

Synthesis of 5-Nitro-1,2,4-Triazol-3-One Via: Conventional Heating, Microwave and Ultrasonication

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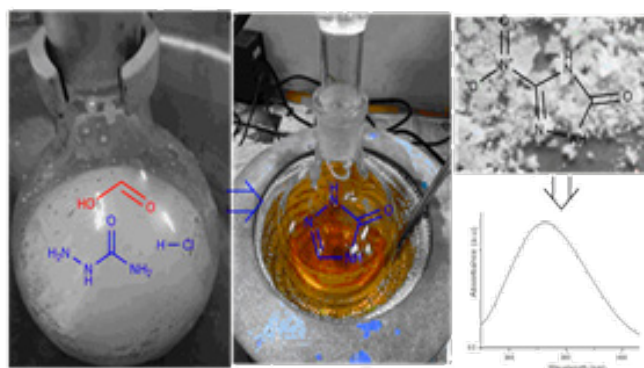
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Abstract

In this laboratory experiment 2,4-dihydro-3H-1,2,5-Triazol-3-one (TO) was synthesized using mixture of semicarbazide hydrochloride (SC.HCl) and formic acid in 1:3 mole ratio. TO was further nitrated using 70% nitric acid (HNO₃) to produce 2,4-dihydro-3H-5-nitro-1,2,5-triazol-3-one (NTO). For the nitration reaction three techniques were employed: conventional heating, microwave assisted and ultrasound assisted reaction. It was found that the extent of gases generation during the reaction was reduced when microwave and ultrasound was employed as compared to the conventional heating method. The time taken for the completion of the reaction was only 15 min when microwave was used.

Graphical Abstract



Keywords: Graduate Education, Green Chemistry, UV-Vis Spectroscopy, Thin Layer Chromatography, Synthesis, Organic Chemistry

Introduction

Most of the students are familiar with the concept of electrophilic substitution reactions where one electrophile (electron deficient species) is attacked by the nucleophilic site (electron rich species) of the reactant, resulting in the substitution of H⁺ electrophile by another electrophile (nitronium ion) NO₂⁺ ion [1]. Ultrasound minimizes production of waste and increases selectivity towards spe-

cific product. Hence, it is an environment friendly technique [2]. Ultrasound has been applied to wide range of reactions including mechanical and dispersive effects on solids, free radical generation and promotion of electron transfer [3]. When ultrasound is applied to a liquid medium, cavitation occurs: a phenomenon where bubbles form and collapse resulting into a release of energy which induces chemical reactions [4].

Microwave assisted synthesis is based on the fact that chemical species absorb electromagnetic radiation into heat and chemical reaction takes place. In recent times several syntheses have been carried out using microwave reactor such as synthesis of polymers, ionic liquids, nano materials, clays, organic compounds as substitution to the conventional method [5-9]. In microwave reactor, the reaction time required for the completion of a chemical reaction is less as compare to conventional heating [10]. Different routes have been suggested for the preparation of TO e.g., refluxing semicarbazide hydrochloride or semicarbazide free base or acetone semicarbazone with formic acid, decarboxylation of 1,2,4-triazol-3-one carboxylic acid but most efficient way is to synthesize it using semicarbazide hydrochloride and formic acid under reflux conditions. Nitrating systems such as fuming nitric acid, 70 % nitric acid, mixture of nitric acid and sulfuric acid, metal nitrate and cyclodextrin nitrate ester with sulfuric acid has been used to achieve the nitration of TO under wide range of temperature conditions (45-70 °C) to obtain NTO with a yield ranging from 43.4 % to 88 % [11-14].

