Synthesis of 1-bromobutane

Evaluation of protocols including a preliminary step of preparation of reagents

Protocol S[1]

The greenness assessment made for protocol S did not include the preparation of reagents. If this step is considered to the greenness, the final evaluation corresponds to Figure 1. Table 1 presents the hazards and scores associated with the substances involved and Table 2 presents the scores used to construct the green stars.

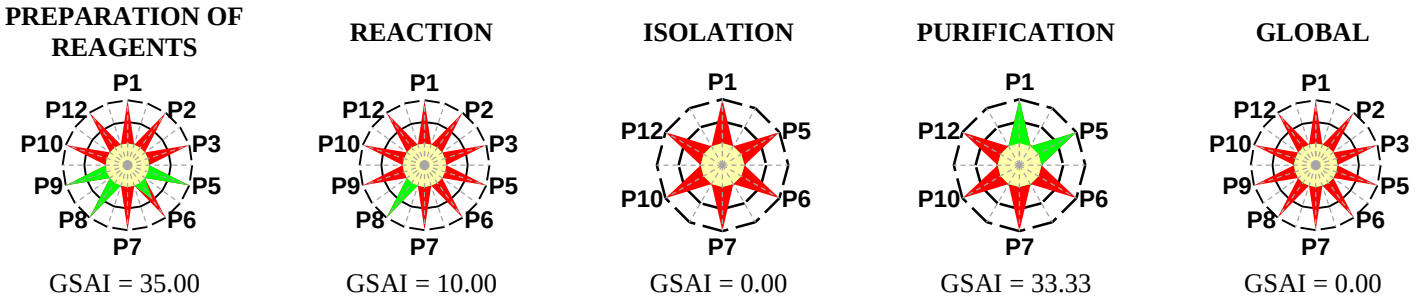

Figure 1. Greenness assessment (GS) for the synthesis of 1-bromobutane, protocol S

Protocol T[2,3]

The greenness assessment made for protocol T did not include the preparation of reagents. If this step is considered to the greenness, the final evaluation corresponds to Figure 2. Table 3 presents the hazards and scores associated with the substances involved and Table 4 presents the scores used to construct the green stars.

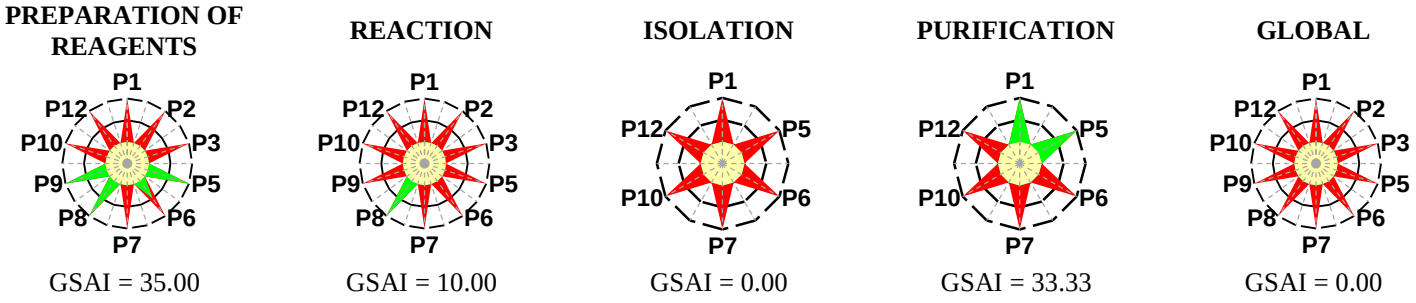

Figure 2. Greenness assessment (GS) for the synthesis of 1-bromobutane, protocol T

Table 1. Hazards for the synthesis of 1-bromobutane, protocol S[α]

