SYNTHESIS OF 1-BROMOBUTANE
Greenness assessment

1. When performing a laboratory experiment it is necessary to always pay attention to the hazards of the substances handled. The **Safety Data Sheets** (SDS) are documents created by chemical manufacturers which contains all information necessary for handling of substances.

1.1. Consult the SDS of the substances involved in this synthesis and fill in the following table (Table 1).

Table 1

Substances involved	Hazard code	Precautionary code
Stoichiometric reagents		
Butan-1-ol (CAS 71-36-3)		
Sodium bromide (CAS 7647-15-6)		
Sulfuric acid (CAS 7664-93-9)		
Auxiliary substances		
Solvents		
p-Xylene (CAS 106-42-3)		
Sodium hydroxide (solution)		
Sulfuric acid (CAS 7664-93-9)		
Water		
Other auxiliary substances		
Anhydrous calcium chloride (CAS 10043-52-4)		
Product		
1-bromobutane (109-65-9)		
Waste		
Butan-1-ol (not reacted)		
But-1-ene		
Calcium chloride		
Dibutyl ether		
Hydrogen bromide		
p-Xylene		
Sodium bromide (excess)		
Sodium hydrogen sulfate		
Sodium sulfate		
Sulfuric acid (dilute solution)		
Water		

2. The **Green Star** (GS) is a holistic metric designed to assess the greenness of a chemical reaction or process. This metric uses the 12 principles of green chemistry to evaluate the greenness and is constructed giving the scores 1, 2 or 3 (the maximum value of greenness, assessed in three levels) to each of the principles following the criteria defined.

2.1. Consult the hazards of the substances involved (Table 1) and fill the following table (Table 2), using the criteria defined in Table II of the supplement.

Table 2

Substances involved	Hazard code	HH	E	P
Stoichiometric reagents				
Butan-1-ol (CAS 71-36-3)				
Sodium bromide (CAS 7647-15-6)				
Sulfuric acid (CAS 7664-93-9)				
Auxiliary substances				
Solvents				
p-Xylene (CAS 106-42-3)				
Sodium hydroxide (solution)				
Sulfuric acid (CAS 7664-93-9)				
Water				
Other auxiliary substances				
Anhydrous calcium chloride (CAS 10043-52-4)				
Product				
1-bromobutane (109-65-9)				
Waste				
Butan-1-ol (not reacted)				
But-1-ene				
Calcium chloride				
Dibutyl ether				
Hydrogen bromide				
p-Xylene				
Sodium bromide (excess)				
Sodium hydrogen sulfate				
Sodium sulfate				
Sulfuric acid (dilute solution)				
Water				

[α]HH – Human Health; E – Environment; P – Physical

2.2. Using the information of the Table 2 and the criteria of Table IV (supplement), fill in the Table 3.

Table 3

Principle	Score	Explanation
P1 - prevention		
P2 - atom economy		
P3 - less hazardous chemical synthesis		
P5 - safer solvents and auxiliary substances		
P6 - increase energy efficiency		
P7 - use renewable feedstocks		
P8 - reduce derivatives		
P9 - catalysts		
P10 - design for degradation		
P12 - safer chemistry for accident prevention		

2.3. Construct the GS in Figure 1. First, mark on each axis the score of the respective principle and paint of green or red the areas that indicate the compliance or non-compliance of the principles, respectively. Then, use the Excel file provided to construct the GS and to calculate the Green Star Area Index (GSAI).

