Synthesis of 3-nitrobenzoic acid – Protocol D

$$C_6H_5COOCH_3 + HNO_3 \rightarrow m-NO_2C_6H_4COOCH_3 + H_2O$$

$$m-NO_2C_6H_4COOCH_3 + NaOH + HCl \rightarrow m-NO_2C_6H_4COOH + CH_3OH + NaCl$$

Preparation of reagents. Place 8 mL (126 mmol) concentrated nitric acid (about 58% excess) in a 125 mL Erlenmeyer flask. Add 8 mL concentrated sulphuric acid. Swirl the flask to thoroughly mix the acids and cool in an ice bath until the internal temperature of the mixture is 5 ºC. Place 20 mL concentrated sulphuric acid in a 250 mL Erlenmeyer flask. Add all at once 10 mL (80 mmol) methyl benzoate to the sulphuric acid. Swirl the flask during the addition of the methyl benzoate and immediately cool the entire mixture in an ice bath until the internal temperature falls to 0-5 ºC. When the internal temperature of both acid mixtures is below 5 ºC, add the nitric acid – sulphuric acid mixture dropwise to the methyl benzoate solution during 5 to 10 minutes. Swirl the 250 mL Erlenmeyer flask vigorously during this addition and keep the mixture as close to 5 ºC as possible. After the addition swirl the flask for several minutes in the ice bath and then allow the solution to warm to room temperature (about 10 to 15 minutes). Swirl the flask occasionally during the warming period. After the mixture has come to room temperature, slowly pour it, with stirring, over 100 g ice in a 600 mL beaker. Swirl the material in the beaker and collect the resulting solid by suction filtration using a Büchner funnel. Wash the solid with 10 mL ice-cold methanol. Air-dry the resulting solid.

Reaction. Place 4 g (100 mmol) sodium hydroxide (between 64% and 100% excess) in a 50 mL Erlenmeyer flask and add 16 mL water. Swirl the Erlenmeyer flask until the sodium hydroxide dissolves. Add methyl 3-nitrobenzoate (about 9 to 11 g – 50 to 61 mmol – obtained in the preparation of reagents) to a 50 mL round-bottom boiling flask. Add the aqueous solution to the round-bottom flask and fit a reflux condenser. Heat the aqueous mixture until the solution boils, and continue ti heat under reflux for 15 minutes. After the reflux period, cool the reaction mixture to room temperature and dilute it with 20 mL distilled water. If the solution is colored, treat the mixture with charcoal and filter hot. Add, with vigorous stirring, the dilute aqueous base mixture to a 250 mL beaker containing 15 mL (180 mmol) hydrochloric acid (between 195% and 260% excess).

Isolation. Swirl the mixture vigorously while cooling in an ice bath until the aqueous solution returns to room temperature. Collect the crude 3-nitrobenzoic acid with the aid of a Büchner funnel and wash the solid with a small amount of distilled water. Air-dry the product.

Purification. Recrystallize the product from 1% aqueous hydrochloric acid.

Safety. Synthesis should be performed in a fume hood. 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. This assessment did not include the preparation of reagents.

