Green Chemistry – The atom economy

Tutor summary

- Divide the students of your tutorial group (*ca* nine students) up into three sub-groups (*ca* three students) right at the beginning of the group session so they have the opportunity to interact together from the start. Let the students know that each member of the sub-groups will have to make a presentation (*Sections B, C* and *D*) and that a single individual from the whole tutorial group will need to make a brief presentation to the whole class (*Section E*).

- Take a register of the group using the attendance sheet/mark sheet supplied. Get the students to <u>sign the sheet</u>. This is necessary for marking purposes and ensures we can track who did what and when. Given that the ITU attracts a relatively high % of the final Chem-2 assessment, we need to be careful about our book-keeping.

- For *Sections B, C* and *D*, let the students work through the problems in their sub-groups but bring the whole group together for *Section E* (the discussion on the basic principles of Green Chemistry). For *Sections B-D*, the three members of each group (*Groups 1-3*) should work through the tasks in parallel, ensuring no 'sleeping' partners.

- The timetable is based around a 35 minute session (*Section B*), 2 x 45 minute sessions (*Sections C* and *D*) and a 15 minute session (*Section E*) that require a reading period, preparation time for oral presentation and then the actual oral presentations (no more than five minute duration). This defines three presentation opportunities for each sub-group of *ca* three students. Different students should give each presentation, though in the plenary session (*Section E*), students could give a second presentation.

- Tutors to inform their tutorial group where their coursework is to be handed in.

- OHP acetates, pens and unused worksheets will be reused.

- The designated person from each tutorial group to present their conclusions to whole class.

- Any suggestions for improvements will be gratefully received.

Good luck.

A	B	C	D	E	F
INTRODUCTION **(48)**	**INTRINSIC ATOM ECONOMIES OF THE MAIN REACTION CLASSES** **(3 ´ 4)**	**ATOM ECONOMY CASE STUDY: THE INDUSTRIAL SYNTHESIS OF IBUPROFEN** **(3 ´ 4)**	**POOR ATOM ECONOMY IN INDUSTRY: CATALYSTS FOR CHANGE** **(3 ´ 4)**	**ITU 4 PRINCIPLES OF GREEN CHEMISTRY** **(12)**	**PLENARY SESSION** **(48)**
Sustainable development	**GRP 1** *Addition reaction: Bromination of cyclohexene.* ***OHP***	**GRP 1** Stereochemical *AND PHARMACOLOGICAL ASPECTS OF IBUPROFEN* ***OHP***	**GRP 1** *'Stoichiometric' ethylene oxidation* *Vs.* *Catalytic ethylene oxidation* ***OHP***	Tutorial group discussion	Tutorial group presentations
Concept of atom economy	**GRP 2** *Substitution reaction: Acyl substitution of ethyl propionate with methyl amine* ***OHP***	**GRP 2** *The Boots Company synthesis of Ibuprofen* ***OHP***	**GRP 2** *'Stoichiometric' nitrobenzene reduction* *vs.* *Catalytic nitrobenzene reduction* ***OHP***		Tutor summary of ITU 4 Coursework
Outline of ITU 4	**GRP 3** *Elimination reaction: DEHYDROHALOGENATION OF TRIMETHYLBROMIDE* ***OHP***	**GRP 3** The BHC Company synthesis of Ibuprofen ***OHP***	**GRP 3** *'Stoichiometric' aromatic nitration* *Vs.* *Catalytic aromatic nitration* ***OHP***	Tutorial group report	Post-evaluation.
	Tutor summary and questions	Tutor summary and questions	Tutor summary and questions	Tutor to lead discussion. Assign tutor group representative	

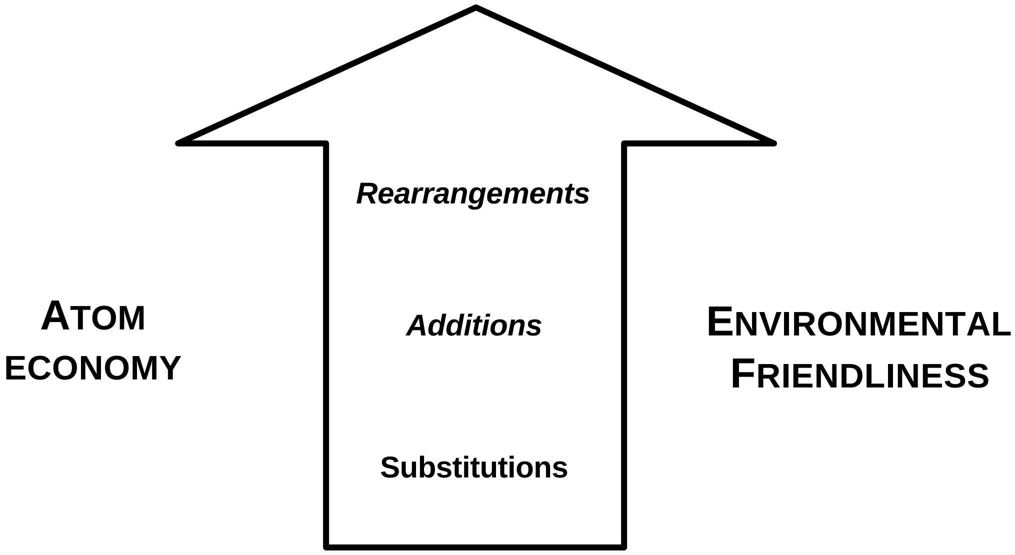
Section B - Tutor Summary

- Percentage yield has, historically, been used to evaluate the efficiency of chemical syntheses. However, this approach provides no information about the extent to which by-products/wastes are formed in a particular reaction.

