Learn Chemistry

Quanticorp R&D: New Products For the Future

Tutor Guide

Developed by Hywel Evans

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QUANTICORP R&D: NEW PRODUCTS FOR THE FUTURE

Contents

HOW TO USE THE RESOURCE

This problem based learning resource is intended for level 6 undergraduate students on BSc Chemistry or related programmes of study. The resource can be adapted to suit the subject knowledge of the students.

The resource is divided into a number of parts which can be used in whole or in part. Some parts give detailed guidance to students whereas others are less prescriptive. However, the resource can be easily adapted to make it more open-ended by omitting some of the student guidance.

The activities contained within the resource require that students study and use material from journal articles. In particular, it is necessary to secure access to the following articles:

1. M. Gerard, A. Chaubey and B.D. Malhotra. Application of conducting polymers to biosensors. *Biosensors & Bioelectronics,* 2002, 17, 345–359.
2. Scherman, O. A., Rutenberg, I.M., and Grubbs, R.H.Direct Synthesis of Soluble, End-Functionalized Polyenes and Polyacetylene Block Copolymers. *J. Am. Chem. Soc*, 2003, **125**, 8515.
3. Moorhead and Wenzel. Two Undergraduate Experiments in Organic Polymers: The Preparation of Polyacetylene and Telechelic Polyacetylene via Ring-Opening Metathesis Polymerization. *J. Chem. Ed*., 2009, **86**, 973.
4. Knoll, K., and Schrock, R., *J. Am. Chem. Soc*., 1989, **111**, 7989.

The resource contains one part which contains laboratory work, however, sample results are provided so the tasks can be undertaken without access to lab facilities.

It is assumed that the tutor has a good grasp of undergraduate chemistry subject knowledge, however, detailed tutor notes are provided which should be used judiciously to support student learning. **The tutor notes are identifiable as red text**.

The following narrative summarises the rationale behind the operation of each part of the resource.

Part 0: New Products for the Future

An e-mail is sent to students to set the scene. The scenario is that the students are employed as development chemists in the R&D department of QuantiCorp, a company which makes immunoassay test kits but wishes to diversify, and they must do some research into prospective new products based on conducting polymer sensors. Students are divided into teams and directed to commence the tasks for Part 1.

The aim and objectives are contained in the e-mail but can be re-iterated after students have had a chance to digest it, as follows:

Aim
To undertake a feasibility study on the possibility of developing a glucose sensor based on conducting polymers.

Objectives

- Prepare a presentation for the Chief Executive on the feasibility of developing a glucose sensor based on a conducting polymer
- Complete an in-depth feasibility study by undertaking background research and laboratory investigations
- Prepare and present a technical summary of the feasibility study for the Head of R&D

Part 1 Getting Started

In this part, students are directed to complete two tasks. Task 1.1 is to make a simple electronic humidity sensor in order so that they can understand the basic principle of sensor operation, with which they may not be familiar; however, this task can be omitted if the resources are not available. Task 1.2 is a literature based activity wherein students must research and summarise a review article on conducting polymer sensors which should give them a basic overview of the field.

Part 2: Presentation

Using the information they have gathered in Part 1, students should now prepare an 'elevator pitch' style presentation for the Chief Executive. In order to facilitate this it is suggested to use the *Message Box* tool which gives a simple framework for structuring the presentation. There are two objectives here: to focus on the important issues using the *Message Box*; and to get students to think about how they should pitch their presentation in a commercial, rather than a purely science oriented, way for the benefit of the Chief Executive.

Part 3: Conducting Polymers

At this point it is necessary to direct the students towards a specific line of inquiry, namely the development of a glucose sensor based on the conducting polymer polyacetylene. It is possible to use other sensor/polymer combinations and adapt the resource to suit, however, the laboratory work is based around synthesis of polyacetylene.

A **problem solving strategy** based on the creative problem solving approach is introduced wherein the students should be encouraged to plan their approach (Task 3.1) and gather the necessary information before attempting to solve the problem. Tasks 3.2 and 3.3 are designed to direct the students to use Wikipedia in the right way - as a quick way to gain an overview and identify key concepts which can then be used as search terms for the primary literature. At the end of this process, the students should now have a method for synthesis of end functionalised polyacetylene, using the Grubb's second generation catalyst, from cyclooctatetraene and a chain transfer agent.

Part 4: Synthesis of Polyacetylene

In this part students are asked to consider how to investigate the synthesis of en-functionalised polyacetylene using the ROMP of COT reaction with Grubb's second generation catalyst. They should be able to easily summarise a suitable procedure using the two papers provided but they are also asked to consider how to investigate the reaction conditions, stoichiometry, structure and conductivity of the product. The students should be allowed a free hand in this because Part 5 gives the opportunity

for the tutor to intervene as much or as little as he/she wishes in the experimental design.

Part 5: Synthesis of Polyacetylene

Here, students are asked to design the experiment. Comprehensive tutor notes are provided to enable the tutor to give advice on the various aspects of the design as follows:

(a) Overall reaction scheme - this should not present a problem.
(b) Investigate the yield – the tutor can give as little or as much guidance on this as he/she feels appropriate, however, the two papers give in Part 4 should provide sufficient information.
(c) Apparatus and special requirements – the use of the equipment to maintain an inert gas atmosphere will probably require advice from the tutor.
(d) Reagents and special requirements – this should not pose a problem except that it may be necessary to specify **dry** reagents. **NB: One of the reagents must be synthesised beforehand.** A method is described in the tutor notes for this part.
(e) COSHH – this should not pose a problem; a blank COSHH form is provided but tutors will probably have their own version.

An **optional handout** *STUDENT NOTES FOR TASK 5.1* is provided if the tutor does not wish to allow students to design their own experiment.

Part 6: Synthesis of Polyacetylene

In this part the actual laboratory synthesis is performed using the procedure designed by the students. Some of the practical elements may require tutor guidance and tutor notes are provided for this purpose.

Part 7: Synthesis of Polyacetylene

Having prepared the polymer students must now perform the analysis using UV-vis, NMR and FT-IT spectroscopies. This part of the lab activity can be tailored to suit the instrumental facilities available, however, the end-functionalised polyacetylene should be soluble in dichloromethane so can be analysed using instrumentation in most chemistry laboratories.

If either Part 6 and/or Part 7 cannot be preformed then the sample data given in Resource 7.1 can be used.

Part 8: Reporting

Students should produce a report of their synthesis and subsequent analytical investigations. The report is intended to be an assessed element which requires students to interpret their results, critically evaluate them, compare them with data from several related papers, retrieve and summarise information from the primary literature and the internet.

The report could be used to satisfy the following assessed learning outcomes with suggested assessment criteria:

Learning Outcome		Assessment Criterion
Knowledge and Understanding		
	Inorganic Chemistry	Overall quality of discussion and extent of additional reading
Laboratory Skills		
	Observation and record keeping	Quality and presentation of NMR, UV-vis and IR spectra
Problem Solving		
	Working on problems	Molar ratios of reactants
	Working on problems	Discussion of effect on yield
	Working on problems	Calculation of theoretical yield
	Working on problems	Calculation of double bonds by: NMR Woodward-Fieser rules HOMO-LUMO transition
	Working on problems	Calculation of cis/trans ratio from IR
Communication		
	Report writing	Correct structure with tables and figures correctly captioned and references correctly cited.
	Information search, retrieval, assessment and use	Use and reference to papers by: Schermann & Grubbs (2001) Scherman et al. (2003) Knoll & Schrock (1989)
		Summary of the effect of iodine doping on conduction

A comprehensive model answer is provided in the tutor notes for assessment and feedback purposes.

Part 9: Conjugation

This part of the project requires the students to investigate how to make the conducting polymer selective for a particular analyte.
In Task 9.1 they are asked to reconsider their initial research from Task 1.2 and also the requirements for selectivity in a sensor by considering the IUPAC definition and some examples of how this can be achieved. The last activity is a link to an article on the enzyme glucose oxidase, however, this can initially omitted to allow a discussion about the ways in which selectivity can be introduced (enzymes being an effective means), and the article introduced subsequently.

Task 9.2 is meant to be a revision of knowledge of functional group chemistry which forms the basis for understanding conjugation reactions, and which is most suitable for conjugation of the enzyme glucose oxidase. The simple answer required here is that it can form a peptide bond at the C- or N- terminus; in reality this is not such a simple reaction to perform under these conditions and requires the use of an activating agent, however, this level of detail is not required to achieve understanding of the basic principle.

Part 10: Conjugation

This part addresses how the polyacetylene can be synthesised to contain appropriate functional groups to allow conjugation of the glucose oxidase enzyme.
Task 10.1 requires students to research conjugation reactions on the internet. The objective is to find a conjugation reaction which will allow conjugation of the C- or N-terminus functional group on the enzyme with an appropriate end-functional group on the polymer. The polymer which they have synthesised contains *tert*-butyldimethylsiloxane functional groups, which will not conjugate with either the C-C or N- terminus on the enzyme. *tert*-butyldimethylsiloxane is an alcohol protecting group, so it may be possible to modify the polymer synthesis to include the trimethylsilyl chloride instead, which is a protecting group for –COOH. This can then be de-protected and conjugated with the N- terminus of the enzyme.

Part 11: Report to the R&D Team Leader

This is the final task, and can form the basis for a second assessment. This can be in the form of a 10-15 minute presentation or a final report.
A powerpoint presentation framework has been provided which can be adapted by the tutor for a plenary session.

Suggested Timetable

Part	Description	Format	Miniumum duration (min)
	Part 0: New Products for The Future		
0	Student Scenario	E-mail sent to students divided into groups	
	Part 1: Getting Started		
1.1	Building a humidity sensor	Student centered practical activity	60
1.2	Using the literature	Student centered library activity	90
	Part 2: Presentation		
2.1	Prepare an elevator pitch	Tutor led activity	30
2.2	Three minute presentation	Tutor led activity with student and tutor feedback	60
	Part 3: Conducting Polymers		
3.1	Planning		30
3.2	Research using the internet	Student centred activity but may require some tutor supervision	30
3.3	Research using the primary literauture	Student centered activity with tutor feedback	30
	Part 4&5: Synthesis of Polyacetylene		
4.1	Using the literature to develop a synthetic method	Tutor led but student centered with tutor feedback	120
5.1	Design an experiment	Student centred with tutor feedback	120
	Part 6: Synthesis of Polyacetylene		
6.1	Laboratory synthesis of polyacetylene	Tutor supervised but student led	180
	Part: Synthesis of Polyacetylene		
7.1	Laboratory investigation of product	Tutor supervised but student led	180
	Part 8: Synthesis of Polyacetylene		
8.1	Reporting	Student centred activity. Tutor guided and assessed.	180

Part 9: Conjugation			
9.1	Research into selectivity of the sensor using the internet	Student centered activity with tutor feedback	120
9.2	Revision of functional group chemistry and conjugation reactions	Student centered activity with tutor feedback	60
Part 10: Conjugation			
10.1	Modify synthetic procedure to allow conjugation of the sensing molecule.	Student centered activity with tutor feedback	60
Part 11: Report to the R&D Team Leader & Plenary			
11.1	Technical summary of investigation	Student oral or written report	120
	Plenary session	Feedback from tutor	30

QUANTICORP R&D PART 0: NEW PRODUCTS FOR THE FUTURE

You are employed as development chemists in the R&D department of QuantiCorp, a high-tech company based in California which manufactures dipstick immunoassay pregnancy test kits. The Chief Executive has decided that it's time to diversify into new areas in order to grow the business and is asking the R&D department to come up with some possible areas for development. A scoping exercise has come up with the possibility of developing a glucose sensor based on conducting polymers. In order to get the best ideas the Chief Executive has decided to split you up into a number of competitive teams to investigate the feasibility of this idea. She wishes to hear your ideas upfront before allowing you undertake a feasibility study. After the feasibility study you will have to report back to the Head of R&D and the best study will be adopted and rewarded with a salary bonus.

TUTOR NOTES FOR SCENARIO

1. E-mail the students with the scenario prior to the first session. At the same time divide them into teams of four.
2. If you wish you can attach the instructions for Part 1 and require students to complete Tasks 1.1 and 1.2 in preparation for Part 2. The advantage of this is that, because Task 1.1 requires access to a set of electronic components, you can allocate times when the students have access to the resource, whereas if you run it as a whole group session then you will need one set for each team.
3. The aim and objectives are contained in the e-mail but can be re-iterated after students have had a chance to digest it, as follows:

Aim

To undertake a feasibility study on the possibility of developing a glucose sensor based on conducting polymers.

Objectives

- Prepare a presentation for the Chief Executive on the feasibility of developing a glucose sensor based on a conducting polymer
- Complete an in-depth feasibility study by undertaking background research and laboratory investigations
- Prepare and present a technical summary of the feasibility study for the Head of R&D

QUANTICORP R&D PART 1 GETTING STARTED

You have just been sent a memo with instructions to present your idea to the Chief Executive for consideration by the end of the week. Panic sets in as you realise that you know nothing about electronic sensors, let alone conducting polymers. Luckily, however, the daughter of one of your team members has just completed a high school science project which looks like it might be of interest and she has agreed that you can use it for training purposes.

Task 1.1 – getting up to speed (60 min.)

Open **Resource 1.1**. Read the instructions for building a simple humidity sensor using the materials supplied. Assemble the sensor and perform the following tests:

Adjust the sensitivity until the LED alarm responds to the humidity of human breath

Wet your index finger and hold it near the sensor without touching so that the LED alarm responds.

Task 1.2 - using the literature (90 min.)

You had some fun with the science project and got the LED to light up in the face of your breath, but now you have to start considering the science in more depth. Open and read the paper by **Gerard *et al*.**[1], and answer the questions below.

1. How could you make this sensor respond to chemicals other than water?
2. How could you make the sensor more specific for the detection of a particular chemical?
3. What are the potential applications for these types of sensor?

When you have finished collate the information.

[1] M. Gerard, A. Chaubey and B.D. Malhotra. Application of conducting polymers to biosensors. *Biosensors & Bioelectronics,* 2002, 17, 345–359

RESOURCE 1.1: SCIENCE PROJECT: A SIMPLE WATER SENSOR

by
Amy V. Clever

(adapted from M. J. Sailor, Water Sensor Experiment, UCSD NanoLab, University of California, San Diego)

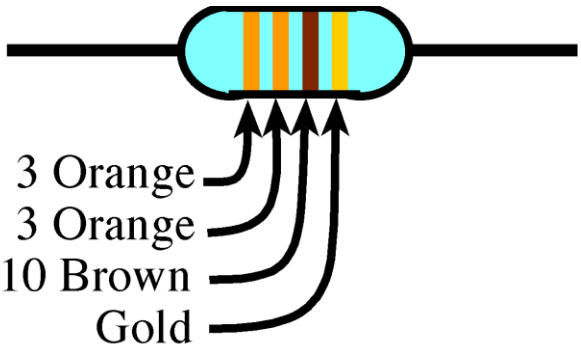
Equipment

9 V Battery
Battery clip
100 kΩ resistor (Brown)
330 Ω resistor (Blue)
npn transistor (2)
red LED
30 pF capacitor (water vapor sensor-see text)
100 kΩ variable resistor
plug-in board
Manual range digital multimeter
Assorted wires

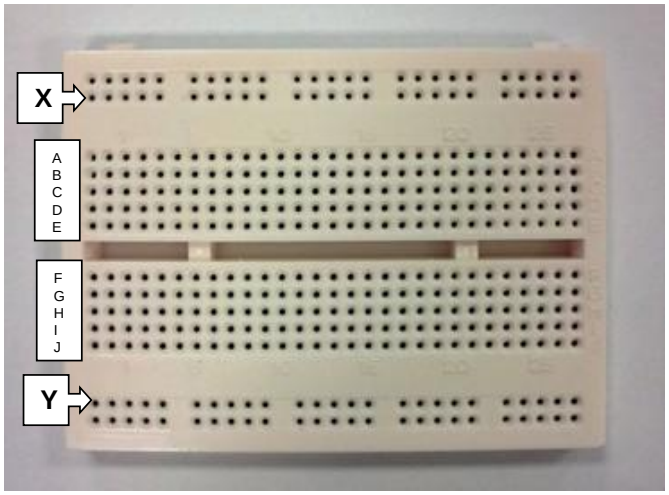
Measuring Resistance

Test the resistance of your skin with the multimeter set to '2000 k' on the **Ω** resitance setting). Now hold the the metal tip of the black probe between the thumb and forefinger of one hand and the metal tip of the red probe in the other. Your skin resistance should read around 500-1000 kΩ. Your skin resistance is therefore between 500,000 to 1,000,000 Ω. If your skin is dry it will register higher; if it is moist you will get a lower reading. This is the principle on which police 'lie detector' tests operate. The lie detector assumes that if you are lying you will sweat, causing the reading to change to a smaller value.

Now test the resistance of the resistors supplied in your kit. The resistors have a color code painted on them in a series of stripes so that you can easily identify their values without having to measure them. The first color band is the tens place, the second color band is the ones, and the third band is called the multiplier. The fourth color band is called the tolerance (it's like the quality of the device), which you can ignore. So the resistor pictured right is orange-orange-brown and should be 3 + (3 x 10) or 330 Ω. When you measure this resistor with your multimeter set to '2000 Ω' it should read pretty close to 330 Ω. The other resistor in your kit (the brown one) has a resistance of 100 kΩ. The color code is: brown = 1, black = 0, and yellow = 10,000.

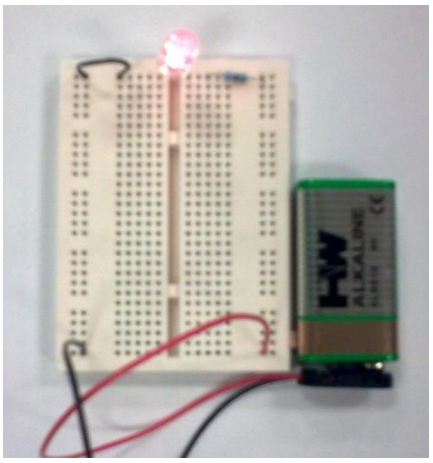


The plug-in board



The plug-in board allows you to connect all the components together. It is wired as follows: all holes in row X are connected together and all holes in row Y are connected together. Each individual column of five holes are connected together. Rows X and Y will be used to supply power from the battery. Each column consists of 5 holes, which are all connected to each other. If you plug something into column 1-D, you can connect it to something else by putting a wire into column 1-A, 1-B, 1-C, or 1-E.

