Most industrial reactions are exothermic, and nearly every large-scale chemical process has at least one step with the potential for thermal runaway, if the conditions are right. The resulting disastrous thermal explosion can cause severe damage to the plant and the environment.

Unpredicted process conditions result from an unanticipated process failure. More often, an anticipated failure creates a condition for which the process chemistry has not been sufficiently investigated and adequate precautions have not been taken. The process, which is known to be safe within normal process conditions, then goes out of control. Many possible scenarios exist.

**Fundamental steps to risk reduction**

Regardless of the particular runaway scenario, there are four fundamental steps to risk reduction (1):

1. Identify the potential for a runaway and quantify its severity.
2. Understand how the thermal runaway is triggered and quantify its likelihood.
3. Define a basis of safety and design a control strategy.
4. Protect against the consequences of thermal runaway.

Although many plants do so, it is generally unwise to default to protective measures and neglect the preceding steps in the identify-understand-control-protect process. Protective measures tend to cover uncertainties in the assessment procedure rather than uncover chances for eliminating the risks (2).

**The role of case studies**

Many case studies in the literature detail thermal runaways that have occurred during industrial-scale chemical synthesis. Studying problems that other companies have encountered and the ways they have been analyzed and (often) solved can be educational. Case studies can be a valuable source of such information (3).

Consider, for example, a diazotization synthesis, in which an –NH₂ group connected to a phenyl ring is converted to a diazonium salt. The information in Table 1 makes it clear that there is a potential for a thermal runaway during such a reaction. The synthesis is typically
highly exothermic, and the diazonium salt may decompose to gaseous products as it is formed. Furthermore, it may become shock-sensitive upon drying (4).

Throughout this article, diazotization is used to illustrate the application of the principles of thermal risk reduction in industrial synthesis. A particularly good example of diazotization involves the synthesis of chloropyrimidines, which are important intermediates in the manufacturing of pesticides and pharmaceuticals. Table 2 presents key information about the process (5).

Small-scale screening tests

Prior to any large-scale laboratory characterization of a reaction’s thermal runaway potential, a preliminary thermal hazards screening must be performed. First, consult “Bretherick’s Handbook of Reactive Chemical Hazards” (6) to determine if the starting materials (or products) have been involved in any past incidents. Consider also the potential reactivity of the process chemicals with the equipment’s materials of construction. The reactants, intermediates and products must all be evaluated for thermal instability. Are any capable of exothermic decomposition upon heating? To what temperature must any be raised to initiate the decomposition? The experimental techniques for gathering such data are described in detail elsewhere (7).

Next, the desired synthesis reaction is carried out on a small scale in the laboratory to prepare a sample for further testing. The crude product (i.e., before neutralization, isolation, washing, etc.) is examined by differential scanning calorimetry (DSC) to determine the heat of decomposition, $\Delta H_d$ (8).

From this, the adiabatic temperature rise, $\Delta T_{ad}$, of the decomposition reaction (the temperature rise that will occur if the exothermic reaction proceeds without any heat transfer into or out of the reaction mass) is estimated (1). This is important, since plant-scale reactors undergoing thermal runaway do so under virtually adiabatic conditions.

The “onset” temperature, $T_o$, of the decomposition reaction (the lowest temperature at which the particular experimental calorimetric apparatus can detect the decomposition) is also estimated. This is important because the likelihood of a runaway depends (in part) on the size of the temperature range separating the desired synthesis and undesired decomposition reactions.

Finally, the adiabatic time-to-maximum rate, $t_{MRad}$, is estimated. This is the time required for the self-heating exothermic decomposition to reach its maximum value for the rate of heat generation under adiabatic conditions. The $t_{MRad}$ influences the choice of the intervention strategy for avoiding a thermal runaway.

Let’s look at the diazotization example. A small sample of the crude reaction product was heated in a differential scanning calorimetry (DSC) test from 25°C to 400°C at 4°C/min. The resulting DSC thermogram is shown in Figure 1. The two upward peaks indicate a decomposition reaction that occurs in two exothermic steps. Each peak is integrated to obtain the corresponding heat of reaction. The temperature at which the curve first departs upward from the horizontal indicates the onset temperature of the exotherm. A second test was conducted using an adiabatic calorimetric method (9) to ascertain if the decomposition reaction proceeds exothermically, producing between 65 and 150 kJ/mole and is usually run industrially at sub-ambient temperatures. Diazonium salts decompose exothermically, producing between 160 and 180 kJ/mole. The decomposition onset temperature is around 130°C, but can range between 20°C and 140°C, depending upon the particular diazonium salt. Many diazonium salts are shock-sensitive. By comparison, nitro compounds may have decomposition onset temperatures as high as 360°C and typically decompose exothermically with between 300 and 500 kJ/mole of energy released.