- Trost's concept of atom economy addresses the failings evident in the yield approach. It asks chemists to consider the degree to which all reactants in a particular synthesis are incorporated into the desired product.

- As our analysis of the Wittig reaction (*Scheme 2*) has demonstrated, although highly efficient in terms of yield many reactions are highly inefficient in the context of atom economy.

- We have also seen that the main classes of chemical reactions exhibit intrinsically different atom economies. In our discussion, we have concluded that additions (Grp 1) are atom economical, substitutions (Grp 2) much less so, and eliminations (Grp 3) inherently atom uneconomical. The final class, which we have not considered in depth, is rearrangements (*e.g.* Diels-Alder). Such transformations effect the reorganisation of constituent atoms within a particular molecule, so by definition rearrangements are 100% atom economical. The intrinsic atom economies (and also the environmental friendliness) of the main reaction classes are illustrated in the diagram below.



Section C - Tutor Summary

- In *Section C* we have focused our attention on the industrial synthesis of Ibuprofen, the active ingredient in many common analgesics (painkillers). The demand for Ibuprofen (>13,000tpa) has soared since it was given over-the-counter status in the mid-eighties.

- We have seen that the original synthesis of Ibuprofen, developed by the Boots Company in the 1960s, comprises of six synthetic steps, all of which employ auxiliary reagents in <u>stoichiometric</u> quantities. At 32%, the atom economy for the synthesis is very poor. Indeed, at present, if the drug were exclusively manufactured via the Boots synthesis, then over 27,000 tonnes of unwanted by-products would enter the waste stream each year!

- The 'green' BHC synthesis has, however, revolutionised Ibuprofen manufacture. With only three steps, all being <u>catalytic</u>, and no need for co-solvents, the new route has an impressive atom economy of 77%. In addition to the environmental gains evident in the process, the manufacturers also enjoy significant economic benefits. Compared to the six-step traditional synthesis, the new three-step synthesis can generate more Ibuprofen in a shorter period of time and with less capital expenditure.

- Innovative chemistry and process technology has dramatically reduced the environmental burden associated with the production of Ibuprofen. The BHC synthesis is now widely regarded as a benchmark for environmental and production efficiency within the pharmaceutical industry.

Section D - Tutor Summary

- In Section D we have compared and contrasted stoichiometric and catalytic processing options for the manufacture of three industrially important bulk chemicals, ethylene oxide, aniline and nitrobenzene.

- Ethylene oxide was traditionally manufactured using the chlorohydrin process. The significant waste burden (large quantities of $CaCl_2$) associated with the process is evident in the lowly atom economy figure of only **23%**. Ethylene oxide is now exclusively manufactured using catalytic methodology. All reactants used in the catalytic synthesis are incorporated into the final product, resulting in **100%** atom economy.

- The traditional synthesis of aniline is the Béchamp process, which simultaneously generates large volumes of iron oxide sludge. At only **35%**, atom economy for the process is poor. In contrast, the catalytic synthesis of aniline has an atom economy of **72%**, with water being the only by-product. The catalytic route is now overwhelmingly the method of choice for aniline production.

- The 'mixed acid' route to nitrobenzene has remained virtually unchanged since its introduction in 1834. The process generates large volumes of spent sulfuric acid, which has to be collected and recycled. Atom economy for the process is low, at **51%**. An alternative synthesis of nitrobenzene, employing a triflate catalyst, has recently been established <u>on a laboratory scale</u>. As well as a significant improvement in atom economy (**87%**), water is the only by-product.

- The examples above clearly demonstrate the environmental (and economical) superiority of catalytic processes over their stoichiometric counterparts. Catalytic methodologies are widely accepted in the chemical sector as the key to operating in an environmentally benign fashion. As well as integrating catalysis into new process designs, it is likely that many existing stoichiometric processes will be replaced by catalytic alternatives.

ITU1 Green Chemistry: The atom economy

Coursework marking scheme

The essay must be structured and present a justified case. Weaknesses in grammar, punctuation and spelling should be penalised. The students are required to apply the concepts of Green Chemistry to suggest improvements in operating procedures within the pharmaceutical industry that could improve their efficiency/environmental (E) factor. They are expected to use examples selected from the actual ITU material in addition to a general review article on the current status of the Green Chemistry movement. The essays should be neat and easy to read but they do not need to be typed.