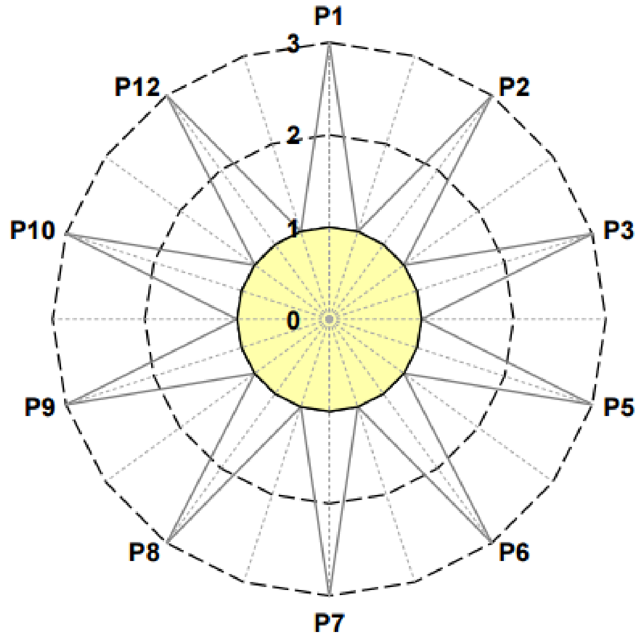

Figure 1. GS to construct

3. Calculate the **yield** of the synthesis performed at macro and microscale. Present all your calculations.

Yield (macroscale) = _______________

Yield (microscale) = _______________

Calculations:

4. The **green chemistry mass metrics** allow to evaluate what happens to atoms in a chemical reaction when they pass from reagents to products or waste. The mass metrics can be of two types: metrics whose goal is to encourage the incorporation of atoms in the product (e.g., Reaction Mass Efficiency) and those who want to minimize the production of waste (e.g., Factor E and Mass Intensity).

4.1. **Reaction Mass Efficiency** (RME) can be determined by the expression:

$$\mathbf{RME} = \frac{\mathbf{m_{product}}}{\mathbf{m_{stoichiometric\ reagents}}} \times \mathbf{100}$$

This metric allows to evaluate the percentage of product obtained in relation to the quantity of stoichiometric reagents used. The ideal value is 100% and it corresponds to the complete transformation of the stoichiometric reagents in the product.

For both scales, determine the value of RME.

RME value (macroscale) = ________________

RME value (microscale) = ________________

4.2. **Factor E** can be determined by the expression:

$$\mathbf{Factor\ E} = \frac{\mathbf{m_{waste}}}{\mathbf{m_{product}}}$$

This metric allows to assess the extent of the formation of waste and its ideal value is 0 (which means that there is no production of waste).

For both scales, determine:

a) the total mass of waste, considering $m_{waste} = m_{total\ reagents} - m_{product}$

m_{waste} (macroscale) = ________________

m_{waste} (microscale) = ________________

b) the value of Factor E

Factor E value (macroscale) = _______________

Factor E value (microscale) = _______________

4.3. **Mass Intensity** (MI) can be determined by the expression:

$$\mathbf{MI} = \frac{\mathbf{m_{total\ reagents}}}{\mathbf{m_{product}}}$$

This metric also allows to assess the extent of the formation of waste and its ideal value is 1 (which means that all reagents are converted in the product and there is no waste production).

For both scales, determine the value of MI.

MI value (macroscale) = _______________

MI value (microscale) = _______________

5. The **Scale Risk Index** (SRI) is an index that allows to distinguish between the micro- and macroscale when the assessment of risk is at stake, taking into account the hazards and the masses of the substances involved in the synthesis as well as the time of the experiment. The lower the value of the SRI, less risks are presented. The value of SRI is calculated from the following expression:

$$SRI = t\left(\sum (s_{Hi} + s_{Ei} + s_{Phi})\, m_i\right)$$

where t is the time for performing the synthesis (time for the reaction + time for the work-up); m_i is the mass of each substance involved; s_{Hi}, s_{Ei} and s_{Phi} are the scores of the human health, environmental and physical hazards of each substance, respectively. SRI is expressed in gram hour (g.h).

5.1. Fill in the following table (Table 4) with the data collected during the experiment.

Table 4

Substances involved	**Mass of the substances (g)**	
	Macroscale	**Microscale**
Stoichiometric reagents		
Sodium bromide		
Butan-1-ol		
Sulfuric acid		
Auxiliary substances		
Sulfuric acid		
Sodium hydroxide		
p-Xylene		
Water		
Anhydrous calcium chloride		
Product		
1-bromobutane		
Byproduct		
Sodium hydrogen sulfate		
Time of the experiment (h)		

5.2. Consult the hazards of the substances involved (Table 1) and fill the following table (Table 5), using the criteria defined in Table V of the supplement.