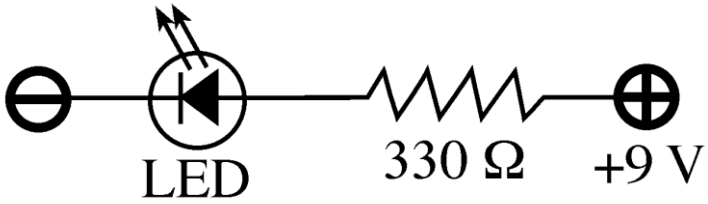
Experiment #1 Wiring up a Light-Emitting Diode (LED)



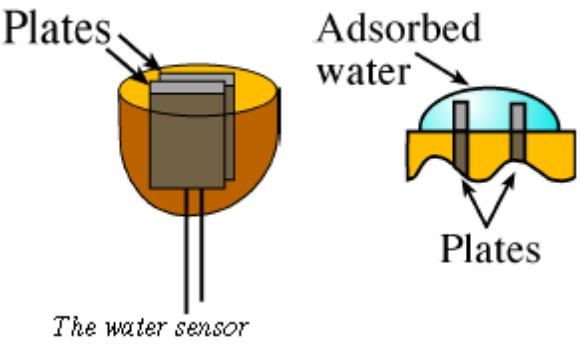
In this experiment you will test how the plug-in board works by lighting up the red lamp provided. It is referred to as a "light-emitting-diode" or LED.

1. Attach the battery clip to the 9V battery then plug the red wire into row X and the black wire into row Y.
2. Plug in the 330 Ω resistor to pinholes 1-X and 1-C.
3. Plug in the LED to holes 1-E and 1-F (longer of the 2 wires should be in 1-F)
4. Plug in the black jumper wire from 1-I to 1-Y

Does the red light come on? If not, you plugged in the LED backwards. The long wire from the LED should be in hole 1-F,not 1-E, which is because a Diode only lets electricity flow in one direction. We say it has a "polarity" because you have to pay attention to which side goes to (+) and which to (-) on the battery. In this last experiment, the resistor was needed to resist the flow of electricity. If you don't use it, too much electricity flows through the LED, causing it to burn out. The resistor is called a "current limiter" because it limits the flow of current, or electricity, in the circuit. The diagram for the circuit you just built is as follows:



Experiment #2 A Water Vapor Sensor

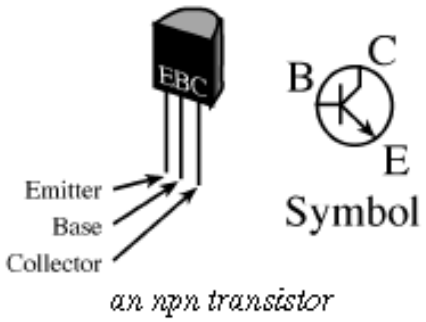


The water sensor

The water sensor. In this project you use a transistor to amplify the signal from the humidity (water) sensor. The humidity sensor works by electrical conductivity; when water vapor condenses on the plates it forms a thin film that conducts electricity between the two plates. In that sense the water sensor is like a resistor except that its resistance value changes depending on the amount of water in the air. It was made by clipping the top off of a 30 pF capacitor using a pair of wire clippers.

Transistor.

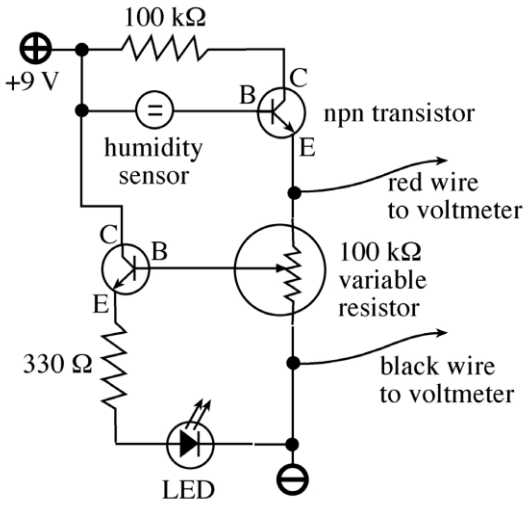
A transistor is an amplifier that will convert the very small change in resistance from the humidity sensor into a larger resistance change that you will measure with your voltmeter. It has three connections; the collector, the base (also called the gate), and the emitter. The collector and the emitter are like the connections to a pipe that carries water, and the base is like the faucet. Ordinarily the base is closed and the resistance between the collector and emitter is very large. When a small voltage is applied to the base, it reduces the resistance between the collector and the emitter, allowing current to flow. Your kit contains a transistor which is marked with the letters E, B, and C, which stand for emitter, base, and collector, respectively.

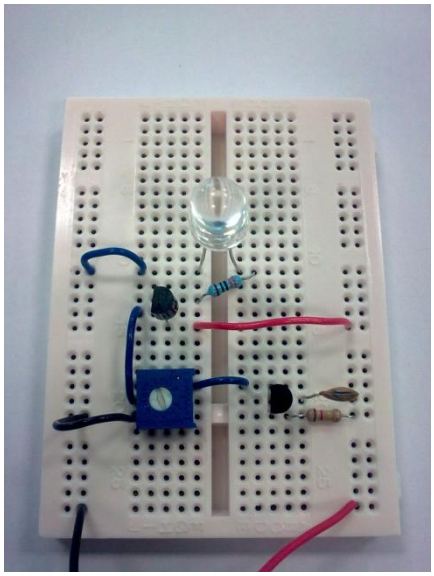


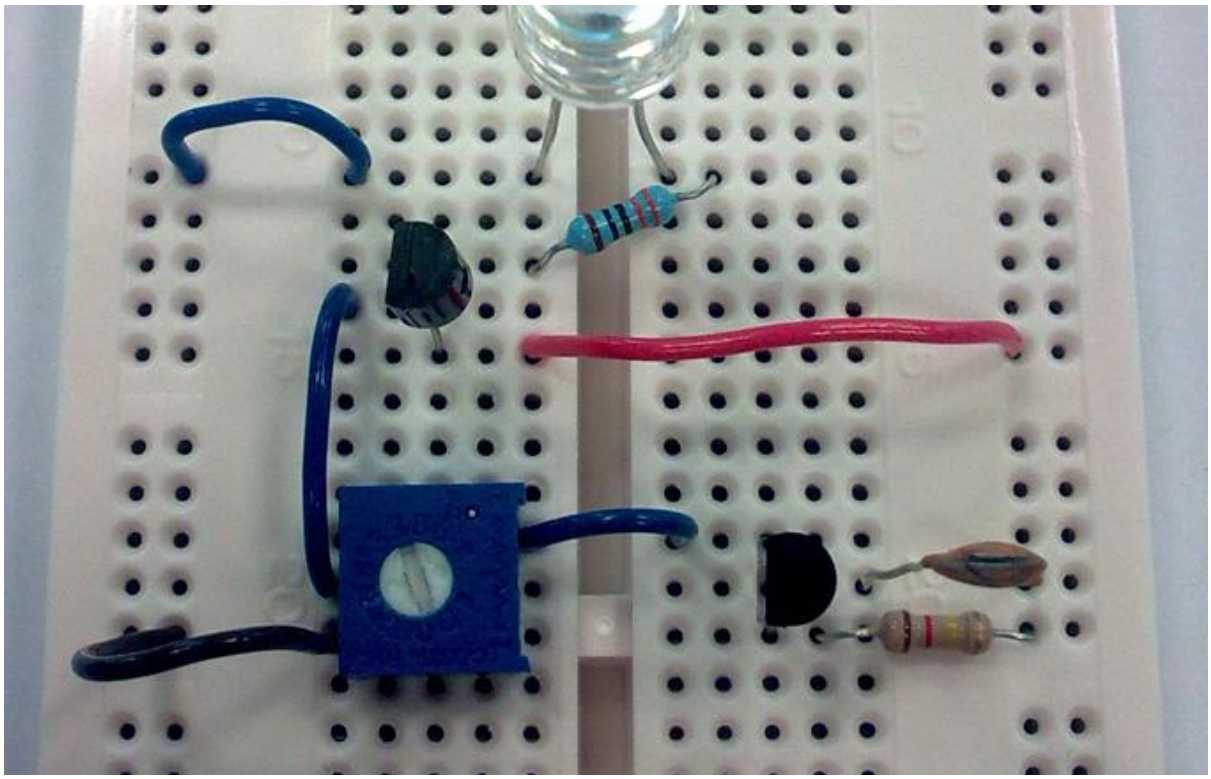
an npn transistor

Wiring up the water sensor

In this part of the experiment, you will create a water vapour sensor with a red LED in the circuit as an over-limit alarm. The LED will light up when the sensor detects a high amount of water vapor. The circuit diagram is shown below, along with a photograph of the circuit.

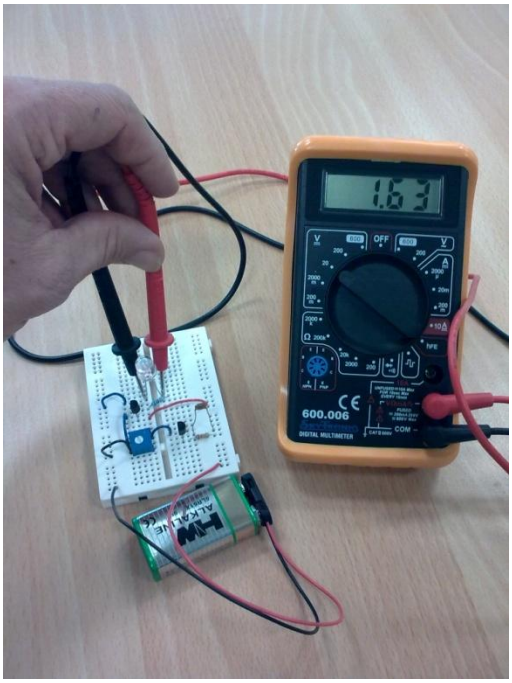






The voltage signal output from the first transistor is sent to the gate of the second transistor. The circuit also incorporates a 100 kΩ variable resistor which allows you to set the threshold level for the over-limit alarm. This circuit is sensitive enough to detect the water vapor on your breath, and can even detect the water evaporating from your skin. If you place your finger close to the sensor without touching it the red light should come on. You will be able to adjust the threshold level where the red light comes on by adjusting the dial on the variable resistor using the paperclip provided. If you find that the red light stays on gently rub the surface of the sensor with some tissue paper to get rid of excess moisture.

You can also measure the voltage reading by touching the probes of the multimeter to the base of the LED legs as shown. You should notice a small change in the voltage reading when you breathe on the sensor.



TUTOR NOTES FOR TASK 1.1

Task 1.1 requires access to some simple electronic components as described in Resource 1.1. These can be obtained from any electronics supplier for relatively little cost.

The activity has trialled both a directed learning and whole group session, and each work quite well.

The following points should be noted:

1. the sensing capacitor will become contaminated after a time so should ideally be freshly prepared;
2. depending on any contamination on the capacitor, it will be necessary to set the variable resistor at the correct resistance otherwise the LED will not respond sensitively.

TUTOR NOTES FOR TASK 1.2

Again, this task can be performed as either a directed learning or whole group session. The reference by **Gerard *et al*.**[2], can be made available on your VLE or as hardcopy during a whole group session.

[2] M. Gerard, A. Chaubey and B.D. Malhotra. Application of conducting polymers to biosensors. *Biosensors & Bioelectronics,* 2002, 17, 345–359

QUANTICORP R&D PART 2: PRESENTATION

Task 2.1 Preparing a presentation for the Chief Executive (30 min)

Your next task is to prepare a presentation for the Chief Executive (CE). She is a busy woman and you will be up against the other teams in the R&D department who want their ideas to be taken on, so you have only five minutes to convey the key information. This is called an 'elevator pitch', so you need to make sure that you get across key points of relevance to the CE. To do this you are going to use a tool called the 'Message Box' (**Resource 2.1**):

Issue

Write down the issue that you need to address, e.g. 'developing capability to produce a new sensor based on conducting polymers'.

Problems

What are the main problems that you expect to encounter when addressing the issue?

Solutions

What are the possible solutions to the problems?

Benefits

Assuming that you are successful what are the direct benefits of your idea, e.g. scientific and production outcomes.

Relevance to audience

In this case the audience will be the Chief Executive so you have to tell her what relevance this has the company's strategic vision and bottom line.

You now have the basic information for a short (**3 min**) presentation which you will present to the Chief Exec.

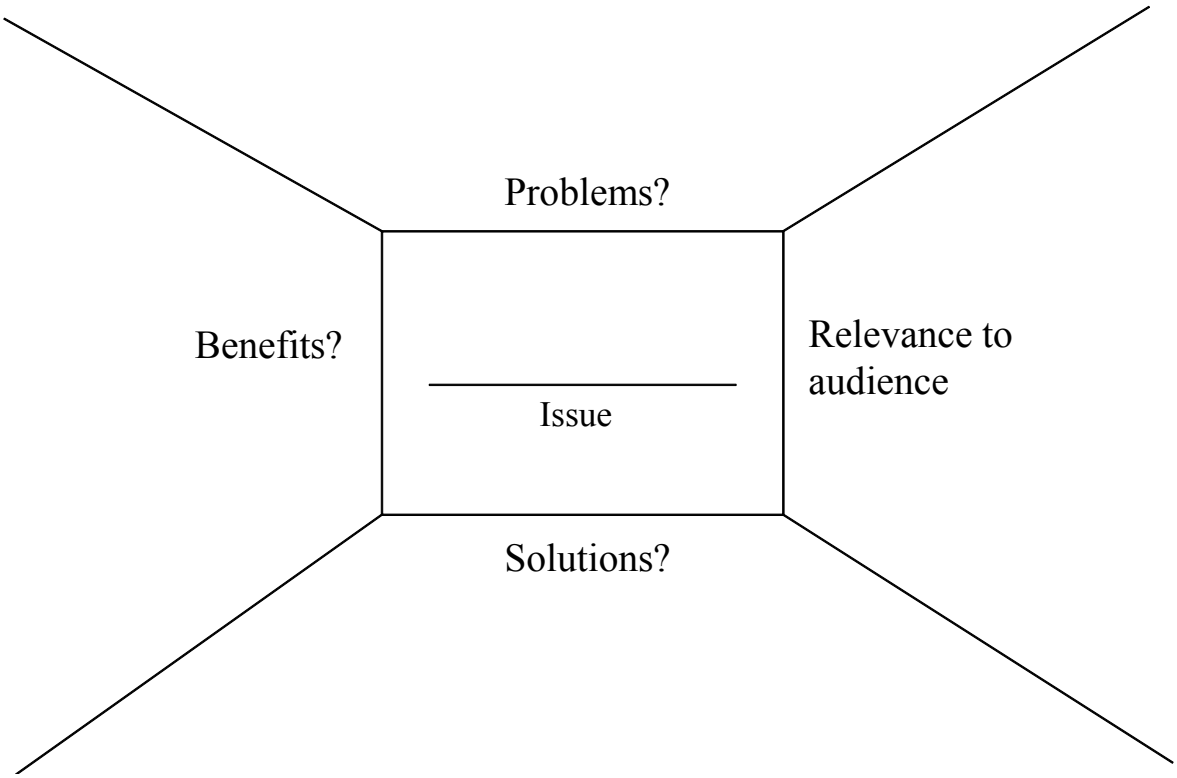
Task 2.2 – presentation to the Chief Executive (60 min)

You have 3 minutes to present your idea to the C.E. Each member of the team should address one of the points in the message box. Remember, your pitch should be clear, concise and coherent, and directly address your remit.

RESOURCE 2.1

Message Box:

Take a few minutes to fill in a one-sentence description of the issue and four supporting facts/arguments which answer the listed questions.



TUTOR NOTES FOR TASK 2.1

The teams should have all the information they need in order to complete this task and the tutor should not intervene at all other than to explain the purpose of the message box.

The message box (see powerpoint presentation 'Message Box.pptx' for a blank copy and a completed example) is a simple way of focussing on the main points of an issue:

Issue: Write down the issue that you need to address. In this case, the issue is for a team to develop a sensor which will be marketed by the company as a new product. Students may wish to target the product at a particular market such as healthcare.

Problems: Write down the problems associated with resolving the issue. Teams should list the technical problems that they will face in development.

Solutions: These will be technical solutions associated with the development of the sensor and a potential market niche that the sensor will occupy.

Benefits: Technological advantages afforded by the sensor, such as sensitivity, unattended operation, low cost etc.

Relevance to audience: Benefits to the company resulting from the technology that is being developed, such as entry into a new market, taking market share from competitors, increased profitability etc. (this will be necessarily somewhat fictional because students do not have access to market research).

The teams should be put under time pressure to keep them on task; **30 minutes** should be sufficient. A variety of online stopwatches can be accessed here. http://www.online-stopwatch.com.

One method which works well is to give each team a piece of flipchart paper and pen so they can bullet-point the outcomes of their message box and use it as a prompt during the presentation.

TUTOR NOTES FOR TASK 2.2

The following method has been trialled and seems to work quite well. Before you start, hand out post-it notes to each team (enough to make comments for all the other teams) and write a list of team names as column headings on the whiteboard. Now give them the following instructions:

1. each team will have a maximum of 3 minutes to give their pitch – this should be timed by the tutor;
2. after a pitch the other teams will have 1 minute to write down **three** good points and **one** area for improvement about the presentation they have just seen;

3. when all the pitches have been presented teams will stick their post-its under the relevant team names on the whiteboard;
4. after all the post-its have been posted teams can collect the feedback for their team.

TUTOR FEEDBACK FOR PART 1

As well as the receiving feedback from other teams in the form of post-it notes the tutor should discuss the following points with the students:

Did the teams address the remit as given in the original e-mail? It states that '*A scoping exercise has come up with the possibility of developing a glucose sensor based on conducting polymers*.' Providing the tutor has not brought attention to the original e-mail during the message box exercise, it is likely that some teams will report on the feasibility of a sensor for an analyte other than glucose!

Was the message clear, coherent and concise? The skill is to develop a message which addresses the key points of the task that they have been set within the 3 minute time limit. Common mistakes are:

- Not using the full 3 minutes
- Lack of clarity
- Going over the 3 minutes (less likely)
- Lack of focus on the message box key points
- Lack of coherence in the presentation, such as not having a clear idea of the sensor that they wish to develop and its technological benefits.

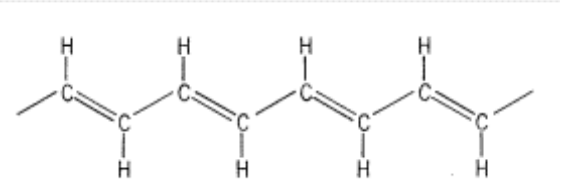
Was the message relevant to the audience? Teams are addressing the Chief Executive who will ultimately want to know if their idea will end up benefitting the company. The students will have no way of knowing this, but they should address this point in the presentation.

QUANTICORP R&D PART 3: CONDUCTING POLYMERS

Market research has identified the following area where there is a market niche:

- A glucose sensor

You initial research has identified the conducting polymer polyacetylene (1) as a possible basis for this type of sensor.



