CHEM22600

Session 2013-2014
Semester 1
PRACTICAL SYNTHETIC CHEMISTRY

Experimental Procedures

"Following recommendations from the HSE the wearing of laboratory coats and safety spectacles will be mandatory in all laboratories where chemicals are being handled. When working in the laboratory legs should be fully covered with trousers or skirt, preferably made of natural fibres. Short skirts or shorts, worn with either bare legs or tights, are not deemed appropriate. Shoes should have enclosed tops – flip flops, sandals or ballerina style pumps are not suitable. Any headscarves must also be made of natural fibre (cotton, linen, silk, wool etc.) as these do not melt and stick to skin in a fire situation."

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Introduction

Welcome to the Synthesis Laboratory.

The importance of synthesis and synthetic expertise cannot be overestimated. New functional molecules are essential for both the maintenance and quality of life. Synthetic chemists provide the expertise and inspiration underpinning discoveries in the life science, catalysis, and materials areas—from new metal complexes with anti-tumour properties, through antiviral compounds, to new and revolutionary molecular electronic devices. It is important that Chemistry graduates are equipped to make significant contributions to these and other areas.

This course is designed to provide further experience of important and modern techniques in practical synthetic chemistry, while illustrating experimentally the chemistry of classes of compounds dealt with in the second year lectures. The course reiterates a number of essential practical techniques that were introduced during your first year and provides a framework for you to improve your technical expertise and confidence in carrying out practical synthetic chemistry. It also involves the interpretation of the spectra of the compounds you make, and therefore complements the training you receive in the Measurements Laboratory Course and in lectures. The course covers areas traditionally viewed as 'inorganic' and 'organic' chemistry. The design of the course emphasises the similarity in techniques used in organic and inorganic research laboratories and in addition it reiterates the importance of keeping laboratory notebooks in good order.

You will start by reviewing your own skills and identifying areas for improvement. The first experiment, A1, is designed to refresh basic manipulative skill in metering reagents and isolation and purification of crystalline solids. Following this, students will conduct a series of experiments designed to improve technique, introduce some new techniques', and test the material taught in lectures. The course continues in the second semester with more advanced experiments, which illustrate a number of techniques that will be new or unfamiliar to you, including synthesis under an inert atmosphere. For the majority of the course you will follow detailed procedures for each experiment.

Section D looks forward to research projects that you will carry out in Years 3 or 4. Exact procedures or methods rarely exist in a research situation and so we have to decide how best to carry out a new experiment based upon our experience and knowledge. You will carry out a retrosynthetic analysis of a simple molecule and suggest a workable synthesis. You will have to decide on *how you might monitor the reaction*, *the appropriate scale to use*, *the solvent*, *the work-up procedure*, and how you *plan* to purify the product. You might need to consult the chemical literature. Finally, you will need to think about the exact procedure that you will adopt and your choice of glassware.

Section E requires you to determine the structure of **TWO** "unknown compounds" – an essential skill set for any chemist. You will be given samples of two compounds and you will be required to determine their structure using spectroscopic techniques, the physical properties of the compound and your knowledge of functional group chemistry. One of these exercises will be in the form of a group exercise where all the members of your BAY will be asked to contribute to solving the unknown's structure. The second exercise will be completed by each student independently.

Please note that is ***your*** responsibility to keep the laboratory clean and tidy. Other students besides you will be housed in these laboratories during the week please do not leave items of equipment or your samples on bench tops or in fume cupboards.

Course Duration, Accommodation, and Structure

Timing and Accommodation

The "Synthesis" laboratory-based practical course ("CHEM2600S") runs for **12 weeks** in total, meeting on **Tuesdays** (10 am – 4 pm) and **Wednesdays** (10 am – 12.30 pm), and is to be accommodated in the "synthesis laboratory" which occupies the **second floor** of the new teaching laboratories. **Please note there will be a lunch break from 12.30 – 13.30 on Tuesdays.** The year group will be split (alphabetically) into **two** groups, **1** and **2**. **Group 2** will *initially* follow a six week course in the synthesis laboratory while *Group 1* will initially be housed in the "measurements laboratory." **You will be informed of which group you are in at the beginning of semester 1.**

FIRST SEMESTER: OVERALL SCHEDULE

Week 1 (*i.e.* week starting 23rd September): Start of laboratory classes.

Group 1: measurements laboratory
Group 2: synthesis laboratory. Students will be given a locker number and will be introduced to their post-graduate demonstrators.

Week 6 (*i.e.* week starting 28th October)

Tidy up your bench set!

Group 2: Please ensure that your last write-up has been completed and uploaded onto the blackboard website by **23.59 on 6th November**.

Week 7 (*i.e.* week starting 4th November): Laboratory switch over date

Group 1: Synthesis laboratory. Students will be given a locker number and will be introduced to their post-graduate demonstrators.
Group 2: Measurements laboratory

Week 12 (*i.e.* week starting 9th December)
Tidy up your bench set!

Group 1: Please ensure that your last write-up has been completed and deposited on the blackboard website by **23.59 on 18th December**.

Lockers and Apparatus

You have been allocated a locker, which is located in one of **11 BAYS**, which contains an individual kit set. You should check the Blackboard website beforehand to obtain your lock number. This will also be displayed on the entrance to the synthesis laboratory. Upon arrival to the laboratory please make sure that your locker contains all of the equipment listed on the check list which the laboratory technician will provide. The care and maintenance of this set becomes **your** responsibility, and indeed, learning the importance of looking after your kit is part of the exercise. *Please ensure that you clean your glassware after each experiment as the technical staff will not be doing this for you*! Locker kits will also contain an NMR tube – it is your responsibility to ensure that you do not misplace this essential piece of glassware as you will be required to run NMR experiments on the samples which you prepare in the laboratory (**please ask your BAY demonstrator to run these spectra for you**). There are no charges for breakages, but you are expected to replace any broken or missing items from the stores (consult the technicians). **We will not return a lab mark for those who fail to return their kit sets, complete and in good condition.**

Year 2 Locker Kit

Item	Size	Qty	Check
Beaker	50 mL	1	
Beaker	100 mL	1	
Beaker	400 mL	1	
Beaker	600 mL	1	
Buchner Flask	250 mL	1	
Buchner Funnel		1	
Buchner Ring		1	
Conical Flask	50 ml	1	
Conical Flask	100 ml	1	
Conical Flask	250 ml	1	
Measuring Cylinder	10 ml	1	
Measuring Cylinder	100 ml	1	
RBF 3 Neck	100 ml	1	
RBF Single Neck	100 ml	1	
Watch Glass		1	
Cork Ring	Small	1	
Suba Seal	B 19	1	
Spatula		1	
Magnetic Stirer Bar		1	
Separating Funnel	250 mL	1	

ONLY ITEMS ON THIS LIST SHOULD BE IN YOUR KIT.
ALL OTHER ITEMS MUST BE CLEANED AND RETURNED.

DO NOT HOARD EQUIPMENT, THIS LEADS TO SHORTAGES.
YOU WILL LOSE MARKS IF YOU DO SO !!!

Date _____

Bay Number _____

Locker Number _____

Student Signature _____

Technician Signature _____

Bays 1,2,12,13	**Graham Booth**
Bays 4,5,6,7	**Mike Hughes**
Bays 8,9,10	**Abbas Askari**

Year 2 Locker Kit: Checklist

The course organisation

The twelve week course is divided into five sections, **A**–**E**:

- In ***first*** semester you will be required to complete the six **"A"** and **"B"** experiments; the **"C"** to **"E"** exercises are to be attempted in second semester;

- Time constraints will normally mean that you will **NOT** be able to carry **"A"**/**"B"** experiments over into second semester laboratory sessions;

- You are **REQUIRED** to hand in the samples/spectra hard copy of the "**SLAB** Experiment Submission Form" for each experiment **BEFORE** being start your next experiment;

- You are asked to complete **all 13 exercises**, section **A** (3 experiments), **B** (3 experiments), **C** (4 experiments), section **D** (1 experiment) section **E** (2 "unknown" exercises).

Supervision and demonstrating

Members of academic staff together with postgraduate demonstrators lead the sessions. Post–graduate demonstrators have been assigned to your "BAY" and will stay with your BAY for the duration of the whole laboratory course. Your assigned post-graduate demonstrator(s) should be your first port of call if you require help and assistance – please make good use of them as they are there to help you!

Your BAY demonstrators will be responsible for:

- taking the attendance register;
- demonstration of practical techniques, running of ^{1}H NMR spectra (**make sure that you make proper arrangements with your demonstrator for the collection of spectra**);
- discussing the underlying theory associated with each experiment;
- providing assistance with the use of SciFinder Scholar and NMR software packages;
- marking of your experiments, completing "SLAB" forms, **giving you feedback** from the marking process, and
- entering data into the marks spread sheets.

Demonstrators

You BAY demonstrator provides a direct feedback mechanism for your progress throughout the course of the laboratory session; if you are at all unhappy with your progress in the laboratory please do not hesitate to contact me either directly or by e-mail (peter.quayle@manchester.ac.uk). All students will do the same experiments, but the different BAYS may do them in differing orders. Please check, on day one of the course, the order in which you will do the experiments.

Attendance

Attendance at laboratory courses is **compulsory** and these modules are **not compensatable**. Failure of a laboratory course could result in expulsion from your degree programme. Regular attendance is vital if you are to achieve a good mark in this module. You will be required to

"sign in" to **each** session (*i.e.* a.m. **and** p.m. on Tuesday; a.m. on Wednesday) by "swiping" you library card in the card reader (**do not confuse this card reader with the wall-mounted reader which unlocks the laboratory door!).**

Course Outline

"S LAB" SEMESTER 1: LABORATORY TIMETABLE

The course in first semester will follow the general outline as shown below. Students are required to complete one experiment per week and submit their write-up, on-line, by the **WEDNESDAY** of the following week (see "***S-Lab Timetable***", below). ***Failure to submit write-ups by the specified date may result in a mark penalty***.

Group 2: Introduction to course on Tuesday a.m. Week 1

Including: health and safety issues, checking of lockers, marking and feedback.

Section A Experiments: Tuesday p.m. Week 1–Wednesday Week 3

A1: Preparation of Metal Acetylacetonate Complex
Techniques: Correct use of balances, clamps and glassware, isolation by vacuum filtration, preparative-scale purification by recrystallization.

A2: Preparation a Nickel(II) Complex by a Template Synthesis
Techniques: Correct setup of reflux apparatus, sample preparation and recording of ^{1}H NMR spectrum.

