7. Hwuche-Hwuche Bark

Summary

Outline of the exercise

Students are presented with a specific chemical problem set in an industrial context. They work in teams representing subsidiaries of a large company called ACE. In the scenario used here an academic chemist claims to have identified a tree bark with remarkable plant growth-enhancing properties. The academic has approached the 'companies' and they must therefore work against a series of deadlines and in competition with each other in order to:

- secure a deal with the academic;
- identify six compounds extracted from the bark using spectroscopic data;
- determine the best way to synthesise the active component; and
- explain the success of their new product in an oral presentation.

This pack contains a complete set of student handouts for the above scenario, examples of six compounds and their spectra, interpretations of these spectra and detailed tutor's guide for running the exercise. Ideas for further scenarios are also given.

Key aims

- To develop the skills of team working and problem solving.
- Time management, information retrieval, and presentation skills also feature strongly in the exercise.

Time requirements

- Approximately 2 hours tutor contact time (see table below)
- 6 hours private study
- 8 hours total student time

Timetable

This exercise requires 8 hours of student work in its current form. It has been run as a one-day event, during the course of a week (using 4 lecture slots), and (in an extended form) over a university term/semester. Because the teams undertake extensive private study, the exercise can be adapted to fit the time constraints of any institution. A basic timetable is given below:

Session	Time	What the tutor does	Handout	What the companies do next
1	30 mins	Sets the scene	1	Prepare bids and submit them (1 hour)
2	5 mins	Gives out spectra	2	Solve structures and submit them (3 hours)*
3	30 mins	Announces 'news'	3a–d, 4	Prepare presentations (2 hours)
4	1 hour			Give presentations

(* An additional 'help' session can be added – see tutor's guide)

S7 Hwuche-Hwuche Bark

Student Handout 1

The product

Dr Barley is a lecturer in the Agricultural Science Department at the University of Rutland. During a trip to Eastern Asia last year, he came across a small community that spread the shredded bark of a local tree – the Hwuche-Hwuche tree – on the soil where they plant their crops; there appeared to be a significant increase in the speed with which some of the crops germinated and grew in this area, but the locals had managed to keep the nature of their 'fertiliser' a secret.

One of the crops which appears to respond to the application of the bark is closely related to maize. On his return to England with samples of the bark, Dr Barley carried out experiments to ascertain whether the development of maize plants could be accelerated using the bark – the results were extremely encouraging, and he is hoping that the material could have commercial value.

Unfortunately, the tree is not widespread, and it would not be viable to use the bark itself, even if further studies confirm its effectiveness. However, Dr Barley would be willing to give samples of the bark (*ca* 1 kg) to your firm for further studies, providing that a suitable agreement is in place – although he will be approaching other companies if you do not respond positively enough. Whether or not he makes an agreement with your firm will depend on long- and short-term financial incentives you offer, as well as on the quality of the associated research programme.

The company

Your company is a subsidiary of a much larger European agrochemical company called ACE. Nevertheless, you are allowed to operate fairly independently, and you have specific products that are entirely under your control. You also have a skilled R&D department, which could easily undertake a medium-term research programme without recourse to ACE. However, if you wished to undertake the large scale production of a new product you would need initial funding from your parent company – or, if the market were large enough, ACE might wish to make the product at one of their larger European plants. Your company has the following profile:

Products	Agrochemicals, mainly bulk fertilisers
Employees	Management and Marketing (8)
(total number: 80)	Production (40)
	Packaging and Distribution (15)
	Maintenance and Services (9)
	R&D (8)
Turnover	ca £25,000,000 p.a.

Initial assignment

You are all members of the research committee, set up by the Managing Director, which meets every month to plan the use of resources. The research plans are influenced by many factors, so the committee members (who are all trained chemists) are the Managing Director (Chairperson), Finance Director, Sales Director, Research Director (overseeing all R&D), and Chief Chemist(s). In response to Dr Barley, you must discuss:

1) What your immediate short-term experiments should be;

2) A likely deal for Dr Barley; and

3) What longer-term plans should be considered if the Hwuche-Hwuche bark looks promising.

