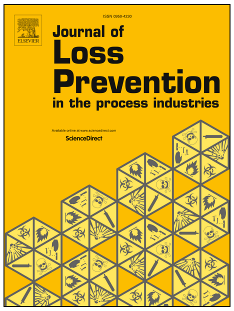

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Reactive Chemical Hazards of Diazonium Salts

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Abstract

Many diazonium salts are thermally unstable and sensitive to friction and shock. Most diazonium salts are known for their violent decomposition hazard in the solid state. There are many industrial and laboratory incidents caused by this group of chemicals. For safety purposes, the hazards related to the preparation and the handling of diazonium salts are discussed. Twelve cardinal rules are provided:

1. Use only a stoichiometric amount of sodium nitrite when generating diazonium salts, avoiding excess sodium nitrite.
2. Check for the excess of nitrous acid by starch-potassium iodide papers and neutralize it.
3. Minimize the presence of nitrous acid by combining amine and acid first, then subsequently adding the sodium nitrite.
4. Keep the temperature below 5°C.
5. Always vent the gases generated.
6. Determine the thermal stability of diazonium compounds in your system.
7. Understand the explosive properties of diazonium salts. If unknown, always assume they are explosive.
8. Never allow the undesired precipitation of diazonium salts out of solution.
9. Analyze the residual diazo compounds in the final product, especially for new process conditions.
10. Quench the remaining diazonium salts before any further treatments.
11. Isolate no more than 0.75 mmol of explosive diazonium salts at one time; also consider the addition of an inert material to stabilize the diazonium salts.
12. Use a plastic spatula when handling the solid. The dried powder should not be “scratched” with a metal spatula or ground finely.

An example of a testing strategy and data interpretation is provided for a process which has multiple steps and two diazonium compounds. Differential Scanning Calorimetry (DSC) and Heat of Mixing calorimetry (HOM) successfully serve as efficient tests to screen thermal stability and gas generation, identifying the candidates for advanced tests.

Keywords: Diazonium salts, Safety guidance, Differential scanning calorimetry (DSC), Reaction calorimetry

1. Introduction

Diazonium salts ($R\text{-}N^{+}\equiv N\cdot X^{-}$) are important intermediates for the preparation of halides and azo compounds. They are commonly used in the Sandmeyer and Sandmeyer-like reactions by reacting with other pseudohalide-type electrophiles (Figure 1). However, diazonium salts are known for violent decomposition hazards at temperatures slightly higher than ambient, so they normally are made in situ and used immediately in further reactions(Fierz, 1952). Some diazonium salts are so unstable, even at ambient conditions, that they are only metastable and are able to explode unpredictably or spontaneously with shock, impact, friction, heat, vibration, or static discharge. There have been multiple historical incidents reported which are related to diazonium salts(Urben, 1999). Ullrich (Ullrich, 1993) mentioned an explosion triggered by mechanically cleaning a valve with unexpected precipitated and dried diazonium salts. A major accident report system (MARS) incident (UKCRHF) described an explosion of about 2 kg of “diazonium solid particulate” upon falling to the ground during inspection of a clarification press, which caused one fatality, six injuries and $3 million in damages. The UK Chemical Reaction Hazards Forum (UKCRHF) recorded a decomposition explosion of wetted 2,4,6-tribromophenyl diazonium bromide salt triggered by friction or impact. Another fatal accident caused by the detonation of supersaturated diazonium chloride salt was reported by UKCRHF as well. There was a reported detonation of benzenediazonium-2-carboxylate hydrochloride when the student touched the material with a metal spatula(Kittsley, 1971). Recently, one of Dow’s R&D labs experienced an explosion due to 8 gram of a dry product made from a diazonium chloride intermediate(Dow, 2014).

To reduce the occurrence of such incidents, a good awareness of the hazards associated with diazonium salts is necessary and appropriate safety rules should be followed.

