

# Synthesis of hippuric acid

## Summary of the analysed protocols

$\text{NH}_2\text{CH}_2\text{COOH} + \text{C}_6\text{H}_5\text{COCl} + 2\text{NaOH} + \text{HCl} \rightarrow \text{C}_6\text{H}_5\text{CONHCH}_2\text{COOH} + 2\text{NaCl} + 2\text{H}_2\text{O}$	(1)
$\text{ClCH}_2\text{COOH} + 2\text{NH}_3 \rightarrow \text{NH}_2\text{CH}_2\text{COOH} + \text{NH}_4\text{Cl}$	(2)
<b>Protocol A<sup>1</sup></b>	
<b>Reaction (R<sub>1</sub>):</b> equation (1), 12.5% exc. sodium hydroxide solution (6M), 30% exc. benzoyl chloride, 500% exc. hydrochloric acid, water (solvent), T ~ 0 °C	
<b>Isolation (I<sub>1</sub>):</b> filtration (suction) → washing (water → ethyl ether)	
<b>Purification (Pu<sub>1</sub>):</b> recrystallization – dissolution (ethanol) → cooling (ice bath) → filtration (suction) → washing (cold ethanol) → drying (oven at T < 100 °C)	
<b>Protocol B<sup>2</sup></b>	
<b>Reaction (R<sub>2</sub>):</b> equation (1), stoichiometric proportions of 10% sodium hydroxide solution and benzoyl chloride, 100% exc. hydrochloric acid, water (solvent), T ~ 0 °C, pH test: Congo red paper	
<b>Isolation (I<sub>2</sub>):</b> filtration (suction) → washing (cold water) → drying (air)	
<b>Purification (Pu<sub>2</sub>):</b> recrystallization – dissolution (chloroform) → reflux → cooling → filtration (suction) → drying (air)	
<b>Protocol C<sup>3</sup></b>	
<b>Reaction (R<sub>3</sub>):</b> equation (1), 26% exc. 10% sodium hydroxide solution, 15% exc. benzoyl chloride, water (solvent), T ~ 0 °C, pH test: Congo red paper	
<b>Isolation (I<sub>2</sub>):</b> ≡ Pr B	
<b>Purification (Pu<sub>3</sub>):</b> recrystallization – dissolution (carbon tetrachloride) → cooling → filtration (suction) → washing (carbon tetrachloride) → dissolution (boiling water) → reflux → filtration → crystallization → filtration (suction) → drying (oven) → decolorizing carbon (auxiliary substance)	
<b>Protocol D<sup>4</sup></b>	
<b>Reaction (R<sub>4</sub>):</b> equation (1), stoichiometric proportion of sodium hydroxide solution (1M), 15% exc. benzoyl chloride, room temperature, pH test: litmus paper and Congo red paper	
<b>Isolation (I<sub>3</sub>):</b> filtration (suction) → drying (vacuum desiccator)	
<b>Purification (Pu<sub>4</sub>):</b> recrystallization – dissolution (carbon tetrachloride) → reflux → filtration → washing (ethyl ether) → drying (vacuum desiccator)	
<b>Protocol E<sup>5</sup></b>	
<b>Preparation of reagents (Prep<sub>1</sub>):</b> equation (2), 2350% exc. ammonium hydroxide, sodium hydroxide and decolorizing carbon (auxiliary substances), distillation, T < 100 °C	
<b>Reaction (R<sub>5</sub>):</b> equation (1), stoichiometric proportion of sodium hydroxide, 10% exc. benzoyl chloride, 50% exc. hydrochloric acid, water (solvent), room temperature	
<b>Isolation (I<sub>4</sub>):</b> filtration → drying (air)	
<b>Purification (Pu<sub>5</sub>):</b> recrystallization – dissolution (carbon tetrachloride) → cooling → filtration (suction) → washing (carbon tetrachloride) → drying (air) → dissolution (boiling water) → filtration → crystallization → concentration of the solution	

<sup>a</sup> → – Sequential

## References

- (1) Universidade de Aveiro, <http://www.ua.pt/ensino/PageDisc.aspx?id=2528> (accessed April 2011).
- (2) Adam Mickiewicz University, <http://www.staff.amu.edu.pl/~psorg/serp.pdf> (accessed April 2013).
- (3) Vogel, A.I. *Elementary Practical Organic Chemistry*. Longmans, Green and Co: London, 1958, pp. 244.
- (4) Robertson, G.R. *Laboratory Practice of Organic Chemistry – 3<sup>rd</sup> edition*. The Macmillan Company: New York, 1954, pp. 328-329.
- (5) Blatt, A.H. et al. *Organic Syntheses, collective volume II*. John Wiley & Sons, Inc.: New York, 1959, pp. 328-330.