Problem 33: Preparation of 2,5-Dimethyl-1-Phenylpyrrole

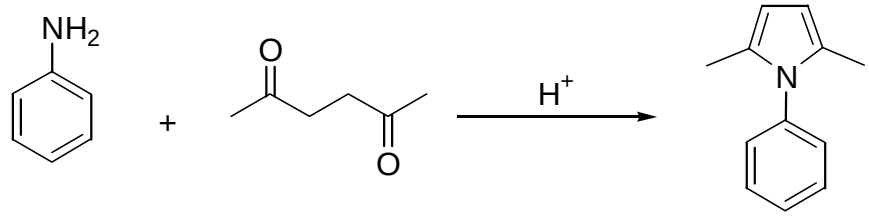
A. INTRODUCTION

There are many different cyclization reactions that produce nitrogen heterocycles, with the **Paal-Knorr** synthesis being one of the most general. In this reaction, a 1,4-dicarbonyl compound is heated with ammonia or a primary amine to produce a pyrrole.

As an example, the condensation of aniline with 2,5-hexanedione leads to 2,5-dimethyl-1-phenylpyrrole (**1**) (a N-substituted pyrrole) that can be easily carried out in a 3h-undergraduate organic laboratory.

B. REACTION AND MECHANISM

The reaction, which takes place, is the following:



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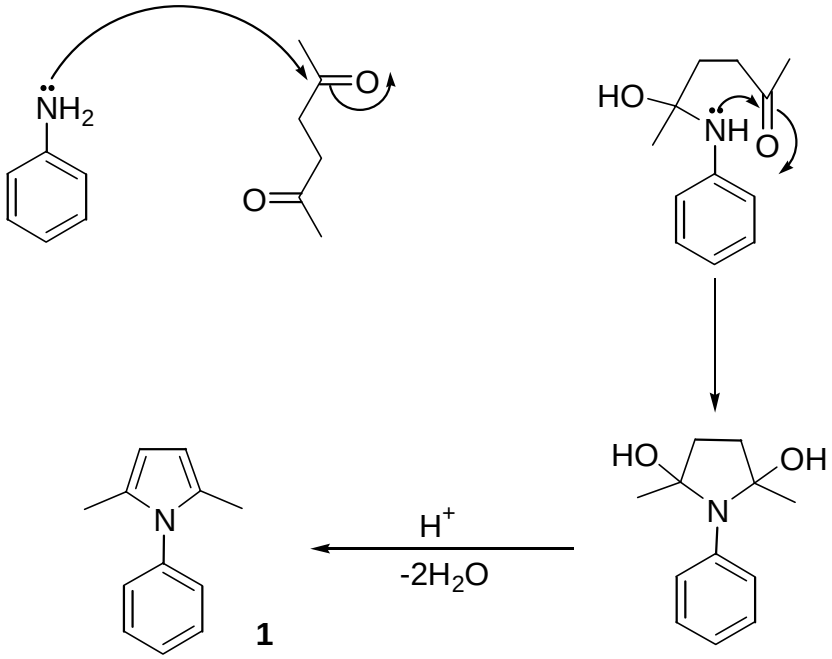
In the first step, the amino-group of aniline attacks one of the two equivalent carbonyl-groups of the 2,5-hexanedione. Afterwards, a second intramolecular nucleophilic attack takes place, resulting in cyclization. Finally, the cyclic compound undergoes two successive dehydrations under acidic treatment to form the final product. The governing force for the two dehydration reactions is the formation of an aromatic system. The proposed mechanism is shown in Scheme 1.



Scheme 1: The proposed mechanism of the 2,5-dimethyl-1-phenyl pyrrole synthesis.

C. LIST OF CHEMICALS:

- Methanol
- Aniline
- 2,5-Hexanedione
- Concentrated HCl
- 0.5 M HCl

D. LIST OF EQUIPMENT FOR EACH STUDENT

1 25 cm^3-round-bottomed flask
1 condenser
3 micrograded syringes
1 10 cm^3 conical flask
1 5 cm^3 measuring cylinder
5 Pasteur pipettes
1 conical sintered glass funnel
1 metal spatula
10 capillary tubes
5 TLC plates
1 developing chamber
3 Eppendorf tubes
2 test tubes (diameter 1 cm, length ca. 10 cm)
1 100 cm^3-Beaker sand bath on heating plates
ice
UV-lamp (254 nm)
eluent (Ethyl acetate-Hexane 1:3)
balance

E. EXPERIMENTAL

Synthesis of 2,5-Dimethyl-1-phenylpyrrole:

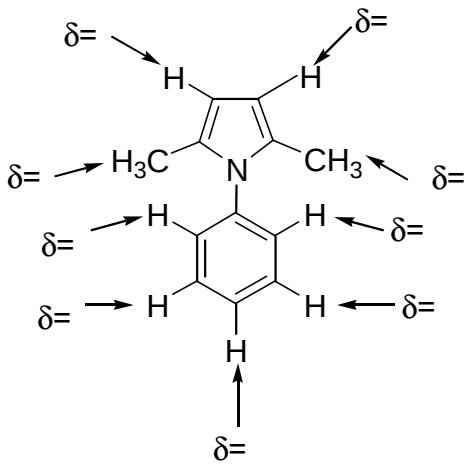
To a round-bottomed flask fitted with a reflux condenser, add 186 mg (2.0 mmol) of aniline, 228 mg (2.0 mmol) of 2,5-hexanedione, 0.5 cm^3 of methanol, and 1 drop of concentrated HCl. Heat the mixture (sand bath) to reflux for 15 min, and then add it to 5.0 cm^3 of 0.5 M HCl, which is kept cool in an ice bath.

The formed crystals are collected by suction filtration and recrystallized from 1 cm^3 of 9:1 methanol/water. The isolated recrystillized product is washed twice with 1 cm^3 of the same mixture of methanol/water, and pressed dry on the filter. The solid is then collected on a piece of filter paper in order to dry further. The dry product is placed in a tare-weighed Eppendorf. The sample tube is closed and weighed. A small amount (ca. 3-5 mg) of the product is placed in another Eppendorf and dissolved in few drops (~5) of acetone. By means of a capillary tube place a drop of this solution on a TLC plate. A similarly prepared sample of the starting material (aniline) is applied next to the product, as a reference, and the TLC plate is eluted with ethyl acetate-hexane 1:3. After elution, the plate is visualized under UV-light (254 nm) and the spots on the plate are drawn with a pencil. The sample tube with the rest of the product is labeled with the name of the product and is given to the supervisor.

