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# Cyclopentadiene: The Impact of Storage Conditions on Thermal Stability

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## Abstract:

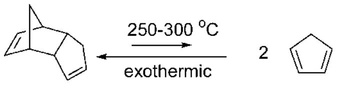
**The potential hazards from cyclopentadiene storage and use on kilogram scale are studied under adiabatic conditions. Cyclopentadiene, a reagent commonly used in organic synthesis, is known to spontaneously dimerize exothermically and thus should be stored cold and used quickly. In the present work we consider the impact of storage conditions such as the container size, volume, temperature, and solvent dilution to assess the potential hazards of a runaway reaction. The results of this analysis clearly show that the hazards are significantly increased as the mass of cyclopentadiene being stored is increased.**

## Introduction

Cyclopentadiene (CPD) is a common precursor in organic syntheses and is used in the preparation of benzonorbornadiene, an intermediate in early routes to varenicline (Scheme 1), which was recently approved as Chantix, an aid to smoking cessation treatment.[1] On gram scale, the usual laboratory precautions allow for safe operation. Careful study is required, however, before transition from the research laboratory to the manufacturing environment. Herein we examine the thermal stability of cyclopentadiene in more detail with particular attention to the relationship between temperature, volume, and solvent dilution for safe storage.

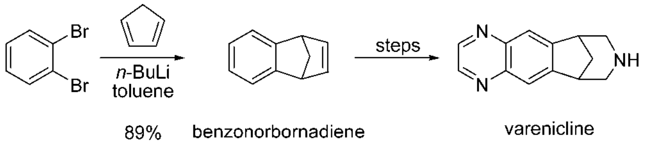
## Cracking and Storage of Cyclopentadiene

Cyclopentadiene is prepared by thermal cracking of the dimer at elevated temperature.



For laboratory scale, we used an *Organic Synthesis* method to prepare CPD.[2] On kilogram scale, however, the general practice of maintaining an inert atmosphere and low storage temperatures followed by immediate use becomes more challenging without dedicated cracking and storage equipment. Consequently, CPD generation and storage risks required further study.

***Scheme 1.*** **Discovery synthesis of varenicline**



Although CPD storage below −20 °C minimizes dimer formation to dicyclopentadiene (DCPD), [3] at room temperature, dimerization is spontaneous and exothermic. To prevent a thermal runaway, since the rate of reaction increases exponentially with temperature, CPD should not be stored in a sealed container without the provision for heat removal.[4] A large-scale incident involving CPD that occurred in 1992 at Nevcin Polymers in The Netherlands illustrates the potential hazards of inadequate heat removal. A 70:30 ratio of CPD to solvent was inadvertently charged to a reactor instead of the intended more dilute 30:70 ratio. As a result of the higher CPD concentration, the temperature rise from polymerization was greater than typically expected and a thermal runaway ensued. This initiated a secondary exothermic decomposition that ruptured the reactor, destroying the plant within a radius of 300 m of the reactor and causing a number of fatalities.[5]

We report here the thermal data obtained from adiabatic calorimetry to quantify the rate of heat evolution from CPD dimerization/polymerization as a function of time and temperature. Adiabatic calorimetry is often used to evaluate the exothermic potential of chemical decompositions. A VSP test (vent-sizing package, by Fauske and Associates) utilizes a 120 mL thin-walled stainless steel container to evaluate the rates of maximum temperature and pressure rise to closely simulate what would occur under low heat-loss conditions. As such, the VSP data can be used to properly size relief vents and used to directly assess thermal runaway behavior on larger scales (i.e., worst case conditions).

