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COMMUNICATION

Biobased synthesis of acrylonitrile from glutamic acid†

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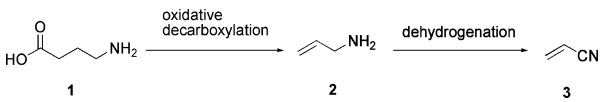
Glutamic acid was transformed into acrylonitrile in a two step procedure involving an oxidative decarboxylation in water to 3-cyanopropanoic acid followed by a decarbonylation-elimination reaction using a palladium catalyst.

Alternative resources for fossil fuels represent a key research area due to the depletion of oil feedstocks, increasing oil prices, insecurity of supply, and environmental concerns. As a consequence a lot of effort has been given to the development of alternative transportation fuels and, to a lesser extent, to the production of bulk industrial chemicals. However, in the last decade chemurgy has regained the interest of a number of research institutions and companies. Amino acids, for instance, appear as an innovative and economically viable source of nitrogen-containing bulk chemicals, avoiding the need of energy-intensive processes to functionalise hydrocarbons with ammonia.[1] We indeed have shown that glutamic acid, available from a wide range of voluminous waste streams such as dried distiller's grains and solubles (DDGS) of the bioethanol production from maize and wheat, can be converted into γ-aminobutyric acid (GABA)[2] and *N*-methylpyrrolidone (NMP)[3] *via* technically and economically feasible routes. DDGS has indeed seen its price drift from $140 to $90 per short tonne between 1980 and 2000.[4] Around 25% of proteins can be found in DDGS from maize, in which glutamic acid is the most abundant amino acid (*ca.* 20%).[5] Considering an assumed volume of 10% of the total transportation market in 2020 will consist of bio-fuels, an additional 100 millions tonnes of protein will be produced, corresponding to *ca.* 20 million tonnes of glutamic acid available as a cheap bio-based feedstock.

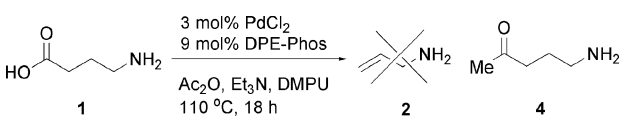
Acrylonitrile is an important bulk chemical used in the production of a number of chemicals and polymers. The annual global production reaches *ca.* 6 million tons with a current price of *ca.* €1900 per ton.[6] Its main industrial production (SOHIO process) is based on the conversion of propene and ammonia at high temperature (400–500 °C) in the presence of metal-oxide catalysts. Recently the first example of the synthesis of acrylonitrile from a non-fossil source (glycerol) was reported using microwave irradiation (47% conversion, 80% selectivity).[7] However, the use of hydrogen peroxide and ammonia was necessary to introduce the nitrogen functionality.

Herein we report the synthesis of acrylonitrile, without the use of additional ammonia, by using glutamic acid in a two step procedure. The first step involves the oxidative decarboxylation of glutamic acid to 3-cyanopropanoic acid in water, followed by a decarbonylation-elimination using a palladium catalyst.

Initially GABA (**1**), obtained from glutamic acid by enzymatic decarboxylation,[2] was used as a starting material. Here it was proposed that oxidative decarboxylation to allylamine (**2**), followed by dehydrogenation would result in the formation of acrylonitrile (Scheme 1). The conversion of an amine such as (**2**) into a nitrile is a well documented transformation in literature and several catalytic processes are available.[8] However this is not the case for the formation of terminal alkenes from carboxylic acids, the first reaction envisaged. Besides the use of a stoichiometric amount of lead tetraacetate, only a few catalytic methods are known and the selectivity towards the terminal alkene is often poor, with alkane or internal alkene formed as side products. Several methods were tested based on literature methods such as the use of a heterogeneous catalyst (Pd/C),[9] silver salts,[10] and homogeneous catalysts.[11] Unfortunately we never succeeded to form allylamine (**2**) from GABA (**1**). Even with protection on the amine function, either no reaction took place, or cyclisation to 2-pyrrolidone occurred. When we applied the reaction conditions we previously developed to selectively form terminal alkenes from carboxylic acids by decarbonylation-elimination,[12] intramolecular decarboxylative acylation was observed,[13] leading to the formation of the ketone (**4**) (Scheme 2).



Scheme 1 Initial approach.



Scheme 2 Decarbonylation-elimination attempts on GABA (**1**).

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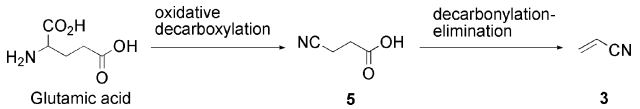
Thus a new strategy was investigated where 3-cyanopropanoic acid (**5**) would be the key intermediate formed from glutamic acid. First an oxidative decarboxylation of the amino acid function of glutamic acid would be performed, followed by a decarbonylation-elimination[12] of 3-cyanopropanoic acid which should give acrylonitrile (**3**) (Scheme 3).



Scheme 3 New approach for the conversion of glutamic acid to acrylonitrile (**3**).