PROBLEMS

a. Record the following data:
   I. The weight of your product:
   II. The calculated theoretical yield:
   III. The obtained yield as a percentage of the theoretical:
   IV. The melting point of the product:
b. Give a design of the thin layer chromatographic plate:
c. Estimate the R_f value of the product:
d. The ^{1}H-NMR ($CDCl_3$) data of the product are:
   δ= 2.04 (s, 6H), 5.91 (s, 2H), 7.22 (m, 2H) and 7.44 (m, 3H)

Indicate on the structure below the appropriate δ values on the protons that are shown with arrows

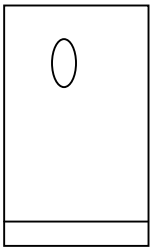


Report

a. Record the following data:

I. The weight of your product:	178 mg
II. The calculated theoretical yield:	342 mg
III. The obtained yield as a percentage of the theoretical:	52%
IV. The melting point of the product:	48°C (lit. 50-51°C)

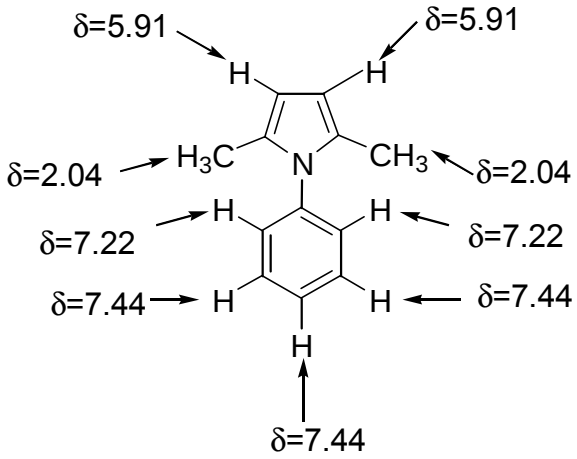
b. Give a design of the thin layer chromatographic plate:



c. Estimate the R_f value of the product: 0.85

d. The ^{1}H-NMR ($CDCl_3$) data of the product are:

δ= 2.04 (s, 6H), 5.91 (s, 2H), 7.22 (m, 2H) and 7.44 (m, 3H)



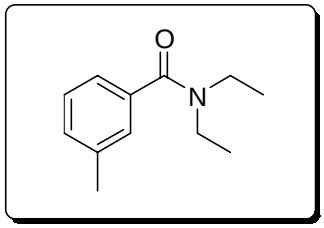
Problem 34: Synthesis of the Insect Repellent DEET

A. INTRODUCTION

DEET is the common name for N,N-diethyl-m-toluamide, a multipurpose insect repellent registered for direct application to human skin. DEET is a unique pesticide because it is applied directly to the human body for the purpose of repelling insects. Because DEET was recognised as one of the few products that are effective against mosquitoes and biting flies, it was registered for use by the general public in the USA in 1957. Approximately 230 products containing DEET are currently registered with the Environmental Protection Agency manufactured by 70 different companies. Every year approximately one-third of the US population is expected to use DEET.

B. THE CHARACTERISTIC FEATURES OF DEET

● The chemical structure is shown below:



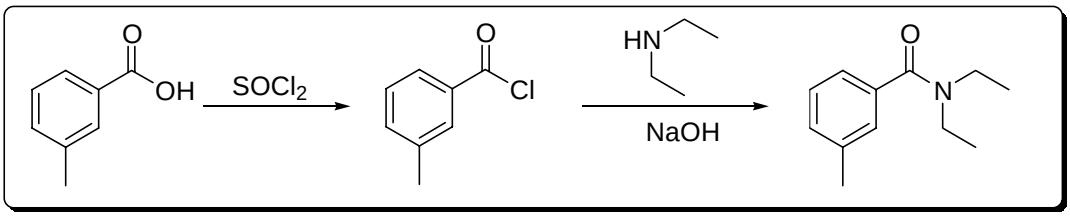
N,N-diethyl-m-toluamide

● Some physical properties are shown in the table below:

Density (25°C)	0.996
Solubility in water	practically insoluble
Solubility in other solvents	soluble in ethanol, ether, chloroform, benzene
Boiling point (at 1 torr)	111°C
Vapour pressure (160°C)	19 torr
Odour	odourless
Colour	colourless

C. SYNTHESIS OF DEET

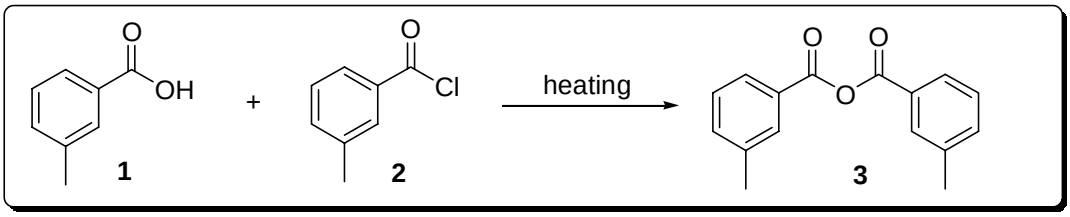
DEET can be prepared starting from m-methyl-benzoic acid (m-toluic acid). First, m-toluic acid is converted to the corresponding chloride. Next, the desired amide is prepared by reacting the active chloride with diethylamine in the presence of base (NaOH).



The activation step using thionyl chloride can be accomplished in two alternative ways:

a. By heating the m-toluic acid with thionyl chloride ($SOCl_2$) and
b. By reacting m-toluic acid at room temperature, with $SOCl_2$ in the presence of a catalytic amount of pyridine.

The activation of m-toluic acid with a catalytic amount of pyridine has an advantage compared to the heating activation concerning the yield and purity of the final product. The heating activation step leads to the creation of by-products as well as the desired product via the anhydride intermediate formation.



