Electronic Supplementary Material (ESI) for Chemistry Education Research and Practice
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Sustainable production of chemicals

Handout

According to the Brundtland Report (1987) „sustainable development is development that meets the needs of the present without compromising the ability of future generations to meet their own needs."

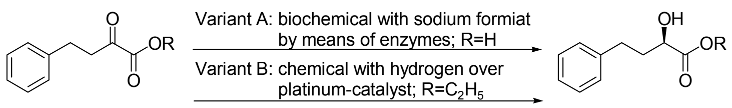
Since the development and safeguarding of wealth is conceivable only in the frame of social harmony, in accordance with a sound environment and on the basis of stable resource availability, the three dimensions environment, economy and social affairs are equally important. Chemistry, as one of the sciences involved, can contribute to a sustainable development, because it represents a starting point for important mass flows. The utilization of resources must not exceed the regeneration rate just as the emission of substances may not exceed the degradation / processing rate within the environment.

However, this goal can only be measured and controlled in few areas of life. Therefore, a pragmatic approach is to choose the least harmful path. Comparing several products, one should prefer the option which

- occasions low costs (e.g. for facilities, raw material extraction, product use → economy)
- is more social (e.g. by fewer accidents, more jobs, no children's work → social affairs)
- protects the environment (e.g. by less waste, emissions, raw materials, land use, by advantageous product properties → environment)

Evaluating potentially opposing results is time consuming and practically impossible in class. A so called life cycle assessment (systematic analysis of the environmental impacts of products during their total lifespan), which highlights only one dimension of the three aspects above, will hardly be conducted in industry due to the effort and costs.

In order to gain an initial overview, a simple mass balance can help, i.e. an illustration of how much raw material or waste can be recorded per product unit. Two alternative syntheses in the production of pharmaceuticals (Scheme 1) will serve as an example. The mass balance (Figure 1) shows a relatively high auxiliary material demand and a high amount of sewage (in kilogram per kilogram product) for variant A of the biochemical, while it reveals that variant B is overall more advantageous. Remarkably, a complete life cycle assessment (Figure 2) according to the method of EcoIndicator 95 shows the same result! As can be seen here, extraction (M4) and the subsequent recycling (M8) most adversely affect the sum of eco points: at the end the stepped line shows more points (Eco 95) for variant A than for variant B.



Scheme 1 Two possible syntheses (variants A and B) of (R)-2-hydroxy-4-phenylbutyric acid (ethylester); a substance which is used in the production of pharmaceuticals.

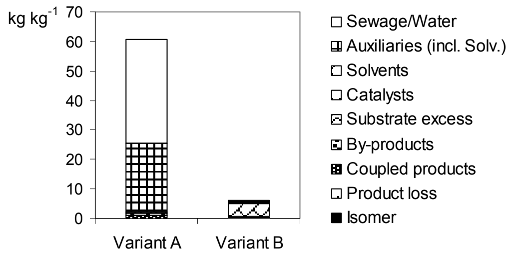
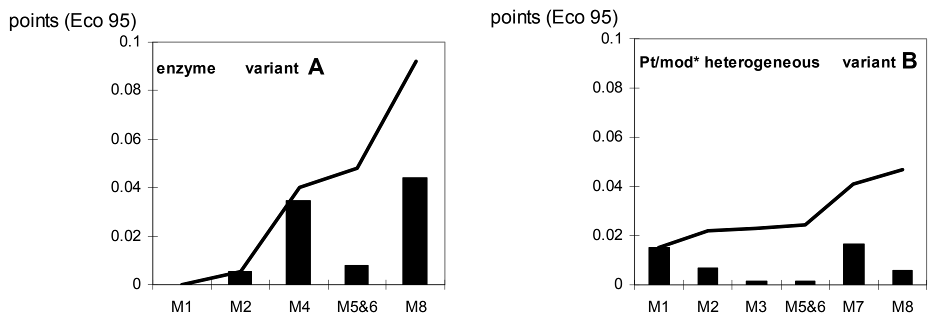


Figure 1 waste (kg) of both variants per kg product.



M1 = catalyst
M2 = reduction
M3 = catalyst removal
M4 = extraction
M5 = solvent drain off
M6 = rectification
M7 = purification
M8 = solvent recycling

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Figure 2 Eco-points for both variants of Scheme 1.

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However, the raw material in Scheme 1 is only an intermediate in a larger synthesis sequence. All substances that are used have to be produced with raw materials and energy, which admittedly is not considered within the life cycle assessment presented above. Actually, the frame of consideration is too narrowly drawn. The preceding step plays an important role for the overall assessment. This becomes clear by means of a small modification, which was done in the development of a production process at the company *Syngenta* (Switzerland) for a chemical applied in agriculture (a so called agrochemical, Scheme 2).

$$A + B + C + NaOH \xrightarrow{\text{Auxiliary material}} \text{Agrochemical} + NaCl + H_2O$$

Scheme 2 Simplified reaction scheme (with substances A, B, C) for the production of an agrochemical.

At the laboratory stage, sodium hydroxide (NaOH) produces a fraction of only 0.47% of the process' overall global warming potential (Figure 3, left hand side), while about a ten percent fraction (Figure3, right hand side) was recorded for the (expensive) auxiliary material (see reaction arrow in Scheme 2). Since the auxiliary material effectively incurs after reaction, it can be recovered to a large extent by means of the application of additional sodium hydroxide. The production of sodium hydroxide in relation to the auxiliary material is much less active regarding global warming. Therefore, the part of the auxiliary material in the total global warming potential could be reduced to about one percent in the final process by means of a slight increase of the amount of sodium hydroxide (Figure 3, left hand side) to 0.72% of the total global warming potential. By not even doubling the amount of sodium hydroxide, not only the global warming effect of the auxiliary material but also its raw material costs were reduced to a tenth part.

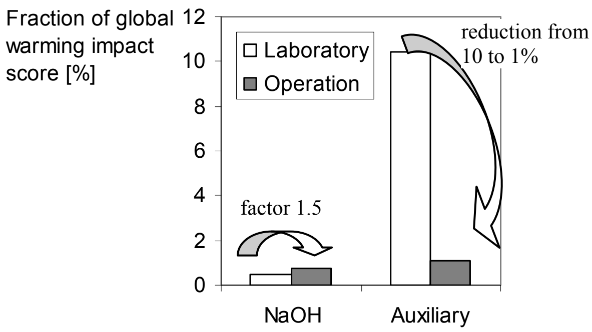


Figure 3 Fractions of global warming scores (% of total impact) for sodium hydroxide and an auxiliary material in the synthesis of an agrochemical (Scheme 2) during the development of a production process from the laboratory scale.

Translated and modified reproduced from Eissen M., Geisler G., Bühler B., Fischer C., Hungerbühler K., Schmid A., Carreira E. M., Mass balances and life cycle assessment, in Green Chemistry Metrics, Measuring and Monitoring Sustainable Processes (Eds.: Lapkin A., Constable D. J. C.), ISBN 9781405159685, John Wiley & Sons Ltd., Oxford, Copyright (2008), pp. 200-227. With kind permission from John Wiley and Sons

While the life cycle assessment, (represented here by the consideration of the global warming potential) makes the impact of doubling sodium hydroxide blatantly obvious (auxiliary: 10% → 1%), practically nothing would be visible in a mass balance! For the auxiliary amount was basically only exchanged by sodium hydroxide. Insofar, a mass balance can give important hints, especially when established for as many synthesis steps as possible, but it cannot replace a complete life cycle analysis.

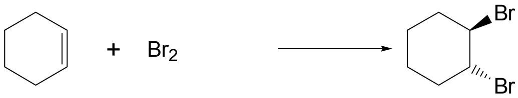
Since life cycle assessment in industry is far away from blanket application, mass balances can be viewed as target-oriented in a first approximation if alternative scenarios deliver the same product. A look at the mass balance of production alone would be shortened, if, for instance, two different agrochemicals were juxtaposed. The sum of eco points within a life cycle assessment contains differences not only within the product life cycle phase *production*, but also in the *utilisation* and *disposal* phase. Specifically, this means that different toxicities of different agrochemicals have an influence as well as a different rate with which an agrochemical has to be brought out on the field. Finally, the carcinogenic soot particles of diesel incineration exhausts of the tractor likewise enter the assessment.

As long as production is the only concern, because one is dealing with the same product in all alternatives, it is a matter of the chemist' field of view, who develops and optimizes syntheses. His examinations can provide the chemical engineer with worthwhile hints about possible alternatives and weak points and can stimulate an interactive discourse with him for the purpose of optimization. Thus, aspects for environmental compatibility can already be considered in early synthesis design, when margins are stills large and costs for process modifications are still small.

Considering partial aspects of the above mentioned three dimensions of sustainability, the following worksheets intend to provide an introduction to the topic.

Production of chemicals: environment, health and safety <u>Worksheet 1</u>

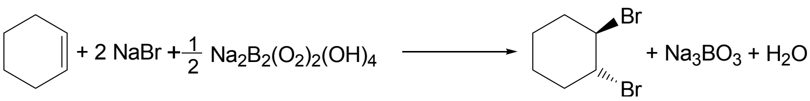
It is impossible to imagine everyday life without products from the chemical industry. One should merely think of plastics and pharmaceuticals. The production must be secure and should pollute the environment as little as possible. The configuration and operation of technical production plants should care for environmental, health and safety aspects as comprehensively as possible. In order to gain insight, the electrophilic bromination of alkenes will be examined exemplarily. These reactions allow access to twofold brominated hydrocarbons (Scheme 1).



Scheme 1 Addition of bromine to cyclohexene

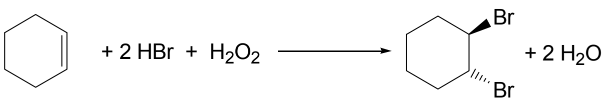
Protocol 1: Cyclohexene (123 g) is stirred in 300 mL carbon tetrachloride (density 1.594 g·mL^{-1}) and 15 mL ethanol (density 0,785 g·mL^{-1}) at -5°C. Bromine (210 g) in 145 mL carbon tetrachloride is added so that the temperature does not exceed -1°C. After reaction, solvent and cyclohexene excess are removed via distillation. The distillation of the product under reduced pressure delivers 303 g dibromocyclohexane (95.3%).

However, bromine is a dangerous substance, which easily evaporates and is very toxic. Against the background of safety aspects it could be more sensible to convert unproblematic bromide compounds, e.g. sodium bromide, with alkenes (Scheme 2, Scheme 3). Nevertheless, bromide ions do not react with the double bound, which is why they have to be oxidized to bromine with an oxidant in the reaction vessel (Problem 1).



Scheme 2 Addition of bromine to cyclohexene with sodium bromide and sodium perborate.

Protocol 2: Sodium bromide (3.06 g) is added to a mixture of sodium perborate (2.29 g) and cyclohexene (1.11 g) in 25 mL acetic acid (density 1.049 g·mL^{-1}) and stirred for two hours. A dilution with water and an extraction with ether are the next steps (on this, albeit, there is no information). After removal of the solvent, the isolation of the product via column chromatography (silica gel, hexane) results a yield of 87%. The coupled product is called sodium borate.



