

Nitration Chemistry in Continuous Flow using Acetyl Nitrate

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Introduction

The adoption of $\text{Ac}_2\text{O}/\text{HNO}_3$ mixtures for aromatic nitrations and the preparation of nitric esters have been reported for laboratory and industrial uses [1]. This system offers the advantage of reduced undesired secondary reactions and selective nitration characteristics, compared to mixed acid solutions [2], [3].

$\text{Ac}_2\text{O}/\text{HNO}_3$ mixtures are on the other hand characterized by a certain explosive behaviour which is generally ascribed to the formation of acetyl nitrate, a species known to undergo violent explosions on heating above 333 K [4]. More than one accident has been recorded in the past in industrial applications of this system [5].

One way to greatly reduce the potential hazard of $\text{Ac}_2\text{O}/\text{HNO}_3$ mixtures is to miniaturize the synthesis apparatus and auxiliary equipment by employing continuous flow chemistry. Continuous flow chemistry is one of the most innovative and rapidly developing fields in chemical engineering, synthesis and process technology [6-10].

Continuous flow reactors are mainly characterized by their high surface-to-volume ratio and channel diameters in the order of several hundred micrometers, which allow the running of highly exothermic or hazardous reactions in a safe manner. Indeed, the heat-transfer rate between the reactor and the surrounding medium can be magnitude of orders faster compared to that for a batch reactor [11].

This paper describes the first results by using acetyl nitrate as nitrating agent for the selective nitration of $\text{N,N}'$ -dialkyl substituted ureas in a continuous flow reaction system. From macroscopic batch reactions with mixed acid as nitrating agent it is well known that always both the mono- and dinitro-substituted products are obtained. With respect to a further processing of the nitroureas to the final DNDA plasticizer a quantitative synthesis of $\text{N,N}'$ -dialkyl- $\text{N,N}'$ -dinitro-urea is preferably wanted to achieve improved energetic properties of the final product.

Experimental

The experiments were carried out in batch mode as well as in continuous mode. For the batch experiments, the reaction was carried out in a reaction calorimeter. The instrument used was a RC1 Reaction Calorimeter, manufactured by Mettler Toledo, equipped with a SV01 glass atmospheric pressure reactor [12].

A mixture of acetic anhydride (Ac_2O) and acetic acid (HAc) was placed to the SV01 vessel and salpetric acid was fed linearly over a certain period of time, while the temperature was maintained at 15°C . The mixture was stirred until no heat release was detected, indicating that the reaction was completed. Then the N,N'-dimethyl-urea dissolved in acetic acid was also fed linearly to the $\text{Ac}_2\text{O}/\text{HNO}_3/\text{HAc}$ mixture, while the temperature was also maintained at 15°C . The agitation rate was constant for both reaction steps at 700 rpm with the glass propeller stirrer. After this the reaction mixture was poured into a water-ice mixture and extracted with CH_2Cl_2 . The extract was washed with water, 5% sodium carbonate and water. The product composition was analysed using HPLC, FTIR and NMR.

For the continuous flow experiments, the schematic representation of the two step nitration of N,N'-dimethyl-urea is shown in Fig. 1. One single step consisted of a PTFE T-mixing element and a downstream PTFE capillary with an internal diameter of 0.1 mm as the reactor. The length of the capillary reactor can be easily adjusted to the needed residence time. Syringe pumps were used to avoid any pulsation and thus to ensure constant stoichiometric conditions. The outlet from the first step was mixed with the third inlet of a solution of acetic anhydride in acetic acid in 2 fold excess to the N,N'-dimethyl-urea. The outlet stream from the second step was quenched directly by flowing into stirred ice-water. As mentioned previously, the samples collected at the outlet were analysed using HPLC.

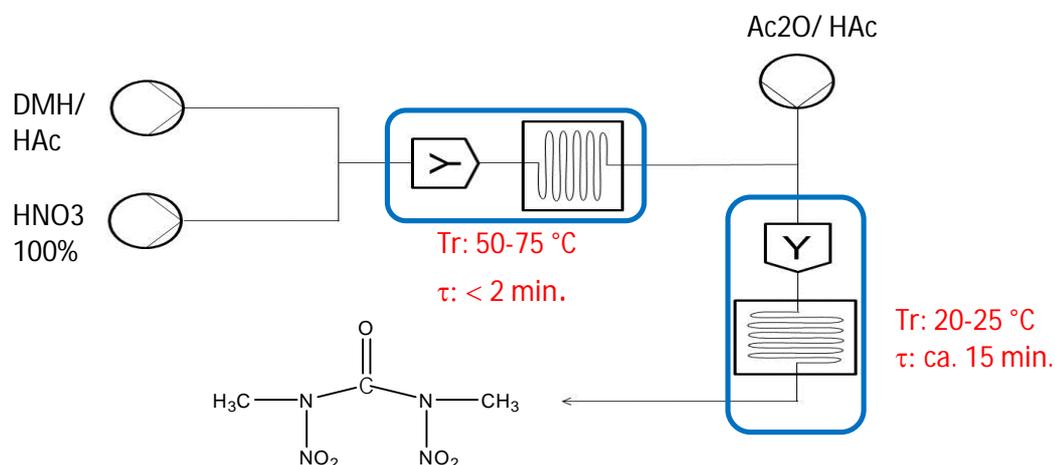


Fig. 1: Schematic representation of the two step nitration of N,N'-diemthyl-urea (DMH) (Ac_2O : Acetic anhydride, HAc: Acetic acid)