D. EXPERIMENTAL

m-Toluic acid (0.5 g, 3.7 mmol), dry ether (0.2 cm^3), pyridine (2 drops), and 99.5% $SOCl_2$ (0.55 cm^3, 7.6 mmol) are stirred for 8 minutes at room temperature in loosely stoppered 5-cm^3 round-bottom flask. The reaction is kept in a fume hood; alternatively, the liberated HCl gas may be directed to an aspirator. The excess $SOCl_2$ was removed at room temperature under water-aspirator vacuum (25 mmHg). The reaction solution was pipetted into a mixture of

diethylamine (1.3 cm^3, 12 mmol) in 10% NaOH (5 cm^3) at 0°C. After stirring for 1 minute, the solution was extracted twice with 15-cm^3 portions of ether. The ether fractions were dried over $MgSO_4$ (or Na_2SO_4) and filtered, and 1 cm^3 of toluene was added to azeotropically remove any traces of both water and pyridine. The solvents were removed in a flash evaporator until dryness. DEET remains as a clear oil in the round-bottom flask.

PROBLEMS

a. Record the following data:

I. The weight of your product:

II. The calculated theoretical yield:

III. The obtained yield as a percentage of the theoretical:

b. During the heating activation of m-toluic acid, the formation of anhydride **3** causes yield reduction because [check the statements that are correct]:

● The anhydride does not react with diethylamine:

● The anhydride reacts with diethylamine affording the desired product as well as some by-products:

● The anhydride reacts readily with diethylamine giving 50% of the desired product plus 50% of the starting m-toluic acid, due to its symmetry:

c. If we want to use infrared (IR) spectroscopy to identify the anhydride **3** formed during the heating activation step of m-toluic-acid, we should look for the characteristic IR-absorption of [check all that apply]:

I. The aromatic C-H stretch at ca. 3065 cm^{-1}:

II. The aliphatic C-H stretch at ca. 2987-2880 cm^{-1}:

III. The symmetrical and asymmetrical C=O stretch of conjugated anhydride at ca. 1763 cm^{-1} and 1720 cm^{-1}

Report

a. Record the following data:

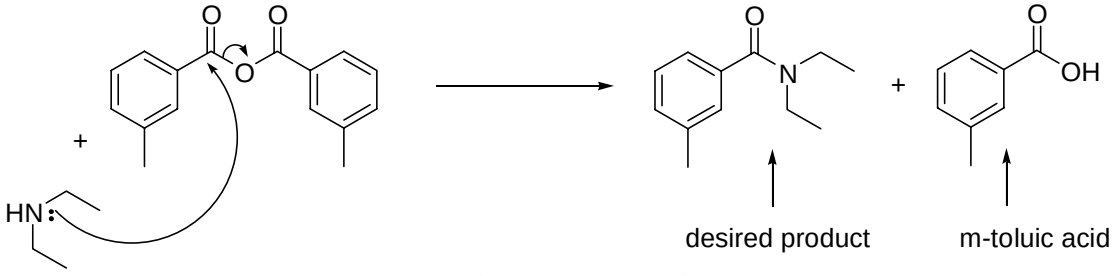
I. The weight of your product:	0.68 g
II. The calculated theoretical yield:	0.70 g
III. The obtained yield as a percentage of the theoretical:	97%

b. During the heating activation of m-toluic acid, the formation of anhydride **3** causes the yield reduction because:

● The anhydride does not react with diethylamine:

● The anhydride reacts with diethylamine affording the desired product as well as some by-products

● The anhydride reacts readily with diethylamine giving 50% of the desired product plus 50% of the starting m-toluic acid, according to the following reaction: X



c. The two strong IR bands at 1763 cm^{-1} and 1720 cm^{-1} are characteristic symmetrical and asymmetrical C=O stretches of conjugated anhydrides.

Problem 35: Solid phase peptide synthesis

A. INTRODUCTION

Solid phase peptide synthesis (SPPS) was introduced by R. B. Merrifield of Rockefeller University (Nobel Prize 1984). This method is based on sequential addition of α-amino and side-chain protected amino acid residues to an insoluble polymeric support. 2-Chlorotrityl chloride resin (Figure 1), whose use has been pioneered by K. Barlos, is an acid labile resin. The steric bulk and the mild acidic conditions required for cleavage make this resin useful in many applications. The base-labile Fmoc-group is used for N-α-protection of amino acids. After removal of this protecting group, the next protected amino-acid is added using either a coupling reagent or pre-activated protected amino-acid derivative. The resulting peptide is attached to the resin through its C-terminus and may be cleaved to yield a peptide acid or amide (depending on the linker used). Side-chain protecting groups are often chosen so as to be cleaved simultaneously with detachment of the peptide from the resin.

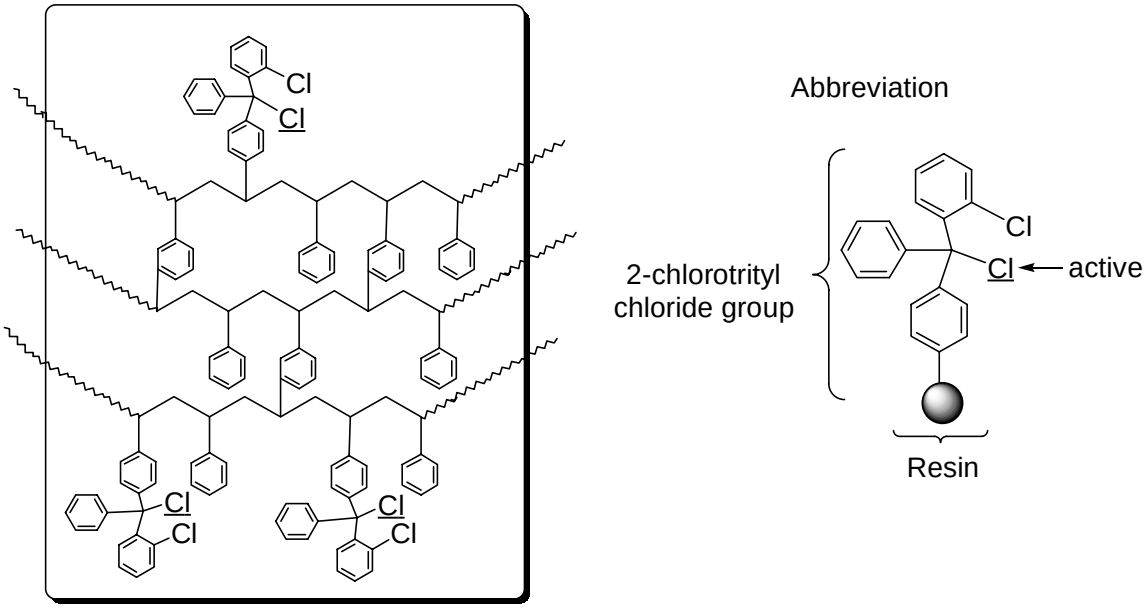


Figure 1: 2-Chlorotrityl chloride group attached to a polymeric support of 1% divinylbenzene cross-linked polystyrene.

