Potential Explosion Hazards with Using DMSO and DMF in Chemical Reactions

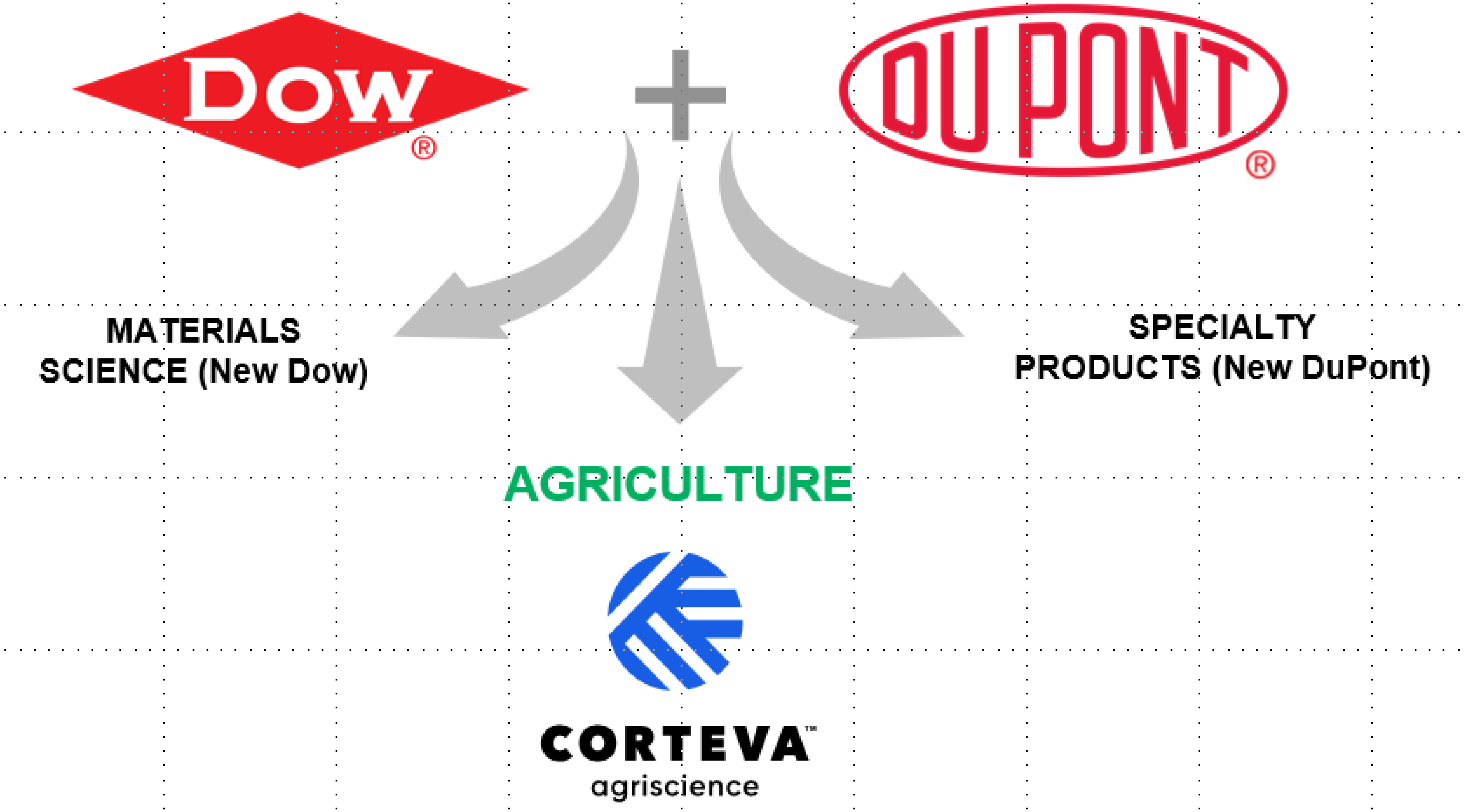
Qiang Yang

Product & Process Technology R&D, Corteva Agriscience

P2SAC Fall Conference, Purdue University, December 10, 2020

Corteva Agriscience™

FOUNDED ON THE RICH HERITAGES OF DOW AND DUPONT



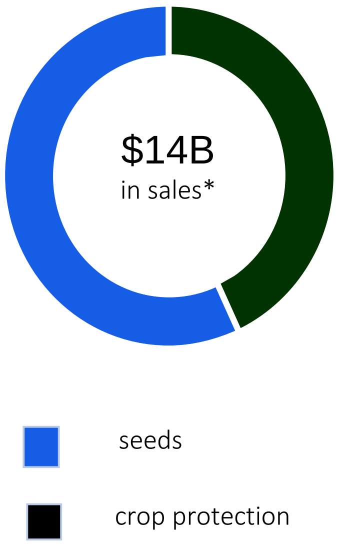
CORTEVA™
agriscience

22,000
people strong

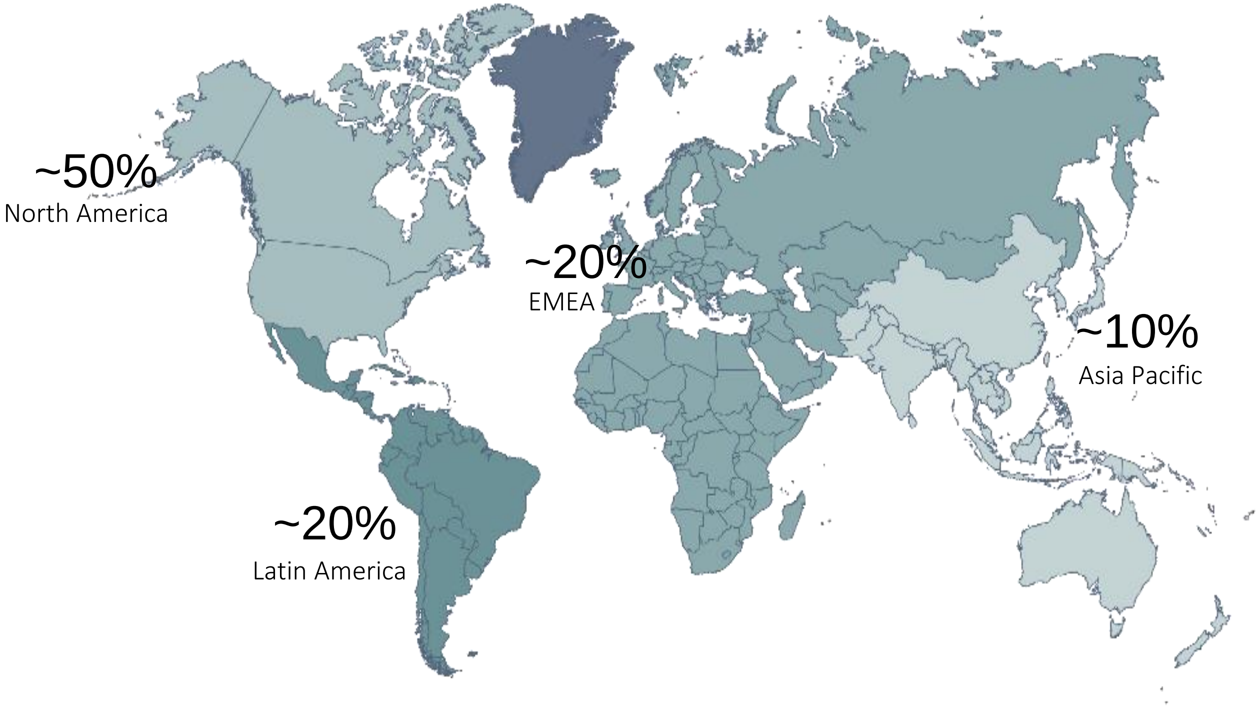
130+
countries

10+
crops

65+
active ingredients



*Excludes revenue associated with remedies



CORTEVA™
agriscience

Our Purpose

To enrich the lives of those who produce and those who consume, ensuring progress for generations to come.

Enrich Lives

Stand Tall

Build Together

Be Curious

Be Upstanding

Live Safely

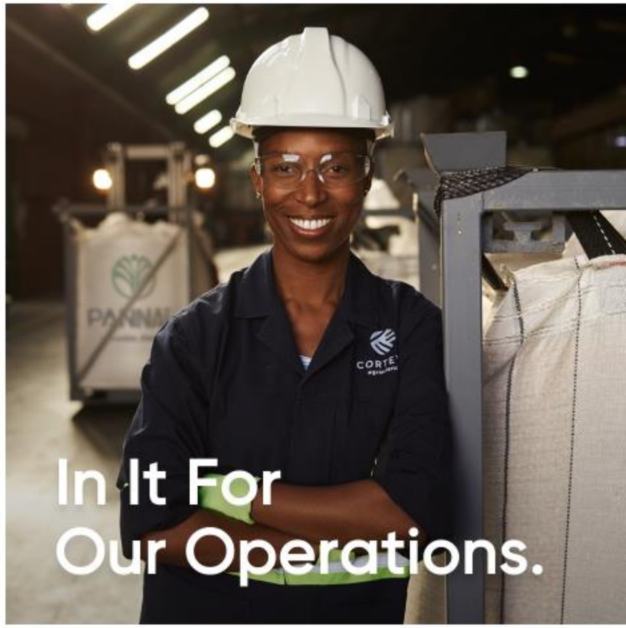
OUR 2030 COMMITMENTS TO SUSTAINABILITY

Learn more at sustainability.corteva.com

- Provide training to 25 million farmers
- Enrich the lives of 500 million smallholder farmers
- Decrease greenhouse gas emissions while increasing yields

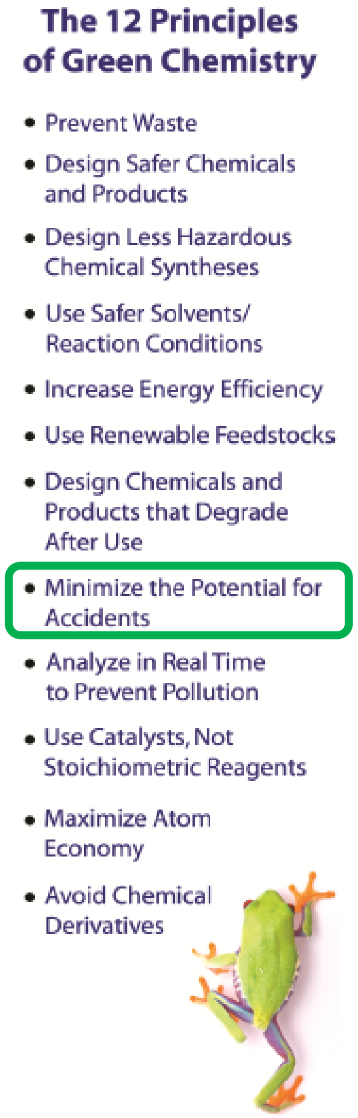
- Improve soil health on 30 million hectares
- Advance water stewardship
- Enhance biodiversity on 10 million hectares

- Keep employees safe
- Empower women, enable youth, and engage communities
- Volunteer 1 million hours
- Increase supply chain transparency



- Require sustainability criteria for new products
- Manage our greenhouse gas emissions
- Use only sustainable packaging
- Increase our sites' sustainability efforts

Why be Concerned with Process Safety?



To avoid incidents like these!

Process Safety Begins in the Lab!

Why?

- Most reactive chemical incidents occur in research laboratories.
- Most incidents involving a chemical reaction could have been prevented, if the process hazards were understood beforehand.

Solution

- Process safety should be considered early to avoid surprises during scale-up. Early identification of significant exotherms should be used to trigger the assessment of thermal hazard risks related to the process before scale-up.
- Personal safety should be considered always. A safe, well-controlled working environment in both the lab and plant is key to avoiding incidents during synthesis, safety studies and manufacturing.

