Safely Scale-up Processes and Accommodate Recipe Changes

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Abstract

Thermal hazards screening can be quickly and cost-effectively performed to obtain the required data for safe scale-up of chemical processes and to accommodate changes to process recipes. Prior to scale-up, it is vital to identify safe temperature and pressure operating ranges, quantify the heat generated from a reaction and the number of moles of gas generated. It is also prudent to determine the heat and gas generation rates in order to safely accommodate the reaction in the given process equipment. These rate data can also be used to verify the adequacy of the existing pressure relief system design. PHA and HAZOP reviews identify credible upset scenarios, and data are required to address these issues. When a process recipe or batch size is changed, data are necessary to quantify the effect of the change on the above parameters. For modifications to existing processes, a management of change (MOC) review should occur. Data addressing issues resulting from these reviews are readily available by performing calorimetry experiments with the Advanced Reactive System Screening Tool (ARSST™) and examples of these applications are provided.

1. Introduction

While general studies found in the literature can be useful for screening thermal hazards, the characteristics of the particular reactions must be determined experimentally [1]. Once the worst credible scenarios are defined by a PHA process or HAZOP, those scenarios should be addressed by experiment. It is advisable to consider abnormal conditions for these upset scenarios. For a more thorough analysis, it is also recommended to perform experiments on raw materials, intermediates as well as any contamination scenarios that are present as identified by a reactivity matrix. The worse credible scenarios are used for the vent sizing analysis, but should also be considered when designing the process equipment and operating procedures. It is recommended that these experiments be performed using a low phi-factor adiabatic calorimeter such as the Advanced Reactive System Screening Tool (ARSST) [2].

1. Determine Safe Operating Envelope

1.1 Safe Temperature for Storage, Transportation or Process Conditions

Data obtained from adiabatic calorimetry experiments can be used to determine safe storage, transportation and processing temperatures for a given reaction. This is accomplished by analyzing the temperature rise rate curve, and obtaining the corresponding kinetics. This information is then used to calculate the time to runaway for a given temperature.

1.1.1 Calculate the Characteristic Time of Adiabatic Runaway

The characteristic time of adiabatic runaway, t (s), can be estimated from the following equation [3]

$$t = \frac{T^2}{\dot{T}B} \qquad \textit{Equation 1}$$

where T (K) is the temperature, $\dot{T}$ (K/s) is the corresponding self-heat rate and B (K) is the activation temperature. If the exposure time for a given temperature is much shorter than the calculated runaway time, then the situation is determined to be safe.

In the low temperature range of interest, i.e. negligible consumption, the reaction rate data, $\dot{T}$ (K/min) is well represented by the following equation.

$$\dot{T} = Ae^{-B/T} \qquad \textit{Equation 2}$$

where A (K/min) is the pre-exponential factor. This expression can be evaluated using ARSST data. The values obtained for B and the corresponding heating rate based on a given temperature can be substituted into Equation 1 to calculate the time to adiabatic runaway. This can be done for a desired temperature range, and a characteristic time to runaway curve can be obtained. Other related quantities (TMR, ADT24, etc.) can be similarly evaluated.

1.1.2 Example for Dicumyl Peroxide

An ARSST experiment was performed on a sample of neat dicumyl peroxide using an external heating rate of 0.8°C/min. The temperature rise rate data were corrected for the external heating rate, which is appropriate at low conversions. From this temperature rise rate curve shown in Figure 1, the kinetic parameters were calculated based on the slope of the data during the Arrhenius portion of the runaway. The resulting expression is

$$\dot{T} = 3.2 \cdot 10^{19} e^{-17,700/T} \qquad \textit{Equation 3}$$

This expression shows that B = 17,700 K. The heating rate values can be calculated over a desired temperature range and the results can be used with Equation 1 to yield a characteristic time to runaway curve for a given temperature range. This curve is shown for the dicumyl peroxide example in Figure 2 where the characteristic time to runaway is given in hours.

Here are examples from the characteristic time to runaway curve shown in Figure 2 for two different temperatures. The characteristic time to runaway at 60°C (-1000/T = -3.0) is 396 hours compared to a temperature of 80°C (-1000/T = -2.83) which gives a time to runaway of 21.9 hours.