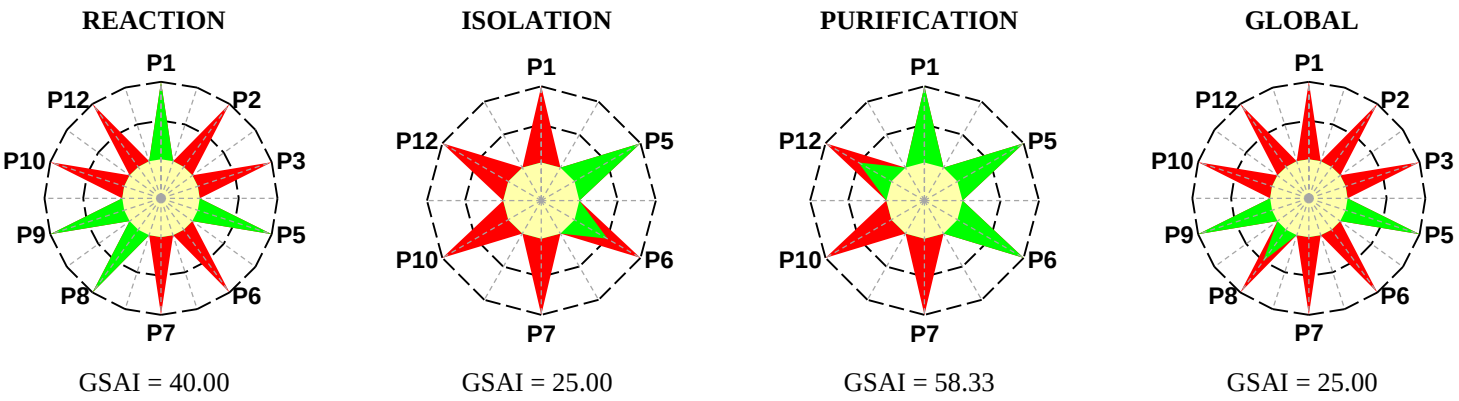

Figure 1. Greenness assessment (GS) for the synthesis of 3-nitrobenzoic acid

Construction of the GS

$$C_6H_5COOCH_3 + HNO_3 \rightarrow m-NO_2C_6H_4COOCH_3 + H_2O$$

$$m-NO_2C_6H_4COOCH_3 + NaOH + HCl \rightarrow m-NO_2C_6H_4COOH + CH_3OH + NaCl$$

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 3-nitrobenzoic acid, protocol D[α]

Substances involved	Step				Hazard code	Score: hazards to...		
	Prep	R	I	Pu		HH	E	P
Stoichiometric reagents								
Hydrochloric acid (CAS 7647-01-0)		✓			H314, H335	3	1	1
Methyl benzoate (CAS 93-58-3)	✓				H302	2	1	1
Methyl m-nitrobenzoate(CAS 618-95-1)		✓			-	1	1	1
Nitric acid (CAS 7697-37-2)	✓				H272 (cat. 3), H314	3	1	2
Sodium hydroxide (CAS 1310-73-2)		✓			H314	3	1	1
Auxiliary substances								
Solvents								
Hydrochloric acid (1% solution)				✓	-	1	1	1
Methanol (CAS 67-56-1)	✓				H225, H301, H311, H331, H370	3	1	3
Water[a,b]	✓	✓	✓		-	1	1	1
Other auxiliary substances								
Activated charcoal (CAS 7440-44-0)		✓			-	1	1	1
Sulphuric acid (CAS 7664-93-9)	✓				H314	3	1	1
Product								
3-nitrobenzoic acid (121-92-6)		✓	✓	✓	H302, H315, H319, H335, H412	2	2	1
Waste								
Hydrochloric acid (dilute solution)				✓	-	1	1	1
Methanol	✓		✓		H225, H301, H311, H331, H370	3	1	3
Nitric acid (dilute solution)	✓				-	1	1	1
Sodium chloride (aqueous solution)			✓		-	1	1	1
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 3-nitrobenzoic acid, protocol D[α]

Green Chemistry Principle	Reaction		Isolation		Purification		Global	
	s	**Explanation**	**s**	**Explanation**	**s**	**Explanation**	**s**	**Explanation**
P1 Prevention	3	Without waste	1	Methanol, H301, H311, H331, H370	3	Waste is innocuous	1	Methanol, H301, H311, H331, H370
P2 Atom Economy	1	Excess of sodium hydroxide and hydrochloric acid > 10%, formation of by-products		NA		NA	1	Excess of sodium hydroxide and hydrochloric acid > 10%, formation of by-products
P3 Less hazardous chemical synthesis	1	Sodium hydroxide and hydrochloric acid, H314, and methanol, H301, H311, H331, H370		NA		NA	1	Sodium hydroxide and hydrochloric acid, H314, and methanol, H301, H311, H331, H370
P5 Safer solvents and auxiliary substances	3	Water and activated charcoal	3	Water	3	1% aqueous hydrochloric acid	3	Solvents and auxiliary substances are innocuous
P6 Increase energy efficiency	1	T > 100 ºC	2	0 ºC ≤ T ≤ 100 ºC	3	Room temperature	1	T > 100 ºC
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	Sodium hydroxide and hydrochloric acid, H314, and methanol, H225, H301, H311, H331, H370	1	Methanol, H225, H301, H311, H331, H370	2	3-nitrobenzoic acid, H302, H315, H319, H335	1	Sodium hydroxide and hydrochloric acid, H314, and methanol, H225, H301, H311, H331, H370

[α]s – Score; NA – Not applicable

References

Durst, H.D.; Gokel, G.W. *Experimental Organic Chemistry – 2nd edition*. McGraw-Hill Book Company: New York, 1987, pp. 493-495.