Submit the names of the research committee of your company, a deal for Dr Barley, and an outline of your longer-term plans by the deadline stated, in a sealed envelope, with your company's name on the outside.

Student Handout 2

Your proposal to Dr Barley has been accepted. He may have accepted offers from other companies, so there is a possibility that you will be working in competition with them. You have secured about 500 g of the Hwuche-Hwuche bark.

To save time, your top chemists have tried to isolate the active component from Hwuche-Hwuche bark, whilst the biologists have been checking that the whole bark does accelerate plant growth. After one month of extraction and chromatography, you believe that you have crude material containing the active component, some of which is sent for biological testing. The rest is found to contain several compounds, and a further month of careful chromatography has allowed you to isolate about 10 mg of each of the six major compounds in (almost) pure form. This is enough for full analytical data to be collected.

Your urgent priority now is to assign the structures correctly – accuracy is more important than speed, but there is nevertheless pressure on you to solve the structures quickly.

- Remember that you are a team – you may wish to divide up the structure solving and then get together to check the proposed structures.
- Consultants may be available to offer advice on the data.*
- You must submit your six proposed structures in a sealed envelope by the deadline given.

*optional "help" workshop, at which specialists offer advice are availabe.

Spectra for the unknowns are given in Appendix C

Student Handout 3a

News from the plant biologists

The active component in the bark is compound **B**. It is three times as effective (weight for weight) as the market leader 'megasprout', for which the active component costs ca £50 per kilo. As with many fertilisers/growth promoters, the active component in 'megasprout' is highly potent, and is diluted down many thousand-fold in the actual product that is spread on crops.

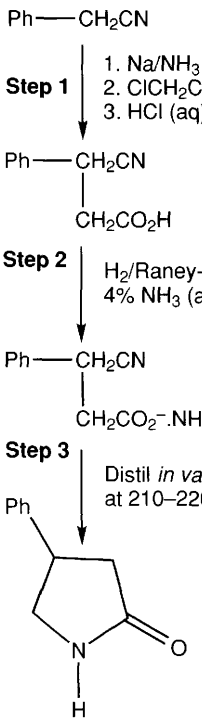
Literature information on B

The commercial viability of the new fertiliser must be established, including details of its synthesis, and the cost of its production.

A quick literature search on compound **B** has provided some useful information. Using this information two possible synthetic routes have been outlined on the following handouts. You must check whether a better synthesis has been published, and also whether there are patents and biological properties reported for compound **B**. In order to cost it, you can assume that bulk materials could be obtained at a third of the Aldrich catalogue price. Gases are very cheap, but their containers are expensive, so bulk prices drop hugely – ammonia costs about £1 per kilo, and hydrogen about £8 per kilo in bulk.

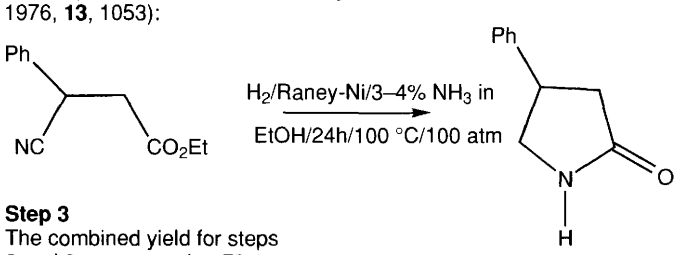
Student Handout 3b

Synthesis of B, Route 1



Step 1
This conversion was reported to proceed in ovarall yield of 75% (see *Chemical Abstract* below).

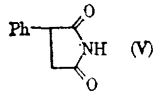
Step 2
Isolated yield and full experimental details were not given for this step. Similar work in 1976 gave the following results (G. Bettoni *et al.*, *J. Heterocyl. Chem.*, 1976, **13**, 1053):