The results of a VSP test of CPD are shown in Figure 1 in which 83 mL (0.81 g/ml, 66.4 g) of cold (−20 °C) CPD was charged to an empty VSP can and the sample was allowed to warm to room temperature, at which time the adiabatic VSP experiment was initiated.[6]

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(1) (a) Varenicline tartrate (Chantix in the US, Champix elsewhere; Pfizer, Inc.). (b) Coe, J. W.; Brooks, P. R.; Vetelino, M. G.; Wirtz, M. C.; Arnold, E. P.; Sands, S. B.; Davis, T. I.; Lebel, L. A.; Fox, C. B.; Shrikhande, A.; Schaeffer, E.; Rollema, H.; Lu, Y.; Mansbach, R. S.; Chambers, L. K.; Rovetti, C. C.; Schulz, D. W.; Tingley, F. D., III; O'Neill, B. T. *J. Med. Chem.* **2005**, *48*, 3474–3477. (c) Coe, J. W.; Wirtz, M. C.; Bashore, C. G.; Candler, J. *Org. Lett* **2004**, *6*, 1589–1592. (d) Brooks, P. R.; Caron, S.; Coe, J. W.; Ng, K. K.; Singer, R. A.; Vazquez, E.; Vetelino, M. G.; Watson, H. H., Jr.; Whritenour, D. C.; Wirtz, M. C. *Synthesis* **2004**, *11*, 1755–1758.

(2) Moffett, R. B. *Org. Synth.* **1963**, *IV*, 238–243.

(3) Cheung, P. Cyclopentadiene and dicylopentadiene. In *Kirk–Othmer Encyclopedia of Chemical Technology*, 5th ed.; John Wiley & Sons: New York, 2001; Vol. 8, pp 219–235.

(4) *Bretherick's Handbook of Reactive Chemical Hazards*, 6th ed.; Butterworth-Heinemann: Oxford, 1999.

(5) Starkie, A.; Rowe, S. *Chem. Br.* **1996**, *Feb*, 34–38.

(6) The specific thermocouple calibration used during the VSP experiment does not accurately track temperature below 24 °C in this case, so only temperatures above 24 °C were recorded.

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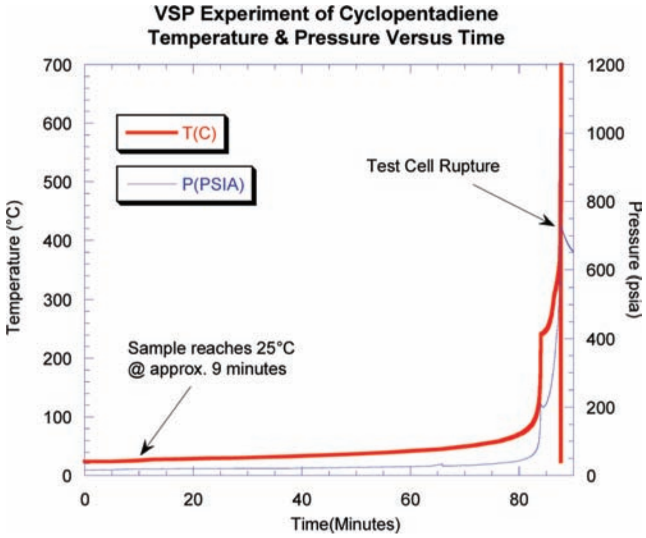

***Figure 1.*** **Thermal runaway observed for CPD under adiabatic test conditions in VSP, in which 83 mL of CPD was charged to the test cell. As the rate of exothermic dimerization increased, the temperature and pressure increased exponentially until the test cell ruptured.**

The VSP test revealed a slow exotherm upon reaching 25 °C that rose to over 200 °C and 200 psi. This was followed by an additional thermal event that achieved even higher temperatures and pressures (700 °C and 1200 psi) before violently rupturing the test cell. Upon cooling, the remaining test cell was examined and had burst around the welded seam at the top. The pressure vessel, lid, walls, and insulation were covered in brown viscous liquid and around this area was a black-brown solid material believed to be thermally decomposed DCPD polymeric products. If we assume the initial portion of the runaway (up to 240 °C) was due solely to dimerization kinetics, then the calculated heat of dimerization is in the range of 30 to 36 kJ/mol.[7]

These data show that the consequences of a runaway reaction in a well-sealed container are severe. The primary exotherm from CPD dimerization is shown as the rate of temperature rise or self-heat rate versus temperature in Figure 2. The magnitude of the rate is evident: the rate of temperature rise approaches 1000 °C/min!