Substances involved	Step				Hazard code	Score: hazards to...		
	Prep	R	I	Pu		HH	E	P
Stoichiometric reagents								
Bromine (CAS 7726-95-6)	✓				H314, H330, H400	3	3	1
Butan-1-ol (CAS 71-36-3)		✓			H226, H302, H315, H318, H335, H336	3	1	2
Hydrobromic acid (CAS 10035-10-6)		✓			H314, H335	3	1	1
Sulphur dioxide (CAS 7446-09-5)	✓				H314, H331	3	1	1
Auxiliary substances								
Solvents								
Hydrochloric acid (CAS 7647-01-0)			✓		H314, H335	3	1	1
Sodium carbonate (5% solution)			✓		-	1	1	1
Sodium hydrogen carbonate (5% solution)			✓		-	1	1	1
Water[a,b]	✓		✓		-	1	1	1
Other auxiliary substances								
Anhydrous calcium chloride (CAS 10043-52-4)			✓		H319	2	1	1
Anhydrous magnesium sulphate (CAS 7487-88-9)			✓		-	1	1	1
Sulphuric acid (CAS 7664-93-9)		✓			H314	3	1	1
Product								
1-bromobutane (109-65-9)		✓	✓	✓	H225, H315, H319, H335, H411	2	3	3
Waste								
Butan-1-ol (not reacted)			✓		H226, H302, H315, H318, H335, H336	3	1	2
Calcium chloride			✓		H319	2	1	1
Carbon dioxide			✓		H280	1	1	2
Dibutyl ether			✓		H226, H315, H319, H335, H412	2	2	2
Hydrobromic acid (excess, dilute solution)			✓		H315, H319	2	1	1
Hydrochloric acid (dilute solution)			✓		-	1	1	1
Hydrogen bromide		✓			H314, H335	3	1	1
Magnesium sulphate			✓		-	1	1	1
Sodium chloride (aqueous solution)			✓		-	1	1	1
Sulphur dioxide	✓				H314, H331	3	1	1
Sulphur trioxide	✓				H271, H314, H330, H350	3	1	3
Sulphuric acid (dilute solution)			✓		-	1	1	1
Water[a,b]			✓	✓	-	1	1	1

[α] Prep – Preparation of reagents; R – Reaction; I – Isolation; Pu – Purification; HH – Human Health; E – Environment; P – Physical
[a] Renewable; [b] Degradable to innocuous products

Table 2. Scores used to construct the green star for the synthesis of 1-bromobutane, protocol S[α]