Step 3
The combined yield for steps 2 and 3 was quoted at 79%

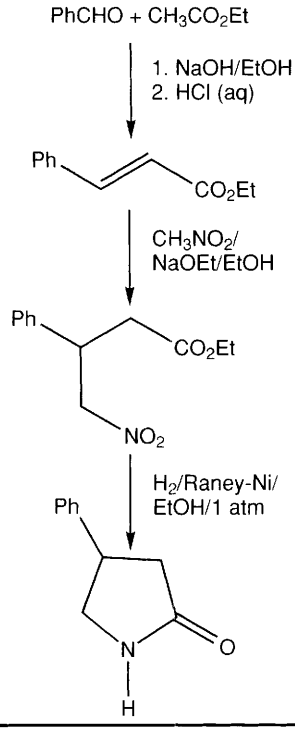
Published data relating to synthesis of B, Route 1 from *Chem Abs.* 1967, 66, 94779y

94779y Synthesis and reactions of β-phenyl-β-cyanopropionic acid. A. G. Chigarev and D. V. Ioffe (Inst. Toksikol., Leningrad). *Zh. Org. Khim.* **3**(1), 85–8(1967)(Russ). Dry $ClCH_2CO_2Na$ (116 g.), m. 215°, was added to $(PhCHCN)^-Na^+$ (prepd. in situ from 117 g. $PhCH_2CN$ and 25.3 g. Na in 1.5 l. liquid NH_3) and stirred 1 hr. to give 74–6% $PhCH(CH_2CO_2H)CN$ (I), m. 74–6°. Crude I boiled 4 hrs. with concd. HCl gave 90% $PhCH(CH_2CO_2H)CO_2H$ (III), m. 165–7°. A soln. of 141 g. III in 110 ml. 26% aq. NH_3 was evapd. to dryness, the residue melted and kept 30 min. at 200–20°, cooled, dissolved in hot EtOAc, filtered, and crystd. to give 75% phenylsuccinimide (V), m. 89–90°, which could be also obtained by heating $PhCH(CH_2CO_2H)CONH_2$ [obtained from I by the Anschutz procedure (*CA* 1, 2702)]. Redn. of V with $LiAlH_4$ gave a 66.5% yield of 3-phenylpyrrolidine, b_2 92–4°, n_D^{20} 1.5545 (picrate m. 159–61°). Esterification of I with MeOH with a catalytic amt. of H_2SO_4 gave 69% $PhCH(CH_2CO_2Me)CN$, m. 50–2°. Hydrogenation of I in 4% aq. NH_3 with Raney Ni gave $PhCH(CH_2CO_2NH_4)CH_2NH_2$, which on heating at 210° cyclized to β-phenylbutyric acid γ-lactam, m. 75°, b_2 178–82°, in 79% yield calcd. on I. CPJR



Student Handout 3c

Synthesis of B, Route 2



Step 1
This conversion was reported to proceed in ovarall yield of 75% (see procedure in Handout 3d).

Step 2
This should proceed by conjugate (Michael) addition of the CH_2NO_2 anion, and should require 1 mol equivalent of base.This type of reaction is well known, and yields of around 80% are expected.

Step 3
This step is in the literature and is claimed to proceed in 75% yield (J. Cologne *et al*., *Bull. Soc. Chim. Fr.*, 1962, 598).

Student Handout 3d

Published data relating to synthesis of B, route 2
From: *Organic Synthesis*, Coll. Vol. I, 1932, 252.

ETHYL CINNAMATE

$$C_6H_5CHO + CH_3CO_2C_2H_5 \xrightarrow{C_2H_5ONa} C_6H_5CH{=}CHCO_2C_2H_5 + H_2O$$

Submitted by C. S. Marvel and W. B. King.
Checked by Henry Gilman, R. E. Fothergill and R. E. Brown.

1. Procedure

In a 2-l. two-necked flask fitted with a short reflux condenser and mechanical stirrer (Note 1) are placed 400 cc. of dry xylene (Note 2) and 29 g. (1.26 atoms) of clean sodium (Note 3) cut in small pieces. The flask is surrounded by an oil bath and heated until the sodium has melted. At this point the stirrer is started and the sodium is broken up into very small particles (Note 4). The oil bath is removed, but stirring is continued until the sodium has solidified in very fine particles. The xylene is then poured off, and to the sodium is added 460 cc. (4.7 moles) of absolute ethyl acetate (Note 5) containing 3–4 cc. of absolute ethyl alcohol (Note 6). The flask is quickly cooled to 0° and 106 g. (1 mole) of pure benzaldehyde (Note 7) is added slowly from a separatory funnel while the mixture is stirred. The temperature is held between 0 and 5° (Note 8). The reaction starts as soon as the benzaldehyde is added, as is shown by the production of a reddish substance on the particles of the sodium. About one and one-half to two hours are required for this addition. The stirring is continued until practically all of the sodium has reacted (one hour after all the aldehyde has been added).