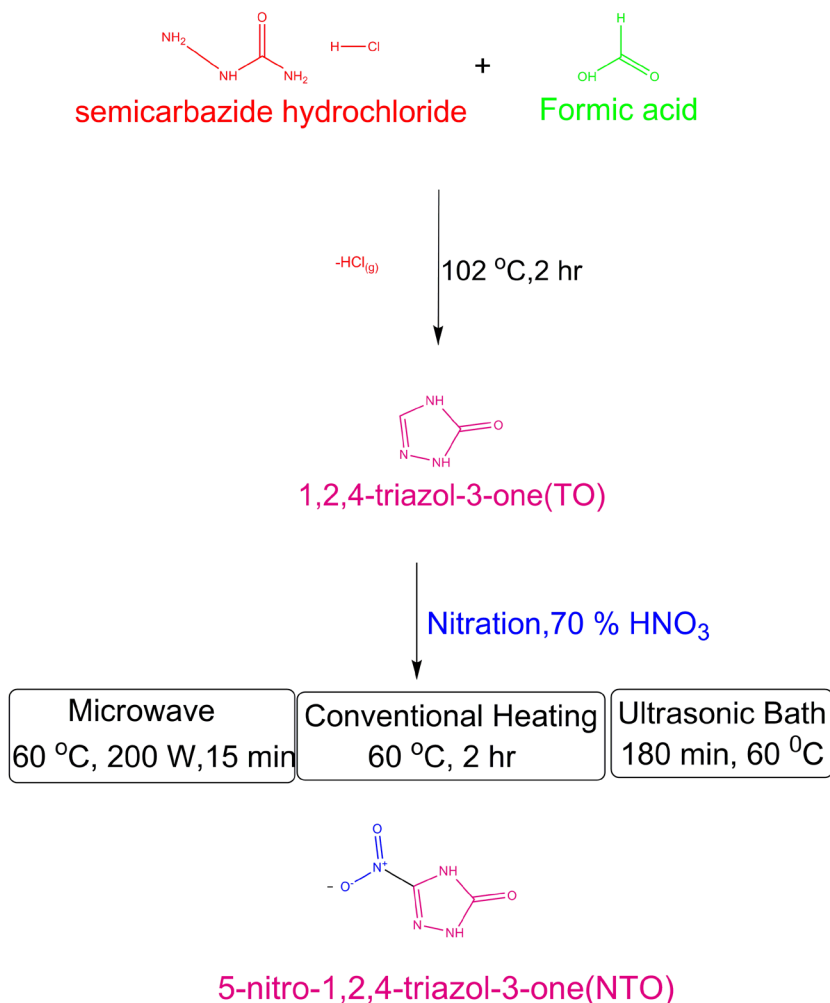
This paper mainly focuses on how the students can learn greener way to synthesize NTO. The synthesis is of two steps and as distil-

lation is also required in the first step it can take two days to synthesize NTO from semicarbazide hydrochloride. Using NMR and IR is not feasible as not all the student have the facility of these instruments and hence, in this paper simple techniques such as silica gel thin layered chromatography (TLC) and UV-VIS spectroscopy is used to confirm the formation of the product. In addition to that NTO is white solid but imparts yellow aqueous solution and is also acidic in nature while TO does not have such properties. This way students can learn how replacing only one group from the molecules results into large difference in the characteristics.

Experiment Overview

In this experiment synthesis of NTO was carried out in two steps. First step involves synthesis of TO by refluxing semicarbazide hydrochloride and formic acid in 1:3 mole ratio. In the second step, produced TO after re-crystallization was nitrated using 70 % analytical grade nitric acid using conventional heating, microwave radiation and ultrasonic bath. The reaction progress was determined by thin layered chromatography using silica gel plates. UV-visible spectroscopy was used to confirm the formation of the product. The reaction Scheme is presented in the Scheme 1.

Scheme 1: Reaction Scheme for The Synthesis Of NTO



Experiment Procedure

Step 1: Synthesis of 1,2,4-Triazol-3-one (TO)

25 mL formic acid (0.6626 mol) was poured into one necked round bottom flask (RBF) and was stirred via a magnetic stir bar and plate. 25 g semicarbazide hydrochloride (0.2242 mol) was slowly added to the formic acid with continuous stirring. After the complete addition of semicarbazide hydrochloride, the solution becomes slurry type, allow it to stir for some time. The mixture was then refluxed at 102 °C. Under this condition hydrochloric acid from is released in the form of gas leaving the semicarbazide free base. Reaction between semicarbazide free base and formic acid produces semicarbazone which upon further heating produces TO. The excess formic acid from the reaction mixture is re-collected by distillation in order to avoid solvent waste. A white solid mass of TO was obtained. To this 75 mL of double distilled water is added and again it was distilled to re-collect the water. The Synthesized TO was filtered, dried in oven at 60 °C for 3hrs and re-crystallized using double distilled water. Yield: 68 % (12.97 g, 0.1525 mol) TO was obtained with melting point (232 0C, reported 234 oC).