Courtesy of Mettler Toledo

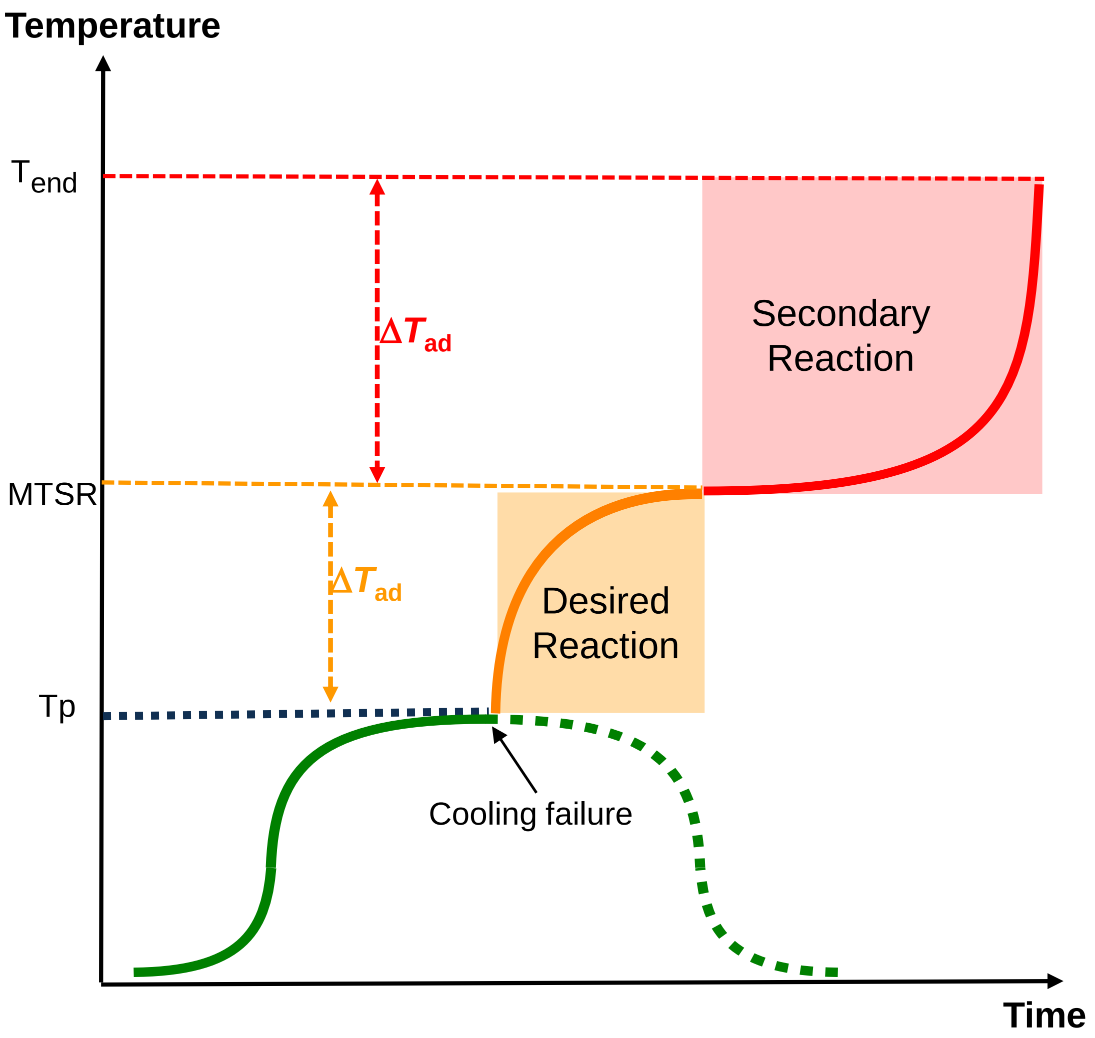
Thermal Hazard Analysis

T_p: Process temperature

ΔT_{ad}: Adiabatic temperature rise

MTSR: $T_p + \Delta T_{ad}$

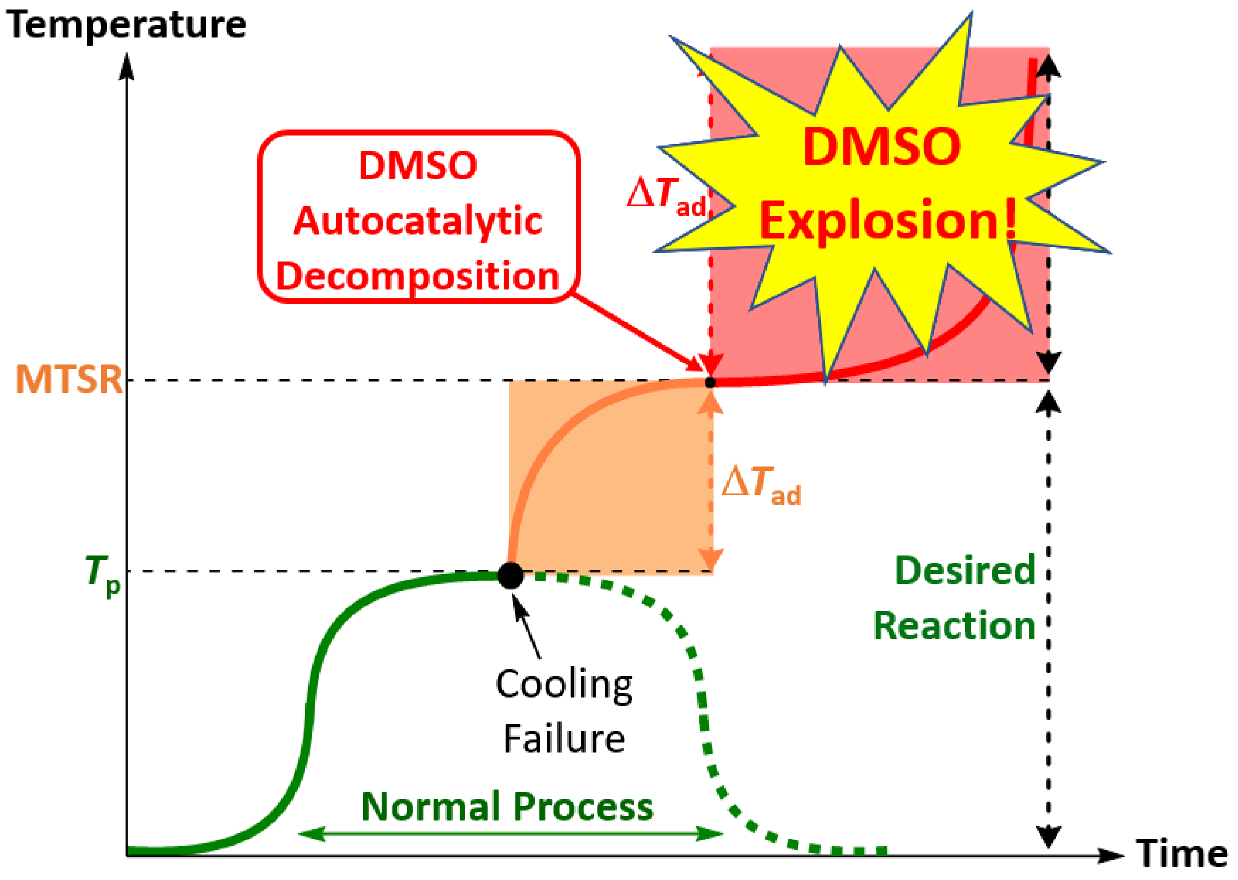
- Desired Reaction can be characterized using Reaction Calorimeters such as RC1 and HF Calorimeter.
- Secondary reaction can be characterized with DSC, ARC, or VSP, etc.
- If the reaction reaches the MTSR, will it trigger a decomposition reaction?
- Is there a potential thermal runaway?