1

You now need a problem solving strategy to guide you in the development. A simple but powerful framework is given below.

1. Identify the problem and decide what you want to achieve:
    a. identify a conducting polymer for development into a sensor;
2. Plan how you want to proceed.
3. Establish what you already know, what you don't know and what you need to find out:
    a. research into synthetic methods;
    b. functionalization of the polymer;
    c. synthesis of the polymer;
    d. conjugation with a sensing molecule;
4. Come up with some solutions, alternative approaches and new ideas
5. Critically evaluate your solutions and decide whether any of them solve the problem
6. Repeat 3-5 as many times as necessary

Task 3.1 – Planning (30 min)

You have been given a specific problem but before going any further you should decide on a plan of action. In your plan you should decide:

- Who will do what
- How the team will communicate and share information
- How often and where you will meet
- A framework and process for solving the problem (it is suggested that you use the framework given above)

Task 3.2 – Research into synthetic methods (30 min)

Your laboratory is equipped with basic laboratory equipment for undertaking synthetic organic chemistry but you only have a limited budget and need an answer quickly . . . so you resort to Wikipedia http://en.wikipedia.org/wiki/Polyacetylene

Answer the following questions and copy the trail of Wikipedia links into the grid below (the first one has been done for you and make sure that you only copy words which are links to another page). You will need to read the whole text of the entries and click forward and back between some of them in order to get all the answers and links:

1. What is the name of the compound most commonly used to prepare polyacetylene?
2. What is the most common synthetic route?
3. What is the name of the catalyst used in this polymerisation method?
4. What will this catalyst tolerate?

polyacetylene

Now go to Google Scholar http://scholar.google.co.uk and enter the text of the links into the search bar.

Within the top ten hits there should be a relevant article by Scherman *et al.* published in 2003 in the *Journal of the American Chemical Society*. Download the full text.

Task 3.3 Functionalization of the polymer (30 min)

Refer to the article you downloaded in Task 3.1 and extract the following information:

1. Outline the reaction scheme for the production of telechelic polyacetylene with functionalized ends by using a chain transfer agent;
2. State the main advantage of the particular catalyst used;
3. Give the structures of the different CTAs that were used.

TUTOR NOTES FOR TASK 3.2

This task is designed to give the students an easy route in to the extensive literature on Ring Opening Metathesis Polymerisation (ROMP) reactions by using Wikipedia to make a list of keywords which they can use to search the literature. They should populate the grid as shown below:

polyacetylene	cyclooctatetraene	ring opening metathesis polymerisation
Grubb's catalyst	functional groups	

Searching on the string

polyacetylene cyclooctatetraene ring opening metathesis polymerisation Grubbs catalyst functional groups

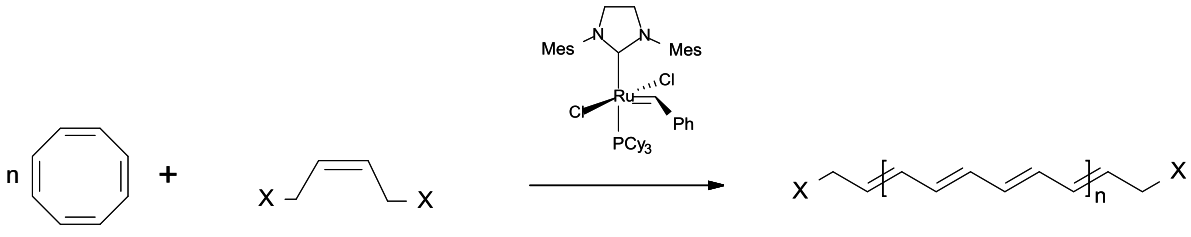
should result in a number of articles of which the most relevant is:

Scherman, O. A., Rutenberg, I.M., and Grubbs, R.H.Direct Synthesis of Soluble, End-Functionalized Polyenes and Polyacetylene Block Copolymers. *J. Am. Chem. Soc*, 2003, **125**, 8515.

In this way they have used Wikipedia, a resource which, while far from authoritative, is a convenient way to gain an overview and list of keywords which can then be used to quickly access the peer reviewed scientific literature. Google Scholar is an very good search engine for this typee of activity and is better than Web of Knowledge at returning relevant articles.

TUTOR NOTES FOR TASK 3.3

The reaction scheme for ROMP of COT with a CTA is given in Scheme 2 from Scherman *et al*.[3] (*J. Am. Chem. Soc*, 2003, **125**, 8515):



2 **5** **1** **4**

[3] Scherman, O. A., Rutenberg, I.M., and Grubbs, R.H.Direct Synthesis of Soluble, End-Functionalized Polyenes and Polyacetylene Block Copolymers. *J. Am. Chem. Soc*, 2003, **125**, 8515

The main advantages of the Grubb's 2nd generation catalyst (1) used here are that it has a high degree of functional group tolerance and it can be used to polymerize COT (2) which has a low ring strain.

The different types of CTA (5) used are given in Figure 1 taken from Scherman *et al*. (*J. Am. Chem. Soc*, 2003, **125**, 8515):

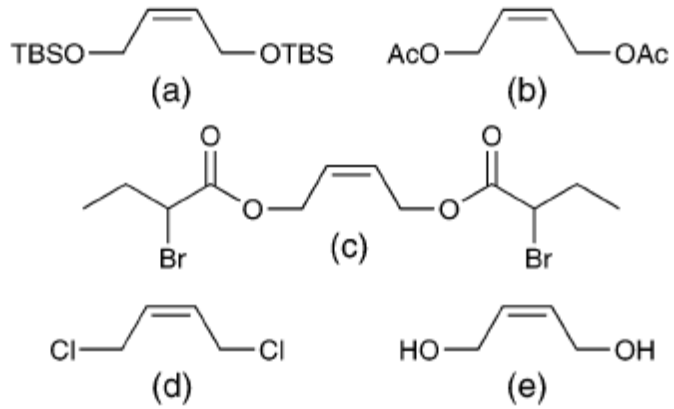


Figure 1. CTAs **5a−e**.

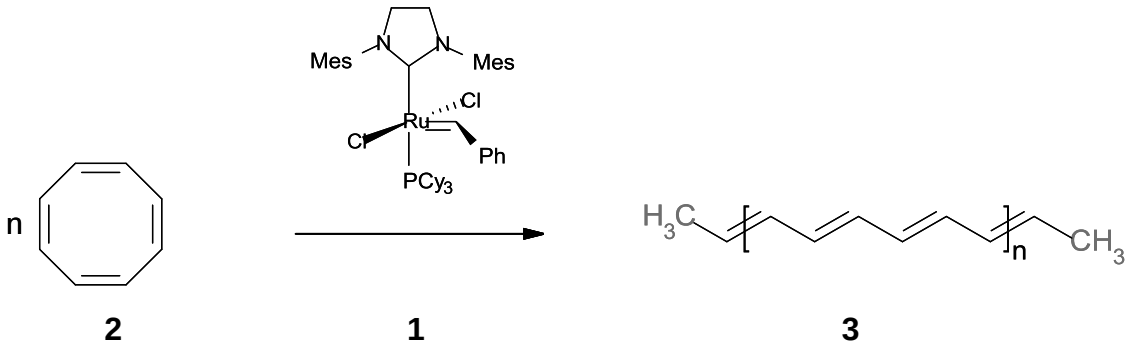
*Reprinted with permission from Scherman, O. A., Rutenburg, I.A., and Grubbs, R.H., J. Am. Chem. Soc., 2003, **125**, 8515. Copyright 2003 American Chemical Society.*

QUANTICORP R&D PART 4: SYNTHESIS OF POLYACETYLENE

In order to test the feasibility of scaling up production of polyacetylene you first need to conduct a lab-scale synthesis. This is step 3c in your problem solving strategy:

1. Identify the problem and decide what you want to achieve:
    a. identify a conducting polymer for development into a sensor;
2. Plan how you want to proceed.
3. Establish what you already know, what you don't know and what you need to find out:
    a. research into synthetic methods;
    b. functionalization of the polymer;
    c. synthesis of the polymer;
    d. conjugation with a sensing molecule;
4. Come up with some solutions, alternative approaches and new ideas
5. Critically evaluate your solutions and decide whether any of them solve the problem
6. Repeat 3-5 as many times as necessary

The basic reaction yields solid polyacetylene (Scheme **1**), but the polymer can be end-functionalized using a chain transfer agent (CTA)



2 **1** **3**

Scheme 1 ROMP of COT reaction

Task 4.1 (120 min)

A survey of the literature has turned up some useful sources of information:

A paper by Moorhead and Wenzel[4] describes the preparation of polyacetylene using the Ring opening metathesis and the Grubb's second generation catalyst, and subsequent investigation of the structure of the polymer.

(a) What was the name and full structure of the CTA used for Experiment 2?
(b) Why was it used?

[4] Moorhead and Wenzel. Two Undergraduate Experiments in Organic Polymers: The Preparation of Polyacetylene and Telechelic Polyacetylene via Ring-Opening Metathesis Polymerization. *J. Chem. Ed.*, 2009, **86**, 973.

Now read the paper by Scherman *et al*.[5]

(c) Summarise the experimental procedure used for the production of $TBSOCH_2$-capped polyacetylene (in solution).
    (i) Which reaction conditions, using CTA **5a**, gave the best and worst yields?
    (ii) How was the CTA reagent **5a** synthesised?

How would you investigate this reaction with respect to:

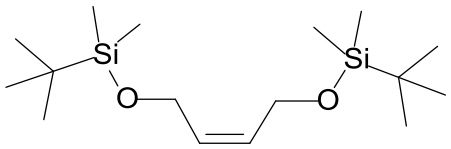
(d) Reaction conditions
(e) Stoichiometry
(f) Structure of the product
(g) Conductivity of the product

[5] Scherman, O. A., Rutenberg, I.M., and Grubbs, R.H.Direct Synthesis of Soluble, End-Functionalized Polyenes and Polyacetylene Block Copolymers. *J. Am. Chem. Soc*, 2003, **125**, 8515.

TUTOR NOTES FOR TASK 4.1

(a) What was the name and full structure of the CTA used for Experiment 2?

The chain transfer agent was *tert*-butyldimethylsilyl-protected *cis*-2-butene diol (**5**).



5

(b) Why was it used?

The TBS-protected *cis*-2-butene diol (**5**) was added to give $TBSOCH_2$-capped polyacetylene (**4**) which is more soluble than the un-functionalized polyacetylene (**3**).

Now read the paper by Scherman** et al.*[6].***

(c) Summarise the experimental procedure used for the production of $TBSOCH_2$-capped polyacetylene (in solution).

0.5 cm^3 (4.44 mmol) COT and 1.6 cm^3 (4.34 mmol) of CTA 5a were added by syringe to a dry Teflon capped vial containing a stir bar, under argon. To this was added 1.0 cm^3 (8.84 x 10^{-3} mmol) of a 7.5 mg cm^{-3} solution of catalyst in CH_2Cl_2 using a syringe. The vial was heated to 55 ºC in an oil bath and the yellow solution turned dark orange within 5 min. After 24 h the solution was dissolved in CH_2Cl_2, precipitated in 100 cm^3 of MeOH with stirring, and filtered through a Buchner funnel to yield a red solid. The solid was dried under reduced pressure to yield 91 mg of polymer (20% yield). Alternatively, the precipitate in MeOH was repeatedly centrifuged and washed with MeOH until the decanted liquid was colourless. The red solid was dissolved in CH_2Cl_2 in an amber vial and the solvent removed under reduced pressure.

(i) Which reaction conditions, using CTA 5a, gave the best and worst yields?

From Table 1 in Scherman *et al*. (*J. Am. Chem. Soc*, 2003, **125**, 8515) the yields were:

Best: [COT]/[CTA] = 2; [COT]/catalyst = 500; yield = 83 %
Worst: [COT]/[CTA] = 3; [COT]/catalyst = 1050; yield = 9 %

(ii) How was the CTA reagent 5a synthesised?

[6] Scherman, O. A., Rutenberg, I.M., and Grubbs, R.H.Direct Synthesis of Soluble, End-Functionalized Polyenes and Polyacetylene Block Copolymers. *J. Am. Chem. Soc*, 2003, **125**, 8515.

CTA 5a was synthesised according to the literature procedure of Corey and Venkates (Corey, E.J., and Venkates, A., *J. Am. Chem. Soc*., 1972, **94**, 6190.)

How would you investigate this reaction with respect to:

(d) Reaction conditions

Reaction conditions that would affect the reaction include:

- Temperature
- Time
- Presence of an inert atmosphere

(e) Stoichiometry

The stoichiometry of the reaction is influenced by the concentration of reactants and catalyst. This can be investigated by performing a series of experiments with different ratios of the three reactants.

(f) Structure of the product

The structure of the product can be investigated using UV-vis (number of double bonds); IR spectrometry (functional groups and *cis/trans* ratio); NMR (confirmation that polymerisation has taken place; existence of an intermediate, and number of double bonds).

(g) Conductivity of the product

A thin film of the polymer can be plated out on a glass slide with electric contacts and the resistance measured using a volt meter.

QUANTICORP R&D PART 5: SYNTHESIS OF POLYACETYLENE

Task 5.1 (120 min)

Design an experiment to investigate the yield for the synthesis of $TBSOCH_2$-capped polyacetylene. You will need to apply your problem solving strategy to:

(a) decide an overall reaction scheme;
(b) investigate the yield;
(c) decide on the apparatus and any special requirements that you will need;
(d) decide on the reagents and any special preparation that they require;
(e) complete a COSHH evaluation of the chemicals.

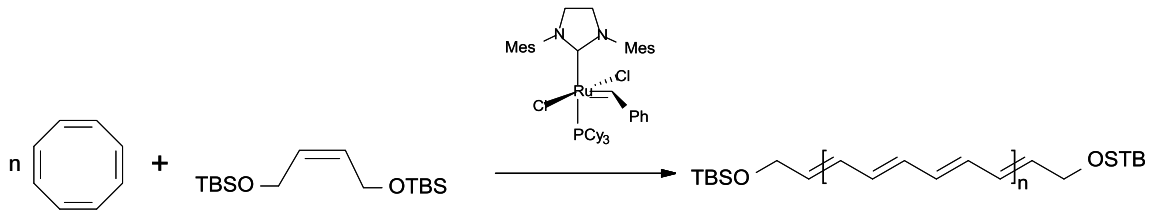
TUTOR NOTES FOR TASK 5.1

The following notes assume that the investigation is performed by six groups of two or three students so you will need to subdivide your teams. If there are more students experiments can be replicated.

Students should be able to complete parts (a), (b) and (e) of this task by reference to the information they have already been given. However, they probably do not have the practical experience necessary to fully complete parts (c) and (d), so will require tutor guidance for this. A separate student handout (**Student Notes for Task 5.1**) for this task is included to facilitate this.

(a) decide an overall reaction scheme;

The correct reaction is Scheme 2



2 **5** **1** **4**

Scheme 2 ROMP of COT with a CTA

(b) investigate the yield;

In Task 4.1 the students were asked to summarise the experimental procedure of Scherman *et al.*[7] and to identify the best and worst yields. This can form the basis for their investigation as follows:

The best and worst yields were:

Best: [COT]/[CTA] = 2; [COT]/catalyst = 500; yield = 83 %
Worst: [COT]/[CTA] = 3; [COT]/catalyst = 1050; yield = 9 %

One possible scenario is to prepare **five** different reaction mixtures as outlined below:

Reaction	**Amount of reactant /** cm^3		
	(5)	**(2)**	**(1)**
1	1.6	0.5	1.0

[7] Scherman, O. A., Rutenberg, I.M., and Grubbs, R.H.Direct Synthesis of Soluble, End-Functionalized Polyenes and Polyacetylene Block Copolymers. *J. Am. Chem. Soc*, 2003, **125**, 8515.

2	1.6	0.75	1.0
3	1.6	1.0	1.0
4	1.6	0.5	0.5
5	1.6	0.5	1.5
6	-	0.5	1.0

The molar masses and densities of the reagents are as follows:

COT (**2**)	Mr = 104.15 g mol^{-1}; ρ = 0.9250 g cm^{-3}
Grubbs 2nd generation catalyst (**1**)	848.97 g mol^{-1}
CTA (**5**)	316.57 g mol^{-1}; ρ = 0.8587 g cm^{-3}

Reaction	**Amount of reactant / mmol**		
	(5)	**(2)**	**(1)**
1	4.34	4.44	8.88×10^{-3}
2	4.34	6.66	8.88×10^{-3}
3	4.34	8.88	8.88×10^{-3}
4	4.34	4.44	4.44×10^{-3}
5	4.34	4.44	17.7×10^{-3}
6	-	4.44	8.88×10^{-3}

Pipette X cm^3 of (**5**) into a 15 cm^3 Quickfit test-tube, seal with a Subaseal and flush with nitrogen. Add Y cm^3 of (**2**) using glass syringe fitted with a stainless steel (s/s) luer-lock needle. To this mixture add Z cm^3 of a 7.5 mg cm^{-3} solution of (**1**) in CH_2Cl_2 using a glass syringe fitted with a s/s luer-lock needle (**NB use separate syringes and needles for each of the reagents)**. The brownish yellow solution should become dark orange after a few minutes. Transfer to a heating block at 55 °C and allow to react for 24 h. Remove and pour the contents into a 150 cm^3 QF conical flask containing 100 cm^3 of methanol, with stirring. Filter the deep red suspension using a 1.8 cm diameter Hirsch funnel and a 250 cm^3 Buchner flask. Allow to dry under vacuum overnight, record the mass of polymer produced and calculate the yield.

(c) decide on the apparatus and any special requirements that you will need;

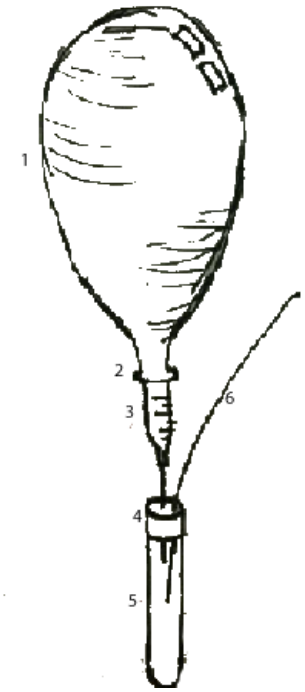
The reaction must be performed in moisture and air-free environment. This can be achieved by flushing the reaction vessel with nitrogen and transferring the reagents by syringe. The following apparatus is required:

- 15 cm^3 Quickfit test-tubes
- Suba-Seals®
- Stainless steel needles
- Gas-tight luer-tipped cannulas for gas transfer from balloon to reagent vessels
- Balloons that can be filled with nitrogen
- Luer fittings (cut down plastic syringes) that can be attached to the balloons
- Nitrogen cylinder with an appropriate luer fitting for filling the balloons

- glass syringes with stainless steel needles – one per group to add catalyst (**1**), and one for each of reagents **2** and **5**.
- 5 cm^3 vials fro preparation of catalyst solution.