Exemplary results

For the batch experiments, the reaction was carried out in a reaction calorimeter. Due to its ability to provide reaction rate data directly, and its in-situ nature, reaction calorimetry has become one of the most powerful tools for providing kinetic data and valuable insights into the reaction.

The heat flow profile obtained from the RC-1 experiment for the in-situ generation of acetyl nitrate as well as the nitration reaction is shown in Fig. 1. Both reactions occurred quite rapidly; therefore the generation of the acetyl nitrate as well as the nitration reaction can be regarded as a feed-controlled reaction system. Even with the shortest dosing-time it was not feasible to realize a kinetically controlled reaction regime in the batch mode. The reaction rate is determined by the feed-rate of the salpetric acid and of the urea respectively.

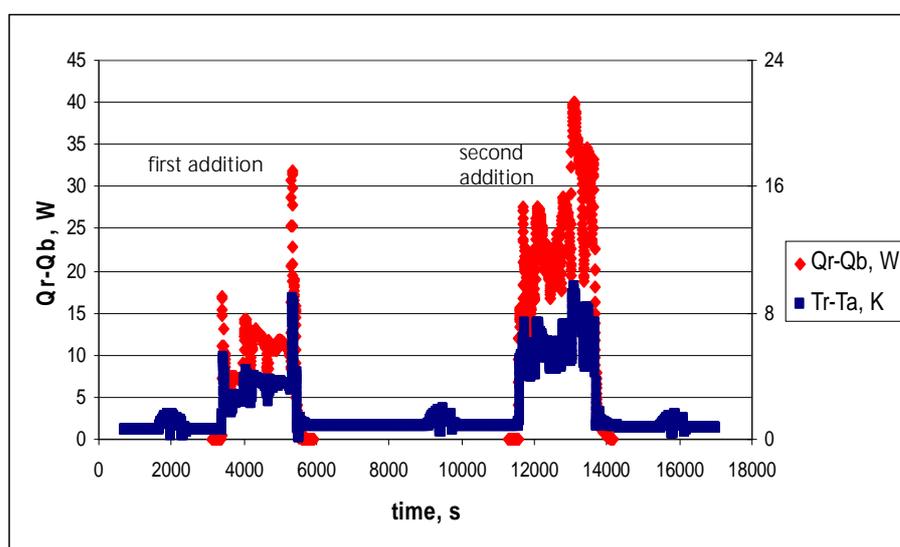


Figure 2: Heat flow profile for the in-situ generation of acetyl nitrate (first addition) as well as the nitration reaction of N,N'-dimethyl-urea (second addition). First addition: 100% salpetric acid was added to a mixture of acetic anhydride and acetic acid. Second addition: N,N'-dimethyl-urea was added to the $\text{Ac}_2\text{O}/\text{HNO}_3/\text{HAc}$ mixture at 15°C.

Further experiments were carried out in continuous mode. The schematic representation of the two step nitration of N,N'-dimethyl-urea (DMH) is shown in Fig. 1. To ensure also isothermal conditions at higher flow-rates, a two-step configuration was developed to spread the released reaction heat over two reaction steps. Due to the in-situ generation of the acetyl nitrate in the second step, the related concentration of acetyl nitrate is low in the reaction mixture. Therefore the hazardous potential of the acetyl nitrate is reduced to a minimum. The reaction proceeded smoothly with precise control on the reactor system to form the desired N,N'-dimethyl- N,N'-dinitro-urea. Yields up to 78 % could be achieved for N,N'-dimethyl- N,N'-dinitro-urea. Appropriate conditions were found to be 2,5 min residence time in the first step at 65°C and 10 min in the second step at 25°C. In comparison with mixed acid as nitrating agent mono nitrated products

could not be found. The HPLC- and $^1\text{H-NMR}$ analysis of the isolated product clearly indicate that only the *N,N'*-dimethyl- *N,N'*-dinitro-urea is formed during the nitration reaction (Fig. 3 and Fig. 4).

Therefore continuous flow reaction systems turned out to be a suitable tool for the safe and highly selective synthesis of *N,N'*-dimethyl- *N,N'*-dinitro-urea using acetyl nitrate as nitrating agent.