Stoessel, F. Basel, CH, *WILEY-VCH Verlag GmbH & Co. KGaA*, 2008

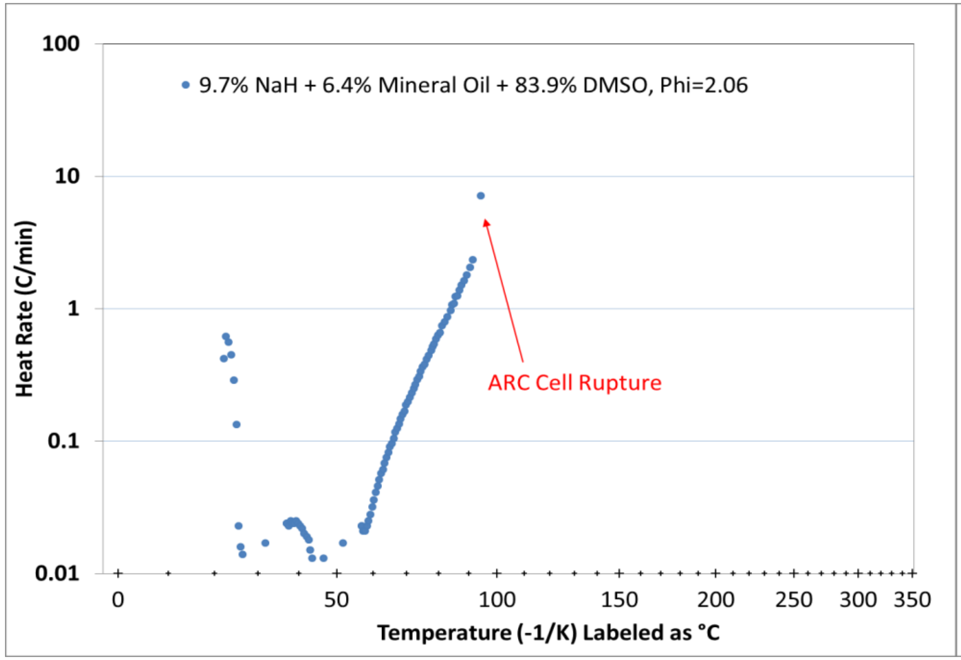
DMSO is Incompatible with a Variety of Substances…

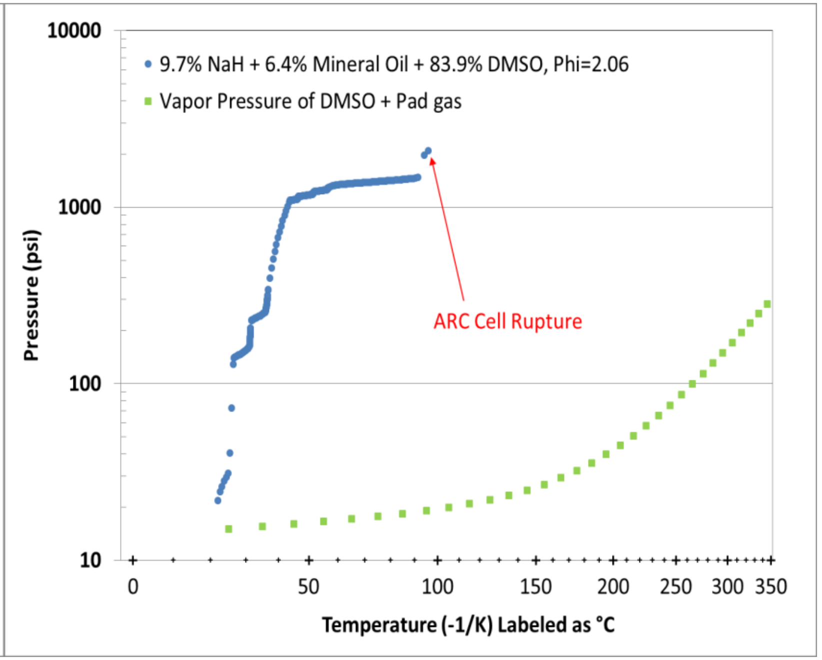
- Bases
- Acids
- Halides
- Metals and metal ions
- Electrophiles
- Oxidants
- Reductants
- **Almost any substances in DMSO will lower the onset temperature and increase the severity of DMSO decomposition.**



Org. Process Res. Dev. **2020**, *24*, 916–939.

