Recycling the undesired enantiomer of naproxen

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

Workshop 1 hand-out

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Part 1 – Team building

In order to complete a team project successfully you should become familiar with each other and the details of the project.

Read through the module book together and make sure everyone understands what the project involves and how it will be assessed. If you have any questions ask the teacher.

Make a list of the different tasks that will need to be completed for the project will be a success and discuss which tasks everyone would like to do.

Part 2 – Process design

Method 1

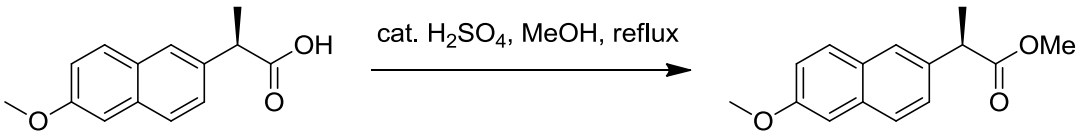

Figure 1: Reaction scheme for method 1

Concentrated sulfuric acid (0.23 mL, 0.43 mmol) was added dropwise to a solution of (*R*)-Naproxen (1 g, 4.35 mmol) in methanol (30 mL). The resulting solution was heated to reflux for 1 hour, allowed to cool to rt and poured into a saturated aqueous solution of sodium bicarbonate (50 mL). This suspension was extracted with ethyl acetate (3 x 30 mL) and the combined organics washed with saturated aqueous sodium bicarbonate (30 mL), dried over $MgSO_4$ and concentrated *in vacuo* to a colourless solid (0.96 g, 91%)

Method 2

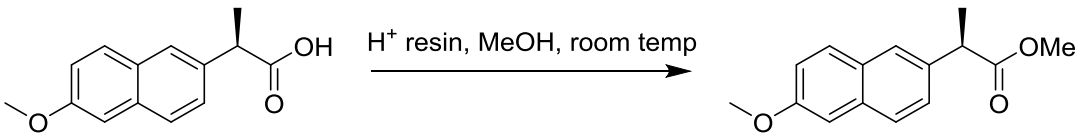

Figure 2: Reaction scheme for method 2

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(*R*)-Naproxen (2 g) was dissolved in methanol (50 mL) containing Dowex-H^+ resin (500 mg) and stirred at 40 °C for 2 days. Reaction mixture filtered to remove resin and concentrated *in vacuo*. Residue dissolved in ethyl acetate (50 mL) and washed with saturated aqueous sodium bicarbonate solution (3 x 20 mL), dried over $MgSO_4$ and concentrated *in vacuo* to a colourless solid (1.91 g, 90%).

A) Use the tables below to compare the raw materials cost of these two methods. First calculate how many kg you would need to make 15 kg of the final product using each method. Then work out the cost to make 15 kg. Assume that (*R*)-naproxen has no cost because it is being produced as a waste product of (*S*)-naproxen at our plant.

Cost calculations

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		£0.00	
c. H_2SO_4	0.23	1.84	0.13		£10.87	
MeOH*	30.00	0.79	37.88		£15.05	
Sodium bicarbonate (aq)	80.00	1.00	80.00		£2.00	
Ethyl acetate*	90.00	0.90	100.33		£37.90	
Total						

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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		£0.00	
H^+ resin	N/A	N/A	0.50		£40.00	
MeOH*	50.00	0.79	63.13		£15.05	
Sodium bicarbonate (aq)	80.00	1.00	80.00		£2.00	
Ethyl acetate*	100.00	0.90	111.48		£37.90	
Total						

*For this exercise we are providing you with laboratory solvent costings but in reality the actual solvent costs would be about ten times less per kg on pilot plant scale than on the lab scale (because of bulk delivery and storage).

B) Amberlyst resin can be used 4 – 5 times. Discuss what impact this would have on the sustainability of each process.

C) The two methods require heating to different temperatures for different lengths of time. Discuss what impact you think this will have on their usefulness in a pilot plant.

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