Table 5

Substances involved	**Hazard code**	**HH**	**E**	**P**
Stoichiometric reagents				
Butan-1-ol (CAS 71-36-3)				
Sodium bromide (CAS 7647-15-6)				
Sulfuric acid (CAS 7664-93-9)				
Auxiliary substances				
Solvents				
p-Xylene (CAS 106-42-3)				
Sodium hydroxide (solution)				
Sulfuric acid (CAS 7664-93-9)				
Water				
Other auxiliary substances				
Anhydrous calcium chloride (CAS 10043-52-4)				
Product				
1-bromobutane (109-65-9)				
Waste				
Butan-1-ol (not reacted)				
But-1-ene				
Calcium chloride				
Dibutyl ether				
Hydrogen bromide				
p-Xylene				
Sodium bromide (excess)				
Sodium hydrogen sulfate				
Sodium sulfate				
Sulfuric acid (dilute solution)				
Water				

$^{\alpha}$HH – Human Health; E – Environment; P – Physical

5.3. Using the data collected in Tables 4 and 5 and the expressions of Table VI, determine the values of SRI for macro and microscale.

SRIH value (macroscale) = ________________

SRIE value (macroscale) = ________________

SRIPh value (macroscale) = ________________

SRI value (macroscale) = ________________

SRIH value (microscale) = ________________

SRIE value (microscale) = ________________

SRIPh value (microscale) = ________________

SRI value (microscale) = ________________

Discussion

1. Using GS, can you discriminate the greenness of the synthesis performed at macroscale from the microscale? Justify your answer.

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2. What can you conclude about chemical greenness of the synthesis at macro and microscale from the values of:

2.1. RME? Justify your answer.

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2.2. Factor E? Justify your answer.

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2.3. MI? Justify your answer.

3. What can you conclude about the risks present at macro and microscale from the values of SRI? Justify your answer.

4. Do you think it is better to use a single metric or multiple metrics simultaneously when evaluating a laboratory experiment? Explain your answer.

SUPPORTING DOCUMENTS

Document 1 – Principles of Green Chemistry

Table I. The principles of green chemistry

Principle	**Description**
P1 - prevention	It is better to prevent waste than to treat or clean up waste after it has been created.
P2 - atom economy	Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
P3 - less hazardous chemical synthesis	Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
P4 - designing safer chemicals	Chemical products should be designed to effect their desired function while minimizing their toxicity.
P5 - safer solvents and auxiliary substances	The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.
P6 - increase energy efficiency	Energy requirements of chemical processes should be recognized for their environmental and economic impacts should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.
P7 - use renewable feedstocks	A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.
P8 - reduce derivatives	Unnecessary derivatization (use of blocking groups, protection/deprotection, and temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate waste.
P9 - catalysts	Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
P10 - design for degradation	Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.
P11 - real-time analysis for pollution prevention	Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
P12 - safer chemistry for accident prevention	Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents including releases, explosions, and fires.

Document 2 – Construction of Green Star

Table II. Scores for classification of substances to construct the Green Star

Hazards		**Score (S)**	**Hazards**		**Score (S)**
H200	Physical	3	H318	Health	3
H201	Physical	3	H319	Health	2
H202	Physical	3	H320	Health	2
H203	Physical	3	H330	Health	3
H204:	Physical	2	H331	Health	3
H205	Physical	3	H332	Health	2
H206	Physical	3	H333	Health	2
H207	Physical	3	H334	Health	3
H208	Physical	3	H335	Health	2
H220	Physical	3	H336	Health	2
H221	Physical	2	H340	Health	3
H222	Physical	3	H341	Health	3
H223	Physical	2	H350	Health	3
H224	Physical	3	H351	Health	3
H225	Physical	3	H360	Health	3
H226	Physical	2	H361	Health	3
H227	Physical	2	H362	Health	2
H228 (category 1)	Physical	3	H370	Health	3
H228 (category 2)	Physical	2	H371	Health	3
H229	Physical	2	H372	Health	3
H230	Physical	3	H373	Health	3
H231	Physical	2	H400	Environmental	3
H232	Physical	3	H401	Environmental	3
H240	Physical	3	H402	Environmental	2
H241	Physical	3	H410	Environmental	3
H242 (Type C & D)	Physical	3	H411	Environmental	3
H242 (Type E & F)	Physical	2	H412	Environmental	2
H250	Physical	3	H413	Environmental	2
H251	Physical	3	H420	Environmental	3
H252	Physical	2	EUH001	Physical	3
H260	Physical	3	EUH006	Physical	3
H261 (category 2)	Physical	3	EUH014	Physical	3
H261 (category 3)	Physical	2	EUH018	Physical	3
H270	Physical	3	EUH019	Physical	3
H271	Physical	3	EUH029	Health	3
H272 (category 2)	Physical	3	EUH031	Health	3
H272 (category 3)	Physical	2	EUH032	Health	3
H280	Physical	2	EUH044	Physical	3
H281	Physical	2	EUH059	Environmental	3
H290	Physical	2	EUH066	Health	2
H300	Health	3	EUH070	Health	3
H301	Health	3	EUH071	Health	3
H302	Health	2	EUH201	Health	3
H303	Health	2	EUH201A	Health	2
H304	Health	3	EUH202	Health	3
H305	Health	2	EUH203	Health	2
H310	Health	3	EUH204	Health	2
H311	Health	3	EUH205	Health	2
H312	Health	2	EUH206	Health	3
H313	Health	2	EUH207	Health	3
H314	Health	3	EUH208	Health	2
H315	Health	2	EUH209	Physical	3
H316	Health	2	EUH209A	Physical	2
H317	Health	2			