---

Table 1. Thermal stability of diazonium salts.

<table>
<thead>
<tr>
<th>Properties</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most aromatic diazonium salts</td>
<td>Not stable at temperatures above 5°C</td>
</tr>
<tr>
<td>The synthesis reaction to prepare the diazonium salt is typically exothermic, producing between 65 and 150 kJ/mole and is usually run industrially at sub-ambient temperatures</td>
<td></td>
</tr>
<tr>
<td>Diazonium salts decompose exothermically, producing between 160 and 180 kJ/mole. The decomposition onset temperature is around 130°C, but can range between 20°C and 140°C, depending upon the particular diazonium salt</td>
<td></td>
</tr>
<tr>
<td>Many diazonium salts are shock-sensitive</td>
<td></td>
</tr>
<tr>
<td>By comparison, nitro compounds may have decomposition onset temperatures as high as 360°C and typically decompose exothermically with between 300 and 500 kJ/mole of energy released</td>
<td></td>
</tr>
</tbody>
</table>
Safety

The conversion of 2-aminopyrimidine to 2-chloropyrimidine can be achieved through a diazonium salt intermediate. This is composed of the diazonium ion (ArN₂⁺, where Ar stands for "aromatic ring") and a counter ion. The general preparation involves treatment of a primary aromatic amine with nitrous acid, which is generated in situ from sodium nitrite and hydrochloric acid.

Run in semi-batch mode, this process consists of the following sequence of steps (11):

- Charge reactor with concentrated HCl and cool to 0°C.
- Add stepwise, with stirring, the reactant (2-amimopyrimidine).
- Cool to −15°C.
- Add stepwise, with stirring over a 5-min period, a cold solution of sodium nitrite.
- Hold the reaction mass between −15°C and −10°C during the nitrite addition.
- Stir the reaction mixture an additional hour at −5°C.
- Neutralize to pH 7 using a 30% sodium hydroxide solution.

As shown in Table 5, the thermal runaway in the diazotization synthesis is considered to be severe based upon the size of the adiabatic temperature rise and ultimate pressure reached by the secondary decomposition reaction.

Potential triggers of thermal runaway

How is the runaway triggered in the normal (desired) process? Will a cooling failure at a critical point in the process lead to a thermal runaway? Will over-addition of catalyst or loss of agitation do the same? The

Table 2. Typical diazotization synthesis.

<table>
<thead>
<tr>
<th>Step</th>
<th>Reaction</th>
<th>Temp.</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NH₂N₂Cl</td>
<td>0°C</td>
<td>Charge reactor with concentrated HCl and cool to 0°C.</td>
</tr>
<tr>
<td>2</td>
<td>NH₂N₂⁺</td>
<td>−15°C</td>
<td>Add stepwise, with stirring, the reactant (2-amimopyrimidine).</td>
</tr>
<tr>
<td>3</td>
<td>Cl⁻</td>
<td>−10°C</td>
<td>Hold the reaction mass between −15°C and −10°C during the nitrite addition.</td>
</tr>
<tr>
<td>4</td>
<td>Neutralize to pH 7 using a 30% sodium hydroxide solution.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Small-scale screening data on the secondary decomposition.*

- Tpo (Carius tube test) = 144°C
- Tor (DSC) > 175°C
- tMRad (ARC) < 1 h
- Hr (DSC) = 296 kJ/kg
- ∆Hr = -431 kJ/kg
- ∆Tad (DSC) > 165°C
- Tp (DSC) = 30°C
- The decomposition occurs in two steps (DSC)
- The data for this example shown in Table 3 represent what is typically required from a series of small-scale thermal screening tests.

Table 4. Large-scale thermal characterization of the synthesis.