Potential Explosion Hazards of DMSO with Bases: NaH

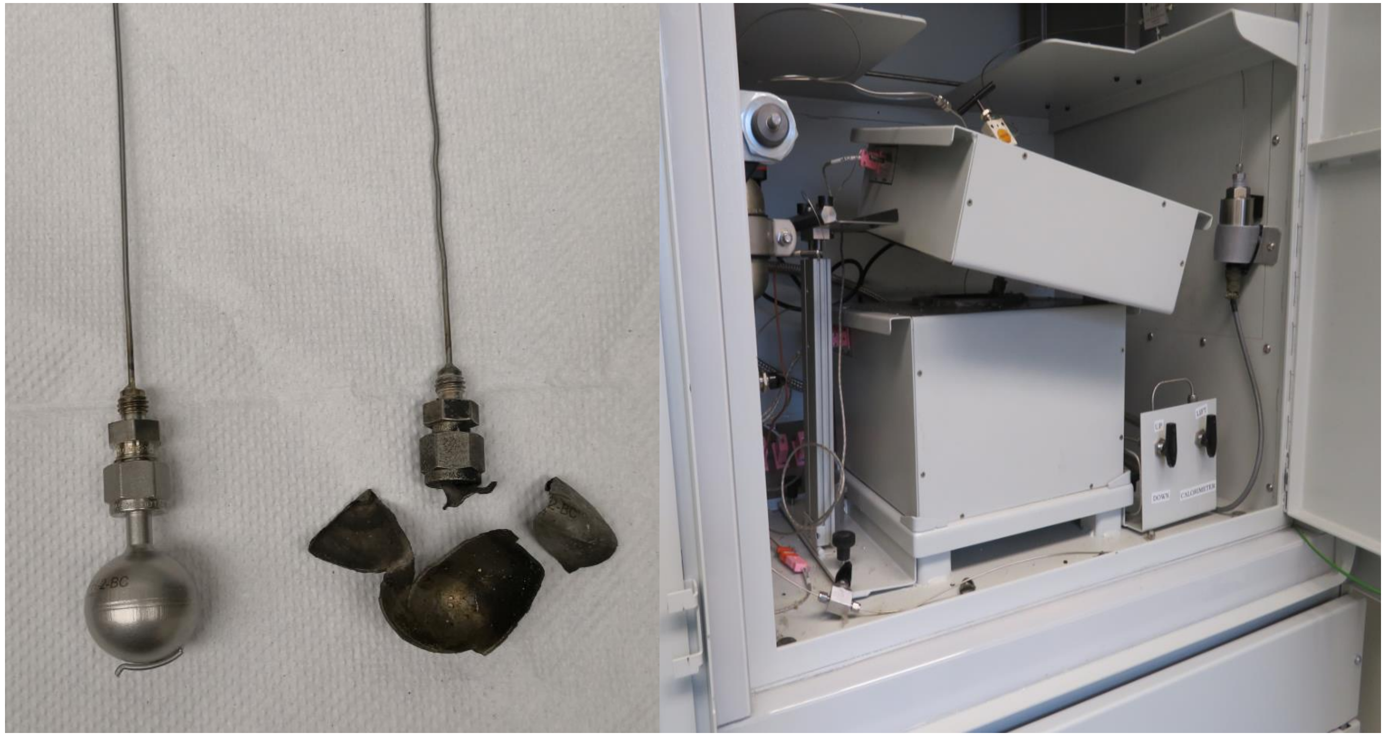




- The ARC analysis was performed with 4.55 grams of a mixture of 16.1% NaH in mineral oil (60 wt%) and 83.9% DMSO.
- ARC recorded two small exothermic events, followed by a significant exothermic event with an onset temperature of 56.8 °C.

Org. Process Res. Dev. **2019**, *23*, 2210–2217.

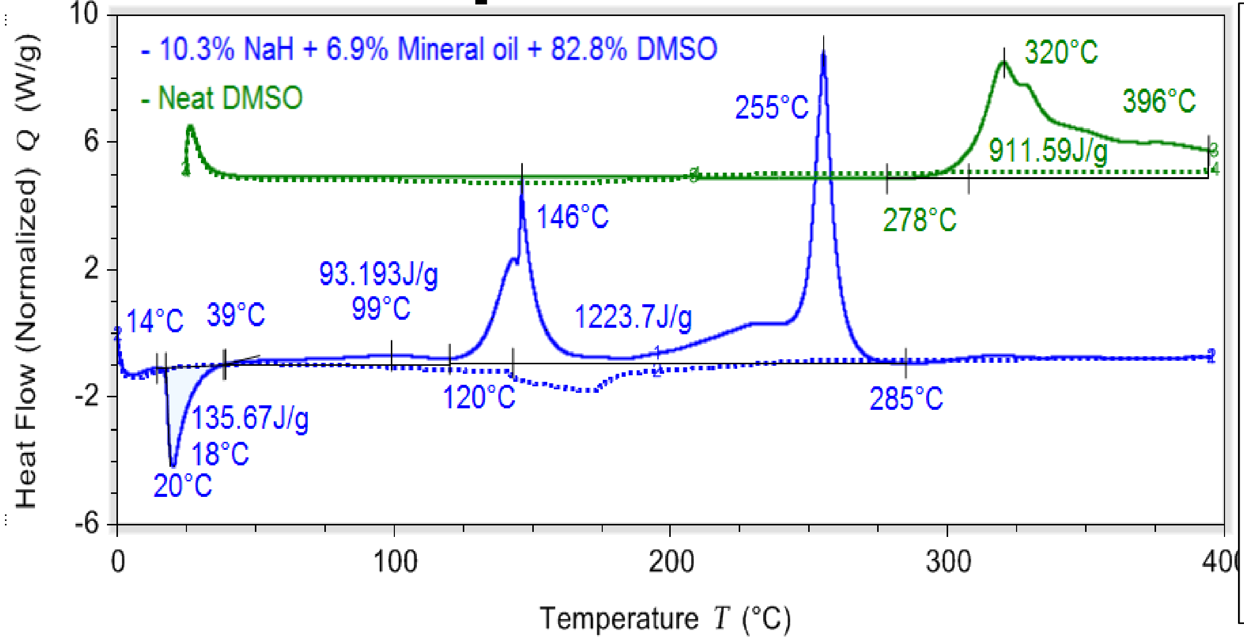
Potential Explosion Hazards of DMSO with Bases: NaH