Scheme 2 Addition of bromine to cyclohexene with hydrogen bromide and hydrogen peroxide

Protocol 3: A mixed and cold (0°C) solution of hydrogen peroxide (35%, 1.94369, density 1.11 g·mL^{-1}, 20 mmol) and of hydrogen bromide (48%, 3.3714 g, density 1.,49 g·mL^{-1}, 20 mmol) is added to a solution (room temperature) of cyclohexene (10 mmol) in 5 mL carbon tetrachloride (density 1.594 g·mL^{-1}) (or dioxane) over the period of time of 10 min. The reaction ends after two hours. The organic layer is washed with water and brine and is dried over sodium sulfate. After removal of the solvent, the product yield is 86%. (The information regarding HBr(aq) und H_2O_2(aq) differs slightly from literature.)

Though there is a great plenty of further bromination methodologies, only these three should be considered exemplarily. Which one would you choose (Problem 3)?

Problem 1 Note the oxidation reaction from bromide ions to bromine (electron transfer reaction).

Problem 2 The *yield* relates the amount of desired product to the amount of the (key-) substrate. Demonstrate that the yield in protocol 1 is 95.3%.

Problem 3 Note criteria which you would consider for your decision.

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Production of chemicals: environment, health and safety **Worksheet 2**

The dimensions economy, environment and social affairs have an influence on the decision for one of several synthesis alternatives.

Economy: costs have to be competitive

Environment: the environment has to be spared by consuming a low amount of raw materials and energy and by keeping emissions as low as possible.

Social affairs: health and safety of employees, residents and the public must be protected.

Producing companies collect all necessary information for a proper basis of decision-making. In the following, at least some of the relevant aspects shall be considered.

1. Resource efficiency
2. Production of waste materials
3. Raw material costs
4. Hazards of applied substances (Worksheet 3)

1. Resource efficiency

The resource efficiency of different synthesis protocols can be compared by determining the amounts of raw materials, solvents, auxiliary materials etc. needed in order to produce one kilogram of product. This is denoted as mass index S^{-1} and presented here exemplarily for protocol 1.

$$S^{-1} = \frac{\text{Raw materials [kg]}}{\text{Product [kg]}} = \frac{123\text{g } C_6H_{10} + 210\text{g } Br_2 + 445\text{mL} \cdot 1.594\,\frac{\text{g}}{\text{mL}}\ CCl_4 + 15\text{mL} \cdot 0.785\,\frac{\text{g}}{\text{mL}}\ \text{ethanol}}{303\text{g dibromocyclohexane}} = 3.4789$$

One kilogram of product is produced with 3.4789 kg of raw materials. → Problem 4

2. Production of waste materials

According to this result, 2.4789 kg of applied substances are not product, and are therefore waste. The environmental factor E is the amount of waste per kilogram of product. → Problem 5, Problem 6 or Problem 8

$$E = \frac{\text{Waste [kg]}}{\text{Product [kg]}} = \frac{751.105\text{g waste}}{303\text{g dibromocyclohexane}} = 2.4789$$

Problem 4 Determine how many kilograms of cyclohexene are necessary per kilogram of product in protocol 1. Determine the corresponding amounts for the other substances as well.

Problem 5 The waste amount of 751g for protocol 1 consists of 709g carbon tetrachloride, 12g ethanol, 14.9g by-products and 15.1g substrate excess of cyclohexene. Calculate how these values can be determined.

Problem 6 Using the results from Problem 5, determine how many kilograms of waste (Ethanol, etc.) are produced per kilogram of product.

Table 1 and 2, and Figure 1 and 2, respectively, show raw materials (see Problem 4) and waste amounts (see Problem 6) for all three protocols. → Problem 7, Problem 8

Substances that are used in work up in protocols 2 and 3 cannot be considered quantitatively and, thus, are considered only qualitatively.

Table 1 Raw materials of protocols 1-3 in [kg / kg product]

Method:	1	2	3
Substrates	1.10	2.27	1.50
Solvents	2.38	9.22	3.83
Water	-	-	1.45
Sum	3.48	11.49	6.78

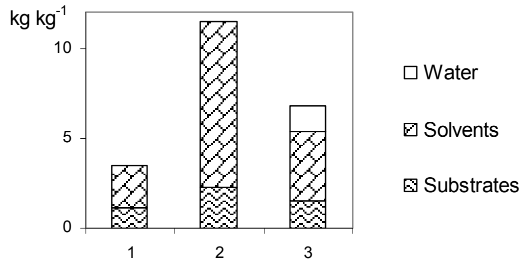

Figure 1 Mass index S^{-1} (see Table 1)

Table 2 Waste of protocols 1-3 In [kg / kg product]

Method:	1	2	3
Coupled products	-	0.60[a]	0.15
By-products	0.049	0.24	0.19
Substrate excess	0.05	0.43	0.16
Solvents	2.38	9.22	3.83
Water	-	-	1.45
Sum	2.48	10.49	5.78

[a] 0.53 kg Na_3BO_3 and 0.07 kg water

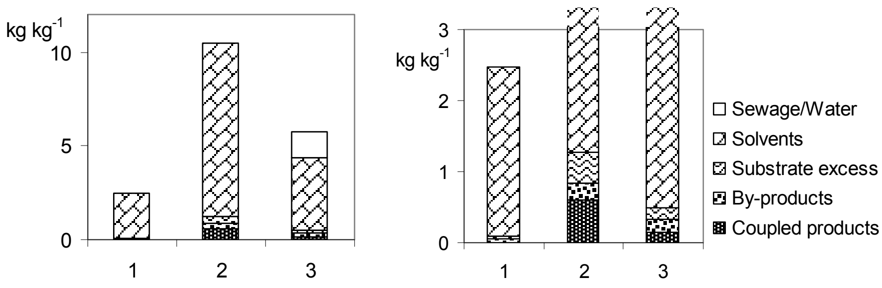

Figure 2 Environmental factor E (see Table 2). The right hand side shows a zoomed presentation in order to make coupled and by-products better visible.

Problem 7 Compare the results presented in Table 1 and 2, and Figure 1 and 2, respectively.

Problem 8 Exercise applying the software EATOS: determining data shown in Table 1 and 2 analogously to Problem 4 and 6 is tedious. Use the software EATOS (file: Eatos.jar) in order to reproduce the resource demand (mass index S^{-1}) and the waste production (environmental factor E) of the three protocols. Substances for which no amounts are indicated in the protocol have to be ignored. Hence, work-up can only be considered qualitatively.

3. Raw material costs

Table 3 Costs of substances that are used in protocols 1 to 3 (Scheme 1 to Sheme 3) on the basis of an Aldrich-chemicals-catalogue.

	Costs [€ kg^{-1}] [a]	Substance amounts per kg product and costs					
		1		2		3	
		[kg]	[€]	[kg]	[€]	[kg]	[€]
Cyclohexene	35.75	0.4059		0.3902		0.3948	
Bromine	32.86	0.6931					
Carbon tetrachloride	90.59	2.341				3.83	
Ethanol	6.44	0.0389					
Sodium perborate	62.20			0.8051			
Sodium bromide	25.70			1.0758			
Acetic acid	7.80			9.22			
Hydrogen bromide (48%)	26.78					0.7777	
Incorporated water	26.78					0.8425	
Hydrogen peroxide (35%)	19.82					0.3269	
Incorporated water	19.82					0.6072	
Sum							

[a] Except for ethanol (catalogue 2003/04) online data from 22/03/2008 were used here in order to present the costs in [€ kg^{-1}].

Problem 9 Determine the raw material costs for the protocols (→Table 3) and present the results graphically in a Figure 3 *Raw material costs* analogue to Figure 1 and 2.

Production of chemicals: environment, health and safety <u>**Worksheet 3**</u>

4. Hazards of applied substances

The **R-phrases** of substances used in protocols 1 to 3 are listed here. The data was taken from the European chemical Substances Informations System (http://ecb.jrc.it/esis/) or from the Aldrich-catalogue.

Bromine		
	26	Very toxic by inhalation
	35	Causes severe burns
	50	Very toxic to aquatic organisms
HBr (aq, 48%)		
	20	Harmful by inhalation
	35	Causes severe burns
H_2O_2 (aq, 35%)		
	5	Heating may cause an explosion
	8	Contact with combustible material may cause fire
	20/22	Harmful by inhalation and if swallowed
	35	Causes severe burns
Sodium bromide		
	-	(Aldrich-catalogue)
Sodium perborate		
	8	Contact with combustible material may cause fire (Aldrich-catalogue)
	23/24/25	Toxic by inhalation, in contact with skin and if swallowed (Aldrich-catalogue)
	36/37/38	Irritating to eyes, respiratory system and skin (Aldrich-catalogue)
Ethanol		
	11	Highly flammable
	23/24	Toxic by inhalation and in contact with skin (Aldrich- catalogue)
	36/37/38	Irritating to eyes, respiratory system and skin (Aldrich- catalogue)
Acetic acid		
	10	Flammable
	35	Causes severe burns
Ether		
	12	Extremely flammable
	19	May form explosive peroxides
	22	Harmful if swallowed
	66	Repeated exposure may cause skin dryness or cracking
	67	Vapours may cause drowsiness and dizziness
Carbon tetrachloride		
	23/24/25	Toxic by inhalation, in contact with skin and if swallowed
	40	Possible risk of cancer
	48/23	Toxic: danger of serious damage to health by prolonged exposure through inhalation
	52/53	Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment
	59	Dangerous for the ozone layer
Dioxane		
	11	Highly flammable
	19	May form explosive peroxides
	36/37	Irritating to eyes and respiratory system
	40	Possible risk of cancer
	66	Repeated exposure may cause skin dryness or cracking

Problem 10 Though the information of the presented worksheets is not sufficient in total for a final decision, the three protocols should be comparatively evaluated regarding a potential production plant. Consider

a) environment, health and safety aspects and

b) costs.

Additional remark: some companies produce hydrogen bromide as a waste product in other processes.

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Production of chemicals: environment, health and safety **Worksheet 3**

4. Hazards of applied substances

The **H-statements** of substances used in protocols 1 to 3 are listed here. The data was taken from Wikipedia (German Version, 17 March 2012).

Bromine

330	Fatal if inhaled
314	Causes severe skin burns and eye damage
400	Very toxic to aquatic life

HBr (aq, 48%)

331	Toxic if inhaled
314	Causes severe skin burns and eye damage
280	Contains gas under pressure; may explode if heated
335	May cause respiratory irritation

H_2O_2 (aq, 35%)

271	May cause fire or explosion; strong oxidizer
332	Harmful if inhaled
302	Harmful if swallowed
314	Causes severe skin burns and eye damage

Sodium bromide

-

Sodium perborate

272	May intensify fire; oxidizer
360	May damage fertility or the unborn child
302	Harmful if swallowed
335	May cause respiratory irritation
318	Causes serious eye damage

Ethanol

225	Highly flammable

Acetic acid

226	Flammable liquid and vapour
314	Causes severe skin burns and eye damage

Ether

224	Extremely flammable liquid and vapour
302	Harmful if swallowed
336	May cause drowsiness or dizziness
EUH019	May form explosive peroxides
EUH066	Repeated exposure may cause skin dryness or cracking

Carbon tetrachloride

351	Suspected of causing cancer
331	Toxic if inhaled
311	Toxic in contact with skin
301	Toxic if swallowed
372	Causes damage to organs through prolonged or repeated exposure
412	Harmful to aquatic life with long lasting effects

Dioxane

225	Highly flammable
351	Suspected of causing cancer
319	Causes serious eye irritation
335	May cause respiratory irritation

Problem 10 Though the information of the presented worksheets is not sufficient in total for a final decision, the three protocols should be comparatively evaluated regarding a potential production plant. Consider

a) environment, health and safety aspects and

b) costs.