When most of the sodium (Note 9) has disappeared, 90–95 cc. of glacial acetic acid is added and the mixture is carefully diluted with water. The ester layer is separated, the water layer is extracted with about 25–50 cc. of ethyl acetate, and the combined ester portions are washed with 300 cc. of 6 *N* hydrochloric acid and then dried with sodium sulfate. The ethyl acetate is distilled from a water bath and the remaining liquid is transferred to a Claisen flask and distilled from an oil bath under reduced pressure. A small fraction comes over below 128°/6 mm. and is discarded. The ethyl cinnamate (Note 10) boils at 128–133°/6 mm.; 168–173°/46 mm. The yield is 120–130 g. (68–74 percent of the theoretical amount). (NB The "notes" are not reproduced here.)

Student Handout 4

Urgent message from ACE

Your parent company ACE has been informed of the potential of Hwuche-Hwuche bark, but is currently reviewing all its major R&D commitments. They plan to announce a series of investments and cuts in about a month's time and they have asked your management team to give a presentation to the ACE board, outlining the potential of the Hwuche-Hwuche bark project. This presentation must last about five minutes (not less than four or more than seven minutes), and will be given by one or two of your management team. The presentations will be in the next few days – check when you are timetabled to speak. Materials for preparing overheads are available.

Presentations might concentrate on two or three of the following points:

- How successful you were at isolating and identifying **B**;
- A plan for the next phases of its development and any investment requirements;
- How you plan to make it, and how much it will cost (including scale up savings);
- How it compares with rival products (for example, cost and properties) or how you might market it – advertising ideas might come in here;
- How much profit it might make (and whether Dr Barley will get a big slice of it).

T7 Hwuche Hwuche bark

This exercise requires three plenary sessions of between three and thirty minutes, and a longer session for final presentations. It can be run over a week, as a one-day exercise, or spread over several weeks, although in this case it may lose some impact. Detailed advice on each session is given below. Although the exercise can be run by a single tutor, there are two instances where additional support might be helpful – during session 1, if the role play is to have maximum impact, and during the optional help session when the presence of three or four 'consultants' is beneficial. Six 'unknown' compounds can be found in this pack; five of the six (excepting the active compound) are available from Aldrich, and spectra and their interpretations are also included (see Appendices C and D).

Session 1

5 mins	Exercise introduced
5 mins	Students split into (pre-arranged) groups
15 mins	Handout 1 provided, and companies encouraged to start the exercise
10 mins	Plenary feedback session Deadline for bids announced

The tutor's introduction to this exercise can be used to set the problem in context and all of the information necessary is found on the student handout (Handout 1). During trialling it was found to be particularly effective if Dr Barley was introduced in a role-play, in which he enters the "office" of the managing director of the company; these roles can be played by the tutor and a colleague respectively. 'Companies' should have approximately six students each, and should assign themselves a company name and identify roles within the group (as described on the handout).

The plenary session can be used to gather feedback from the students concerning the short-, medium- and long-term considerations of the project, and all groups should be called upon to put forward suggestions. These might include, for example, getting the deal with Dr Barley, details of plant testing, identifying the components, lead compounds, development of a market compound, factors influencing success or otherwise (including cost, toxicology, and environmental issues) and time-scales. A summary of the points made in the discussion, given at the end of the plenary session, can be useful.

Finally, announce a deadline for submitting bids.