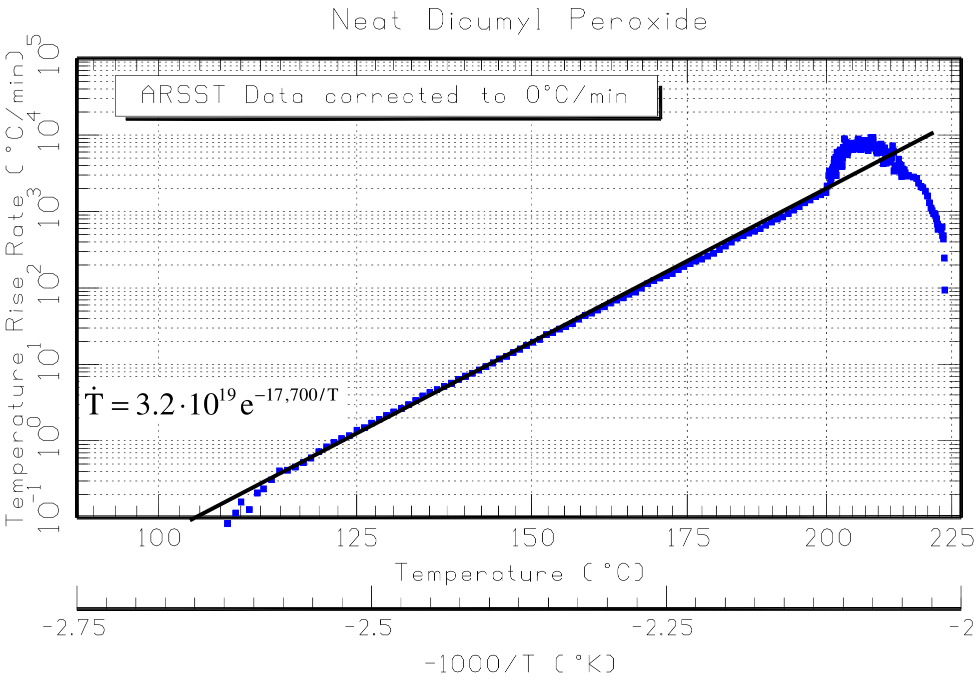

Figure 1. Temperature rise rate curve with kinetic data curve fit based on ARSST data.

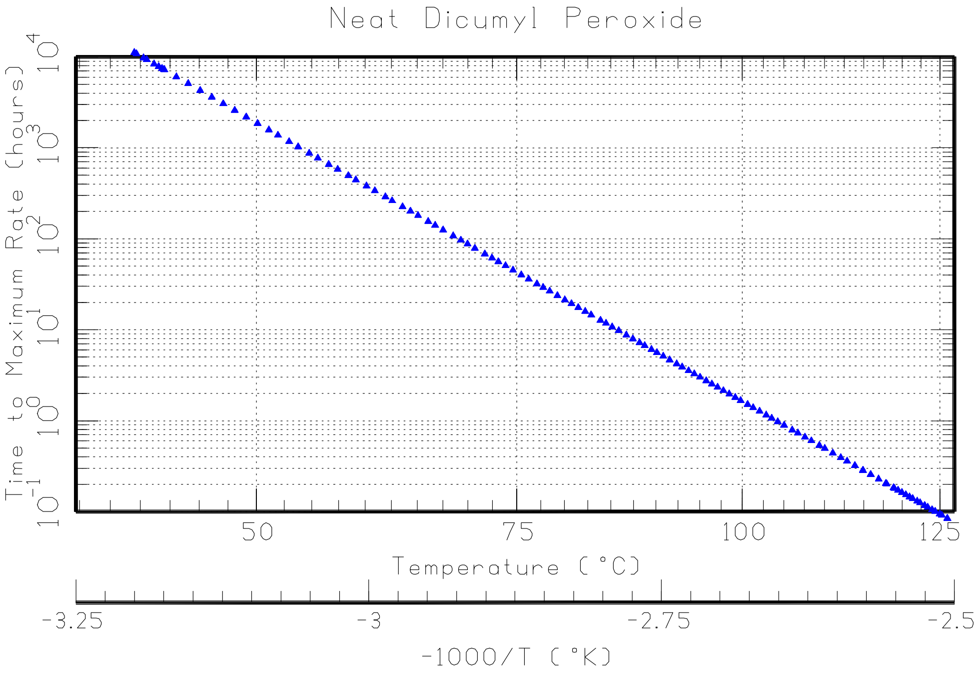

Figure 2. Characteristic time to runaway curve for neat dicumyl peroxide.

1.2 Safe Pressure Range of Operation

1.2.1 Determine Moles of Non-condensable Gas Generated

It is important to calculate the amount of non-condensable gas that forms during a low phi factor adiabatic calorimeter experiment. This is accomplished by comparing the final pressure after cooldown to the initial pressure of the experiment at the same corresponding temperature. Figure 3 illustrates an example of this for 8.8 g of di-tert-amyl peroxide where the reference temperature is 30°C.

By examining the raw data file from the experiment, the final pressure is observed to be 116.3 psig and the initial pressure is –12.4 psig at a reference temperature of 30°C. The difference of these values yields the change in pressure which is 128.7 psi. This change in pressure can be used to calculate the number of moles of non-condensable gas that was formed. This is accomplished by using the ideal gas law.