Table III. Criteria and scores (S) for classification of substances regarding degradability and renewability

Characteristics	Criteria	Score
Degradability	Not degradable and may not be treated to render the substances degradable to innocuous products	3
	Not degradable but may be treated to render the substances degradable to innocuous products	2
	Degradable and breakable to innocuous products	1
Renewability	Not renewable	3
	Renewable	1

Table IV. Criteria and scores (S) to construct the Green Star$^{\alpha}$

Green Chemistry Principle	Criteria	S
P1 – Prevention	Waste is innocuous (S=1, Table II)	**3**
	Waste involves a moderate hazard to human health and environment (S=2, Table II, for at least one substance)	**2**
	Waste involves a high hazard to human health and environment (S=3, Table II, for at least one substance)	**1**
P2- Atom Economy	Reactions without excess of reagents (≤10%) and without formation of by-products	**3**
	Reactions without excess of reagents (≤10%) and with formation of by-products	**2**
	Reactions with excess of reagents (>10%) and without formation of by-products	**2**
	Reactions with excess of reagents (>10%) and with formation of by-products	**1**
P3 – Less hazardous chemical synthesis	All substances involved are innocuous (S=1, Table II)	**3**
	Substances involved have a moderate hazard to human health and environment (S=2, Table II, for at least one substance)	**2**
	At least one substance involved has a high hazard to human health and environment (S=3, Table II)	**1**
P5 – Safer solvents and auxiliary substances	Solvents and auxiliary substances are not used, but if used are innocuous (S=1, Table II)	**3**
	Solvents or/and auxiliary substances are used but have a moderate hazard to human health and environment (S=2, Table II, for at least one substance)	**2**
	At least one solvent or auxiliary substance has a high hazard to human health and environment (S=3, Table II)	**1**
P6 – Increase energy efficiency	Room temperature and pressure	**3**
	Room pressure and temperature between 0 and 100 ºC when cooling or heating is needed	**2**
	Pressure different from room pressure and/or temperature > 100 ºC or less than 0 ºC	**1**
P7 – Use renewable feedstocks	Raw material/ feedstocks involved are renewable (S=1, Table III)	**3**
	At least one raw materials/feedstock involved is renewable, water is not considered (S=1, Table III)	**2**
	None of raw materials/feedstocks involved are renewable, water is not considered (S=3, Table III)	**1**
P8 – Reduce derivatives	Derivatizations or similar operations are not used	**3**
	Only one derivatization or similar operation is used	**2**
	More than one derivatization or similar operations are used	**1**
P9 – Catalysts	Catalysts are not used and if used are innocuous (S=1, Table II)	**3**
	Catalysts are used but have a moderate hazard to human health and environment (S=2, Table II)	**2**
	Catalysts are used and have a high hazard to human health and environment (S=3, Table II)	**1**
P10 – Design for degradation	All substances are degradable and break down to innocuous products (S=1, Table III)	**3**
	All substances not degradable may be treated to render them degradable to innocuous products (S=2, Table III)	**2**
	At least one substance is not degradable nor may be treated to render it degradable to innocuous products (S=3, Table III)	**1**
P12 – Safer chemistry for accident prevention	Substances used have a low hazard to cause chemical accidents (S=1, Table II, considering health and physical hazards)	**3**
	Substances used have a moderate hazard to cause chemical accidents (S=2, Table II, for at least one substance considering health and physical hazards, no substances with S=3)	**2**
	Substances used have a high hazard to cause chemical accidents (S=3 , Table II, for at least one substance considering health and physical hazards)	**1**

$^{\alpha}$ P8 – In the present case, derivatizations are not used and the criterion involves the number of stages: 3 = one stage, 2 = two stages and 1 = more than two stages.