Additional remark: some companies produce hydrogen bromide as a waste product in other processes.

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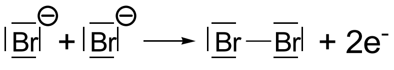
Solution to Problem 1

$2\,Br^- \rightarrow Br_2 + 2e^-$ or 

Solution to Problem 2

$$\text{Yield} = \frac{n(\text{Product})}{n(\text{Key-substrate})} = \frac{\frac{m(\text{Dibromocyclohexane})}{M(\text{Dibromocyclohexane})}}{\frac{m(\text{Bromine})}{M(\text{Bromine})}} = \frac{\frac{303\text{ g}}{241.953\ \frac{\text{g}}{\text{mol}}}}{\frac{210\text{ g}}{159.808\ \frac{\text{g}}{\text{mol}}}} = \frac{1.252\text{ mol}}{1.314\text{ mol}} = 0.953$$

Solution to Problem 3

Possible criteria are:

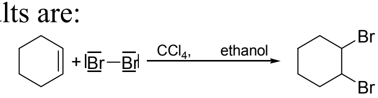
Economy	Environment	Social affairs
Raw material costs Raw material availability Production plant costs (e.g. safety technology) Availability of a manufacturing plant Disposal costs Yield Time demand Utilization of by-products Purity of product	Environmental compatibility of resource extraction Emissions (e.g. CO_2, solid waste) into the environment Resource efficiency Energy consumption Life cycle assessment	Health of employees and residents → process safety Emitted substances are harmless for the public

A reliable decision is not possible without further examinations. Worksheet 2 presents approaches for an examination.

Solution to Problem 4

$$\frac{123\text{ g Cyclohexene}}{303\text{ g Dibromocyclohexane}} = 0.4059\,\frac{\text{g}}{\text{g}} = 0.4059\,\frac{\text{kg}}{\text{kg}}$$

Analogous results are:



Details in the reference: (Org.Syn 1943, 2, 171)	123 g	210 g	445 mL	15 mL	303 g
Amended in [g]:	123 g	210 g	709 g	12 g	303 g
Converted in [kg / kg product]:	0.4059	0.6931	2.341	0.0389	1

(Note: the second line shows rounded values, which is why minor differences in the third line appear, where results were determined exactly.)

Solution to Problem 5

The amounts for carbon tetrachloride and ethanol are already shown in the solution to Problem 4.

Determination of substrate excess (assuming that the key-substrate is converted completely):

Substance	Mass [g]	Molecular weight [g mol^{-1}]	Amount of substance [Mol]	Excess [Mol]	**Excess [g]**
Cyclohexene	123	82.145	1.49735224 ($=\frac{123}{82.145}$)	0.18327535 ($\approx 1.497 - 1.314$)	**15.0551537** ($= 82.145 \cdot 0.18327535$)
Bromine	210	159.808	1.31407689($=\frac{210}{159.808}$)		

Determination of the amount of by-product (yield 0,953)

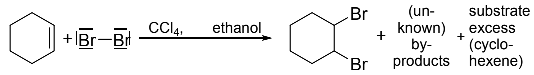
Substance	Mass [g]	Molecular weight [g mol^{-1}]	Amount of substance [Mol]	Amount of substance, which is not converted to the product. [Mol]	**Mass of by-products,** which result from both substrates [g]
Cyclohexene	123	82.145	1.49735224 ($=\frac{123}{82.145}$)	0.06176756 ($\approx 1{,}314 \cdot (1 - 0{,}953)$)	5.07389617 ($= 82.145 \cdot 0.06176756$)
Bromine	210	159.808	1.31407689($=\frac{210}{159.808}$)	0.06176756 ($\approx 1{,}314 \cdot (1 - 0{,}953)$)	9.87095014 ($= 159.808 \cdot 0.06176756$)
				Sum:	**14.9448463**

Solution to Problem 6

If 14.94 (see second table in the solution of Problem 5) are considered instead of 14.9 , the result will be 0.0493 $\frac{kg}{kg}$.

$$\frac{14.94\text{ g Cyclohexene}}{303\text{ g Dibromocyclohexane}} = 0.0493\,\tfrac{g}{g} = 0.0493\,\tfrac{kg}{kg}$$

Analogous results are:



	Cyclohexene	Br_2	CCl_4	ethanol	Dibromocyclohexane	(unknown) by-products	substrate excess (cyclohexene)
Details in the reference: (Org.Syn 1943, 2, 171)	123 g	210 g	445 mL	15 mL	303 g		
Amended in [g]:	123 g	210 g	709 g	12 g	303 g	14.9 g	15.1 g
Converted in [kg / kg product]:	0.4059	0.6931	2.341	0.0389	1	0.0493	0.0497

(Note: the second line shows rounded values, which is why minor differences in the third line appear, where results were determined exactly.)

Solution to Problem 7

The comparison of the three protocols makes clear that protocol 1 is the best regarding applied raw material amounts and produced waste material. Solid waste (0.53 kg Na_3BO_3 / kg product) has to be disposed of according to protocol 2. The generation of by-products in protocols 2 and 3 diminishes the yield. (Supporting hint: with protocol 3 cinnamic acid can be brominated yielding 99% according to the literature. The mass index remains at $S^{-1} = 4.8$ (without water $S^{-1} = 3.7$), which is still higher compared to protocol 1.) In this comparison, even raw materials for the work-up in protocols 2 and 3 are missing. In literature no data are giving (Scheme 2 to 3). Thus, at least qualitatively further solvents and washing waters need to be considered. (However, it can be assumed that a column chromatography for purification of the product would not be conducted in a technical scale.)
The lowest amount of solvent is used in protocol 1. In the first instance this means a generation of higher waste amounts for the other protocols. Potential recycling means the application of a correspondingly high amount of energy. However, the protocols are not (yet) optimized so that the utilization of lower amounts is conceivable. Especially substrate excesses have to be reduced in case of a higher production volume.
The generation and presence of water in protocols 2 and 3 implicates a treatment of wastewater, which can entirely be omitted in protocol 1.

Solution in short form

Protocol 1 is the best. Aspects:

- solid waste (0.53 kg Na_3BO_3 / kg product) in protocol 2
- high amount of by-product in protocols 2 and 3
- aqueous work-up in protocols 2 and 3 is not considered yet, but has to be kept in mind as well.
- low amount of solvent in protocol 1
- potential recycling → correspondingly high amounts of energy
- protocol 1 copes without water → no wastewater treatment is necessary

Solution to Problem 8

The tabular values can be reproduced. The problem should motivate an introduction to the application of the software EATOS. After entering the stoichiometry and substance amounts of the synthesis protocols, a column diagram can be established which shows the data being presented in the table. The software executes conversions (see Problem 4 to 6). Synthetic protocols can thereby be presented comparatively in short time.

Hint: Concerning impure raw materials, e.g. 48% hydrogen bromide, the entry of substance amount in the unit 'mol' delivers a false calculation because of a programming error. Therefore, it has to be converted to 'g' or 'mL' beforehand. These data are already given in protocol 3. Sample calculation:

$$m(HBr) = n(HBr)\cdot M(HBr) = 0.02\text{mol}\cdot 80.9119\,\tfrac{g}{mol} = 1.618\text{g} \quad \text{and} \quad m(HBr-\text{solution}) = \frac{m(HBr)}{\text{fraction}} = \frac{1.618\text{g}}{0.48} = 3.3714\text{g}$$

Besides, in the literature the substance amounts in 'mL' are not identical with the quantity in 'mol'. Deviating from literature, 48% HBr(aq) and 35% H_2O_2(aq) are presented in protocol 3 instead of 47% and 30%, respectively. No commercial products were available by Aldrich with these concentrations, yet its data concerning density and costs should be considered.

Electronic Supplementary Material (ESI) for Chemistry Education Research and Practice
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Solution to Problem 9

The results are presented in bold in the following table. In order to make transparent the determination of costs in [€ kg^{-1}], Aldrich's data are presented. Data regarding the molecular weight are not used. Purity plays a role for the determination of the water fraction for hydrogen bromide (48%) and for hydrogen peroxide (35%).

Sample calculation:

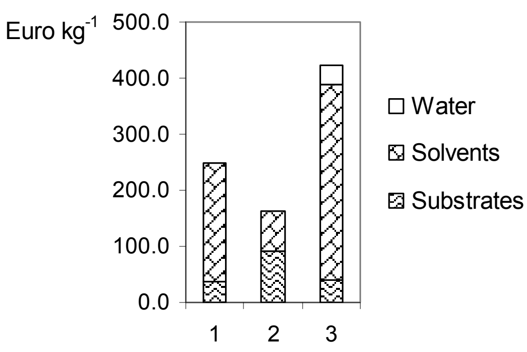
$$\text{Cyclohexene: Costs}\left(\text{cyclohexene}\right) = \frac{72.4\ \text{Euro}}{0.81\,\frac{\text{kg}}{\text{L}} \cdot 2.5\text{L}} \approx 35.75\,\frac{\text{Euro}}{\text{kg}}$$

Table 3 (supplemented) Costs of the substances applied in protocols 1 to 3 (Scheme 1 to 3) with data from an Aldrich-catalogue.

	Substance data		Product of the company Aldrich				Costs	Substance amounts per kg product and costs					
								1		2		3	
	molecular weight [g mol^{-1}]	density [g mL^{-1}]	Product number	Packa-ging size	Price [€]	Purity or fraction	[€ kg^{-1}] [a]	[kg]	[€]	[kg]	[€]	[kg]	[€]
Cyclohexene	82.15	0.81	125431	2.5 L	72.4	0.99	35.75	0.4059	**14.5**	0.3902	**14.0**	0.3948	**14.1**
Bromine	159.81	3.119	207888	1 L	102.5		32.86	0.6931	**22.8**				
Carbon tetrachloride	153.82	1.594	289116	6 L	1500	0.995	90.59	2.341	**212.1**			3.83	**347.0**
Ethanol	46.0688	0.785	458600	25 L	126.4	_	6.44	0.0389	**0.3**				
Sodium perborate	199.62		244120	0.5 kg	31.1		62.20			0.8051	**50.1**		
Sodium bromide	102.89		220345	3 kg	77.1	0.99	25.70			1.0758	**27.6**		
Acetic acid	60.05	1.05	W200611	25 kg	195	0.995	7.80			9.22	**71.9**		
Hydrogen bromide (48%)	80.91	1.49	268003	1 L	39.9	0.48	26.78					0.7777	**20.8**
Incorporated water						0.52	26.78					0.8425	**22.6**
Hydrogen peroxide (35%)	34.02	1.11	349887	0.5 L	11	0.35	19.82					0.3269	**6.5**
Incorporated water						0.65	19.82					0.6072	**12.0**
Sum									**249.6**		**163.6**		**423.0**

[a] Except for ethanol (catalogue 2003/04) online data from 22/03/2008 was used here, in order to present the costs in [€ kg^{-1}].