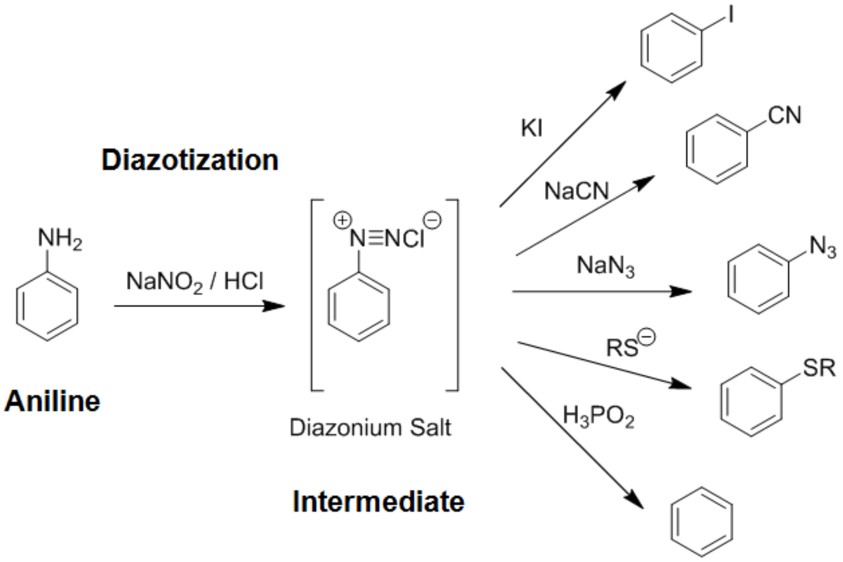


Figure 1, Sandmeyer and Sandmeyer-like reaction examples

2. Hazards during the preparation of diazonium salts

The most common method to make diazonium salts is treatment of primary amines such as aniline with an aqueous solution of nitrous acid (HNO_2) prepared from sodium nitrite ($NaNO_2$) and a mineral acid (e.g. HCl, H_2SO_4). Normally, a considerably greater amount of mineral acid than the two equivalents necessary on the basis of the stoichiometry of diazotization should be used. This helps the formation of the nitrosating agent and then accelerates the formation of diazonium products. However, a stoichiometric amount of sodium nitrite often is used to prevent an excess of nitrous acid, which exerts a very unfavorable effect on the stability of diazonium salts and potentially interferes with further transformations. Due to the potential instability of diazonium salts, it is important to use the amount of nitrite required for the reaction as accurately as possible. Some researchers recommended testing for excess of nitrous acid by starch-potassium iodide papers and neutralizing it by adding urea, sulfamic acid, or hydrazine at the end of the diazotization reaction. Even in the process of making diazonium salts, the presence of nitrous acid should be minimized. A high concentration of nitrous acid is subject to a rapid decomposition releasing toxic gases of NO_x. Under certain conditions, this gas generation is much faster than that from the decomposition of diazonium salts, which results in a large venting of gas and low yield of the desired products. Therefore, combining the primary amine and mineral acid, and subsequently adding sodium nitrite, is more practical and widely used.

During the preparation of diazonium salts, the reaction temperature is a key safety parameter. In aqueous solutions, most diazonium salts are unstable at temperatures above 5°C, with the diazo functional group tending to be lost as nitrogen gas. To retain the diazo group for further steps, low temperatures need to be maintained as long as the diazonium salts are present in the system. On the other hand, the formation of the diazo group from a primary amine and nitrous acid is an exothermic reaction, with a reaction enthalpy of between -65 kJ/mol and -150 kJ/mol, depending on the mineral acid used (Grewer, 1999). Meanwhile, most aqueous diazotization reactions are fast reactions at -10 to 5°C. For example, the reaction rates of the diazotization reaction in aqueous hydrochloric and hydrobromic acids are close to the rate of diffusion in the solution. In order to control the reaction temperature, either sufficient cooling capacity is required to quickly remove the heat of reaction, or the feed rate controlled to limit the heat generation rate. Direct pre-add of ice into the reactor is an effective heat removal method and widely used in the dye industry.

In semi-batch process mode utilizing simultaneous temperature and feed control, extra caution is needed. For example, Partington (Partington, 2002) investigated a 500-gallon reactor failure with a manual temperature control system. The vessel failure was caused by the reactant accumulation due to over cooling and fast heat release from those reactants during the following heating step, triggering the decomposition of the diazonium salt. Gas generation from decomposition of diazonium salt is another safety consideration in the preparation of diazonium salts, especially when high nitrous acid is present. A gas venting system is suggested to prevent the pressure buildup in the reactor, as well as safety relief devices to protect the equipment.