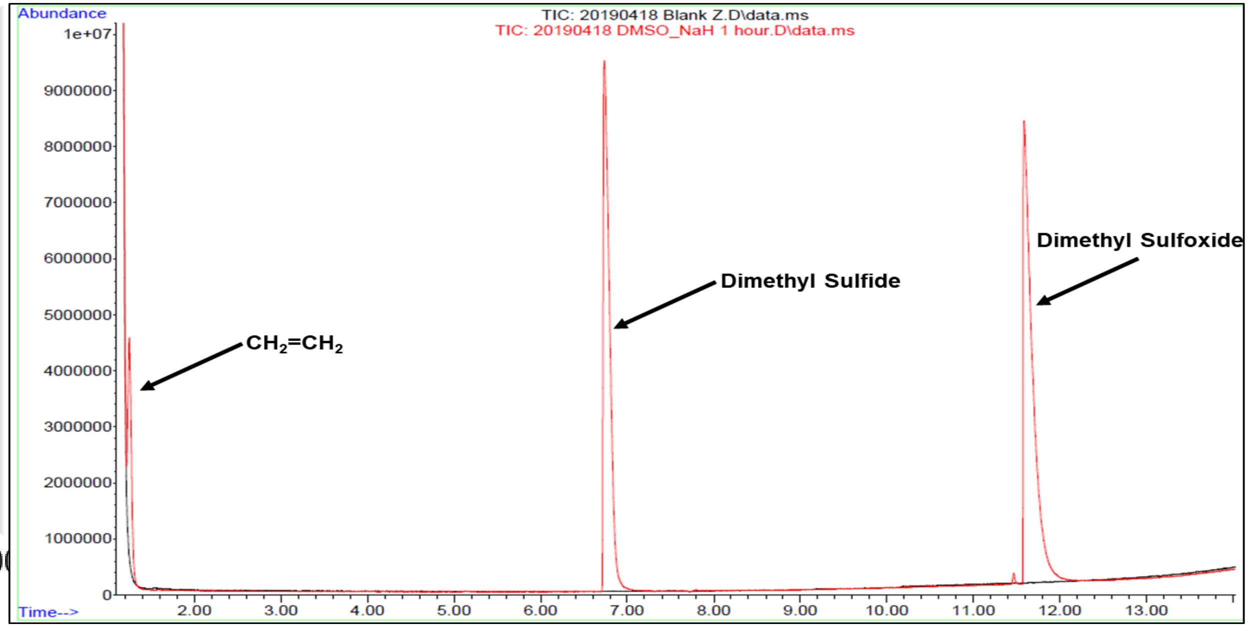


- This exotherm caused the rupture of an ARC cell designed with an average burst pressure of 14,500 psi.
- The force generated from this explosion was strong enough to displace the reactor housing.

Org. Process Res. Dev. **2019**, *23*, 2210–2217.

Potential Explosion Hazards of DMSO with Bases: NaH

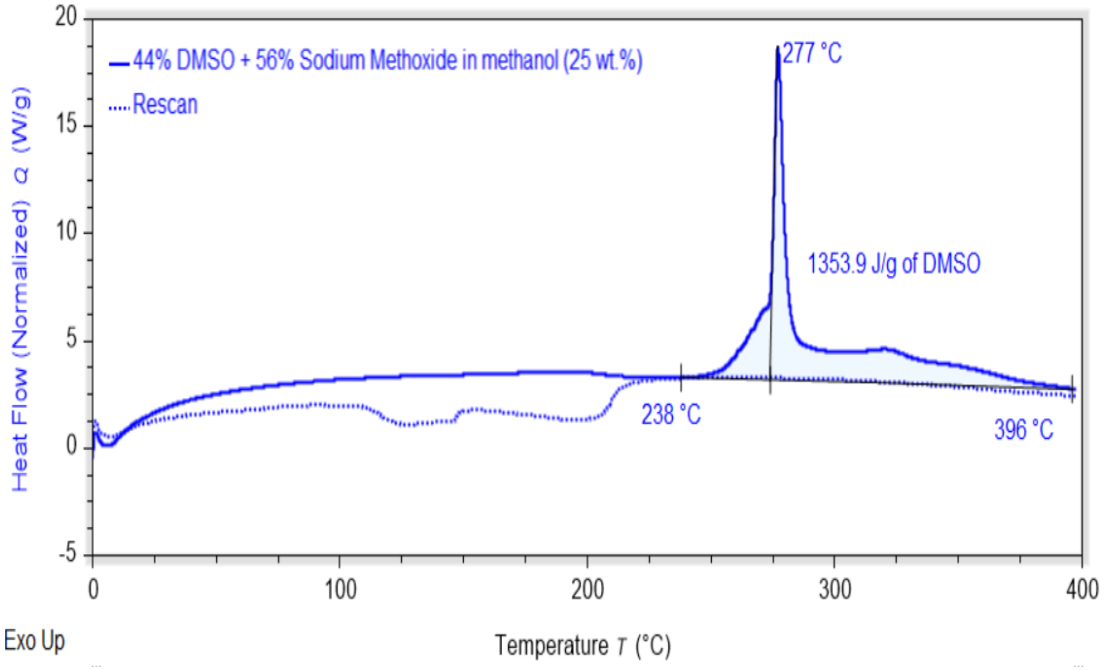


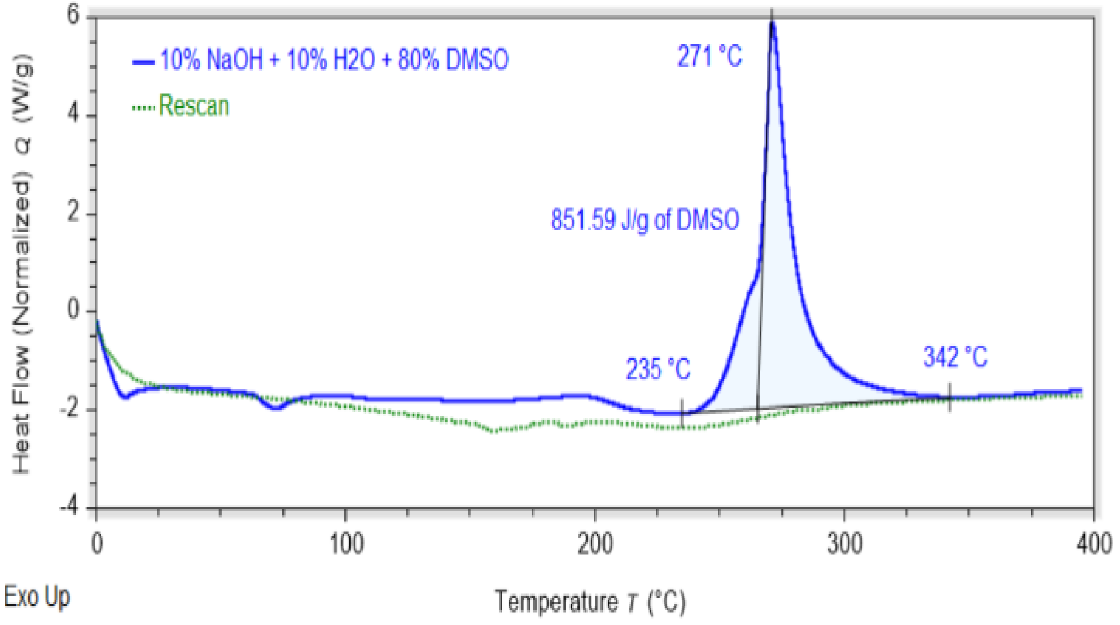


- The minor event (39 °C to 120 °C) generated a significant amount of non-condensable gases that raised pressure from 129 to 1289 psi.
- The combined total heat release of –810.2 J/g was deemed explosive according to the Yoshida correlation.
- Gaseous products from the minor event include ethylene ($CH_2=CH_2$) and dimethyl sulfide (CH_3SCH_3).