- Reaction is instantaneous at −10°C
- Reaction rate is feed-controlled
- Reaction rate approaches zero quickly once the feed is stopped
- Slow feed rates are required if the reaction is to be kept at the process temperature
- No accumulation of reactants was observed in the 2 L, glass-jacketed reactor at −10°C = Tp, provided the feedrate was kept below 5.2 g/min and the mixture was stirred
- ∆Hr = -296 kJ/kg of reaction mixture
- Cₚ = 2.6 kJ/kg°C
- ∆Tad = 114°C
- MTSR = 104°C (based upon Tp = −10°C)

Table 5. Large-scale thermal characterization of the synthesis reaction.

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- ∆Tad = 114°C
- MTSR = 104°C (based upon Tp = −10°C)

*Unless otherwise noted, the data refer to the decomposition of the crude product.

Large-scale thermal characterization

If the screening tests indicate that it is safe to do so, a large-scale (kg) characterization of the desired synthesis reaction is performed. A reaction calorimeter is ideal for this purpose (7). The objective is to obtain quantitative data on the heat of reaction, ∆Hr, and the isothermal rate of reaction for the specific synthesis. From these data, the adiabatic temperature rise and the maximum temperature that can be reached by the runaway of the synthesis reaction, MTSR, can be calculated. These data are critical for the safe optimization and scaleup of the process.

Let’s return to the diazotization example. The synthesis was carried out in a reaction calorimeter, which simulates the actual semi-batch process and records the power output from the exothermic reaction as a function of the amount of reactant dosed over time. The resulting reaction profile is shown in Figure 2. The area under the power output curve is integrated to yield the heat of reaction per kg of reaction mass. The reaction profile shows that this reaction is instantaneous (at −10°C) and that the rate of diazotization is feed-controlled and approaches zero quickly once the feed is stopped. There is no accumulation of reactant at the experimental feed rate. Table 4 summarizes for the example the data typically required from a large-scale thermal characterization of a synthesis reaction.

Evaluating the severity of the hazard

The severity of the runaway is best characterized by the adiabatic temperature rise, the rate of pressure rise, and the ultimate pressure reached. The adiabatic temperature rise links the heat of reaction to the rate of reaction. For example, if the effect of temperature on the reaction rate is such that a 10 K increase doubles the rate, then an adiabatic temperature rise of 100 K will cause a 1,000-fold rate increase. Since the reaction is exothermic, such a substantial rate increase represents a huge increase in power output that must be countered by the plant’s cooling capacity. If the reaction is run in a solvent or is gas-generating, this rate increase will result in a formidable rate of vaporization or pressurization during the runaway.

As a general rule, if the adiabatic temperature rise is greater than 200 K, or if the boiling point is surpassed, the runaway is generally considered to be of high severity (1). Runaways that quickly reach very high pressures of non-condensable gas are assigned a high severity rating regardless of the size of the adiabatic temperature rise.
The paramount hazard of a synthesis process is loss of thermal control of the desired reaction (2). The runaway of the desired reaction can trigger a secondary decomposition. Such decompositions are typically highly energetic.

Understanding just how the runaway is triggered is key to keeping the process under thermal control. Process control involves eliminating triggers — i.e., those conditions that initiate runaway. For example, even a highly exothermic and rapid process step can be kept under control if adequate external cooling is provided to the reaction batch or if the reaction exotherm is tempered by significant vaporization of a low-boiling solvent.

For the diazotization synthesis, an obvious trigger is loss of jacket cooling. Other triggers include an excessively fast feed rate, and the buildup of the diazonium salt solid on the internal reactor wall (which may occur due to improper agitation such as might result from the selection of the wrong type of agitator). Decomposition of any dry residue may be initiated by friction or by shock/impact. Long residence times in the reactor may act as a trigger if the reaction mass is sensitive to isothermal aging. Table 5 summarizes the potential triggers for the diazotization synthesis.