A3: Ferrocene
Techniques: Carrying out reactions under an inert atmosphere; Isolation by vacuum filtration; Sublimation, organometallic chemistry.

Section B Experiments: Tuesday a.m. of Week 4–Wednesday a.m. of Week 6

B1: The Synthesis of Glucose Pentaacetae
Techniques: Reaction set-up, recrystallisation, filtration, melting point, infrared spectroscopy, ^{1}H NMR spectroscopy, determination of optical rotation.

B2: Peptide Synthesis
Techniques: Reaction set-up, recrystallisation, infrared spectroscopy, ^{1}H NMR spectroscopy, spectroscopic analysis.

B3: The Synthesis of Gramine
Techniques: TLC, filtration, recrystallisation, melting point, infrared spectroscopy, NMR spectroscopic analysis.

Clear-up: Wednesday Morning of Week 6

Group 1: Introduction on Tuesday a.m. Week 7

Complete the cycle of experiments as above in weeks 7-12
Clear-up: Wednesday Morning of Week 12

“S-LAB” SEMESTER 1: LABORATORY TIMETABLE

SLAB Semester 1						
Group 2	Exp. A1	Exp. A2	Exp. A3	Exp. B1	Exp. B2	Exp. B3
Date of Experiment	24/09/2013	01/10/2013	08/10/2013	15/10/2013	22/10/2013	29/10/2013
Deadline for write up*	02/10/2013	9/10/2013	16/10/2013	23/10/2013	30/10/2013	06/11/2013
Group 1						
Date of Experiment	05/11/2013	12/11/2013	19/11/2013	26/12/2013	03/12/2013	10/12/2013
Deadline for write up*	13/11/2013	20/11/2013	27/11/2013	04/12/2013	11/12/2013	18/12/2013

*** Write-ups should be submitted to Blackboard by 23.59 together with an electronic copy of the relevant COSHH form and Lab Absence form (where applicable).**

SAFETY

ALL substances should be treated as toxic (even salt, oxygen and water can kill you under certain conditions!). Absorption through the skin may be dangerous as well as ingestion and inhalation through the mouth, nose, ears, eyes, etc. Some materials appear to have little immediate effect, but may cause problems in the long term – carcinogens are an obvious example. *If at* ***any time you are unsure of what you are doing ask for advice.***

When working in the laboratory YOU MUST adhere to the following safety regulations:

- Wear safety spectacles **at all times**;
- ALWAYS wear a **laboratory coat** when in the synthesis laboratory;
- **Open-toed shoes** and **sandals** are **not appropriate footwear** for use in the laboratory;
- **Adopt a sensible dress code which affords you adequate protection** in the case of fire or spillages; long hair is to be tied-back;
- Note the location of the emergency exits and the first aid boxes;
- Note the location of the CO_2 fire extinguishers and fire blankets and familiarise yourself with their mode of operation;
- Use pipette fillers at all times when pipetting chemicals;
- Wear protective gloves when using acids and bases or other harmful substances;
- Dispense concentrated acids in fume hoods only;
- Label all samples with your name date and the substance name;
- Dispose of waste organic solvents etc in the specially marked bottles provided;
- Dispose of **sharp items**, *e.g.* needles etc in the **specially marked containers provided**;
- Clear up any chemical spillage **immediately**.

Hazardous Chemicals: CoSHH forms

The law requires that **any one** using chemical compounds assess the hazards associated with their use before starting, and then take appropriate action to minimise the risks to themselves and others. **Any one includes you!**

You will therefore complete a *CoSHH* (**C**ontrol of **S**ubstances **H**azardous to **H**ealth) *form* (similar to those used in the departmental research laboratories) **before** starting each experiment. An electronic version of this form has been uploaded onto the S-LAB website.

i) Read through your next experiment the night before you come into the laboratory;
ii) Complete the online COSHH form;
iii) Save a copy of your completed COSHH form on your computer;
iv) Print out a copy of the ***completed*** COSHH form and have it signed by your demonstrator **before** starting your experiment;
v) upload a copy of each completed COSHH form with your report when submitting your experiment for marking.

The completed form must be shown to a demonstrator or member of staff **before** you start your experiment. If it is satisfactory, the demonstrator will sign it and enter fill in the appropriate section of your SLAB form. ***Only then may you start your experiment***. You will not be allowed to start an experiment without this authorisation.
The risks associated with using any chemical compound are a combination of what it does it comes in contact with you or someone else (toxic, narcotic, irritant, corrosive, lachrymator, carcinogen,

laxative, etc.,) and its potential for escaping control. A CoSHH form asks for information on both aspects.
Information on toxicities of known compounds is included in suppliers catalogues (a legal requirement). Note these, and read and include the numbers of the compound's "Hazard statements" (H-numbers) and Precautionary statements (P-numbers) in the entry for the compound in your CoSHH form. Details of lethal doses are not required, but your assessment should note whether the compound is toxic by skin contact, inhalation, or ingestion. Note any relevant decontamination (commonly, irrigate with large volumes of cold clean water) and disposal procedures.
The potential for a compound to escape control depends on the quantities used, on the physical form of the compound, and on what you are doing with it. For each compound, your CoSHH entry should include the quantity to be used, whether it is a solid, liquid or gas, and its mp or bp. Any reactivity properties likely to cause handling difficulties should also be noted (e.g., ^{n}BuLi can spontaneously ignite in air…!).

CoSHH forms are a basis for action, so don't just fill in and forget. Act upon what you have found out when you run your experiment. If in doubt, check with a demonstrator or staff member.
A list of useful reference books is given at the end of this note.

You must hand your CoSHH form in with the appropriate experiment write-up; failure to do so will result in a mark of zero being recorded.

Books:

Seiler, Sigel and Sigel	'Handbook of Toxicity of Inorganic Compounds'
The Royal Society of Chemistry	'Hazards in the Chemical Laboratory'
	'Dangerous Properties of Industrial Materials'
	'The Merck Index'

Accidents

- All technical staff has had training in emergency first aid. In the event of an accident, seek immediate assistance;

- Staff will provide first aid for cuts, burns, and chemical contact, inhalation or ingestion. They are trained to assess the need for further treatment, and, if necessary call the ambulance service.

- Generally, splashes to the skin and eyes should be washed with copious amounts of water.

- Removal of reagents insoluble in water will be facilitated by cleaning the contaminated area with soap.

- Dry burns should be treated by covering the afflicted area with a new dry sterile dressing from the first aid box. If you inhale gas or dust particles and feel faint, immediately leave the area.

- If, in the unlikely event that you do ingest a chemical, wash your mouth out with copious amounts of water and inform the first aider of what the chemical was.

We are legally obliged to record all accidents requiring treatment.

Year 2 Synthesis Lab Chemical Risk Assessment

Student	Dates From: / / To / /	Expt. ref. no. (*e.g.* A2 etc)
Bay Number	Emergency contact no.	

Reaction Equation (including ALL products/by-products)

Overnight reaction? Yes / No

Temperature Range

Substance (use a second sheet if necessary)	**Phys. Form**	**Quantity**	**Risk Phrases**	**Summary of Hazards** *e.g.* Highly Flammable, Toxic, Explosive, Carcinogenic, Mutagenic, Lachrymatory

Primary Control Measures
ALL chemical reactions, workups, and purifications MUST BE conducted within a fume hood, while wearing safety glasses, lab coat and chemically resistant gloves.

Secondary Control Measures

Double glove (chemical resistant only) ☐ Other (specify)

Remove hazardous materials from vicinity ☐

Visible warning notice ☐

Faceshield ☐

Blast shield ☐

In Emergency, *e.g.* in the event of evacuation, the following measures should be taken to ensure the reaction is safe to leave:

CoSHH form used in the Synthesis Laboratory

N.B. CoSHH forms are a basis **for action**, so **don't just fill in and forget**. Act upon what you have found out when you run your experiment. **If in doubt, check with a demonstrator or staff member. You must keep your CoSHH form with you whilst working in the lab.**

"SLAB" Experiment Submission Forms

For each experiment that you perform in the laboratory you will also be asked to fill out an "**SLAB Experiment Submission Form**". This provides both the student and staff with an additional record of attendance and attainment. This form should be signed by your BAY demonstrator at the start of each experiment on presentation of the COSHH form and completed when the experiment is marked. Your BAY demonstrator will keep the top copy and place it in your file. The duplicate copy is for your records: please do not loose this document! Once completed and returned to you this form should provide a useful source of information concerning your progress.

SLAB Year 2

University of Manchester: School of Chemistry
2nd Year Synthesis Laboratory

MANCHESTER 1824
The University of Manchester

EXPERIMENT SUBMISSION FORM

STUDENT NAME	BAY	GROUP	EXPERIMENT

	Demonstrator's Signature	Date
COSHH Completed		
Practical Completed		
Sample Handed In		

Sample Feedback	Spectra Feedback
Mark	**Mark**

No marks will be awarded if this form is not completed. You must retain the bottom copy of this form and hand the top copy in with your spectra, to your bay demonstrator.

"SLAB" Experiment Submission Form

Course Assessment: Writing up Experiments and Submission of Reports

The course assessment will be based upon:

- the results of your experiments;
- the quality/quantity of your samples (**marked out of 10**);
- the quality of your reports**: all laboratory reports must be submitted for marking/archival reference *via* blackboard** (using the electronic **SLAB** Experiment Write-up form).
- All experiments require a write-up which must be completed as outlined in the "Experiment Write-up Guide" and **submitted to the appropriate blackboard site**. You should **also** use your laboratory notebook for the **recording initial observations**, calculation of yields etc. Your notebook will be checked periodically in order to ensure that observations etc. are recorded correctly.

Marks are not allocated solely on the basis of attendance: merely attending the laboratory will not gain you marks!

Time management in this course is essential: you cannot "overrun" from one section to another. You are **required to write-up each experiment as they are carried out**.

On completing an experiment you should also present the following to your BAY demonstrator:

- Properly ***labelled*** samples from the experiment which we will retain;
- Properly ***annotated*** spectra of starting materials/products (these should have your name and University ID no. appended);
- A mark of "zero" will be returned if samples are not properly labelled or spectra not properly annotated with your name/|ID number;
- A properly ***completed*** CoSHH form for the experiment;
- An "**SLAB** Experiment Submission Form" for the experiment;
- A paper copy of each completed **SLAB** Experiment Write-up form (this is for our records in case of an irretrievable blackboard failure).
- Reports will be marked as a "**zero**" if a properly completed CoSHH form is not returned with the **SLAB** Experiment Write-up form;

Your BAY demonstrator will fill in the SLAB completion form and will allocate marks for the sample and spectra (**out of a maximum of 10**). We will retain the top copy and the duplicate (yellow copy) be returned to the student for your records. The sample mark will then be entered into the laboratory spread sheet. Students should check with their BAY demonstrator that all of their marks have been properly recorded in the Laboratory Spread Sheet.

Post-graduate demonstrators have been assigned to specific experiments and will mark **online** assignments for experiments **A2**, **B1** and **B2** (**each of these online assessments is worth 20 marks**). You should receive feedback for these assignments by the Monday **after** submission.

Write-ups for experiments **A1**, **A3** and **B3** will me marked in your presence in the laboratory in the week following the completion of the experiment: **could you please print out a copy of your report for these experiments and bring them to the laboratory for marking? This exercise should provide you with direct feedback concerning your write-ups.**

Illness and Absence

There are penalties for late submission of write-ups. If there are any **extenuating** circumstances as to why work cannot be completed or marked you must see a member of academic staff as soon as practicable. If you have been ill or have been on interview *etc.* complete the electronic version of the "**Lab Absence Form**" which is on the S-LAB website and present this to the staff demonstrator. The signed form should then be returned to G.20 as soon as you resume your studies. You should then upload the electronic copy of your absence form together with the appropriate write-up to the relevant assessment box on Blackboard.

Feedback

Return of marks

It is important that you receive regular feedback concerning your progress during your stay in the Synthesis Laboratory. This will be forthcoming from:

i) Your BAY demonstrators when you hand in the completed "SLAB" forms;
ii) Direct feedback from your BAY demonstrator when marking experiments **A1**, **A3** and **B2** which will take in the laboratory. You will be able to see exactly where marks are gained in your write-up and ask questions concerning the improvement of the presentation of your work prior to completing the next write-up;
iii) The marks for each experiment which will be returned to you on a regular basis (together with written comments) *via* Blackboard;
iv) Discussions with demonstrators and staff when in the laboratory (**please make use of this very valuable resource!**).

If you are at all concerned with your progress, or have questions relating to assessment, please consult Dr. Peter Quayle (Peter.quayle@manchester.ac.uk) without delay.

You will automatically receive feedback and marks for each experiment that you submit to Blackboard: this will enable you can gauge your progress throughout the course. Tutors will also be sent your marks so that they can monitor your progress.

Office Hours

The "**office hours**" for CHEM22600s will be Tuesdays and Thursdays@ 4.00 – 5.00 p.m. If you wish to discuss any aspect of the course you will be able to do so with Dr. Quayle - simply turn up at Dr. Quayle's office (room 4.02c) at these times.

I will organise a feedback session to be held in the synthesis laboratory (date to be arranged) where issues associated with the presentation of write-ups can be discussed.

Laboratory Notebook

The reasons for keeping a laboratory notebook are several in number and include: to record what you have done and your ***raw data***, so as to enable you to repeat the experiment at a later date; to enable you to write a report; to enable someone else to repeat the work that you have done; and to avoid the possibility of loosing scraps of paper that have important information written on them. Ask yourself honestly at the end of each session: if you were only given your laboratory notebook

in a year's time would you be able to repeat the experiment or more importantly would somebody else? If the answer to this question at the end of any session is no then you need to record more detail. Your notebook will also be where most of your experimental write-ups appear.

The importance of this may not seem relevant to you now, but when you get a job in industry or carry on in academic research your laboratory notebooks will be of primary importance; for example, patents and or publication in journals will be based upon the data you have recorded in your note books; if you move on to another position and someone has to carry on the project they were working on, your notebook will be an invaluable source of information to them. Notebooks can be used as legal documents in court cases, for example in disputed cases of intellectual property rights (IPR). Your notebook will be retained by the School after you have submitted all your write-ups for assessment.

You Must:

- Put your name and BAY number on the outside cover;
- include the date of an experiment;
- put the title of the experiment;
- put the equations or structural formula diagrams for the experiment, so you know what you're doing and can work out what is the limiting reagent;
- have a list of reagents, how much you used in g and moles and the number of equivalents;
- include observations/calculations *etc*;
- include a calculation of the theoretical yield based on the limiting reagent;
- include any observations and problem encountered and how they were overcome.

Copying and Plagiarism

- You will be assessed on the material you present. Copying from another student, or using sections from a textbook or the web, or any other source without attribution (and justification) is unacceptable. Students suspected of acting in a plagiaristic manner will be investigated as outlined in the University Regulations.

• Samples and Spectra

Only samples labelled with *your name*, submission date, and the compounds identity will be accepted (see the model write-up below for information on correct labelling).
IR and NMR spectra that *you record* are part of the assessment. These also should be labelled and dated. The use of data from other students, without attribution, will result in a zero mark for that experiment. Any students knowingly providing data for others will also get zero for that experiment.

Useful Reference Material

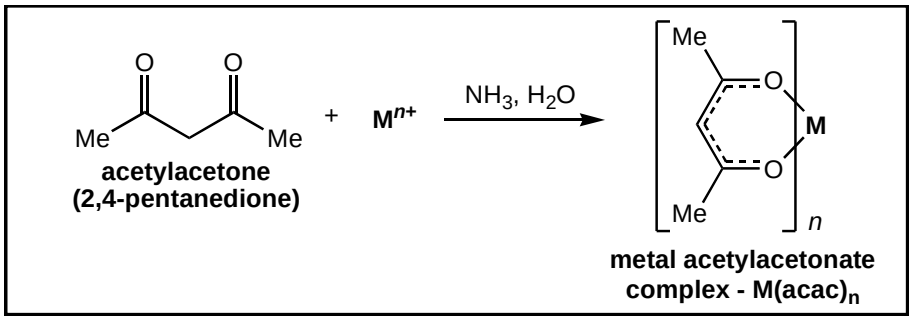
The set texts for your course "Clayden" ("Organic Chemistry" by Clayden, Greeves, Warren and Wothers, 1st Edition) and "Housecrotft and Sharpe" ("Inorganic Chemistry" by Housecroft and Sharpe) provide an invaluable source of background material which you should consult before carrying out your experiments and completing your write-ups.

General Laboratory techniques: "Experimental Organic Chemistry," 2nd Edition, by L. M. Harwood, C. J. Moody and J. M. Percy
Spectroscopy: "Organic Structures from Spectra", 4th Edition, by L. D. Field, S. Sternhell and J. R. Kalman.

EXPERIMENT A1

PREPARATION OF METAL ACETYLACETONATE COMPLEXES

Introduction



In this experiment you prepare and purify a metal acetylacetonate complex type and record its IR spectrum and melting point. In later experiments (measurement lab) you will prepare other examples.

Practical Skills Developed/Reinforced: Correct use of balances and glassware; Preparative-scale recrystallisation; Isolation by vacuum filtration.

Relevant Lecture Courses: CHEM10312, solution chemistry and d-block chemistry; CHEM20410, introducing carbon acids.

Hazard Assessment of Chemicals Handled

Acetylacetone	*Flammable, Harmful if swallowed.*
Sodium acetate	*Irritant to respiratory tract, eyes, and skin. Harmful if absorbed through skin.*
Petroleum ether (60–80)	*Highly flammable.*
Manganese(II) chloride tetrahydrate	*Harmful by inhalation and if swallowed, irritating to eyes, respiratory system, and skin.*
Toluene	*Irritant , vapours may cause drowsiness and dizziness. May be harmful if absorbed through skin, swallowed, or inhaled.*
Potassium permanganate	*Contact with combustible material may cause fire. Harmful if swallowed.*

DO NOT BEGIN THE EXPERIMENT BEFORE YOU HAVE COMPLETED YOUR COSHH FORM FOR THIS EXPERIMENT AND HAD IT CHECKED AND SIGNED BY YOUR DEMONSTRATOR

EXPERIMENTAL PROCEDURE

HANDLE ALL CHEMICALS INVOLVED IN THE FUME CUPBOARD AND CARRY OUT THE REACTIONS IN A FUME CUPBOARD. AVOID INHALATION OF VAPOURS. TOLUENE, ETHANOL, ETHYL ACETATE, AND PETROLEUM ETHER ARE VERY FLAMMABLE – AVOID OPEN FLAMES. TAKE GREAT CARE USING AMMONIA SOLUTION – IT IS CORROSIVE AND CAN CAUSE BURNS. DISPOSE OF ALL CHEMICAL WASTE AS INSTRUCTED. AS USUAL NO CHEMICALS ARE TO BE DISPOSED OF IN BINS, AND ALL GLASS MUST BE DISPOSED OF IN THE GLASS BINS (THAT INCLUDES TLC SPOTTERS AND DISCARDED VIALS).

Preparation of Tris(acetylacetonate)manganese

For this experiment you will need two spotlessly clean, **DRY** 100 mL conical flasks and a glass filter funnel which should be put to warm in an oven at 60°C.

Synthesis

In a 100 mL conical flask, dissolve hydrated manganese(II) chloride (1 g) and sodium acetate (2 g) in water (40 mL), and then add acetylacetone (***a.k.a.* 2,4-pentanedione**, 4 mL). Stir the mixture until the acetylacetone is well dispersed and then add slowly, with stirring, 10 mL of the 0.125 M solution of potassium permanganate. To this mixture add a further solution of sodium acetate (2 g) in water (10 mL) and heat the resulting mixture on a hotplate with *occasional* stirring, bringing the temperature up to 60 °C for 20 minutes. Allow the solution to cool to room temperature, filter off the crystalline precipitate with a Hirsch or Büchner funnel (use vacuum), wash it with a small amount of water and partially dry it by drawing air through it. Spread the solid out on a filter paper and leave it to dry further in air for a few minutes.

Purification by Recrystallisation

Put the dry solid into one of your dry 100 mL conical flasks and, **IN A FUME CUPBOARD**, add some toluene, just enough to dissolve the solid (no more than 15 mL) as you heat it on a hotplate for a few minutes. Heating will dissolve the product but not the insoluble impurities (such as MnO_2). Filter the warm solution through a fluted filter paper (don't try to use vacuum!) placed in the warm filter funnel placed in the other clean, dry 100 mL conical flask (see the beginning of this experiment).

Add petroleum ether 60–80 (40 mL) to the hot filtrate and allow to cool down to room temperature. If no precipitate has appeared after a few minutes, add another portion (20 mL) of petroleum ether and scratch the wall of the conical flask under the solution with a glass rod. Filter the crystals on a Hirsch funnel (use vacuum) and wash them with a small amount of petroleum ether. Let them dry in the air.

i) Record the weight, percentage yield, and the IR spectrum of your product.

ii) Record the melting point of your product. With the help of a demonstrator find a literature melting point of the product and compare with your value.

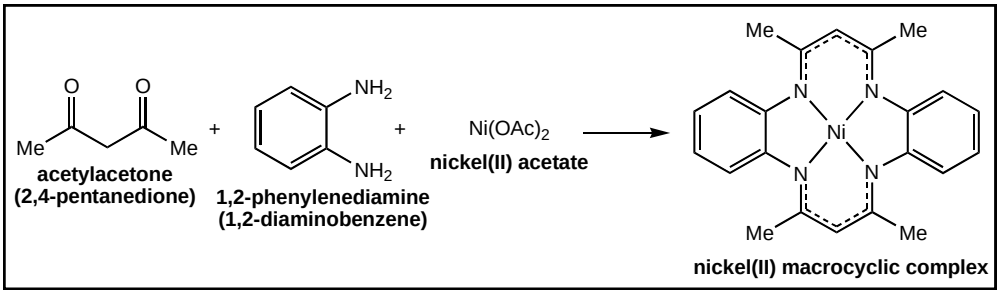
WASTE DISPOSAL:

Please dispose of any waste in the specially labelled "A1 Waste containers" which are in BAY 11. <u>DO NOT</u> pour organic waste from this experiment into general waste containers as this may result in a violent exotherm. DO NOT pour aqueous waste from this reaction down the drain or into the organic waste containers.

Experiment A2

Spontaneous Self-Assembly; Preparation a Nickel(II) Complex by a 'Template Synthesis'

NOTE: This experiment requires a 3-hour reflux. Set it up as soon as you arrive in the laboratory on Tuesday morning.



In this experiment you prepare and purify the nickel(II) macrocyclic complex and measure its IR and ^{1}H NMR spectra and melting point.

Practical Skills Developed/Reinforced: Correct use of reflux > 100 ˚C; Isolation by crystallisation; Efficient use of time.

Relevant Lecture Courses: CHEM10312, solution chemistry and d-block chemistry; CHEM30311, ligand design; CHEM20411,organic synthesis.

Hazard Assessment of Chemicals Handled

Acetylacetone	*Flammable, harmful, toxic if swallowed. Irritating to eyes,*
1,2-Phenylenediamine (1,2-diaminobenzene)	*Harmful by inhalation and contact with skin. Toxic if swallowed. Irritating to eyes. Limited evidence of a carcinogenic effect – possible carcinogen.*
Nickel(II) acetate tetrahydrate	*Toxic, possible carcinogen. Harmful if swallowed, may cause sensitization by skin contact. Avoid contact with skin.*
1-Butanol	*Flammable, harmful. Irritating to respiratory syste and skin. Risk of serious damage to eyes. Vapours might cause drowsiness and dizziness.*
Methanol	*Flammable, toxic. Danger of serious irreversible effects through inhalation, contact with skin, and if swallowed. Irritating to eyes and skin.*

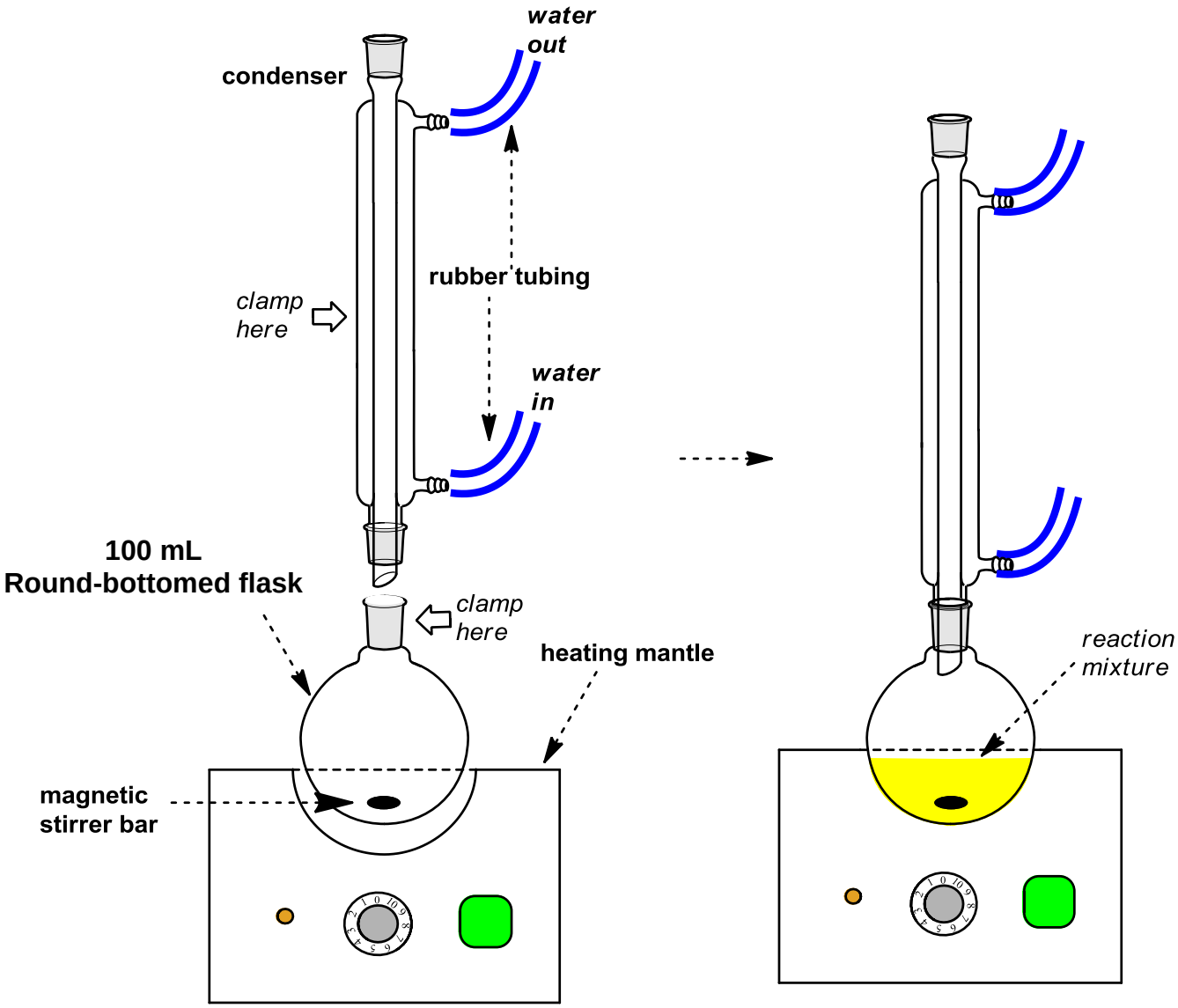
DO NOT BEGIN THE EXPERIMENT BEFORE YOU HAVE COMPLETED YOUR COSHH FORM FOR THIS EXPERIMENT AND HAD IT CHECKED AND SIGNED BY YOUR DEMONSTRATOR

EXPERIMENTAL PROCEDURE

HANDLE ALL CHEMICALS INVOLVED IN THE FUME CUPBOARD AND CARRY OUT THE REACTIONS IN A FUME CUPBOARD. AVOID INHALATION OF VAPOURS. 1-BUTANOL IS FLAMMABLE – AVOID OPEN FLAMES. TAKE GREAT CARE HANDLING 1,2-PHENYLENEDIAMINE AND NICKEL(II) ACETATE. DISPOSE OF ALL CHEMICAL WASTE AS INSTRUCTED. AS USUAL NO CHEMICALS ARE TO BE DISPOSED OF IN BINS, AND ALL GLASS MUST BE DISPOSED OF IN THE GLASS BINS (THAT INCLUDES TLC SPOTTERS AND DISCARDED VIALS).

Preparation of the Nickel(II) Macrocyclic Complex

You need to set up the apparatus as shown below:



Notes:

1) Make sure your apparatus is clean and dry.

2) You might need to use an adapter or two, but keep the number as small as possible – ideally you should not need any.

3) Make sure your clamps are set up correctly.

4) **We have <u>two</u> types of heating mantle. If you have one which <u>stirs</u>, add a magnetic stirrer bar to the reaction mixture BEFORE heating is started. If you have one that doesn't, add one or two boiling chips <u>PRIOR</u> to heating. <u>Addition of either a stirrer bar or anti-bumping granules to the HOT reaction mixture will result in a violent reaction.</u>**

Experimental Method

To the 100 mL round-bottomed flask add, nickel(II) acetate tetrahydrate (1.0 g), 1,2-phenylenediamine (1.8 g), 1-butanol (25 mL) and acetylacetone (1.7 mL). Heat the pale purple mixture to reflux (with stirring if available: ***if not*** add a few ant-bumping granules to the cold reaction mixture ***before*** heating) and continue reflux for **3 hours**, during which time a deep green colouration should develop. ***You are advised to use this time to begin writing up this experiment or completing the previous write-up.***

Once the reflux time is complete (precise timing is not critical, but better with more than 3 hours than less, especially if there was no stirring), **Cool to room temperature**: ***Either***, if you are not time-constrained, by switching off the heat source and leaving *in situ* to cool slowly; any agitation should be very gentle and infrequent, to avoid excessive nucleation of crystallites. Less nucleation means fewer, larger crystallites, which are easier to filter and wash. ***OR***, if you are time-constrained, by removing from the mantle (**be careful** handling the hot flask: 1-butanol boils at 117 ˚C) and placing in a cool water bath, or in a stream of running cold water. When cool add methanol (5 mL). Place the flask in an ice/salt bath and cool the reaction mixture to –5 ˚C. A solid should precipitate out of solution. The dark colouration may make this difficult to see.

Collect the precipitate by vacuum filtration (use a Büchner flask and Büchner funnel or glass sinter), and wash the solid (while in the Büchner funnel/sinter) with ice-cold methanol (10 mL)). Dry the solid by allowing air to be drawn through it for 10–15 minutes.