In addition, it was reported that several diazonium salts were produced by organic nitrites (typically pentyl nitrite) in organic solvents such as acetic acid, ethanol, or dioxane(Zollinger, 1996). The diazonium salts were either separated from the solution by vacuum distillation or precipitated by addition of a nonpolar solvent. Such an isolation operation is not recommended before understanding the stability of the diazonium salts. An example of a stability study is provided in a later section.

3. Violent decomposition of diazonium salts

Although in most cases, the diazonium salts are made in situ and immediately consumed in further treatment, the violent decomposition hazard and the potential explosive property of those materials brings a significant safety concern. Diazo compounds tend to decompose at low temperature compared to other high energy function groups. As Grewer (Grewer, 1999) reported, typical ADT_{24} (temperature at which the adiabatic induction period is 24 hr) for the decomposition of diazonium salts was 80°C, while ADT_{24} for chemicals with nitro groups was between 190°C to 280°C (depending on the other substituents). They also gave a reaction enthalpy of -160 kJ/mol and -180 kJ/mol associated with the decomposition of the diazo functional group. Other researchers reported that bases, transition metal impurities (e.g. Cu, Sn), excess of nitrous acid and direct sunlight significantly accelerated the decomposition behavior and greatly lowered the detected onset temperature. For example, the detected onset temperature of benzenediazonium chloride in one reaction mixture was determined to be 35°C by DSC in our lab, which is significantly lower than the literature data, 80°C. The thermal stability characterization data from the literature may not necessarily apply across all experimental conditions. Therefore, thermal stability studies of diazonium compounds should be considered for each new process.

4. Explosion hazard of diazonium salts

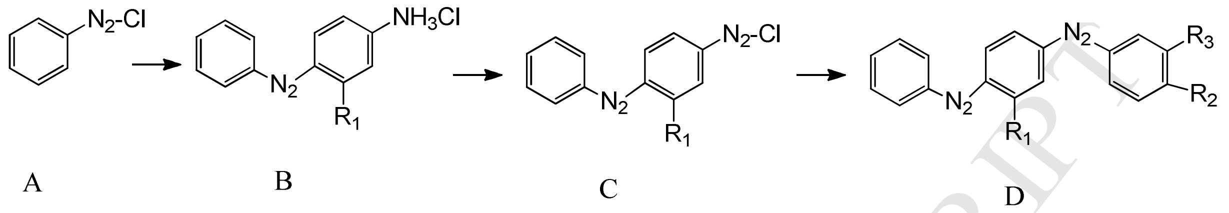
Besides the violent decomposition hazard, many diazonium salts tend to be explosive in the solid state. Of those, chromates, nitrates, picrates, sulfides, triiodides, xanthates, and particularly perchlorates are highly explosive and sensitive to friction, shock, heat and radiation. Chloride and bromide salts also exhibit a highly explosive potential. Ullrich (Ullrich, 1993) gave a list of the selected explosive diazonium salts. From a safety standpoint, diazonium salts never should be allowed to precipitate out of the solution during the reaction before a sample is fully characterized by reactive chemical tests with proper sample preparations (drying period and temperature). There are several industrial incidents caused by the unintentional precipitation of diazonium salts, which caused explosions, fatalities, injuries and property damage. To prevent this, it requires understanding of the solubility limit of the diazonium salts in the solution and the safety margin of the reaction operations. The UKCRHF suggested a method to determine the supersaturation of the diazonium salts. An analysis (such as IR examination, Nujol IR for solids; typical 2200~2300cm^{-1}) of the post-reaction mixture that has contained diazo compounds is also a best practice to ensure that the final product after the dediazonization is free of the diazonium salts. This is especially important to do when the process conditions are changed (e.g. a new recipe, reaction time and/or temperature). If the diazo compounds are co-precipitated with the desired product during the reaction, such analysis is even more necessary because the dediazonization reaction in further treatments will be limited by the mass transfer in the crystal phase and the coating effect of the products, increasing the possibility to have undesired residual of diazonium salts in the final product. The failure of such analysis and the lack of awareness of the presence of diazonium intermediates have caused several events in different laboratories. The remaining diazonium salts should be quenched before any further treatments, especially drying and heating. There are various methods studied to remove diazonium compounds, but unfortunately there is no universal one. Adding an aqueous solution of hypophosphorous acid (H_3PO_2), in some cases in the presence of a catalyst (e.g. 0.05~0.10% Cu^{2+}), is often suggested. For an intentional isolation of a diazonium salt, it must be considered hazardous and confined to a small scale. It is recommended that no more than 0.75 mmol of explosive diazonium salts should be handled at one time. The addition of other salts (e.g. $ZnCl_2$) to form the so-called diazonium metal double salts, or other compounds (e.g. 18-crown-6 ether), to form a crystalline complex can considerably stabilize the isolated diazonium salts. Furthermore, such diazonium salts should never be heated above 40°C and the dried powder should not be “scratched” with a metal spatula or ground finely(Zollinger, 1996).