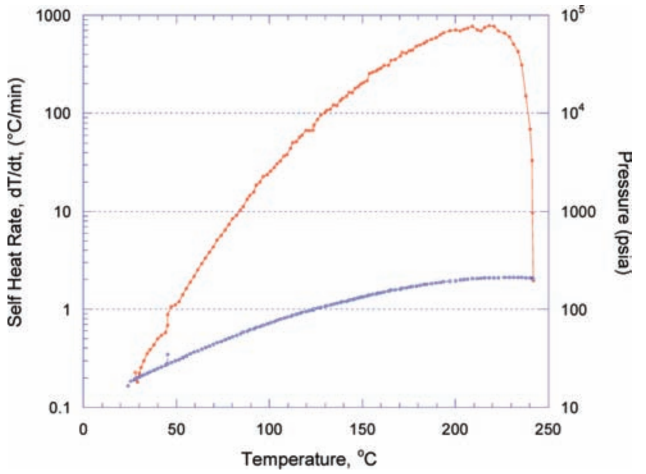

***Figure 2.*** **Thermal runaway observed for CPD under adiabatic test conditions in VSP plotted as self-heat rate $dT/dt$ (°C/min) versus temperature (°C).**

The initial exotherm is clearly due to dimerization of CPD to DCPD occurring as a thermal runaway reaction. When the temperature exceeds 200 °C, thermal decomposition of the DCPD is observed. This is apparent from a comparison of the differential scanning calorimetry (DSC) data for CPD and DCPD as shown in Figure 3. The DSC trace for CPD (Figure 3A) clearly shows that the exotherm due to dimerization occurs with a heat evolution of approximately 520 J/g or 34.4 kJ/mol. At higher temperatures secondary exothermic events are observed as seen in the bimodal heat flow curves. We believe this is evidence for the heat of polymerization to higher polymers of DCPD and other decomposition pathways.[8] This is supported by the DSC trace of DCPD (Figure 3B). At temperatures above 200 °C a bimodal exotherm is clearly seen, but no significant exotherm is observed below 200 °C.

Good consistency was obtained from DSC and VSP for the heat of dimerization with 34 kJ/mol measured from DSC and 30–36 kJ/mol calculated by VSP. This is approximately half of the energy that is reported for heat of dimerization in Kirk–Othmer Encyclopedia of Chemical Technology,[3] who reports 75 kJ/mol. One possibility is that the Kirk–Othmer reference of 75 kJ/mol includes both heat of dimerization and decomposition. Our DSC results support this as the combined contributions of dimerization (34 kJ/mol) and decomposition energy (34 kJ/mol) is 68 kJ/mol, comparable to 75 kJ/mol from Kirk–Othmer.

Dilution in solvent can be used to significantly reduce the severity of the runaway reaction by providing additional heat capacity and by slowing the second and higher order reactions. For example, a 50 wt % CPD in heptane solution was studied, and a maximum self-heat rate of 0.2 °C/min and maximum pressure of only 28 psi were observed.[9] Dilution, however, requires larger storage capacity for extended periods prior to use, as well as compatibility of the additional solvent in the next-step reaction.

On the basis of these observations and additional thermal experiments (e.g., DSC, ARC), two recommendations for safe CPD storage are proposed:

- Store pure CPD (packed in dry ice) at −40 to −50 °C with an internal temperature monitoring device for volumes of 1–5 L. This provides an approximately 50 °C margin of safety from the critical ambient temperature.

Caution: If CPD is being collected from a thermal cracker the receiver should always be maintained below −40 °C.

- For larger volumes immediately dilute the CPD directly from the thermal cracker with 10 vol of solvent (heptanes) and store cold (at −20 °C or lower to minimize dimer formation). Agitation of the CPD–heptane solution in a jacketed temperature-controlled vessel is recommended for large volumes.