B. SYNTHESIS OF THE DIPEPTIDE H_2N-SER-ALA-OH

The synthesis of the above dipeptide is accomplished by the Fmoc-strategy using 2-chlorotrityl chloride resin as the solid support. The reactions that take place are illustrated in Figure 2.

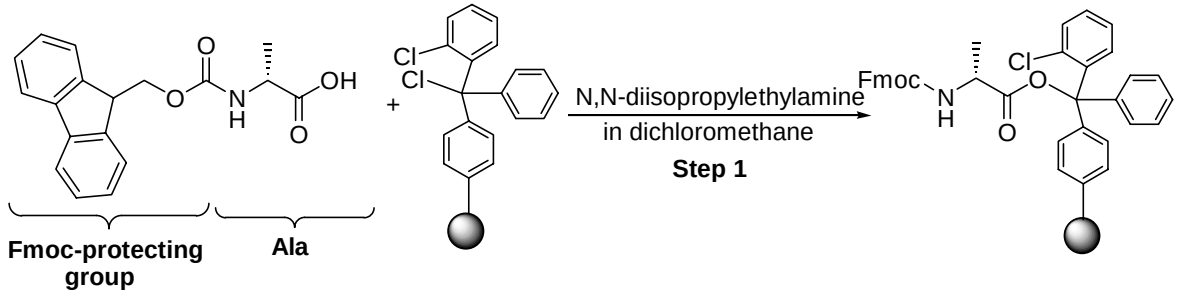


Figure 2a: Synthesis of H_2N-Ser-Ala-OH using the Fmoc strategy on 2-chlorotrityl chloride resin (Step 1).

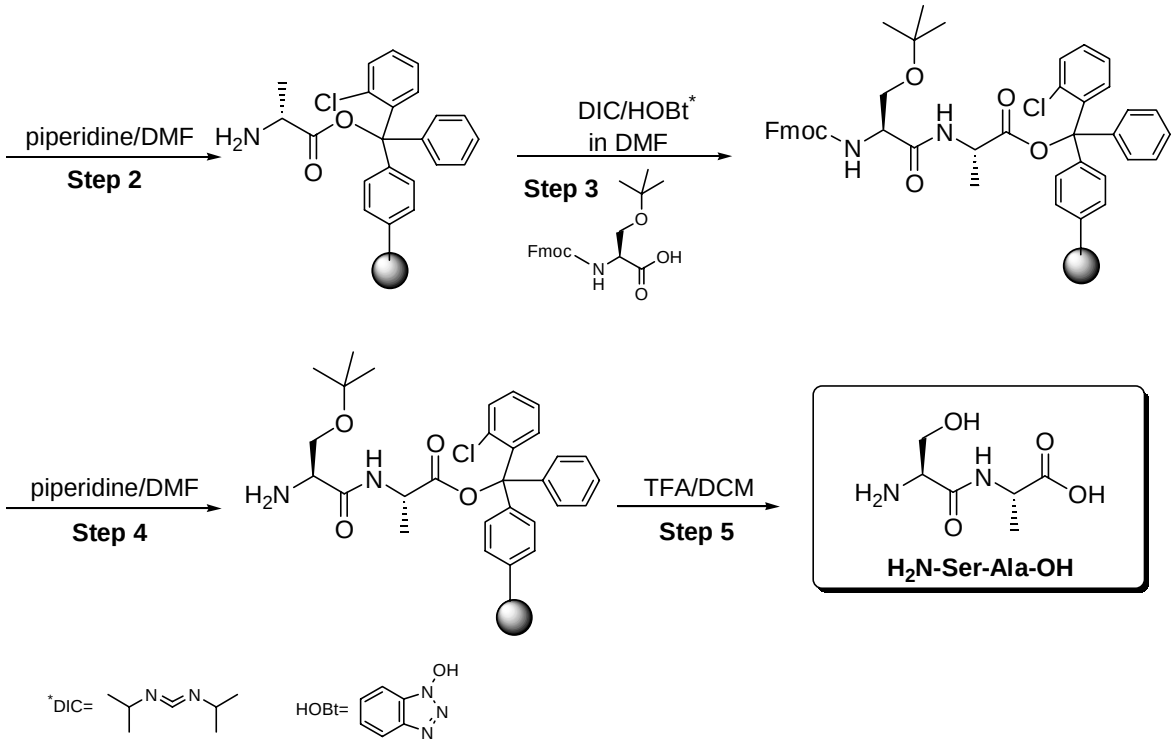


Figure 2b: Synthesis of H_2N-Ser-Ala-OH using the Fmoc strategy on 2-chlorotrityl chloride resin (Steps 2-5).

C. ESTIMATION OF LEVEL OF FIRST RESIDUE ATTACHMENT

This procedure takes place after the completion of Step 1.

1. Take a UV cell
2. Weigh 2 mg dry Fmoc-amino acid-resin into the UV cell. Dispense freshly prepared 20% solution piperidine/DMF (3 cm^3) into the cell.
3. Agitate the resin mixture using a Pasteur pipette for 2-3 minutes.
4. Place the cell in a spectrophotometer. Read the absorbance (A_{sample}) at 290 nm.
5. Using another UV cell, read the absorbance of 20% solution piperidine/DMF (3 cm^3) at the same wavelength (A_{blank})
6. Estimate the level of first residue attachment using the equation:

Fmoc loading= $\frac{n}{m} = \frac{A_{sample} - A_{blank}}{1.75m}$, where n is the amount of Fmoc-amino acid-resin (in mmol) and m the mass of resin (in g).