For the disposal of waste containing diazonium salts, the diazo compounds should be removed first from the solution by adding quenching agents, such as H_3PO_2 solution. If the storage of such waste is necessary, always consider venting of the gas generated from the decomposition of diazonium salts.

5. An example of the testing strategy and data interpretation

The following compounds (A to D) are used in the dye industry. Starting from aniline, two diazonium intermediates (A and C) are made in situ and subsequently converted to azo compounds (B and D) by coupling reactions. Since the azo group is another high energy group(Koxsk, 2008), thermal stability tests were conducted for all these compounds to understand the safety margin of the process. As suggested by Frurip(Frurip D. B., 2004), screening calorimeters and simple reaction calorimeters should be applied first to identify candidates for further advanced tests. Differential Scanning Calorimetry (DSC) was used to study the thermal stability of potential energetic materials (from A to D), while Heat of

Mixing calorimetry (HOM, a reaction calorimetry, also called “2-drop” mixing calorimetry) was used to determine the reaction heat and gas generation of the desired reactions. Detailed information about those instruments and the standard test methods used in The Dow Chemical Company can be found in other references(Frurip D. a., 2007)(Whiting, 1988)(Frurip D. , 1995).



These four compounds were handled either in aqueous solution or organic solvents (xylene and excess aniline). The solvents and other chemicals in these samples are all inert in the testing temperature range, so any exothermic behavior should be caused by these high energy compounds. DSC results for different samples are presented in Figure 2. Among those samples in aqueous solution or in organic solvent, compound A is the one with the highest risk regarding thermal decomposition, because it has the lowest detected onset temperature. Since this detected onset temperature is just 40 degrees away from the process temperature (0°C), time to max rate may be unacceptably short. There is a creditable risk that this undesired reaction may occur when there is a slight deviation from normal processing conditions (Hofelich, 2002). The amount of ice to maintain cooling of the vessel should be pre-defined based on the heat release from the reaction, with sufficient ice present to maintain the temperature of the reaction mixture during the preparation step and until the next step where A is completely consumed. Based on the DSC onset temperature and the activation energy of -114 kJ/mol from the literature (Crossley, 1940), the time to max rate (TMR) in the adiabatic condition (Hofelich, 2002) was calculated to be 37 hrs. However, during an actual process upset with a cooling failure and no additional ice, additional heat input from side chemistry will provide additional heat, leading to a shorter TMR. Either a very conservative correction factor should be applied to ensure more than enough cooling capability is present, or more advanced modeling or more advanced testing is needed to better simulate the heat removal requirements for the reactor.

In order to investigate the solvent effect (water in this sample) on the detected onset temperature, another sample of A was tested by DSC after being dried in situ in the DSC ampoule by purging with nitrogen gas. This nitrogen-dried sample showed the same detected onset temperature (within the uncertainty range) as the first exothermic event, but with an additional exothermic peak around 200°C. Hence, there was no observed solvent effect on the first exotherm. The second exotherm does not appear in the aqueous sample, either due to the endotherm behavior of the slow vaporization of water into the headspace or due to water dilution which lowers the occurrence of forming azo compounds (similar to B). Even for this nitrogen-dried sample, the energy of the first exotherm is still much lower than the literature data (-1.5 kJ/g for pure A) (Urben, 1999). This is reasonable because the testing sample contained other salts (e.g. NaCl as the other product of the desired reaction, Aniline Hydrochloride as the intermediate) and was not purified. In spite of that, Yoshida’s correlation (Yoshida, 1987) with the onset and energy of the first exotherm predicts that this solid is a shock sensitive solid. This is consistent with the literature (Ullrich, 1993) stating that compound A is an explosive chemical, with an impact sensitivity of only 3 J. Overall, the big safety concern in this process is the explosion from the precipitation of compound A, especially when dried. Therefore, maintaining a completely solubilized reaction mixture throughout the process is critical for maintaining safe operating conditions.