Warning: Pure CPD and diluted CPD must be prepared and packed at or below the recommended storage conditions. It is

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(7) Heat of dimerization = MW × Phi × cp × $\Delta T$ MW = (66.1 g/mol)(1.16)(1.8 J/gC)(260 °C)KJ/1000J = 35.9 kJ/mol assuming an initial temperature of −20 °C where $\Delta T$ = 260 °C or 30 kJ/mol assuming an initial temperature of 20 °C.

(8) Wilson, P. J.; Wells, J. H. *Chem. Rev.* **1944**, (34), 1–50.

(9) Other solvents have not been evaluated.

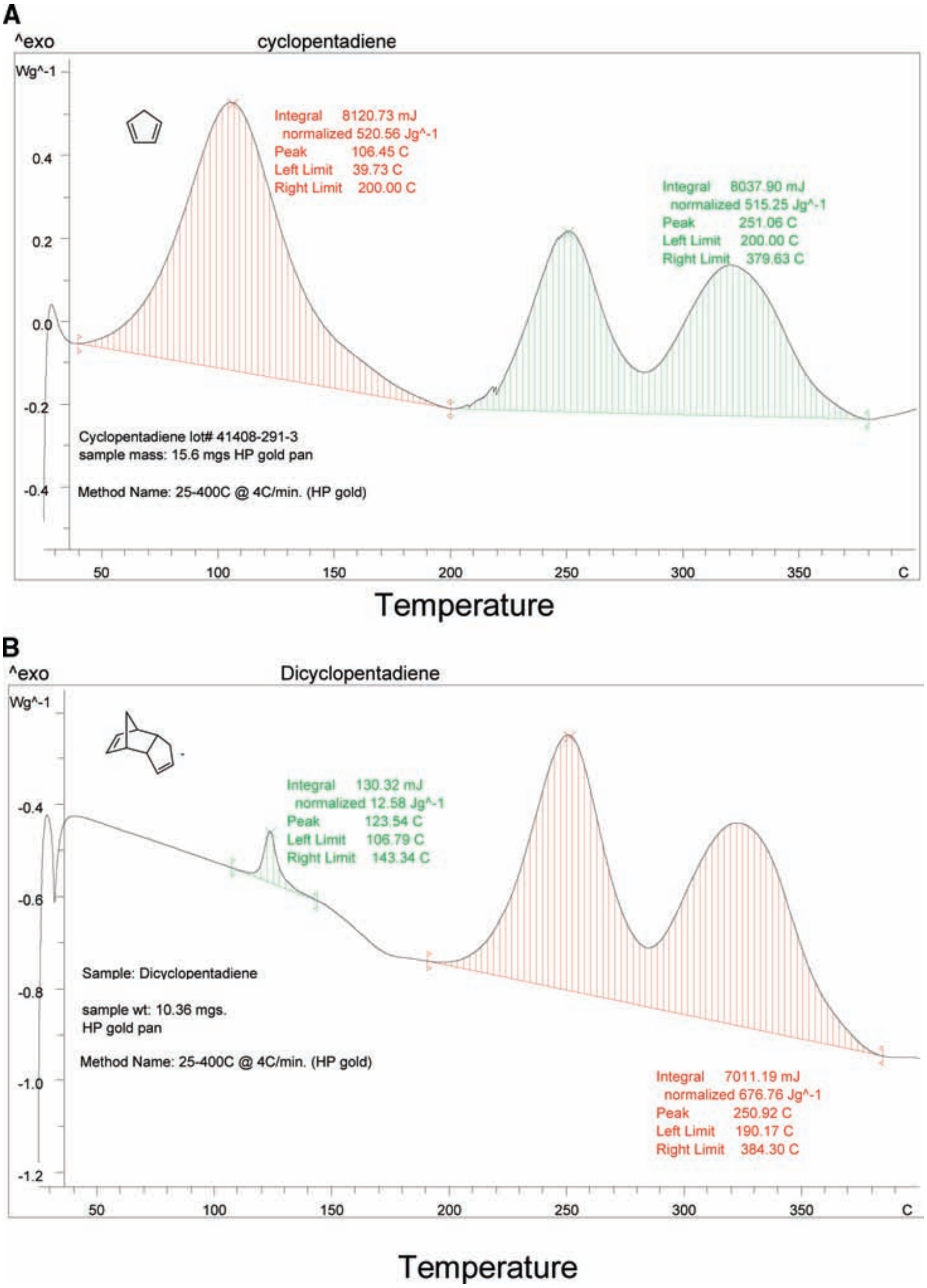

***Figure 3.*** **Differential scanning calorimetry of (A) CPD and (B) DCPD scanned from ambient to 400 °C in gold-plated stainless steel crucibles. The area shaded under the curves indicate the integral or total heat liberated from the exothermic event.**

a common industrial mistake to assume that placing a drum packed at room temperature into a −20 °C cold room complies with “store at −20 °C”. For example, CPD that is allowed to warm up before placing into cold storage could still thermally run away; this is because the safe storage conditions are calculated on the basis of the dimerization kinetics of CPD at those prevailing storage conditions.

## Discussion of Energy Balance

Given that CPD is used frequently on gram scale it is worth discussing the thermal data in the context of storage conditions. The thermal runaway data presented here for CPD, as measured in the adiabatic calorimeter, represents a worst case scenario under low heat loss conditions with no stirring. It is similar to what would happen if you placed cold CPD and sealed it in a well-insulated Dewar bottle. The slow exothermic dimerization would cause the temperature to rise, ultimately speeding the reaction rate until thermal runaway occurs as demonstrated on 83 mL scale in Figures 1 and 2.

In the following section we describe the extrapolation to other storage containers and their respective heat transfer rates.

## Convective Heat Transfer

In convection, the mode of heat transfer is through fluid motion from either natural convection or forced convection such

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(10) Janna, W. S. *Engineering Heat Transfer*; PWS Publishers: Boston, 1986.

(11) Ferguson, H. D. *J. Hazard. Mater.* **1994**, *37*, 285–302.

(12) The heat generation rate was corrected for the Phi Factor of the test cell. The Phi Factor was 1.16.