Syringes, quickfit test-tubes and vials should be dried and kept in a dessicator before use.

Attach the inert gas balloon to a Luer fitting (cut down plastic syringe). It is a good idea to place a layer or two of Sellotape or blueroll between the balloon and retaining clip to prevent pinching the balloon rubber.



1. Balloon filled with N_2
2. Retaining clip
3. Luer fitting
4. Suber seal
5. Reaction vessel
6. Cannulas

Slowly fill your balloon with the appropriate gas at the cylinder located at a fume cupboard. Either pinch the neck of the balloon with your fingers or cap the Luer fitting with a cork-stoppered needle to retain gas until you return to your apparatus.

Quickfit vessels are often capped with Suba-Seals® for this type of work. Before puncturing the seal it is advisable to make a marker pen dot at the location you're going insert a cannula or needle as this will make relocating the puncture point much easier and negate compromising the seal with many random puncture sites.

Remember that if you are purging a vessel you will need somewhere for gas to escape! When using a cannula as a vent, it is advisable to confirm that this is actually occurring by dipping the open end in a small beaker of solvent or water. Never cause a sharp bend or constriction in a cannula.

(d) decide on the reagents and any special preparation that they require;

The experiment can be performed effectively with reagents prepared at the following concentrations:

Grubb's 2nd generation catalyst (1), 7.5 mg cm^{-3} solution in CH_2Cl_2. The catalyst can be purchased from Sigma-Aldrich in 100 mg vials. A solution should be made up fresh in the lab (see Tutor Notes for task 6.1)

COT (2). A yellow liquid which can be bought from Sigma-Aldrich in 5g bottles which should be enough for the experiments described here.

TBS-protected *cis*-2-butene diol (5). This is a clear liquid which must be synthesised beforehand. The following method can be scaled up as appropriate:

Add 1.235 g (14 mmol) of *cis*-butene-1,4,-diol to 2.36 g (34.7 mmol) of imidazole in a 25 cm^3 round-bottomed flask equipped with a magnetic flea and 8 cm^3 pressure equalizing funnel. To the funnel add 5 g of dimethyl-*tert*-butylsilyl chloride in 5 cm^3 of dimethyl formamide and 2 cm^3 of dichloromethane (DCM may be a better solvent than DMF). Fit the funnel with a suitable size Suba-seal and purge with nitrogen from a balloon by briefly breaking the joint at the round bottom flask.

The addition of the silylating agent is exothermic and should result in more of the imidazole going into solution. Leave the reaction mixture to stir for 48 h then rotary evaporate off the DCM to leave the remaining DMF solution. Add this to c.a. 40 cm^3 H_2O in a 100 cm^3 separating funnel and extract into hexane (2 x 20 cm^3). Wash with 10cm^3 H_2O before drying over anhydrous Na_2SO_4 (the imidazole catalyst is soluble in water but not in hexane so is removed in this step). Gravity filter the hexane solution and rotary evaporate to yield 3.98 g of colourless, almost odourless oil (91.5 % yield).

(e) complete a COSHH evaluation of the chemicals.

Students should complete COSHH assessments using the procedure specific to the institution. A sample COSHH assessment form is given in **Resource 5.1**

STUDENT NOTES FOR TASK 5.1

Optional handout

Reagents

The experiment can be performed effectively with reagents prepared at the following concentrations:

- Grubb's 2nd generation catalyst (**1**) – a 7.5 mg cm^{-3} solution in CH_2Cl_2
- COT (**2**) – a yellow liquid
- TBS-protected *cis*-2-butene diol (**5**) – a clear liquid which has been previously synthesised.

Dry CH_2Cl_2 is also required for preparation of the catalyst solution and solubilising the polymer.

Investigating the stoichiometry of the reaction

The effect of reagent concentration on yield can be investigated by students working in six pairs with different ratios of reactants, and pooling the information afterwards. Prepare **six** different reaction mixtures as outlined in Table **1**.

Table 1 Reaction mixtures

Reaction	**Amount of reactant /** cm^3		
	X (5)	**Y (2)**	**Z (1)**
1	1.6	0.5	1.0
2	1.6	0.75	1.0
3	1.6	1.0	1.0
4	1.6	0.5	0.5
5	1.6	0.5	1.5
6	-	0.5	1.0

The molar masses and densities of the reagents are as follows:

COT (2)	M_r = 104.15 g mol^{-1}; ρ = 0.9250 g cm^{-3}
Grubbs 2nd generation catalyst (1)	M_r = 848.97 g mol^{-1}
CTA (4)	M_r = 316.57 g mol^{-1}; ρ = 0.8587 g cm^{-3}

Procedure

Pipette X cm^3 of (**5**) into a 15 cm^3 Quickfit test-tube, seal with a Suba-Seals® and flush with nitrogen. Add Y cm^3 of (**2**) using glass syringe fitted with a stainless steel (s/s) luer-lock needle. To this mixture add Z cm^{-3} of a 7.5 mg cm^{-3} solution of (**1**) in CH_2Cl_2 using a glass syringe fitted with a s/s luer-lock needle (**NB use separate syringes and needles for each of the reagents)**. The brownish yellow solution should become dark orange after a few minutes. Transfer to a heating block at 55 °C and allow to react for 24 h. Remove and pour the contents into a 150 cm^3 QF conical flask containing 100 cm^3 of methanol, with stirring. Filter the deep red suspension using a 1.8 cm diameter Hirsch funnel and a 250 cm^3 Buchner flask. Allow to dry under vacuum overnight, record the mass of polymer produced and calculate the yield.

Performing the experiment in an inert atmosphere

The following equipment can be used to provide an inert atmosphere in the reaction vessel. Provide this on the bench and advise students on its use as appropriate:

- Balloons that can be filled with nitrogen
- Luer fittings (cut down plastic syringes) that can be attached to the balloons
- Nitrogen cylinder with an appropriate luer fitting for filling the balloons
- Gas-tight luer-tipped cannulas for gas transfer from balloon to reagent vessels
- Quick-fit test tubes (15 cm^3) with Suba-Seals®

Attach the inert gas balloon to a Luer fitting (cut down plastic syringe). It is a good idea to place a layer or two of Sellotape or blueroll between the balloon and retaining clip to prevent pinching the balloon rubber.

Slowly fill your balloon with the appropriate gas at the cylinder located at a fume cupboard. Either pinch the neck of the balloon with your fingers or cap the Luer fitting with a cork-stoppered needle to retain gas until you return to your apparatus.

Quickfit vessels are often capped with Suba-Seals® for this type of work. Before puncturing the seal it is advisable to make a marker pen dot at the location you're going insert a cannula or needle as this will make relocating the puncture point much easier and negate compromising the seal with many random puncture sites.

Remember that if you are purging a vessel you will need somewhere for gas to escape! When using a cannula as a vent, it is advisable to confirm that this is actually occurring by dipping the open end in a small beaker of solvent or water. Never cause a sharp bend or constriction in a cannula.

RESOURCE 5.1

COSHH Assessment

Faculty/Department:	School/Section:
Assessment No.	Assessor:
Description of procedure or experiment *(Include how long and how often this is carried out and the quantity of substance used)*	
Identify the persons at risk:	Staff ☐ Contractors ☐ Public/students ☐
Name the substance involved in the process, the supplier (if known) and the information source.	

Classification *(state the category of danger, tick all that apply)*


☐ Very Toxic


☐ Toxic

☐ Corrosive


☐ Harmful


☐ Irritant


☐ Sensitising


☐ Biological

☐ Oxidising


☐ Extremely Flammable


☐ Highly Flammable


☐ Flammable


☐ Environmental

Hazard Type (tick all that apply)

☐ Gas ☐ Vapour ☐ Mist ☐ Fume ☐ Dust ☐ Liquid ☐ Solid ☐ Other (State)

Route of Exposure (tick all that apply)

☐ Inhalation ☐ Skin ☐ Eyes ☐ Ingestion ☐ Other (State)

Workplace Exposure Limits (WELs) *please indicate n/a where not applicable*

Long-term exposure level (8hrTWA):	Short-term exposure level (15 mins):

State the Risks to Health from Identified Hazards (include Risk Phrases)

Control Measures: *(for example extraction, ventilation, training, supervision). Include special measures for vulnerable groups, such as disabled people and pregnant workers. Take account of those substances that are produced from activities undertaken by another employer's employees. (include Safety Phrases)*
Can a less hazardous substance be used? Yes ☐ No ☐ If so why is it not being used?
Is health surveillance or monitoring required? Yes ☐ No ☐

Personal Protective Equipment *(state type and standard)*			
 ☐ Dust mask		 ☐ Visor	
 ☐ Respirator		 ☐ Goggles	
 ☐ Gloves		 ☐ Overalls	
 ☐ Footwear		 ☐ Other	

First Aid Measures
Spillage/Uncontrolled Release Procedures
Storage
Disposal of Substances & Contaminated Items
Hazardous Waste ☐ Skip ☐ Run to Drain ☐ Return to Supplier ☐ Other ☐ (If Other Please State):.....

Name of Assessor:	Signed:	Date:
Name of Safety Manager/ HOS/ HOD:	Signed:	Date:
Review Date:	Signed:	Date:

Review Date:	Signed:	Date:
Review Date:	Signed:	Date:

QUANTICORP R&D PART 6: SYNTHESIS OF POLYACETYLENE

Task 6.1 (120 min)

Perform a synthesis of TBSOCH$_2$-capped polyacetylene.

TUTOR NOTES FOR TASK 6.1

The actual laboratory synthesis is relatively straightforward providing the reagents are prepared as specified and not cross contaminated. Many students will not have the necessary practical skill to correctly perform these procedures under time pressure in the laboratory. However, in order that they don't just 'follow a recipe' with pre-prepared reagents it is advisable to approach the laboratory activity as a step-by-step learning activity as outlined below.

Step 1 Preparation of Grubb's Catalyst solution

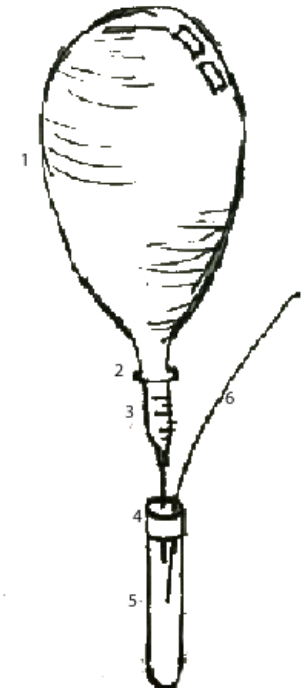
This is a critical step in the synthesis – get this wrong and nothing works. It is suggested that you follow the guidelines below:

Task students to prepare individual catalyst solutions for their particular experiment using a dry 5 cm^3 vial and dry CH_2Cl_2. It is surprising how difficult some students find this relatively simple procedure so you will need to reiterate the following points and demonstrate the correct technique at the outset:

(a) they should prepare about 0.5 cm^3 more solution than they will actually need;
(b) it is easiest to prepare the solution by weight using an analytical balance and you should demonstrate this at the outset For example, for reaction 1:
    i 1.0 cm^3 of a 7.5 mg cm^{-3} catalyst solution is required for the reaction so they should prepare about 1.5 cm^3;
    ii they will need to weigh out 11.3 mg and add 2.0 g of solvent so they need to know what 11.3 mg actually looks like on the end of a microspatula and that it is easiest to add the solvent to the vial using a Pasteur pipette;
(c) when the groups have prepared their solutions get them to bring them to the front of the lab to compare. If they have done this correctly they should have a clear reddish-purple solution and the volumes should be in proportion to each other.

Step 2 Flushing the reaction vessel with nitrogen

It is worth demonstrating the correct procedure for this. The reaction vessel with Suba-Seal® and cannula should look like the diagram below.



7. Balloon filled with N_2
8. Retaining clip
9. Luer fitting
10. Suber seal
11. Reaction vessel
12. Cannulas

Step 3 Adding the reagents to the reaction vessel

It is important to add the COT (2) and CTA (5) first – dedicated syringes for each of these reagents should be supplied. **Then** add the catalyst (1) last using a separate syringe for each group. The liquids are quite viscous so it is necessary to uptake **slowly** with the syringe to prevent air bubbles forming.

Step 4 Reaction

The reaction proceeds quite quickly and can be left in the heating block overnight. However, it is sometimes quite vigorous so should be kept under observation initially in case the Suba-Seal® blows off.

QUANTICORP R&D PART 7: SYNTHESIS OF POLYACETYLENE

Task 7.1 (180 min)

Using the analytical techniques identified in Task 4.1 to investigate the structure of your product.

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STUDENT NOTES FOR TASK 7.1

Solubility

It is necessary to dissolve the product in an appropriate solvent in order to perform some of the spectroscopic investigations. Test the solubility of each of the products from reactions 1-6 in the following solvents:

- CH_2Cl_2
- Pentane
- Acetone
- Ether

UV-vis Spectroscopy

Add ~1 mg (a small speck) of your red solid to approximately 4 cm^3 of an appropriate solvent (discuss this with the tutor before proceeding) and record the UV-Vis spectrum between 250 and 600 nm.

IR Spectroscopy

Record the IR spectrum of ~ 2mg your red solid.

NMR Spectroscopy

Dissolve 10 mg of polymer in an appropriate solvent (discuss this with the tutor before proceeding) and acquire a proton NMR spectrum. Integrate the polyene (δ ~ 6-7 ppm) methylene (δ ~ 4.2 ppm) backbone peaks.

TUTOR NOTES FOR TASK 7.1

If you have preformed the laboratory synthesis then the structure of the polymer can be investigated using UV-vis, IR and NMR spectroscopy

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Solubility

The $TBSOCH_2$-functionalized polyacetylene should be readily soluble in CH_2Cl_2 and pentane. However, the un-functionalized polymer from reaction 6 will be quite insoluble.

Spectroscopic Analysis

Sample spectra which can be used if do not perform the synthesis and analysis are given in Resource 7.1. These can be handed out to the students and used for Task 8.1.