By comparing all DSC data for compounds A-D (Figure 2), it is shown that the detected onset temperature of the first exotherm increases with the molecular weight. This indicates that the other atoms present help to thermally stabilize the high energy functional groups. From the comparison, it is concluded that the second exotherm in the nitrogen-dried sample A is attributed to a similar decomposition pathway observed in compound B, which is formed by the coupling reaction between two molecules of A. This provides tangible evidence of such a side reaction occurring during the preparation step for A.

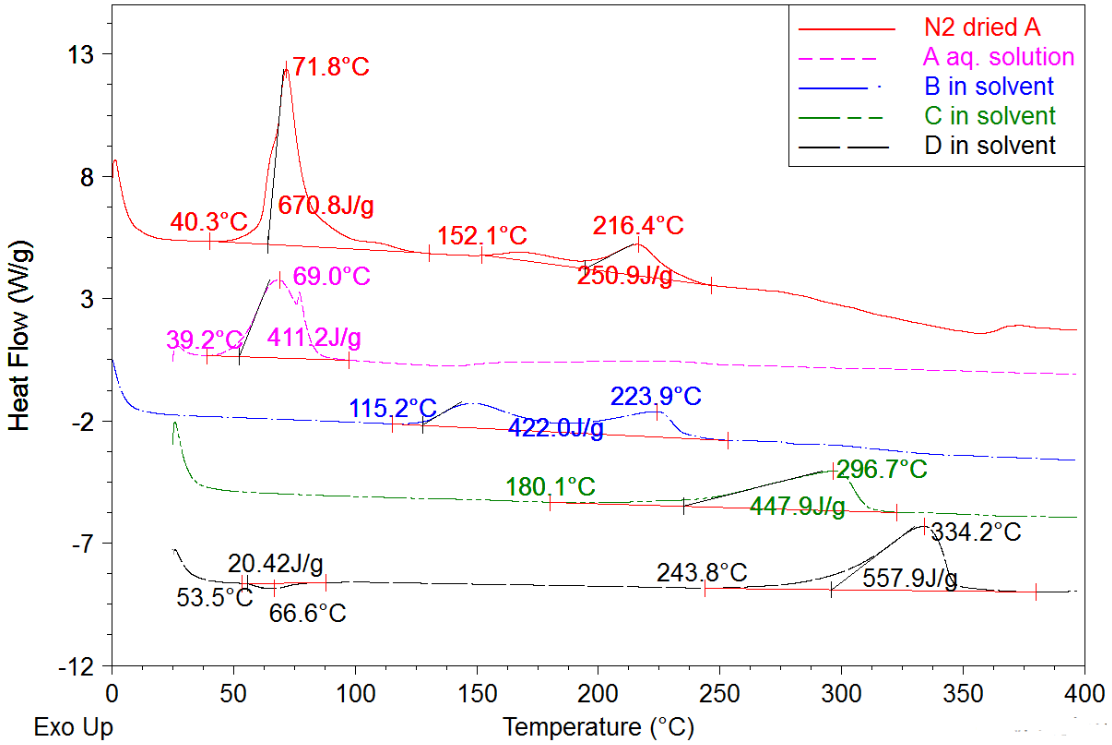


Figure 2, DSC curves for compound A to D; test condition, headspace gas: Nitrogen, temperature range: room temperature to 400°C, temperature rate: 10°C/min, test cell: glass cell

For both quality concerns and safety concerns, the occurrence of decomposition reactions represented by the DSC curves above should be minimized in a normal process. Good temperature control is needed to ensure controlled energy release (heat and gas) in the reactor system. Knowing the heat of reaction of the desired reaction is critical for controlling energy release. HOM testing is a screening method to determine those values. An example of a HOM result is shown in Figure 3. The energy release was recorded during the preparation of A with the desired recipe and normal processing conditions. These data indicate that the energy generation is -125 J/g based on the final mixture, corresponding to -110 kJ/mol of A by assuming 100% conversion to compound A. The energy based on the mass of the final mixture is preferred for scaling purposes, while the value based on moles of A is more useful for chemistry correlation. However, the assumption of 100% conversion to A is not accurate since there are side reactions occurring, as indicated by DSC. As a result, the energy measured should be correlated to the mass of the reaction mixture and the ice demand based on that number vs. assigning a heat of reaction value based on moles of substrate.   In this case, the heat flux curve indicates that the energy releases rapidly at the beginning of mixing before reaching its maximum at the end of the injection. This suggests that this reaction probably is limited by mass transfer, so an effective way to control the reaction rate would be to control the reactant feed rate.