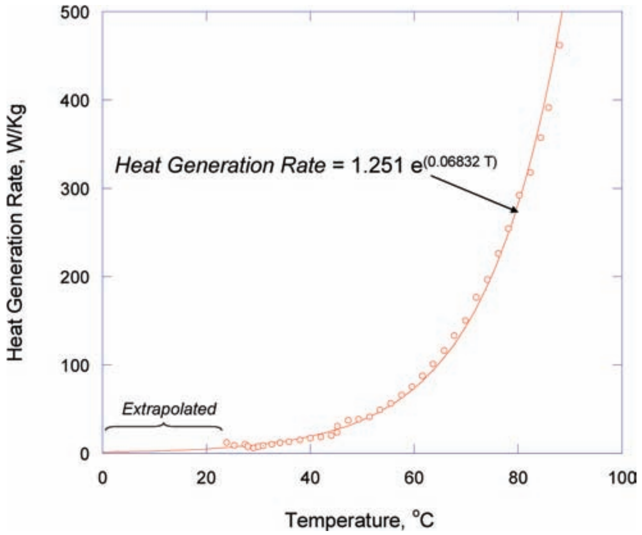

***Figure 4.*** **Thermal (VSP) data for CPD converted to heat generation rate versus temperature.**

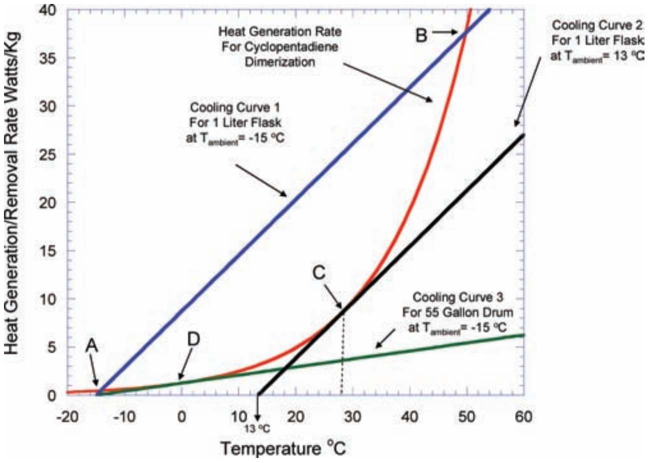

***Figure 5.*** **Heat generation and heat removal (i.e., cooling) analysis. Point A: stable operating point for a 1-L flask of CPD. Point B: an unstable operating point. Point C: unstable critical ambient temperature for 1-L flask of CPD. Point D: unstable critical ambient temperature for 55-gal drum of CPD. Heat loss curves are based on quiescent conditions (no agitation).**

as via fluid pumping or fan. Under convective heat transfer, heat is transferred from an object to the surroundings according to eq 1, known as Newton's Law of Cooling[10]

$$q = h_c A(T - T_\infty) \tag{1}$$

where $h_c$ is the average convection heat transfer coefficient, $A$ is the surface area, and $(T - T_\infty)$ is the temperature difference driving force between the object and the air temperature, $T_\infty$. The larger the temperature difference, the faster the heat transfer rate will be, for a given $h_c$. Physically, the $h_c$ value is the film conductance, so if the object is well-insulated, it will have high resistance to heat transfer and thus a low $h_c$ value where $h_c$ typically has units of W/m$^2$K. The following discussion makes reference to measured heat transfer coefficients for storage vessels containing liquids while being cooled in air (e.g., in nonagitated vessels).[11] The measurements were performed with water as the liquid inside the vessel. Because the dominant resistance to heat transfer, through natural convection, lies on the air side of the vessel, the application of the measured values to approximate CPD storage conditions was deemed justified.

## Heat Generation

To perform the energy balance we set out to understand the rate of heat evolution for dimerization of neat CPD. Consider Figure 4, which is a plot of rate of heat release of CPD versus temperature.[12] The rate of heat release is directly proportional to the rate of reaction which in turn increases exponentially with temperature according to eq 2 for a first order reaction:

$$q = \Delta H_r V k C_a = \Delta H_r V C_a A\ e^{(-E/RT)} \equiv [\text{units of W} = \text{J/s}] \tag{2}$$

A least squares curve fit of the heat generation rate data between 25 and 75 °C produced the following equation, after normalizing to the mass of the CPD, where $T$ has units of °C (Figure 4):

$$\text{W/kg} = 1.2511\ e^{(0.0683217T)} \tag{3}$$

Because temperatures below 24 °C were not tracked by the VSP, the equation is extrapolated to −20 °C using the least squares fit. Figure 5 shows three cooling curves overlaid onto the heat generation curve from Figure 4 to illustrate the effect of ambient storage temperature and vessel size. Of special interest are the intersection points at A, B, C, and D:

•Cooling curve **1** is for a 1-L flask cooled in air for a storage condition ($T_{\text{ambient}}$) of −15 °C.

•Cooling curve **2** is the cooling curve for the same 1-L flask for a storage condition of +13 °C

•Cooling curve **3** is the cooling curve for a 55-gal drum stored at −15 °C.

Cooling curve **1** (Figure 5) intersects the heat generation curve at two points, points A and B, and represents steady-state conditions, as this is where the heat generation equals the cooling rates. However, point A represents a stable operating condition, whereas point B represents an unstable operating condition. Clearly any slight perturbation in temperature above point B causes the heat rate to exceed the cooling rate causing thermal runaway or explosion to result. Any perturbation near point A, on the other hand, results in the system returning to point A. The slope of the cooling curve is determined from the data taken from Table 1 and substituting into eq 1. In this case

$$Q_{\text{cooling curve } \mathbf{1} (\text{1-L flask})} = 0.58\ \text{W/kgK}\ (T - (-15\ °\text{C})) \tag{4}$$

where −15 °C represents the ambient temperature for this cooling curve as noted by where it crosses the $x$-axis at zero heat loss.