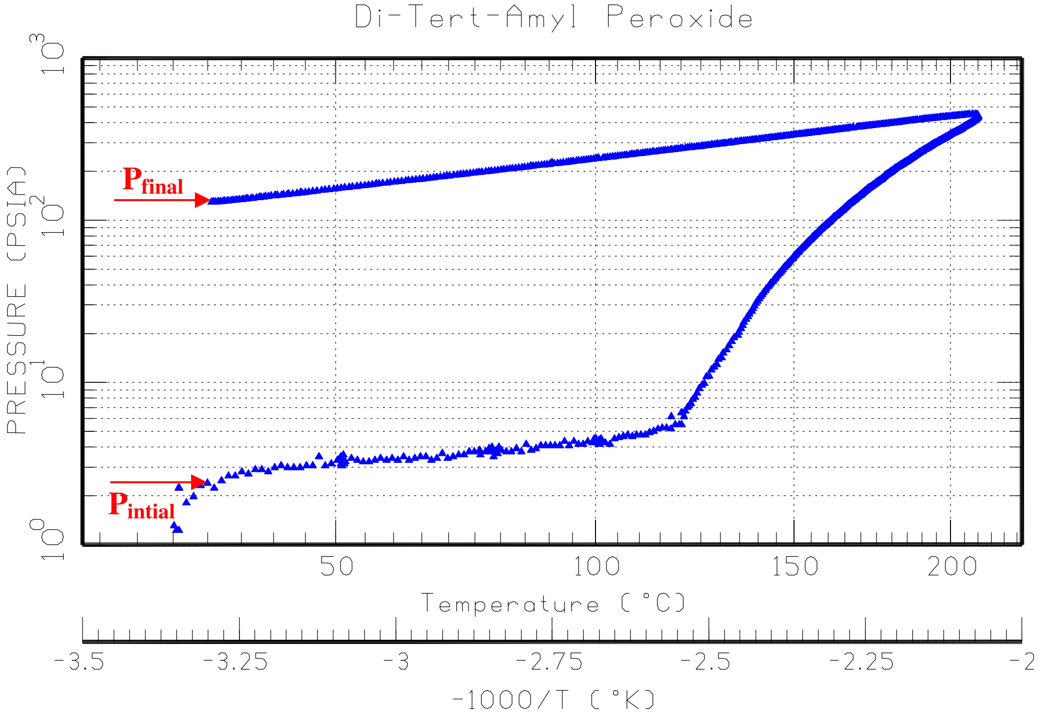

Figure 3. Pressure vs. temperature curve used to determine amount of non-condensable gas generated from an ARSST experiment.

$$n = \frac{PV}{RT} = \frac{128.7\ \text{psi}\ (0.012\ \text{L})}{1.206 \frac{\text{psi}\cdot\text{L}}{\text{mol}\cdot\text{K}} (303\ \text{K})} = 0.0042\ \text{mol} \qquad \textit{Equation 4}$$

where n is the number of moles, P is the pressure difference (psi), V is the freeboard volume (L), R is the universal gas constant and T is the temperature (K). The non-condensable gas can be scaled up to a process vessel given the mass charge and void volume of the vessel. If the process vessel volume is 4000 gallons and the charge mass is 20,000 lb, then the amount of non-condensable gas produced is given by Equation 5.

$$n = \frac{0.0042\ \text{mol}}{8.8\ \text{g}}\left(\frac{453.6\ \text{g}}{\text{lb}}\right)(20{,}000\ \text{lb}) = 4330\ \text{mol} \qquad \textit{Equation 5}$$

The non-condensable gas may be accommodated in one of two ways: contained by the vessel or properly released via an adequate relief system design.

1.2.2 Understand Temperature and Pressure Relationship

It is also useful to look at the temperature and pressure histories on the same graph to understand whether the temperature and pressure begin increasing more rapidly starting at the same time or if one precedes the other. Having this knowledge provides an understanding of which measurable parameters could anticipate an upset condition while processing. In addition, it also allows for a proper control system to be designed to identify a potentially unstable condition that could lead to a runaway.

An example of this type of graph is given for a polymerization of styrene and methyl methacrylate with 0.5% Vazo-64 as an initiator. These results are illustrated in Figure 4.

