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TECHNICAL NOTE

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Process Safety Evaluation of a Tungsten-Catalyzed Hydrogen Peroxide Epoxidation Resulting In a Runaway Laboratory Reaction

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S *Supporting Information*

ABSTRACT: An investigation of a runaway chemical reaction in the laboratory highlighted the potential hazards of oxidation chemistry involving hydrogen peroxide in the presence of tungsten catalysts. Under the process conditions, a combination of a high adiabatic temperature rise, an unstable target molecule, and a potentially incompatible mixture of hydrogen peroxide and tungsten catalyst produced a reaction mixture capable of high rates of self-heating and self-pressurization. Under conditions of poor heat removal, a runaway chemical reaction and loss of containment resulted. Tungsten species can catalyze the decomposition of hydrogen peroxide at low onset temperatures. The safety aspects of this synthetic methodology must be thoroughly assessed prior to scale-up.

INTRODUCTION

Recently, a loss of containment occurred in a chemistry laboratory. The chemist was attempting to apply a literature procedure[1] for the epoxidation of 2,4-pentadien-1-ol (Scheme 1) to the methyl analogue, *trans*,*trans*-2,4-hexadien-1-ol, **1** (Scheme 2) in order to synthesize **2**. Initially, the chemist ran a 5-g reaction without incident, although the product quality and yield were mediocre. The reaction scale was then increased to 30-g. After an overnight hold at ambient temperature in a round-bottom flask, it was observed the next morning that all the reaction material had exited the flask. Uncertain as to the cause of this loss, the chemist repeated the 30-g reaction. A few minutes after adding hydrogen peroxide, the contents were violently ejected from the flask from a 'popped' stopper. The flask was hot to the touch; it was unclear whether gas evolution had occurred.

The literature procedure is run as a batch process in which an allylic alcohol is added in one portion to a mixture of reagents (tungstic acid, sodium acetate, and 30% hydrogen peroxide in methanol) at ambient temperature, and the reaction mixture is stirred overnight. The reaction must be run under inert gas. The incident experiment differed from the literature reference in using the homologated starting component (*trans*,*trans*-2,4-hexadien-1-ol) and in an increase in the catalyst loading (10× literature values). A significant reaction byproduct is the diether **3**, resulting from ring-opening of the desired epoxide with methanol.

Only one citation for the target epoxide **2** can be found in the literature,[2] which quotes no preparative procedure or reference. The thermal and chemical stability of this moiety therefore comes into question. The chemist was unable to supply a sufficiently pure sample of **2** for DSC. The entire synthetic approach to the final target molecule was discontinued due to a lack of progress in several of the stages including, but not confined to, the epoxidation. Therefore potential improvements in the transformation of **1** to **2** through other methodologies were not explored,[3] and a feasible synthesis of **2** remained unresolved. Nevertheless, an investigation into the process safety aspects of this chemistry was undertaken, with a particular emphasis on evaluating the effectiveness of our laboratory risk assessment procedures.

Process Safety Considerations. Hydrogen peroxide in combination with tungstic acid is a popular reagent for the oxidation of several functional groups, olefins in particular. Epoxides, diols, and carboxylic acids have been synthesized by this methodology.[4] A new manufacturing route for adipic acid via direct oxidation of cyclohexene with 30% hydrogen peroxide in the presence of a tungsten catalyst has been reported as a 'greener' alternative to current methodologies.[5]

The potential hazards of working with hydrogen peroxide on scale are well documented, particularly as concentration increases.[6] The processing equipment materials of construction must be carefully assessed as concentrated hydrogen peroxide may decompose violently in contact with iron, copper, chromium, and other metals, with flammable oxygen as the byproduct. Catastrophic incidents have occurred due to the uncontrolled decomposition of hydrogen peroxide interacting with metal components and contaminants. Nevertheless, there is no direct mention of a potential incompatibility between hydrogen peroxide and tungsten species in the process safety literature.[7]

Some recent papers[8] have described the process safety aspects of the hydrogen peroxide−tungstic acid system on scale-up. The chemical process under examination was performed in a semibatch fashion and showed significant control of heat output through addition rate, thus providing some measure of safety. Nevertheless, an aqueous solution of $Na_2WO_4-H_2O_2$ is described as unstable at 25 °C, although significantly stabilized in the presence of DMA coordination. Therefore, despite its frequent use as a synthetic tool, the hydrogen peroxide−tungstic acid system

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must be carefully evaluated for safety in the context of the proposed process in order to avoid an incident.