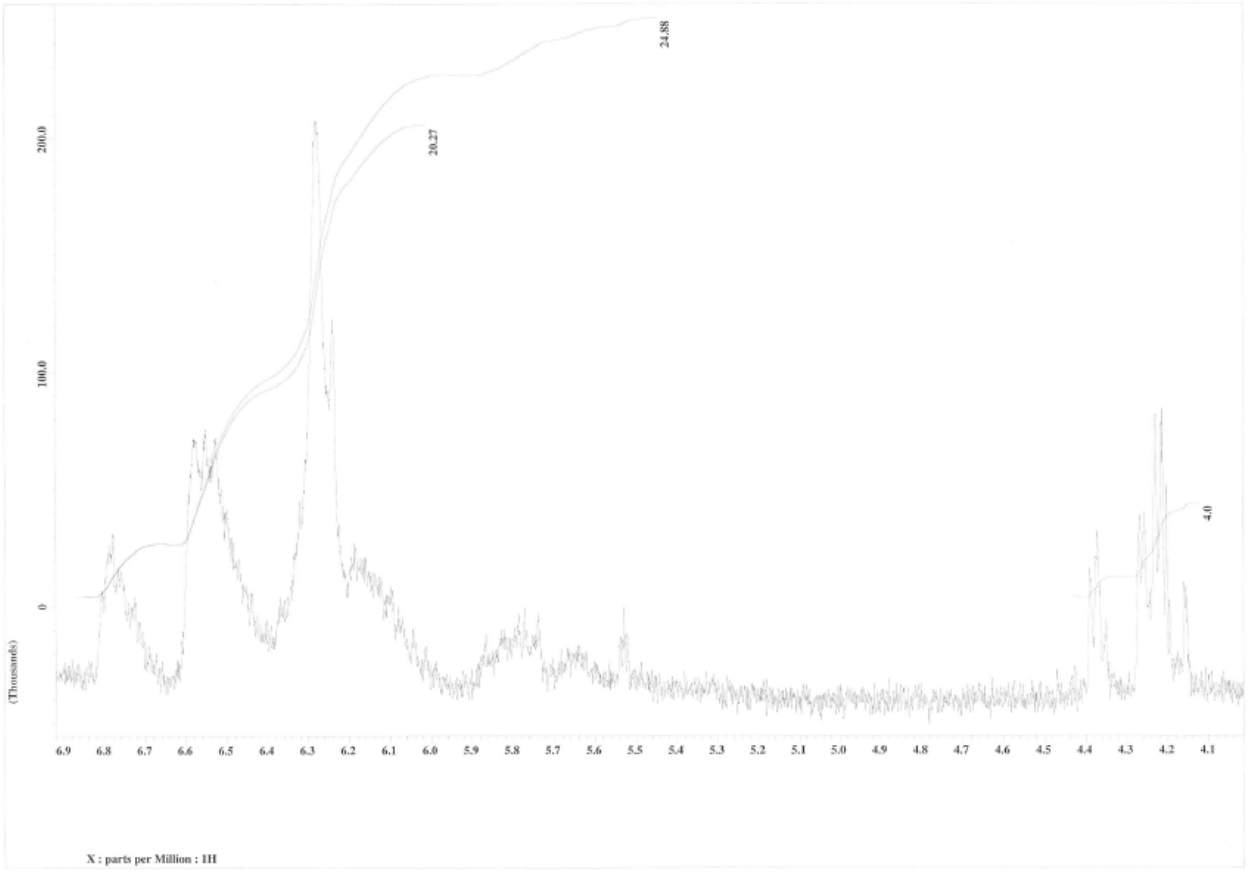

Figure 1 nmr spectrum of end functionalised polyacetylene for Reaction 4

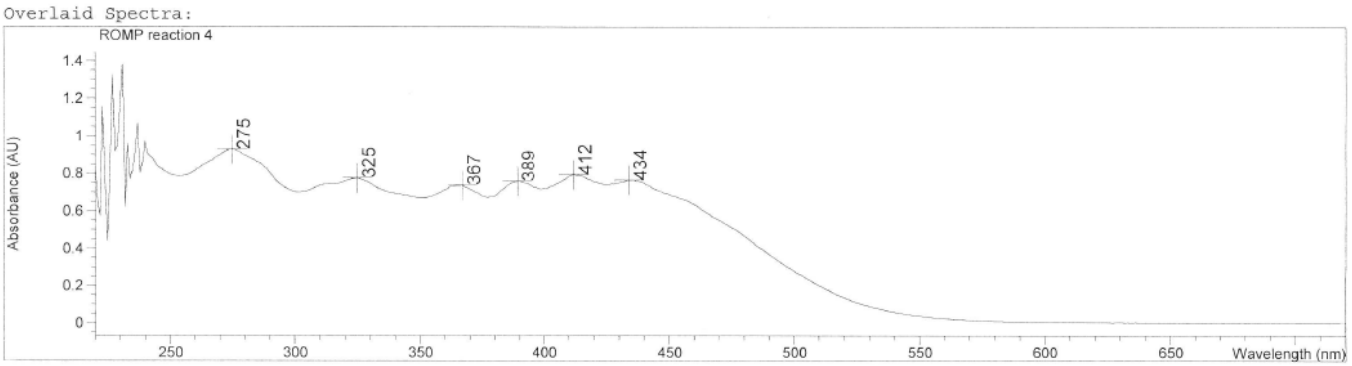

Figure 2 UV-vis spectrum of end functionalised polyacetylene for Reaction 4

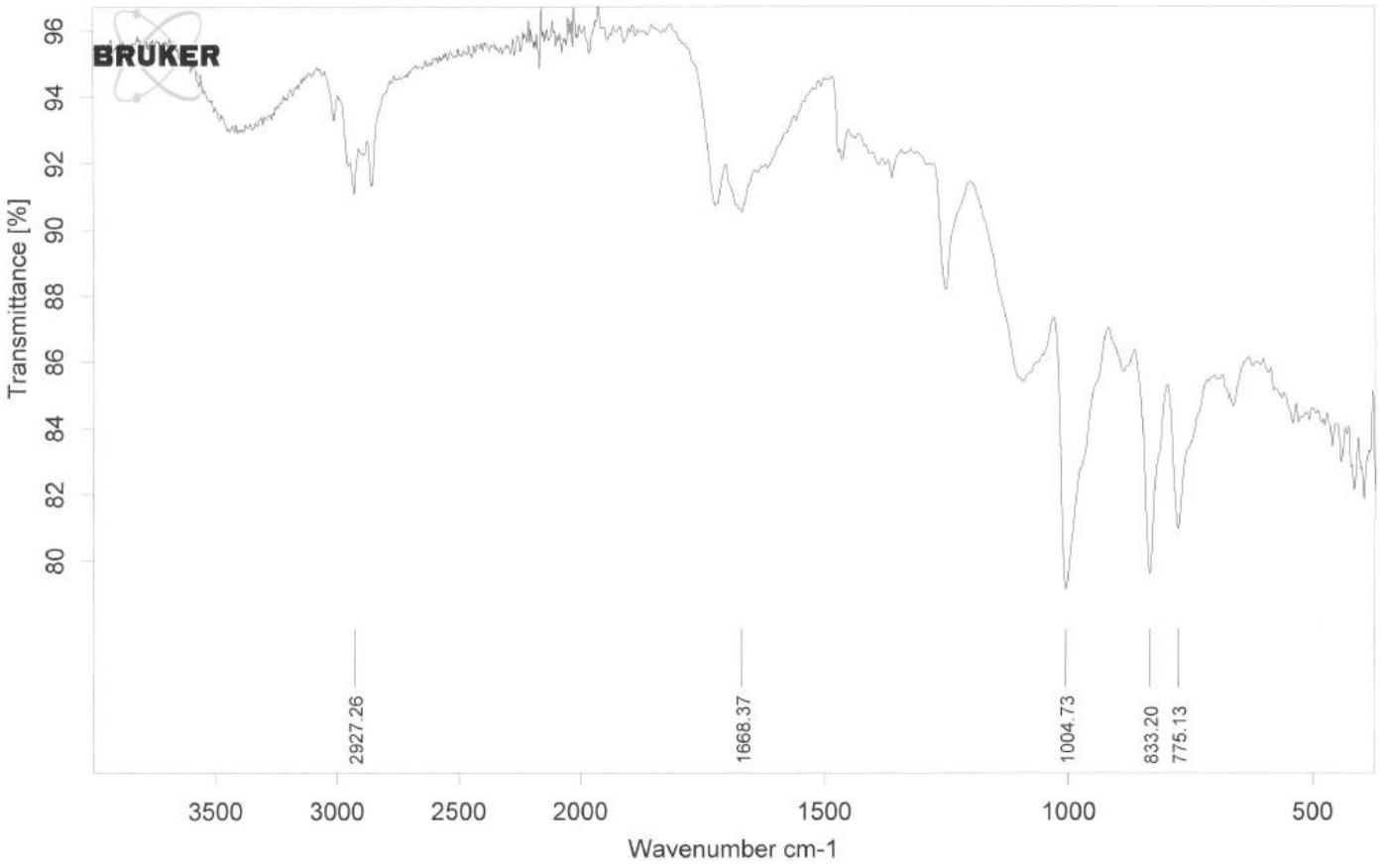

Figure 3 FT-IR spectrum of end functionalised polyacetylene for Reaction 4

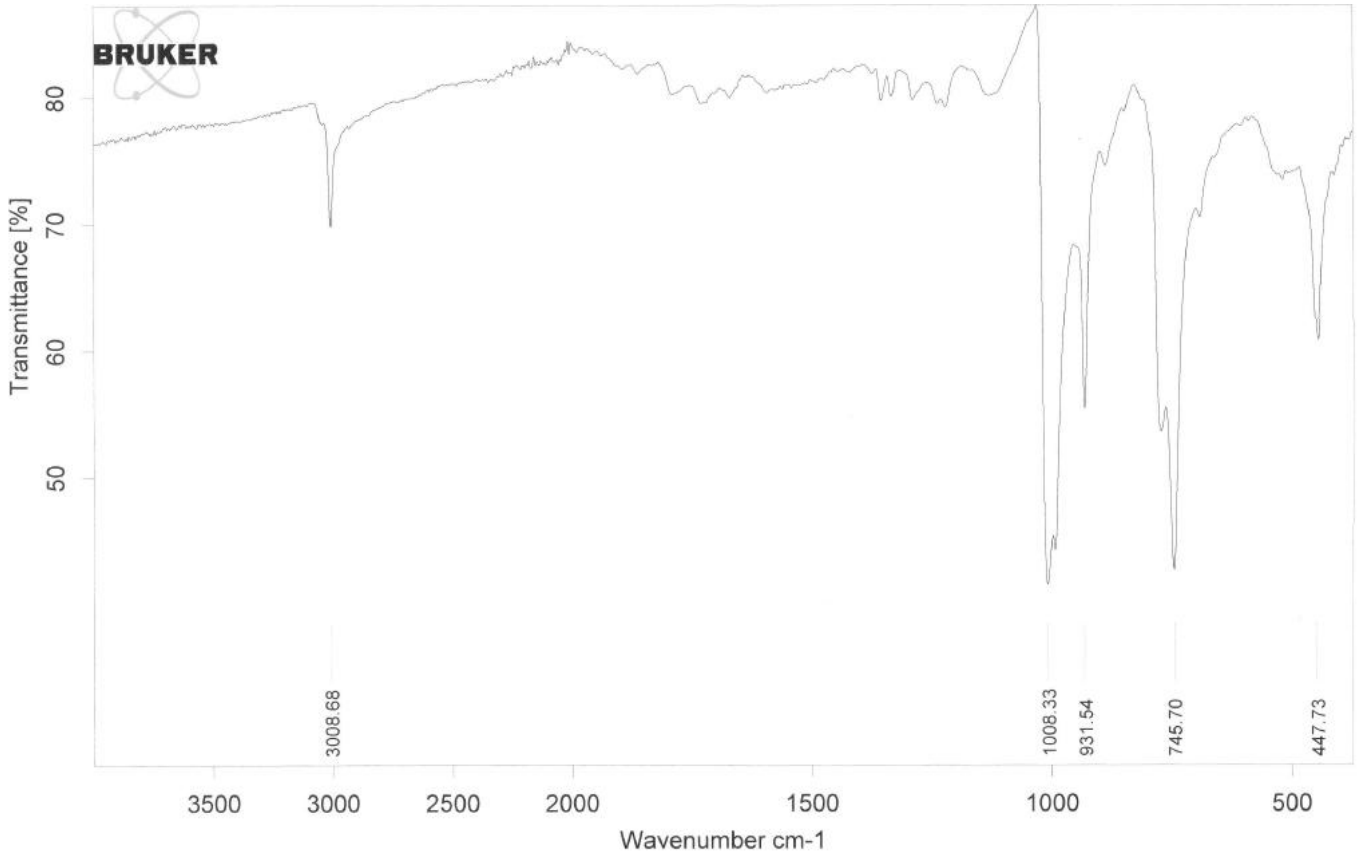

Figure 4 FT-IR spectrum of end functionalised polyacetylene for Reaction 6

QUANTICORP R&D PART 8: REPORTING

Task 8.1 (180 min)

Prepare a report of your investigation. This should include a full experimental procedure and COSHH assessment. Address the following in your discussion:

Analysis of the Product

NMR

Using your spectrum for the polymer product, ratio the integrals for the polyene and methylene peaks and estimate the number of double bonds.[8]

UV-vis Spectroscopy

Conjugated compounds are those that contain alternating double and single bonds. Here the π orbital of the double bond overlaps with the σ orbital of the single bond. This allows for the π electrons to delocalise (become dissociated for one particular atom). As the amount of conjugation increases the π → π* transition becomes lower in energy, so absorption in the UV-vis spectrum occurs at longer wavelengths. It follows then, that the number of double bonds, and hence the length of the polyacetylene chain, can be estimated from the UV-vis spectrum.

A simple method for calculating λ_{max} for the π → π* transition is to follow the Woodward-Fieser rule, as follows:

1. A polyacetylene with two double bonds will have λ_{max} at 217 nm
2. For each additional conjugated double bond λ_{max} will increase by +30 nm increments

Use these rules to calculate the number of conjugated double bonds from the UV-vis spectrum of your sample of polyacetylene.

Refer to Tables V and VI, Figures 13 and 15, and the associated discussion on pages 7999-8000 in the paper by Knoll and Shrock.[9] Use this information to estimate the number of double bonds in your polyene.

Compare the three methods which you have used to calculate the number of double bonds and comment on their accuracy.

Now calculate the average number of monomer units per polymer chain

IR Spectroscopy

Compare your spectrum with that of Scherman *et al.*[8] and identify the principal peaks in the FT-IR spectrum which correspond with the major features of the product polymer. Estimate the relative proportions of the *cis* and *trans* isomers.

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8 Scherman, O. A., Rutenburg, I.A., and Grubbs, R.H., *J. Am. Chem. Soc*., 2003, **125**, 8515.

9 Knoll, K., and Schrock, R., *J. Am. Chem. Soc*., 1989, **111**, 7989

Effect on Yield

Using your figure for the average number of monomer units per polymer chain, calculate the theoretical yield.

Calculate molar ratios of the reactants for each of the reactions 1-5. Discuss the effect on yield.

Conductivity of the Poylmer

Access the information on conducting polymers at the Nobel Prize site[10] by downloading the text file containing the advanced information [(advanced information) The Nobel Prize in Chemistry: Conductive Polymers]. Read the article and summarise, in your own words, how doping with iodine makes the polymer conducting (about *400 words*).

[10] The Nobel Prize in Chemistry 2000: Advanced Information http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2000/advanced.html [accessed 25 Nov 2011].

TUTOR NOTES FOR TASK 8.1

Analysis of the Product

NMR Spectroscopy

A typical 1H NMR spectrum is shown in Figure 2 from the paper by Scherman *et al.*[11] *(J. Am. Chem. Soc*., 2003, **125**, 8515) and is reproduced below.

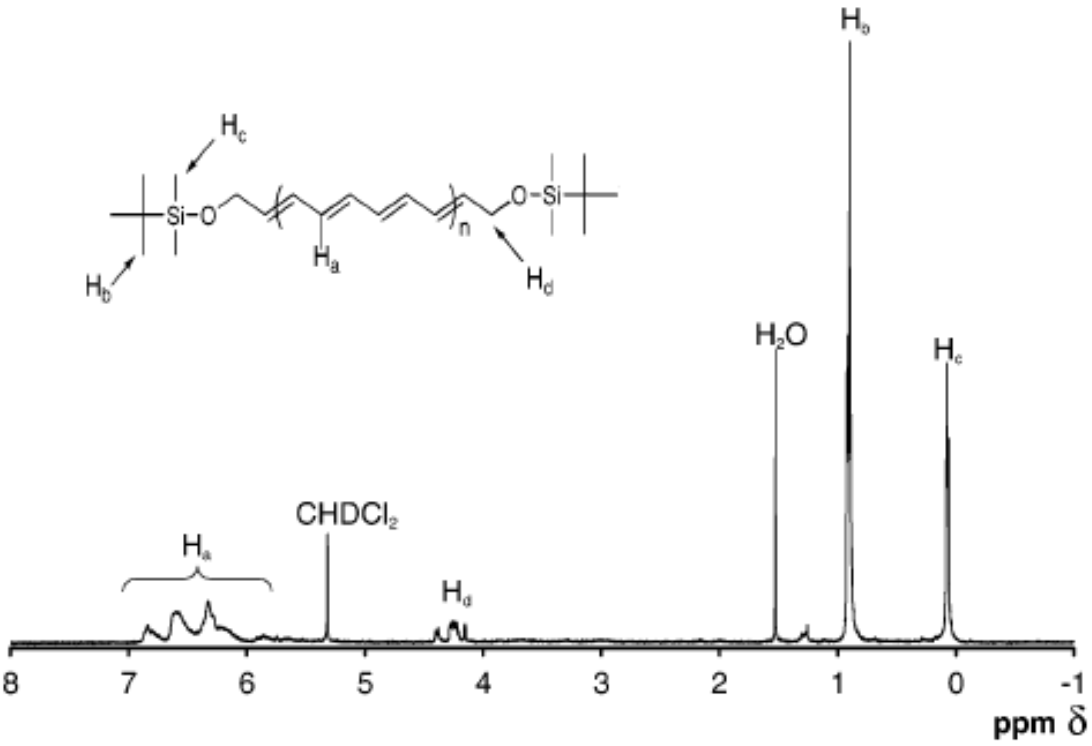

Figure 2. ^{1}H NMR spectrum of telechelic polyene **6a** in CD_2Cl_2.

*NMR spectrum of TBSO functionalized polyacetylene in CD_2Cl_2 (reprinted with permission from Scherman, O. A., Rutenburg, I.A., and Grubbs, R.H., J. Am. Chem. Soc., 2003, **125**, 8515. Copyright 2003 American Chemical Society).*

There are 8 polyene backbone protons (H_a) at δ = 6-7 ppm for every 4 double bonds, or each molecule of COT, incorporated into the polymer chain; and 4 allylic CH_2 protons (H_d) around δ = 4.2 ppm regardless of the polymer chain length.

Hence the number of double bonds (b) is given by: $b = 2H_a/H_d$

and the number of monomers (n) by: $2n = H_a/H_d$

Using the spectrum for reaction 4 given in Resource 7.1:

H_a = 20.27 – 24.88

b ~ 10.1 – 12.4

[11] Scherman, O. A., Rutenburg, I.A., and Grubbs, R.H., *J. Am. Chem. Soc*., 2003, **125**, 8515

n ~ 2.5 – 3.1

UV-vis Spectroscopy

A typical UV-vis spectrum is shown in Figure 3 from the paper by Scherman *et al. (J. Am. Chem. Soc*., 2003, **125**, 8515) and reproduced below.

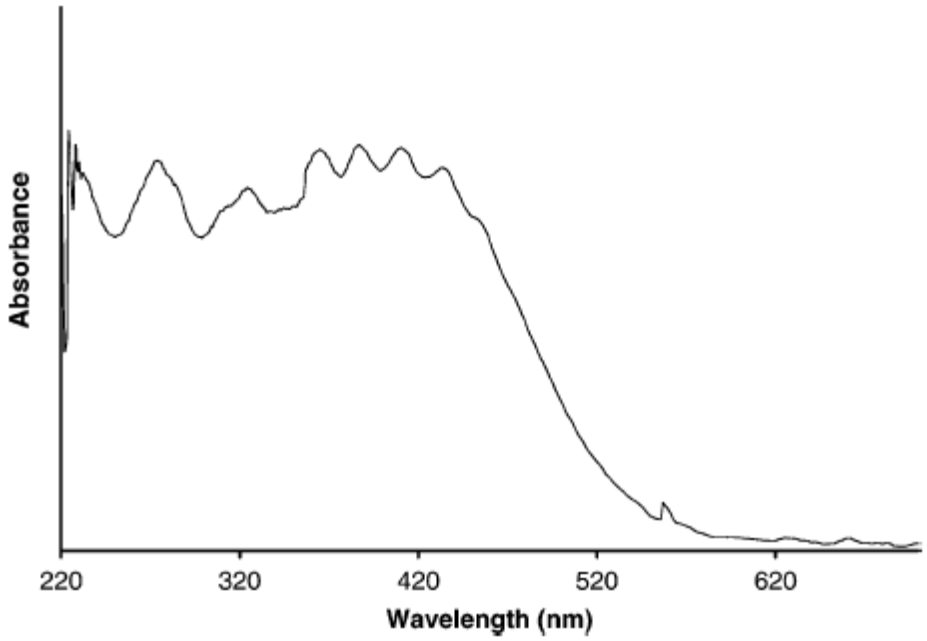

Figure 3. UV−vis spectrum of polyene **6a** in CH_2Cl_2.

*(reprinted with permission from Scherman, O. A., Rutenburg, I.A., and Grubbs, R.H., J. Am. Chem. Soc., 2003, **125**, 8515. Copyright 2003 American Chemical Society)*

Using the Woodward-Fieser rule the number of double bonds is as follows:

λ_{max} ~ 412 nm (this must be estimated for the hump between 350-500 nm)

Number of double bonds = 2 + (412 – 217)/30
= 2 + 6.5
= 8.5

Using the spectra given in Resource 7.1 it students may find it difficult to estimate λ_{max} due to the presence of unreacted monomer contaminating the spectrum. However, they should be able to identify the lower energy transitions between 350-500 nm and compare with the data of Knoll and Schrock.

From the paper by Knoll and Shrock[12]:
Table V from the paper by Knoll and Shrock *(reprinted with permission from Knoll, K. and Schrock., J. Am. Chem. Soc*., 1989, 111, 7989*, 8515. Copyright 1989 American Chemical Society)* for a seres of *n-enes* in pentane, is reproduced below.