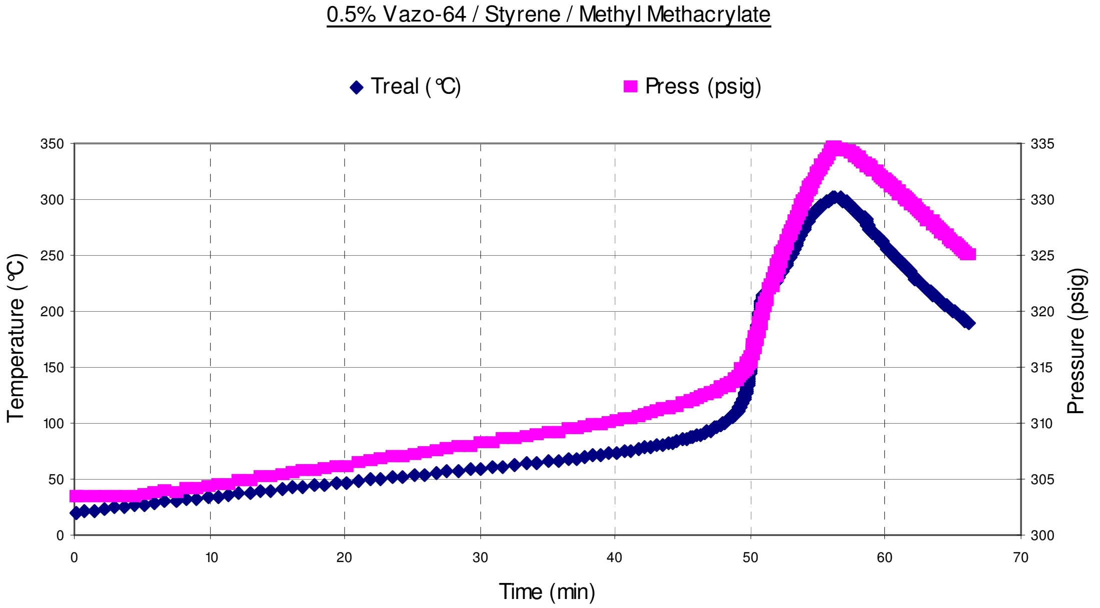

Figure 4. Temperature and pressure history for a runaway reaction polymerization in the ARSST.

2. Calculate Heat of Reaction, ΔH_r

2.1 Theory for Heat of Reaction Calculation

The following assumptions are made in order to obtain the equation for calculating the heat of reaction. It is assumed that the heat of reaction and heat capacity are constant throughout the reaction, and that there is zero conversion of the limiting reagent at the onset temperature of the reaction. This yields the following equation for heat of reaction [4].

$$\Delta H_r = -\frac{\phi c_v ATR}{m/m_t} \qquad \textit{Equation 6}$$

where ΔH_r is the heat of reaction per unit mass of limiting reagent (cal/g, keeping consistent with the convention that ΔH_r term is negative for exothermic reactions), ϕ is the phi-factor or thermal inertia for the experiment (dimensionless), c_v is the specific heat of the mixture at constant volume (cal/g-°C), ATR is the adiabatic temperature rise, m is the mass of limiting reagent (g) and m_t is the total mass of reacting mixture (g).

In the ARSST, the sample is externally heated throughout the experiment and this must be accounted for when calculating the adiabatic temperature rise (ATR). This is accomplished by the following expression.

$$\begin{aligned} &ATR = T_{max} - T_o - \Delta T_{external} \\ &where\ \Delta T_{external} = \dot{T}_{external} \cdot \Delta time = \frac{dT}{dt}\Big|_{ext} (t_{max} - t_o) \end{aligned} \qquad \textit{Equation 7}$$

where T_{max} is the maximum temperature reached during the exotherm (°C), T_o is the temperature at which the heating rate deviates from the background heating rate (°C), $\dot{T}_{external}$ is the background rate due to constant power applied to the sample, t_{max} is the corresponding time at the T_{max}, and t_o is the corresponding time at T_o.

2.2 Example of ΔH_r Calculation for Di-tert-butyl peroxide

In this experiment, 25% di-tert-butyl peroxide was mixed with 75% pentadecane (a high boiling point organic). The sample charge to the ARSST test cell was 7.8 g. This sample was heated at an external rate of approximately 2°C/min for the duration of the experiment including the exotherm. The ϕ-factor can be calculated for this ARSST experiment using the following equation.

$$\Phi = \frac{m_s c_s + m_{tc} c_{tc}}{m_s c_s} \qquad \textit{Equation 8}$$

where m_s is the mass of the sample (g), c_s is the specific heat of the sample, m_{tc} is the mass of the test cell and c_{tc} is the specific heat of the test cell. The specific heat of the test cell is taken as the value for pyrex glass which is 0.2 cal/g-°C. The specific heat for a mixture at constant volume is estimated in this example using the specific heat for the mixture at constant pressure. This quantity is calculated according to the following equation.

$$c_v \approx c_p = m_{DTBP}(c_{p,DTBP}) + m_{C15}(c_{p,C15})$$

$$c_p = 0.25\left(0.58\frac{cal}{g\cdot°C}\right) + 0.75\left(0.66\frac{cal}{g\cdot°C}\right) \qquad \textit{Equation 9}$$

$$c_p = 0.64\frac{cal}{g\cdot°C}$$

Substituting these values into equation 8 leads to the following expression.

$$\Phi = \frac{7.8\,(0.64) + 1.45\,(0.2)}{7.8\,(0.64)} = 1.06 \qquad \textit{Equation 10}$$

The maximum temperature observed for the exotherm can be observed from the temperature rise rate curve as shown in Figure 5. This graphs shows that T_{max} is 241°C and T_o is 120°C.