RESULTS AND DISCUSSION

Theoretical Calculations. In order to provide a quick estimate of the potential enthalpy of the desired process, some theoretical calculations were performed. A simple epoxidation with hydrogen peroxide can be modeled as:

$$\text{Olefin} + \text{hydrogen peroxide} \rightarrow \text{epoxide} + \text{water}$$

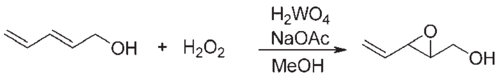
Using values of $\Delta H_f = -187.8$ kJ/mol for H_2O_2[9] and $\Delta H_f = -285.4$ kJ/mol for water[10] the enthalpy of epoxidation (condensed state) for several typical examples[11] can be calculated (Table 1).

It follows that −235 kJ/mol can be used as an average estimation for the epoxidation. Under the reaction conditions (using the heat capacity of methanol), a predicted adiabatic temperature rise of 147 °C can be calculated. This heat is sufficient to bring the reaction mixture to reflux and vaporize ~52% of the total methanol. Therefore, in the batch mode, depending on the kinetics of the transformation, a significant inherent potential exists for overheating and loss of containment.

The side reaction of **2** to **3** is expected to be a low-enthalpy process, approximately −20 kJ/mol (CHETAH calculations)[12] and will not significantly affect the overall thermal evaluation of the process.

Reaction Calorimetry. The process was studied in a Mettler Toledo RC1 reaction calorimeter to determine the thermodynamic profile.[13] Hydrogen peroxide (30%) was added over 30 min to a suspension of sodium acetate and tungstic acid with *trans,trans*-2,4-hexadien-1-ol in methanol. During the actual addition, a small exotherm was observed (131 kJ/kg; ~5% of total). The heat generated during the hydrogen peroxide addition was sufficient to raise the reaction temperature 8 °C. Immediately upon completion of addition, heat output temporarily decreased. This was quickly followed by a second exothermic event which appears to be autocatalytic (Figure 1).[14] A maximum rate of heat output was reached ~2 h postaddition. No gas evolution was observed during this process. A sample taken at 1 h postaddition was analyzed by GC/MS and showed a mixture of 78% **1** and 22% of the desired epoxide **2**. A very small amount of alcohol oxidation to corresponding unsaturated aldehyde (<1%) was observed.[15] The final product mixture contained 9% unreacted **1** and 91% **3**. The enthalpy of reaction and the adiabatic temperature rise (Table 2) agree well with theoretical models. While the principle reaction component is byproduct **3**, the principle contributor to the overall enthalpy is from the epoxidation process, not the ring-opening.

Scheme 1. Model reaction; epoxidation of 2,4-pentadien-1-ol



Scheme 2. Runaway reaction; epoxidation of *trans,trans*-2,4-hexadien-1-ol

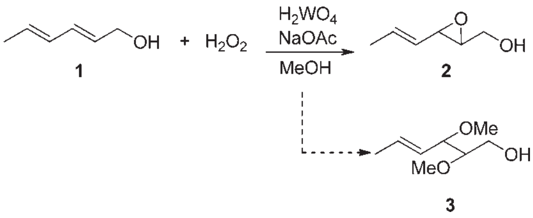
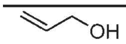
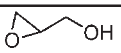
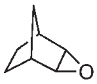


Table 1. Theoretical models of the enthalpy of epoxidation

Olefin	ΔH_f (kJ/mol)	Epoxide	ΔH_f (kJ/mol)	ΔH_{rxn} (kJ/mol)
	-172		-298	-224
	4.3		-131	-233
	53		-98	-249