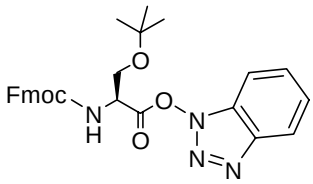
D. EXPERIMENTAL

Step 1: Dissolve Fmoc-Ala-OH (62 mg, 0.2 mmol) in dry CH_2Cl_2 (2 cm^3) by adding DIPEA (N,N-diisopropylethylamine) (139 μL, 0.8 mmol). Add this solution to a fine sintered glass manual SPPS reaction vessel containing 2-Chlorotrityl chloride Resin (200 mg, 0.2 mmol; loading 1.0 eq Cl/g resin) in 1 cm^3 DCM, shake for 30 minutes and then filter. To end-cap any remaining reactive trityl groups, add HPLC grade methanol (0.2 cm^3) and mix for 15 minutes. Filter the resin and wash it 3x2 cm^3 (DCM/MeOH/DIPEA=17/2/1), 3x2 cm^3 DCM and dry the resin in a dessicator over KOH.

Step 2: Estimate the level of first residue attachment as described before. Remove the Fmoc-protecting group using freshly prepared 20% solution piperidine/DMF (3 cm^3). Filter after 5

minutes and repeat with another 3 cm^3 of 20% solution piperidine/DMF. Wash the resin with DMF (3x2 cm^3) and DCM (3x2 cm^3).

Step 3: Dissolve Fmoc-Ser(OBu^t)-OH (383 mg, 1 mmol) and HOBt (135 mg, 1 mmol) in a sample vial in the minimum volume of DMF. Then add dropwise DIC (156 μL, 1 mmol) and stir the mixture for 20 minutes. This results in the formation of the corresponding active ester, which has the structure shown below:



Add this solution to the resin, which has been swollen in 1 cm^3 DMF. Agitate gently for 1 hour and then filter, wash with DMF (3x2 cm^3) and DCM (3x2 cm^3). Then, perform a Kaiser test to ascertain the completeness of the reaction, as described below.

Kaiser test:

Prepare the following solutions:

1. Dissolve 5 g of ninhydrin in 100 cm^3 EtOH.
2. Dissolve 80 g of liquified phenol in 20 cm^3 of EtOH.
3. Add 2 cm^3 of a 0.001 M aqueous solution of potassium cyanide to 98 cm^3 pyridine.
4. Transfer a few resin beads to a small glass tube and add 2 drops of each of the solutions above.
5. Mix well and heat in boiling water for 5 minutes. A positive test indicated by blue resin beads means that the coupling step should be repeated until a negative Kaiser test is achieved.

Step 4: Removal of Fmoc-protecting group is accomplished using the same procedure described in Step 2.

Step 5: Wash resin with isopropanol and ether (3x2 cm^3) and air-dry it by application of vacuum for 10 minutes. Add to the dry resin the cleavage reagent (3 cm^3 0.5% TFA/DCM) and leave to stand at room temperature with occasional agitation for 1 $^1/_2$ hours. Collect the filtrate and wash the resin with the cleavage reagent (3x2 cm^3). Evaporate the combined filtrates until dryness. Add cold ether (5 cm^3) and agitate the solid precipitated with a spatula. Leave for 10 minutes, decant the supernatant liquid and repeat once more with 5 cm^3 of ether. The product H_2N-Ser-Ala-OH is obtained by filtration through a sintered glass funnel.

PROBLEMS - Report

a. Record the following data:

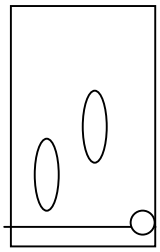
I. The weight of your product: 8 mg

II. The calculated theoretical yield: 12.3 mg (for level of first residue attachment 0.35)

III. The obtained yield as a percentage of the theoretical: 65%

IV. The melting point of the product: 210-213°C

b. Give a design of the thin layer chromatographic plateof the following compounds using $CHCl_3$/MeOH=(9/1) as the eluent system:



i) Fmoc-Ala-OH

ii) Fmoc-Ser(OBu^t)-OH

iii) H_2N-Ser-Ala-OH

c. Estimate the R_f value of the above products: i) 0.25, ii) 0.40, iii) 0

d. Report the observed angle of rotation α and the specific rotation $[\alpha]_D^t$ of your product using a polarimeter and applying the following equation:

$[\alpha]_D^t = \frac{\alpha}{lc}$, where: t = temperature (25°C), D refers to the sodium D line (589.0 nm), l = 1 dm, and c = 6 g/100 cm^3 in aq HCl. α = 1.91°, $[\alpha]_D^t = -31.8^o\ dm^{-1}\ g^{-1}\ cm^3$

Problem 36: Phase diagram and enthalpy of vaporization

Introduction

This experiment will allow you to construct a significant portion of the liquid – gas equilibrium curve in a phase diagram for water. The data will be used to determine an average value for the enthalpy of vaporization for the same compound making use of the Clausius – Clapeyron equation.

Theory

Every liquid can come to equilibrium with its vapor. The vapor pressure of a single-component liquid depends on the nature of the liquid and the temperature. At the temperature where the vapor pressure is equal to the total pressure applied to the liquid, the liquid boils. The normal boiling point is achieved when the pressure is 1 atm (= 1.013 bar = 101 325 Pa).

A phase diagram displays pressure versus temperature (or vice versa). For most compounds there are regions of the diagram where each phase (i.e., solid, liquid, gas) is shown and their boundaries are the two-phase equilibrium curves.

The Clapeyron equation is derived from basic Thermodynamics. It states that the slope of any equilibrium curve is equal to the ratio of the change in molar enthalpy upon phase change over the corresponding molar volume change and over the temperature, viz., $\frac{dP}{dT} = \frac{\Delta h}{T\Delta V}$. If we are interested in the liquid-gas or solid-gas equilibrium, we may assume that the gas follows the ideal gas state equation and that the molar volume of the gas is much larger than that for the condensed phase. With these assumptions, the Clausius – Clapeyron equation is derived: $\frac{d \ln P}{d\left(1/T\right)} = -\frac{\Delta h}{R}$. The derivative on the left-hand side of the equation is the slope of the lnP versus T^{-1} diagram.