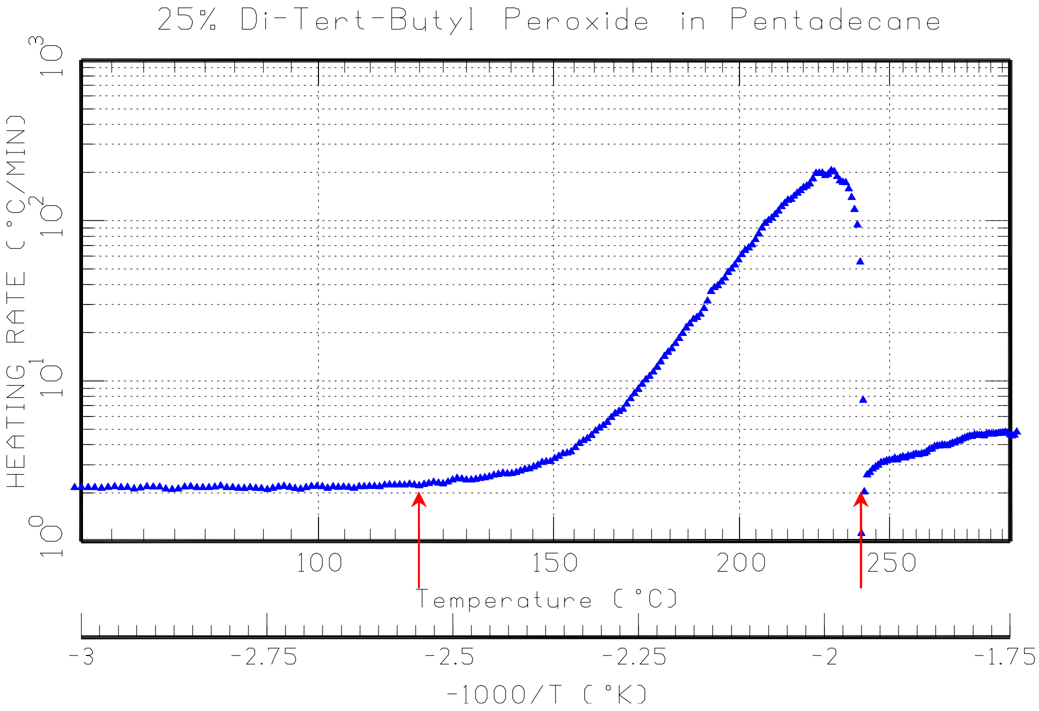

Figure 5. Determine T_o and T_{max} using temperature rise rate curve for 25% di-tert-butyl peroxide and pentadecane in the ARSST.

By examining the raw data file, the corresponding time associated with these temperatures can be identified. These values are 60.0 minutes and 42.8 minutes, respectively. These values can then be substituted into equation 4 in order to obtain the adiabatic temperature rise.

$$\begin{aligned}
\text{ATR} &= T_{\text{max}} - T_{\text{o}} - \Delta T_{\text{external}} \\
\text{ATR} &= 241 - 120 - 2.1\frac{^{\circ}\text{C}}{\text{min}}(60.0 - 42.8)\,\text{min} \qquad \textit{Equation 11} \\
\text{ATR} &= 85^{\circ}\text{C}
\end{aligned}$$

These values can then be substituted into Equation 6 to obtain the value for the heat of reaction. In this example, the heat of reaction is given by the following expression.

$$\begin{aligned}
\Delta H_r &= -\frac{\phi c_v(\text{ATR})}{m/m_t} = \frac{-1.06(0.64)(85)}{0.25} \\
\Delta H_r &= -231\frac{\text{cal}}{\text{g}} = -34\frac{\text{kcal}}{\text{mol}}
\end{aligned} \qquad \textit{Equation 12}$$

This value agrees well with the literature value of 36-37 kcal/mol obtained from bond dissociation energy considerations as well as with other calorimeter values. Values obtained from the VSP2 are 42.4 kcal/mol and the ARC yielded a value of 43 kcal/mol [4].