Slowing the addition rate of hydrogen peroxide does not significantly improve the inherent safety of the process (Figure 2). The overall enthalpy of reaction and the product profile were the same for the two experiments. Under the slower dosing regimen, reaction initiation now occurs during the addition phase. However, most of the heat output (87% thermal conversion) evolved postaddition, with the capacity to raise the reaction mixture to the boiling point and vaporize ~53% of the total methanol content. These results differ little from the 30-min addition. The safety profile was somewhat improved in that the maximum rate of heat output was significantly lowered, so that a greater degree of temperature control is possible. Nevertheless, some serious safety considerations remain, and the process still depends upon external cooling to prevent a runaway situation.

If the $H_2O_2-H_2WO_4$ epoxidation is autocatalytic in nature, the resulting process safety profile will be problematic. Functioning in practice as a batch reaction, a worst-case scenario will depend on the magnitude of exotherm from the desired epoxidation and the ability of the proposed equipment to effectively remove heat from the system. In a vessel configuration with excellent heat transfer and cooling capacity, such as the RC1, a runaway situation is avoided. In equipment of poorer cooling capacity, some loss of control will result with a rise in temperature. Any secondary reactions which may initiate as a result of this temperature increase, such as the decomposition of a reaction component, will increase the exothermicity of the process and increase the negative consequence from inadequate cooling. Among these possibilities, target molecule **2** does not appear to be either chemically or thermally stable; its secondary decomposition may contribute additional heat output with possible pressurization due to gaseous byproduct. Therefore, an uncontrolled temperature excursion can lead to the thermal decomposition of the desired product, generating even more heat output and accentuating the runaway scenario. Another secondary reaction, possibly due to the decomposition of excess hydrogen peroxide, would intensify the worse-case scenario. Hydrogen peroxide decomposition is highly exothermic (98 kJ/mol) and the effect of temperature is such that a temperature increase of 10 °C can increase the rate of decomposition by a factor of 2.3.[16] In the event of gross contamination, decomposition can accelerate, and even H_2O_2 concentrations as low as 10% can be brought to the boiling point. As H_2O_2 accumulates in the reaction mixture, the intensity of a decomposition event will increase. Further experimentation was performed in other instrumentation to examine that possibility.

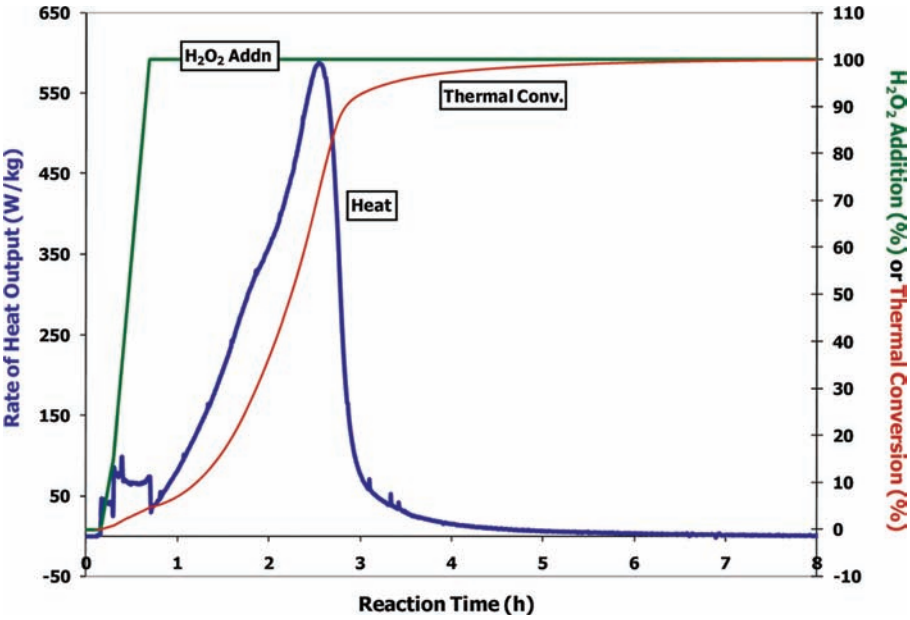


Figure 1. Enthalpy of reaction in the RC1.