Org. Process Res. Dev. **2019**, *23*, 2210–2217.

Potential Hazards of DMSO with Bases: NaOMe and NaOH

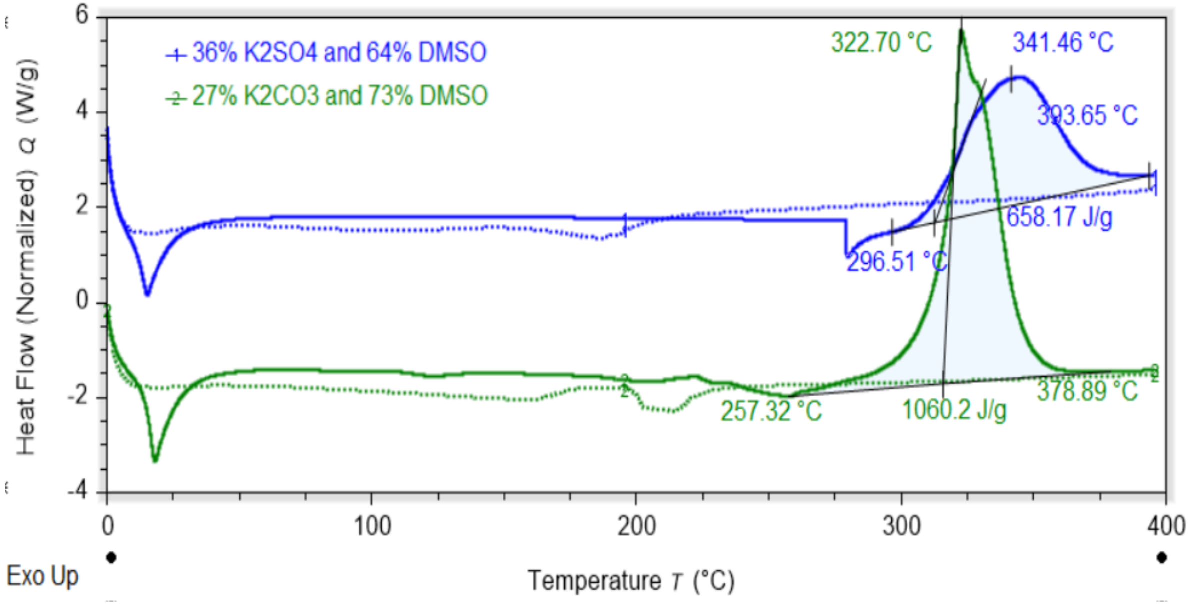




- DSC of a mixture of 56% NaOMe solution in MeOH (25 wt% in MeOH) and 44% DMSO showed a lower onset temperature of 238 °C, with a total energy of –1354 J/g (normalized to the mass of DMSO).
- DSC of a mixture of 20% aqueous NaOH (50 wt%) and 80% DMSO detected an exothermic event at 235 °C, with a total energy output of –852 J/g of DMSO.
- The sharp narrow peaks are characteristic of autocatalytic reactions that represent much more significant hazards of thermal decomposition

Org. Process Res. Dev. **2020**, *24*, 916–939.