Figure 3 Raw material costs (Table 3) for the production of dibromocyclohexane. Water indicated in protocol 3 arises from the solution of hydrogen bromide and hydrogen peroxide.



Solution to Problem 10

a) The type of applied substances has an impact on the choice and utilization of an appropriate process technology. Elaborate technology for the handling of volatile bromine can indeed be omitted in protocols 2 and 3. However, in protocols 1 and 3 the problematic solvent carbon tetrachloride remains, which is toxic and environmentally pollutive. Furthermore, it is suspected to have a carcinogenic effect. This is also true for dioxane, which can be used in protocol 3 as well. Besides, it is flammable and may form explosive peroxides just as diethyl ether in protocol 2. The hydrogen peroxide and hydrogen bromide solutions in protocol 3 are corrosive, as is bromine – but at least they are not as volatile as bromine.

Therefore, the omission of bromine in protocol 3 does not represent a central improvement, since comparable protection measures have to be taken for the employees due to the other substances. However, protocol 2 presents an improvement regarding hazards by means of the substances used. Acetic acid is corrosive, however, not as toxic as carbon tetrachloride. Nevertheless, the fire hazard of sodium perborate in combination with organic solvents has to be considered. Apart from that, this is true also for hydrogen

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peroxide, for which the Aldrich-catalogue remarkably only indicates the R-phrase 34. However, in protocol 2 significant amounts of solid waste are produced (0.53 kg kg^{-1}), meaning that the disposal thereof as well as the production of sodium perborate burden the environment.
The solvents pollute the environment as well. In case they are recycled, the expenses for provision of energy have to be considered. As we are dealing with laboratory rather than optimized synthesis protocols, not much can be said regarding the efficiency of solvent application at the present status. In case the disposal (of a part) is done by incineration, significant amounts of hydrogen chloride accumulate, which cause a salt load in the sewage if neutralized. Furthermore, the formation and presence of water in protocols 2 and 3 implies a wastewater treatment, which can totally be omitted in protocol 1.
Depending on which arguments are considered to be more important, the bottom line could be: protocol 3 falls back on problematic substances even whilst abandoning bromine, and shows no significant improvement in this regard compared to protocol 1, because plant technology cannot be simplified substantially. High waste amounts in protocol 2 do not justify a departure from the usual bromination (protocol 1), assuming controllable security technologies and recyclability of large quantities of solvents. If hydrogen bromide accrues in a company's other processes, its application for the bromination of alkenes could be sensible. The utilization of a coupled or a by-product which otherwise would have had to be treated as waste means a sensible utilization, which preserves the environment. In this case, protocol 3 could be preferable.

b) In protocol 2, solid waste (0.53 kg Na_3BO_3 / kg product) has to be disposed of, and the costs initially remain unknown. The formation of by-products in protocols 2 and 3 diminishes the utilization of the organic compound to be converted. This is a serious disadvantage in case a different, more cost-intensive alkene is converted, when the yield is comparable. (Additional information: protocol 3 yields 99% product converting cinnamic methyl ester.) Regarding the solvents applied, conclusions are only reliable to a certain extent. After all, the protocols are not (yet) optimized versions, so that the utilization of lower amounts of solvent is conceivable. Costs for solvents will be relativized correspondingly. Therefore, raw material costs (Table 3 and Figure 3) reveal that protocol 2 would be the best, however, significant changes are possible by optimization. Hence, results can only be considered to be preliminary. The efficiency of solvent utilization will also depend on recyclability and on (partial) solvent disposal, however, a statement is not possible according to present knowledge. This is also valid for substrate excess, which needs to be reduced in case of a larger production amount. The formation and presence of water in protocol 2 and 3 entails a wastewater treatment with corresponding costs, which can completely be omitted in protocol 1. The type of substances applied has an impact on the choice and the utilization, respectively, of an appropriate process technology. Elaborate technology for handling the highly volatile bromine can be omitted in protocols 2 and 3. However, the problematic solvent carbon tetrachloride remains in protocols 3 and 1. Therefore, the omission of bromine by means of protocol 3 represents no central improvement, since comparable protective measures have to be taken for the employees regardless. Indeed, hydrogen bromide, which potentially arises as a coupled product in different processes, e.g. during the bromination of aromatic compounds, could sensibly be applied in protocol 3.

Therefore, the next step in the development of an efficient synthesis design consists in the more concrete modelling of corresponding process technologies, and goes beyond mass balancing on the basis of literature protocol, requiring much more additional information.

Supporting material: Figures 1 to 3 in colour

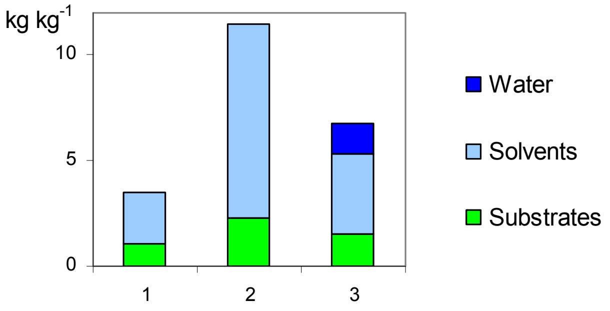

Figure 1 Mass index S^{-1} (see Table 1)

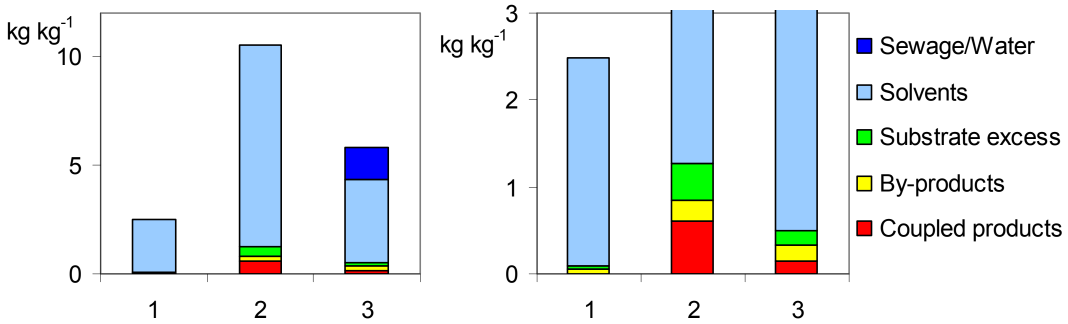

Figure 2 Environmental factor E (see Table 2). The right hand side shows a zoomed presentation in order to make coupled and by-products better visible.

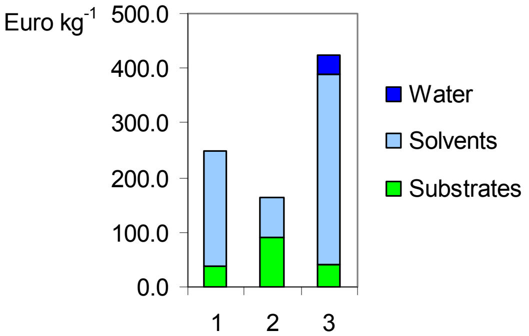

Figure 3 Raw material costs (Table 3) for the production of dibromocyclohexane. Water indicated in protocol 3 arises from the solution of hydrogen bromide and hydrogen peroxide.

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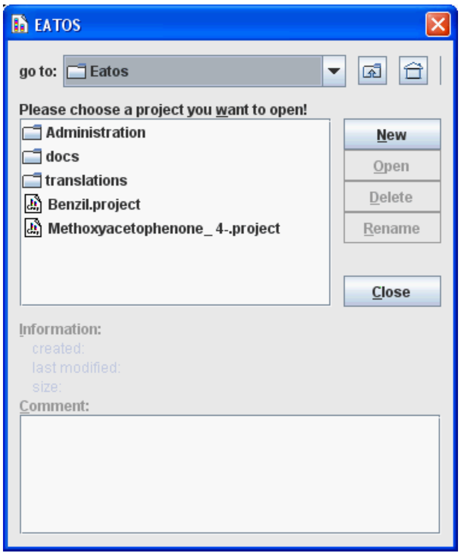
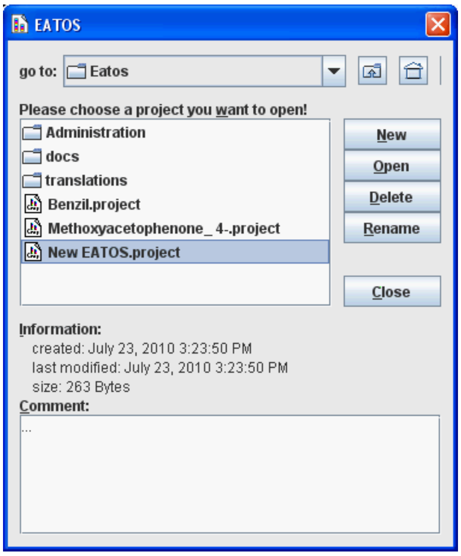
Detailed presentation of Problem 8: application of the software EATOS for the determination of a mass balance, e.g. of the environmental factor E.

After download via http://www.metzger.chemie.uni-oldenburg.de/eatos/ the software has to be started by double-clicking on the file "Eatos.jar".

Button: New

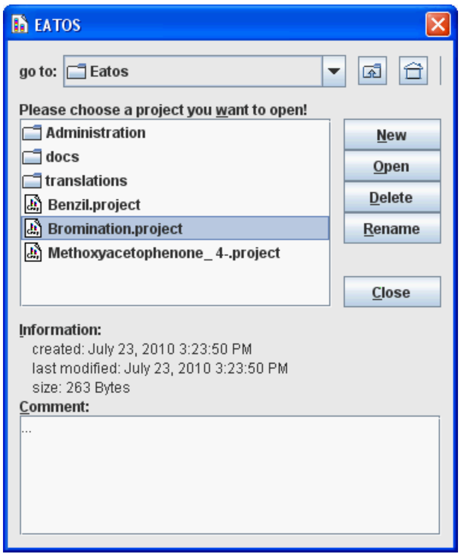


Button: Rename

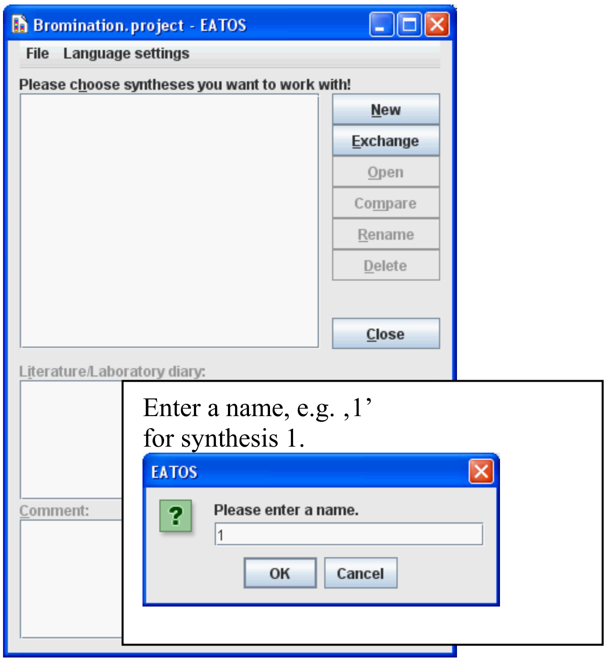


Click in the text ‚New EATOS.project' and note new name (e.g. Bromination.project). Confirm with ENTER/RETURN. The ending ‚.project' has to be kept.