3. Evaluate Temperature and Pressure Rise Rates

3.1 Screening Methodology

The ARSST is commonly used as a screening method for identifying highly reactive mixtures and quantifying those results. Often times, a threshold value for the allowable heating rate and pressure rate will be determined. Mixtures that exceed this threshold should be further evaluated to determine safe operating conditions.

3.2 Example of Shock Sensitive Compound Stabilization

Pinacol Borane (PinB) is a compound that is known to be shock sensitive. This makes processing a challenge. The compound can be stabilized in a variety of ways. One method of stabilization is to combine the PinB with triethyl amine (TEA). This provides a stabile mixture as illustrated in Figure 6 where the blue curves represent temperature rise and pressure rise rates for PinB alone, and the red curves represent temperature rise and pressure rise rates for the PinB and TEA mixture. The stabilized mixture of PinB and TEA is illustrated by the temperature rise rate which does not exceed approximately 2°C/min (which is close to the applied external heating rate) and is much less than the 7,600°C/min observed for the neat PinB. Likewise, the pressure rise rate for the stabilized PinB and TEA does not exceed approximately 3 psi/min compared to the 20,000 psi/min pressure rate observed for the neat PinB.

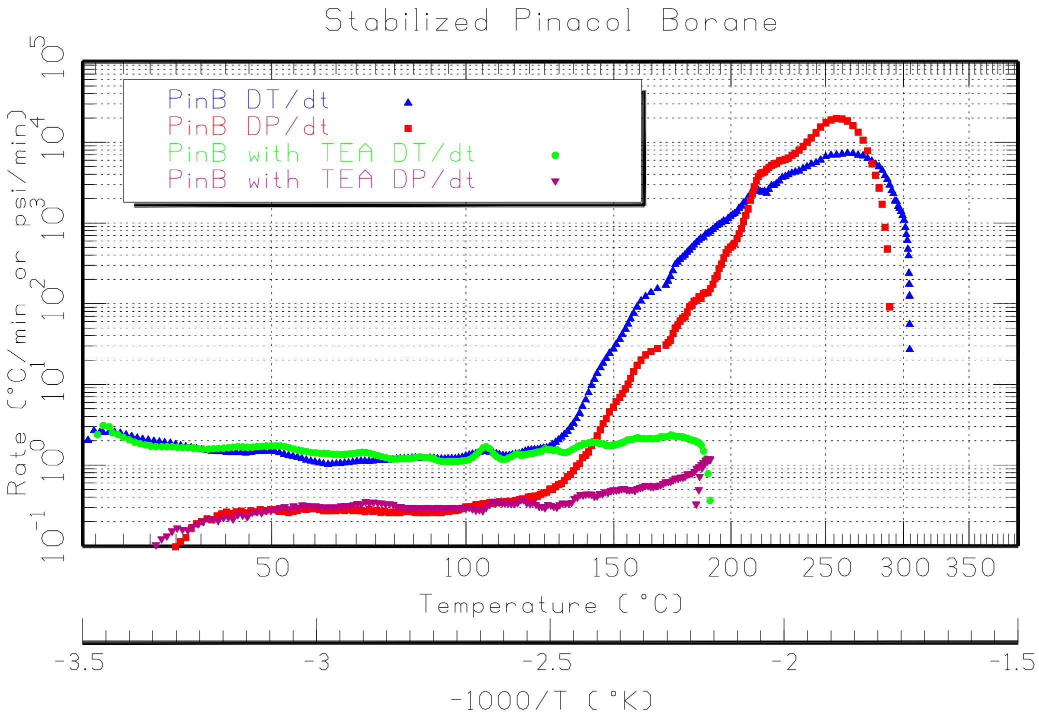

Figure 6. Temperature rise and pressure rise rates for neat pinacol borane compared to stabilized mixture of pinacol borane with triethyl amine in the ARSST.

4. Quantify Recipe Changes

When modifications are made (or proposed) to a process recipe, the effects should be quantified with low phi-factor adiabatic calorimetry experiments. The time required for this effort is minimal when using the ARSST, and the knowledge gained regarding the process is valuable. Scale-up is not recommended without understanding the expected and unexpected chemistry. The impact of recipe changes should be identified by a Management of Change (MOC) review, and should be considered as part of process development or pilot plant support.

4.1 Determine Effect on Temperature Rise and Pressure Rise Rates

It is important to quantify any effect that the recipe has on the rates of temperature and pressure rise for a mixture. Changing one component can affect the results of an experiment, possibly making it more or less energetic. These results should be quantified with a simple low phi-factor adiabatic calorimetry experiment.

4.1.1 Change in Initiator Concentration

In this example, the initiator concentration for the styrene / methyl methacrylate mixture was increased from the initial value of 0.5% Vazo-64 up to 1.0% Vazo-64. A comparison of the temperature rise rate and pressure rise rate curves are shown in Figure 7.

