Biobased synthesis of acrylonitrile from glutamic acid

Jérôme Le Nôtre, a Elinor L. Scott, a* Maurice C. R. Franssen, b Johan P. M. Sanders a

General Information:
All reactions were carried out in standard glassware except for palladium-catalysed reactions performed in Schlenk tubes glassware under a positive pressure of nitrogen. Sensitive liquids and solutions were transferred via syringe. Concentration of solution was carried out by using a rotary evaporator, and generally followed by removal of residual solvents on a vacuum line. Unless otherwise stated, all commercial reagents and solvents were used without additional purification. Proton nuclear magnetic resonance spectra (1H NMR) were recorded on a Bruker AM-400 (400 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0 ppm for TMS. Coupling constants, J, were reported in Hertz (Hz). Carbon 13 nuclear magnetic resonance spectroscopy (13C NMR) was recorded on Bruker AM-400 (100 MHz) and was fully decoupled by broad band decoupling. Chemical shifts were reported in ppm referenced to the centre line of a triplet at 77.0 ppm of chloroform-d. GC-MS analyses were performed on a CE Instrument GC 8000 Top (capillary column SGE-Forte, 30 m x 0.25 mm, 0.25 μm) chromatograph linked to an Automass II Finnigan MAT (70 eV) apparatus.

Oxidative Decarboxylation of Glutamic acid to 3-cyanopropanoic acid (5).

Using N-bromosuccinimide (NBS) or 1,3-dibromo-5,5-dimethylhydantoin (DBDMH): To a stirred solution of glutamic acid (2.93 g, 20 mmol) in a pH 5 phosphate buffer (90 mL) was slowly added a solution of N-bromosuccinimide (NBS, 1.07 g, 60 mmol) in 20 mL of DMF. (For each aliquot addition the reaction mixture turned slightly yellow and a strong CO2 evolution is observed while the coloration disappeared). At the end of the addition the orange solution was stirred overnight at room temperature. The reaction was carefully quenched with Na2S2O3.5H2O till the coloration disappeared, and then extracted with Et2O (3 x 50 mL). After washes and drying over MgSO4 the solvent was removed by evaporation. 1H NMR analysis of the crude showed a mixture of the product and succinimide. The crude was extracted with a minimum amount of Et2O (30 mL) to solubilise the product, succinimide was filtered off and re-extracted two times following the same procedure. The three filtrate solutions were collected and concentrated to afford 3-cyanopropanoic acid (5, 713 mg, 36% yield).

The reaction was repeated with 30 mmol of 1,3-dibromo-5,5-dimethylhydantoin (DBDMH) instead of NBS and after purification the product (5) was isolated in 40% yield (801 mg).

Using bromide salt and sodium hypochlorite:
In an ice-bathed round bottom flask were introduced glutamic acid (2.93 g, 20 mmol), NaBr (0.21 g, 10 mol%), and 50 mL H2O. NaOCl solution (15 wt% in H2O, 24.8 mL, 60 mmol) was added dropwise under a good stirring (for each drop of NaOCl
solution, the reaction mixture turned orange and a strong CO₂ evolution was observed while the coloration disappeared. After 1 hour stirring at 4 °C the reaction mixture was carefully quenched with Na₂S₂O₃·5H₂O. NaCl was then added till saturation and the reaction mixture was extracted with Et₂O (4 x 30 mL). The collected organic layers were dried over MgSO₄ and evaporated to dryness. ¹H NMR analysis of the crude showed 3-cyanopropanoic acid (5, 850 mg, 43% yield) as the major product and the corresponding aldehyde as a minor product (85% purity). A 94% purity towards 3-cyanopropanoic acid (5) was obtained after one recrystallisation in Et₂O.

An alternative work-up procedure consisted in evaporating the water after reaction and quenching. The resulting paste was extracted with Et₂O (4 x 30 mL), the collected organic layers were dried over MgSO₄ and evaporated to dryness. NMR analyses of the crude showed 3-cyanopropanoic acid (5, 1.39 g, 70% yield, 90% purity).

3-Cyanopropanoic acid (5): ¹H NMR (D₂O): δ = 2.79-2.74 (m, 2H), 2.73-2.68 (m, 2H); ¹³C NMR (D₂O): δ = 174.9, 120.8, 29.3, 12.4; IR (cm⁻¹): 3202, 2253, 1692.

Decarbonylation-Elimination of 3-cyanopropanoic acid (5):²
In a Schlenk tube under a positive pressure of nitrogen were introduced palladium(II) chloride (26.8 mg, 3 mol%), bis(2-diphenylphosphino phenyl)ether (DPE-Phos, 244.3 mg, 9 mol%), 3-cyanopropanoic acid (500 mg, 5.0 mmol), and hydroquinone (0.2 mg, 40 ppm). Dry 1,3-Dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU, 30 mL) was then added followed by degassed acetic anhydride (1.0 mL, 10 mmol) and degassed triethylamine (0.7 mL, 5 mmol). The reaction mixture was heated at 110 °C for 18 hours. After reaction, an aliquot of the mixture was analysed by ¹H NMR spectroscopy. Another aliquot was filtered through a short plug of silica and the solution was diluted and analysed by GC-MS. The rest of the crude reaction mixture was submitted to distillation under atmospheric pressure. The second fraction showed a steady boiling temperature (bp: 76-78 °C), was analysed by NMR spectroscopy and GC-MS, and corresponds to acrylonitrile (3, 46 mg, 17% yield).

Acrylonitrile (3): ¹H NMR (CDCl₃): δ = 6.22 (dd, 1H, J = 17.9 Hz, 0.87 Hz), 6.07 (dd, 1H, J = 11.7 Hz, 0.87 Hz), 5.65 (dd, 1H, J = 17.9 Hz, 11.7 Hz); ¹³C NMR (CDCl₃): δ = 137.2, 116.9, 107.7; MS (EI): m/z (%) = 53 (100) [M⁺], 52 (80), 51 (35).

References