Button: Open



Button: New



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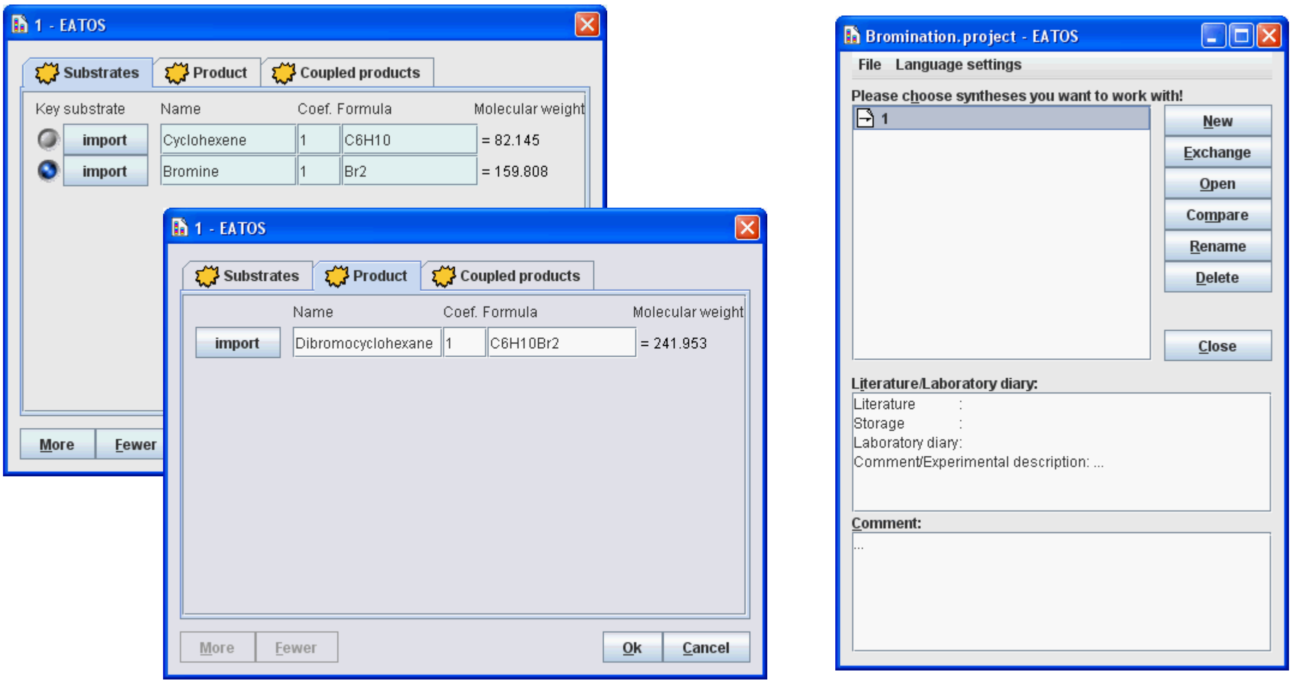
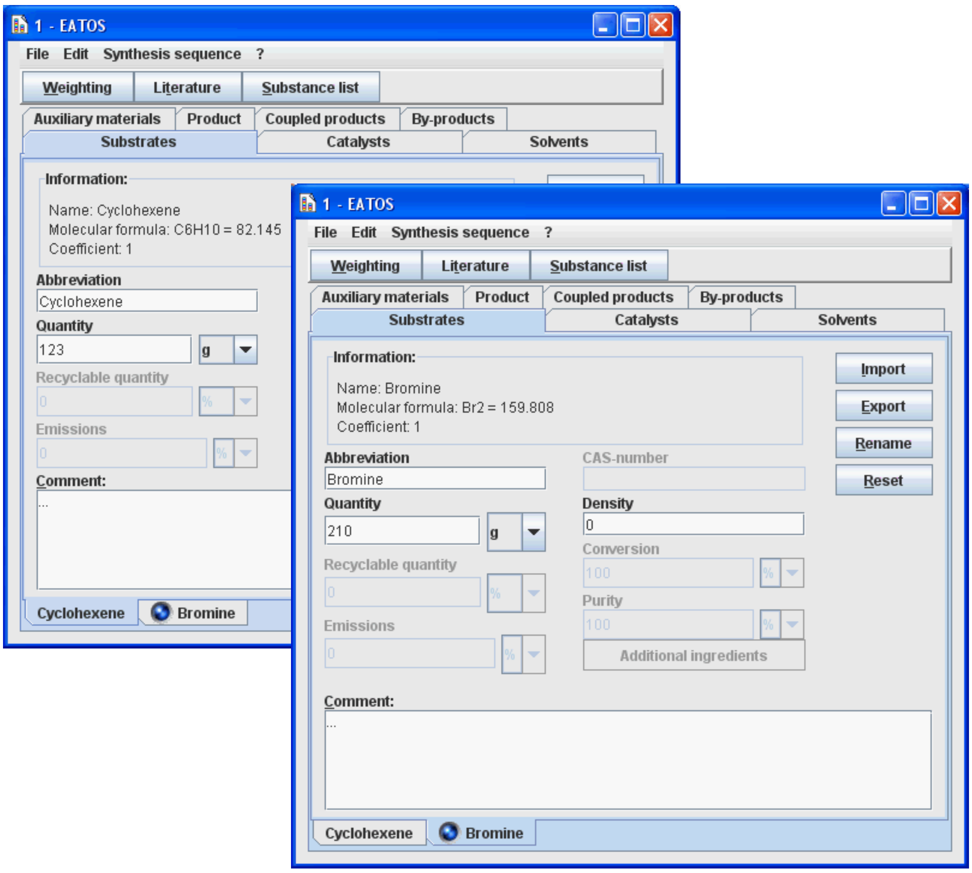
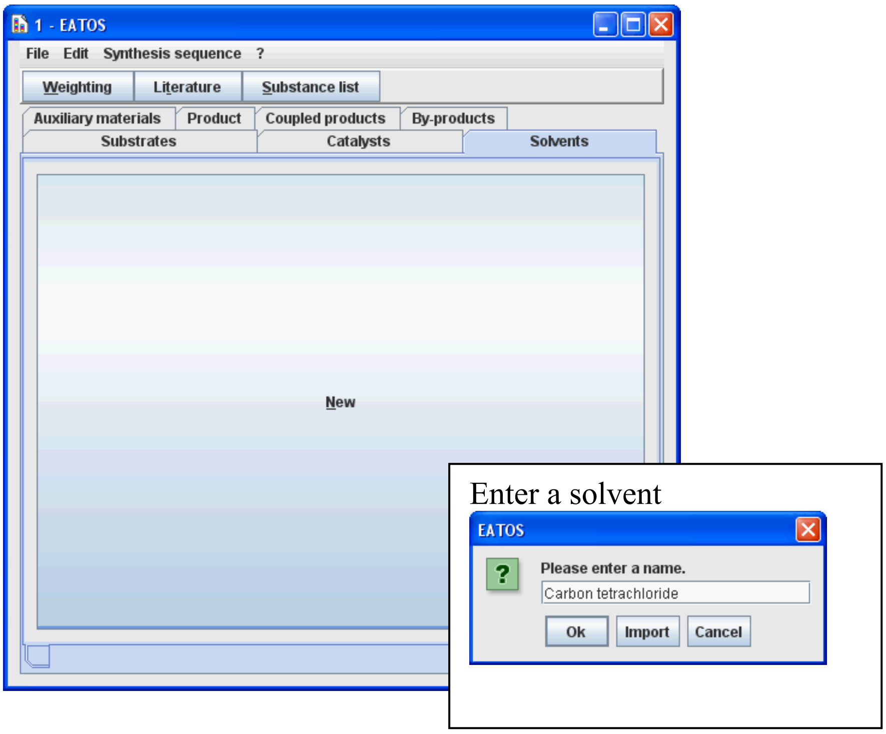
Enter the stoichiometry: the blue dot has to be set at the substrate which is in shortfall, i.e. to which the yield relates. Click synthesis 1 and the button: Open



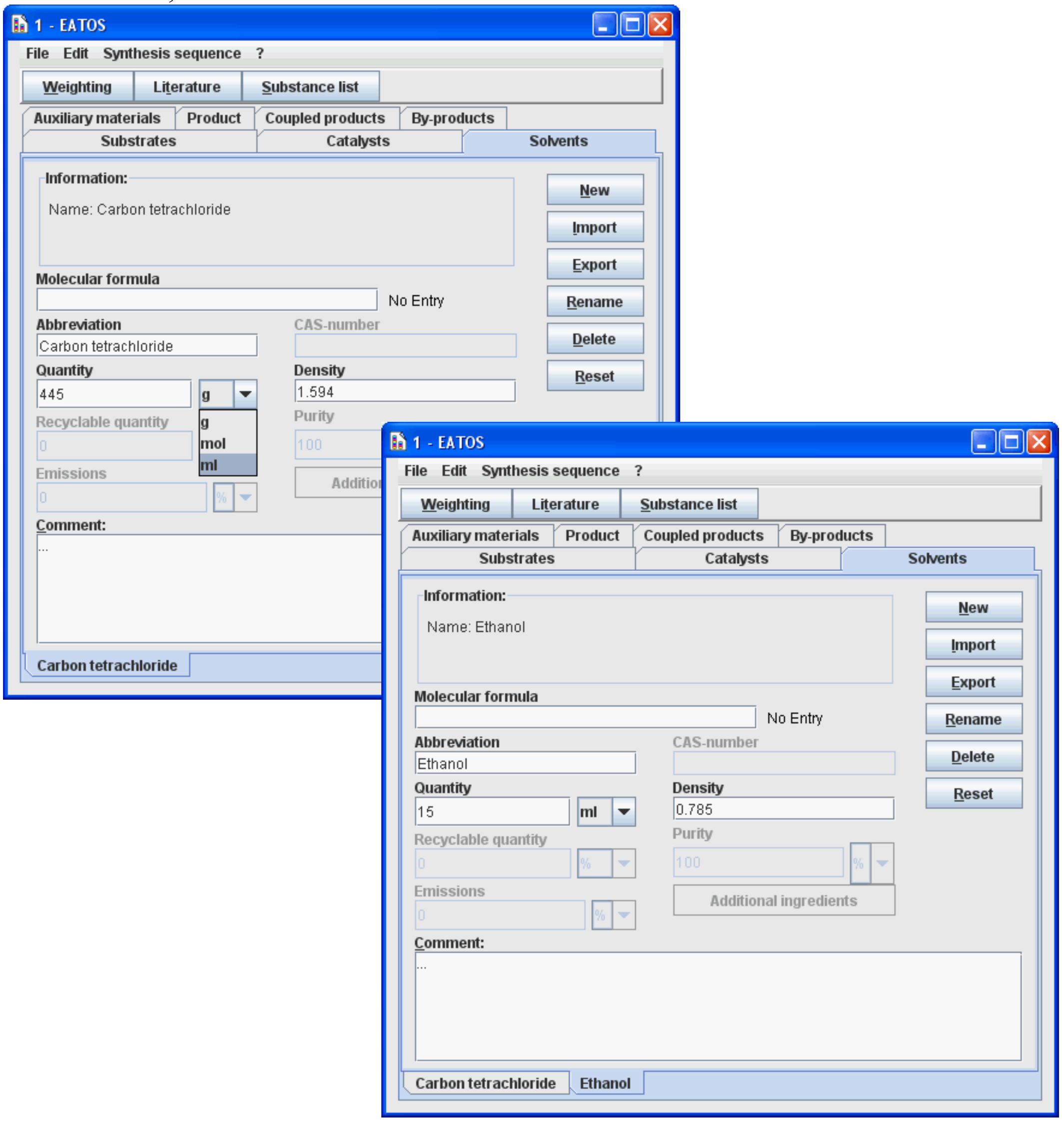
Note the amounts of substrates.