Table 2. Enthalpy of reaction as measured by RC1

thermal parameter	value
enthalpy of reaction	2616 kJ/kg
	257 kJ/mol
adiabatic temperature rise	155 °C
maximum rate of heat output	588 W/kg
	88 W/L
specific heat capacity of the reaction mixture:	2.64 kJ/kg·°C

Thermal Stability Experiments. A series of experiments was run in the Advanced Reactive System Screening Tool (ARSST) to study both the thermal runaway and the potential interaction between hydrogen peroxide and tungstic acid (Table 3).[17] The ARSST was chosen as the most appropriate equipment available in our laboratory for this investigation due to its stirring capacity, low phi conditions, pressure measurement, and excellent containment. Baseline experiments (entries 1−2) were run to investigate the possible incompatibility of hydrogen peroxide and tungstic acid under the reaction conditions, varying the catalyst concentration. A similar experiment (entry 3) using sodium tungstate rather than tungstic acid plus sodium acetate tested the possible effects of the buffer. Identical experiments were run in the presence of **1** to simulate the runaway, varying the catalyst loading (entries 4−5). Entry 5 most closely mimics the actual laboratory runaway conditions. Another set of experiments was performed (entries 6−7) in the absence of tungsten catalyst in order to examine the underlying decomposition of hydrogen peroxide in the reaction medium. A final experiment (entry 8) was run on the reaction mixture in the absence of methanol to investigate any possible solvent effects. For entries 1, 2, 4, 5, and 7, the pH of the initial reaction mixture was 6.3; entries 3 and 6 showed a pH of 8 and 7.5 respectively.

Although the use of a tungsten catalyst with hydrogen peroxide to perform oxidations is standard methodology, it is clear that there is a potential safety issue involved in this reagent combination (entries 1−3). In the presence of tungsten catalyst, the decomposition of hydrogen peroxide initiates at a low temperature with the production of noncondensable gas. (Pressure appears a more sensitive indicator of the onset of decomposition than temperature.) As expected, the severity of the decomposition event is a function of catalyst loading, particularly with respect to the self-pressurization rate and the total amount of gaseous byproduct produced as a result of the decomposition. The lower onset temperatures may be due to the greater energy output in a stationary equipment configuration, allowing the ARSST to detect heat output above its sensitivity levels at early temperatures. Even moderate tungsten catalyst loadings (entries 1 and 4) can initiate a secondary decomposition of hydrogen peroxide at temperatures commonly used for oxidation chemistry.

At the same catalyst loading, the use of sodium tungstate produces a far more severe safety issue than the combination of tungstic acid and sodium acetate (entries 2 and 3). Extremely high rates of self-heating and self-pressurization are achieved using sodium tungstate. Buffered pH conditions appear to provide a stabilizing effect on hydrogen peroxide which is not present under slightly higher pH conditions.

Permanent noncondensable gas formation, presumably oxygen, was observed in all of these decompositions. The residual overpressure of 11.6 psi (entry 2) can be estimated to be 9.5 mmol of gas, requiring decomposition of ~32% of the original hydrogen peroxide loading. The evolution of oxygen as a byproduct has serious safety consequences. Insufficient inerting can lead to a situation in which the reaction headspace is in the flammable range. Ignition from an unintended source may lead to a very serious fire.

The simulations of the laboratory incident (entries 4 and 5) with **1** present produced severe self-heating scenarios. At the same catalyst loading as that of the laboratory incident (entry 5), rates of self-heating above the tracking capacity of the instrumentation and high self-pressurization rates were achieved (see Figure 3). However, unlike the control reactions (entries 1−3), permanent formation of noncondensable gas was found to be a minor byproduct. This suggests that most of the hydrogen peroxide has reacted with **1** and is no longer available to decompose to gaseous byproduct.

