Recycling the undesired enantiomer of naproxen

A context/problem-based learning (C/PBL) resource

Workshop 1 – Answers

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Produced for the Royal Society of Chemistry

Workshop 1 – answers

During the first part of this session have a quick chat to each group and answer any questions they may have.

Groups should identify the following activities as a minimum. They may be more explicit.

- Planning the experiments
- Carrying out the esterification reaction
- Testing different conditions for the racemisation
- Testing different conditions for the hydrolysis
- Analysing the results
- Deciding on new conditions to test
- Carrying out the reaction on a large scale
- Writing the presentation (introduction, proposed route, discussion of lab work, tables figures)
- Writing final reports

They don't need to begin planning reactions at this stage. They should focus on deciding who will focus on each aspect of the lab work and begin thinking about how to fairly divide up the presentation.

Part A

Students should bear in mind the yield of the reactions (91% for method 1 and 90% for method 2) when scaling up. Simple ratios can be used to scale up the weight used in the prep to the weight needed to make 15 kg.

Setting the cost of (*R*)-naproxen as £0 is a simplification. There would be some costs associated with purifying it from the waste solutions from (*S*)-naproxen manufacture, but they would be the same for both methods, so it is reasonable enough to omit them.

Directly scaling up the work up procedures in this way would not be carried out on a plant scale, but is the simplest way to directly compare the methods.

Table 1: Method 1 costs

Material	Volume / mL	Density / g cm^{-3}	Mass used in prep / g	Mass needed to make 15 kg / kg	Raw material cost / kg	Cost to make 15 kg
(*R*)-naproxen	N/A	N/A	1.00	15.63	£0.00	
c. H_2SO_4	0.23	1.84	0.13	1.95	£10.87	£21.23
MeOH*	30.00	0.79	37.88	591.86	£15.05	£8,907.49
Sodium bicarbonate (aq)	80.00	1.00	80.00	1250.00	£2.00	£2,500.00
Ethyl acetate*	90.00	0.90	100.33	1567.73	£37.90	£59,423.27
Total						**£70851.99**

Table 2: Method 2 costs

Material	Volume / mL	Density / g cm^{-3}	Mass used in prep / g	Mass needed to make 15 kg / kg	Raw material cost / kg	Cost to make 15 kg
(*R*)-naproxen	N/A	N/A	2.00	15.71	£0.00	
H^+ resin	N/A	N/A	0.50	3.93	£40.00	£157.07
MeOH*	50.00	0.79	63.13	495.80	£15.05	£7,460.73
Sodium bicarbonate (aq)	80.00	1.00	80.00	628.27	£2.00	£1,256.54
Ethyl acetate*	100.00	0.90	111.48	875.52	£37.90	£33,182.21
Total						**£42,056.55**

Part B

Pros: some money saved in raw materials and waste costs.

Cons: may require extra plant operations to recover from one reaction and transfer to the next.

Will depend on how the plant is set up whether it is worth recycling it.

Part C

There is no absolutely correct answer to this as many factors relating to the size and set up of the plant will have an impact on the cost of heating to different temperatures and on the hourly overheads for a process.

If a plant has a source of cheap heating (for example a nearby steam generator which is always on to power other processes) then the differences in the cost of heating to 40 °C and to reflux may not be very significant. Whereas, if the heating has to come directly, via electricity for example, then a small difference in temperature may make a large difference in cost.

If the plant is large and several processes are running at any given time then the fixed hourly costs of running the reaction might be relatively small, as building would be open and some of the workers would be there even if the process wasn't running. However, in a smaller plant the plant might be shut down between batches and so the costs of running a process for longer would be more noticeable.