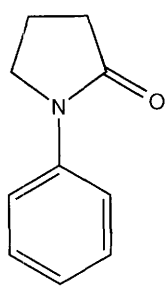
Session 2

This session can be very short, and simply requires that Handout 2 and spectra are given to the students. Handout 2 tells each of the companies that their offer to Dr Barley has been accepted, and introduces the problem solving aspect of the exercise **(spectra for this exercise can be found in appendix C)**. An element of urgency, and therefore pressure, can be brought in if the companies are made to realise that they are in competition with each other. The emphasis should be on the importance of finding the correct structures (for which marks are given) and on team work.

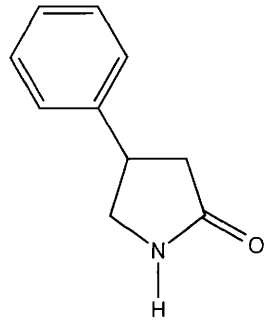
Optional workshop with consultants

An extra session offering guidance on identification of the unknown compounds can be useful. Students should not be told whether their structures are right or wrong. Other colleagues, postgraduate students or research assistants might be involved as consultants. Interpretations of the spectra for the six unknowns in this pack are provided in Appendix D.

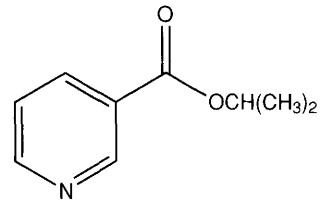
Hwuche Hwuche Bark – structures of substances isolated from bark



A



B



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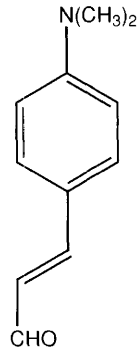
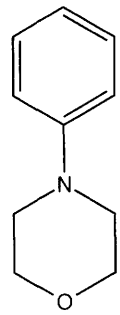
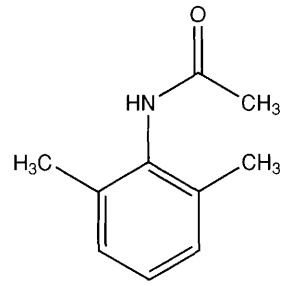


D



E



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Session 3

5 mins	Identify unknown structures and request IUPAC names for them. At least one copy of Aldrich should be available per company
15 to 25 mins	Collect submissions of compound names Distribute handouts 3a–d Distribute handout 4 while companies are studying handouts 3a–d

The purpose of this session is initially to name the compounds and find out which of them are commercially available. The correct structures should be displayed so that all of the students are working on the same compounds at this stage. Of the six compounds used in this teaching pack five can be located in Aldrich, and the name for the sixth (the active compound) should be determined. Marks should be awarded for correctly naming each of the structures.

Handouts 3a–d explain the second part of this session. Students are now required to examine the literature provided on the synthesis of the active compound and decide how it might best and most cost effectively be prepared commercially. They are then required to give a presentation (see Handout 4) which addresses the industrial production of the fertiliser.

Session 4

Students give their presentations during this final session, the length of which depends on the number of groups involved. Presenters should remain outside the room until they have given their presentations, as it may be unfair for a later presenter to see an earlier presentation. The managing director of ACE can chair the session, and provide a short summary of the exercise at the end.

An assessment scheme is provided in this pack, based on various aspects of the exercise, and prize(s) can be awarded to the best companies; if students have taken part with enthusiasm, this helps the exercise to end on a high.

Adapting the exercise

This exercise can be easily modified. The basic format breaks down into:

a) The introduction, in which a commercial possibility (or problem) is set in context, and companies are established. Some general discussion helps the companies to get started, to identify roles, and to think about some longer-term issues.

b) An urgent problem solving session tackling specific chemical questions – identifying unknown compounds (of appropriate difficulty), a literature search, or the analysis of data relating to a process.

c) A solution to the problem can be identified within the overall context of the exercise.

d) A final presentation – a report, an oral presentation, or a poster.

Additional scenarios

Outlines are given below for various scenarios which could be used in a similar manner to the Hwuche-Hwuche bark exercise developed here.

■ Contamination scare

A company employee has spotted several dead fish near the (harmless?) effluent outflow. The company must respond before it becomes public. What should they do?

Session 1

Students are divided into two groups representing companies and environmental control units respectively.