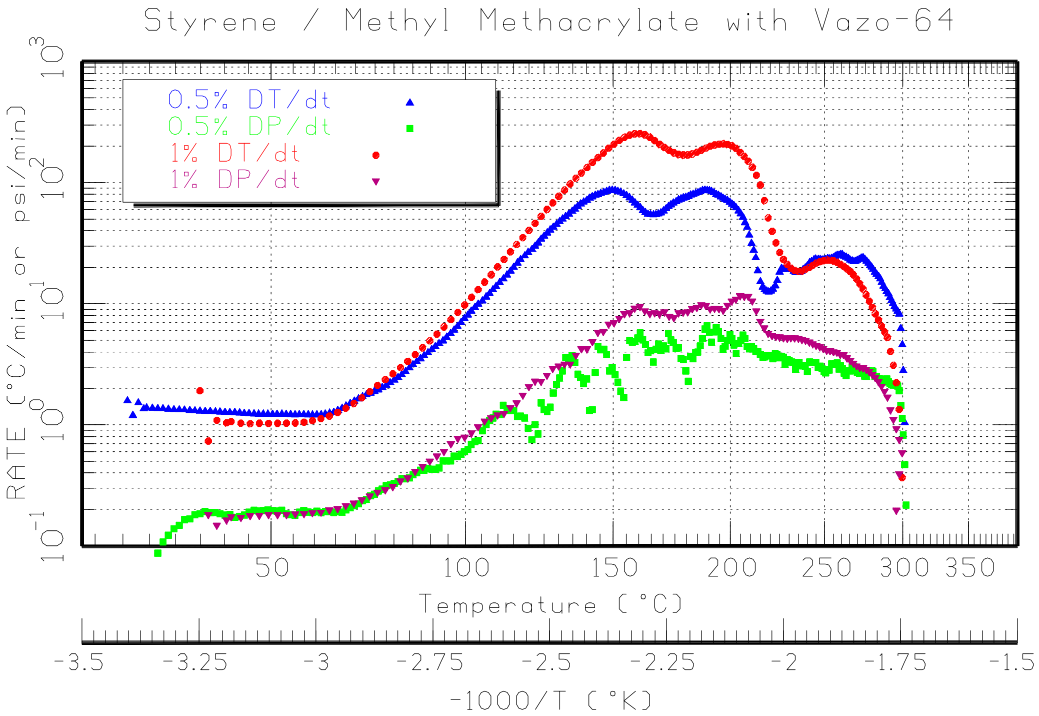

Figure 7. Temperature rise and pressure rise rates for two different initiator concentrations for a styrene and methyl methacrylate polymerization reaction in the ARSST.

Figure 7 clearly shows that the small increase in initiator concentration increases the maximum temperature rise rate by more than 100°C/min. There is a minimal change in the maximum pressure rise rates. Given these changes in the temperature rise rate and pressure rate values, the relief system design should also be re-evaluated to verify that it is sufficient.

4.2.1 Change in Monomers

In this example, 10% glycidyl methacrylate was added to the reaction mixture of styrene and methyl methacrylate. The initiator concentration for both experiments was 0.5% Vazo-64. A comparison of the temperature rise rate and pressure rise rate curves are shown in Figure 8. There is a small increase in the peak heating rate values at 150°C and 180°C for the recipe containing the glycidyl methacrylate. Pressure rise rates for each of the reactions appear to be quite similar. Even though the rate changes are small, it is still advisable to verify that the relief system can accommodate the rates obtained based on the change in recipe.

4.2 Re-Evaluate Relief System Requirements

Data must be re-evaluated to determine if the system classification has changed (vapor, gassy or hybrid). The system must be sized accordingly to verify that relief system requirements are adequate to accommodate the recipe change.