[12] Knoll, K., and Schrock, R., *J. Am. Chem. Soc*., 1989, **111**, 7989

Table V. UV–vis Data for *all-trans*-Polyenes[a]

	$1^1B_u \leftarrow 1^1A_g$				$3^1A_g \leftarrow 1^1A_g$		$2^1B_u \leftarrow 1^1A_g$
	0–0	0–1	0–2	0–3	0–0	0–1	0–0
$2t_2$	237.2 (0.688)	227.8 (1.00)	219.8 (0.948)				
$3t_3$	275.6 (0.766)	264.8 (1.00)	255.6 (0.779)				
$4t_4$	311.4 (0.897)	297.4 (1.00)	284.8 (0.683)	274.6 (0.369)			
$5t_5$	343.0 (0.991)	325.8 (1.00)	311.0 (0.615)	297.8 (0.294)	237.8 (0.062)		
$6t_6$	371.2 (1.00)	351.0 (0.931)	334.2 (0.558)	319.0 (0.258)	258.2 (0.037)	250.0 (0.032)	
$7t_7$	396.2 (1.00)	373.6 (0.906)	355.6 (0.520)	338.0 (0.239)	277.6 (0.035)	267.8 (0.026)	
$8t_8$[b]	418.8 (1.00)	394.0 (0.869)	374.0 (0.531)	354.2 (0.254)	296.4 (0.046)	285.6 (0.033)	239.0 (0.123)
$9t_9$[c]	438.8 (1.00)	411.2 (0.921)	390.2 (0.574)	371.8 (0.290)	313.6 (0.080)	301.8 (0.059)	253.0 (0.179)
$10t_{10}$	456.4 (0.977)	427.8 (1.00)	405.2 (0.638)	382.6 (0.310)	330.8 (0.099)	317.6 (0.056)	267.8 (0.165)
$11t_{11}$	468.8 (0.921)	439.4 (1.00)	414.4 (0.657)	393.4 (0.340)	346 (0.106)	330 (0.071)	282 (0.159)
$13t_{13}$	494 (0.921)	462 (1.00)	438 (0.757)	412 (0.450)	370 (0.214)	352 (0.143)	306 (0.186)
$8t_8$	450.4 (1)	423.2 (0.953)	400.0 (0.571)				
$9t_9$[d]	473.0 (1)	444.2 (0.982)	418.8 (0.582)	397.6 (0.292)			
$10t_{10}$[d]	493.2 (1)	462.2 (0.977)	435.2 (0.611)	414 (0.303)			
$11t_{11}$[d]	510.2 (0.867)	476.4 (1)	449.0 (0.702)	422 (0.403)			
$13t_{13}$[d]	540.2 (0.871)	504.6 (1)	474.4 (0.726)	447 (0.427)			

[a] UV–vis data are listed in nanometers. Relative extinction coefficients are listed in parentheses. The solvent is *n*-pentane, unless otherwise noted. The assignments of transition 2 and transition 3 (last three columns) are tentative. [b] In dichloromethane the first three transitions (ϵ in L mol^{-1} cm^{-1}) are 432 (111 000), 406 (103 000), and 384 (64 300). [c] In dichloromethane the first three transitions (ϵ in L mol^{-1} cm^{-1}) are 452 (114 000), 424 (101 000), and 402 (65 000). [d] In carbon disulfide.

Table V. UV–vis Data for *all-trans*-Polyenes[a]

	$1^1B_u \leftarrow 1^1A_g$				$3^1A_g \leftarrow 1^1A_g$		$2^1B_u \leftarrow 1^1A_g$
	0–0	0–1	0–2	0–3	0–0	0–1	0–0
$2t_2$	237.2 (0.688)	227.8 (1.00)	219.8 (0.948)				
$3t_3$	275.6 (0.766)	264.8 (1.00)	255.6 (0.779)				
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$10t_{10}$[d]	493.2 (1)	462.2 (0.977)	435.2 (0.611)	414 (0.303)			
$11t_{11}$[d]	510.2 (0.867)	476.4 (1)	449.0 (0.702)	422 (0.403)			
$13t_{13}$[d]	540.2 (0.871)	504.6 (1)	474.4 (0.726)	447 (0.427)			

[a] UV–vis data are listed in nanometers. Relative extinction coefficients are listed in parentheses. The solvent is *n*-pentane, unless otherwise noted. The assignments of transition 2 and transition 3 (last three columns) are tentative. [b] In dichloromethane the first three transitions (ϵ in L mol^{-1} cm^{-1}) are 432 (111 000), 406 (103 000), and 384 (64 300). [c] In dichloromethane the first three transitions (ϵ in L mol^{-1} cm^{-1}) are 452 (114 000), 424 (101 000), and 402 (65 000). [d] In carbon disulfide.

The wavelengths of the corresponding transitions taken from Figure 3 in the paper by Scherman *et al.* (*J. Am. Chem. Soc., 2003, **125**, 8515)* and from reaction 4 in Resource 7.1 are given in Table 2.

Table 2 Peaks in the UV-vis spectrum for polyacetylene in CH_2Cl_2

Reference	No. Of double bonds	$1^1B_u \leftarrow 1^1A_g$				$3^1A_g \leftarrow 1^1A_g$		$2^1B_u \leftarrow 1^1A_g$
		0-0	0-1	0-2	0-3	0-0	0-1	0-0
Knoll & Schrock	8	432	406	384				
Knoll & Schrock	9	452	424	402				
Scherman *et al.*	8-9	440	420	390	370			
Reaction 4	8-9	434	412	389	367	325		275

Note that these samples were dissolved in CH_2Cl_2 wheras the data taken from Knoll and Shrock is mostly for polyacetylene dissolved in pentane. However, they do quote some limited data and give the first three transitions for the 8t polymer as 432, 406 and 384 nm and for the 9t polymer as 452, 424 and 402. (i.e. shifted approximately 14 nm lower in wavelength).

Taking this data in total, the number of double bonds is estimated to be:

Scherman *et al*. between 8 and 9, hence **n = 2.3**

Reaction 4 (Resource 4.2) between 8 and 9, hence **n = 2.3**

IR Spectroscopy

The IR spectrum given in Figure 4 of the paper by Scherman *et al. (J. Am. Chem. Soc., 2003, **125**, 8515)* is shown below. In this the peaks are assigned as follows:

- the peak at ~745 cm^{-1} can be attributed to the *cis* C-H out-of-plane vibrational mode;
- the peak at 773 cm^{-1} is more difficult to assign depending on the mixture of cis and trans isomers;
- the peak at 1011 cm^{-1} is due to the *trans* C-H out-of-plane vibrational mode.

The relative sizes of the peaks at 745 cm^{-1} and 1011 cm^{-1} give an indication of the amounts of *cis* and *trans* isomers, in this case more *trans* than *cis*. The results shown indicate equal amounts of *cis* and *trans*.

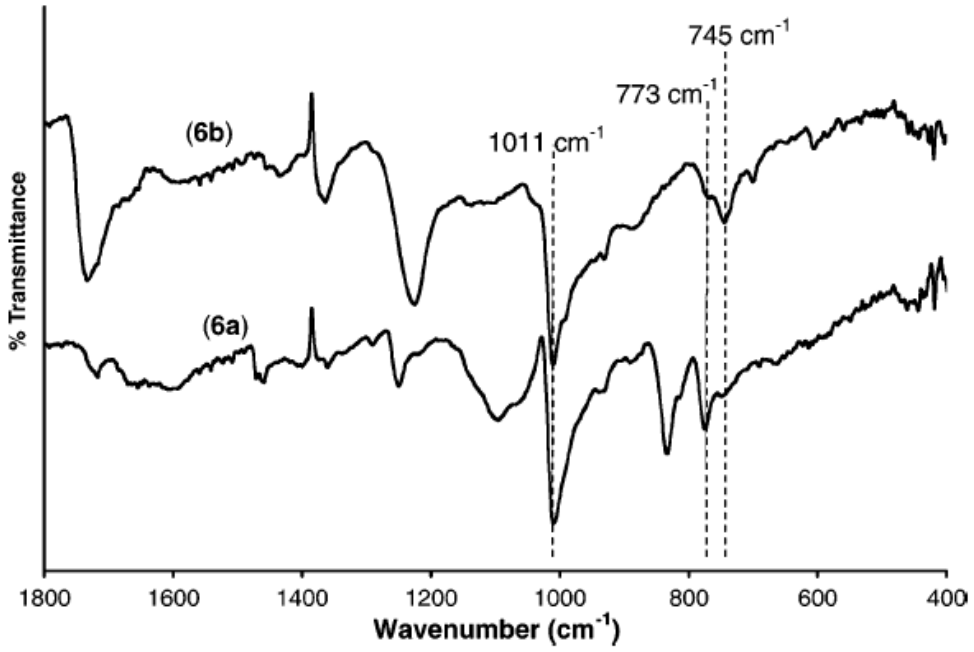


Figure 4. FT-IR % transmittance spectra of polyenes **6a** and **6b** in KBr pellets.

*FT-IR spectrum of polyacetylene (reprinted with permission from Scherman, O. A., Rutenburg, I.A., and Grubbs, R.H., J. Am. Chem. Soc., 2003, **125**, 8515. Copyright 2003 American Chemical Society).*

In comparison, the results for Reaction 6 in Resource 7.1 indicate equal amounts of *cis*- and *trans*-isomers, whereas the results for Reaction 4 indicate that the peak at ~745 cm^{-1} is barely visible as a shoulder on the peak at ~775 cm^{-1}, so there would seem to be much more *trans*- than *cis*-. .

Effect on Yield

The molar masses and densities of the reagents are as follows:

COT (2)	Mr = 104.15 g mol^{-1}; ρ = 0.9250 g cm^{-3}
Grubbs 2nd generation catalyst (1)	848.97 g mol^{-1}
CTA (5)	316.57 g mol^{-1}; ρ = 0.8587 g cm^{-3}

Table 3 Reaction mixtures

Reaction	Amount of reactant						COT/ CTA	COT/Grubbs
	CTA		COT		Grubbs			
	cm^3	mmol	cm^3	mmol	cm^3	mmol		
1	1.6	4.34	0.5	4.44	1.0	8.83E-03	1	500
2	1.6	4.34	0.75	6.66	1.0	8.83E-03	1.5	750
3	1.6	4.34	1.0	8.88	1.0	8.83E-03	2	1000
4	1.6	4.34	0.5	4.44	0.5	4.42E-03	1	1000
5	1.6	4.34	0.5	4.44	1.5	13.25E-03	1	335
6	-		0.5	4.44	1.0	8.83E-03	-	500

There are two ways of working out the theoretical yield:

For un-functionalized polyacetylene e.g. Reaction 6

If we assume that all the COT is used to make polyacetylene then the theoretical yield is equal to the mass of COT used.

Mass COT used = 0.46 g
Hence, theoretical yield ≈ 0.46 g

For $TBSOCH_2$- functionalized polyacetylene e.g. Reaction 4

Once the average number of monomers per polymer chain are known the theoretical yield can be calculated as follows:

The average number of monomers (n) per polymer molecule has been calculated to be between 2-3

2 moles of CTA are required for each mole of COT, so the limiting reagent is COT.

Hence, average number of moles of polymer = (moles of COT)/n

So, if n = 2.5

Average number of moles of polymer = $4.44 \times 10^{-3}/2.5$
= 1.776×10^{-3} mol

But
2 moles of $TBSOCH_2$- are added for each mole of polymer.

So, average M_r polymer = (n x M_r COT) + (2 x M_r $TBSOCH_2$-)

M_r COT = 104.15 g mol^{-1}
M_r $TBSOCH_2$- = (7x12.01) + (17x1.01) +15.99 + 28.01 = 145.24 g mol^{-1}

So M_r polymer = (2.5 x 140.15) + (2 x 145.24)
= 550.86 g mol^{-1}

Theoretical yield = moles of polymer x M_r polymer

Theoretical yield = 1.776×10^{-3} x 550.86
= 0.98 g

From Table 1 in Scherman *et al.* (*J. Am. Chem. Soc*., 2003, **125**, 8515) the yields were:

Best: [COT]/[CTA] = 2; [COT]/catalyst = 500; yield = 83 %
Worst: [COT]/[CTA] = 3; [COT]/catalyst = 1050; yield = 9 %

The mechanism of polyCOT growth is shown in Figure 6 from the paper by Hilf and Kilbinger[13] and reproduced below.

[13] Hilf, S. And Kilbinger, A.F.M. *Nature Chemistry*, 2009, **1**, 537.

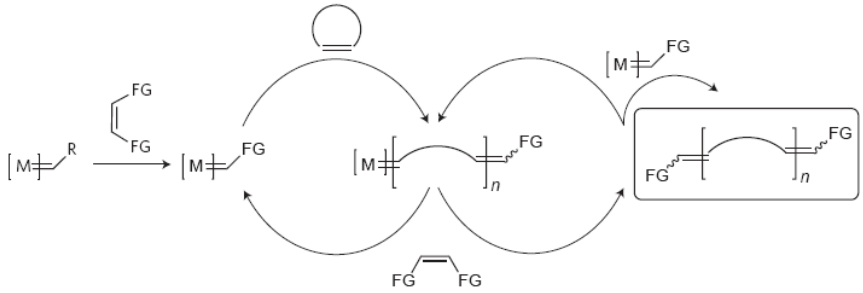


Figure 6 | Mechanism for the formation of telechelic polymers by application of chain-transfer agents (CTAs). The incorporation of the CTA, and therefore the molecular weight determination, relies on both the polymerization kinetics and the equilibration of the CTA into the polymer by cross-metathesis. Polymers with low polydispersity index can be obtained by pulsed addition of monomer to a highly reactive catalyst in the presence of a CTA. FG: functional group.

Conductivity of the Polymer

Metals are conducting because there is practically no energy gap between the highest occupied (valence band) and lowest unoccupied (conduction band) orbitals.

These bands are only partially filled with electrons so that, with even a weak electric field, the electrons easily redistribute: electrons at higher energy and holes at lower energy.

In a polymeric material the band gap is defined by the energy gap between the HOMO (highest occupied molecular orbital) and LUMO (lowest occupied molecular orbital).

Polyacetylene would not normally expected to be a conductor because the band gap between the HOMO and LUMO is too large. Hence, it is found to be a semiconductor with an intrinsic conductivity of about 10^{-5} to 10^{-7} S m^{-1}.

Doping that transforms polyacetylene to a good conductor of electricity is oxidation (or *p*doping).

$[CH]_n + 3x/2\ I_2 \rightarrow [CH]_n^{x+} + xI_3^-$ oxidative doping

It is not the counter ion, I_3^-,but the charges on the polymer that are the mobile charge carriers.

The iodine dopant will remove or to add electrons to the polymer by abstracting an electron under formation of an I_3^- ion). If an electron is removed from the top of the valence band of polyacetylene a vacancy (hole) is created.

There are two types of hole, **polarons** and **solitons**.

A polaron is a radical cation which is localised, partly by Coulomb attraction to its counterion (I_3^-) which also has very low mobility.

However, mobility of a polaron along the polyacetylene chain can be high and charge is carried along. However, since the counterion (I_3^-) is not very mobile, a high concentration of counterions, and hence a high degree of doping, is required so that the polaron can move in the field of close counterions.

Neutral solitons are stable free radical defects which can propagate along the chain but may not carry any charge. However, it may contribute to charge transfer between different chains, called ”intersoliton hopping” where an electron jumps between localized states on adjacent polymer chains and exchanges an electron with a closely located charged soliton.

All conjugated polymers do not carry solitons, but polarons can be found in most of them. Charge transport in polaron-doped polymers occurs via electron transfer between localized states being formed by charge injection on the chain.