Method

By trapping water in a sealed container, heating the apparatus and monitoring the pressure and the temperature, we can record a section of the phase diagram.

Apparatus

A simple heater (100-200 W), a 0-200 °C thermometer, a 0-20 bar pressure gauge (Bourdon tube), insulating aluminium foil, a steal tube, H_2O.

Procedure

Assemble the apparatus: wrap tightly together water containing tube (copper tube 10 cm long, 6 mm dia., plugged on one end and fitted with pressure gauge) and thermometer with Al foil; insert assembly in core of heater coil; support properly. Apply power to heater. Monitor pressure and temperature and interrupt heating when either 16 bar or 180 °C are exceeded. Start recording pressure and temperature for every division on the pressure gauge, while the apparatus is cooling down until the temperature has reached below 80 °C. Enter your measurements in a table with 3 columns: point number, pressure (units), temperature (units).

Analysis – Presentation

Draw all recorded points on a P vs. θ graph (phase diagram). Spot out any irregularities, i.e., highly divergent measurements. Extend the above table to include columns for lnP, T, 1/T. Calculate lnP, T, 1/T. Draw diagram of lnP vs. 1/T. Draw a straight line through the points of the latter diagram. Determine the slope of the line and calculate the enthalpy of vaporization for water.

Results – Discussion – Additional questions

Summarize your results. Estimate the normal boiling point of water based on your measurements. Compare to the known value and comment on any divergence. Likewise calculate the cooking temperature in a pressure cooker equipped with a safety valve which weighs 3 N and has a piston diameter of 6 mm.

Problem 37: <u>SOME CHEMISTRY OF IODINE</u>

The following chart contains some of the known compounds of the halogens at various oxidation states. Note that the oxidation number ranges in general from –1 to +7, but fluorine differs significantly from the other halogens in that it has no stable oxyacids.

Oxidation State	*Fluorine*	*Chlorine*	*Bromine*	*Iodine*
+7		$HClO_4$, ClO_4^-		H_5IO_6, IO_4^-
+5		$HClO_3$, ClO_3^-	$HBrO_3$, BrO_3^-	HIO_3, IO_3^-
+3		$HClO_2$, ClO_2^-		
+1		HClO, ClO^-	HBrO, BrO^-	HIO, IO^-
0	F_2	Cl_2	Br_2	I_2
-1	HF, F^-	HCl, Cl^-	HBr, Br^-	HI, I^-

A glance at the chart should convince you that oxidation-reduction reactions are a very important part of halogen chemistry.

Although iodine will show some chemistry unique to itself, many of its reactions are typical of other halogens. In this experiment we shall investigate some reactions of iodine and note the influence of hydrogen ion concentration on the equilibria.

PROCEDURE

Caution: Solid iodine and its vapor will cause burns and stains on skin or clothing. Its vapors are poisonous and even small quantities will irritate the mucous membranes, if inhaled. *Avoid unnecessary contact.*

Use 13x100 mm test tubes throughout this experiment except in Part IIb.

Preliminary Experiment-The Starch Iodine Test.

Prepare a dilute solution of iodine by adding one or two small iodine crystals to about 5 cm^3 of tap water. Warm slightly, add 3 or 4 drops of starch solution, and observe. This is a very sensitive test for molecular iodine.

Note: The color is due to a starch-iodine complex which is attributed to the ability of I_2 molecules to fit into the long, hollow spaces between the helical coils which constitute the starch molecule. The fit is close and the interaction strong enough to give the intense color even at very low iodine concentrations.

Part I. Some Reactions of Iodide Ion I^-.

a. To 2 cm^3 of 0.1 M potassium iodide (KI) add an equal volume of 0.1 silver nitrate ($AgNO_3$). Note the result.

b. To 2 cm^3 of 0.1 M potassium iodide (KI) and 5 cm^3 of starch solution add a drop or two of commercial bleach (5% NaOCl) solution. Note the result. Continue to add the bleaching solution until there is a second color change. How do you account for this?

c. To 2 cm^3 of 0.1 M potassium iodide (KI) and 5 cm^3 of starch solution add about 5 drops of 3% H_2O_2. Note the result.

Part II. Some Reactions of Iodate Ion IO_3^-.

a. Pour about 5 cm^3 of saturated solution of KIO_3 into each of two test tubes.

1. Add 3 cm^3 of 0.1 M KI and 2 cm^3 of 6 M H_2SO_4 to one of the test tubes. Decant the supernatant liquid from the solid produced. Filter, if necessary. Wash the solid with water. Do you recognize the solid? Run an identification test you have used previously to confirm your inference.
2. Add 3 cm^3 of 0.1 M KI and 2 cm^3 of 6 M KOH to the second test tube. What do you conclude about the role of hydrogen ion in the reaction between iodide and iodate ions?

3. Add 3 cm^3 of an acidified solution of 0.1 M sodium sulfite (Na_2SO_3), 2 cm^3 of 6 M H_2SO_4 and 3 or 4 drops of starch solution. What do you observe?

Part III. Reaction of I_2 in a Basic Solution.

a. To a few crystal (about 0.5 g) of solid iodine add from a dropper about 10 drops of 6 M potassium hydroxide, KOH. Shake the test tube gently until the solid iodine disappears and the solution is colorless. You may need to warm the solution gently and add a few more drops of 6 M KOH. You will identify the product of this reaction in Part d.

b. Cool the solution and make it acidic by adding sufficient (10 drops or slightly more) 6 M HNO_3 to neutralize the base added previously. Note the product of this reaction. What do you think it is?

c. Make the solution basic again by adding a few drops of 6 M KOH. Warm gently and add a few drops of 6 M KOH, if necessary, until a color change is observed. Discard the solution.

d. Repeat the procedure outlined in Part a. Cool under the cold water tap until a solid crystallizes from the solution. Decant the supernatant liquid and save it for part (2) below.

1. Dry the white solid by heating the test tube gently. Allow it to cool. Dissolve the white solid in 5 cm^3 of water. Add 5 cm^3 of 1 M sodium sulfite (Na_2SO_3), 2 cm^3 of 6 M H_2SO_4 and 3 or 4 drops of starch solution. Note the result. Compare it with that obtained in Part IIb.
2. To the decanted liquid add 5-10 drops of 0.1 M silver nitrate $AgNO_3$; shake the test tube and note the result. Compare the product with that obtained in Part Ia.