Enter a new solvent.



Button: New, in order to enter the solvent ethanol.



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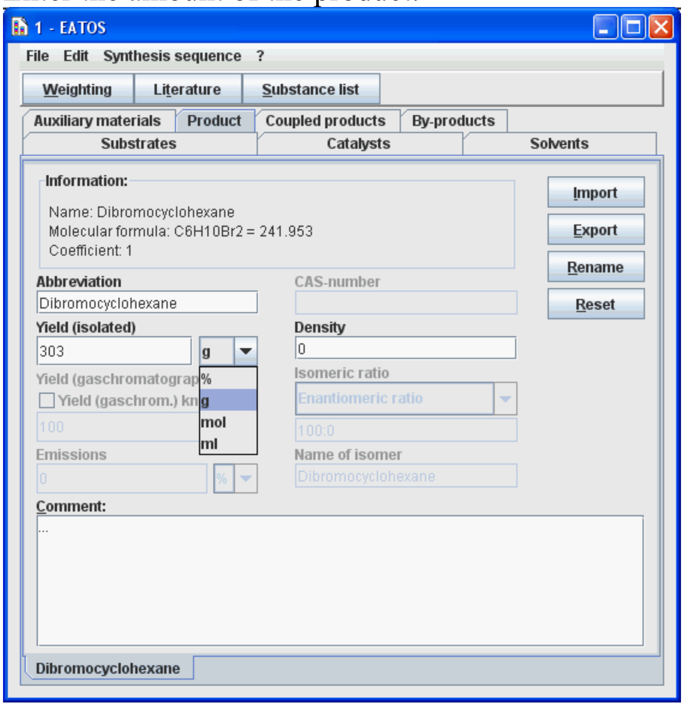
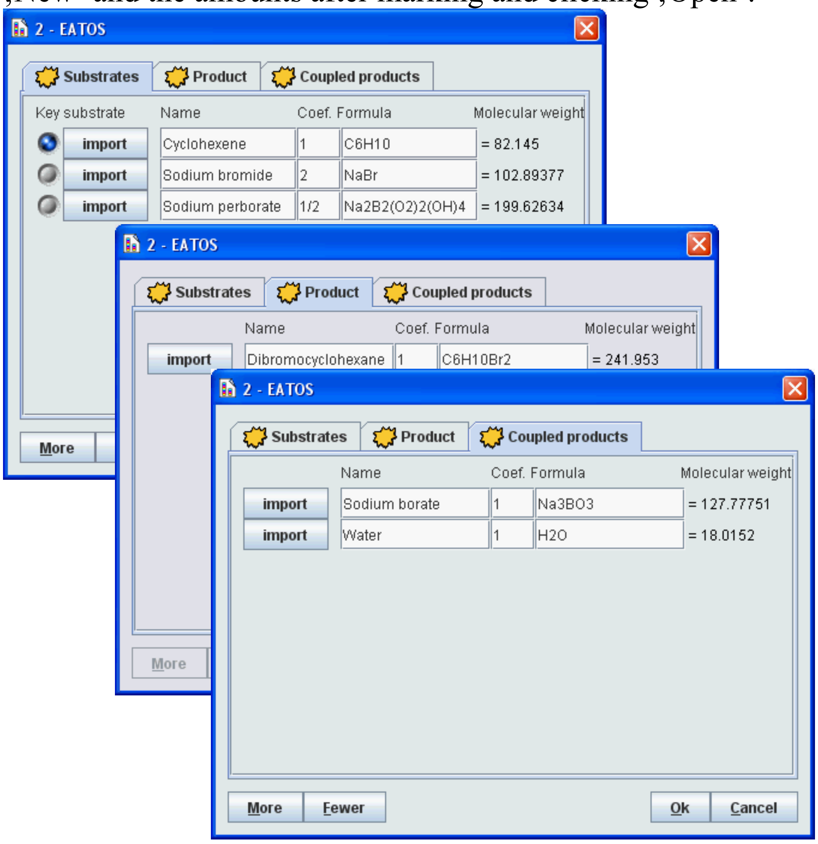
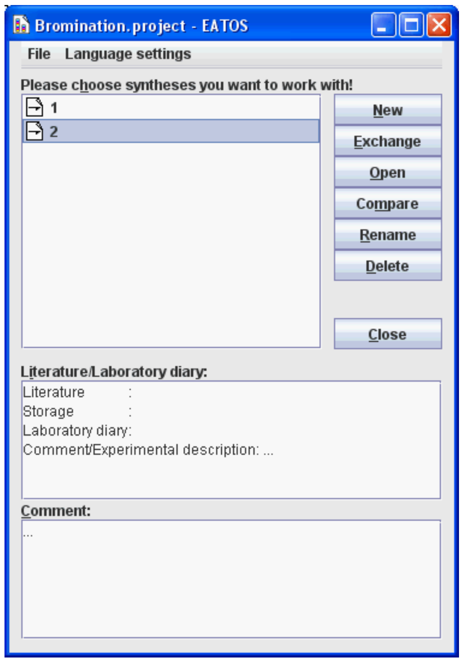
Enter the amount of the product.



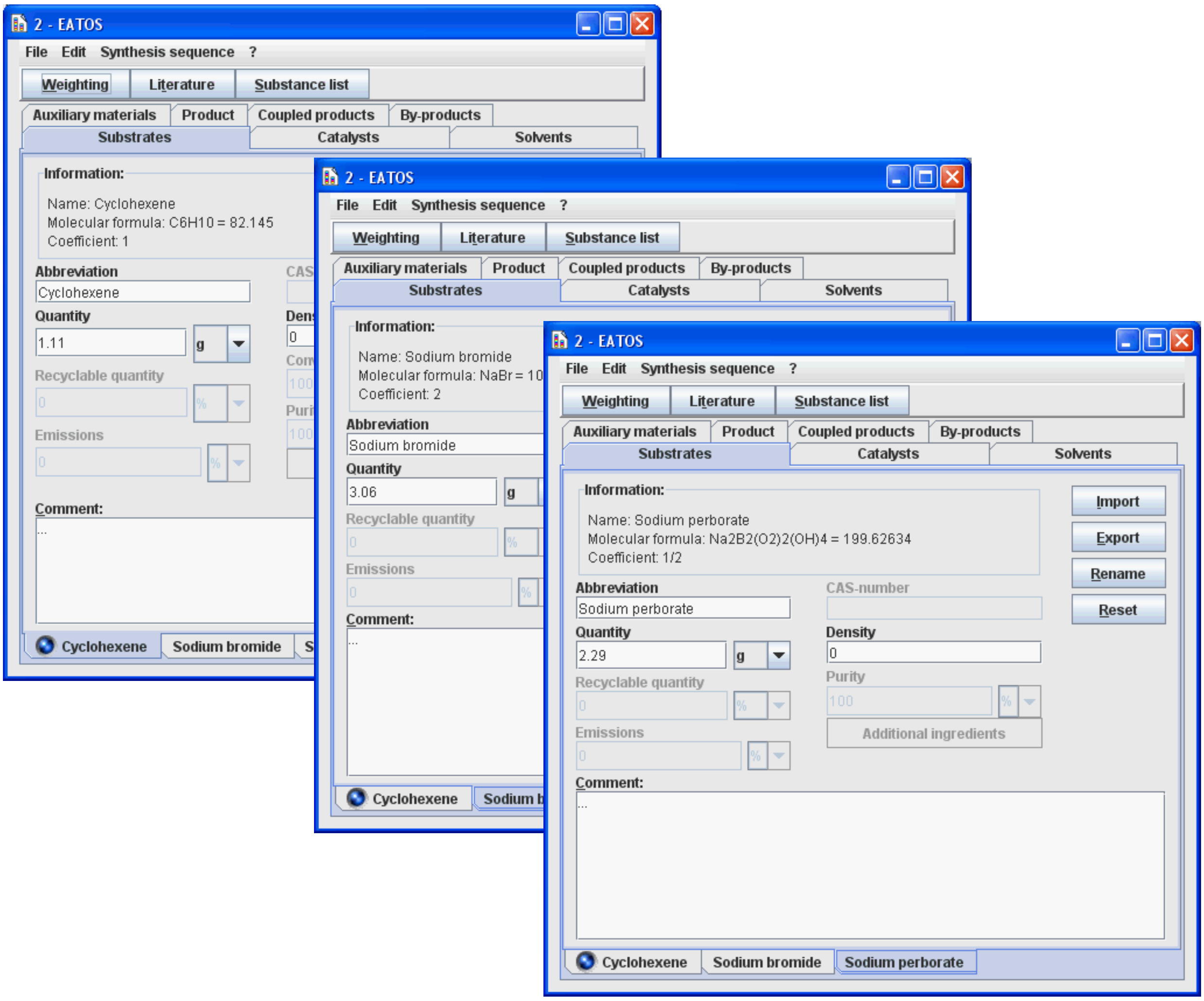
After closing the window, the stoichiometry of a second synthesis can be entered via the button ‚New' and the amounts after marking and clicking ‚Open'.