Green Chemistry Principle	Preparation of reagents		Reaction		Isolation		Purification		Global	
	s	Explanation	s	Explanation	s	Explanation	s	Explanation	s	Explanation
P1 Prevention	1	Sulphur trioxide, H314, H330, H350, sulphur dioxide, H314, H331	1	Hydrogen bromide, H314, sulphur dioxide, H314 and H331	1	Butan-1-ol that does not reacted, H318	3	Waste is innocuous	1	Butan-1-ol that does not reacted, H318, hydrogen bromide, H314, sulphur dioxide, H314 and H331, sulphur trioxide, H314, H330, H350
P2 Atom Economy	1	Excess of sulphur dioxide > 10%, formation of by-products	1	Excess of hydrobromic acid > 10%, formation of by-products		NA		NA	1	Excess of hydrobromic acid and of sulphur dioxide > 10%, formation of by-products
P3 Less hazardous chemical synthesis	1	Bromine, H314, H330 and H400, sulphur dioxide, sulphur trioxide, H314, H330, H350	1	Butan-1-ol, H318, hydrobromic acid and sulphuric acid, H314, sulphur dioxide, H314 and H331, 1-bromobutane, H411, hydrogen bromide, H314		NA		NA	1	Butan-1-ol, H318, hydrobromic acid, hydrochloric acid and sulphuric acid, H314, bromine, H314, H330 and H400, sulphur dioxide, H314 and H331, 1-bromobutane, H411, hydrogen bromide, H314, sulphur trioxide, H314, H330, H350
P5 Safer solvents and auxiliary substances	3	Solvents and auxiliary substances are not used	1	Sulphuric acid, H314	1	Hydrochloric acid, H314	3	Solvents and auxiliary substances are not used	1	Hydrochloric acid and sulphuric acid, H314
P6 Increase energy efficiency	2	0 ºC ≤ T ≤ 100 ºC	1	T > 100 ºC	1	T > 100 ºC	1	T > 100 ºC	1	T > 100 ºC
P7 Use renewable feedstocks	1	Substances not renewable	1	Substances not renewable	1	Substances not renewable	1	Substances not renewable	1	Substances not renewable
P8 Reduce derivatives	3	One stage	3	One stage		NA		NA	1	Three stages
P9 Catalysts	3	Without catalysts	1	Sulphuric acid, H314		NA		NA	1	Sulphuric acid, H314
P10 Design for degradation	1	Substances not degradable	1	Substances not degradable	1	Substances not degradable	1	Substances not degradable	1	Substances not degradable
P12 Safer chemistry for accident prevention	1	Bromine, H314, H330 and H400, sulphur dioxide, sulphur trioxide, H314, H330, H350	1	Butan-1-ol, H318, hydrobromic acid and sulphuric acid, H314, sulphur dioxide, H314 and H331, 1-bromobutane, H225, hydrogen bromide, H314	1	Butan-1-ol, H318, 1-bromobutane, H225, hydrochloric acid, H314	1	1-bromobutane, H225	1	Butan-1-ol, H318, hydrobromic acid, hydrochloric acid and sulphuric acid, H314, bromine, H314, H330 and H400, sulphur dioxide, H314 and H331, 1-bromobutane, H225, hydrogen bromide, H314, sulphur trioxide, H314, H330, H350

[α]s – Score; NA – Not applicable

Table 3. Hazards for the synthesis of 1-bromobutane, protocol T[α]

Substances involved	Step				Hazard code	Score: hazards to...		
	Prep	R	I	Pu		HH	E	P
Stoichiometric reagents								
Bromine (CAS 7726-95-6)	✓				H314, H330, H400	3	3	1
Butan-1-ol (CAS 71-36-3)		✓			H226, H302, H315, H318, H335, H336	3	1	2
Hydrobromic acid (CAS 10035-10-6)		✓			H314, H335	3	1	1
Sulphur dioxide (CAS 7446-09-5)	✓				H314, H331	3	1	1
Auxiliary substances								
Solvents								
Sulphuric acid (CAS 7664-93-9)			✓		H314	3	1	1
Water[a,b]	✓		✓		-	1	1	1
Other auxiliary substances								
Anhydrous calcium chloride (CAS 10043-52-4)			✓		H319	2	1	1
Sodium carbonate (CAS 497-19-8)			✓		H319	2	1	1
Sulphuric acid (CAS 7664-93-9)		✓			H314	3	1	1
Product								
1-bromobutane (109-65-9)		✓	✓	✓	H225, H315, H319, H335, H411	2	3	3
Waste								
Butan-1-ol (not reacted)			✓		H226, H302, H315, H318, H335, H336	3	1	2
Calcium chloride			✓		H319	2	1	1
Carbon dioxide			✓		H280	1	1	2
Dibutyl ether			✓		H226, H315, H319, H335, H412	2	2	2
Hydrobromic acid (excess, dilute solution)			✓		H315, H319	2	1	1
Hydrogen bromide		✓			H314, H335	3	1	1
Sodium sulphate (aqueous solution)			✓		-	1	1	1
Sulphur dioxide	✓				H314, H331	3	1	1
Sulphur trioxide	✓				H271, H314, H330, H350	3	1	3
Sulphuric acid (dilute solution)			✓		-	1	1	1
Water[a,b]			✓	✓	-	1	1	1

[α] Prep – Preparation of reagents; R – Reaction; I – Isolation; Pu – Purification; HH – Human Health; E – Environment; P – Physical
[a] Renewable; [b] Degradable to innocuous products

