

Synthesis of hippuric acid – Protocol B



Reaction. In conical flask prepare 19 mL (63 mmol) of 10% sodium hydroxide solution (stoichiometric proportions) and dissolve in it 2.3 g (30 mmol) of glycine. Add 3.5 mL (30 mmol) of benzoyl chloride (stoichiometric proportions) in 5 portions to the solution. Shake vigorously after each addition until all the chloride has reacted. Transfer the solution to a beaker and rinse the conical flask with a little water. Place a few pieces of crushed ice to the solution and add slowly 5 mL (60 mmol) of hydrochloric acid (about 100% excess) with stirring until the mixture is acid to Congo red paper.

Isolation. Collect the resulting crystalline precipitate of hippuric acid, upon a Büchner funnel, wash with cold water and drain well.

Purification. Place the solid in a round bottom flask with 10 mL of chloroform and heat under reflux. Allow the mixture to cool down. Filter the product on Büchner funnel, and dry on air on Petri dish.

Safety. See hazards associated with the reagents in Table 1.

Greenness Assessment. The evaluation was performed using the Green Star (GS) and the results are shown in Figure 1.

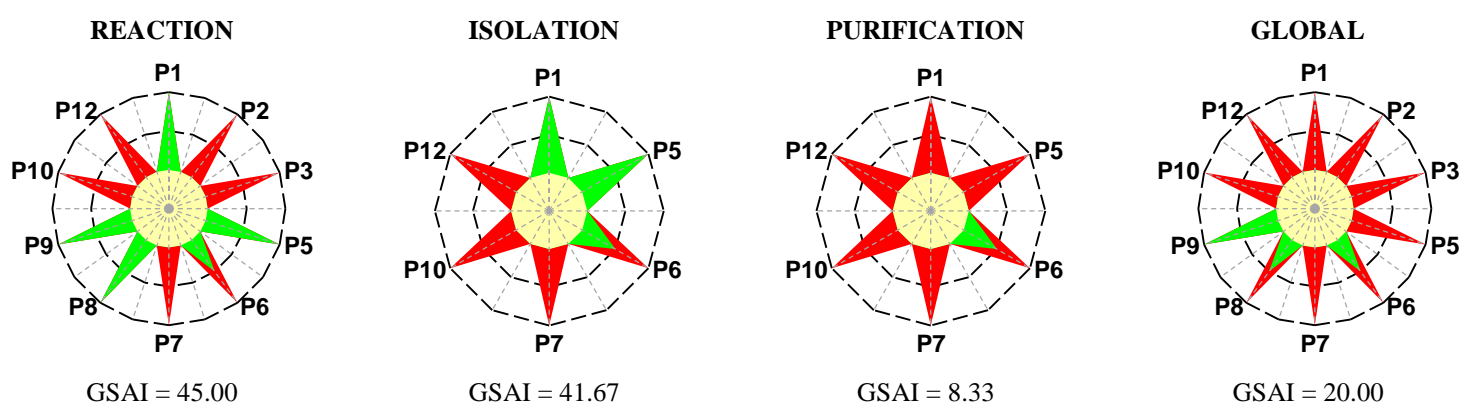


Figure 1. Greenness assessment (GS) for the synthesis of hippuric acid

Construction of the GS



Table 1 presents the hazards and scores associated with the substances involved and Table 2 presents the scores used to construct the green stars.

Table 1. Hazards for the synthesis of hippuric acid, protocol B^α

Substances involved	Step			Hazard code	Score: hazards to...		
	R	I	Pu		HH	E	P
Stoichiometric reagents							
Benzoyl chloride (CAS 98-88-4)	✓			H302, H312, H314, H317, H332	3	1	1
Glycine (CAS 56-40-6)	✓			-	1	1	1
Hydrochloric acid (CAS 7647-01-0)	✓			H314, H335	3	1	1
Sodium hydroxide (10% solution)	✓			H314	3	1	1
Auxiliary substances							
Solvents							
Chloroform (CAS 67-66-3)			✓	H302, H315, H351, H373	3	1	1
Water ^{a,b}	✓	✓		-	1	1	1
Product							
Hippuric acid (495-69-2)	✓	✓	✓	H302, H315, H318, H335	3	1	1
Waste							
Benzoic acid			✓	H318, H335	3	1	1
Chloroform			✓	H302, H315, H351, H373	3	1	1
Hydrochloric acid (dilute solution)		✓		-	1	1	1
Sodium chloride (aqueous solution)		✓		-	1	1	1
Water ^{a,b}		✓		-	1	1	1

^α 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 hippuric acid, protocol B^a

Green Chemistry Principle	Reaction		Isolation		Purification		Global	
	s	Explanation	s	Explanation	s	Explanation	s	Explanation
P1 Prevention	3	Without waste	3	Waste is innocuous	1	Benzoic acid, H318, and chloroform, H351, H373	1	Benzoic acid, H318, and chloroform, H351, H373
P2 Atom Economy	1	Excess of hydrochloric acid > 10%, formation of by-products		NA		NA	1	Excess of hydrochloric acid > 10%, formation of by-products
P3 Less hazardous chemical synthesis	1	Benzoyl chloride, sodium hydroxide and hydrochloric acid, H314, hippuric acid, H318		NA		NA	1	Benzoyl chloride, sodium hydroxide and hydrochloric acid, H314, hippuric acid and benzoic acid, H318, chloroform, H351, H373
P5 Safer solvents and auxiliary substances	3	Water	3	Water	1	Chloroform, H351, H373	1	Chloroform, H351, H373
P6 Increase energy efficiency	2	0 °C ≤ T ≤ 100 °C	2	0 °C ≤ T ≤ 100 °C	2	0 °C ≤ T ≤ 100 °C	2	0 °C ≤ T ≤ 100 °C
P7 Use renewable feedstocks	1	Substances not renewable	1	Substances not renewable	1	Substances not renewable	1	Substances not renewable
P8 Reduce derivatives	3	One stage		NA		NA	2	Two stages
P9 Catalysts	3	Without catalysts		NA		NA	3	Without catalysts
P10 Design for degradation	1	Substances not degradable	1	Substances not degradable	1	Substances not degradable	1	Substances not degradable
P12 Safer chemistry for accident prevention	1	Benzoyl chloride, sodium hydroxide and hydrochloric acid, H314, hippuric acid, H318	1	Hippuric acid, H318	1	Chloroform, H351, H373, hippuric acid and benzoic acid, H318	1	Benzoyl chloride, sodium hydroxide and hydrochloric acid, H314, hippuric acid and benzoic acid, H318, chloroform, H351, H373

^as – Score; NA – Not applicable

References

Adam Mickiewicz University, <http://www.staff.amu.edu.pl/~psorg/serp.pdf> (accessed April 2013).