium borohydride:

To a solution of 4-methyl-4'-nitro-benzophenone (2 g) (*from experiment* 6-6) in 20 ml of toluene a freshly prepared suspension of 1 g sodium borohydride in 20 ml ethanol is added while stirring. The mixture is stirred for one additional hour. Then it is poured into a separating funnel with was previously filled with water (80 ml) and extracted three times with 40 ml diethyl ether each. The ether extracts are washed with water to neutral reaction, dried with sodium sulfate, and filtered. Then the solvent is removed. Calculate the raw yield in your lab journal. Recrystallise from ethanol/water and determine yield and melting point.

Advice: No value of the melting point can be found in the library of the institute.

3. Reduction of benzophenone with hydrazine/potassium hydroxide solution:

You are working with a carcinogenic compound!

Work in the "Stinkraum"

- Stick the attached warnings at the front of the fume hood!
- Follow the warning hints given at the beginning of this script!
- Use a syringe to measure the hydrazine. Use a long canula! Never immerse the syringe into the storage bottle, but only the canula! Operate as follows:
 - Fix the bottle with a clamp that it may not tip over,
 - stick the cannula firmly to the syringe,
 - Suck the hydrazine into the syringe
 - (a little more than necessary),
 - as shown in the figure turn down the syringe. On doing this leave the cannula in the bottle ¹,
 - press the air out of the syringe,
 - press out as much of the liquid, that the remaining substance is exactly the needed amount,
 - never press out the hydrazine too strongly, because the cannula which is only sticked to the syringe will jump away and the liquid will be spilled.

If the canula is too short to reach the surface of the liquid, ask your assistant for advice.

 \Rightarrow Have a little diluted hydrogen peroxide solution ready to clean the syringe when the hydrazine is measured. Fill it into the syringe. This will completely decompose all traces of hydrazine. After rinsing with water you may use the syringe for other purpose without any risk.

In a small three neck flask diethylene glycol (30 ml) and potassium hydroxide (6 g) are heated carefully up to 180-190 °C. (*What do you observe?*) The obtained solution is cooled down to ca. 100 °C, and hydrazine hydrate (80 %, 5 ml) and benzophenone (4,5 g) are added. The mixture is refluxed for two hours. (Temperature in the flask ca. 140 °C) Then the product is distilled out of the mixture together with water and hydrazine. Distilled water is continuously replaced through a dropping funnel. The speed of this addition has to be as slow as the temperature of the mixture doesn't go down. Over all 100 ml are to be distilled.

• Take care about hydrazine residues when taking apart the distillation apparatus!

¹ Don't be afraid! The cannula is flexible. Consider that the connection of the syringe is not centered but shifted aside. If you hold the Syringe the right way the connection is placed on top and when you press the pistil, first the air bubble is removed.

Freie Universität Berlin - Institut für Chemie und Biochemie - Organisch-chemische Praktika

Completely immerse all glass ware into dilute hydrogen peroxide solution (ca. 1 % is sufficient at all, so do not waste this reagent! Wear gloves!) Hydrazine is thereby decomposed within a few seconds.

• In order to decompose the hydrazine in the distillate diluted hydrogen peroxide is added until gas evolution stops.

The distillate is extracted three times with hexane, the organic phase is washed with diluted sulfuric acid and water, dried with sodium sulfate and filtrated.

Disposal advice: All water layers are flushed into the drain. The residue of the steam distillation is added to the organic solvent waste.

Then the solvent is removed. The remaining oil is distilled in a ball tube oven in a membrane pump vacuum. Carry out a protocol of your distillation and examine pressure/temperature yield and melting point/refractive index of each fraction obtained!

4. Reduction of Phthalimide with zinc/sodium hydroxide:

In a motar zinc dust (18 g), copper sulfate (0,1 g), and water (3,5 ml) are mixed intensively to a thick paste. The paste is moved into a 250 ml-round bottom flask, and a 20% solution of sodium hydroxide (40 g) is added. (*Don't forget to rinse the motar with the lye!*) With stirring and cooling by means of an ice bath, phthalimide (14,7 g) is added in small portions at such a rate that the temperature in the flask doesn't rise above 8 °C. When addition is completed, stirring is continued for 30 min. Then water (40 ml) is added, and the mixture is heated with vigorous stirring in a PEG-bath (bath temperature: ca. 100 °C) until evolution of ammonia has ceased.

Caution: Thermometers are destroyed in the concentrated lye!

To examine the evolution of ammonia you have first to suck off the ammonia in the gas volume of the apparatus. Remove the heating bath, then hold a glass tube which is attached to a membrane pump into the apparatus, and suck air through it! Heat again! The reaction is finished if no new ammonia is evolved anymore within the next 10 min. Generally the reaction takes about 10 hours. The reaction may be disrupted.

After cooling down the mixture is concentrated to a volume of about 40 ml by distillation under reduced pressure. The material is filtered, and the pH of the filtrate is adjusted to 3 with hydrochloric acid (25 %, ca. 22 ml). The mixture consists of two layers (*What do these layers consist of?*) and is refluxed for one hour. The mixture is slowly cooled down by leaving it in the switched off heating bath, then stored in the refrigerator over night. The precipitate is filtered with suction. Write down the raw yield in your lab journal.

Disposal advice: The mother liquor is combined with the precipitate of the reducing agent which was yielded by filtration. If anything remains not dissolved as few as possible hydrochloric acid is added. The obtained solution is neutralized with a solution of sodium carbonate (Caution: Vigorous foaming!) and the obtained precipitate (What is it?) is put in the designated collecting vessel.

The product is recrystallized from water/ethanol. Determine yield and melting point.

Freie Universität Berlin - Institut für Chemie und Biochemie - Organisch-chemische Praktika

Questions to be answered before conducting the experiment:

- 1. Briefly outline the selectivity of reductions with some of the usual complex metal hydrides!
- 2. Write down the stoichiometric equations and explicit mechanisms of the reactions to be conducted.
- 3. Figure out methods for evaluating purity of products and their structural identification.

Tasks to be solved after conducting the experiment:

4. Check purity and identity your products according to Q. 3)!

Lit.: part 4: Org. Synth. Col. Vol. II, 526-527

- 5 -

- 7 -

WS 2008

Caution

In this fume hood hydrazine is used.

(Experiment 8-3, part 3)

Hydrazine is carcinogenic, toxic and allergenic!

No other apparatus is allowed in this fume hood!

Name: Room: Date: