Learn Chemistry

Faster Greener Chemistry? Catalyst Synthesis and Evaluation

Student Guide

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This resource was produced as part of the National HE STEM Programme

National HE STEM Programme

RSC | Advancing the Chemical Sciences

www.rsc.org/learn-chemistry

Registered Charity Number 207890

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Introduction - About context/problem based learning

Context/Problem Based Learning (C/PBL) is a teaching methodology that aims to increase students' engagement with a subject by designing courses based upon real-life applications of the principles, techniques and experiments that students encounter in their undergraduate courses. These real world contexts are presented in the form of problem scenarios which are ill-defined and have a number of satisfactory solutions. Learners work in small groups to solve problems and acquire new knowledge and then present the outcomes or product. This approach provides you with the opportunity to develop valuable transferable skills such as communication, team working and problem solving. You are encouraged to take control of your learning and academic staff adopt the role of facilitator or guide during this process.

About this resource

This case study focuses on the synthesis, characterisation and evaluation of a range of up to nine manganese(III) salen complexes that are employed as catalysts in the oxidation of alkenes to epoxides. You are asked to adopt the role of a chemist employed in a campus company that specialises in catalysts, Chem Cat Ltd. The company has been contracted to carry out some consultancy work for a large pharmaceutical multinational, HugePharma Ltd. You will work as part of a team and will report to the Chem Cat Ltd. laboratory manager according to the brief outlined in a letter from the Chemical Development Manager in HugePharma Ltd. The pharmaceutical company have specifically requested that green chemistry (also known as sustainable chemistry) principles be implemented to their full potential in the epoxidation process as they need to maintain their Integrated Pollution Prevention and Control (IPPC) licence.

Your team are required to:

1. Prepare and characterise one of a range of Mn-salen complexes using a two step synthesis.
2. Evaluate the performance of the catalyst in a reference reaction (epoxidation of stilbene).
3. Assess the relative costs and the environmental impact of this process and of alternative procedures with reference to suitable metrics.

To do this, you need to devise and perform several laboratory experiments to obtain the results required to make a recommendation to HugePharma Ltd.

The context is based on information from the literature, including journal articles and reviews, patents, textbooks, some articles in Chemistry World and Chemical & Engineering News and environmental protection agency websites. Salts of Mn(III), particularly those that contain salen type ligands (salen is bis(salicylaldehyde)ethylene diamine), have been found to show catalytic activities of significant interest. The main application of these properties to date has been in the asymmetric epoxidation of alkenes (e.g. Jacobsen’s catalyst) and oxidation of a variety of organic substrates. As a result, Mn-salens have been employed at commercial scale to oxidise a wide range of organic compounds. The process often uses sodium hypochlorite (bleach) as the oxidant. It is an environmentally friendly reagent as it breaks down into sodium chloride, water and oxygen. It is also inexpensive and has an efficient atom economy. Modifications are being investigated to reduce the environmental impact further as several of the catalysts can be recovered and recycled, and reactions in the absence of organic solvent and in supercritical carbon dioxide have been performed.

You will work in groups and your tutor will guide you through the workshop and laboratory sessions so that you complete the experimental work, report and presentation required in a stepwise manner over a number of weeks. Descriptions of each session and clear guidelines are provided in this document which you should read carefully. By the final workshop session, you and your group will be ready to submit your report and you

will present your findings to your class. This case study resource aligns with the RSC Chemistry for Tomorrow's World priority areas of "Water and Air" and "Raw Materials and Feedstocks".

How is the resource delivered?

The case study is designed to be delivered as a laboratory based course, made up of 8 three-hour sessions, 4 workshop sessions and 4 laboratory sessions. When combined with independent study and writing-up time, it is intended that this resource will require a total of 50 learning hours (a total of 24 contact hours plus 26 hours of self study). As such, it represents approximately 2.5 European Transfer Credit System (ECTS) or 5 UK credits of work or 1.5 US credits.

Assessment

This case study resource has three main elements: planning laboratory experiments, conducting experiments and analysis and reporting of data obtained.

Therefore, assessment focuses on; (i) the planning of the group project, most conveniently monitored using a wiki (see Appendix 2), (ii) student lab books on experiments conducted (see Appendix 5), and (iii) the reporting, analysis and recommendations arising out of the data obtained. More details on assessment are provided at appropriate points in this guide and the assessment components and a guideline weighting are provided in Table 1 below.

Table 1: Assessment components

Activity	Group / individual	% mark allocation (guideline)
Contribution to group (based on effort and effective collaboration - evidenced by participation in lab and workshop sessions, summaries of meetings and contribution to group wiki)	Individual	10
Peer assessment by other group members (based on frequency and quality of contributions, both online and face-to-face)*	Individual	5
Lab notebook and individual work submitted on a weekly basis	Individual	30
Reflective piece	Individual	10
Final wiki report (Criteria are relevant content, accuracy, structure, clarity, literature references)	Group	30
Presentation - feedback from tutor and peers and assessment by tutor (criteria are visual impact, effectiveness of oral communication, relevant content, accuracy, structure, clarity, references to the literature and understanding).	Group	15

* Peer assessment is an optional but recommended assessment component and your tutor will advise on whether it is being implemented.

Class organisation

The learning resource is designed so that you work in small groups (typically three students) to complete the brief provided together. Your tutor will advise you as to the other students who will be in the group you will be working in. Table 2 which follows provides a breakdown of what each lab and workshop session will entail. Further detail for each session is included in the relevant sections throughout this guide. The assessment components (Table 1) require that each student submits a laboratory book as well as a short reflective statement for individual assessment. The group work assessed is the presentation and the group wiki report

and the group meeting summaries which provide a record of how the group collaborated and their rate of progress. Your tutor will log into each group's wiki at regular intervals (probably once per week) and provide brief feedback on progress reported. You will receive feedback at various stages throughout the process. The weekly work assigned (Table 3) is designed so that you are preparing elements of your final report as you go along and are obtaining regular feedback.

Group work and organisation

It is suggested that you choose a team name initially. This helps to develop your group identity and allows you to begin the process of listening to each other's suggestions and arriving at a decision. As a group, you should discuss and decide how to deal with the tasks you have been assigned during each weekly session. A list of actions should be compiled before you leave each session (i.e. things that must be done before the next session). Name the people responsible for completing each action and arrange a time when the group will have a short meeting to review what has been done before the next session. You will need to meet regularly outside of the laboratory / classroom to ensure that you are making good progress.

There are 3 roles that should be assigned to group members each week on a rotating basis: Chair, Reporter and Editor. The Chair prepares the agenda for meetings, runs the group meeting/discussions, listens with an open mind to all group members, and ensures that everyone in the group has the opportunity to contribute. The Reporter should prepare a summary of the meetings (attendance, decisions made and resulting actions, people responsible and dates to be completed as well as progress reported) and should post these on the group wiki by the day specified by your tutor. The Editor is responsible for reviewing the wiki content to ensure a consistent style, coherency and an overall structure and will also liaise with authors when changes or additions to content are required. You should adopt each role at least once during the project and should remember to nominate these roles during each session (note than an Editor is not needed until session 2). A good overview on effective group work is presented in Chapter 3 of Study and Communication Skills for the Chemical Sciences; Overton, T., Johnson, S., Scott, J.; Oxford University Press (2011).

A word about wikis

A wiki is an excellent tool for facilitating group learning, communication and collaboration while allowing your tutor to monitor and assess individual contributions. The wiki for each group is intended to provide a means to produce a report in a format that each group member can access, modify and review. Your group should aim to include evidence of all preparatory work as well as the final report on the wiki by adding comments, files and links and by using a wiki page to coordinate group planning and communication. This ensures that group members receive credit for their entire contribution and also provides a very useful archive that contains material relevant to your project only. If you have not used a wiki before, your tutor will demonstrate the basic tasks involved in the first session. Wikis are regularly used in organisations to allow groups to collaborate on projects and documents and to share knowledge and the ability to use one is a valuable transferable skill. For example, a wiki has been established to develop policy in the area of green chemistry in California (http://cagreenchem.wikidot.com/start). Extensive guidelines concerning the use of wikis are provided in Appendix 1 to this guide. In addition to your group wiki, your tutor may use a class wiki or a Virtual Learning Environment (VLE) to support this module and to communicate with the entire class and they will advise you of this at the beginning of the module.

Navigating this student guide

An overview of this C/PBL case study is presented in Tables 2 and 3. Further details for each session are included in the relevant sections throughout this Student Guide. The Appendices to this guide contain

guidelines on the various tasks that form part of this C/PBL project and should be read within the first week and referred to regularly from then on. The briefing pack that you receive in Week 1 is a valuable source of information and should be read carefully and then consulted on an ongoing basis.

Table 2: Schedule of Activities for Workshops (WS) and Laboratory Sessions (Lab)

Session (3 hrs)	Title	Activities (during and between sessions)
1 (WS 1)	Introduction to the project and planning for first synthetic step	Tutor led: • Introduction presentation and assignment into groups • Demonstration of a sample wiki if possible (adding and editing pages, uploading files and adding comments) Class activity: • Discussion on green chemistry, environmental legislation (Annual Environmental Reports and Integrated Pollution Prevention and Control licences) and the role of catalysts and desirable properties they should have. • Discussion on selecting a suitable scale for the first step and preparation of a procedure
2 (Lab 1)	First synthetic step (reaction of diamine and salicylaldehyde to form the ligand intermediate)	Student led: • Writing of procedure in advance • Preparation of ligand intermediate • Prediction of expected IR and NMR spectra for the salicylaldehyde starting material used and the intermediate prepared. • Begin group literature research on alternative procedures/oxidants • Maintain independent lab book and group wiki
3 (Lab 2)	Second synthetic step (preparation of catalyst)	Student led: • Writing of procedure in advance • Preparation of catalyst • Prediction of expected IR spectrum for the catalyst prepared • Interpretation of IR and NMR spectra of the salicylaldehyde used and the intermediate prepared • Preparation of a 1 page summary on literature research on alternative epoxidation conditions (recommend one experiment to be attempted) • Maintain independent lab book and group wiki
4 (Lab 3)	Evaluation of catalyst performance in a reference reaction (epoxidation of *trans*-stilbene)	Student led: • Writing of procedure in advance • Epoxidation using sodium hypochlorite in duplicate / triplicate • Prediction of expected IR and NMR spectra for the *trans*-stilbene starting material used and the epoxide prepared • Evaluation of alternative oxidation procedures found based on criteria provided (yield, catalyst loading, solvent, type of oxidant, complexity of the procedure) and recommend which should be attempted in the future. • Interpretation of IR spectrum obtained of catalyst • Maintain independent lab book and group wiki
5 (Lab 4)	Evaluation of catalyst performance using alternative conditions (and completion of evaluation of catalyst using sodium hypochlorite)	Student led: • Writing of procedure in advance • Epoxidation reaction using alternative conditions (e.g. different oxidant or solvent) in duplicate / triplicate. • Complete catalyst performance evaluation • Analyse data from all groups to determine the most effective catalyst • Maintain independent lab book and group wiki

6 (WS 2)	Costing and assessment of environmental impact for oxidation procedures performed	Student led: • Use ChemSpider to find vendors and costings for raw materials for the synthesis of the catalyst and the epoxidation reaction. • Use guidelines on metrics and recommended reading sources to evaluate the environmental impact of each process as well as the potential for further development
7 (WS 3)	Clinic for formative feedback on draft reports	Tutor led class activity: 'Clinic' where each group: • has submitted 1 page 'work in progress' summary and their draft report in advance on which they receive feedback • discusses any problems or queries • receives feedback on their summary and on their wiki draft report as it is at that point
8 (WS 4)	Oral presentations	Student led: • PowerPoint presentation to peers summarising the work performed and their recommendations followed by questions from the tutor, guest tutor (if present) and other students • Submission of final report (with feedback from presentation incorporated) and individual reflective piece for assessment within a week Tutor led: • General oral feedback from tutor (optional written feedback on each presentation to each group from tutor and peers)

As this module is continuously assessed, you should submit an assignment or present/prepare work each week by the deadlines shown in Table 3 below. The weekly work is designed so that you are preparing elements of your final report as you go along. It is very important that you submit assignments on or before the deadline and that you check the schedule below carefully. You should also check how your tutor has specified that the work is submitted. It is recommended that all group work is uploaded to a Work Submitted page on the wiki so that it is easily accessible but you may also be asked to submit a hard copy. The time spent on individual and group work between each session should be between 1 and 3 hours.

Table 3: Work to be completed after each weekly session

Stage	**For submission after the session by the following (day of week to be added) at (time to be added)**
Week 1 (Introduction) Date for completion of tasks:	**Group** • Modified experimental procedure for step 1 (catalyst ligand preparation).* • Summary of group meeting posted on group wiki. **Individual** • Short version of chemical safety assessment.* • Maintain group wiki and independent lab book. * The procedure and safety assessments should be typed and structures should be drawn using chemical drawing software.
Week 2 (Ligand preparation) Date for completion of tasks:	**Group** • Modified experimental procedure for step 2 (catalyst preparation). • Short version of chemical safety assessment. • Summary of group meeting posted on group wiki. • Begin research on alternative epoxidation conditions for Mn-salen catalysts. **Individual** • Predicted IR and ^{1}H NMR spectra for salicylaldehyde starting material and ligand intermediate. • Maintain group wiki and independent lab book.

Week 3 (Catalyst preparation) Date for completion of tasks:	**Group** • Modified experimental procedure for epoxidation of stilbene using standard conditions. • Summary of group meeting posted on group wiki. • One page summary on research carried out (on alternative conditions for epoxidation of alkenes with Mn-salen catalysts and recommended experiment to try). • Short version of chemical safety assessment. • Predicted IR spectrum for catalyst with suggestion as to why NMR analysis of catalyst is not useful. **Individual** • Interpretation of IR and ^{1}H NMR spectra obtained of ligand intermediate and of salicylaldehyde starting material. • Maintain group wiki and independent lab book.
Week 4 (Catalyst evaluation 1) Date for completion of tasks:	**Group** • Modified experimental procedure for epoxidation of stilbene with catalyst using alternative conditions. • Short version of chemical safety assessment. • Predicted ^{1}H NMR spectra for stilbene and stilbene oxide. • Evaluate alternative oxidation procedures found based on criteria provided (yield, catalyst loading, solvent, cost of raw materials (in reaction and work up), type of oxidant, complexity of the procedure) and recommend which should be attempted in the future. • Summary of group meeting posted on group wiki. **Individual** • Interpretation of IR spectrum obtained of catalyst. • Maintain group wiki and independent lab book.
Week 5 (Catalyst evaluation 2, alternative conditions) Date for completion of tasks:	**Group** • Compilation and sharing of data on group results (yields and conversions) for reference epoxidation reaction (using sodium hypochlorite). • Determination of most effective catalyst based on this data for the reference reaction and prediction of how catalyst structure & efficiency are related. • Summary of group meeting posted on group wiki. **Individual** • Interpretation of ^{1}H NMR spectra obtained of crude product from stilbene epoxidation using sodium hypochlorite. • Maintain group wiki and independent lab book.
Week 6 (Costing and green metrics workshop) Date for completion of tasks:	**Group** • Analysis of ^{1}H NMR spectra obtained of crude products from alternative stilbene epoxidation to determine percentage conversion. • Compilation and sharing of data on group results for alternative epoxidation reaction. • Comparison of results for the reference and alternative oxidation reactions. • Costing of raw materials and solvents for synthesis (including work up) of the catalysts prepared, and for the epoxidation reactions. Identify any resulting issues (most and least expensive materials). • Evaluation of the environmental impact of each process with reference to appropriate metrics and provide recommendations for further development. • Draft group report on wiki ready for preliminary review. • Work in progress summary on draft group report posted on group wiki (provide link from Table of Contents). • Summary of group meeting posted on group wiki. **Individual** • Maintain group wiki and independent lab book.

Week 7 (Clinic for formative feedback) Date for completion of tasks:	**Group** • Incorporation of feedback from clinic workshop into the group's wiki report. • Consideration of the scope for each synthesis step to be improved and recommendations for future work. • Practise group presentation to ensure it is coherent, structured, accurate and meets the time requirements (the wiki itself can be used as a visual aid or, alternatively, it may be preferred that PowerPoint slides be prepared). • Summary of group meeting posted on group wiki. • Maintain group wiki.
Week 8 (Oral presentations) Date for completion of tasks:	**Group** • Incorporation of feedback from presentation into the group's wiki report. • Final editing and completion of group's wiki report. • Submission of wiki report **Individual** • Reflective piece to be submitted. • Lab book to be submitted. • Peer assessment of other students in the group (optional).

Learning outcomes

On completion of this C/PBL resource, you should be able to do the following, within the context provided:

1. Use a literature procedure to write a laboratory procedure (including a list of materials and equipment required) to prepare organic and organometallic compounds on a suitable scale.
2. Prepare a short chemical risk assessment for the experimental work to be undertaken.
3. Plan time in the laboratory effectively in order to complete the synthesis and evaluation of the catalyst assigned.
4. Keep an accurate and current record of experimental details and data in a laboratory notebook.
5. Interpret experimental data and predict and assign spectra to confirm the identity and purity of products.
6. Use appropriate databases to find relevant information on raw material costing for the process and on recent developments to improve the environmental impact it has (alternative solvents and oxidants etc.).
7. Evaluate the efficiency, relative costs and the environmental impact of the oxidation procedures used for the epoxidation of *trans*-stilbene.
8. Identify aspects of each reaction performed that adhere to the principles of Green Chemistry and those that do not.
9. Use the results obtained for all catalysts evaluated to predict how catalyst structure and efficiency are related.
10. Produce a professional report, including an executive summary and an assessment of the scope for each step to be improved. This must be supported by the relevant experimental data and a laboratory notebook.
11. Prepare an oral presentation on the findings from the study to present to the company that commissioned the project.
12. Prepare a short individual reflective statement on the group process, transferable skills developed and the extent to which the stated learning outcomes were met.

Transferable skills development

You will be asked to reflect on the development of the skills listed below at the end of the project. It is recommended that you record some notes as you go along on what areas you are finding challenging as well as progress that you feel you are making to make this task easier. The specific ways in which it is intended that key skills will be developed during this C/PBL case study are described below:

- Team work: you work in groups to complete the task assigned, use a wiki to facilitate collaboration and meet between sessions to review progress.
- Organisation and planning: you prepare procedures on a suitable scale and plan your time in the laboratory effectively.
- Communication skills: you present (oral presentation) and report (wiki and final report) on the scientific work performed in keeping with the context.
- Drawing conclusions and recommendations from data: you justify decisions, assumptions and conclusions made with reference to results from other groups and supporting literature in order to produce a logical and clearly reasoned scientific report.
- Numeracy: you apply the relevant green chemistry metrics to your experimental results.
- Professional role and responsibilities: you adopt the role of a professional chemist and are required to consider the environmental impact and costing of the processes you have been working on.
- Problem solving: you work in groups to address the brief presented in the context scenario.
- Information technology skills: you use a wiki to collaborate and develop your ability to use word-processing, spreadsheet, presentation, chemical drawing and library database software.
- Metacognition: you reflect on the process involved in working on the brief given, the extent to which the stated learning outcomes were met and to which your transferable skills were developed.

Session 1 (Workshop 1): Introduction to the project and the first synthetic step

The purpose of the introduction session is to:

1. Introduce you to the case study context and outline the schedule of work, the learning outcomes, and assessment components and criteria.
2. Introduce or revise the principles of green chemistry and environmental reporting requirements for commercial producers of fine chemicals (Annual Environmental Reports and Integrated Pollution Prevention and Control licences), as well as the role of catalysts and desirable properties they should have.
3. Provide information on the literature references to be consulted to plan the first synthetic step in the production of a Mn-salen catalyst for alkene epoxidations. You will be is assigned a specific catalyst to prepare.
4. Demonstrate how to use a sample wiki (adding and editing pages, uploading files, adding comments and accessing page histories).

Getting started

Project briefing pack

This guide contains a briefing pack of information from HugePharma Ltd., the organisation that has requested that some consultancy work be carried out by your team (see pages 12 to 25). You should read the letter from HugePharma Ltd. which outlines the tasks involved and begin to review the other material provided. This pack is an important source of information and should be read carefully and then consulted on an ongoing basis.

The experimental procedure

Your group will be assigned a particular catalyst to prepare. **The scale you will work on requires that you synthesise 0.5 g of the catalyst assuming a 70% yield in each of the two steps involved.** Check this scale with your tutor in case there are any modifications required.

You will need to consult the original research article that describes a method for synthesising these catalysts: Asymmetric Olefin Epoxidation with Sodium Hypochlorite Catalyzed by Easily Prepared Chiral Mn(III) Salen Complexes, Zhang, W., Jacobsen, E.N., Journal of Organic Chemistry, 1991, 56, 2296-2298. Use the information in this paper to establish the quantities of starting materials that you will need for the scale you are working on and to jointly prepare an experimental procedure that you will use next week to prepare your salen ligand. You will need to show all calculations clearly so that your work can be checked.

Group organisation

Working in your assigned groups, compile an initial list of actions for your group work, and assign responsibilities and due dates. Ensure that you refer to Table 3 to check the tasks that are ongoing and those that need to be completed by the following week. Consider what you need to do and what information you need to obtain. Arrange a time when the group will have a short meeting to review progress before the next lab session and select the Chair and Recorder for this week's meeting (see the Group Work and Organisation section on page 3). These positions should rotate each week. As a group you will find the best way of working, but initially it may be useful to upload files with draft work to the wiki in advance of the weekly group meeting, and then discuss what will be added to the page at the meeting. It is important that you contribute to your group taking account of your relevant skills and experience but it is also expected that you will contribute to areas you are less experienced in to learn more about them.

The wiki

It is recommended that a table of contents page is set up based on the scientific report headings requested in the briefing pack received from HugePharma Ltd (see A Word about Wikis on page 3 and Appendix 1). In addition, the wiki should be used as a forum to organise meetings and work to be done, prepare draft work

and outlines, share relevant file and links, ask questions of other group members and provide feedback by leaving comments on pages. It will develop into a very useful archive of information for your group if used effectively and organised well. Care should be taken to name each page, file and link clearly, to note what changes were made when editing a page and to identify each comment as to its content so that information can be found easily.

Reflective statement

Your final task on completion of the course work will be is the production of a reflective piece. It is recommended that, towards the beginning of the project, you become familiar with the topics that need to be addressed by reading the guidelines provided in Appendix 9 so that relevant notes can be made over the course of the project.

Guidelines

Guidelines are provided in the appendices on:

- Using a wiki
- Preparing laboratory procedures
- Compiling chemical safety information
- IR and NMR spectra prediction
- Writing up your lab notebook
- Preparing presentations
- Plagiarism
- Writing your reflective piece
- Writing your executive summary

These should be read and adhered to when preparing written work.

Tasks to complete before session 2:

- Review the assessment criteria and schedules provided (Tables 1 to 3).
- Become familiar with how to navigate the group wiki and how to add and edit pages, add files and add comments. Add a Table of Contents and a Group Planning and Communication main page (see Appendix 1).
- Meet as a group to review progress on the list of actions for your group. The Chair will have prepared a short agenda and the Recorder will post a short meeting summary (of decisions made and progress reported) on the wiki by the day specified by your tutor.
- Submit a group experimental procedure for the preparation of the salen ligand on a suitable scale (via the wiki and/or directly to your tutor). These should be typed and structures should be drawn using a chemical drawing package. (Accelyrs Draw and ChemSketch are both available to download free of charge). **You will not be allowed to begin lab work in Session 2 until this task has been satisfactorily completed.**
- Add information on the first experiment available in advance (materials, equipment, literature reference etc.) to your lab notebooks.
- **Individually** submit a short chemical safety assessment for the synthesis procedure.

Desired learning outcomes

On completion of this session and the related independent learning hours you will able to:

- Understand the context based scenario and be aware of how the module will be assessed.
- Prepare an experimental procedure on a suitable scale and identify materials and equipment required as well as any chemical safety issues.

HugePharma Ltd.,
Chemical Development Department (Europe Division)
Warner Industrial Park, Gladwell Road, Carrigstown

Project briefing pack

- Letter from Chemical Development Manager
- Guidelines for structure of scientific report
- Twelve Principles of Green Chemistry
- Current epoxidation method
- Epoxidation route to be examined
- Literature review

HugePharma Ltd.,
Chemical Development Department (Europe Division)
Warner Industrial Park, Gladwell Road, Carrigstown

To: Managing Director, Chem Cat Ltd., University Industry Centre, Bridgeford.
Re: Consultancy project – Synthesis and Evaluation of Manganese(III) Salen Catalysts

Further to our meeting last week, we would like to confirm that HugePharma Ltd. are engaging the services of Chem Cat Ltd. to undertake consultancy work on a project to synthesise and evaluate Mn(III) salen catalysts suitable for epoxidation of alkenes. As you are aware, we require a process that implements Green Chemistry principles to their full potential to ensure that we comply with environmental legislation and maintain our Integrated Pollution Prevention and Control (IPPC) licence.

As previously agreed, the following deliverables are required to be completed within a two month period:

- Preparation on a lab scale and characterisation of up to nine Mn-salen complexes using the two step procedure described in the original literature reference (W. Zhang and E. N. Jacobsen, *Journal of Organic Chemistry*, 1991, **56**, 2296-2298).
- Evaluation of the relative performance of each catalyst using a reference reaction (the epoxidation of *trans*-stilbene). Criteria for catalyst evaluation are: (i) the yield and purity of the catalyst prepared, (ii) conversion to and yield of *trans*-stilbene epoxide (based on crude product). The results should be shown to be reproducible by performing the reference reaction in duplicate or triplicate.
- Prediction of how catalyst structure and efficiency are related based on the results from the reference reactions.
- Evaluation of the relative costs and the environmental impact of the procedure used and of at least one alternative epoxidation procedure (different oxidant or reaction conditions). If time allows, it would be useful if the alternative conditions could be trialled. Environmental impact evaluations should include a comparison with our current method of alkene epoxidation using mCPBA (P. L. Robinson, C. N. Barry, J. W. Kelly and S. A. Evans Jr., *J. Am. Chem. Soc.*, 1985, **107**, page 5217).
- A scientific report on the findings from the study (including an executive summary for non-technical management staff). Information on the scope for each synthesis step to be improved and recommendations for future work should be provided. We are particularly interested in modifications to the oxidation reaction and yield, solvent, cost of raw materials (in reaction and work up), complexity of the procedure, catalyst loading, potential for catalyst recovery and type of oxidant are all important considerations.
- We may also require that some of your staff give an oral presentation on the report after it has been submitted.

I have attached our corporate guidelines for the structure of scientific reports. A copy of the relevant literature review work carried out by one of our Chemical Development teams and of the contract for your signature will be sent to your office by courier today.

Chem Cat Ltd. has a good reputation in this field and therefore I look forward to receiving the scientific report prepared by your staff in due course. As discussed at our meeting, further work on this project may be commissioned based on the findings from this initial work.

Yours sincerely,

Josephine Buckley

Dr. J. Buckley,

Chemical Development Director.

HugePharma Ltd.,
Chemical Development Department (Europe Division)
Warner Industrial Park, Gladwell Road, Carrigstown

Guidelines for Structure of Scientific Reports

Reports should be a maximum of 2,000 words (not including figures, tables etc.) and should contain the following elements:

1. Report title, date submitted and author name(s).
2. An executive summary (aimed at a non-technical audience, maximum 200 words)
3. The main body of the report to include:
   - Aims and objectives
   - Background information and related previous work
   - Experimental details
   - Results and discussion
   - Conclusion including recommendations
   - Glossary of definitions for any unfamiliar terminology used to ensure clarity.
4. References should be formatted according to the Royal Society of Chemistry Publishing author guidelines format. (See page eleven of the document at this link: http://www.rsc.org/images/Guidelines_tcm18-186308.pdf)

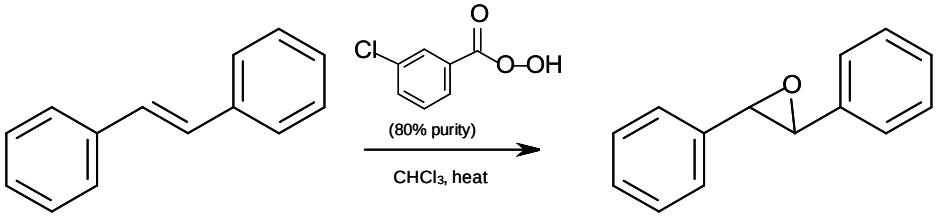
Any alternative epoxidation methods should align with the Twelve Principles of Green Chemistry as set out by P. Anastas and J. Warner, in Green Chemistry: Theory and Practice (Oxford University Press: New York, 1998).

The Twelve Principles of Green Chemistry:

1. It is better to prevent waste than to treat or clean up waste after it is formed.
2. Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4. Chemical products should be designed to preserve efficacy of function while reducing toxicity.
5. The use of auxiliary substances should be made unnecessary wherever possible, and innocuous when used.
6. Energy requirements should be recognised for their environmental and economic impacts, and should be minimised. Synthetic methods should be conducted at ambient temperature and pressure.
7. A raw material or feedstock should be renewable rather than depleting wherever technically and economically practicable.
8. Unnecessary derivatisation should be avoided whenever possible.
9. Catalytic reagents are superior to stoichiometric reagents.
10. Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.
11. Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
12. Substances and the form of a substance used in a chemical process should be chosen so as to minimise the potential for chemical accidents.

Current method:

The established epoxidation method uses a peroxyacid (*meta*-chloroperoxybenzoic acid (mCPBA)) as the oxidant in the conversion of an alkene to the corresponding epoxide. mCPBA is the peroxy acid employed because of its relative ease of handling. The reaction scheme for epoxidation of stilbene is shown below. This procedure is not enantioselective and gives a yield of 90 % for the conversion of *trans*-stilbene.



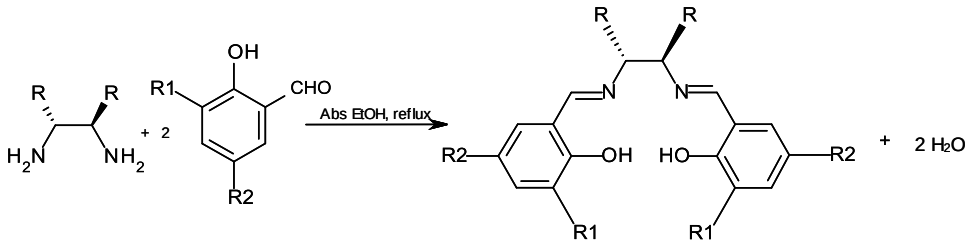
Reference: P.L. Robinson, C.N. Barry, J.W. Kelly, S.A. Evans Jr., *J. Am. Chem. Soc.*, 1985, **107**, 5210–19.

It is requested that Chem Cat Ltd. investigate the use of Jacobsen's catalyst to carry out a "greener" epoxidation of the model compound *trans*-stilbene. This alternative method would also facilitate enantioselective epoxidations to be performed should the need arise.

Epoxidation route to be examined:[7]

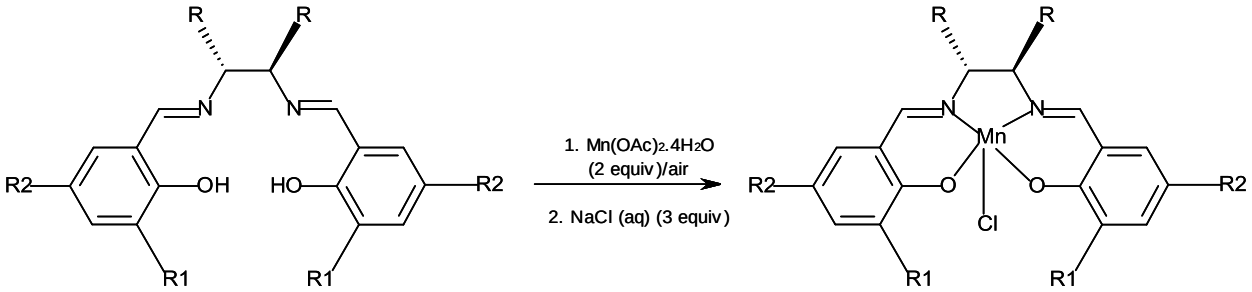
Reference: W. Zhang and E. N. Jacobsen, *Journal of Organic Chemistry*, 1991, 56, 2296-2298

Step 1- Synthesis of catalyst ligand:



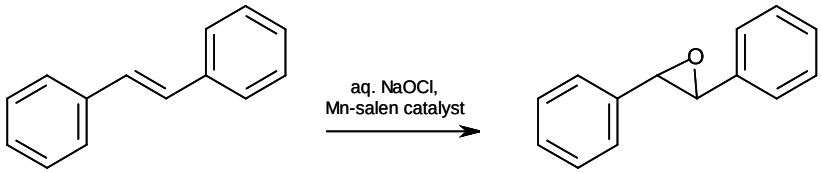
(R=H or $–CH_2CH_2CH_2CH_2$-, R1=H or *t*-butyl, R2= Cl, OMe, H, *t*-butyl, or NO_2)

Step 2- Synthesis of Mn-salen catalyst complex:



(R=H or $–CH_2CH_2CH_2CH_2$-, R1=H or *t*-butyl, R2= Cl, OMe, H, *t*-butyl, or NO_2)

Step 3 – Epoxidation of trans-stilbene using the Mn-salen catalyst:



Literature review - annotated bibliography

Key to superscripts used to classify texts:

A: General topic reading – directly related

B: General topic reading – not directly related

C: Specific reference to Mn-salen catalysed epoxidation reaction

News stories

Herbert C. Brown Award For Creative Work In Synthetic Methods [A]

Yarnell, A.; Chemical & Engineering News, January 21, 2008, 86 (3), 57

Citing him as "the preeminent developer of synthetic methods of his generation," this article reports the conferring of an American Chemical Society award on Prof. Eric Jacobsen. His discovery and use of catalysts for enantioselective catalytic reactions, including epoxidation, have garnered him great respect. Jacobsen's chiral metal salen catalysts have widespread use in academic and industrial applications for the enantioselective epoxidation of olefins. The preparation of a key intermediate in the synthesis of Indinavir (Crixivan®), a HIV protease inhibitor drug, is given as an example of use on a multiton commercial scale.

Chiral Chemistry [B]

Stinson, S.C.; Chemical & Engineering News, May 14 2001, 79(30), 45-57

and Rouhi, A.M., Chemical & Engineering News, June 14 2004, 82 (24), 47-62

These articles discuss the ever increasing demand and sales of single-enantiomer chiral compounds. While the references to applications may be dated, this does provide a useful overview of the importance of these compounds in the pharmaceutical industry. A number of applications and synthetic routes are discussed throughout the reports.

Epoxidation Catalyst Immobilized In Ionic Liquid [A]

Freemantle, M.; Chemical & Engineering News, May 22 2000, 78 (21), 8-9

Chemists in South Korea immobilised Jacobsen’s catalyst in a room temperature ionic liquid in order to improve ease of recovery and recycling of the homogeneous chiral catalyst in asymmetric epoxidation of alkenes. They showed that the immobilised catalyst can be recycled five times with only a slight decrease in enantioselectivity and activity.

Enzymes at Work [B]

Thayer, A.M.; Chemical & Engineering News, August 14 2006, 84 (33), 15-25

This report discusses the option of using enzymes as alternative catalysts for epoxidation. The benefits of this technology are considered along with the reluctance of chemists to apply the technology.

Text books

Green Chemistry: Theory and Practice[A]

Anastas, P.T., Warner, J.C., Oxford University Press, 1998

This text book defines green chemistry and the tools used to achieve it. It sets out the twelve principles, exploring each principle individually. Tools for the evaluation of effects of chemistry, feedstocks and starting materials, reaction types and methods of improving reactions are also provided alongside examples of green chemistry in action. While this text book is over 10 years old, it is a key text written by authors who first conceived the principles of this approach.

Green Chemistry: An Introductory Text (2nd Edition) [A]

Lancaster, M., RSC Publishing, 2010

This updated edition of Mike Lancaster's textbook discusses a number of key green chemistry topics including waste minimisation, feedstocks, green metrics, efficient processes, catalysis, and greener solvents. There is a strong focus on new green methods which have been commercialised, and comparing new synthetic pathways with those used in the past. Chapters of particular relevance include Ch.1: Principles and Concepts of Green Chemistry (22 pages), Ch. 3: Measuring and Controlling Environmental Performance (28 pages), Ch. 4: Catalysis and Green Chemistry (48 pages), Ch. 8: Designing Green Processes (24 pages), and Ch. 9: Industrial Case Studies (31 pages).

Sustainable Solutions for Modern Economies[B]

Höfer, R. (Ed.), Royal Society of Chemistry, 2009

Giving an overview of the topic of sustainable solutions for development, this text book sets a useful context for the overall project. In particular, the introductory chapters cover the history of the concept of sustainability and its economic importance. Case studies showing applications of sustainable industrial processes should also be useful to give an impression of changes occurring in industry due to this important consideration.

Organic Chemistry[C]

Clayden, J., Greeves, N., Warren, S., 2nd edition, Oxford University Press, 2012.

Chapter 43 describes the application of Jacobsen's catalyst to the synthesis of Indinavir (Crixivan®), a HIV protease inhibitor drug and, in chapter 41, the conditions under which the catalyst is applied in organic synthesis are discussed.

Oxford Chemistry Primers 96: Applied Organometallic Chemistry and Catalysis[C]

Whyman, R., Evans, J. (Ed.), Oxford University Press, 2001

This primer provides an overview of homogeneous and heterogeneous organometallic catalysis, providing an account of the principal commercial applications in industry. Section 7.6 focuses on asymmetric

epoxidation including the Sharpless method and use of Jacobsen's catalyst. Applications of the Jacobsen catalyst in production of enantiomerically pure amino-alcohols as precursors for HIV and cancer treatments are mentioned along with potential barriers to commercialisation such as availability of ligands and catalyst stability on a large scale.

Modern Oxidation Methods (2nd Edition) [A,C]

Bäckvall, J.E. (Ed.), WILEY-VCH Verlag GmbH & Co. KGaA, 2010, pages 37 - 80, 371 - 421

This text book would be of use when researching new methods of oxidation. Of particular interest are the discussions in Chapter 2 on transition metal catalysed epoxidations of alkenes and information in Chapter 11 on manganese catalysed oxidation with hydrogen peroxide. This provides a useful context for comparison of different methods of epoxidation.

Methods and Reagents for Green Chemistry: An Introduction [A,C]

Tundo, P., Perosa, A., Zecchini, F. (Eds), John Wiley & Sons, 2007, pages 191 - 229

Part 3 of this text book covers "Green catalysis and biocatalysis", giving an over view of the importance of catalysis in green chemistry, waste minimisation and sustainable development. Chapter 11 focuses on metal catalysed enantioselective oxidation processes, reporting results based on use of Jacobsen's catalyst and related catalytic species. Substitution of groups at almost all positions on the catalyst structure have been investigated for the influence on yield and enantioselectivity of the catalyst, although no clear conclusion is drawn on this topic. This chapter also reports the industrial use of manganese salen catalysts for production of a potassium channel activator (BRL 55834), which has potential to be used as a bronchodilator, as shown in the scheme below (Figure A).

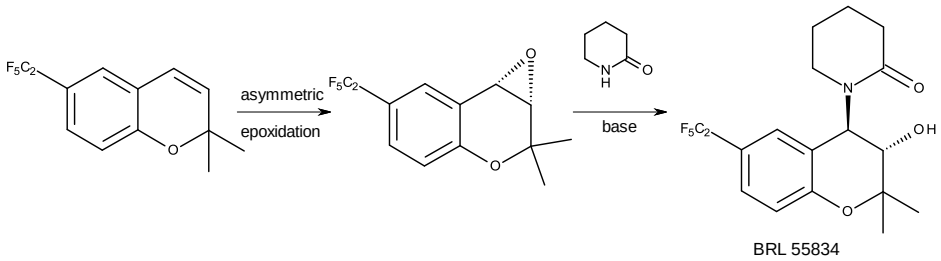


Figure A: Asymmetric epoxidation in the production of a pharmaceutical ingredient

Process Chemistry in the Pharmaceutical Industry. Chapter 19: Chiral (Salen)Mn(III) complexes in Asymmetrc Epoxidations: Practical Synthesis of *cis*-Aminoindanol and Its Applications to Enantiopure Drug Synthesis [A,C]

Editor: Gadamasetti,K.G., Chapter authors: Senanayake, C.H., Jacobsen, E.N.; Marcel Dekker Inc., 1999, pages 347-368

Two enantiomers of a chiral drug often display different biological activity; therefore a practical and reliable route for production is important to the pharmaceutical industry. This chapter focuses on the development of a practical chiral (salen)Mn catalyst for asymmetric epoxidation of unfunctionalised alkenes, and a practical application of salen(Mn)-based epoxidation methodology to the synthesis of enantiopure *cis*-aminoindanol and its applications in drug synthesis. Chiral salen complexes of all the first row transition metals have been prepared, with Mn(III) derivatives displaying superior selectivity and the highest turnover in epoxidation of most alkenes. The synthesis of (salen)Mn(III) complexes is readily accomplished by heating an ethanolic solution of a salen ligand to reflux with two equivalents of $Mn(OAc)_2.4H_2O$ in air (see Figure B).

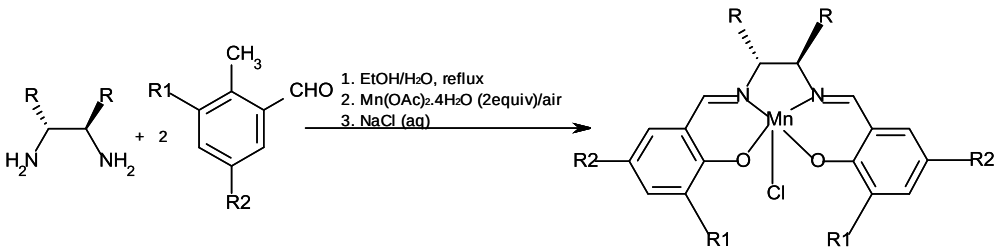


Figure B: Summary of synthesis procedure for Jacobsen's catalyst

It was reported that good enantioselectivity in olefin epoxidation requires 1) a dissymmetric diimine bridge derived from a C2 symmetric 1,2-diamine, and 2) bulky substituents on the 3 and 3' positions of the salicylide ligand. In general, electron donating or sterically demanding substituents on the 5 and 5' position also improve enantioselectivity. The most widely used catalyst in this class uses a *t*-butyl substituent at the 3 and 3' position.

A variety of stoichiometric oxidants are effective for (salen)Mn-catalysed epoxidations, but aqueous sodium hypochlorite was found to be a practical option. Conditions have been developed involving a two-phase system, with an aqueous phase containing commercial bleach and an organic phase containing a solution of substrate and catalyst in a suitable solvent. On lab scale, the reaction is carried out within a few hours in dichloromethane at 0^oC. Alternative solvents include 1,2-dichloroethane, *tert*-butyl methyl ether, ethyl acetate and toluene. Work-up is accomplished by phase separation and epoxide isolation by recrystallisation, distillation or chromatography. In general, complete substrate conversion can be achieved using 0.1 to 5 mol% of catalyst.

This system has been further developed by the Merck[14] and Sepracor[15] research groups for the production of *cis*-1-amino-2 indanol, an important pharmaceutical precursor. Applications for this in drug synthesis could include HIV protease inhibitors, synthesis of (S)-oxybutynin (Diropan®) which is a prescribed muscarinic receptor antagonist and production of (R)-Ketoprofen, a non-steroidal anti-inflammatory drug (NSAID).

Green Chemistry Metrics - Measuring and Monitoring Sustainable Processes. Chapter 5: Mass Balances and Life Cycle Assessment [A,C]

Lapkin, A, Constable, D. J.C., (Chapter authors: Eissen, M., Geisler, G., Bühler, B., Fischer, C., Hungerbühler, K., Schmid, A., Carreira, E. M.), John Wiley & Sons, 2008.

Chapter 5 of this book examines mass balances and life cycle assessment, focusing on enantioselective epoxidation of styrene as a case study (section 5.3.2). This comparison gives a useful introduction to the complexity of the number of different considerations which must be taken into account when evaluating a reaction. The use of Jacobsen's catalyst is compared to enzymatic conversion of styrene to styrene oxide. Mass intensity, environmental (E-) factor and cost index are calculated for both processes. The results found the enzymatic process to be greener although many factors must be balanced by the writers before reaching this conclusion.

Research Papers

Asymmetric Olefin Epoxidation with Sodium Hypochlorite Catalyzed by Easily Prepared Chiral Mn(III) Salen Complexes[A,C]

Zhang, W., Jacobsen, E.N., Journal of Organic Chemistry, 1991, 56, 2296-2298.

This is the original paper published by Jacobsen *et al.* reporting the effectiveness of manganese salen catalysts for the epoxidation of asymmetric olefins to give enantiopure products. The described synthesis is simpler than those previously reported and is a highly practical procedure using commercial bleach as the stoichiometric oxidant (see Figure C).

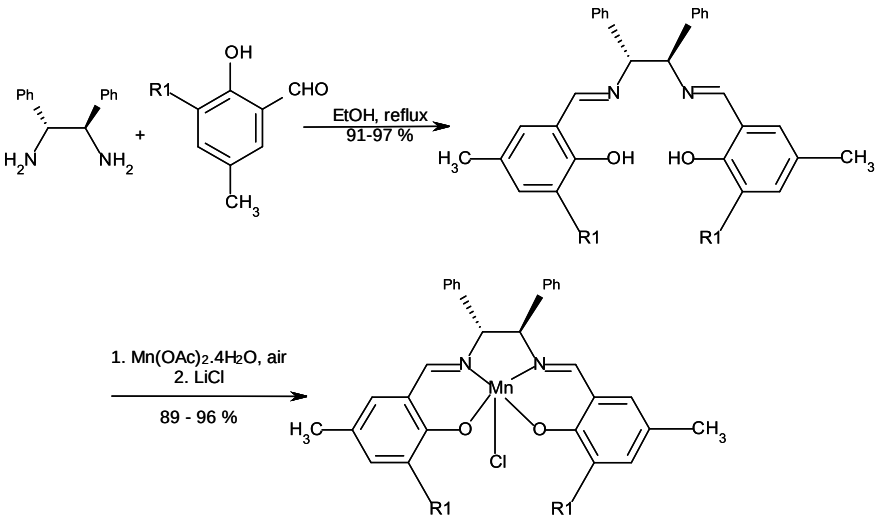


Figure C: Synthesis of Jacobsen's catalyst using conditions stated in the original reference

The catalyst is isolated in excellent yields and can be stored for prolonged periods of time without any precautions to exclude light, air or moisture. This route for olefin epoxidation claims to embody several appealing features, such as good isolated yields of epoxide, inexpensive reagents, and mild conditions.

Synthesis and Use of Jacobsen's Catalyst: Enantioselective Epoxidation in the Introductory Organic Laboratory[A,C]

Hanson, J., *Journal of Chemical Education*, 2001, 9, 1266-1268

This paper describes the use of Jacobsen's catalyst in an undergraduate teaching environment. The preparation was used to introduce students to a new synthetic method, to teach common techniques used in running reactions and characterising compounds, and to reinforce concepts learned in the accompanying lecture course. The methodology was reported to be reliable, safe, and inexpensive enough to be performed by large numbers of relatively inexperienced students. The paper and accompanying supplementary information provide a detailed description of the practicalities associated with implementing this laboratory session. The enantioselectivity of the catalyst, an aspect not addressed in this project, was also examined.

Asymmetric Processes Catalyzed by Chiral (Salen) Metal Complexes[A,C]

Larrow, J.F., Jacobsen, E.N., *Topics in Organometallic Chemistry*, 2004, 6, 123-152

This chapter reviews progress in the application of chiral salen ligands in asymmetric transformations, comparing the use of different metal catalysts. It is reported that the ligands are relatively simple to produce, display high enantioselectivities and are active on a broad range of substrates. In this comprehenensive review, a number of topics are covered including salen ligand synthesis, epoxidation reactions, epoxide ring opening reactions, carbonyl addition processes and cycloaddition processes.

A Simple and Versatile Method for Alkene Epoxidation Using Aqueous Hydrogen Peroxide and Manganese Salophen Catalysts[A,C]

Liu, S.Y., Nocera, D.G., *Tetrahedron Letters*, 2006, 47, 1923–1926

This paper and the accompanying supplementary information describes a versatile method for the catalytic epoxidation of a range of olefins using manganese salophen catalysts. This method varies from that reported by Jacobsen *et al.*, in that aqueous H_2O_2 is used as the oxidising agent in the presence of an organic additive. This system claims low catalyst loading, short reaction times, and a simple reaction procedure.

Recoverable chiral salen complexes for asymmetric catalysis: recent progress[A,C]

Zulauf, A., Mellah, M., Hong, X., Schulz, E.; *Dalton Trans*., 2010, 39, 6911–6935

This review reports on the various metal centred chiral salen-type complexes (including Jacobsen's catalyst) which have already been reported as asymmetric catalysts for the preparation of a wide range of enantioenriched products. When these complexes are efficiently recovered and recycled, the procedures have proven positive in terms of atom economy and overall economical savings. The paper summarises recent results (2006–2009) dealing with the use of recyclable chiral salen complexes.

Manganese-Based Organic and Bioinorganic Transformations[A,C]

Melikyan, G.G., *Aldrichimica Acta*, 1998, 31, 50-64

This review covers a number of applications of manganese compounds in synthetic chemistry including radical bond formation, manganese salen complexes, manganese porphyrins, and DNA-cleaving agents. Providing a overview of each use, this provides background reading for the use of Mn salen complexes in catalytic asymmetric epoxidation and related reactions, giving a large number of relevant citations.

Chromium- and Manganese-salen Promoted Epoxidation of Alkenes[A,C]

McGarrigle, E.M., Gilheany, D.G., *Chemical Reviews*, 2005, 105, 1563-1602

This review (40 pages) comprehensively covers the development of Cr(salen) and Mn(salen) mediated asymmetric epoxidation focusing in particular on progress between 1999 and March 2004. The review only considers salen complexes with a particular general structure which Jacobsen's catalyst shares. Heterogeneous and supported catalysts are not included. Pages 1569 – 1589 focus on manganese catalysed asymmetric epoxidation, discussing early results in this field, subsequent modifications and the reaction mechanism.

Practical Asymmetric Synthesis[A,C]

Davies, I. W., Reider, P. J., *Chemistry and Industry*, 1996, 11, 412-415

This article discusses several case studies on asymmetric synthesis strategies performed on a commercial scale. The first example discussed is the production of Indinavir (Crixivan®), a HIV protease inhibitor by Merck. The conditions under which Jacobsen's catalyst was utilised in this synthesis and some process improvements that were made are discussed.

Metal Acetylacetonate Synthesis Experiments: Which Is Greener? [B]

Ribeiro, M.G.T.C., Machado, A.A.S.C., *Journal of Chemical Education*, 2011, 88, 947–953

This paper describes a scenario in which learners are asked to carry out a synthetic procedure, calculate its green chemistry metrics and suggest improvements. In this case, the students are challenged to use the 12 principles to review and modify metal acetylacetonate synthesis. A "green star" metric is used alongside conventional green chemistry mass metrics to evaluate the improvement in greenness. This metric helps students to become familiar with both the 12 principles and green chemistry mass metrics and to gain experience in modifying synthetic chemistry to improve its greenness.

Patents[C]

U.S. Patent No. 5,637,739 Chiral Catalysts and Epoxidation Reactions Catalyzed Thereby

and U.S. Patent No. 5,663,393 Chiral Catalysts and Epoxidation Reactions

Jacobsen, E.N., Zhang, W., Deng, L.; 1997

These patents cover the use of chiral catalysts for enantioselective epoxidation and oxidation of prochiral alkenes. The catalyst described is Jacobsen's catalyst or a structurally similar Mn(salen) complex.

US Patent No. 6,031,115: Process for Preparing Epoxides **and** International Patent No. WO 93/1706 Process for Preparing Enantiomerically Pure Fluorinated Epoxychromans

Bell, D., Fedouloff, M., Turner, G.; 2000; SmithKline Beecham plc

This patent covers the use of Jacobsen type catalysts for the production of pharmaceutical grade ingredients.

Website[B]

The Green Chemistry Network website; http://www.greenchemistrynetwork.org/

This body aims to promote awareness and facilitate education, training and practice of Green Chemistry in industry, government, academia and schools. The main page has a useful links menu that includes a section on Educational Resources and on Environmental Agencies and Commissions.

Some additional sources that may be useful:

The following texts contain some information on environmental management and control in organisations;

- N. Stanley, Active Pharmaceutical Ingredients – Development, Manufacturing and Regulation, 2nd edition, Informa Healthcare, 2010 (see chapter on Environmental Control)
- M.K. Theodore and L. Theodore, Introduction to Environmental Management, CRC Press, 2009
- C. Sheldon and M. Yoxon, Environmental Management Systems, 3rd edition, Routledge, 2006

Session 2 (Laboratory 1): First synthetic step - reaction of a diamine and a salicylaldehyde derivative to generate a catalyst ligand

Aim / Goal of this Laboratory session:

The primary goal of this session is for you to carry out the experimental procedure to synthesise and isolate the salen ligand assigned. It should take your group about two hours from set-up to isolation of the product.

Further Information

You will carry out characterisation of the ligand by TLC, melting point, ^{1}H NMR, ^{13}C NMR (if required) and FT-IR spectroscopy. Samples of each salicylaldehyde starting material should also be characterised by ^{1}H NMR and FT-IR spectrocopic analysis.
You should be writing up your lab book as you go along according to the guidelines provided.

Take some time before the end of the session to plan the work that your group needs to do before the next session; compile a list of actions and assign responsibilities and due dates. Arrange a time when the group will have a short meeting to review progress before the next lab session and select the Chair, Recorder and Editor for this week's meeting.

Tasks to complete before session 3:

- Meet as a group to review progress on the list of actions for their group. The Chair will have prepared a short agenda, and the Recorder will post a short summary of decisions made and progress reported on the wiki.
- Submit an experimental procedure for the preparation of the Mn-salen catalyst on a suitable scale as well as a short chemical safety assessment (via the wiki and/or directly to the tutor). These should be typed and structures should be drawn using a chemical drawing package. **You will not be allowed to begin lab work in Session 3 until this task has been satisfactorily completed.**
- Begin research on alternative epoxidation conditions for Mn-salen catalysts.
- **Individually** submit a prediction of the expected IR and NMR spectral characteristics of the salicylaldehyde starting material used and the ligand intermediate prepared.
- Add information on the characterisation and yield for the first synthetic step to your lab notebook, and add information on the second experiment available in advance on the second synthetic step (materials, equipment, literature reference etc.).

Desired learning outcomes:

On completion of this session and the related independent learning you will able to:

- Prepare an experimental procedure on a suitable scale and identify materials and equipment required as well as any chemical safety issues.
- Predict the IR and NMR spectral characteristics of the compounds that you will be preparing and of the salicylaldehyde starting material used.
- Collaborate in a face-to-face meeting and using a wiki.

Session 3 (Laboratory 2): Preparation of a Mn-salen catalyst

Aim / Goal of this Laboratory session:

The primary goal of this session is to carry out the experimental procedure to synthesise and isolate the Mn-salen catalyst assigned. It should take almost three hours from set-up to tidy-up. The procedure requires that air be bubbled through the reaction mixture to allow in situ oxidation from Mn(II) to Mn(III).

Further Information

As this synthetic step will take most of the session to complete, you will carry out most of the characterisation of the catalyst complex in the next session.
You should be writing up your lab book as you go along according to the guidelines provided.
Take some time before the end of the session to plan the work that your group needs to do before the next session; compile a list of actions and assign responsibilities and due dates. Arrange a time when the group will have a short meeting to review progress before the next lab session and select the Chair, Recorder and Editor for this week's meeting.

Tasks to complete before session 4:

- Meet as a group to review progress on the list of actions for your group. The Chair will have prepared a short agenda and the Recorder will post a short summary of decisions made and progress reported on the wiki by the day specified by the tutor. The Editor should be reviewing any page content that is being uploaded.
- Submit a group experimental procedure for the oxidation of stilbene using the Mn-salen catalyst you prepared on a suitable scale as well as a short chemical safety assessment (via the wiki and/or directly to the tutor). These should be typed and structures should be drawn using a chemical drawing package. **You will not be allowed to begin lab work in Session 4 until this task has been satisfactorily completed.**
- Submit a prediction from the group of the expected IR spectral characteristics of the catalyst prepared and suggest why NMR analysis will not be useful.
- Carry out research as part of your group on alternative alkene oxidation conditions using Mn-salen catalysts, by looking at some of the suggested references and conducting searches on a scientific database using selected keywords. Each group should have posted a summary of the research carried out and information obtained with references used (one page maximum) on your group wiki in advance of the next session.
- **Individually** submit an interpretation of your IR and ^{1}H NMR spectra obtained of the ligand intermediate and of the salicylaldehyde starting material.
- Add information on the characterisation and yield for the second synthesis step to your lab notebook, and add information on the epoxidation reaction available in advance (materials, equipment, literature reference etc.).

Desired learning outcomes:

On completion of this session and the related independent learning hours you will able to:

- Determine the overall yield of catalyst obtained.
- Perform literature research to identify alternative oxidation conditions.
- Prepare an experimental procedure on a suitable scale for the oxidation of *trans*-stilbene and identify materials and equipment required as well as any chemical safety issues.
- Characterise the salicylaldehyde starting material used and the salen ligand prepared
- Predict the IR spectral characteristics of the catalyst prepared
- Collaborate in a face-to-face meeting and using a wiki.

Session 4 (Laboratory 3): Evaluation of the catalyst performance in a reference reaction - epoxidation of *trans*-stilbene

Aim / Goal of this Laboratory session:

The primary goal of this session is to carry out the experimental procedure to epoxidise *trans*-stilbene to give *trans*-stilbene oxide using the Mn-salen catalyst assigned. The experiment takes about three hours from set-up to tidy-up if the reaction mixture is left stirring for 2 hours.

Further Information

As this synthetic step will take most of the session to complete, you will carry out most of the characterisation of the product in the next session. You should be writing up your lab book as you go along according to the guidelines provided.

Ensure that you have checked with your tutor to find out which alternative oxidation conditions you will be using next week as well as the relevant literature reference. Take some time before the end of the session to plan the work that your group needs to do before the next session; compile a list of actions and assign responsibilities and due dates. Arrange a time when the group will have a short meeting to review progress before the next lab session and select the Chair, Recorder and Editor for this week's meeting.

Tasks to complete before session 5:

- Meet as a group to review progress on the list of actions for your group. The Chair will have prepared a short agenda, and the Recorder will post a short summary of decisions made and progress reported on the wiki by the day specified by the tutor. The Editor should be reviewing any page content that is being uploaded.
- Submit a group experimental procedure for the oxidation of stilbene under alternative conditions using the Mn-salen catalyst you prepared on a suitable scale as well as a short chemical safety assessment (via the wiki and/or directly to the tutor). Your tutor will have advised you on which literature reference to use. Structures should be drawn using a chemical drawing package. **You will not be allowed to begin lab work in Session 5 until this has been satisfactorily completed.**
- Submit a prediction from the group of the expected IR and NMR spectral characteristics of the *trans*-stilbene starting material and stilbene oxide product.
- As a group, evaluate all alternative oxidation procedures found based on the criteria provided in the company brief supplied (yield, solvent, complexity of the procedure, catalyst loading, potential for catalyst recovery and type of oxidant) and recommend which should be attempted in the future.
- On an **individual** basis, interpret the IR spectrum obtained of the Mn-salen catalyst.
- Add information on the characterisation and yield for the third experiment (oxidation of *trans*-stilbene) to your lab notebook. Add information available in advance on the next experiment (materials, equipment, literature reference etc.) to your lab notebook.

Desired learning outcomes:

On completion of this session and the related independent learning hours you will able to:

- Perform the epoxidation of stilbene with sodium hypochlorite using the catalyst prepared.
- Characterise the catalyst prepared using IR spectroscopy.
- Predict the NMR and IR spectral characteristics of the organic compounds being used in Session 4.
- Prepare an experimental procedure on a suitable scale for the oxidation of *trans*-stilbene using alternative conditions, and identify materials and equipment required as well as any chemical safety issues.
- Evaluate the alternative oxidation methods found the previous week, and recommend which should be attempted in the future.
- Collaborate in a face-to-face meeting and using a wiki.

Session 5 (Laboratory 4): Alternative method for epoxidation of *trans*-stilbene using the Mn-salen catalyst

Aim / Goal of this Laboratory session:

The primary goal of this session is to carry out the alternative experimental procedure (for example, using hydrogen peroxide as the oxidant) to epoxidise *trans*-stilbene to give *trans*-stilbene oxide using the Mn-salen catalyst assigned.

Further Information

You should be writing up your lab book as you go along according to the guidelines provided. Take some time before the end of the session to plan the work that your group needs to do before the next session; compile a list of actions and assign responsibilities and due dates. Arrange a time when the group will have a short meeting to review progress before the next lab session and select the Chair, Recorder and Editor for this week's meeting.

When planning your prediction of how catalyst structure and efficiency are related for the reference reaction from Session 4, you will need to ensure that you obtain crude yield and percentage conversion results from all other groups and compile them. If the epoxidation reaction was performed in duplicate or triplicate, the crude yield and percentage conversion results should be used to calculate actual yields and the mean and standard deviation of these actual yields can then be calculated. The expected trends have been reported in the literature and you should examine whether the following structural changes have resulted in any variations in the actual yields;

1. The nature of the diamine used to generate the catalyst ligand (ethylene or cyclohexane).
2. Electronic effects of substituents at the 5 and 5' position.

Tasks to complete before session 6:

- Meet as a group to review progress on the list of actions for your group. The Chair will have prepared a short agenda, and the Recorder will post a short summary of decisions made and progress reported on the wiki by the day specified by the tutor. The Editor should be reviewing any page content that is being uploaded.
- Submit a group analysis of the results for all of the catalysts prepared (yield of catalyst from the two step preparation, average yield and conversion for the reference epoxidation reaction using sodium hypochlorite). This will require the determination of the percentage conversion to stilbene oxide based on the NMR data obtained.
- Produce a prediction of how catalyst structure and efficiency might be related, based on the results from the reference reactions and supporting literature references.
- On an **individual** basis, interpret the ^{1}H NMR spectra obtained of the crude products from the first stilbene epoxidation (using hypochlorite).
- Add information on the characterisation and yield for the fourth experiment (epoxidation using alternative conditions) to your lab notebook.

Desired learning outcomes:

On completion of this session and the related independent learning hours you will able to:

- Perform the epoxidation of *trans*-stilbene using the catalyst previously prepared under alternative conditions (e.g. using hydrogen peroxide as the oxidant).
- Characterise the stilbene epoxide product from the previous week, and determine the crude yield and the extent of conversion based on NMR analysis.
- Compare the effectiveness of all catalysts prepared in the reference reaction, and predict how structure is related to efficiency.
- Collaborate in a face-to-face meeting and using a wiki.

Session 6 (Workshop 2): Assessing the cost, performance and environmental impact of the reactions performed

Aim / Goal of this Laboratory session:

The purpose of this workshop session is to see how to:

1. Use ChemSpider (www.chemspider.com) to find vendors and costings for raw materials for the synthesis of the catalyst and the epoxidation reactions.
2. Use recommended reading sources and the guidelines provided on metrics to evaluate the environmental impact of each process and the potential for further development.

Further Information

Take some time before the end of the session to plan the work that your group needs to do before the next session; compile a list of actions and assign responsibilities and due dates. Arrange a time when the group will have a short meeting to review progress before the next lab session and select the Chair, Recorder and Editor for this week's meeting.

You will be given a deadline for submission of the draft wiki report and work in progress summary, which will be during or shortly after this workshop session.

Costing

You should prepare an estimate for the cost of synthesising 100g of stilbene oxide by the original and alternative methods using the catalyst you synthesised. The costing can assume a yield of 90% for each synthetic step but you should also note the actual yield you obtained. You must remember to include VAT (20 %) on all raw materials to be purchased as well as a rough estimate of overhead costs (add 25% to the raw material subtotal if the synthesis will take 2 days and add an extra 10% for each additional day needed). The template shown below is available from your tutor as an Excel file and it is recommended that it is used to prepare the costing.

Template for Costing for Synthesis of 100 g of Target Compound

Name of Chemical	Name of Vendor	Purity Grade and Product Number	Quantity Required (g or ml)	Unit Size	Cost per Unit (€ or £)	No. of Units Required	Total Cost Including VAT*	Actual Cost to Produce 100 g of Target Compound (€ or £)
Example only- Acetone	Jupiter Chemicals	Reagent grade, >99.5%, Prod. no. 179124	450 ml	500 ml	23.80	1	28.56	25.70
							Subtotal:	
							Overheads:**	
* Value Added Tax = 20%							Total Cost per 100 g:	

**Including labour, consumables, utilities - Add 25% to the subtotal if the process will take 2 days and add an extra 10% for each additional day if needed.

The overall cost per 100 g calculated can be used to compare the original and alternative oxidation reactions carried out in sessions 4 and 5 and, if required, to discriminate between catalysts that show similar conversion rates and environmental impact. Other useful information that should be noted is which raw materials are most and least expensive in the quantities required. Although not a green chemistry consideration, this information is important to be aware of in a commercial environment.

Green chemistry metrics

Reaction metrics are used to measure the "green credentials" of a reaction, and provide a useful comparison tool to quantify improvements made when altering reaction conditions. By focusing only on product yield,

chemists may miss the opportunity to improve the environmental credentials of a synthesis. A green chemist should influence the behaviour of synthetic chemists to move away from solely focusing on yield, and routinely consider environmental impacts. Table 4 shows how the application of green chemistry principles can deliver both economic and environmental benefits.

Table 4: Economic and environmental benefits from application of green chemistry principles[5]

Process Improvement	Environmental Benefit	Economic Benefit
Atom economy	Less by-products and waste formed	Incorporate more of inputs into output, improving cost efficiency
Solvent reduction	Use lower volumes of potentially hazardous materials and have less solvent waste	Reduced volume means lower storage requirements and less energy to heat process
Reagent optimisation	Use catalysts rather than solely stoichiometric reagents to reduce inputs and recycle components	Improved selectivity and efficiency
Energy Reduction	Lower emissions related to power generation and use	Reduced costs
In situ analysis	Lower risk of exposure or release of analyte into environment.	Real time data increases efficiency, avoiding down time by detecting problems promptly
Safety	Use of non-hazardous materials and improved safety procedures lower the risk of environmental exposure, spillages, fire or explosions.	Increases worker safety and less downtime due to accidents

Reaction yield, atom economy, and mass intensity will be used to examine the reactions set out in this case study. The ideal value for atom economy and yield is 100 %, while for mass intensity it is 1. Reaction yield will affect the mass of product obtained and therefore a low yield will result in a poorer mass intensity value.

$$\text{Atom economy} = \frac{\text{molecular weight of product}}{\text{sum of molecular weight of reactants}} \times 100$$

$$\text{Mass intensity} = \frac{\text{total mass used in process (kg)}}{\text{mass of product (kg)}} \times 100$$

$$\text{Percentage yield} = \frac{\text{actual yield of product}}{\text{theoretical yield of product}} \times 100$$

Metrics should be calculated for the reactions that follow:

- Synthesis of salen ligand (see Figure 1)
- Preparation of manganese salen catalyst (see Figure 2)
- Epoxidation using a Mn-salen catalyst and hypochlorite solution (see Figure 5)
- Epoxidation using a Mn-salen catalyst and hydrogen peroxide or other alternative conditions examined (see Figure 6)

To assist you, an overview of the steps involved is given below, and the calculation of the metrics for the existing standard epoxidation method used by HugePharma Ltd. has been provided to you as a worked example.

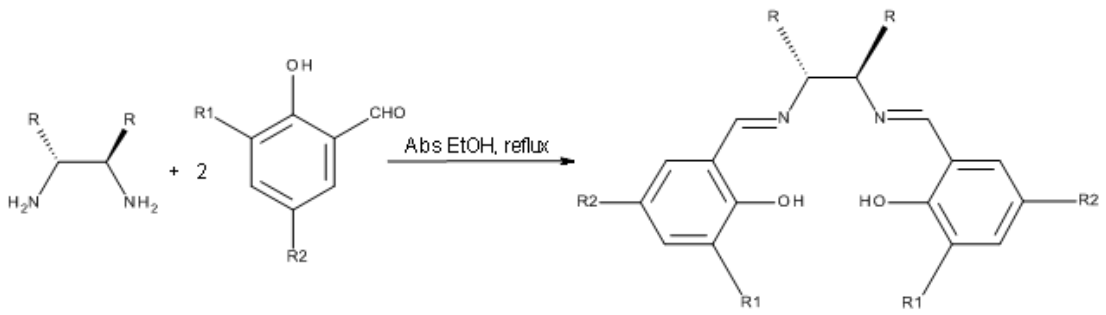


Figure 1: Step 1 - Reaction of diamine and salicylaldehyde derivative to form a salen ligand[3]

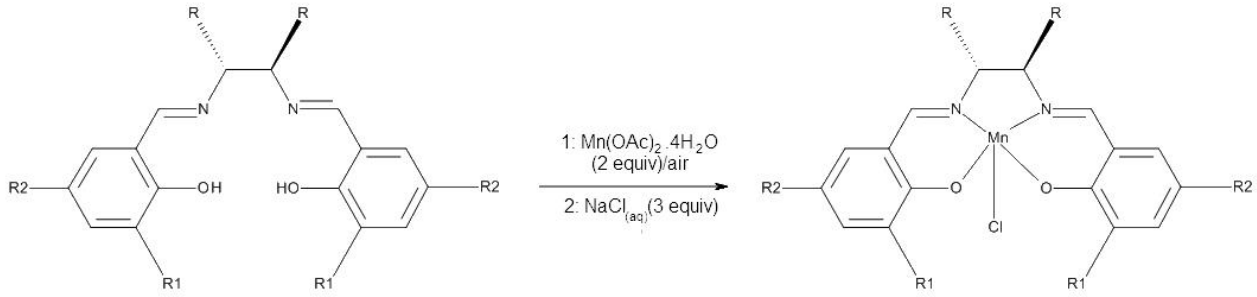


Figure 2: Step 2 - Synthesis of a manganese salen catalyst[3]

Epoxidation of *trans*-stilbene

Current method:[1]

The established epoxidation method referred to by HugePharma Ltd. utilises a peroxyacid (*meta*-chloroperoxybenzoic acid (mCPBA)) as the oxidant for the conversion of an alkene to an epoxide. mCPBA is the preferred peroxy acid because of its relative ease of handling. The reaction scheme for epoxidation of *trans*-stilbene is shown in Figure 3. This procedure is not enantioselective.

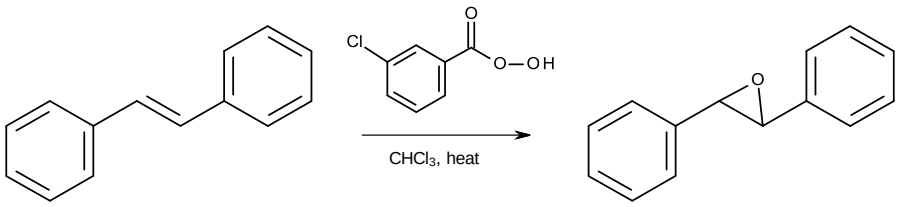


Figure 3: Peracid epoxidation of stilbene

Catalytic asymmetric epoxidation methods:

The area of asymmetric epoxidation was initially pioneered by Sharpless[6] using catalysts based on titanium tetraisopropoxide and chiral dialkyl tartrate, forming an enantiomerically enriched product depending on the enantiomeric form (+ or -) of tartrate used (Figure 4). The oxidant used is *tert*-butyl hydroperoxide.

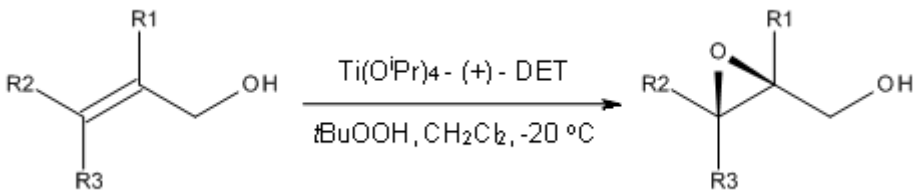


Figure 4: Sharpless epoxidation of allylic alcohols[6]

This method has proven effective for the production of complex carbohydrates but requires an allylic alcohol starting material. Oxidation of simple olefins shows very little enantioselectivity, therefore this method is not suitable for the epoxidation of *trans*-stilbene.

In 1991, Jacobsen *et al.* published details of their epoxidation catalysts based on chiral Schiff base ligands around a manganese centre (Figure 5).[2] When used in the presence of sodium hypochlorite (bleach), these catalysts have been shown to efficiently transform a wide range of alkene substrates in high yields, and enantiomeric excesses in the region of 90 %.

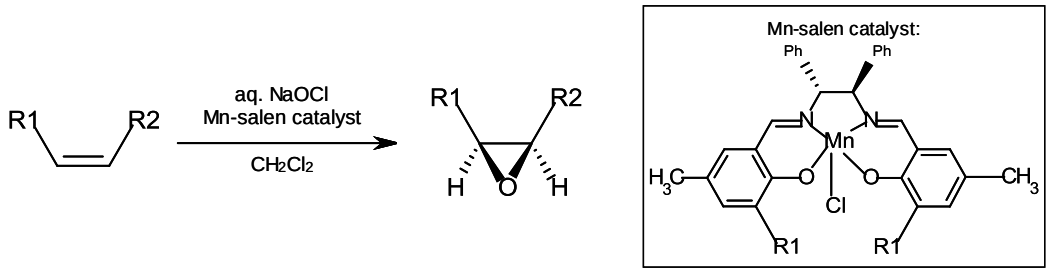


Figure 5: Epoxidation of alkenes with sodium hypochlorite using a Mn-salen catalyst (e.g. Jacobsen's catalyst)[2]

Catalytic asymmetric epoxidation method using hydrogen peroxide with Mn-salen catalyst:

An alternative method has been reported by Liu and Nocera[7] using Jacobsen's catalyst in the presence of hydrogen peroxide to perform the epoxidation of alkenes (Figure 6). This procedure is reported to employ "green" methods through the use of this simple and cheap oxidising agent which should significantly improve the atom economy.

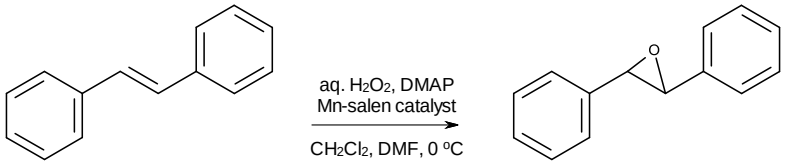


Figure 6: Epoxidation of stilbene with hydrogen peroxide using a Mn-salen catalyst (e.g. Jacobsen's catalyst)[7]

Worked example: Epoxidation of *trans*-stilbene using mCPBA

Stilbene oxide may be prepared by reacting 5.0 g (0.028 mol) *trans*-stilbene with *m*-CPBA (6.0 g, 0.028 mol, 80%) in 50 mL hot chloroform as shown in Figure 3. This reaction is reported to occur with a 90 % product yield.

Reaction metrics calculations:

Atom economy = [m.w. Stilbene oxide / (m.w. Stilbene + m.w. mCPBA)]*100
= [196.24/(180.25+172.57)]*100
= 55.62 %

Mass intensity

Assumptions:

- Calculations are based on producing 1 kg of product in 100 % yield. (The result can then be adjusted based on the actual yield)
- Chemicals used in product work-up are not included.
- Water is not included in mass intensity calculations. (Process Mass Intensity, an alternative metric, does include process water).

1 kg stilbene oxide = 1000/196.24 moles
= 5.0958 moles therefore require 5.0958 moles of stilbene starting material
Scale factor = 5.0958 moles / 0.028 moles = 181.99
(Based on using 0.028 mole stilbene in the epoxidation)
Scaling from procedure:
Mass of stilbene = 5.0958*180.25/1000 = 0.9185 kg
Mass of mCPBA = 181.99*(0.028*172.57) / 1000*0.80 = 1.099 kg
Density of $CHCl_3$ = 1.492 g mL^{-1}
Mass of $CHCl_3$ = 181.99*0.05*1.492 = 13.577 kg

Mass intensity (100 % yield)	= 0.9185 + 1.099 +13.577 = 15.5945
Mass intensity (90 % yield)	= 17.33

(Note that the mCPBA used has a specification of 80% purity and the extra 20% mass has not been factored in here to keep the example relatively straightforward. If this extra 20% is included, 0.2748 kg should be added to the total and the mass intensity calculated is 15.87)

Issues with this method:

- Low atom economy
- Heat required to maintain operating temperature; energy input required.
- Chloroform as solvent; carcinogen, restrictions on use.
- mCPBA is shock sensitive; safety hazard on large scale
- Cannot be used to produce one enantiomer over another

Useful references

M. Lancaster, *Green Chemistry: An Introductory Text* (2nd Edition), RSC Publishing, Cambridge, 2010

P. T. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice* Oxford University Press, USA, 2000.

Tasks to complete before session 7:

- Meet as a group to review progress on the list of actions for your group. As always, the chair should have prepared a short agenda and the scribe will post a short summary of decisions made and report progress on the wiki by the day specified by the tutor. The Editor should be reviewing any page content that is being uploaded.
- Prepare a group analysis of the costing for the raw materials and materials required for work up for the two oxidation processes carried out (including catalyst preparation) for production of 100 g of

trans-stilbene oxide and identify any issues (e.g. which materials are most and least expensive in the quantities required).

- Prepare a group analysis of the environmental impacts of two oxidation processes with reference to green chemistry metrics including recommendations for improvements that may be possible.
- As a group, analyse the ^{1}H NMR spectra obtained of the crude products from the *trans*-stilbene epoxidation under alternative conditions to determine the percentage conversion.
- Prepare a group analysis comparing the results (yield and conversion) for the reference and alternative oxidation reactions for all catalysts.
- Submit a draft wiki report with a one page work in progress summary describing which areas of the final report the group feel they have addressed and which ones they have yet to complete with details on who is responsible and due dates. Any clarifications required or queries should also be noted.
- Ensure the experimental details in your lab notebooks have been completed (characterisation and conclusions).

Desired learning outcomes:

On completion of this session and the related independent learning hours you will able to:

- Plan for the scope of future development work on each process.
- Compare the results obtained in the epoxidation reactions performed (using the reference procedure and an alternative one).
- Cost the raw materials for two oxidation processes.
- Compare the environmental impacts of each oxidation process with reference to the appropriate metrics.
- Prepare a draft report including a work in progress summary.
- Collaborate in a face-to-face meeting and using a wiki.

Session 7 (Workshop 3): Clinic for formative feedback on draft reports

Aim / Goal of this Session:

The purpose of this workshop session is to:

1. Discuss your work to date with your tutor and obtain formative feedback (as an entire class and as an individual group) from your tutor on which areas of the report you need to work on and which ones have been addressed satisfactorily.
2. Discuss any queries your group have on the assignment any problems that have been encountered.
3. Identify the tasks remaining and plan for when they will be achieved.

Further Information

In this workshop you will have the opportunity to receive formal feedback from your tutor who will highlight any areas that require work as well as any misunderstandings and identify the strengths of the work produced to date. It also gives you the opportunity to review your work as a group and to complete any tasks that you have not been able to do to date while your tutor is speaking to other groups.

Your tutor will provide specific guidelines for the final presentation of your work that will take place in Session 8. You should have time to at least plan the work required to produce and give your presentation. General guidelines for preparing presentations are provided in Appendix 6. Remember to refer back to the original brief from HugePharma Ltd. to ensure that your presentation is addressing each aspect.

Tasks to complete during session 7:

- Note and act on feedback provided from your tutor.
- Review your work as a group and identify tasks that need to be completed.
- Complete any outstanding work from previous workshops and discuss the consideration
- Plan and begin preparations for your presentation.

Tasks to complete before session 8:

- Incorporate feedback from your tutor into the group report and presentation.
- Add information to the wiki on your consideration of the scope for each synthesis step to be improved and recommendations for future work.
- Meet as a group to finalise your presentation. Practise it several times as a “dry run” and ensure it meets the time requirement and is relevant, coherent, structured and accurate.
- Post information on who attended any meetings as well as the tasks completed at them on your wiki.
- Continue to update and edit the wiki by uploading files and summaries, drafting sections of the proposal and responding to contributions from other group members.
- The structure, coherence and consistency of style and formatting of the final report are important considerations at this stage.
- If the executive summary was not submitted with the draft report, it now needs attention.

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Desired learning outcomes for session 7:

On completion of this session and the related independent learning hours you should be able to:

- Communicate effectively when receiving formative feedback to ensure that the maximum benefit is obtained
- Act on constructive criticism and suggestions
- Prioritise the remaining work to be done
- Prepare and present an informative and visually engaging presentation on your group project that encapsulates your findings.
- Collaborate in a face-to-face meeting and using a wiki.

Session 8 (Workshop 4): Oral presentations

Aim / Goal of this Session:

The purpose of this workshop session is to:

1. Present your group's work to your peers and tutor summarising the work undertaken, your recommendations and answer any questions they may have.
2. Obtain oral feedback from your tutor (with optional written feedback on each presentation to each group from your tutor and peers)
3. Learn about alternative approaches to the project from the other presentations and provide a supportive audience with constructive feedback to your peers.

Further Information

In this workshop your group will present your work and recommendations to the company and you will listen to and assess the presentations of the other groups in your class. Your tutor may opt to invite some guest tutors who have a background in green chemistry or who work or have worked in industry to provide additional feedback.

You should be prepared to provide others with constructive feedback as well as receive constructive feedback from your peers and tutor. It is important to realise your role as an audience member for your peers. You should contribute to a supportive environment by listening attentively, making some eye contact with the presenter, asking any questions you have in a respectful and non-confrontational way and (if requested to) making some constructive comments on the peer feedback forms for the group assigned. Listening to the other group's presentations also provides a very useful opportunity to see how others approached the same project and to assess what you might incorporate from their methods in the future.

You will be reminded about the deadline for the submission of your final report (generated from your wiki). At this stage, your executive summary should be the main task remaining as it cannot be prepared once the main body of the proposal has been written. In addition, it is expected that you will incorporate any relevant feedback (oral or written) from your tutor into the report after your presentation. You should note down the oral feedback and ask for clarification from your tutor at the end of the session if needed.

Your final task is the production of a reflective piece and this should be done once all other tasks are complete. The deadline for submission of your reflective piece will usually be several days after that for the group report to give you some time to complete it. Along with any notes you made during the process, you should also find that reviewing some of the group wiki will be helpful. Guidelines are given in the appendices.

Tasks to complete by the end of the module:

- Incorporation of feedback from the presentation into the group report.
- Final editing and completion of group's wiki report.
- Printing out and submitting the final report in the format specified (wiki or PDFs or Microsoft® Word). You may also be required to submit your report for checking by plagiarism detection software.
- Lab book to be submitted by the deadline provided.
- Preparing and submitting your individual reflective piece.
- If requested, submission of any marked group or individual work in hard copy that was previously returned.

Desired learning outcomes of session 8:

On completion of this session you should be able to and the related independent learning hours you should be able to:

- Present findings in a professional manner.
- Evaluate your work and the work of others.
- Provide a supportive audience and constructive feedback to your peers.
- Act on feedback provided that is relevant to your written report.
- Produce a professional report, including an executive summary and an assessment of the scope for each step to be improved, that is supported by the relevant experimental data and a laboratory notebook as well as references to the literature.
- Prepare a short individual reflective statement on the group process, transferable skills developed and the extent to which the stated learning outcomes were met.

Appendices: Student guidelines

The following guidelines should be adhered to when preparing course work.

Appendix 1: Using a wiki

A wiki is "a collaborative website consisting of one or more pages that allow authorised users to contribute to or edit page content." (source: http://usermanual.pbworks.com/Glossary)

Note that although many wikis are open access, those described for this project are secure and only people invited to join the group / wiki by the tutor administrator will have access.

Why use a wiki?

- Wiki software is very easy to use and allows you to work and to write collaboratively to produce a report / presentation / webpage.
- The wiki is a means of generating a very useful archive of all of the information that is relevant to the assignment as the project proceeds.
- It provides the added flexibility of being able to work anywhere that a PC or laptop and internet connection are available at any time.
- All previous versions of each page can be accessed using the Page History function which means that no work can be permanently overwritten or deleted.
- Contributions made by each member can be easily tracked to assess their quality, quantity and whether they were made across the entire timeframe of the assignment.
- Peer feedback and review is facilitated by the comments and page editing option.
- The assignments and the feedback provided can be accessed easily and stored indefinitely for future reference and are available in a flexible format (pages can usually be saved as PDFs).
- Wikis are regularly used in organisations to allow groups to collaborate on projects and documents and to share knowledge and the ability to use one is a valuable transferable skill. For example, a wiki has been established to develop policy in the area of green chemistry in California (http://cagreenchem.wikidot.com/start) (further references on the use of wikis in organisations are provided towards the end of this Appendix).

What do you need to be able to do?

Instructions on the technical details in relation to using the selected wiki are given on its website.

The common tasks you will perform using the wiki are:

- adding and editing wiki pages
- adding comments and links to pages and
- inserting tables and chemical schemes / structures.

Most chemical drawing software allows for structures to be saved as images (the required format is usually specified in the help menu).

If you have a specific technical problem, it is recommended that you check any guidelines that have been provided to you by your tutor and also ask the other members of your group for help. If you are still having a problem, you should then contact your tutor.

Always remember:

- Use folders, link related pages and name files and pages in a logical and structured way so that you can find information on the wiki easily. To help with this, names are provided that should be used for

the pages that will make up the main body of your report / presentation and for other some pages to facilitate group organisation and communication (see the end of this section).

- References should be cited when necessary and all information should be put into your own words.
- **Ensure that the information is accurate, will not offend anyone and is not plagiarised.**
- Try to keep the page to a reasonable length. Long pages can cause the reader to lose interest. Try to arrange data in sensible subcategories with pages for each to make it more engaging for the reader.
- You may find it helpful initially to add an outline of the content planned for a page at the top of it.
- The minimum knowledge level of your target audience is non-technical management at HugePharma Ltd.; the target audience is their chemical development team.
- Note that there is a space limit on each wiki page. If you find that a page is no longer accepting edits, you have probably reached the limit. You will need to add a new page, and link to this page from the end of the existing one to continue that section.

Netiquette and online communication

The concept of "netiquette" is very important because when you are communicating online, there are no visual cues (you can't see the face of the person or people you are in contact with). This means that it is more difficult to communicate clearly and it is more likely that a comment may be misunderstood or misinterpreted. Also, you should remember that all comments made on a wiki remain in the page history even after they are deleted.

It is recommended that you read over a comment carefully before you add it to the wiki to make sure that it is clear and there aren't any spelling mistakes that will make it confusing. You should be respectful and polite to each other, and be conscious of not offending or insulting anyone. Use of capital letters only is the online equivalent of shouting at someone and should be avoided. The same approach applies in any professional environment.

Ground rules for your group

You may want to consider establishing some ground rules about working in your groups such as remaining respectful towards a group member who you feel is not contributing, providing constructive feedback to peers (e.g. posting a comment first before making changes to someone else's work), responding to a query or message within a reasonable timeframe, communicating with the group to let them know if you will be late or absent and consulting with the group in relation to important decisions.

Remember that working in a group can be very productive, but it requires communication, planning and compromise.

Peer feedback and review

In the initial weeks, your group could consider waiting until a group member asks for feedback or editing of their contribution before making changes to their work. It is helpful if contributors are specific about feedback required (e.g. proof-reading for grammar, spelling and formatting or aspects such as relevance, structure, clarity and validity of the conclusions drawn). It is recommended that feedback and changes are constructive. A comment should address what was done well, and also the areas where it was felt changes were required and why.

Structure of your wiki report

The following are the names of the pages that it is recommended be used to make up the main body of your report / presentation:

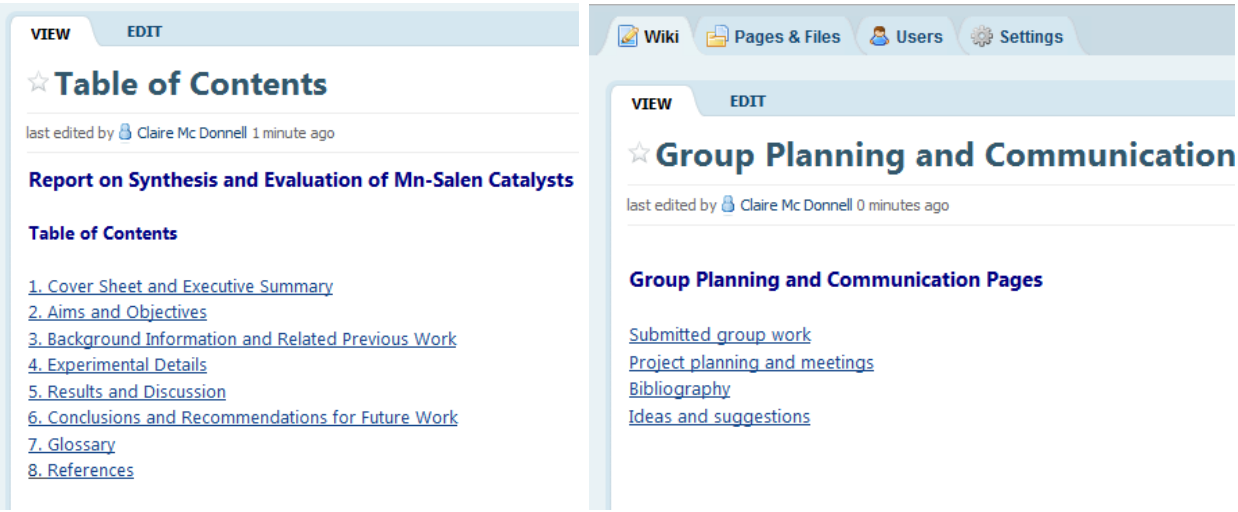
- Table of contents (with links to the other report component pages, see example that follows)
- Cover sheet and executive summary
- Aims and objectives

- Background information and related previous work
- Experimental details
- Results and discussion (this can be subdivided into separate results and discussion pages, or into pages such as Catalyst evaluation based on reference reaction, Use of alternative conditions, Costings and evaluation of environmental impact, Prediction of relationship between catalyst structure and performance and Scope for improvement for synthetic steps)
- Conclusion and recommendations for future work
- Glossary
- References

Your group should consider adding a main page to the wiki called 'Group Planning and Communication' (see example below) to the wiki that can have the following pages linked to it:

- Submitted group work - Use this page to submit any assignments you are asked to submit via the wiki.
- Project planning and meetings - Use this page for summaries of your group's weekly meetings and any other project planning. Some wikis include templates for reporting on meetings that could be incorporated here.
- Ideas and suggestions - Use this page as a sounding board and suggestion box for general issues.
- Bibliography - Use this page to post links or citations to useful websites, videos, articles or textbooks. Each one must include a short summary of why this information source is useful and refer to a specific page/section in it if necessary.

Screenshots of a Sample Wiki Showing Pages Linked to the Two Main Pages



Assessment of wikis

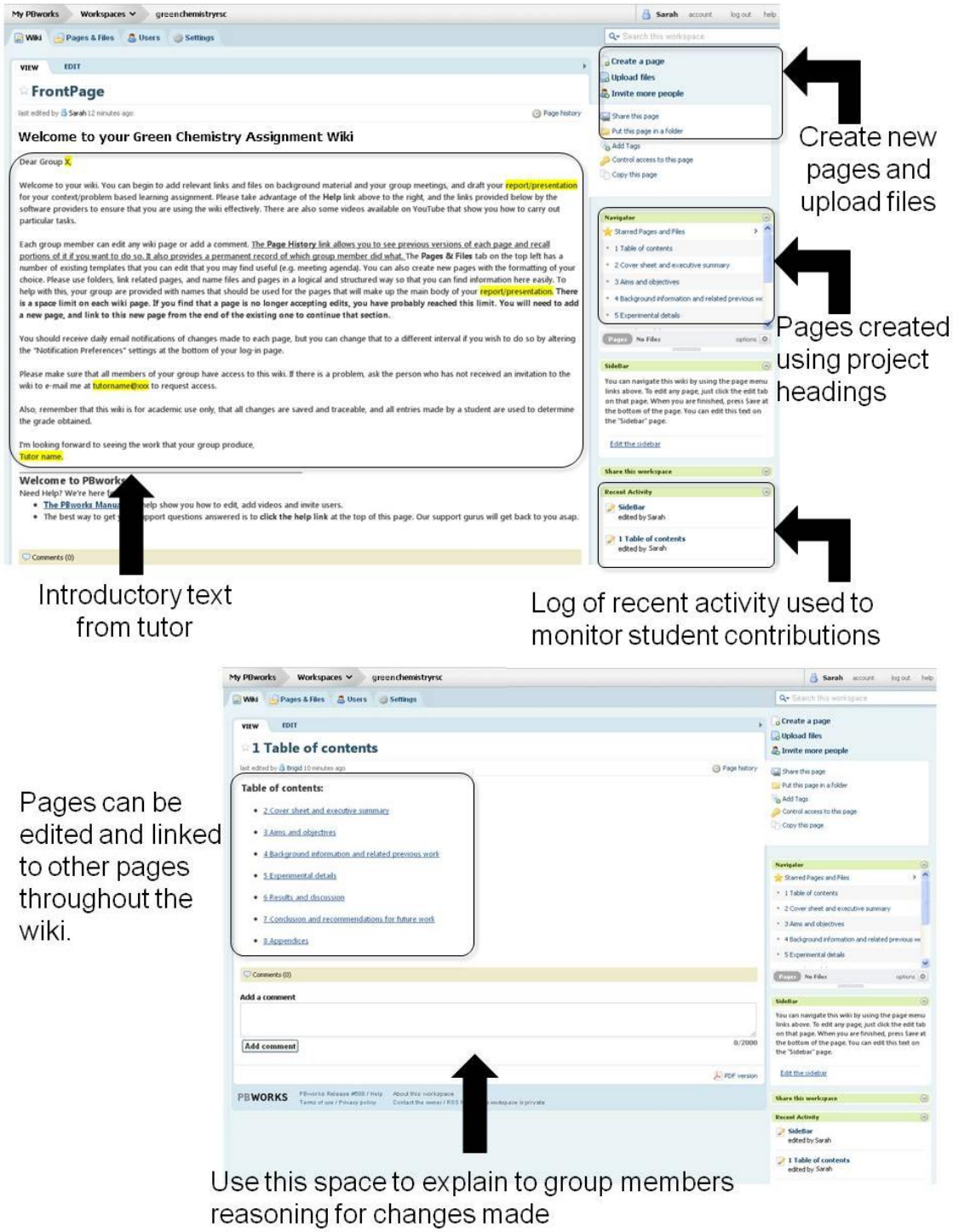
The main criteria used to assess your contribution to the wiki are the effort you put in and the extent of collaboration with the rest of your group that you were involved in.

References on the use of wikis in organisations:

- "Corporate Wiki Users: Results of a Survey", A. Majchrzak, C. Wagner & D. Yates, *WikiSym'06, Proceedings of the 2006 international symposium on Wikis*, D. Riehle, J. Noble, Eds. (ACM Press, 2006), vol. Odense, De, pp. 99-104, accessed 18 October 2011 at https://blog.itu.dk/MVOL-F2010/files/2010/02/corporate-wiki-users-results-of-a-survey.pdf

- A wiki to develop policy in the area of green chemistry in California is available here http://cagreenchem.wikidot.com/start and is reported here:
- http://eponline.com/articles/2009/02/09/calif-launches-wiki-to-develop-green-chemistry-regulations.aspx
- Ganfyd wiki is a medical database that can be edited by registered medical practitioners and viewed by anyone: http://www.ganfyd.org/index.php?title=Main_Page
- Mayweg, A.; Hofer, U.; Schnider, P.; Agnetti, F.; Galley, G.; Mattei, P.; Lucas, M.; Boehm, H. J., ROCK: the Roche medicinal chemistry knowledge application - design, use and impact. *Drug Discovery Today* **2011,** *16* (15-16), 691-696.

Screenshots Showing Main Features of a Wiki



Appendix 2: Preparing laboratory procedures

The literature procedures provided will need to be modified so that the scale is appropriate to prepare the quantity required **(0.5 g of catalyst based on a 70% yield in each of the two steps involved).** You must also consider the equipment and glassware available in your laboratory.

The following format is suggested:

- Give the title of the experimental procedure, the author names and the date.
- Draw a reaction scheme for the synthetic step, and give the relevant literature reference underneath.
- Include, in a tabular format, information on the reagents to be used (amount in g or mL, concentration in moles or mmoles, equivalents, density (if required) in g cm^{-3} and quality or purity).
- Try to use the same number of significant figures for all quantities measured (see Table 5).

Table 5: Suggested layout for information on reagents used

Chemical	Quantity (mass or volume)	Molar mass (g/mol)	No. of moles (mol)	Density (g/cm^3)	Equivalents
4-Fluoroacetophenone, reagent grade	5.0 g	138.14	0.036	N/A	1.0

- List the apparatus needed (remember to specify the size and quantity and whether any glassware needs to be dried in the oven)
- You should write the procedure to be followed in the present tense in the same way that those in your laboratory manuals are presented e.g. "Add 50 cm^3 of absolute ethanol to…., Filter the mixture under gravity to isolate the product" etc.
- Structure the procedure so that it is clear and easy to follow.
- Include details of any analysis to be performed at the end of the procedure.
- At the end of the procedure, the calculations used to determine the scale required should be shown so that they can be clearly followed. All units should be included.

Appendix 3: Preparing chemical safety data

A table of all chemical substances to be used should be prepared for each experiment under the headings shown in Table 6. Any significant hazard and handling issues identified should be discussed with your tutor in advance of the session, and the measures to deal with it should be included in your procedure and report.

Material safety data sheets (MSDS) can be obtained from the chemical vendor's website (for example Sigma Aldrich). These will provide the GHS hazard pictogram, CAS number, hazard classification and hazard statements and risk phrases. Occupational Exposure Limit values (OELs) are set by national authorities as limits for concentrations of hazardous compounds in workplace air. These values are an important tool for risk assessment and management. Sources of this information for specific countries are listed on: http://osha.europa.eu/en/topics/ds/oel/index.stm (last accessed 11.01.12).

Table 6: Example Safety Data Sheet

Substance name	CAS no	Hazard Classification	Hazard statement/Risk phrase	Route of exposure	OELV
trans-1,2-diamino cyclohexane 	1121-22-8	Danger, skin corrosion, causes burns **DANGER**	H314 Causes severe skin burns and eye damage.	Skin Contact, Inhalation	

Further Information:
Sigma Aldrich website (free acces): http://www.sigmaaldrich.com/
Chemspider database (free access): http://www.chemspider.com/

Appendix 4: Prediction of IR and NMR spectra

You are required to submit an estimated ^{1}H NMR and IR spectrum for some of the starting materials and compounds prepared that you have submitted for analysis over the course of the project. It is important to have worked out what you expect to see in the spectrum of a particular compound.

Infrared spectrum prediction can be provided in the format shown in Table 7, listing expected vibrations and the corresponding frequency range.

Table 7: Infrared Spectrum Absorption Bands Predicted for a Given Compound

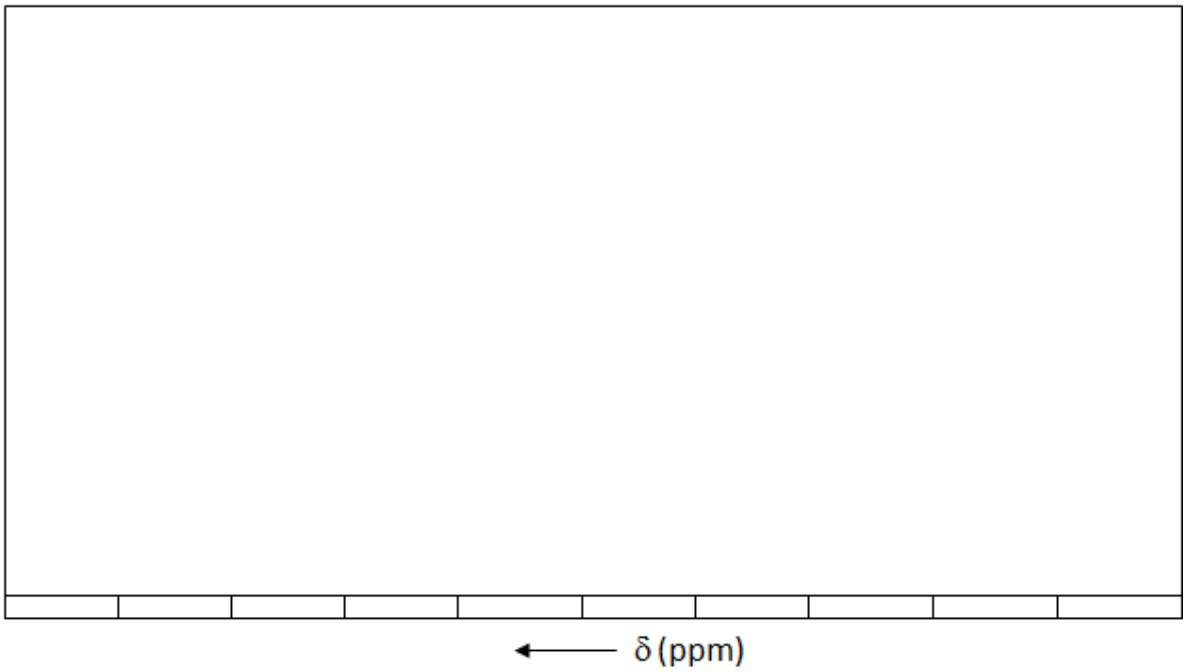
Vibration	**Frequency range and intensity**
C=O stretch (amide)	1630-1680 cm^{-1} (strong)

For ^{1}H NMR spectra, you will need to draw out the structure of your compound showing all of the protons present in order to begin estimating the spectrum. The next step is to establish which protons are equivalent based on their chemical environment. Labelling the equivalent protons on the structure with the same letter may help. You may find using the template provided in Table 8 helpful for presenting the information. Ensure that you explain why a particular approximate chemical shift is assigned and that you explain how the number of protons on the neighbouring carbons is used to determine the spin-spin coupling.

Table 8: Prediction of ^{1}H NMR Spectrum

No of signals in spectrum					
Chemically equivalent protons					
Approx. chemical shift (ppm)					
Integration					
Spin-spin coupling					

Blank spectrum for sketching a predicted ^{1}H NMR spectrum



Appendix 5: Writing up your laboratory notebook

Why Keep a Laboratory Notebook?

A laboratory notebook is your record of the work you completed in the lab. You are required to keep a laboratory notebook for the duration of the work, and submit this at the end. In industry and in research labs, the notebook is the property of the company or supervisor respectively. They are extremely important legal documents that must be able to withstand the scrutiny of a court if required. Without a notebook, patents could not be filed, and academics would not be able to publish papers. Most importantly, the notebook should be a "live" document, written as you work.

Tips on how to keep a notebook and what should be included:

- The notebook should have an overall organised structure that can be clearly followed.
- Use the laboratory notebook to reflect on your work periodically, question your approach, write in comments about what you are thinking, different approaches you might take, and how subsequent results might be interpreted.
- A laboratory notebook is also important to provide information to somebody who may want to repeat your work. As such, it should be clear and legible.
- **The notebook should be hardback A4, with lines on the front and back pages.** Ideally the pages should be pre-numbered, and if they are not, number the pages in the top right hand corner. You should write in permanent ink (never pencil), and date each page.
- On the cover, write your name, lab and module name. Leave the first few pages blank, so that you can add a Table of Contents as you progress through the book, which will list the experiments (both successful and unsuccessful) you completed.
- Write on both left and right pages, with a clear consistent formatting throughout the book. It may be useful to use the right hand page for your 'neat' record and the left hand page for 'rough' notes. (Note that even rough notes should be clear and labelled with appropriate units if required).

- Do not remove pages from the notebook and do not use correcting fluid. If you make a mistake, draw a thin line through the work.
- Do not use the notebook for indecipherable notes to yourself– everything should be clear for somebody else to follow, including rough calculations and ideas.
- You should take your lab book with you as you go around the lab. It should be next to you at the balance so that you can enter your measurements directly as you go along. It should be next to you as you set up a reaction so that you can record any observations directly into it.

What to put in the notebook

- Your notebook should include (but is not limited to) the following:
- Start a new double page for each experiment; the top of the page should be dated, labelled with an experiment code (usually your initials followed by a number, *e.g.* JJ1) and a title.
- The aim of the experiment should then be stated. For synthetic projects, it is often appropriate to draw a reaction scheme here. If the work is based on information from a journal article, this source should be referenced under the scheme.
- Include in a tabular format (see Table 5 earlier) the reagents used (amount in g or cm^3/mL, concentration in mol, equivalents, density (if required) in g cm^{-3}, quality/purity). If you have already prepared a table with this information using Microsoft Word, it can be printed out and pasted in to your notebook instead of transcribing the information by hand. For the solvent, record the amount used and if anhydrous. Try to use the same number of significant figures for all quantities measured.
- List the apparatus (size, how it was cleaned, if dried in the oven- for how long and at what temperature?)
- You should write the method used in the passive voice and in the past tense (e.g. 50 cm^3 of methanol was added to…, The mixture was filtered under gravity, etc).
- Include reaction times, colours and appearance of reagents, water type used (deionised, distilled, tap…), solution strength, experimental observations (e.g. striking colour change, formation of a precipitate), sketches of TLC plates (indicating eluent, visualisation method and R_f values), instrument details, and anything else *you* would like to know if you were repeating this work.
- Include the outcome of the experiment in a short conclusion, even if it is negative.
- If repeating an experiment, make sure to note any deviations from the previous procedure – at least one full procedure should be provided however.
- For spectroscopic/chromatographic studies, include concentrations of analyte, solvent used for analysis, visualisation methods (e.g. UV, permanganate stain) and R_f values. Indicate whether the compound prepared contains any impurities.
- If an experimental set-up is unusual or new to you, a sketch of the apparatus is useful.
- Any calculations or numbers used in calculations (e.g. theoretical and actual yields) should be annotated correctly so that it is clear where the numbers you are using come from. Remember to check the number of significant figures you should have in your final answer. It is sufficient to show a detailed calculation for one set of data and then summarise the calculation and refer to where it has been provided in detail if it is repeated for similar sets of data.

Chemical safety information

Ensure that you include a table of the chemical safety information already compiled for the experiment in your lab notebook (see Table 6). If it was typed, it can be pasted into the lab notebook.

Appendix 6: Oral presentation guidelines

When preparing a presentation, take care to:

- Tailor the tone and content to the audience
- Be informative and interesting
- Keep to the appropriate timing
- Make slides simple and visually engaging

Figures 7 and 8 show sample presentation slides. Version 1 on the left in Figure 7 shows the common mistake of overloading slides with information. Remember you will be talking about the slides when they are shown and so can provide the additional detail then. Version 2 on the right expresses the same information, but the use of images and bullets makes it easier for the audience to take the information on board.

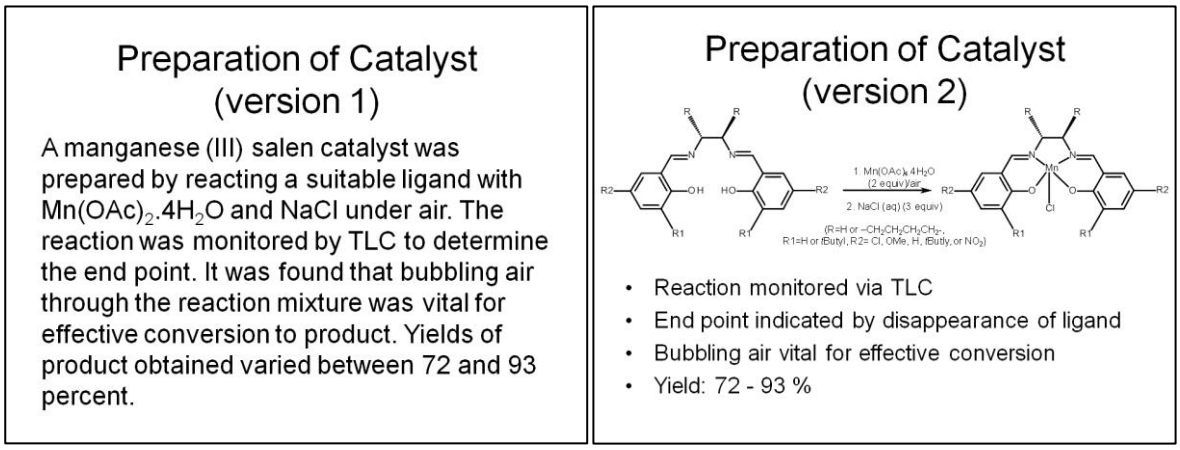


Figure 7: Dos and don'ts in slide preparation

As Figure 8 below shows, when you have chosen the best content for the slide, it is important to present it well. Ensure pictures are big enough and clear so that the audience can read the detail. Make use of the space available to you, and use a reasonable font size (preferably minimum size 20 in Arial).

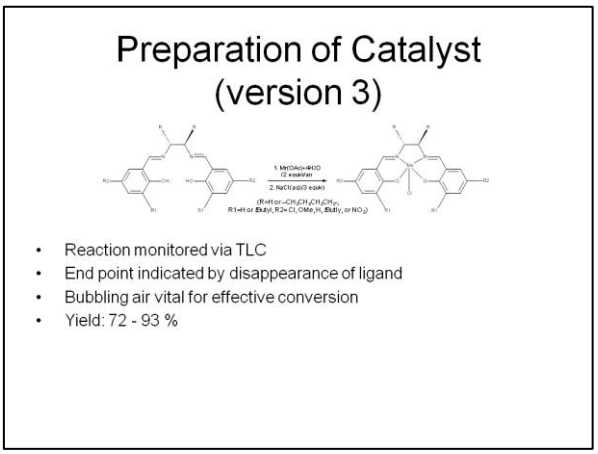


Figure 8: Poor use of slide space.

Remember to:

- Keep slides simple – large font, simple colours

- Bulletise text - aim for a maximum of 6 bullet points containing 6 words on average
- Pictures speak a thousand words, but make sure that they are clear and big enough
- Don't over use animations as they can be distracting
- Credit sources and provide references

It is important to carefully structure your presentation to ensure it flows well. Content can be split into three categories:

- Beginning - introduce topic on level suitable to audience
- Core - longest section covering key messages
- End - summarise results and emphasise main point

Plan your content carefully. It may not be necessary or possible to include all of the data you collected so be critical when choosing what to include. Too much information may cause you to overrun the time slot, and result in loss of marks or having to stop before you reach the final slide.

When delivering the presentation be sure to:

- Practice several times, preferably with an audience
- Check you can use the technology
- Be confident – make eye contact and try to smile
- Speak slowly and clearly
- Face your audience when you speak
- Avoid blocking the screen
- Stay calm - if you make a mistake or something goes wrong; you may be the only one who notices so take your time, correct the mistake, and move on.
- Take your time answering questions, and if you don't know an answer, just say so.

Useful resources:

- Key Skills for Scientists – Getting the Message Across, ed. Natalie Mansfield, Royal Society of Chemistry, 2007
- Effective Communication for Science and Technology, Joan van Emden, 2001, Palgrave, Hampshire (Chapters 6 & 7)
- Chapters 11 and 12 of Study and Communication Skills for the Chemical Sciences, Tina Overton, Stuart Johnson, Jon Scott; Oxford University Press, Oxford, 2011.

Appendix 7: Plagiarism

Plagiarism is not acknowledging the work of others. Therefore, all work which is not of your own creation must be accompanied by a reference which gives a detailed description of the item from which you have obtained information (e.g. article, website, book).

Important things to remember:

- Make sure that you acknowledge any information that you obtain from a particular source by including a reference.
- You should not reproduce information word for word from a reference even when you have acknowledged the source. The only exception is for a quotation, however direct quotations should be used sparingly. You are expected to communicate the information in your own words.
- Failure to meet these requirements means you have plagiarised work. This is the same as stealing someone else's work.
- If you are found to have plagiarised material, marks will be deducted.
- References should be formatted according to the Royal Society of Chemistry Publishing author guidelines format. (See page eleven of the document at this link: http://www.rsc.org/images/Guidelines_tcm18-186308.pdf)

Useful resource:

- Study and Communication Skills for the Chemical Sciences, Tina Overton, Stuart Johnson and Jon Scott, 2011, Oxford University Press, Oxford (Chapter 10)

Appendix 8: Guidelines for an executive summary

An executive summary provides an overview in non-specialist language to an executive/management audience. It is generally about one tenth the length of the whole report, and is directed at managerial readers who may not read the whole report, and who may not have the relevant technical knowledge.

The purpose of an executive summary is:

- To provide the reader with a shortened version of a report to allow them to identify the key information quickly.
- To act as a navigational tool for the report. An overview should help the reader to understand and access the more detailed information in the main body of the report.
- To help the reader to decide whether they need to read the whole report.

Common difficulties when preparing an executive summary are:

- Deciding on core information.
- Linking the information into a coherent piece of writing that stands alone and is clearly written and structured.

The summary should be organised under descriptive headings highlighted in bold. It should be formatted with consideration for fast accessibility of information and the convenience of the reader. The structure should follow that of the body of the report and non-technical terms should be used as far as possible. No tables or figures should be used. Do not forget to mention whether any further / recommended work is required.

Use the brief provided from the company asking you to carry out this work to help you to decide on the important information to be included. You may find it helpful to prepare your executive summary in the format of a letter in response to that sent by HugePharma Ltd. originally which outlined the work that was required. This format is acceptable once this executive summary letter includes the components listed below.

You should make sure that you have included:

- A statement that places the work in context
- The method used (summary of synthetic steps in 1-2 sentences)
- The main results
- The main conclusions
- Your main recommendations

The information above on writing executive summaries has been sourced from;

Chapter 3 of *Writing For Science and Engineering* by Heather Silyn-Roberts, Butterworth-Heinmann, Oxford, 2000.

Appendix 9: Guidelines for your reflective piece

In this short report (500 to 800 words approx), you should:

1. Briefly describe your role in the project and the contribution you made.
2. Discuss how you experienced working in a team (consider both the positive and negative aspects).
3. Discuss any changes that you would make to how you and your group went about the project if you were repeating it.
4. Summarise what you found to be most the interesting aspect of the project as well as the most challenging aspect.
5. Consider whether you think the project was useful to your learning and whether all of the learning outcomes (see page 8) were met.
6. Assess whether you have developed the transferable skills listed on page 9 further as a result of this project. Highlight any that you think are particularly important or that you have now gained confidence in.
7. Consider whether you have found that writing a reflective piece like this helps you to review what you learned over the course of the project.

This reflective piece is assessed based on:

- **content** (60% - there are no right or wrong opinions but you must make sure that you discuss **all** of the topics listed above)
- **presentation** (10%) and
- **coherence, accuracy and structure** (30%).

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