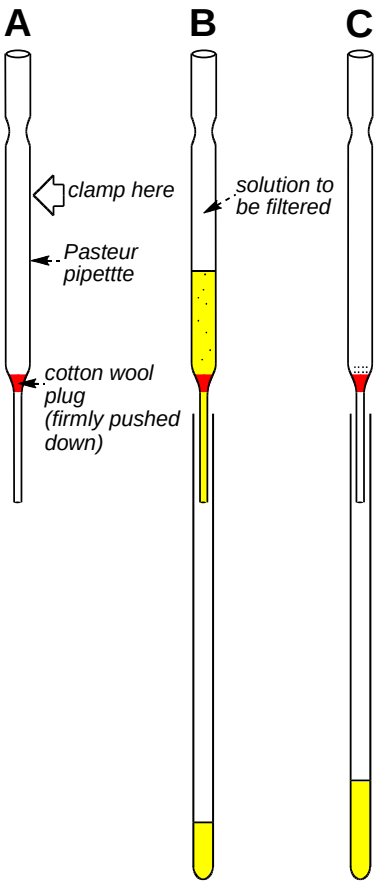
i) Record the weight and colour, calculate the percentage yield, and record the melting point, IR spectrum and ^{1}H NMR spectrum of your product.

ii) With the help of a demonstrator find a literature melting point of the product and compare with your value.

^{1}H NMR Sample Preparation

Prepare a sample for ^{1}H NMR analysis. It is important in this case to use a well-washed sample. It should be dark purple in colour. Impure material may make recording of NMR difficult. Weigh out ~ 5–10mg (0.005–0.010 g) of your product into a small vial, and dissolve it in ~0.75 mL of deuterochloroform ($CDCl_3$) **[CARE: $CDCl_3$ - Irritant , vapours may cause drowsiness and dizziness. $CDCl_3$ may be harmful if absorbed through skin, swallowed, or inhaled. Perform this operation in a fume cupboard]**.

This solution (free of any undissolved solid) must now be transferred into a clean dry NMR tube and the NMR tube capped. To achieve this, use a (glass) Pasteur pipette prepared for use as a filter as outlined below:



A – Clamp a Pasteur pipette (**gently**) and push a small plug of cotton wool into the constriction as shown. Handle the glass pipettes carefully as they break easily. The cotton wool plug will act as the 'filter paper'.

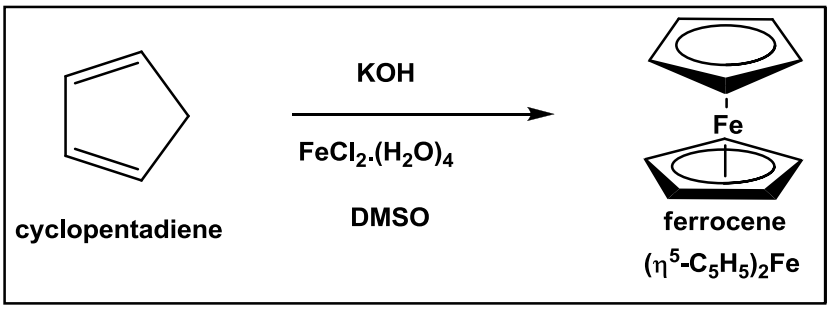
B – Place a clean dry NMR tube under the pipette and add the solution to be filtered to the pipette. Force the solution through the plug by applying **gentle** pressure from a Pasteur pipette bulb (**DO NOT use compressed air or the nitrogen supply for this**).

C – Carefully remove the used Pasteur pipette and dispose of it appropriately (wash it through with a little solvent and then put it into the waste glass container).

Now cap the NMR tube and arrange with your demonstrator the running of the ^{1}H NMR spectrum of your sample.

EXPERIMENT A3

PREPARATION OF (BIS-CYCLOPENTADIENYL)IRON(II) – "FERROCENE"



Introduction

In this experiment you will prepare ferrocene: you will gain experience in working under an inert atmosphere and purify your product by sublimation.

Practical Skills Developed/Reinforced: Carrying out reactions under an inert atmosphere; Isolation by vacuum filtration; Sublimation.

Relevant Lecture Courses: CHEM20310, organometallic chemistry; CHEM10412, aromatic chemistry.

Hazard Assessment of Chemicals Handled

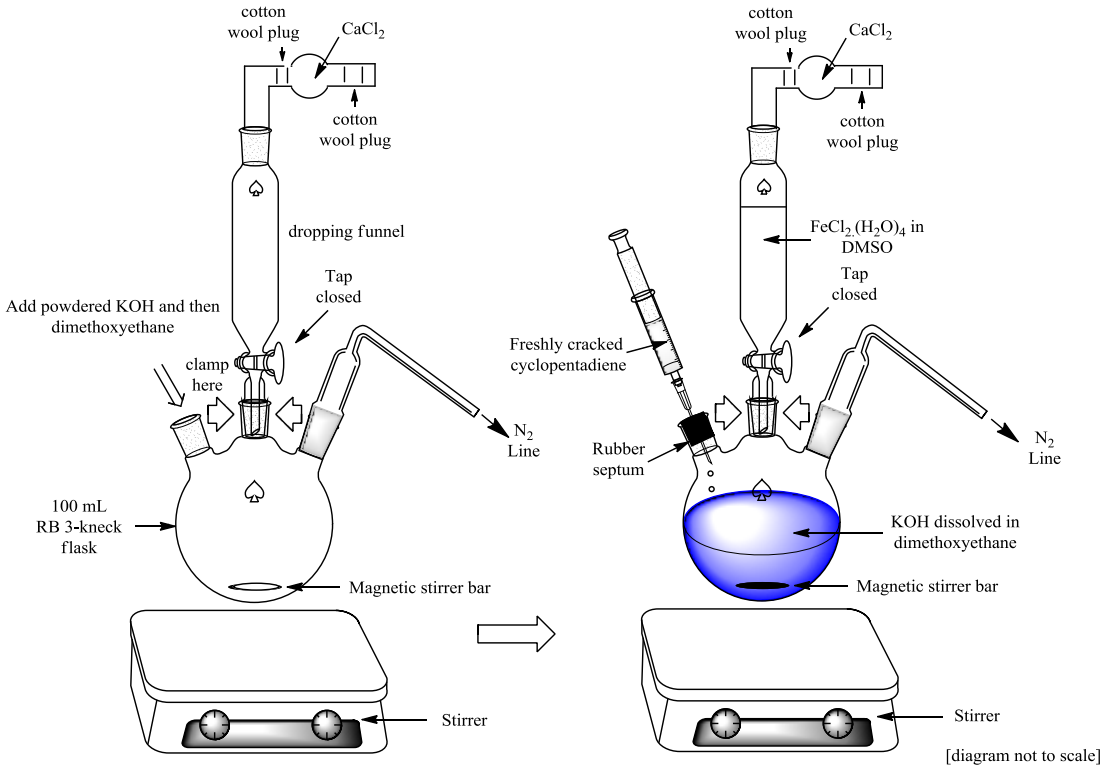
cyclopentadiene	*Highly flammable. Irritating to eyes. Vapours may cause drowsiness and dizziness. Highly flammable. Harmful if swallowed*. ***Stench***.
Dimethylsulfoxide	*Highly flammable. Irritating to eyes. Vapours may cause drowsiness and dizziness. Odour.*
Potassium hydroxide powder	*Highly corrosive. Avoid contact with skin.*
Concentrated Hydrochloric acid	*Highly corrosive. Avoid contact with skin.*
1,2-Dimethoxyethane	*Highly flammable. Irritating to eyes. Vapours may cause drowsiness and dizziness. Odour.*

DO NOT BEGIN THE EXPERIMENT BEFORE YOU HAVE COMPLETED YOUR COSHH FORM FOR THIS EXPERIMENT AND HAD IT CHECKED AND SIGNED BY YOUR DEMONSTRATOR

EXPERIMENTAL PROCEDURE

HANDLE ALL CHEMICALS INVOLVED IN THE FUME CUPBOARD AND CARRY OUT THE REACTIONS IN A FUME CUPBOARD. AVOID OPEN FLAMES. TAKE GREAT CARE HANDLING POTASSIUM HYDROXIDE AND DIMETHYLSULFOXIDE. DISPOSE OF ALL CHEMICAL WASTE AS INSTRUCTED. AS USUAL NO CHEMICALS ARE TO BE DISPOSED OF IN BINS, AND ALL GLASS MUST BE DISPOSED OF IN THE GLASS BINS (THAT INCLUDES TLC SPOTTERS AND DISCARDED VIALS).

You need to set up the apparatus as shown below:



Notes:

1) Make sure your apparatus is clean and dry.

2) You might need to use an adapter or two, but keep the number as small as possible – ideally you should not need any.

3) Make sure your clamps are set up correctly.

Preparation of Ferrocene

ALL operations for this experiment are to be carried out in a fume cupboard. If any of the reagents come into contact with your skin please consult a demonstrator or a member of the technical staff immediately. Cyclopentadiene has a nasty odour. Please dispose of the organic and inorganic wastes in the appropriate waste containers which have been placed in BAY 11 fume cupboard.

To a stoppered 100 mL 3-necked RB flask equipped with dropping funnel (please make sure that the tap is initially closed) add a magnetic stirrer bar followed by **powdered** KOH* (8g, 142.6 mmol)) (**CARE: powdered KOH is highly corrosive**). You must wear gloves when carrying out this operation and avoid inhalation of the powder. Then add 1,2-dimethoxyethane (24 mL) to the KOH and seal the flask with a rubber septum. Purge the flask with a stream of nitrogen and slowly stir the contents of the flask until the KOH dissolves. After approximately 5 minutes the KOH should have dissolved and freshly cracked cyclopentadiene† (2.0 mL, 26.6 mmol) (**CARE**: ***stench. Use only in a fume cupboard. Do not put waste material down the***

* **This will be supplied by the technical staff.**
† **Freshly cracked cyclopentadiene will be made available to you on the morning of the experiment.**

sink: use the designated waste containers) is added drop-wise from a syringe through the rubber septum. After the addition of cyclopentadiene is complete stir at room temperature for 10 minutes.

Meantime grind $FeCl_2.4H_20$ (2.6 g, 13.1 mmol) into a fine powder (this **MUST** be done in a fume cupboard) and dissolve in dimethylsulfoxide (12 mL) (**CARE: do not allow contact of this solution to your skin**). Transfer the ferrous chloride solution to the addition funnel. Purge the flask with nitrogen for 5 minutes and then begin the slow addition of the $FeCl_2$ solution by slowly opening the tap on the dropping funnel. The rate of addition is adjusted so that the entire solution is added over 15 minutes. Upon completing the addition of the ferrous chloride close the dropping funnel tap and stir the reaction mixture vigorously for an additional 30 minutes while maintaining a steady flow of nitrogen through the flask. The reaction mixture darkens and often appears dark green in colour at this stage.