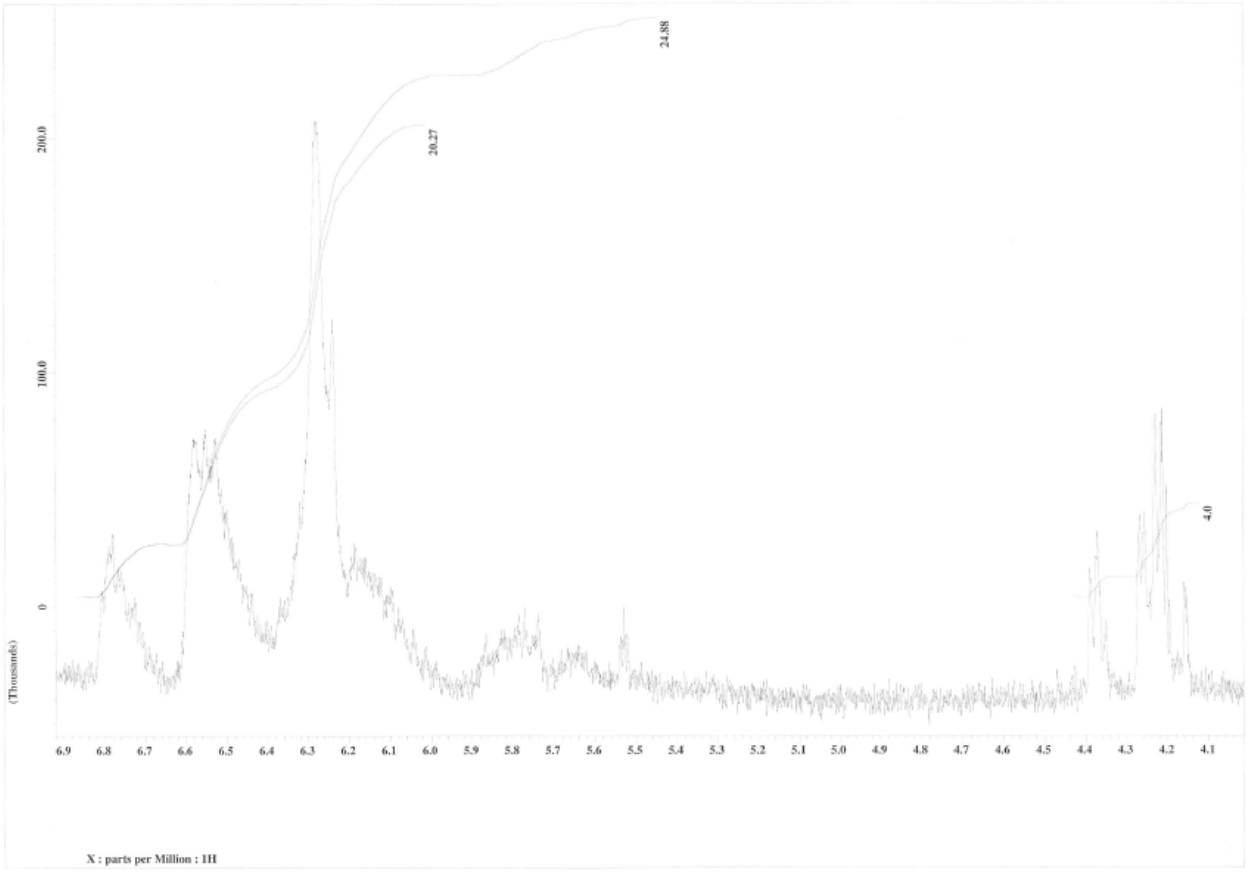


Figure 5 nmr spectrum of end functionalised polyacetylene for Reaction 4

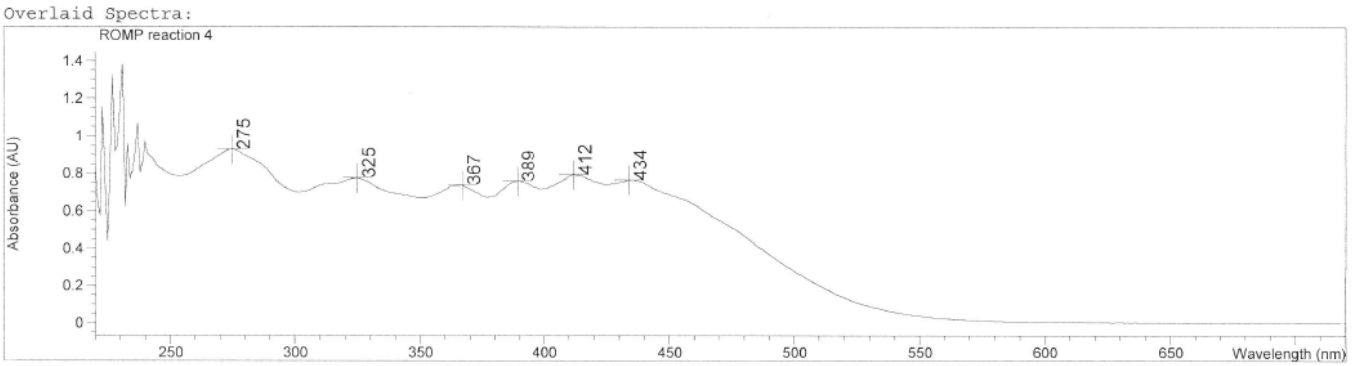


Figure 6 UV-vis spectrum of end functionalised polyacetylene for Reaction 4

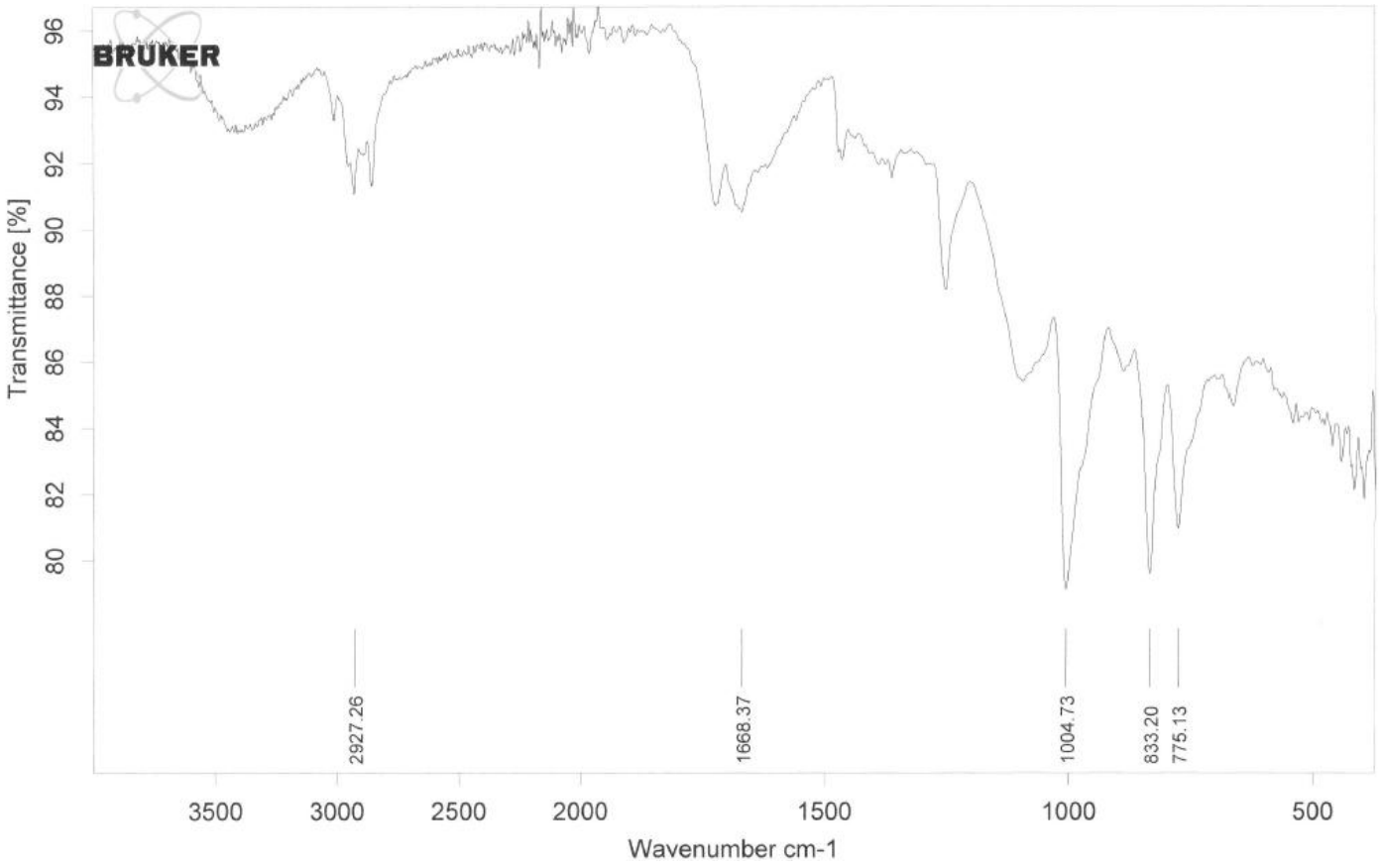


Figure 7 FT-IR spectrum of end functionalised polyacetylene for Reaction 4

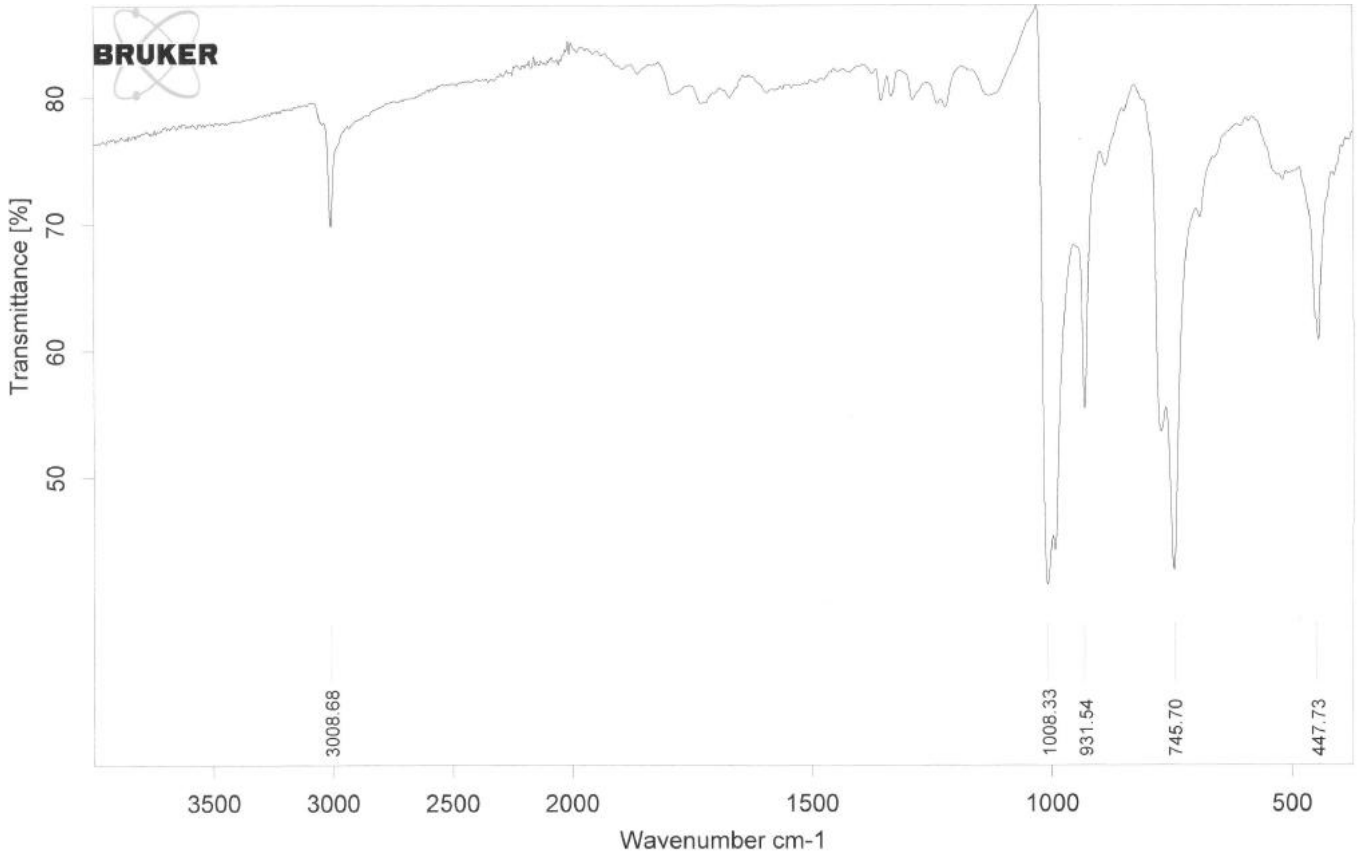


Figure 8 FT-IR spectrum of end functionalised polyacetylene for Reaction 6

QUANTICORP R&D PART 9: CONJUGATION

The final step in your problem solving strategy is to alter the polymer to make it sensitive to a specific analyte:

1. Identify the problem and decide what you want to achieve:
    a. identify a conducting polymer for development into a sensor;
2. Plan how you want to proceed.
3. Establish what you already know, what you don't know and what you need to find out:
    a. research into synthetic methods;
    b. functionalization of the polymer;
    c. synthesis of the polymer;
    d. **conjugation with a sensing molecule**;
4. Come up with some solutions, alternative approaches and new ideas
5. Critically evaluate your solutions and decide whether any of them solve the problem
6. Repeat 3-5 as many times as necessary

Before you can do this you first have to decide on the type of sensing molecule you will need to attach and the method of conjugation.

Task 9.1 Selectivity for glucose

Review Task 1.2 and list the ways which you identified to make the sensor more specific for the detection of a particular chemical.

The IUPAC recommendations on *Selectivity in Analytical Chemistry*[14].in particular the discussion of '*Useful interactions*' and '*Selectivities in methods*' gives examples of different types of selectivity shown in the matrix below:

Chemical reactions	Surface adsorption	Associate formation
Absorption of radiation	Electrochemical reactions	Enzyme reactions
Immunochemical reactions	Separation selectivity	Detection selectivity

In your teams, consider the following questions for 10-15 minutes:

1. Do any of these correspond with your findings?
2. Can you think of specific examples which demonstrate these different types of selectivity?
3. From your reading of the literature, which of these examples has the most obvious application for a glucose sensor?

[14] IUPAC. Selectivity in analytical chemistry (IUPAC recommendations 2001). *Pure Appl. Chem*, 2001, **73**, 1381.

4. Follow this link to the Protein Data Bank http://www.rcsb.org/pdb/101/motm.do?momID=77 and read the article on the 'Molecule of the Month'.

Task 9.2 Conjugation with the sensing molecule

A conjugation reaction is a synthetic reaction wherein a foreign molecule is covalently linked with an endogenous biological molecule to give a product known as a conjugate.

Biological molecules are like any other chemicals in that they have a variety of functional groups which can react with other molecules, so you can make use of these to carry out a variety of conjugation reactions.

1. Quickly brush up on your functional groups by matching the structures in Resource 9.1 to the names below:

Alcohol

Alkene

Amine

Amide

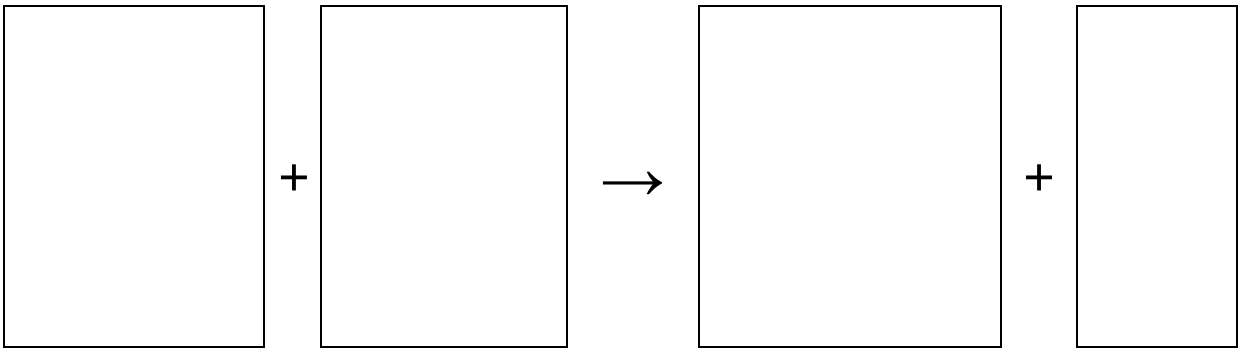
Carboxylic acid

Ester

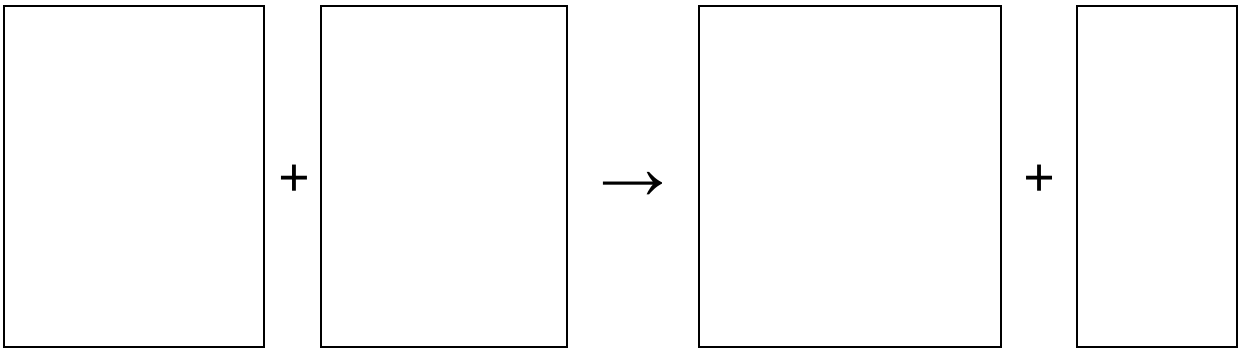
Hemiacetal

2. Now use Resource 9.2 to draw reaction schemes which match the following statements:

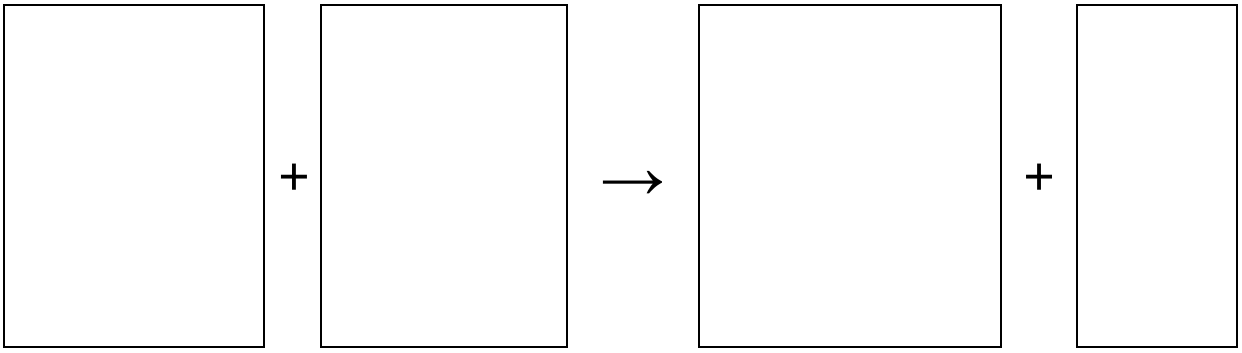
(a) Monosaccharides contain hemiacetal functional groups and undergo condensation reactions to form disaccharides.



(b) Amino acids contain carboxylic acid and amine functional groups and undergo condensation reactions to form peptides.



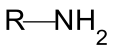
(c) Fatty acids and glycerol contain carboxylic acid and alcohol functional groups respectively and undergo condensation reactions to form triacylglycerols.

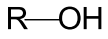


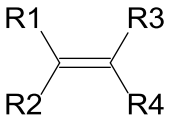
3. Follow the link to the Protein Database http://www.pdb.org/
   (a) search for *glucose oxidase*
   (b) scroll down to the entry for 1GPE GLUCOSE OXIDASE FROM PENICILLIUM AMAGASAKIENSE and click on the name;
   (c) Click on the *Sequence* tab at the top of the page and scroll down to view the protein chain sequence;
   (d) Note the first three letters in the chain - these are the 1-letter codes for the first three amino acids;
   (e) Look up the 1-letter symbols on the *Sigma-Aldrich Amino Acid Reference Chart* http://www.sigmaaldrich.com/life-science/metabolomics/learning-center/amino-acid-reference-chart.html and draw the structures;
   (f) Read the following extract from Wikipedia http://en.wikipedia.org/wiki/N-terminus and draw the structure of the tri-peptide formed from these three amino acids. Identify the N- and C- terminus;

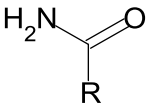
4. Suggest a possible reaction scheme for conjugation of glucose oxidase with another functional group.

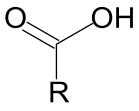
RESOURCE 9.1

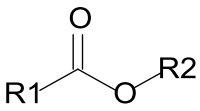


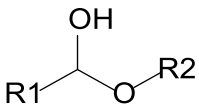




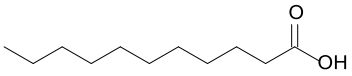


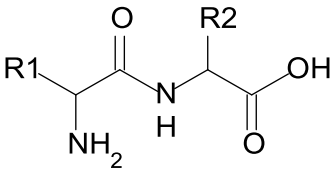


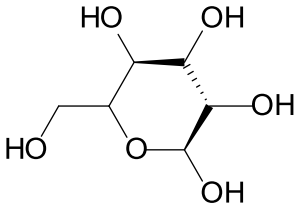


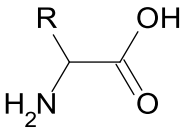


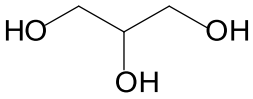
RESOURCE 9.2

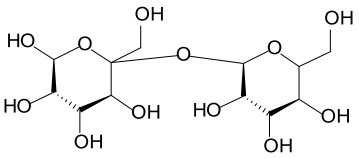

O
OH


O
R2
R1
N
H
OH
NH2
O


HO
OH
OH
HO
O
OH


R
OH
H2N
O


HO
OH
OH


OH
OH
HO
O
O
O
HO
OH
HO
OH
OH
OH

TUTOR NOTES FOR TASK 9.1

Draw a matrix on the whiteboard and collate the information from the teams. The chances are that the students will, as a group and with some prompting from the tutor, come up with many examples similar to those given below.