QUESTIONS

1. Write the equations for the reactions observed in Parts Ia, Ib, Ic.
2. a. How did the results in Part IIId(1) compare with those obtained in Part IIb?
   b. How did the test with 0.1 M silver nitrate in Part IIId(2) compare with the results of Part Ia?
   c. What do you conclude about the ionic species formed when I_2 reacts with 6 M KOH as in Part IIIa?
3. Write the equation for the self-oxidation-reduction reaction of iodine in a basic solution. Write the equation for the reverse reaction in an acid solution.
4. In which oxidation state do the halogens most commonly occur in nature? Explain your answer in terms of the electronic structure of this species for chlorine.
5. How would you prepare elemental fluorine, F_2? Consult an oxidation-reduction table to check the feasibility of your method.
6. Find the geometry, using the VSEPR model, for the following anions of the halogen oxoacids: ClO_2^-, ClO_4^-, BrO_3^-, IO_6^-.

Answers

1. Ia : $I^-(aq) + Ag^+(aq) \rightarrow AgI\downarrow$ (yellow precipitate)

Ib : $2I^-(aq) + OCl^-(aq) + 2H^+(aq) \rightarrow I_2$ (comp.) $+ Cl^-(aq) + H_2O$

The solution was deep blue colored . The color is due to the starch-iodine complex.

I_2 (comp.) $+ OCl^-(aq) + H_2O \rightarrow IO_3^-(aq) + 5Cl^-(aq) + H^+(aq)$

In excess of NaOCl the iodine was further oxidized to iodate.

Ic : $2I^-(aq) + H_2O_2 + 2H^+(aq) \rightarrow I_2 + 2H_2O$

The solution was deep blue colored . The color is due to the starch-iodine complex.

2. a. In Part IIb the sulfite ions (SO_3^{2-}) was reacted with an excess of iodic ions (IO_3^-) (saturated solution of KIO_3) and in the presence of starch indicator the deep-blue starch-iodine color increased systematically as a result of the following of reactions:

$$IO_3^- + 3SO_3^{2-} \rightarrow I^- + 3SO_4^{2-}$$
$$5I^- + IO_3^- + 6H^+ \rightarrow 3I_2 + 3H_2O$$

In Part IIId the iodate ions (IO_3^-) are reacted with an excess of sulfite ions (SO_3^{2-}). With the excess of sulfite, free iodine periodically appears and disappears as a result of the following sequence of reactions:

$$IO_3^- + 3SO_3^{2-} \rightarrow I^- + 3SO_4^{2-}$$
$$5I^- + IO_3^- + 6H^+ \rightarrow 3I_2 + 3H_2O$$
$$3I_2 + 3SO_3^{2-} + 3H_2O \rightarrow 6I^- + 6H^+ + 3SO_4^{2-}$$

The net reaction is the oxidation of iodates to iodides and the starch indicator oscillates between deep blue and almost colorless as the iodine concentration pulsates.

b. In Part IIId(2) the product is the same (yellow precipitate) with that obtained in Part Ia, following the reaction:

$$I^-(aq) + Ag^+(aq) \rightarrow AgI\downarrow$$

c. The anionic species formed when I_2 reacts with 6 M KOH as in Part IIIa was the iodates (IO_3^-) and iodides (I^-) anions.

3. The equation for the self-oxidation-reduction reaction of iodine in a basic solution is:

$$3I_2 + 6OH^- \rightarrow 5I^- + IO_3^- + H_2O$$

and the reverse of this reaction in an acid solution:

$$5I^- + IO_3^- + 6H^+ \rightarrow 3I_2 + 3H_2O$$

4. As X^-, oxidation state (1-), as the result of their electronic configuration:…..$ns^2\ np^5$.

5. The only practicable method of preparing F_2 gas is based on the electrolysis of fluoride salts, i.e., potassium fluoride (KF) dissolved in anhydrous HF:

$$KF + HF \rightarrow F_2 + H_2 \text{ (electrolysis)}$$

$$2F^- \rightarrow F_2 + 2e^- \quad E^o = -2{,}87 \text{ V}$$
$$2H^+ + 2e^- \rightarrow H_2 , \quad E^o = 0{,}00 \text{ V}$$
$$2F^- + 2H^+ \rightarrow F_2 + H_2 , \quad \Delta E = -2{,}87 \text{ V}$$

6. ClO_2^-: bent
   ClO_4^-: octahedral
   BrO_3^-: tetrahedral
   IO_6^-: trigonal pyramidal T-shaped

Problem 38: <u>Preparation of the complex salt $Cu(NH_3)_4SO_4 \cdot H_2O$</u>

Anhydrous copper sulphate, $CuSO_4$, is white. When it is dissolved in water, the resulting solution is sky blue because of the formation of the complex ion $Cu(H_2O)_6^{2+}$, or $Cu(H_2O)_4(H_2O)_2{}'^{2+}$ or $Cu^{2+}(aq)$. The six water molecules are not equivalent due to the Jahn-Teller effect.

The hydrated solid salt of copper sulfate, $CuSO_4 \cdot 5H_2O$ which may be written as $Cu(H_2O)_4 \cdot SO_4 . H_2O'$ is also blue.

If a solution of NH_3 is added to a solution of $Cu^{2+}(aq)$, the colour becomes intensely blue because of the formation of a new complex:

$$Cu^{2+} + 4NH_3 <=> Cu(NH_3)_4^{2+} + \text{water}$$

In solutions containing 0.01 to 5 M NH_3 the complex $Cu(NH_3)_4^{2+}$ is mainly formed. In lower concentrations of NH_3 formation of complexes containing fewer NH_3 molecules is favored, that is $Cu(NH_3)_3(H_2O)^{2+}$, $Cu(NH_3)_2(H_2O)_2^{2+}$ and $Cu(NH_3)(H_2O)_3^{2+}$. In concentrations of NH_3 higher than 5 M, $Cu(NH_3)_5(H_2O)^{2+}$ is also formed. Under these conditions the predominant complex is $Cu(NH_3)_4^{2+}$.

$$K_{form} = \frac{\left[Cu(NH_3)_4^{2+}\right]}{\left[Cu_{aq}^{2+}\right]\left[NH_3\right]^4}$$

K_{form} has a large value, that is the equilibrium is shifted to the right, while K_{inst}, which is defined as $1/K_{form}$, is small, hence the complex $Cu(NH_3)_4^{2+}$ is <u>stable</u>.