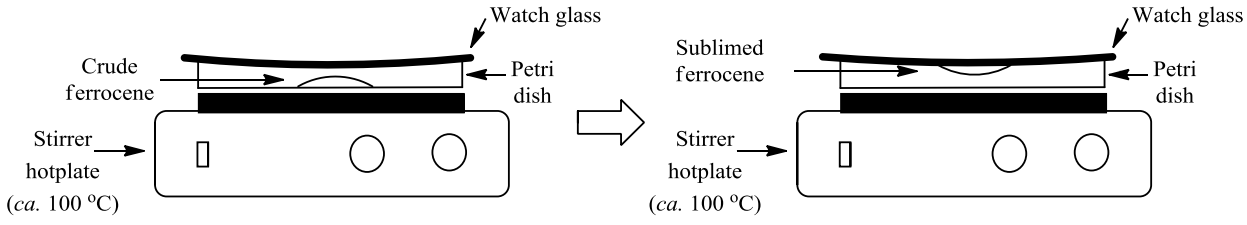
In a fume cupboard carefully add concentrated hydrochloric acid (18 mL) to 50 g of crushed ice in a 600 mL beaker (**CARE: HCl is corrosive**) and slowly add the reaction mixture to the ice-cold acid solution. The resulting slurry is stirred for about 15 minutes and the orange precipitate is collected on a Büchner or Hirsch funnel and washed with four 5-mL portions of water. The moist solid is spread out on a large watch glass and dried between two large pieces of filter paper and then in a vacuum desiccator overnight. Record the mass of your crude product: ensure that your BAY demonstrator has noted your crude yield in the appropriate "SLAB" form.

WASTE DISPOSAL

ALL aqueous extracts from this reaction should be collected in the "A3 AQUEOUS WASTE" container which will be kept in fume cupboard number 11. DO NOT pour any aqueous waste from this reaction directly into the sinks in either the laboratory or fume cupboards. Organic waste should be collected in the appropriate container in the BAY 11 fume cupboard.

Purification of Ferrocene by Sublimination

After drying record the crude yield of product. **Purify 0.3 g of the crude product by sublimation**. The following set up will be used in this procedure:



Place 0.3 g of your crude product into a Petri dish and cover with a watch glass. Place the Petri dish onto a stirrer hotplate and gradually warm the hotplate up to *ca.* 95 °C (**overheating may result in product loss**). As the Petri dish is heated ferrocene will sublime onto the underneath surface of the watch glass. Do not

overheat the Petri dish (i.e. keep to < 100 °C) as this will lead to charring of the product. Once the ferrocene has sublimed onto the watch glass carefully removed the Petri dish from the hot plate and collect the purified product.

i) Record the mass and percentage yield of your purified sample of ferrocene;

ii) determine its melting point (use a sealed capillary: consult your demonstrator about this);

iii) record the IR and ^{1}H NMR spectra of your product.

iv) With the help of a demonstrator find the literature melting point of the product and compare with your value;

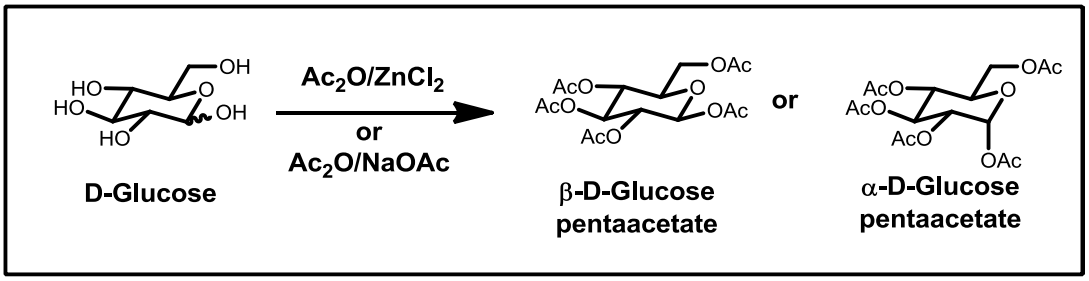
v) Fill in the appropriate SLAB submission form so that your BAY demonstrator can now apportion marks for yield, quality of product and spectra.

PRACTICAL PROCEDURES: "B" EXPERIMENTS

EXPERIMENT B1

THE SYNTHESIS OF GLUCOSE PENTAACETATE

Introduction (*Suggested reading: Clayden, 6, 14, 49*).



In this experiment you will prepare glucose pentaacetate from glucose. Glucose is the primary product of photosynthesis and is the prototypical member of the carbohydrate class of natural products. Glucose is transformed in nature into biopolymers such as cellulose and starch. Carbohydrates are key to many biological "recognition" processes - and provide the basis for blood group typing. In this experiment you will prepare **one** of the **two** possible anomers of glucose pentaacetate. ^{1}H NMR spectroscopy, in conjunction with other physical data (melting point, optical rotation), will then be used to determine the structure of the product obtained in your reaction.

Practical Skills Developed/Reinforced: Recrystallization; IR and ^{1}H NMR spectroscopy, introduction to carbohydrate chemistry, determination of specific rotation.

Relevant Lecture Courses: CHEM10101, aldehydes and ketones; CHEM10412, carbonyl group chemistry; CHEM20411 (carbonyl and heterocylic chemistry) and also the ^{1}H NMR spectroscopy lectures at the beginning of year 2.

Hazard Assessment of Chemicals Handled

Acetic anhydride	*Harmful if swallowed. Irritating to eyes, respiratory system and skin*. *Reacts with water to produce acetic acid which is an irritant.*
Zinc chloride	*Deliquescent*. *Harmful if swallowed. Irritating to eyes and skin*.
Methanol	*Harmful if swallowed. Flammable. Avoid inhalation. Vapours may cause drowsiness and dizziness.*
Sodium acetate	*Skin irritant, avoid contact with skin and eyes.*

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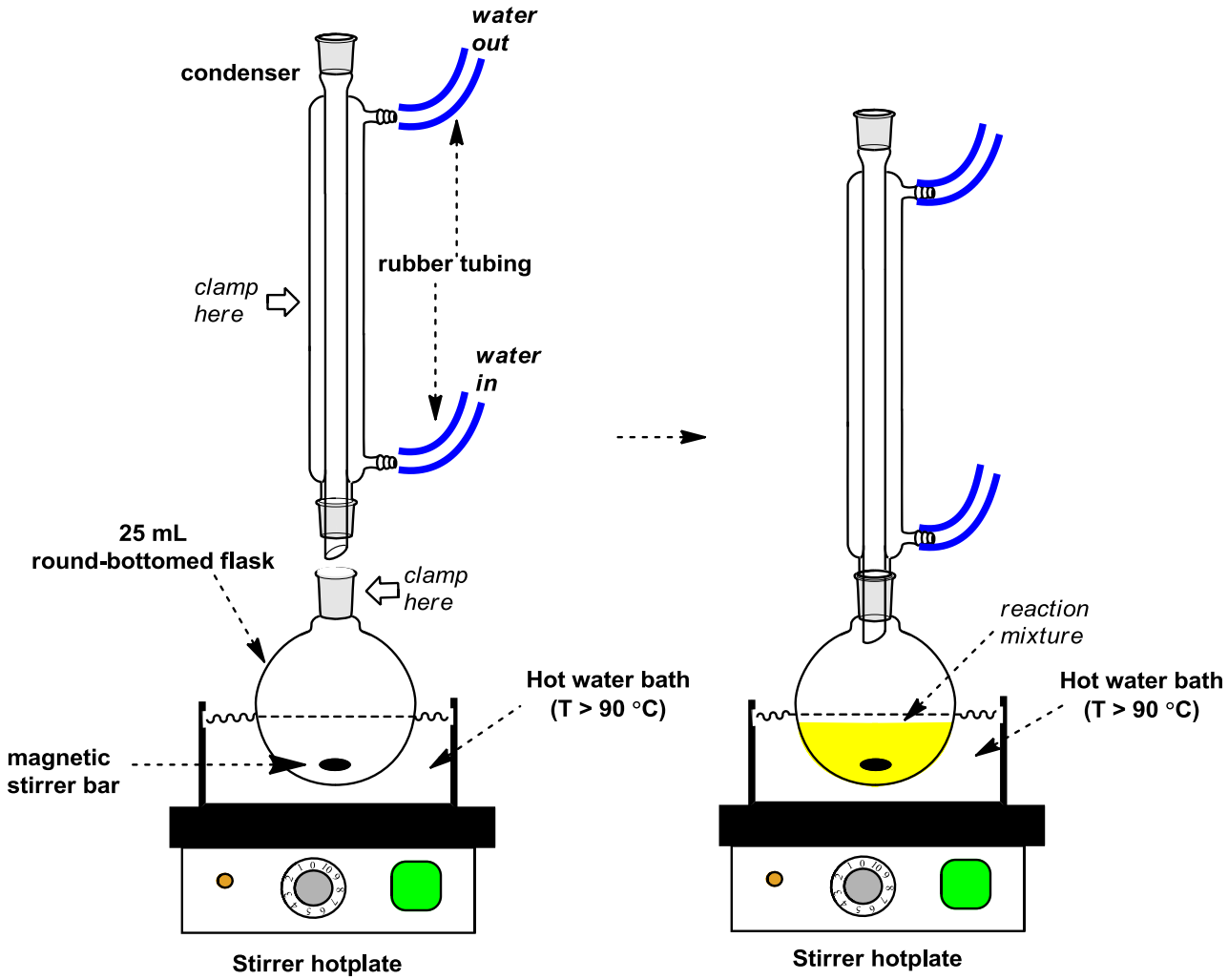
DO NOT BEGIN THE EXPERIMENT BEFORE YOU HAVE COMPLETED YOUR COSHH FORM FOR THIS EXPERIMENT AND HAD IT CHECKED AND SIGNED BY YOUR DEMONSTRATOR

HANDLE **ALL** CHEMICALS INVOLVED IN THE FUME CUPBOARD AND CARRY OUT THE REACTIONS IN A FUME CUPBOARD. AVOID INHALATION OF VAPOURS. **METHANOL** IS **FLAMMABLE** – AVOID

OPEN FLAMES. **ZINC CHLORIDE** IS AN IRRITANT: AVOID CONTACT WITH SKIN. DISPOSE OF ALL CHEMICAL WASTE AS INSTRUCTED. AS USUAL NO CHEMICALS ARE TO BE DISPOSED OF IN BINS, AND ALL GLASS MUST BE DISPOSED OF IN THE GLASS BINS (THAT INCLUDES TLC SPOTTERS AND DISCARDED VIALS)

You need to set up the apparatus as shown below:



Notes:

1) Use a stirrer-hotplate to maintain the water bath at a temperature **> 90 °C**; **remember to replenish the water as it evaporates.**

2) Make sure your apparatus is clean and **dry**.