Step 2: Nitration of TO to produce NTO

In a one necked round bottom flask, 6 mL, 70 % nitric acid was cooled below 5 °C under stirring condition. To this nitric acid 1 g, 1,2,4-triazol-3-one (TO) was slowly added maintaining the temperature of the mixture below 5 °C. Using the similar method total 3 reaction mixtures was prepared. These reaction mixtures were used further for the nitration using conventional heating, Microwave assisted and ultrasound assisted method. The progress of the reaction was monitored using silica gel TLC employing Ethyl acetate:n-Hexane in 8:2 volume ratios as a mobile phase. The TO spot did not move but the spot corresponding to that of NTO moved far (Rf=0.8) with the mobile phase because of its polarity as a result

of of the presence of the nitrate group. During the nitration brown fumes of nitrogen dioxide were released and solution turned brownish. The mechanism of the reaction is depicted in Scheme 2.

Nitration Using Conventional Heating

In around bottom flask containing the reaction mixture was heated on a water bath at 60-65 oC. This temperature range was found to be suitable for the nitration of TO as the higher temperature results in the decomposition of the product. After 90 min white solid formation starts in the mixture and reaction was completed in 120 min. The reaction mixture was poured onto ice. The precipitates of NTO were filtered and washed with chilled water to remove excess nitric acid. After drying, NTO was re-crystallized using absolute alcohol. Yield: 72 % (1.10 g) of NTO was obtained.

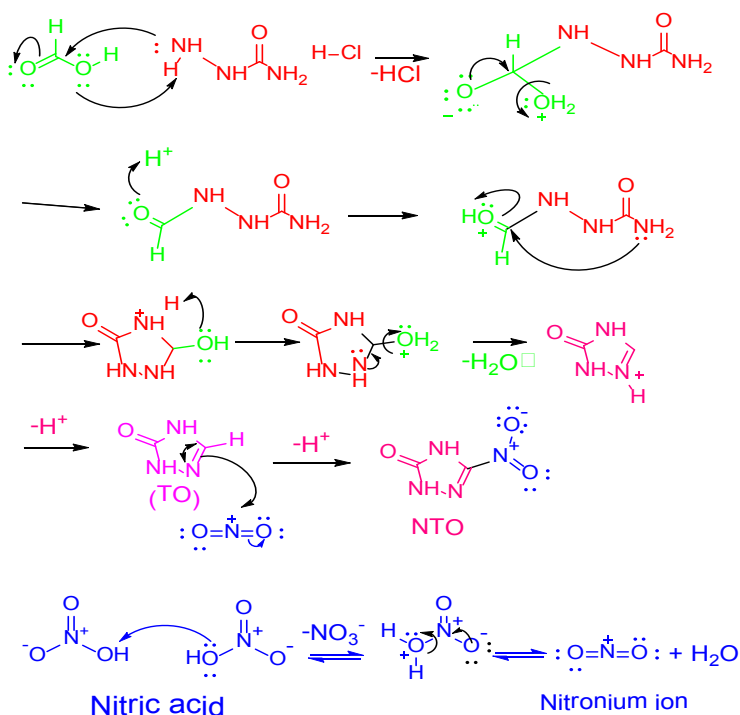
Nitration Microwave Radiation

The content was transferred into a 3 necked flask. Microwave reactor (Uwave-1000; serial no.: UW162) assembly was set up. The reaction mixture was heated at 60 °C, 200 W for 15 min. Precipitation formation started after 8 min. After the completion of the reaction, the mixture was poured onto ice, Filtered, dried and NTO was re-crystallized by absolute alcohol. The yield obtained was 68.5 % (1.05 g NTO).

Nitration Using Ultrasound Radiation

The reaction mixture was irradiated with ultrasound using ultrasonic bath (Life care, serial no.:2K1802005) at 60 °C. The reaction was slow and took 180 min to complete the reaction. After the completion of the reaction, the mixture was poured onto ice, Filtered, dried and NTO was re-crystallized by absolute alcohol. 65 % (1 g) yield of NTO was obtained.

Scheme 2: Mechanism of The Reaction



Result and Discussions

During refluxing of formic acid and semicarbazide hydrochloride, hydrochloride gas was released and hence one can assume that all the semicarbazide hydrochloride has been reacted once the gas is not released anymore. The obtained solid after re-crystallization was 232 °C which matches with that of TO from literature that is 234 °C. NTO is white crystalline solid which did not melt but instead decomposes at around 273 °C. TLC plate was used to confirm the formation of NTO. As depicted in Figure 1, as NTO possess nitro group, it is more polar in nature as compare to TO and hence travel far along with the solvent ($R_f=0.8$). In the starting of the reaction only one spot corresponding to that of TO (1) was present as reaction proceeds 2 spots corresponding to that of TO and brown spot of NTO were visible (2). Once the reaction is completed Spot corresponding to that of TO disappear indicating that TO has been used up.