The transformation of amino acids into nitriles has been studied in the past and different reaction conditions are available in the literature. For the reaction to proceed a catalytic amount of bromide cation "Br^+" is needed. Different bromide cation sources can be used either using brominated agents or a mixture of bromide anion and oxidant. For instance sodium hypobromite has been used for the oxidative decarboxylation of amino acids.[14] The use of *N*-bromosuccinimide[15] as well as trichloroisocyanuric acid have also been reported.[16]

A combination of HBr and hydrogen peroxide,[17] a bromide salt with hydrogen peroxide,[18] or with tetrabutylammonium peroxydisulfate[19] as oxidant have been used for bromination reaction and could be good candidates for the transformation of amino acids into nitriles. Moreover those reagents can present a better activity in the presence of vanadium catalysts.[20] This combination with vanadium is directly inspired by nature, where haloperoxidase enzymes are known to perform this oxidation reaction.[21] Hager *et al.* have described the use of bromoperoxidase with hydrogen peroxide and potassium bromide for the transformation of valine and tyrosine.[22]

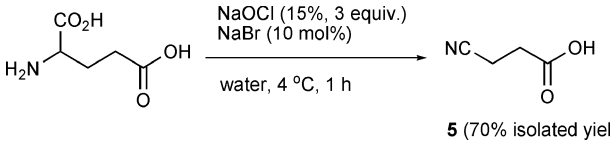
First we decided to try *N*-bromosuccinimide (NBS, 3 equivalents) and 1,3-dibromo-5,5-dimethylhydantoin (DBDMH, 1.5 equivalents) in phosphate buffer pH 5 at room temperature for 4 h.[15b] Although the conversion into 3-cyanopropanoic acid (**5**) was almost complete, side products were formed and purification of the crude mixture remained difficult. However 3-cyanopropanoic acid (**5**) was isolated in *ca.* 40% after chromatography over silica gel. By trying the combination of hydrogen bromide with hydrogen peroxide we did not observe any conversion of glutamic acid into 3-cyanopropanoic acid (**5**).

We then decided to use *in situ*-generated sodium hypobromite on glutamic acid by reacting sodium bromide and sodium hypochlorite (Table 1). During the dropwise addition of sodium hypochlorite it was observed that the reaction mixture changed colour temporarily (from pale yellow to brown-orange) and gas (CO_2) was evolved. It is known that at least 2 equivalents of oxidant are needed to convert an amino acid function into a nitrile group.[14] However using 2 equivalents of sodium bromide and sodium hypochlorite, only 57% conversion into 3-cyanopropanoic acid (**5**) was obtained after 1 h at 0 °C (Table 1, entry 1). Optimisation of the reaction conditions showed that an excess of sodium hypochlorite was needed (Table 1, entry 2), but only a catalytic amount of sodium bromide is required to reach full conversion (Table 1, entries 3–5), with an optimum of 0.1 equivalent based on glutamic acid (Table 1, entry 4). The reaction was repeated on a larger scale (20 mmol of glutamic acid) and the isolated yield amounted to 70% (Scheme 4).

Table 1 Optimisation of the oxidative decarboxylation of glutamic acid using a combination of sodium bromide and sodium hypochlorite[a]

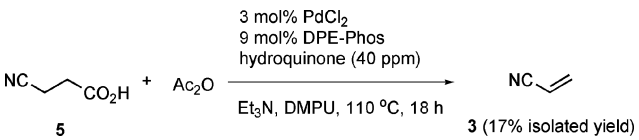
Entry	NaBr (equivalent)	NaOCl (equivalent)	Conversion (%)[b]
1	2	2	57
2	3	3	100
3	0.5	3	100
4	0.1	3	100
5	0.01	3	5

[a] Reaction conditions: glutamic acid (1 mmol, 147 mg), D_2O (2 mL), 0 °C, 1 h. [b] Determined by ^1H NMR.



Scheme 4 Glutamic acid to 3-cyanopropanoic acid (**5**) using sodium bromide and sodium hypochlorite.

Recently we reported the optimisation of a catalytic system able to selectively transform aliphatic carboxylic acids into terminal alkenes under relatively mild conditions.[12] The reaction follows a decarbonylation-elimination reaction pathway using acetic anhydride. Acetic acid and carbon monoxide are then produced and can be potentially recycled and reused. 3-Cyanopropanoic acid (**5**) was reacted under these optimised reaction conditions as depicted in Scheme 5. The reaction was performed on 0.5 to 1 g scale and after 18 h reaction carbon monoxide was detected in the reaction atmosphere. The crude mixture was analysed by proton NMR and showed a full consumption of the starting material and the presence of acrylonitrile (**3**), which was confirmed by GC-MS analysis. Purification was performed using a micro-distillation set-up and acrylonitrile (**3**) was isolated, in pure form, in 17% yield. The low isolated yield can be explained by the fact that, despite the presence of a stabilizer (hydroquinone), some insoluble black material was present in the reaction mixture, which could come from the degradation of the starting material or the polymerisation of the product.



Scheme 5 Decarbonylation/elimination reaction of 3-cyanopropanoic acid (**5**).

In conclusion, we show that acrylonitrile can be prepared in two steps from glutamic acid. The first step consists of an oxidative decarboxylation using *in situ*-generated sodium hypobromite leading to the formation of 3-cyanopropanoic acid. We are currently studying the possibility of improving this transformation by the use of enzymes such as haloperoxidases,[21] or by exploring the use of a greener oxidant for the reaction, such as molecular oxygen.[23] The second step allowed the conversion

of 3-cyanopropanoic acid into acrylonitrile by a palladium-catalysed decarbonylation-elimination reaction. Although the isolated yields need to be improved, we showed that the conversion was high and we hope that further study of this transformation, especially towards the stability of acrylonitrile during the reaction, will lead to better results. Moreover it appeared to us that 3-cyanopropanoic acid constitutes an interesting and promising intermediate for the preparation of other bulk chemicals and further results will be reported in due course.

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