2) There may be an initial **exotherm** when the acetic anhydride and zinc chloride are mixed;

3) Quench the reaction **slowly** as this may also be **exothermic**.

EXPERIMENTAL PROCEDURE

You must carry out this reaction in a fume cupboard. You must use gloves in order to protect your skin when manipulating the reagents used in this reaction.

This experiment will run in two groups:

Group A: those students who are housed in BAYS 1, 3, 5, 7, 9, 11, 13, and

Group B: those students who are housed in BAYS 2, 4, 6, 8, 10, 12

Group A Students:

To a 25 mL round bottom flask add the D-glucose provided (1g), zinc chloride (0.2g: **CARE: deliquescent, skin irritant**), acetic anhydride (5 mL: **CARE: skin irritant; avoid inhaling vapour**) and a magnetic stirrer bar. Attach a reflux condenser equipped with a $CaCl_2$ guard tube, and heat to 90 $^oC^{‡}$ with stirring for 1 hour. After one hour, remove from the source of heating and allow the reaction mixture to cool down to room temperature. **Carefully** (**this may cause an exotherm**) poor the contents of the round bottom flask into a 400 mL beaker containing 100 mL of ice water and stir for up to 1 hour or until sufficient crystals have been produced. A sticky oil may initially separate out at this stage which slowly solidifies on stirring. Collect the crude crystals of D-glucose pentaacetate by vacuum filtration. Recrystalise the crude glucose pentaacetate from the minimum of hot methanol (**CARE: do not use a naked flame – use in a fume cupboard**).

i) Record the yield of your recrystallised product, its melting point, IR and ^{1}H NMR spectra.

ii) With the help of a demonstrator find literature melting points for the two possible products from this reaction and compare with your value.

iii) Determine the optical rotation of your product (consult your demonstrator about this).

iv) With the help of a demonstrator find the literature value for the optical rotation of the two diastereoisomeric pentaacetates and compare with your value in order to predict which anomer you have prepared.

v) Use the ^{1}HNMR data to verify which anomer you have prepared (discuss the use of the Karplus equation with your demonstrator in order to complete this assignment).

vi) Fill in the appropriate SLAB submission form so that your BAY demonstrator can now apportion marks for yield, quality of product and spectra.

Group B Students:

To a 25mL round bottom flask add the D-glucose which provided (1g) sodium acetate (0.8g: **CARE - irritant**) acetic anhydride (5 mL: **CARE: skin irritant; avoid inhaling vapour**) and a magnetic stirrer bar. Attach a reflux condenser which is equipped with a $CaCl_2$ guard tube and heat to 90 ^oC with stirring for 1.5 hours. Allow the reaction mixture to cool down to room temperature then poor the contents onto 75 mL of ice water and stir until white crystals are formed. Collect the crude crystals of glucose pentaacetate by vacuum

‡ The water bath should be maintained at > 90 °C in order for the reaction to go to completion.

filtration. Recrystallise the crude D-glucose pentaacetate from the minimum of hot methanol (**CARE: do not use a naked flame – use in a fume cupboard**).

i) Record the yield of your recrystallised product, its melting point, IR and ^{1}H NMR spectra.

ii) With the help of a demonstrator find literature melting points for the two possible products from this reaction and compare with your value.

iii) Determine the optical rotation of your product (consult your demonstrator about this).

iv) With the help of a demonstrator find the literature value for the optical rotation of the two diastereoisomeric pentaacetates and compare with your value in order to predict which anomer you have prepared**.**

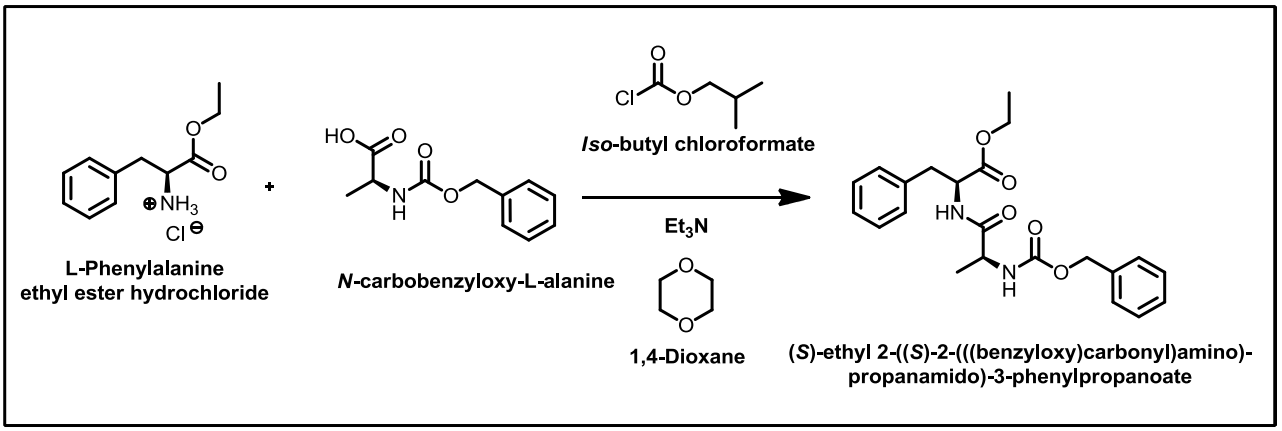
v) Use the ^{1}HNMR data to verify which anomer you have prepared (discuss the use of the Karplus equation with your demonstrator in order to complete this assignment).

vi) Fill in the appropriate SLAB submission form so that your BAY demonstrator can now apportion marks for yield, quality of product and spectra.

EXPERIMENT B2

THE SYNTHESIS OF A DIPEPTIDE

Introduction (*Suggested reading: Clayden, Chs. 25 and 52*).



In this experiment you will prepare a dipeptide from two amino acids, via the activation of a free carboxylic acid as its anhydride. The structure of the peptide will be conformed buy an analysis of its ^{1}H NMR and IR spectra.

Practical Skills Developed/Reinforced: Recrystallisation, IR and ^{1}H NMR spectroscopy, introduction to peptide chemistry.

Relevant Lecture Courses: CHEM10101, aldehydes and ketones; CHEM10412, carbonyl group chemistry; CHEM20411 (peptide chemistry) and also the ^{1}H NMR spectroscopy lectures at the beginning of year 2.

Hazard Assessment of Chemicals Handled

Triethylamine	*Harmful if swallowed. Irritating to eyes, respiratory system and skin*.
Iso-butylchloroformate	*Harmful if swallowed. Irritating to eyes and skin; librates HCl upon reaction with water. Avoid inhaling vapour- irritating to respiratory system.*
THF	*Harmful if swallowed. Flammable. Avoid inhalation. Vapours may cause drowsiness, dizziness and headaches. Forms explosive peroxides on standing in sunlight.*
Petroleum ether	*Harmful if swallowed. Flammable. Avoid inhalation. Vapours may cause drowsiness and dizziness and headaches.*
1,4-Doxane	*Harmful if swallowed. Flammable. Avoid inhalation. Vapours may cause drowsiness, dizziness and headaches. Forms explosive peroxides on standing in sunlight.*
Dichloromethane	*Harmful if swallowed. Avoid inhalation. Vapours may cause drowsiness, dizziness and headaches. Suspected liver toxin.*

DO NOT BEGIN THE EXPERIMENT BEFORE YOU HAVE COMPLETED YOUR COSHH FORM FOR THIS EXPERIMENT AND HAD IT CHECKED AND SIGNED BY YOUR DEMONSTRATOR

HANDLE **ALL** CHEMICALS INVOLVED IN THE FUME CUPBOARD AND CARRY OUT THE REACTIONS IN A FUME CUPBOARD. AVOID INHALATION OF VAPOURS. **THF, 1,4-DOXANE, TRIETHYLAMINE and PETROLEUM ETHER** ARE **FLAMMABLE** – AVOID OPEN FLAMES. ***ISO*−BUTYLCHLOROFORMATE** IS AN IRRITANT: AVOID CONTACT WITH SKIN. **DICHLOROMETAHANE** IS TOXIC BY INHILATION –USE IN THE FUME CUPBOARD. DISPOSE OF ALL CHEMICAL WASTE AS INSTRUCTED. AS USUAL NO CHEMICALS ARE TO BE DISPOSED OF IN BINS, AND ALL GLASS MUST BE DISPOSED OF IN THE GLASS BINS (THAT INCLUDES TLC SPOTTERS AND DISCARDED VIALS)

EXPERIMENTAL PROCEDURE

You must carry out this reaction in a fume cupboard. You must use gloves in order to protect your skin when manipulating the reagents used in this reaction.

Generation of mixed anhydride:

To a dry 50 mL conical flask add *N*-carbobenzyloxy-L-alanine (446 mg) and a solution of triethylamine (0.2 mL) dissolved in 1,4-dioxane (10 mL). Cool the mixture to ~ 5 °C in a water/ice bath (this should be at a temperature of ca. 3 °C). Cool a solution of *iso*-butylchloroformate (0.27 mL: **CARE: irritant**) in 1,4-dioxane (10 mL) to 5 °C and slowly add this solution solution to the solution of carbobenzyloxy-L-alanine using a Pasteur pipette over a 15 min period. After the addition of the *iso*-butylchloroformate is complete continue to stir the reaction mixture for a further 30 minutes in order to complete the formation of the mixed anhydride.

Peptide coupling step:

In the meantime prepare a solution of L-phenylalanine ethyl ester hydrochloride (430 mg) in water (10 mL). To this solution add triethylamine (0.2 mL: **CARE: irritant**) dissolved in 1,4-dioxane (10 mL: **CARE: flammable**) and cool this mixture to ~ 5 °C in a water/ice bath. Slowly add this solution to the mixed anhydride prepared above using a Pasteur pipette at 5 °C over a 15 min period. Allow the reaction to reach room temperature whilst stirring (15-20 minutes).