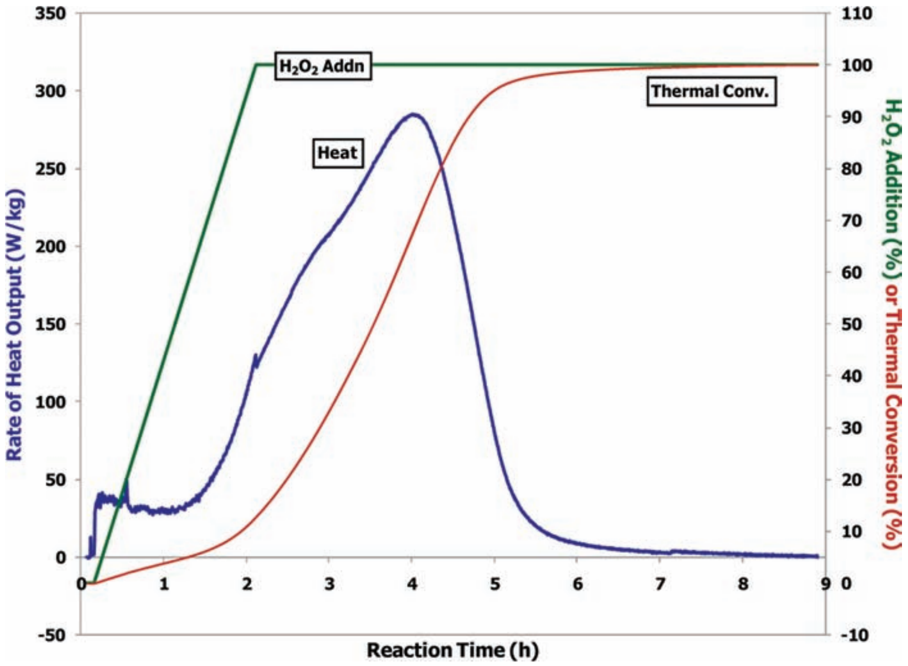


Figure 2. Enthalpy profile; 2-h charge of H_2O_2.

Table 3. ARSST experiments on reaction mixtures

		self-heat rate (°C/min)		self-pressurization rate (psi/min)		
entry	experimental conditions	maximum rate	initiation temperature	maximum rate	initiation temperature	pressure gain (psi)
1	0.01 equiv of H_2WO_4; no **1**	82	47 °C	2.4	42 °C	1.7
2	0.1 equiv of H_2WO_4; no **1**	71	40 °C	11.5	33 °C	11.6
3	0.1 equiv of Na_2WO_4; no **1**	8300	45 °C	618	40 °C	13.7
4	0.01 equiv of H_2WO_4; with **1**	4970	40 °C	70	35 °C	0.3
5	0.1 equiv of H_2WO_4; with **1**	6760	42 °C	480	35 °C	0.3
6	No H_2WO_4 catalyst; with **1**	314	65 °C	309	55 °C	4.9
7	No H_2WO_4 catalyst; no **1**	15	105 °C	7.9	95 °C	12
8	0.1 equiv of H_2WO_4; no **1**; no methanol	3730	45 °C	7510	35 °C	30

The decomposition of hydrogen peroxide in the absence of tungstic acid catalyst, under the reaction conditions (entry 6; with **1** present), also results in thermal decomposition with permanent gas generation. The rates of self-heating and self-pressurization are midway between those observed in control experiments and experiments containing **1**. However, the initiation temperatures of decomposition are significantly higher, near the boiling point of methanol. Without the contributing factor of tungsten-catalyzed decomposition of hydrogen peroxide, a solvent vaporization barrier may prove sufficient to prevent a runaway situation.

Entries 6 and 7 show that, in the absence of catalyst, the underlying decomposition of hydrogen peroxide is a relatively moderate event, initiating at higher temperatures than for the other processes. The greater severity of the entry 6 decomposition process suggests that, even in the absence of catalyst, some oxidative process transforms substrate **1** to a less stable molecular entity, which then decomposes with additional heat output.