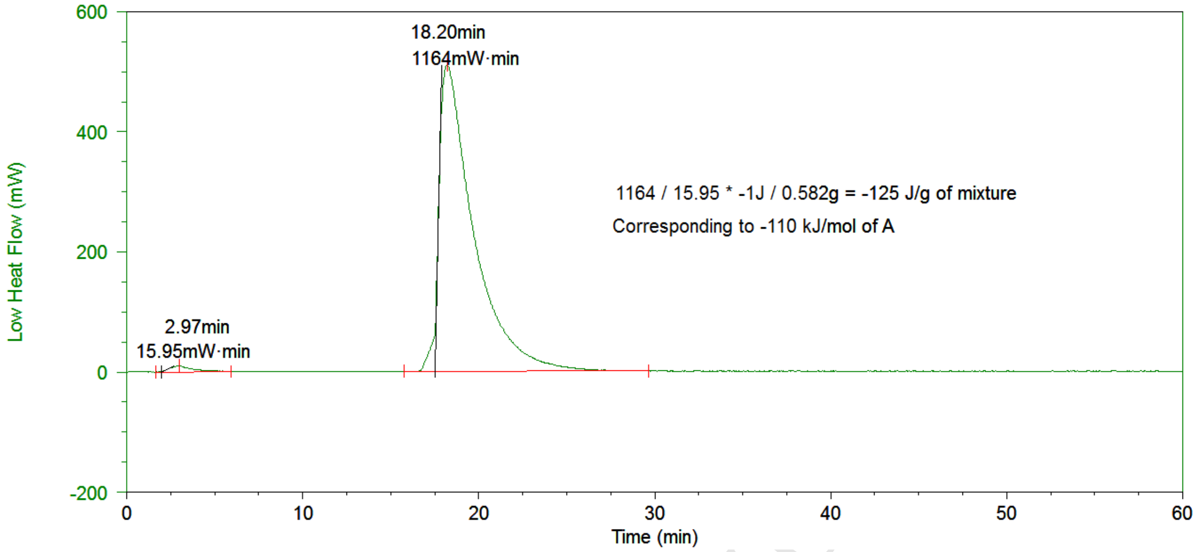


Figure 3, Heat flux curve of the HOM for the step to make compound A; test condition, headspace gas: Air, temperature: 5°C, glass cell with stirring bar

Since the failure of reactor vessels is directly caused by overpressure in most cases, the gas generation is a key factor that needs to be considered during the safety evaluation. Pressure data is used for comparison with the Maximum Allowable Working Pressure (MAWP) of the vessel and/or to evaluate the need for vent relief design. HOM data provides the information to screen the scenarios and identify the worst case for possible advanced tests. The pressure data for each step from A to C are presented in Figure 4. The gas generation rates for steps A and B are very close, while that for step C is much faster at the beginning (a small leak developed in this test). The reason for the fast rate in C is due to the extra amount of HNO_2 used in this step. Since HNO_2 exhibits a fast gaseous decomposition rate in this process, it is important to evaluate the potential for a mis-loading scenario where HNO_2 solution is solely produced in the reactor due to wrong material feed or a reversed feeding order. As shown in Figure 4, the gas generation from HNO_2 solution is much faster than the other solutions. Therefore, if there is a credible scenario where this could occur by mistake, the gas rate of this chemistry should be quantified by advance testing to ensure adequate vent relief design.