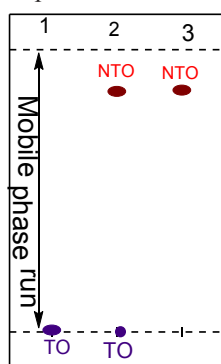


Figure 1: Tlc Run Using Ethylacetate:n-hexane in 8:2 Volume Ratio (1) Before Reaction (2) During The Reaction (3) After The Reaction

UV-Visible spectroscopy (Shimadzu UV-1800) was used to verify the formation of NTO. As depicted in Figure 2, aqueous solution of TO did not absorb between 800-260 nm and hence it does not interfere with the spectra of NTO. NTO because of the nitro group absorbs between 250-500 nm and aqueous solution of NTO exhibits yellow color. As NTO is acidic in nature, its UV-VIS spectra are pH dependent. As pH of the solution is decreased it absorbs at lower wavelength. The aqueous solution of 0.0001 M NTO exhibited similar spectra for NTO synthesized using Conventional, Microwave and ultrasound method as depicted in Figure 2.

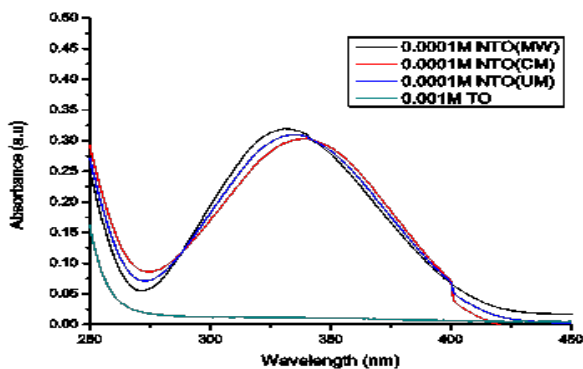


Figure 2: UV-VIS spectra of 0.0001M NTO and 0.001M TO in

Aqueous Solution: UM=Ultrasound Method, CM=Conventional Method and, MW=Microwave Method.

In the nitration, 70 % HNO_3 is used and the nitronium ion (NO_2^+) is generated as depicted in Scheme 2. This nitronium ion being an electrophile substitutes 'H' from TO at C-5 to produce NTO. NTO is acidic in nature, its assay could be carried using acid-base titration. In this way students can utilize basic chemistry knowledge to approximate the purity of NTO produced. Further this product's structure can be confirmed using IR and NMR spectroscopy.

As NTO is water soluble, during the washing of the precipitates with chilled water precipitates of NTO are also washed away with water and hence, overall yield is decreased after washing.

Hazards

Ethyl acetate and n-hexane used as a mobile phase for TLC are volatile flammable liquids and they should be avoided contact with the flame source. Silica gel causes respiratory tract irritation. Formic acid and hydrogen chloride gas possess acute oral toxicity, causes skin corrosion and vapors are harmful as well and hence the reaction must be done in a fume hoods with proper mask. Semicarbazide hydrochloride, TO and NTO possess acute toxicity if swallowed, caused skin and eye irritation and hence, contact with these substances should be avoided. Longer exposure should be avoided. As Semicarbazide hydrochloride and NTO decomposes at higher temperature, Heating at higher temperature must be avoided and contact with flame or friction or spark should also be avoided. Proper care must be need such as wearing lab gloves, lab apron, mask and lab goggles is a must.

Conclusions

Microwave is more suitable technique to carry out nitration of TO as it requires only short for the completion of the reaction. On the other hand, ultrasound assisted using water bath as it was carried out at lower temperature requires most time. In the conventional heating method, the product may decompose because of overheating and hence, microwave assisted synthesis is preferable. For the students it is beneficial to carry out reaction using microwave as batches of the reaction can be done within short time limit. Solvents used are re-collected after the reaction which is one step towards green chemistry that the student can learn. As UV-visible spectroscopy and TLC techniques are easily available to the students confirming the formation of the product employing these techniques quite feasible. Here are the main points that can be concluded.

Table 1: Comparison of Microwave, Ultrasonic and Conventional Heating Method for The Synthesis of NTO at 60 °C

Method	Time (min)	Yield of NTO (%)
Conventional heating	120	72
Microwave Heating	15	68.5
Ultrasonic	180	65

- Nitration using microwave irradiation is more feasible be-

cause of short time for the reaction completion.

- TLC and UV-Visible spectroscopy easily available methods to confirm formation of the new product.
- Solvent re-collected after the reaction by distillation can be utilized again and hence, waste is avoided.

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