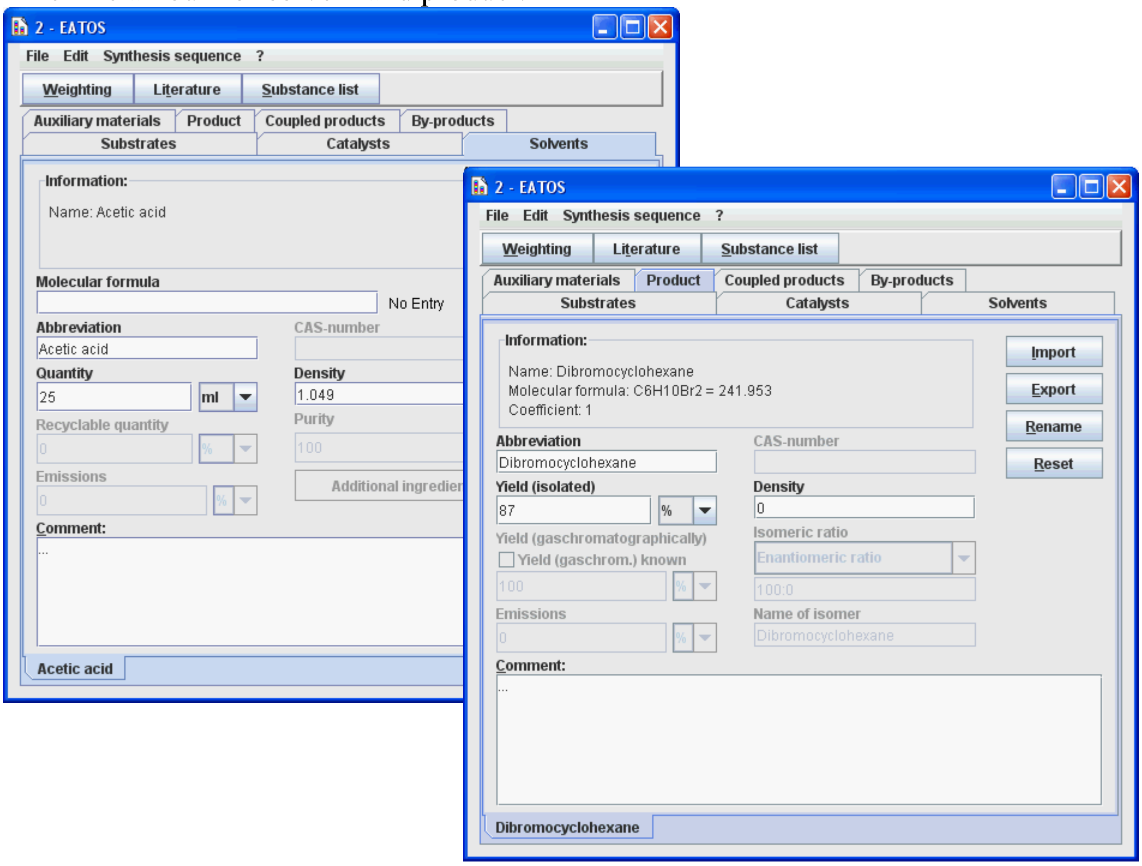


Click on 'More' or 'Fewer', in order to change the number of substrates or coupled products.

Note the amounts of substrates.



Enter the amount of solvent and product.



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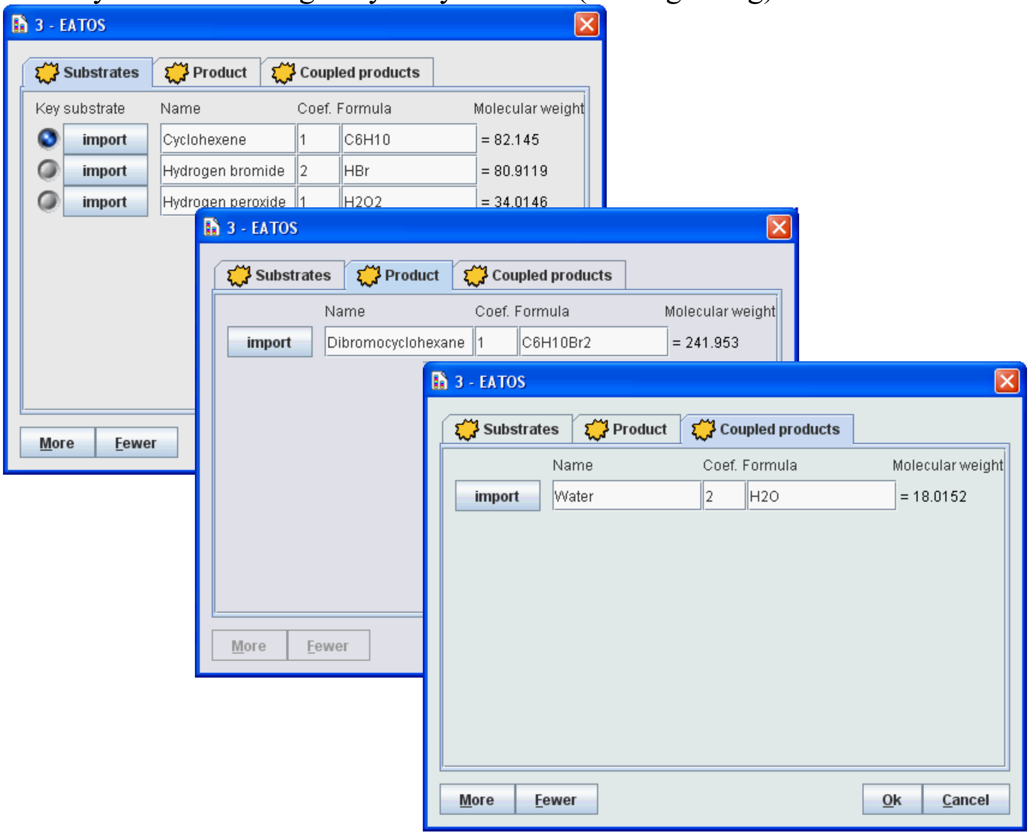
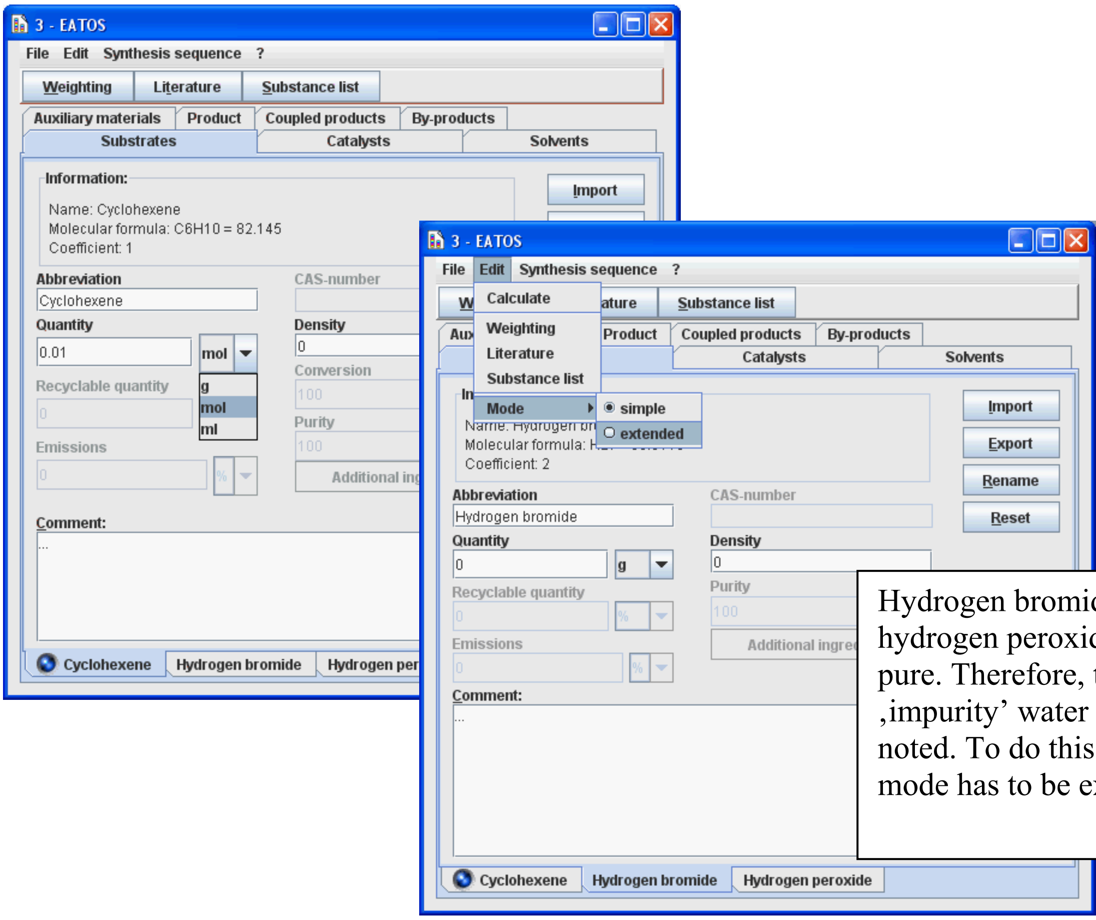
Enter synthesis 3 analogously as synthesis 1 (see beginning)



Enter the amounts of substrates.



Hydrogen bromide and hydrogen peroxide are not pure. Therefore, the ‚impurity' water has to be noted. To do this, the mode has to be extended.