Chemical reactions Chemical spot tests (eg. for nitroglycerine)	Surface adsorption Quartz crystal microbalance	Associate formation Complexometric reactions (eg. EDTA titrations)
Absorption of radiation Infra-red spectrometry UV-vis spectrometry	Electrochemical reactions Polarography	Enzyme reactions Glucose oxidase reaction with glucose
Immunochemical reactions Pregnancy test kit	Separation selectivity Chromatography Semi-permeable membranes	Detection selectivity Mass spectrometry Atomic emission spectrometry

The intention here is to direct the students to use an enzyme as the selective sensing element. They may well have come to this conclusion in any case:

Directed Learning: instruct students to follow this link to the Protein Data Bank http://www.rcsb.org/pdb/101/motm.do?momID=77 and read the article on the 'Molecule of the Month'.

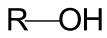
TUTOR NOTES FOR TASK 9.2

The intention with this task is to get the students to think of way of covalently linking an enzyme to a substrate; ultimately they will need to attach the enzyme glucose oxidase to the conducting polymer polyacetylene.

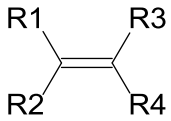
The first two sub-tasks are simply to remind them of some functional group chemistry and the types of reactions that occur between the functional groups of the main classes of biological molecules, namely proteins, sugars and lipids.

1. Quickly brush up on your functional groups by matching the structures in Resource 9.1 to the names below:

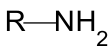
Alcohol



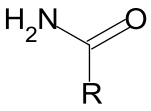
Alkene



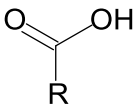
Amine



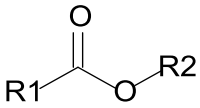
Amide



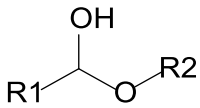
Carboxylic acid



Ester

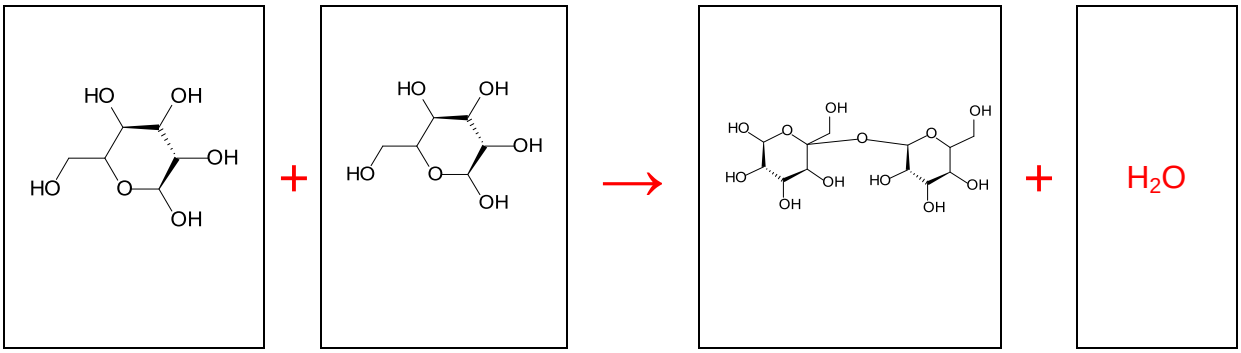


Hemiacetal

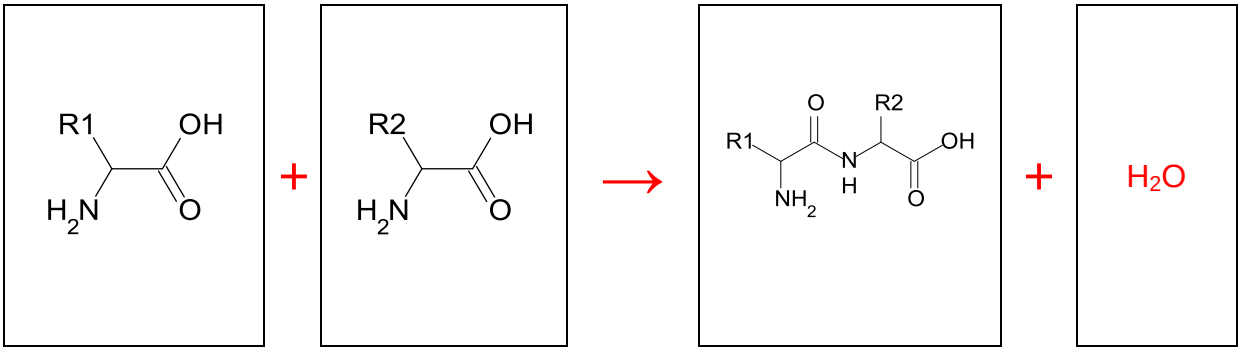


2. Now use Resource 9.2 to draw a reaction schemes which match the following statements:

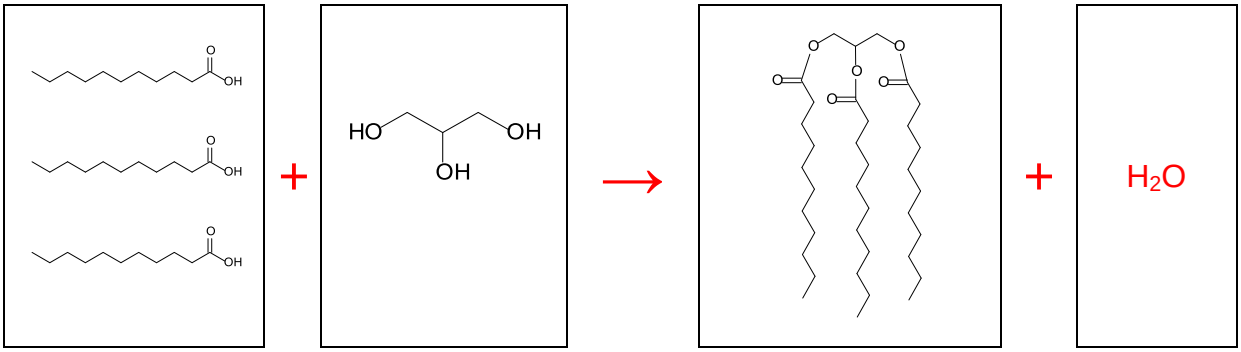
(a) Monosaccharides contain hemiacetal functional groups and undergo a condensation reaction to form a disaccharide.



(b) Amino acids contain carboxylic acid and amine functional groups and undergo a condensation reaction to form a peptide.



(c) Fatty acids and glycerol contain carboxylic acid and alcohol functional groups respectively and undergo a condensation reaction to form triacylglycerol.



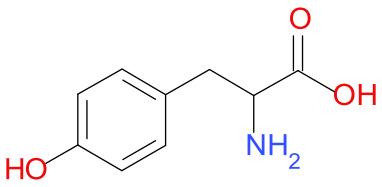
After the teams have completed these tasks they should feedback to the whole group via the tutor and consider the reactions of the functional groups. This leads into the next task which is to examine the structure of the glucose oxidase enzyme and identify the functional groups that occur at the C- and N- terminus.

3. Follow the link to the Protein Database http://www.pdb.org/
   (a) search for *glucose oxidase*
   (b) scroll down to the entry for 1GPE GLUCOSE OXIDASE FROM PENICILLIUM AMAGASAKIENSE and click on the name;
   (c) Click on the *Sequence* tab at the top of the page and scroll down to view the protein chain sequence;
   (d) Note the first three letters in the chain - these are the 1-letter codes for the first three amino acids;

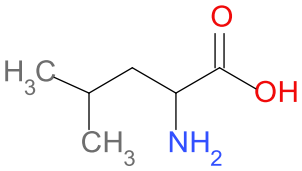
Y L P

   (e) Look up the 1-letter symbols on the *Sigma-Aldrich Amino Acid Reference Chart* http://www.sigmaaldrich.com/life-science/metabolomics/learning-center/amino-acid-reference-chart.html and draw the structures;

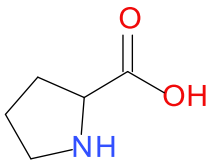
Y Tyrosine



L Leucine

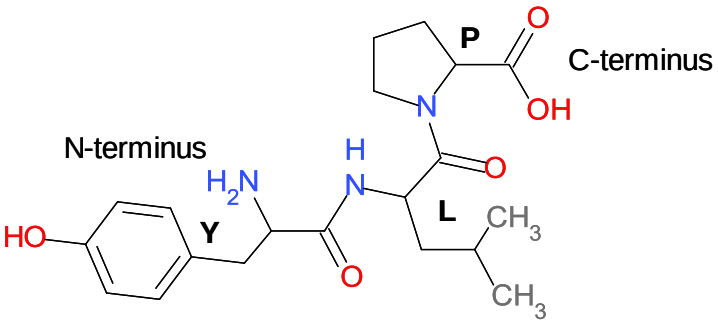


P Proline



   (f) Read the following extract from Wikipedia http://en.wikipedia.org/wiki/N-terminus and draw the structure of the tri-peptide formed from these three amino acids. Identify the N- and C- terminus;

*The **N-terminus** (also known as the **amino-terminus**, **NH_2-terminus**, **N-terminal end** or **amine-terminus**) refers to the start of a protein or polypeptide terminated by an amino acid with a free amine group (-NH_2). The convention for writing peptide sequences is to put the N-terminus on the left and write the sequence from N- to C-terminus. When the protein is translated from messenger RNA, it is created from N-terminus to C-terminus.*



The conclusion that can be drawn is that the ends of the amino acid chains that make up glucose oxidase will have a free amino group at one end, the N-terminus, and a free carboxylate functional groups at the other end, the C-terminus.

4. Suggest a possible reaction scheme for conjugation of glucose oxidase with another functional group.

The functional groups at the C- and N- termini can undergo condensation reactions with amino and carboxylate functional groups respectively. However, these reactions can be with any substrate which has the appropriate functional group, not just other amino acids or proteins.

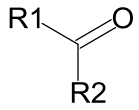
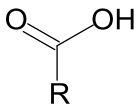
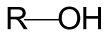
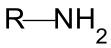
QUANTICORP R&D PART 10: CONJUGATION

Task 10.1 Review the reaction scheme for synthesis of your telechelic polymer (60 min)

- What is the definition of a telechelic polymer?
- What are the functional groups on the ends of the polymer?
- How were these introduced?
- Will this allow you to conjugate it with a protein?

Go to http://www.organic-reaction.com/organic-synthesis/protecting-groups/, find out the purpose of the functional group which you have used and complete the relevant row in the table below.

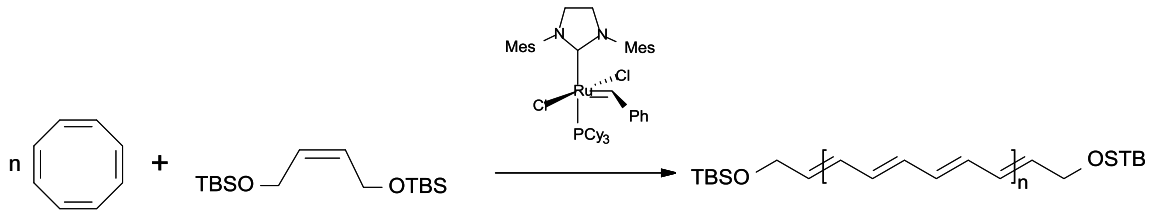
Find a similar reaction for the –COOH functional group and complete the row in the table.

		Reaction conditions	
Functional group	Structure after protection	Protection	De-protection
			
			
			
			

Propose a modified reaction scheme for synthesis of your telechelic polymer so that it can be conjugated with a protein.

TUTOR NOTES FOR TASK 10.1

Review the reaction scheme for synthesis of your telechelic polymer:



2 **5** **1** **4**

What is the definition of a telechelic polymer.

A telechelic polymer is a di-end-functional polymer where both ends possess the same functionality

What are the functional groups on the ends of the polymer?

The functional groups are *tert*-butyldimethylsiloxane groups.

How were these introduced?

They were introduced by reacting tert-dibutyl-1,4-dimethylsiloxane with *cis*-butene-1,4,-diol .

Will this allow you to conjugate it with a protein?

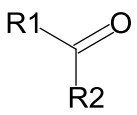
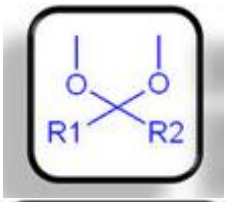
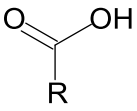
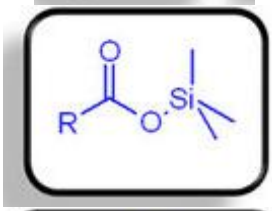
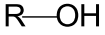
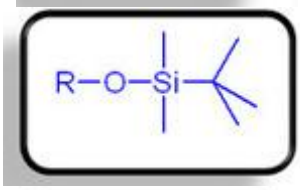
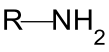
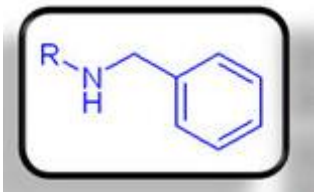
No

Go to http://www.organic-reaction.com/organic-synthesis/protecting-groups/, find out the purpose of the functional group which you have used and complete the relevant row in the table below.

The *tert*-butyldimethylsiloxane group is a protecting group for an alcohol functional group

Find reactions for the other functional groups and complete the table.

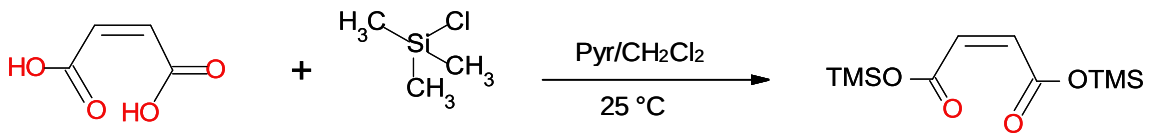
Some examples from the website are given below, but there are others.

Functional group	Structure after protection	Reaction conditions: Protection	Reaction conditions: De-protection
		Dimethyl acetal protection MeOH, dry HCl, 25 °C	50 % CF_3COOH, $CHCl_3$, H_2O, 0 °C TsOH, acetone, 25 °C
		Ester silyl protection Me_3SiCl/Pyr, CH_2Cl_2, 25 °C	$Bu_4N^+F^-$, DMF, 25 °C K_2CO_3, MeOH, H_2O, 25 °C
		Ether silyl protection TBDMSCl, imidazole, DMF, 25 °C	$Bu_4N^+F^-$, THF, 25 °C
		Benzyl (Bn) protection BnCl, aq. K_2CO_3, reflux BnBr, Et_3N, CH_3CN	H_2, Pd-C, ROH HCO_2NH_4, Pd-C, ROH reflux

Trimethylsilyl chloride can be used to protect a carboxylate functional group.

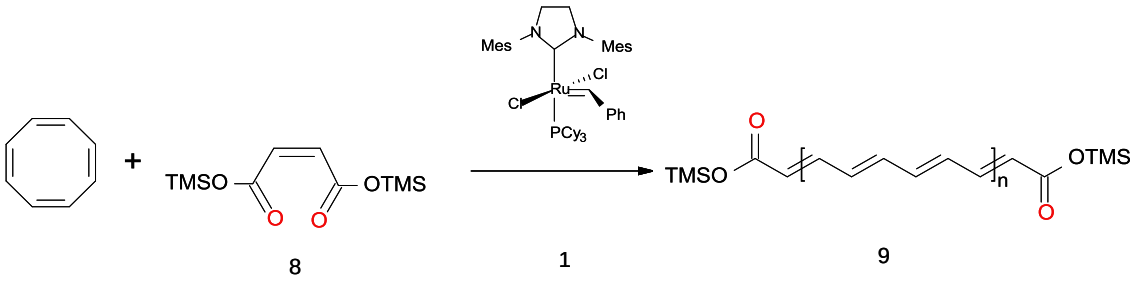
Propose a modified reaction scheme for synthesis of your telechelic polymer so that it can be conjugated with a protein.

1. **Protection of chain transfer agent**
   In the original reaction scheme *cis*-butene-1,4,-diol was protected using dimethyl-*tert*-butylsilyl chloride. However, for subsequent functionalisation with the GOD protein we require either a carboxylic or amine functional group. One solution is to protect ***cis*-butene-1,4,-dicarboxylic acid** (**6**) with trimethylsilyl chloride (**7**).



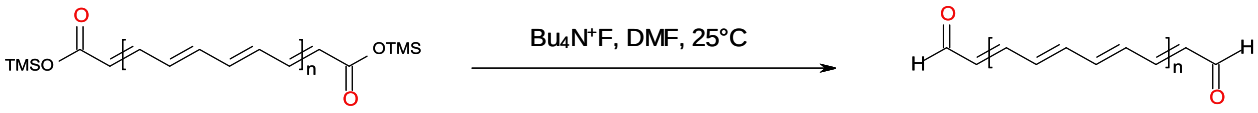
6 7 8

2. Polymerisation and end-functionalisation



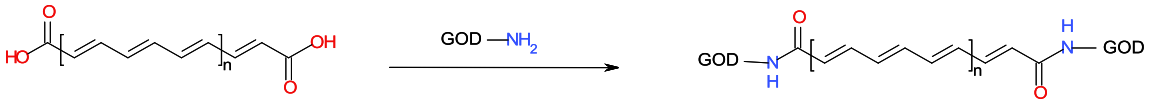
8 1 9

3. Deprotection



9 10

4. Conjugation with GOD



10 11

In practise, an activating agent such carbodiimide would be used to form an activated ester prior to reaction with GOD.

QUANTICORP R&D PART 11: REPORT TO THE R&D TEAM LEADER

Task 11.1 Preparing a report for the R&D Team Leader (120 min)

Your final task is to prepare a technical summary for the R&D Team Leader describing the outcome of your investigation. You need to convince the Team Leader of the scientific and technical merit of your proposal so that it can be taken to the pilot stage, so the science must be convincing. You can use your problem solving strategy as a basis as follows:

1. Identify the problem and decide what you want to achieve:
2. Outline your plan
3. Present your solution
4. Summarise the scientific and technical basis for your solution
5. Critically evaluate your solution, including the benefits and potential risks of proceeding.

You will be advised whether this is to be in the form of a presentation or a written report.