A range of possible chemicals from the fictitious company, and their toxicity levels, should be provided by the tutor. Students need to identify suitable analytical methods which could be used to identify these. Methods chosen should be practicable for the undergraduate laboratory. Contaminants chosen could be organic or inorganic, highly toxic trace materials requiring tricky physical chemistry to quantify, or less toxic compounds present in larger amounts.

Session 2

In the laboratory, samples are provided which contain acceptable (measurable) levels of three contaminants, but dangerous levels of one. Students must identify this contaminant. Data could be provided if an appropriate laboratory session were not available.

Session 3

Companies must identify how to reduce the level of the contaminant in the effluent by looking at the industrial process (provided by the tutor). Environmental units must prepare a one-page report outlining their case for prosecuting the company.

Session 4
The problem has gone public. In the final session, a series of short TV interviews take place between an interviewer (environmental unit representative) and a company representative – the former asking questions to show how awful the company is, and the latter trying to defend their position and subsequent action.

Cheaper production costs

This exercise could be based on organic, inorganic or physical chemistry, and is a much simpler exercise to run. It involves identifying a synthetic process [for example, an actual commercial procedure (perhaps an old one), or a suitable synthesis that is not actually commercial], which could be improved by:

a. changing the synthetic route (new organic synthesis);

b. using a better inorganic reagent or catalyst; or

c. modifying the reaction conditions.

Session 1
The exercise starts with an outline of the process, and a discussion concerning the process. From the information given, the teams must estimate the cost of making the product.

Session 2
An emergency memo arrives indicating that a rival is undercutting their price, and they must reduce their cost by 30%. The teams need to use literature, catalogues, and their skill to develop a modified procedure that reduces the cost as much as possible.

Session 3
It is useful to have a halfway workshop in which groups can discuss their ideas with a consultant (ie with a tutor). It is then revealed that company cuts are due, and only the really competitive products will survive.

Session 4
At a series of presentations, the company management (*ie* the tutor) will hear proposals from teams about making their product more competitive. Assessment can be based on presentations and/or a single A4 report, and/or a poster. The winning team is the one which presents the most convincing case that they can reduce the cost.

Silent witness

Teams of students represent chemists in a forensic science department. There are any number of possibilities for inventing a crime, and getting the teams to try and solve it using chemical evidence, provided as the exercise unfolds. It would be possible to end such an exercise with a court case, particularly if there was conflicting evidence that defence and prosecution teams could use.

New pharmaceutical leads

This exercise could closely follow the Hwuche-Hwuche bark format presented in this chapter, with medicinal chemistry considerations replacing agrochemical factors.

Extending the exercise

Some possibilities for extending the exercise are:

- Addition of more (and/or harder) unknowns;
- Addition of a financial management component (*eg* companies have a budget from which they must buy spectra or consultancy help);
- A substantial literature search, to explore syntheses and properties of an active compound;
- Production of a final report (to a specific format).

Subsequent exercises

The 'Hwuche-Hwuche Bark' project establishes 'companies' that work well as teams (even though there may be some clashes of personality), and these teams can be used in the three subsequent exercises, extending the basic scenario:

- Annual Review Presentations – where students give individual talks to their colleagues, as part of the company's annual review of its graduate employees.
- Interviews – where the companies advertise, interview, and appoint a new employee; all of the students must apply for a job in another company.
- Posters – where the company teams each prepare a poster on a new potential area of research.

These are stand-alone exercises, but the use of the companies from the 'Hwuche-Hwuche Bark' exercise adds realism, encourages development of team skills, and saves time.

Assessment

An assessment scheme is provided below.

a) Offer to Dr Barley (/10)
Top marks should be awarded for offers that do not cost too much, but would be likely to secure the material.

b) Structures (/24)
For each structure: 4 marks (correct), 2 marks (close), or 0 marks (incorrect).

c) Names of the compounds (/6)
For each compound correctly named – 1 mark.

d) Presentations (/20):
(i) Quality of science (/8)
(ii) Quality of presentation (including visual aids) (/8)
(iii) Did they engender confidence and enthusiasm? (/4)

Company	Offer	Structures	Names	Presentation	Total (/60)