Cooling curve **2** (Figure 5) illustrates the extreme case in the 1-L flask scenario if the ambient storage condition is too

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(13) Boudart, M. *Kinetics of Chemical Processes*; Butterworth-Heinemann: Woburn, MA, 1991.

***Table 1.*** **Heat transfer data and results calculated for CPD**[a]

| | heat transfer coefficent[b] W/m$^2$K | heat transfer area m$^2$ | specific rate of heat transfer W/kgK | critical internal temperature (calcd)°C | critical ambient temperature (calcd)°C |
|---|---|---|---|---|---|
| 100-mL flask (glass) | 12[c] | 0.01 | 1.2[c] | 39 | 24 |
| 10L flask (glass) | 12[d] | 0.048 | 0.58 | 28 | 13 |
| 55-gallon drum (steel) | 8.5[d] | 2.16 | 0.083 | −0.4 | −15 |

[a] Note the heat transfer coefficients for the flask and drum were measured values for water as cited in Ferguson et. al. Legend: W = watts or J/s, m = meters, K = Kelvin, kg = kilograms. [b] Janna (ref 10, p 18) cites heat transfer coefficient range of 5–25 W/m$^2$K for natural convection in air. [c] The data for the 100-mL flask data were estimated from the *U* value of the 1-L flask data, but correcting for surface area to volume ratio, a value of 1.2 W/KgK was obtained. [d] Heat transfer data from Ferguson et al..[11] These data are for nonagitated storage vessels. Agitated vessels typically have much higher heat transfer coefficents.

warm. Based on these conditions an unstable critical point exists at point C as shown. This is the highest ambient condition where the heat generation equals the cooling rate. However, point C represents an unstable and unsafe operating condition because a slight elevation in temperature could initiate a thermal runaway. Point C indicates that the inside flask temperature would be 28 °C while the ambient air temperature is +13 °C. The ambient temperature can easily be seen graphically as the temperature where the cooling curve crosses the *x*-axis: by definition this is where ($T = T_\infty$) so ($T - T_\infty$) = 0 and heat loss is zero. To further elaborate, point C on Figure 5 represents a critical point and is described as the point on the heat generation curve where the slope is equivalent to the slope of the heat loss curve. At this point it follows that the critical ambient temperature can be determined numerically via the derivative of eq 3 set to equal the slope of the heat loss curve according to eq 5.

$$\frac{\mathrm{d}Q_{\text{heat generation}}}{\mathrm{d}T} = 0.068321 \times 1.2511\ \mathrm{e}^{(0.068321 T_{\text{critical}})} = 0.58\ \mathrm{W/kgK} \quad (5)$$

Solving for $T_{\text{critical}}$ we find $T_{\text{critical}}$ = 28 °C. (See Table 1). Substituting $T_{\text{critical}}$ back into the eq 3 and setting $Q_{\text{heat generation}} = Q_{\text{heat loss}}$ gives $T_{\text{ambient}}$ = 13 °C and this generates eq 6 for cooling curve **2**.

$$Q_{\text{cooling curve }\mathbf{2}(\text{1-L flask at 13 °C})} = 0.58\ \mathrm{W/kgK}\ (T - 13\ °\mathrm{C}) \quad (6)$$

To illustrate the influence of storage container size, the calculated cooling curve **3** for a 55-gal steel drum is shown in Figure 5. It shows that at point D, where the heat generation curve intersects the cooling curve, critical internal temperature of the drum would be approximately −0.4 °C. The critical *ambient* temperature is found to be −15 °C for storing a 55-gal drum of CPD. The cooling curve **3** is described by eq 7:

$$Q_{\text{cooling curve }\mathbf{3}} = 0.083\ \mathrm{W/kgK}\ (T - (-15\ °\mathrm{C})) \quad (7)$$

The main difference between cooling curves **1** and **3** is the much lower rate of cooling per kilogram from the 55-gal drum as indicated by the difference in the specific heat transfer rate (Table 1, 0.58 vs 0.083 W/kgK for the 1-L flask and drum, respectively). Curves **1** and **3** indicate that for the same *ambient* temperature of −15 °C, a stable storage condition exists for the 1-L flask, but this is clearly an unsafe operating condition for the 55-gal drum.