Product isolation:

Upon completion of the reaction add water (60 mL) and extract this mixture with dichloromethane (2 x 50 mL: **CARE: irritant and toxic**). **Combine the lower, dichloromethane, layers** and wash them with dil.HCl (3M, 2 x 40mL) being sure to retain the lower, dichloromethane layers. Wash the combined dichloromethane layers with dilute aqueous sodium carbonate (3M, 2 x 20 mL) and then with water (1 x 20 mL). Dry the organic extracts (remember this is the lower layer) with anhydrous sodium sulphate. Remove the sodium sulphate by filtration (use a glass funnel and fluted filter paper.) and transfer the dried organic extracts into a **pre-weighed weighed** RBF flask. Remove the solvent on a rotary evaporator and triturate the residue with 20-30 mL of 40/60 petrol. The desired product should now solidify into a colourless solid which can be isolated by filtration using a Buchner funnel (**CARE: flammable - do not use a naked flame; use in a fume cupboard**).

i) Record the yield of your recrystallised product, its melting point, IR and ^{1}H NMR spectra.

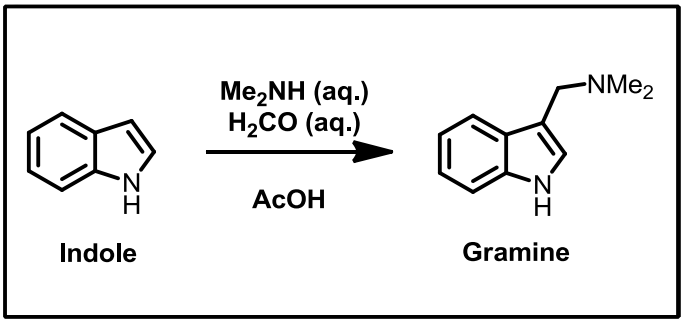
ii) With the help of a demonstrator find literature melting points for products of this reaction and compare this with your value.

iii) Fill in the appropriate SLAB submission form so that your BAY demonstrator can now apportion marks for yield, quality of product and spectra.

EXPERIMENT B3

THE SYNTHESIS OF GRAMINE: THE MANNICH REACTION

Introduction (*Suggested reading: Clayden, Chs. 27 and 43*).



In this experiment you will prepare gramine, a useful synthetic intermediate, which possesses an indole skeleton. The procedure exemplifies the "Mannich Reaction" – a "cascade" process of chemical reactions which has extensive use both in heterocyclic and aliphatic chemistry. The identity of the product will be confirmed by ^{1}H nmr spectroscopy, IR spectroscopy and comparison of melting point with that in the literature.

Practical Skills Developed/Reinforced: Recrystallization; IR and NMR spectroscopy, introduction to heterocyclic chemistry.

Relevant Lecture Courses: CHEM10101, aldehydes and ketones; CHEM10412, carbonyl group chemistry; CHEM20411 (carbonyl and heterocylic chemistry) and also the ^{1}H NMR spectroscopy lectures at the beginning of year 2.

Hazard Assessment of Chemicals Handled

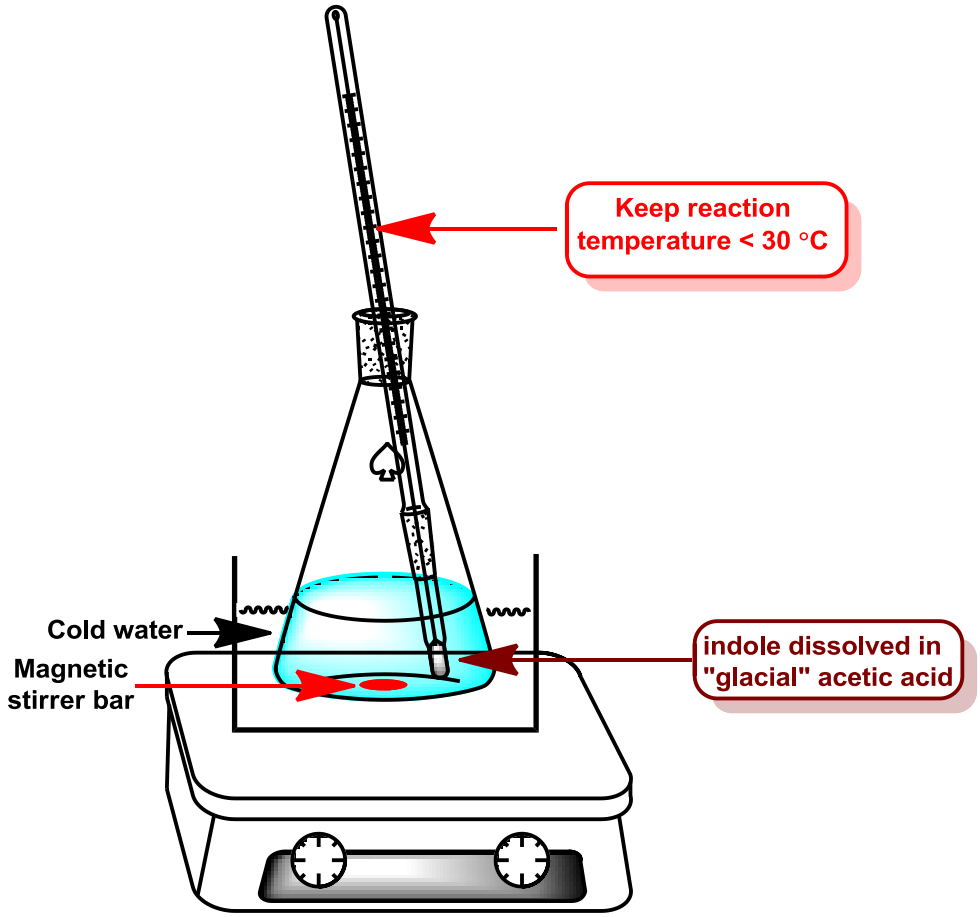
Indole	*Harmful if swallowed. Irritating to eyes, respiratory system and skin. Odour*
Aqueous formaldehyde	***Cancer suspect agent.*** *Avoid inhalation of vapour and contact with skin. Irritating to eyes, respiratory system and skin. Vapours may cause drowsiness and dizziness.*
Aqueous methylamine	*Toxic, irritant, Harmful if swallowed. Irritating to eyes, respiratory system and skin*
Acetone	*Harmful if swallowed. Toxic, irritant, flammable. Irritating to eyes, respiratory system and skin. Avoid inhalation. Vapours may cause drowsiness and dizziness.*
Aqueous sodium hydroxide	***Highly caustic:*** *do not allow to come into contact with skin or eyes. Harmful if swallowed.*

DO NOT BEGIN THE EXPERIMENT BEFORE YOU HAVE COMPLETED YOUR COSHH FORM FOR THIS EXPERIMENT AND HAD IT CHECKED AND SIGNED BY YOUR DEMONSTRATOR

HANDLE **ALL** CHEMICALS INVOLVED IN THE FUME CUPBOARD AND CARRY OUT THE REACTIONS IN A FUME CUPBOARD. AVOID INHALATION OF VAPOURS. **ACETONE** IS **FLAMMABLE** – AVOID OPEN FLAMES. AQUEOUS **SODIUM HYDROXIDE** IS **CAUSTIC**: AVOID CONTACT WITH SKIN. DISPOSE OF ALL CHEMICAL WASTE AS INSTRUCTED. AS USUAL NO CHEMICALS ARE TO BE DISPOSED OF IN BINS, AND ALL GLASS MUST BE DISPOSED OF IN THE GLASS BINS (THAT INCLUDES TLC SPOTTERS AND DISCARDED VIALS)

AQUEOUS FORMALDEHYDE IS A CANCER SUSPECT AGENT. DO NOT INHALE VAPOURS

You need to set up the apparatus as shown below:



Notes:

1) Clamp the kneck of the flask in order to prevent spillage of its contents.
2) Ensure that you have some ice so that you can change the ice-water during the quenching of your reaction
3) Use a thermometer to monitor the temperature of your reaction.

Experimental procedure.

You must carry out this reaction in a fume cupboard. You must use gloves in order to protect your skin when manipulating the reagents used in this reaction.

To a 50 mL conical flask add "glacial" acetic acid[§] (20 mL: **CARE! CORROSIVE**) and a magnetic stirrer bar. With stirring then add indole (1g, 8.6 mmol) followed by 40% aqueous dimethylamine solution (3 mL: **CARE! This reagent is a skin irritant**). There will be a light exotherm during this addition: it is wise therefore to place the conical flask in a cold water bath on top of a magnetic stirrer so that the temperature of the reaction mixture does not rise above 30 °C during the addition process. Allow the mixture to cool to less than 30 °C and add 35% aqueous formaldehyde solution (2 mL: **CARE! Only use this reagent in a fume cupboard. Do not inhale vapour. Cancer suspect agent**) and stir for 1 hour at room temperature.

After one hour pour the reaction onto about 100 g of ice which has been placed into a beaker. Stir the reaction mixture vigorously with a spatula and **carefully** add 30% sodium hydroxide solution[**] (45 mL) (**CARE: this is a caustic reagent – do not allow this reagent to come into contact with your skin**) so that the temperature does not rise above 5 °C. You may have to add more ice at this stage in order to control the temperature rise. After the addition is complete check the pH of the reaction mixture in order to ensure that it is now basic. A solid should now precipitate from solution, which should be collected using vacuum filtration. Wash the solid with 3 X 15 mL of ice-cold water, and allow to dry on the vacuum filter for 15 minutes. Collect the solid and dry between two pieces of filter paper and then in a vacuum desiccator. Record the appearance and crude yield of your product. Recrystallise your product from hot acetone using the minimum quantity (< 15 mL) of hot acetone (**CARE: use in a fume cupboard**).

Remember to dispose of all aqueous waste in the appropriate waste containers.

i) Record the mass and calculate the yield of your recrystallised product.

ii) Record melting point, IR and ^{1}H NMR spectra.

iii) With the help of a demonstrator find the literature melting point of the product and compare with your value.

iv) Fill in the appropriate SLAB submission form so that your BAY demonstrator can now apportion marks for yield, quality of product and spectra.

[§] **Use the "glacial" acetic acid provided by the technicians.**

[**] **This reagent will be provided by the technical staff. DO NOT use "dilute NaOH"**