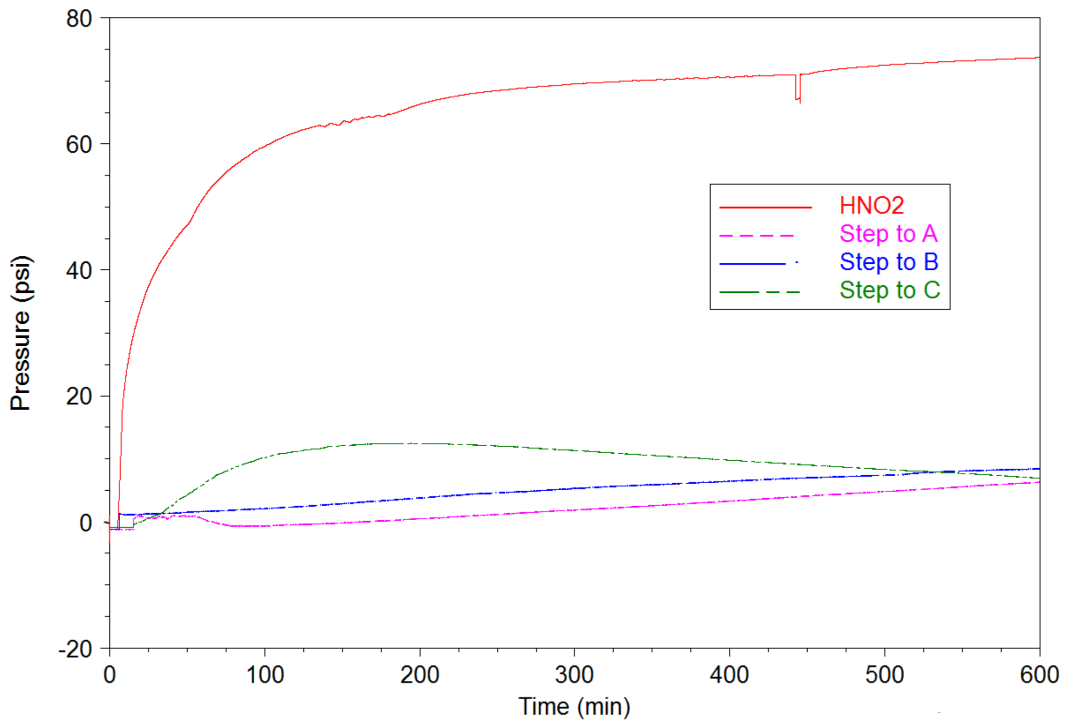


Figure 4, pressure curves of the HOM for difference steps; test condition, headspace gas: Air, temperature: 5°C, glass cell with stirring bar

In Summary, from the DSC data presented, compound A is the one with the highest safety risk. This requires good control of temperature and the reactant feed rate during the preparation process. Also, the precipitation of this compound should be avoided. The HOM tests give the expected energy release of the desired process and the potential for gas generation to ensure adequate cooling is present and to screen for the need for advanced testing for pressure relief design.

6. Summary:

For the safe handling of diazonium salts, the following cardinal rules are recommended:

1. Use only a stoichiometric amount of sodium nitrite when generating diazonium salts, avoiding excess sodium nitrite.
2. Check for the excess of nitrous acid by starch-potassium iodide papers and neutralize it;.
3. Minimize the presence of nitrous acid by combining amine and acid first, then subsequently adding the sodium nitrite.
4. Keep the temperature below 5°C.
5. Always vent the gases generated.
6. Determine the thermal stability of diazonium compounds in your system.
7. Understand the explosive properties of diazonium salts. If unknown, always assume they are explosive.
8. Never allow the undesired precipitation of diazonium salts out of solution.
9. Analyze the residual diazo compounds in the final product, especially for new process conditions.
10. Quench the remaining diazonium salts before any further treatments.

11. Isolate no more than 0.75 mmol of explosive diazonium salts at one time; also consider the addition of an inert material to stabilize the diazonium salts.
12. Use a plastic spatula when handling the solid. The dried powder should not be “scratched” with a metal spatula or ground finely.

The cardinal rules proposed in this paper were derived, in part, from a thorough review of the literature, including standard and widely used sources used by Process Safety professionals(Urben, 1999)(Zollinger, 1996). It must be noted, however, that we have little direct or extensive experience in several of these proposals and therefore we urge the reader to use appropriate caution when applying these to any chemical process.

An example of a chemical process involving diazonium intermediates and azo compounds was provided for testing strategy and data interpretation. DSC and HOM serve as efficient tests to screen the thermal stability and gas generation, while identifying the potential need for advanced tests.

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Highlights:

1, The reactive chemical hazards of diazonium salts were systematically discussed, including the preparation, handling, reaction and killing the salts.

2, Twelve cardinal rules were provided to mitigate the reactive chemical hazards of diazonium salts.

3, An example of quick experimental determination of the reactive chemical hazards of such compounds was provided.