From these results it is possible to conclude that a thermal runaway reaction would be expected to occur from CPD dimerization if the critical ambient temperature is reached or exceeded. The critical temperature is vessel-size-dependent. Although not shown in Figure 5 (but included in Table 1), the critical ambient temperature for a 100-mL flask was calculated to be approximately 24 °C, 11 °C warmer than for a 1-L flask (+13 °C) and 39 °C *warmer* than for the 55-gal drum (−15 °C). Clearly, as the scale of operation increases, the potential hazard increases significantly. For small unsealed storage vessels, there is a wider margin of safe operating temperatures than for larger vessels.

This discussion has focused on defining temperatures that may result in runaway reactions under sealed conditions. Another practical concern is storing at temperatures low enough to minimize dimerization to maintain CPD purity/potency. Kirk–Othmer reported a rate of 0.5 mol %/h dimerization at 0 °C and 1 mol %/h at 10 °C and thus recommended storing CPD at temperatures below −20 °C where dimerization is less than 0.05 mol %/h. This translates to less than 0.6% of dimer after 12 h at −20 °C.

## Conclusions

We have examined the thermal behavior of CPD dimerization in the context of storage conditions that could lead to thermal runaway reactions. Cold storage temperatures were recommended to minimize dimerization (for purity/potency) as well as to mitigate the potential for a runaway reaction. Given the wide-spread use of CPD it should be borne in mind that as the volume of CPD increases, the safe critical storage temperature decreases significantly. These data clearly demonstrate that provision should always be made to provide pressure relief to avoid overpressurization and the possibility of explosion in the event a thermal runaway occurs.

**Experimental.** For the VSP test, 83 mL (0.81 g/mL, 66.4 g) of cold (−20 °C) CPD was charged to an empty VSP can, and the sample was allowed to warm to room temperature at which time the adiabatic VSP experiment was started. The VSP test cell was 38 g. The Phi Factor correction was 1.16. The heat generation plot was calculated as follows: $q = [(m_{\text{test cell}} Cp_{\text{test cell}}) + (m_{\text{cpd}} Cp_{\text{cpd}})] \times \mathrm{d}T/\mathrm{d}t$ or $q = [(38.4\ \mathrm{g} \times 0.5\ \mathrm{J/gK}) + (83\ \mathrm{mL} \times 0.8\ \mathrm{g/mL}) \times (1.8\ \mathrm{J/gK}))] \times \mathrm{d}T/\mathrm{d}t = 138.7\mathrm{J/K} \times \mathrm{d}T/\mathrm{d}t$. Normalization to kilograms and using 66.4 g of CPD in the experiment, the proportionality factor becomes $138.7\ \mathrm{J/K} \times (66.4\ \mathrm{g})^{-1} \times (1000\ \mathrm{g/kg}) = 2090\ \mathrm{J/kgK} \times (\mathrm{d}T/\mathrm{d}t) \times (\mathrm{min}/60\ \mathrm{s}) = 34.8 \times \mathrm{d}T/\mathrm{d}t$ where $\mathrm{d}T/\mathrm{d}t$ has units of °C/min and $Q$ is W/Kg.

The VSP was from Fauske and Associates (Burr Ridge, Illinois).

For the DSC experiments, the samples were weighed to the nearest 0.1 mg into a gold-plated stainless steel high pressure crucible. The lid was crimped on with a crimper. The sample was heated from 25 to 400 °C at 4 °C/min using a Mettler 821 DSC.

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