Document 3 – Calculation of Scale Risk Index

Table V. Scores to classify the hazards of substances for calculation of Scale Risk Index

Hazards		**Score (S)**	**Hazards**		**Score (S)**
H200	Physical	2	H318	Health	2
H201	Physical	2	H319	Health	1
H202	Physical	2	H320	Health	1
H203	Physical	2	H330	Health	2
H204:	Physical	1	H331	Health	2
H205	Physical	2	H332	Health	1
H206	Physical	2	H333	Health	1
H207	Physical	2	H334	Health	2
H208	Physical	2	H335	Health	1
H220	Physical	2	H336	Health	1
H221	Physical	1	H340	Health	2
H222	Physical	2	H341	Health	2
H223	Physical	1	H350	Health	2
H224	Physical	2	H351	Health	2
H225	Physical	2	H360	Health	2
H226	Physical	1	H361	Health	2
H227	Physical	1	H362	Health	1
H228 (category 1)	Physical	2	H370	Health	2
H228 (category 2)	Physical	1	H371	Health	2
H229	Physical	1	H372	Health	2
H230	Physical	2	H373	Health	2
H231	Physical	1	H400	Environmental	2
H232	Physical	2	H401	Environmental	2
H240	Physical	2	H402	Environmental	1
H241	Physical	2	H410	Environmental	2
H242 (Type C & D)	Physical	2	H411	Environmental	2
H242 (Type E & F)	Physical	1	H412	Environmental	1
H250	Physical	2	H413	Environmental	1
H251	Physical	2	H420	Environmental	2
H252	Physical	1	EUH001	Physical	2
H260	Physical	2	EUH006	Physical	2
H261 (category 2)	Physical	2	EUH014	Physical	2
H261 (category 3)	Physical	1	EUH018	Physical	2
H270	Physical	2	EUH019	Physical	2
H271	Physical	2	EUH029	Health	2
H272 (category 2)	Physical	2	EUH031	Health	2
H272 (category 3)	Physical	1	EUH032	Health	2
H280	Physical	1	EUH044	Physical	2
H281	Physical	1	EUH059	Environmental	2
H290	Physical	1	EUH066	Health	1
H300	Health	2	EUH070	Health	2
H301	Health	2	EUH071	Health	2
H302	Health	1	EUH201	Health	2
H303	Health	1	EUH201A	Health	1
H304	Health	2	EUH202	Health	2
H305	Health	1	EUH203	Health	1
H310	Health	2	EUH204	Health	1
H311	Health	2	EUH205	Health	1
H312	Health	1	EUH206	Health	2
H313	Health	1	EUH207	Health	2
H314	Health	2	EUH208	Health	1
H315	Health	1	EUH209	Physical	2
H316	Health	1	EUH209A	Physical	1
H317	Health	2			

Table VI. Expressions to calculate the Scale Risk Index[α]

Index	Abbreviation	Expression
Scale Risk Index for Human health hazards	SRIH	$SRIH = t \sum s_{Hi} m_i$
Scale Risk Index for Environmental hazards	SRIE	$SRIE = t \sum s_{Ei} m_i$
Scale Risk Index for Physical hazards	SRIPh	$SRIPh = t \sum s_{Phi} m_i$
Scale Risk Index	SRI	$SRI = t (\sum (s_{Hi} + s_{Ei} + s_{Phi}) m_i)$ $SRI = SRIH + SRIE + SRIPh$

[α] t – time for performing the synthesis (time for the reaction + time for the work-up); m_i – mass of each substance involved; s_{Hi} – score of the human health hazards; s_{Ei} – score of the environmental hazards; s_{Phi} – score of physical hazards of each substance; scores from Table V.

An automatic model to construct the green star may be uploaded in:

http://educa.fc.up.pt/documentosQV/EV/Construction%20of%20Green%20Star_10_points_GSAI.xlsx