### Table 5. Thermal risk assessment.

<table>
<thead>
<tr>
<th>Likelihood</th>
<th>Diazonium salt intermediate is unstable at temperatures only slightly above the process temperature, which is much lower than the maximum temperature that can be reached by the synthesis reaction during a thermal runaway.</th>
</tr>
</thead>
</table>
|            | $T_p (\sim 10^\circ C) < T_{oi} (30^\circ C)$. $T_{oi} (30^\circ C) < MTSR (104^\circ C)$. $MTSR (104^\circ C) = \text{Boiling point of the reaction batch (100^\circ C)}$. Secondary decomposition will rapidly accelerate in the runaway. $t_{MRad} < 8 \text{ h}$.
|
| Severity   | The secondary decomposition reaction is gas-producing and moderately exothermic. $\Delta T_{ad} (DSC) > 165^\circ C$. $P_{ult} (ARC) = 430 \text{ psig at 174^\circ C}$. |
| Risk       | High — A rapid gas-generating secondary decomposition reaction occurs with substantial heat generation at temperatures well below the boiling point of the reaction batch and is easily reached by the synthesis reaction in the event of a cooling failure. The rapid decomposition results in very large reactor pressures due to noncondensible gas formation. The boiling point is not expected to act as a safety barrier. The $t_{MRad}$ for the secondary decomposition is much less than 8 h. |
| Potential triggers | • Inadequate process cooling  
• Excessively high feedrates  
• Inadequate agitation  
• Excessively high reactant concentrations  
• Loss of solvent  
• Incorrect pH adjustment  
• Isolation and drying of the reaction intermediate  
• Formation of dry residue in pipes, valves and ventilation ducts, and on reactor walls  
• Long residence times in the reactor |
| Consequences of a thermal runaway | A reactor explosion with substantial damage to persons and facility  
Nitrous gases in the decomposition products are an environmental danger |

### Nomenclature

- $BP$ = boiling point temperature  
- $C_p$ = constant-pressure heat capacity  
- $\Delta H$ = heat of reaction  
- $\Delta H_d$ = heat of decomposition  
- $\Delta H_r$ = heat of reaction  
- $MTSR$ = maximum temperature reached by the synthesis reaction  
- $P_{ult}$ = largest pressure reached by the runaway  
- $t_{MRad}$ = adiabatic time-to-maximum rate  
- $\Delta T_{ad}$ = adiabatic temperature rise  
- $T_f$ = [what is $T_f$?]  
- $T_{oi}$ = onset temperature  
- $T_{oc}$ = onset temperature for crude product  
- $T_{op}$ = onset temperature for pure product  
- $T_{or}$ = onset temperature for pure reactant  
- $T_{po}$ = onset temperature for noncondensible gas formation

**Figure 1.** DCS thermogram for diazotization synthesis.
Likelihood of the hazard

The likelihood of a runaway is generally considered low if $t_{MRad} > 24$ h, and high if $t_{MRad} < 8$ h \((I)\). Thermal runaways that accelerate quickly under adiabatic conditions are difficult to deal with, because very little time is available for operators to respond once alerted to the emergency condition \((10)\).

Ordinarily, the safe design of a process is based upon the $MTSR$ for the desired synthesis reaction, since the primary strategy is to avoid reaching the conditions required for the undesired secondary decomposition. In highly critical runaway scenarios, the onset temperature for the secondary decomposition reaction may be just slightly above the process temperature and well below the $MTSR$. In this case, the heat release from the secondary reaction must be accounted for, and the $I$ and $P_{ult}$ of the secondary reaction are of primary concern.

In the case of the diazotization synthesis, the likelihood of a runaway is high. As shown in Table 5, the decomposition onset is only 40°C above the process temperature and is well below both the boiling point of the reaction batch and the $MTSR$. The relationship between the important temperatures in the thermal runaway scenario is shown in Figure 3. The $I$ for the decomposition reaction is less than one work shift (8 h).

Risk

Qualitatively, the thermal risk is the product of the severity of the hazard and the likelihood of the hazard \((1)\).

The risk is high in the case of the diazotization example. Should a cooling failure occur at the process temperature ($T_p = -10°C$), the synthesis reaction will undergo a thermal runaway and potentially self-heat to 104°C ($MTSR$). The solvent boiling point, $BP$, is 100°C. The exothermic undesired decomposition will be triggered at 31°C ($T_o$) long before the boiling point is reached. Should there be insufficient solvent to provide cooling or should the solvent be boiled or carried off, the undesired decomposition reaction can self-heat to 196°C ($T_f$). Before reaching this temperature, a substantial volume of permanent gas will have been formed ($T_{po} = 144°C$) by the decomposition.

The relatively high thermal risk of the diazotization synthesis stems from the fact that the reaction is typically highly exothermic and the diazonium salt intermediate is often thermally unstable and may decompose as it is formed. There are many ways to trigger the undesired decomposition reaction. The consequence is a reactor explosion with substantial damage to persons and the facility. Nitrous gases are a decomposition product and a danger to the environment. A summary of the thermal risk assessment is given in Table 5.