The equilibrium is established quickly, that is, complex $Cu(NH_3)_4^{2+}$ is <u>labile</u>.

Complexes in which the corresponding equilibrium is established slowly are called <u>inert</u>.

Due to the lability of the complex $Cu(NH_3)_4^{2+}$ the NH_3 molecules that are bound to the central ion Cu^{2+} are quickly and continuously exchanged with non-complexed NH_3 molecules, which are present in the solution as well as with molecules of the solvent (water).

Experiment

1. 6.25 g of hydrated copper sulfate $CuSO_4 \cdot 5H_2O$ are dissolved in a mixture of 10 cm^3 of concentrated NH_3 solution and 6 cm^3 of distilled water. The intensely blue solutions of the complex $Cu(NH_3)_4^{2+}$ will be formed according to the previous equilibrium.

2. The complex salt $Cu(NH_3)_4SO_4 \cdot H_2O$ is less soluble in a mixture of ethanol–water than in water. (Explain why). By adding 10 cm^3 of ethanol to the aqueous solution and cooling, a precipitate is formed. Is the dissolution in a mixture of ethanol – water endothermic or exothermic?

3. The precipitated salt is filtered under vacuum and washed sequentially by (a) a mixture of equal volumes of ethanol and concentrated solution of NH_3, (b) pure ethanol and (c) finally ether.

4. The so obtained crystals are placed in a desiccator. If a drying compound is used that can react with NH_3, e.g. $CaCl_2$, gas phase NH_3 will be bound and the complex will decompose in order to maintain the solid-gas equilibrium. A compound not reacting with NH_3 must be used, like CaO.

5. The binding of Cu(II) with NH_3 can be shown qualitatively as follows:

0.3 g of the starting material $CuSO_4 \cdot 5H_2O$ are dissolved in 10 cm^3 water, a few drops of Na_2CO_3 2 M solution are added and then a blue precipitate of $CuCO_3$ is formed. A similar solution of $Cu(NH_3)_4SO_4 \cdot H_2O$ does not give the previous reaction since Cu(II) is in the form of $Cu(NH_3)_4^{2+}$.

Under which conditions formation of $CuCO_3$ would be possible from the solution of the complex salt $Cu(NH_3)_4SO_4 \cdot H_2O$?

$$Cu(NH_3)_4^{2+} <=> Cu^{2+}(aq) + 4NH_3$$

Removal of NH_3 would shift the equilibrium to the right:

(a) by heating

(b) by addition of $CaCl_2$

(c) by addition of HCl.

Why is the complex salt more soluble in water than in ether?

Problem 39: <u>EDTA titration of magensium and calcium in water samples</u>

The term "hardness" of water refers to salts, mainly of Ca^{2+} and Mg^{2+} with the ions Cl^-, SO_4^{2-} and HCO_3^-.

By boiling water, the soluble salts of HCO_3^- are transformed to insoluble salts of CO_3^{2-}:

$$2HCO_3^- \quad <=> \quad H_2O + CO_2\,(g) + CO_3^{2-}$$

$$Ca^{2+} + CO_3^{2-}: \quad <=> \quad CaCO_3\,(\text{insoluble})$$

The hardness that is due to such salts disappears by boiling the water, hence the term non-permanent hardness.

The hardness which is due to Cl^- and SO_4^{2-} is permanent because it does not disappear by boiling the water.

Total hardness is the sum of permanent and non-permanent hardness.

The hardness of water is expressed in mg CaO / 100 cm^3 H_2O (Deutch degrees, D^o), in mg $CaCO_3$ / 100 cm^3 H_2O (French degrees, F^o) and in mg $CaCO_3$ / 1000 cm^3 H_2O (American way of expressing hardness).

Procedure:

Determination of the total hardness of water. Titration with EDTA.

1. 50 cm^3 of H_2O are measured accurately. Instead of "hard water" a solution containing a quantity of Mg^{2+} and Ca^{2+} ions may be used.

2-3 cm^3 of buffer solution $NH_3 - NH_4Cl$ having pH=10 are added and 3-4 drops of a solution (in alcohol) of melan eriochrome T, 0.5% (indicator). The solution turns red-violet because of the formation of a complex between Mg^{2+} and the indicator.

2. A solution of the dissodium salt of EDTA of known concentration 0.01 F which is equivalent to 1mg $CaCO_3$ / cm^3 EDTA (question 1) is added with stirring.

The ions Ca^{2+} and Mg^{2+} form 1:1 complexes with EDTA. EDTA will form complexes with all the free Ca^{2+} and Mg^{2+} ions and finally it will also bind with the ions Mg^{2+} which are to the indicator, replacing it. At this point, which is the titration end point, the colour of the solution turns from red to blue because of the liberation of the indicator. At pH=10, the colour change is clear and the determination of the equivalence point more accurate.

If V is the volume of the EDTA solution consumed and C its concentration in mg $CaCO_3$ equivalent to 1 cm^3 of EDTA solution and the volume of the water sample used is 50 cm^3, the hardness of water in mg $CaCO_3$ / 100 cm^3 H_2O is given by: $F^o=2VC$.

If C=0.01F ~ 1mg $CaCO_3$ / 1 cm^3 EDTA then $F^o=2V$.

Questions

1. Prove that an EDTA concentration of 0.01F is equivalent to 1mg $CaCO_3$ per 1 cm^3 EDTA.
2. If the volume of water sample is 25 cm^3, how will the hardness in F^o be calculated?
3. Express the experimentally determined hardness in D^o and in mg $CaCO_3$ / dm^3 H_2O.
4. If the water contains Ca^{2+} but no Mg^{2+}, is it possible to use the above method for the determination of the concentration of Ca^{2+} ? Which modification of the method is necessary?
5. Fluoride ions are added to the water supply of many cities for the protection of teeth. If the water non-permanent hardness is 1.0×10^{-3} M, is it possible for the fluoride concentration to reach the desired value of one part per million before it starts to form insoluble CaF_2? For the solubility product of CaF_2 use the value 1.7×10^{-10}.