A comparison of entries 2 and 8 demonstrates the mitigating effect of the solvent as a heat sink. Self-heating and self-pressurization initiated at a very low onset temperature. This interaction led to an exotherm which became critical at ~65 °C. Methanol appears to have no role in promoting the decomposition process, but functions as a heat sink to slow and mitigate the severity of the runaway reaction.

In the actual laboratory runaway, all of the questionable process safety parameters combined to lead to a critical situation. The reaction first proceeds to form the desired epoxide **2** in a highly exothermic process. However, **2** is chemically and thermally unstable at the resulting temperatures, and decomposes to produce more heat. Once temperature is sufficiently elevated, the tungsten-catalyzed decomposition of hydrogen peroxide initiates, with the evolution of additional heat output and gaseous byproduct. All of these processes will self-accelerate, especially under conditions of poor heat removal. A mixture of solvent vapor and gaseous byproduct pressurizes the vessel configuration; a loss of containment through the point of exit with least resistance results.

Application to Laboratory Risk Assessment Procedures. Due to this investigation, our laboratory risk assessment procedures were reassessed for gaps which might result in future accidents. A number of factors, including a very high potential adiabatic temperature rise, autocatalytic kinetics, thermal instability of the desired product, and a potential chemical incompatibility not explicitly

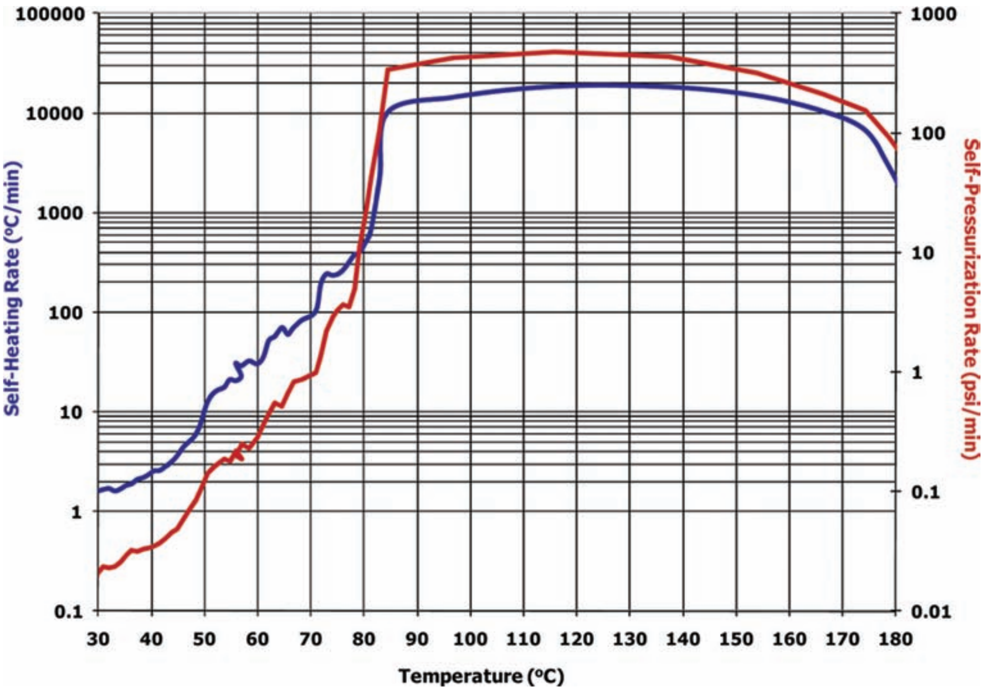


Figure 3. ARSST data for entry 5; self-heating and self-pressurization of the reaction mixture.

documented in a major safety compilation such as Bretherick's, all contributed to the thermal runaway. The chemist, performing reasonable due diligence in evaluating the process risks prior to running the chemistry, would not be likely to uncover of any of these factors. Unknown chemical hazards may occasionally be encountered; however, adherence to established laboratory safety procedures, such as the use of work-shields and an uncluttered workspace, mitigated the severity of this incident to a simple cleanup job.