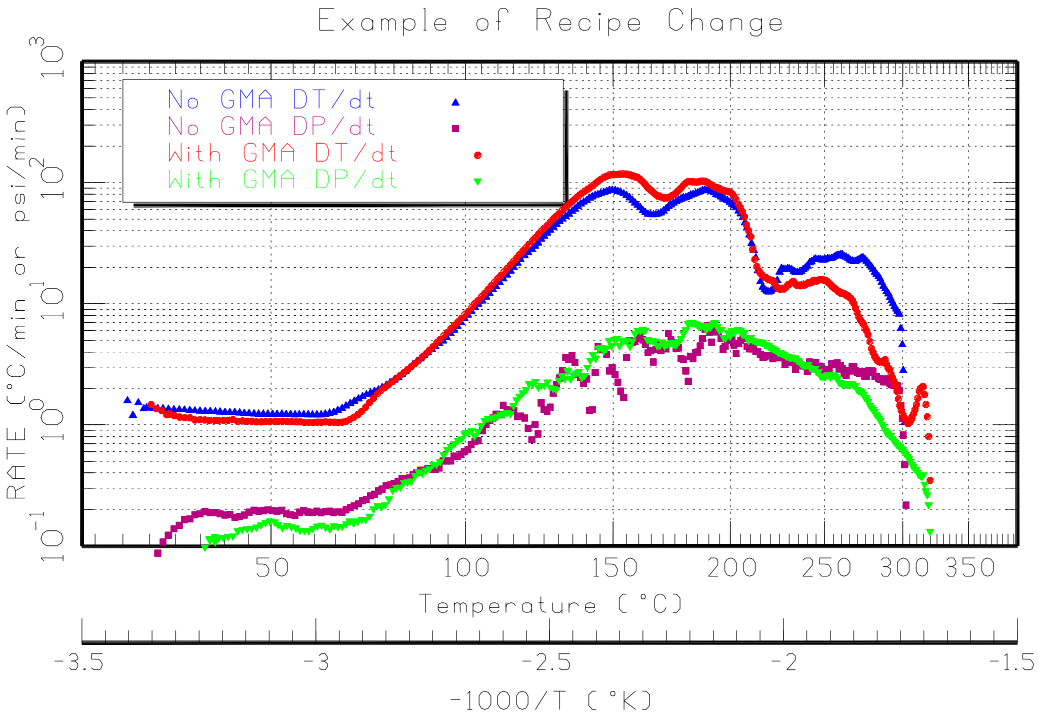

Figure 8. Temperature rise rate and pressure rise rates for two different polymerization reactions in the ARSST.

5. Vent Sizing Application

5.1 Determine Allowable Heating and Pressure Rise Rates

An easy to use mechanistic based equation is provided below that is consistent with all available relevant experimental data and incident information. For condensed-phase (vapor, gassy and hybrid systems), the generalized screening equation [3] is given by the following equation.

$$A_v = \frac{3.5 \cdot 10^{-3}}{P\left[1 + \frac{1.98 \cdot 10^{3}}{P^{1.75}}\right]^{0.286}} \left(\frac{\left(\dot{T} + \dot{P}\right) V}{C_D} \right) \qquad \textit{Equation 13}$$

where A_v (m^2) = vent area, P (psig) = relief set or peak relief pressure, $\dot{T}$ (°C min^{-1}) = rate of temperature rise, $\dot{P}$ (psi min^{-1}) = rate of pressure rise (resulting from 10 g test sample in the ARSST), V (m^3) = volume of reactants, C_D = discharge coefficient, and depending on the system, inputs for the rate of temperature rise and rate of pressure rise are defined in Table 1.

Table 1. Defined Inputs For Use With Equation 10

System	$\dot{T}$	$\dot{P}$
Vapor[*]	$\dot{T}$ (P)	0
Gassy	0	$\dot{P}_{max}$
Hybrid	$\dot{T}$ (P)	$\dot{P}$ (P)

P is the relief set pressure and $\dot{P}_{max}$ (psi min^{-1}) is the maximum rate of pressure rise measured in the ARSST with a 10 gm sample. For a given vessel and its respective relief system piping (used to calculate the discharge coefficient), equation 13 can be used to determine allowable temperature and pressure rise rates.

$$\dot{T}+\dot{P}=\frac{A_v P\left[1+\frac{1.98\cdot 10^3}{P^{1.75}}\right]^{0.286}}{3.5\cdot 10^{-3}}\left(\frac{C_D}{V}\right) \qquad \textit{Equation 14}$$

This is extremely useful in pilot plant operations where a limited number of vessels are available with a pre-determined maximum allowable working pressure (MAWP) and relief set pressure.

6. Summary

Safe, cost-effective and efficient process scale-up can be accomplished through low phi-factor adiabatic calorimetry such as the ARSST. The data can be applied directly to process scale due to the low phi-factor of the experiment. Valuable data regarding safe temperature and pressure operating ranges, heat generated from a reaction and the number of moles of gas generated can be obtained. It is also prudent to determine the heat and gas generation rates in order to safely accommodate the reaction in the given process equipment. These rate data can also be used to verify the adequacy of the existing pressure relief system design. Data addressing issues resulting from PHA or MOC reviews are readily available by performing calorimetry experiments with the Advanced Reactive System Screening Tool (ARSST™).

FAI would like to thank Max Sarvestani of Boehringer-Ingelheim Pharmaceuticals for his contribution of data to this paper.

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[*] In case of "foamy" vapor systems, vent area estimated from Eq. 1 is multiplied by a factor of 2. Note that system characterization and flow regime (foamy versus non-foamy) can be determined from ARSST data.

7. References

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