Table 4. Scores used to construct the green star for the synthesis of 1-bromobutane, protocol T[α]

Green Chemistry Principle	Preparation of reagents		Reaction		Isolation		Purification		Global	
	s	Explanation	s	Explanation	s	Explanation	s	Explanation	s	Explanation
P1 Prevention	1	Sulphur trioxide, H314, H330, H350, sulphur dioxide, H314, H331	1	Hydrogen bromide, H314, sulphur dioxide, H314 and H331	1	Butan-1-ol that does not reacted, H318	3	Waste is innocuous	1	Butan-1-ol that does not reacted, H318, hydrogen bromide, H314, sulphur dioxide, H314 and H331, sulphur trioxide, H314, H330, H350
P2 Atom Economy	1	Excess of sulphur dioxide > 10%, formation of by-products	1	Excess of hydrobromic acid > 10%, formation of by-products		NA		NA	1	Excess of hydrobromic acid and of sulphur dioxide > 10%, formation of by-products
P3 Less hazardous chemical synthesis	1	Bromine, H314, H330 and H400, sulphur dioxide, sulphur trioxide, H314, H330, H350	1	Butan-1-ol, H318, hydrobromic acid and sulphuric acid, H314, sulphur dioxide, H314 and H331, 1-bromobutane, H411, hydrogen bromide, H314		NA		NA	1	Butan-1-ol, H318, hydrobromic acid and sulphuric acid, H314, bromine, H314, H330 and H400, sulphur dioxide, H314 and H331, 1-bromobutane, H411, hydrogen bromide, H314, sulphur trioxide, H314, H330, H350
P5 Safer solvents and auxiliary substances	3	Solvents and auxiliary substances are not used	1	Sulphuric acid, H314	1	Sulphuric acid, H314	3	Solvents and auxiliary substances are not used	1	Sulphuric acid, H314
P6 Increase energy efficiency	2	0 ºC ≤ T ≤ 100 ºC	1	T > 100 ºC	1	T > 100 ºC	1	T > 100 ºC	1	T > 100 ºC
P7 Use renewable feedstocks	1	Substances not renewable	1	Substances not renewable	1	Substances not renewable	1	Substances not renewable	1	Substances not renewable
P8 Reduce derivatives	3	One stage	3	One stage		NA		NA	1	Three stages
P9 Catalysts	3	Without catalysts	1	Sulphuric acid, H314		NA		NA	1	Sulphuric acid, H314
P10 Design for degradation	1	Substances not degradable	1	Substances not degradable	1	Substances not degradable	1	Substances not degradable	1	Substances not degradable
P12 Safer chemistry for accident prevention	1	Bromine, H314, H330 and H400, sulphur dioxide, sulphur trioxide, H314, H330, H350	1	Butan-1-ol, H318, hydrobromic acid and sulphuric acid, H314, sulphur dioxide, H314 and H331, 1-bromobutane, H225, hydrogen bromide, H314	1	Butan-1-ol, H318, 1-bromobutane, H225, sulphuric acid, H314	1	1-bromobutane, H225	1	Butan-1-ol, H318, hydrobromic acid and sulphuric acid, H314, bromine, H314, H330 and H400, sulphur dioxide, H314 and H331, 1-bromobutane, H225, hydrogen bromide, H314, sulphur trioxide, H314, H330, H350

[α]s – Score; NA – Not applicable

References

(1) Vogel, A.I. *A Text-Book of Practical Organic Chemistry*. Longmans, Green and Co, Ltd: London, 1948, pp. 277-281.

(2) Blatt, A.H.; Gilman, H. *et al*. *Organic Syntheses, collective volume I – 2nd edition*. John Wiley & Sons, Inc: New York, 1958, pp. 25-41.

(3) Fourneau, M. E. *et al*. *Synthèses Organiques*. Masson et Cie, Éditeurs: Paris, 1935, pp. 179-182.