Preventive measures

Knowing the thermal risk, we can define a safety basis for the process. Control strategies can then be put into place to prevent thermal runaway. These include running the process in semi-batch mode and controlling the rate of reactant feed to ensure that there can never be enough potential energy in the reactor at any given time to trigger a secondary decomposition reaction. An alarm and trip mechanism can be installed that shuts off the reactant inlet flow should the temperature of the reaction batch warrant it.

Additionally, the process can be run in a suitable low-boiling solvent to keep the reactant concentrations low and to provide tempering by vaporization. In this case, the sol-
vent boiling point acts as a safety barrier as the process is run open to the atmosphere through a properly sized reflux condenser. Quantitative data on the maximum rate of heat generation during self-heating are needed if the required cooling capacity is to be assessed. Independent cooling of the condenser is necessary.

To protect against the disastrous consequences of a thermal explosion, consider incorporating the following safety measures in the process design:

- adding an emergency pressure-relief system capable of venting the pressure evolved during the thermal runaway
- containing the pressure by designing a reactor strong enough to withstand the maximum pressure developed
- draining the reactor bottom to a suitable catch-tank during the very early stages of runaway
- adding a reaction-rate inhibitor chemical to reduce the rate of the runaway reaction to a safe value
- crash cooling the reactor contents by adding a suitable cold solvent during the early stages of runaway.

The selection of the correct safety measures depends on the runaway scenario that the design is intended to address. For example, controlling the feed rate in a semi-batch process will not be effective if the kinetics of the reaction at the process temperature permit the accumulation of reactant. Use of a low-boiling-point solvent will not be an effective safety barrier if the secondary decomposition reaction generates noncondensable gas rapidly at lower temperatures. Emergency pressure-relief systems, such as bursting disks and vent valves, may be impractical if the required vent areas are very large, if a moderate temperature rise does not cause enough pressure increase to actuate the system, or if the rate of pressure generation to be vented is so large as to indicate a detonation.

The diazotization synthesis presents a considerable thermal risk. It cannot be run safely as a batch process, but must be run in semi-batch mode. The desired reaction can be completed under thermal control using a suitably low feed rate and adequate reactor cooling. Tempering by solvent vaporization is not likely to be an effective safety barrier, since the rapid exothermic decomposition reaction is triggered well below the boiling point. Various control and protective measures must be taken, including careful control of the feed rate and making ready an independent emergency backup cooling system. Reactor venting should be considered only as a last resort. (Data to support the calculation of the required vent size are not presented here.) Table 6 summarizes the recommended safety measures.

### Table 6. Safety measures selection.

<table>
<thead>
<tr>
<th>Measure Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Run the process in semi-batch mode</td>
<td></td>
</tr>
<tr>
<td>Select a suitably low feed rate based on the kinetic data obtained from the reaction calorimetry</td>
<td></td>
</tr>
<tr>
<td>Ensure sufficient cooling capacity to easily handle the maximum rate of heat generation from the exothermic synthesis reaction</td>
<td></td>
</tr>
<tr>
<td>Do not isolate or dry the intermediate</td>
<td></td>
</tr>
<tr>
<td>Protective measures must be taken:</td>
<td></td>
</tr>
<tr>
<td>1. Make ready a backup independent cooling system to the reactor</td>
<td></td>
</tr>
<tr>
<td>2. Provide careful control of the feed rate to prevent overcharging</td>
<td></td>
</tr>
<tr>
<td>3. Provide careful control of the batch temperature and inlet temperature of the dosed reactant</td>
<td></td>
</tr>
<tr>
<td>4. Provide careful pH control</td>
<td></td>
</tr>
<tr>
<td>5. Install a high-temperature alarm and trip to shut off the reactant feed</td>
<td></td>
</tr>
<tr>
<td>6. Provide for the possibility of emergency reaction quenching</td>
<td></td>
</tr>
<tr>
<td>7. Reactor venting should be considered, but only as a last resort</td>
<td></td>
</tr>
<tr>
<td>8. The crude product should be purified at once and the pure product stored</td>
<td></td>
</tr>
</tbody>
</table>

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**Acknowledgments**

The author thanks Mr. David Y. Kohn, Dr. Robert Venugopal and Ms. Victoria Jones for their assistance in preparing this article.

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**Literature Cited**