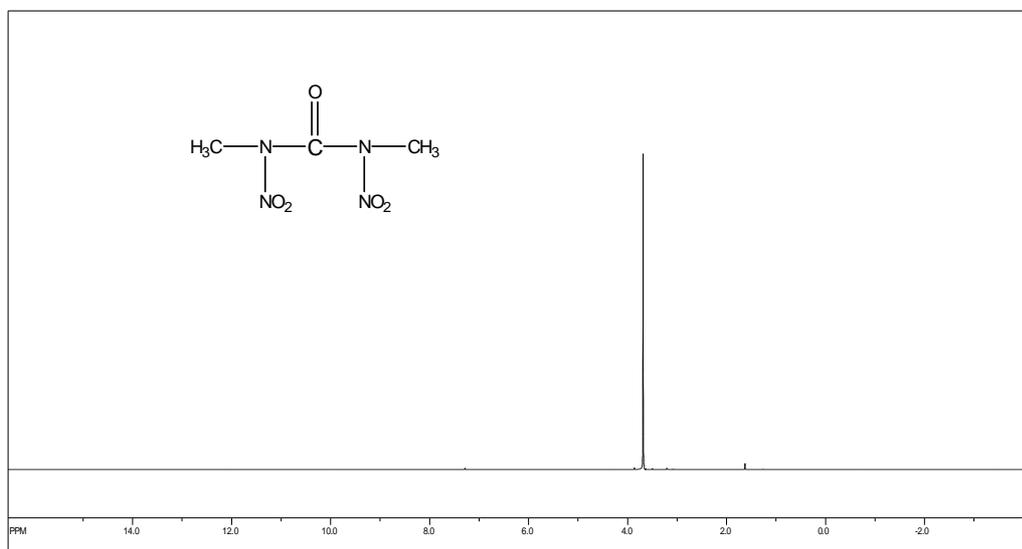


Fig. 3: $^1\text{H-NMR}$ spectrum of *N,N'*-dimethyl- *N,N'*-dinitro-urea

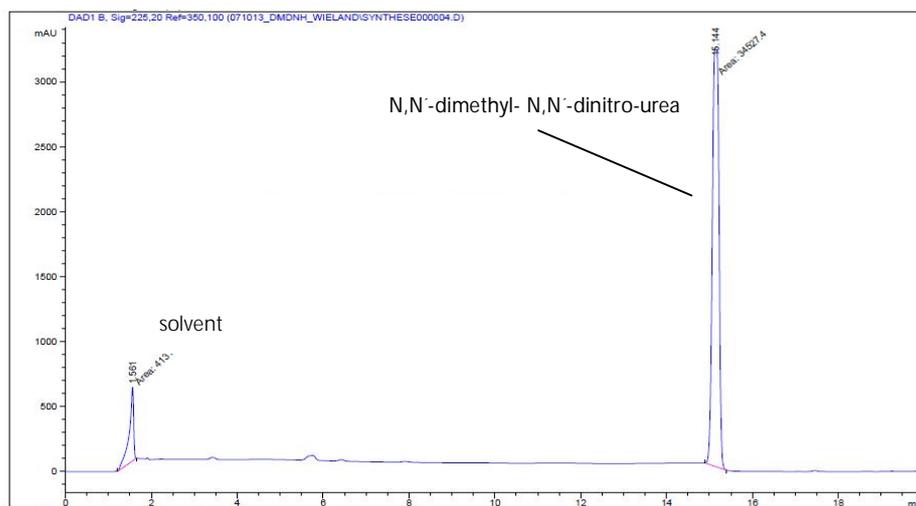


Fig. 4: HPLC chromatogram of *N,N'*-dimethyl- *N,N'*-dinitro-urea

Summary

As a result, the developed two step continuous flow reaction system are especially predestined for the safe and highly selective synthesis of N,N'-dimethyl- N,N'-dinitro-urea using acetyl nitrate as nitrating agent. The flow experiment provided only the dinitrated product, in contrast to the less selectivity by using mixed acid as nitrating agent.

Nitrations with acetyl nitrate in continuous flow provide a safe alternative to running dangerous exothermic reactions in batch and offers increased process safety and improvements in product selectivity as well as significant time savings, especially in the screening of reaction parameters to find the optimal conditions. The refined conditions can then be directly translated to the production of larger amounts by increasing the flow rate, using multiple reactors in parallel, and/or prolonging the running time of the system.

Continuous flow technology can therefore be regarded as a key technology for highly selective nitrations using acetyl nitrate as nitrating agent. Moreover one of the great benefits of using continuous flow technology, besides efficient mixing and increased reactor control, is the increased run-to-run and reactor-to-reactor reproducibility. This is a major concern especially in producing energetic materials.

Literature

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