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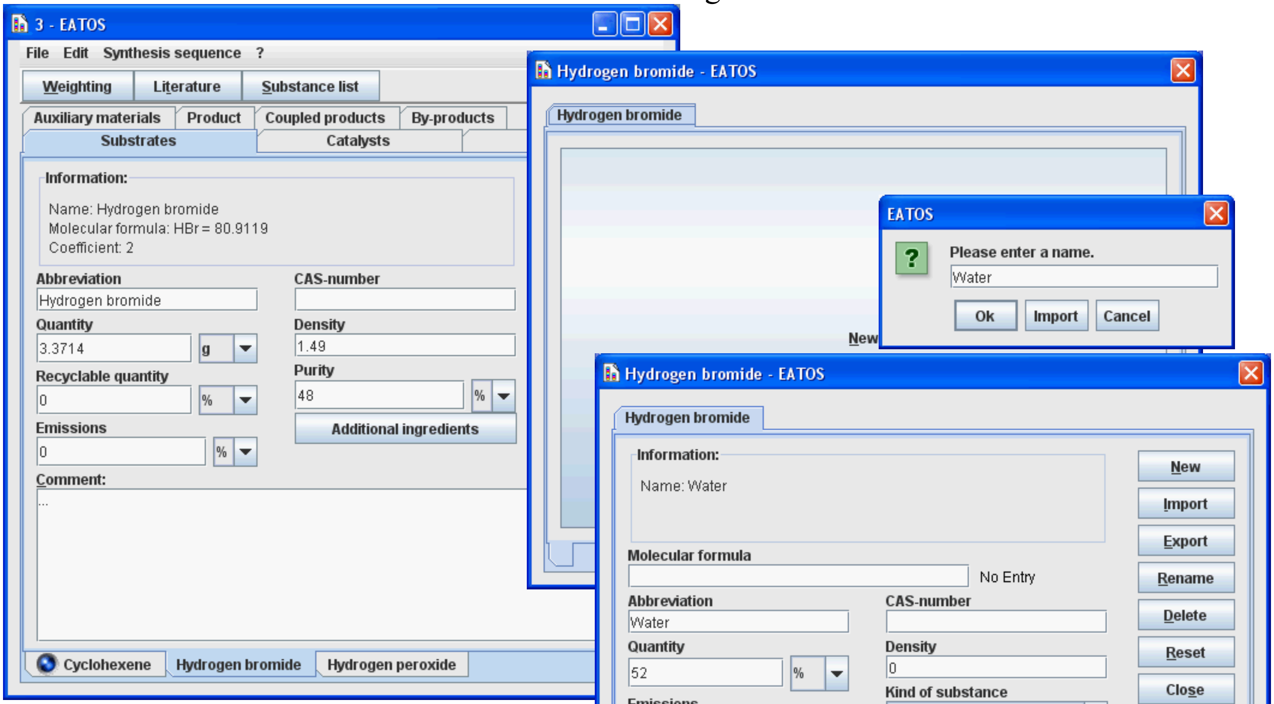
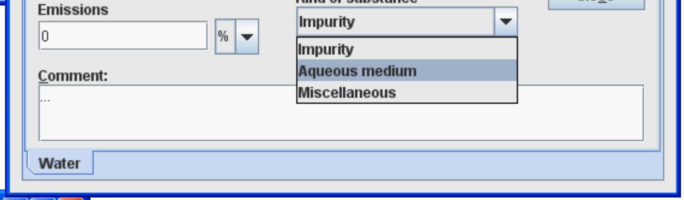
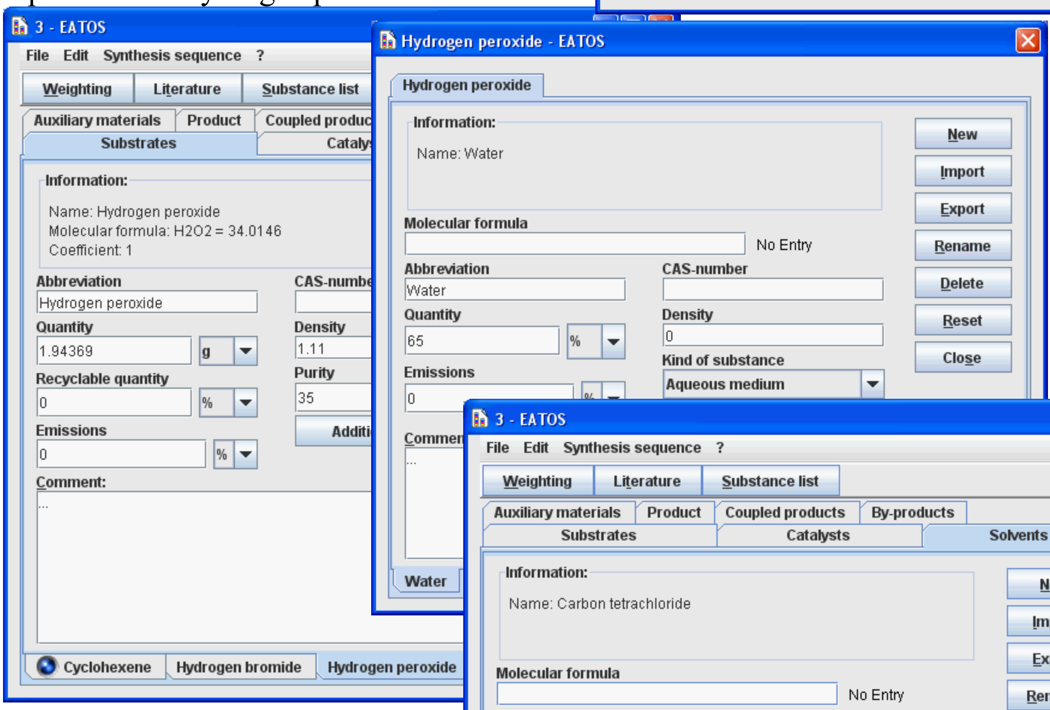
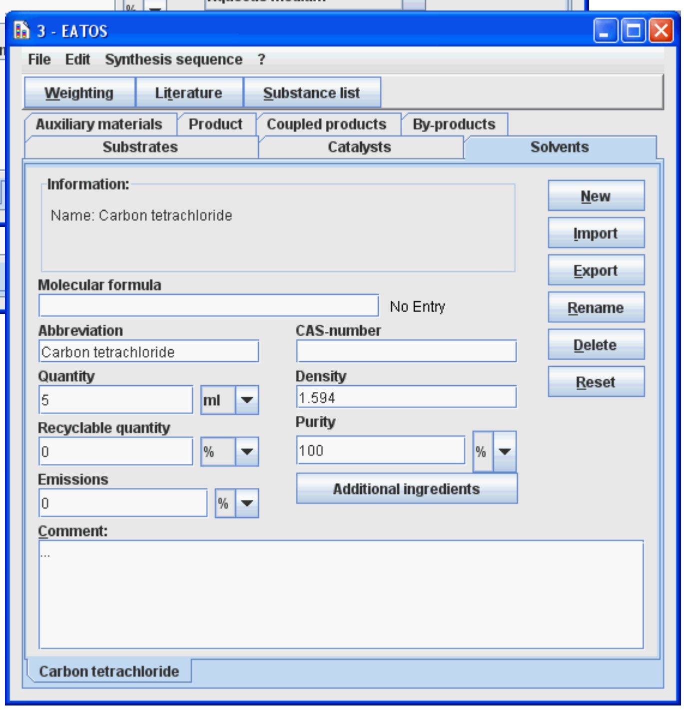
Choose the extended mode and click on "Additional ingredients" in order to enter water at 52%.





After "Close" this procedure will be repeated with hydrogen peroxide.





Then, enter the solvent.

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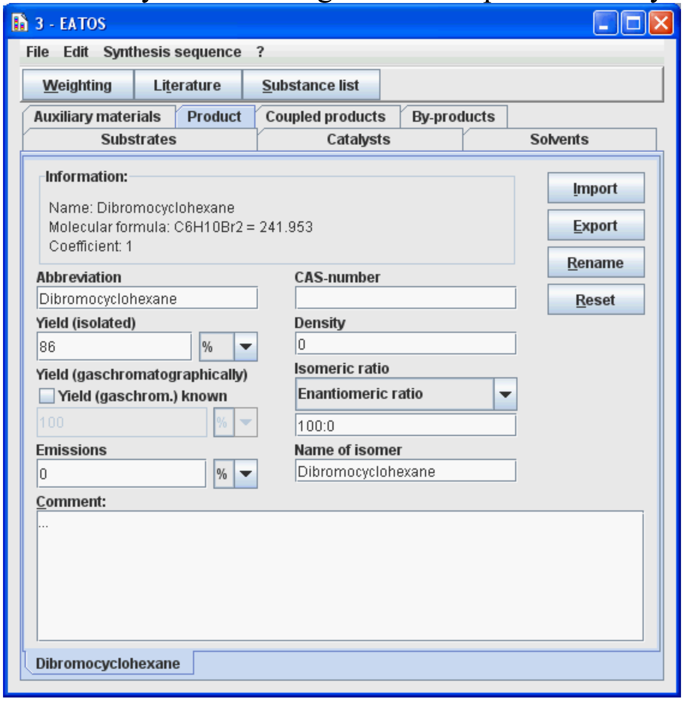
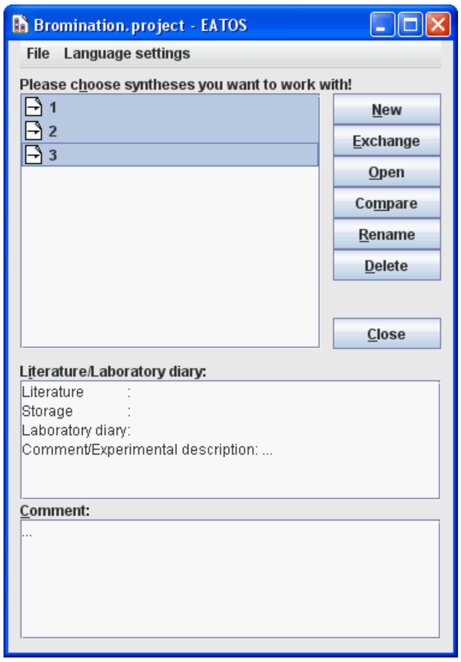
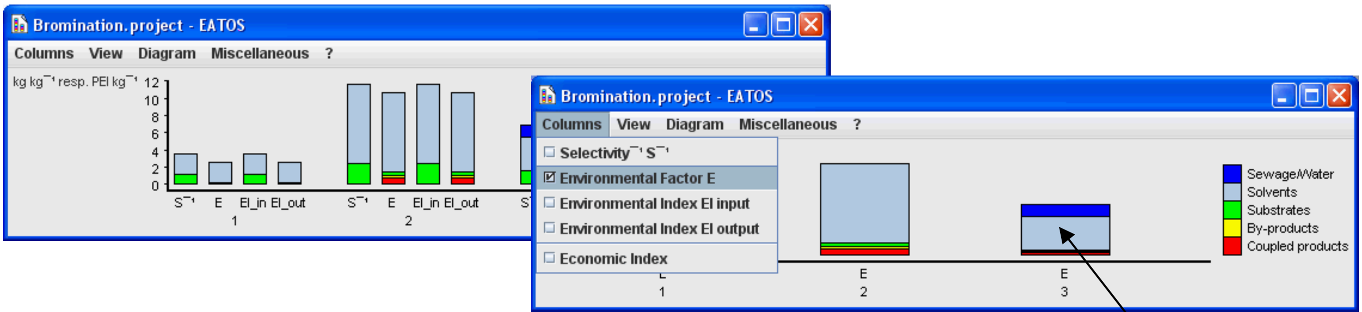
After listing the yield and closing the window "3 – EATOS", mark these three syntheses by holding the Ctrl-key and selecting them. Compile a chart by using the button "Compare".



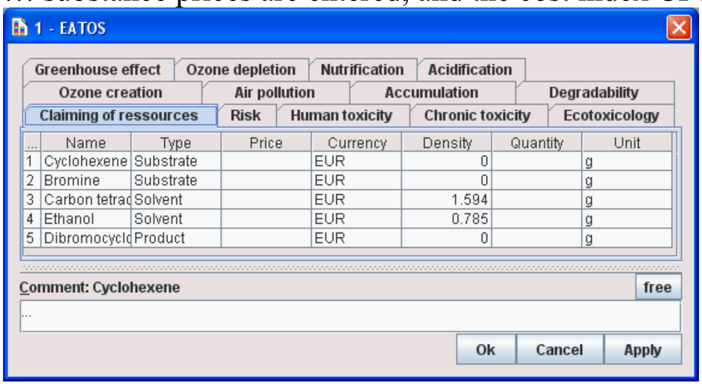


A column diagram appears showing the mass index S^{-1}, environmental factor E and the environmental indices EI_in and EI_out. The latter two columns would reveal a potential environmental impact (PEI kg^{-1}), if R-phrases or other qualitative properties have been listed choosing the button "Weighting". Because this is not topic of the work sheets, only mass index S^{-1}, environmental factor E and, after clicking on "Weighting" …



The underlying values can be shown by clicking on the segments of the columns.

… substance prices are entered, and the cost index CI comes into consideration.



Further functionalities are shown in the user's manual.