In our laboratory, risk assessment procedures and process safety involvement often do not initiate until at least the 100-g scale. However, chemists should be aware that low molecular weight components can generate more potential energy on a weight basis and thus may require safety assessment at a smaller scale. Reactions run at relatively high concentration with high catalyst loadings can also increase the potential risks of a laboratory runaway through a diminished heat sink and faster kinetics.

■ CONCLUSIONS

The laboratory runaway epoxidation was caused by the uncontrolled heat and gas generation from a combination of a very high adiabatic temperature rise, autocatalytic kinetics, thermal instability of the desired product, and a secondary decomposition process of hydrogen peroxide catalyzed by the tungsten catalyst. Once the reaction was scaled such that the heat output exceeded the cooling capacity of the system, the temperature of no return for the vessel configuration was easily achieved, leading to a runaway situation.

Although commonly used as a synthetic methodology for a wide variety of oxidations, tungsten can catalyze the decomposition of hydrogen peroxide at relatively low onset temperatures with concurrent pressurization. The severity of this decomposition will depend on reaction conditions such as catalyst loading, excess of hydrogen peroxide and reaction concentration. Oxygen byproduct can produce an enriched atmosphere in the presence of flammable organic solvent, leading to a severe combustion hazard. Any scale-up of this methodology should involve a thorough process safety assessment in the context of the process and proposed equipment configuration.

■ EXPERIMENTAL SECTION

General Procedure for ARSST Screening. A stock solution of *trans,trans*-2,4-hexadien-1-ol in methanol (24% w/w) was used. A 10-mL spherical glass test cell was loaded with the stock solution (4.90 g; 12.0 mmol **1**), sodium acetate (295 mg; 3.6 mmol; 0.3 equiv), and tungstic acid (300 mg; 1.2 mmol; 0.1 equiv). The equipment was assembled according to the Fauske instructions, using a glass thermocouple. A new center tube was used to avoid the introduction of metal corrosion. The vessel was purged with nitrogen several times; 30% H_2O_2 (2.04 g; 1.86 mL; 18.0 mmol; 1.5 equiv) was added via the center tube. The vessel was pressurized to 300 psi and the appropriate heating protocol (2 °C polynomial) was applied.

General Procedure for Reaction Calorimetry in the RC1. The Mettler AP00.01 80 mL reaction calorimeter was loaded with a solution of *trans,trans*-2,4-hexadien-1-ol **1** (9.00 g; 91.70 mmol; 1.0 equiv) in methanol (36 mL; 28.55 g; 4 vol), anhydrous sodium acetate (2.26 g; 27.5 mmol; 0.3 equiv) and tungstic acid (2.29 g; 9.71 mmol; 0.1 equiv), and the temperature was set at 20 °C [400 rpm]. A calibration was performed. At a constant rate over a specified time (either 30 or 120 min) was added 30 % hydrogen peroxide (14.05 mL; 15.59 g; 137.5 mmol; 1.5 equiv). The reaction medium was maintained at 20 °C overnight, followed by a calibration.

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Detailed ARSST study results. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) The Mettler Toledo Autochem RC1e midtemperature reaction calorimeter with 80 mL capacity was used.

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(16) For hydrogen peroxide thermodynamic properties and H_2O_2 self-accelerated decomposition, see the following: (a) http://www.h2o2.com/technical-library/physical-chemical-properties/thermodynamic-properties/default.aspx?pid=33&name=H2O2-Thermodynamic-Properties; (b) http://www.h2o2.com/technical-library/physical-chemical-properties/thermodynamic-properties/default.aspx?pid=42&name=Self-Accelerated-Decomposition

(17) Advanced Reactive Systems Screening Tool (ARSST) manufactured by Fauske and Associates. For more information, see: Fauske, H. *Process Saf. Prog.* **2006**, *25*, 120.