Potential Hazards of DMSO with a Weaker Base, Na_2CO_3

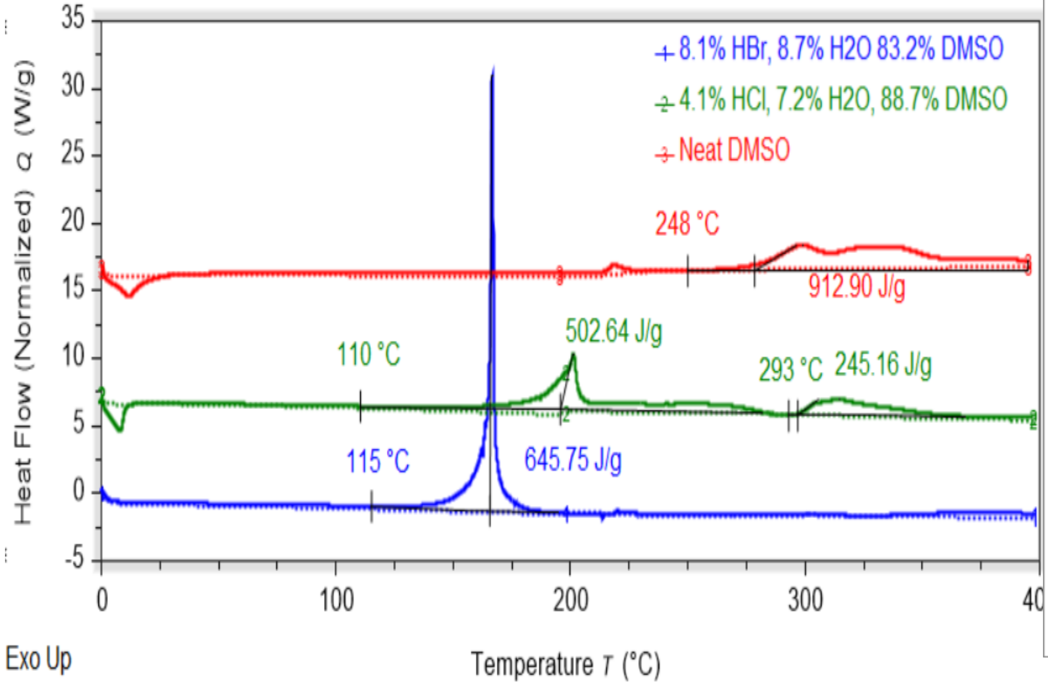


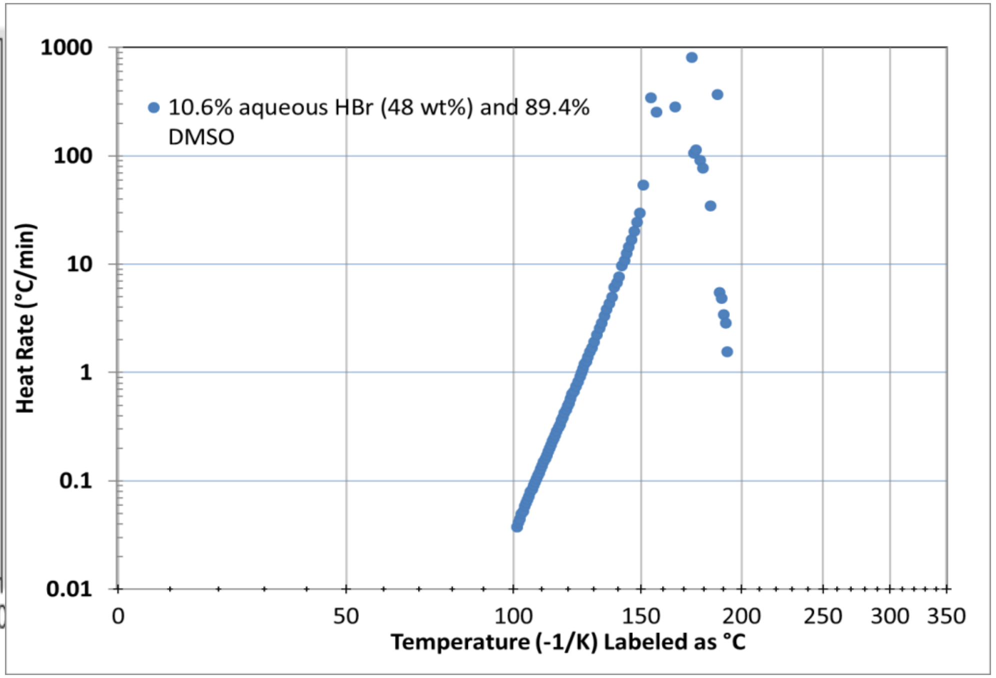
- DSC of a mixture of 73 wt% of DMSO and 27 wt% of K_2CO_3 showed a significant exothermic event with an onset temperature of 257 °C and an energy release of –1060 J/g (normalized to the mass of DMSO).
- A control experiment of a mixture of 36 wt% of K_2SO_4 and 64 wt% of DMSO indicated decomposition occurred at ca. 296 °C with a total energy release of –658 J/g (normalized to the mass of DMSO).

Org. Process Res. Dev. **2020**, *24*, 916–939.

Potential Explosion Hazards of DMSO with Acids

- An explosion occurred in 1983 from a mixture of DMSO and *p*-nitrotoluenesulfonic acid in a 2000-gallon reactor at 60 °C.
- Another explosion occurred in 1991 during the vacuum distillation of an old mixture of 88% DMSO, 7% water, and 5% 2-bromomethyl-1,3-dioxane. HBr was detected as one of degradants.
- DSC and ARC analysis of HBr/DMSO and HCl/DMSO mixtures:

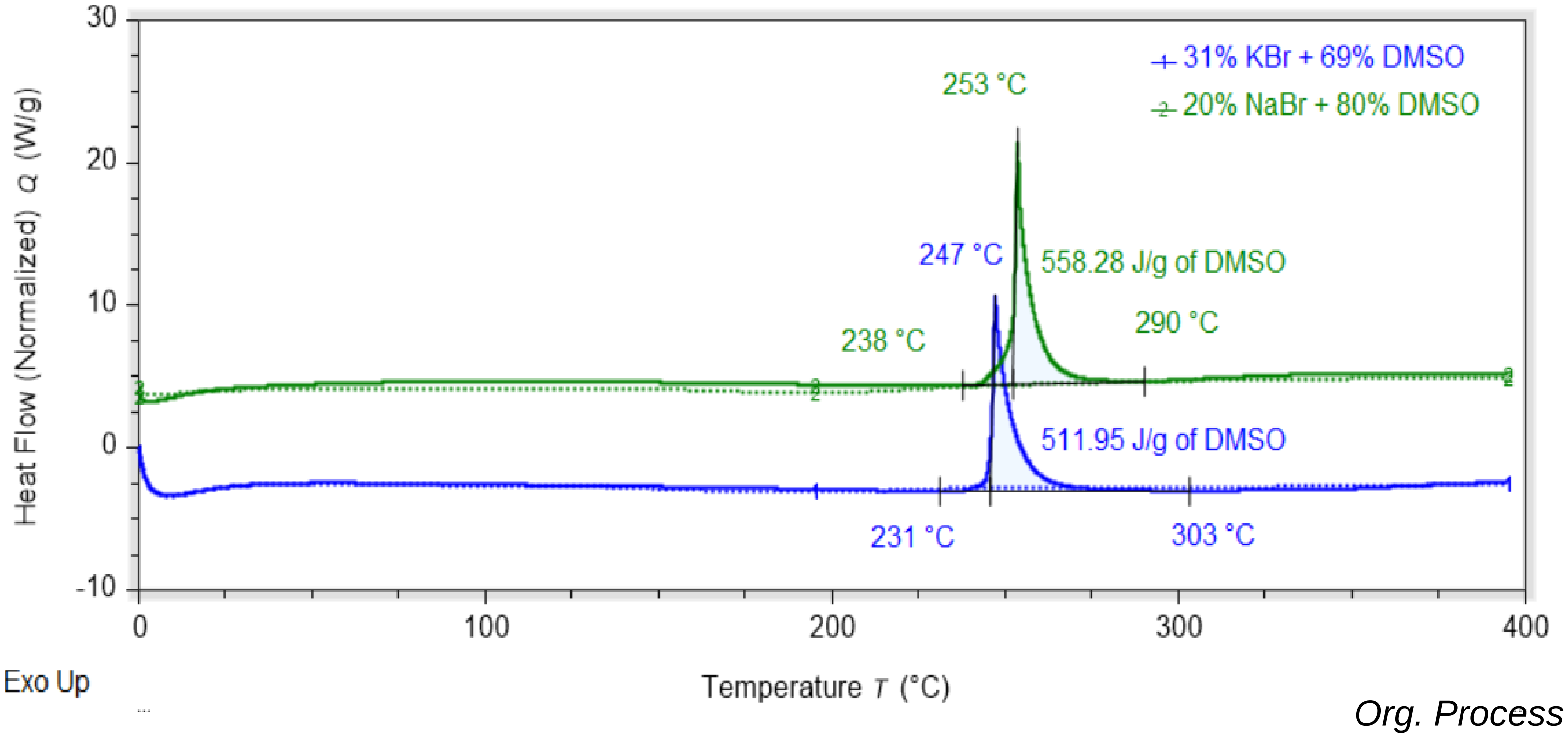




Org. Process Res. Dev. **2020**, *24*, 916–939.

Potential Explosion Hazards of DMSO with Halides

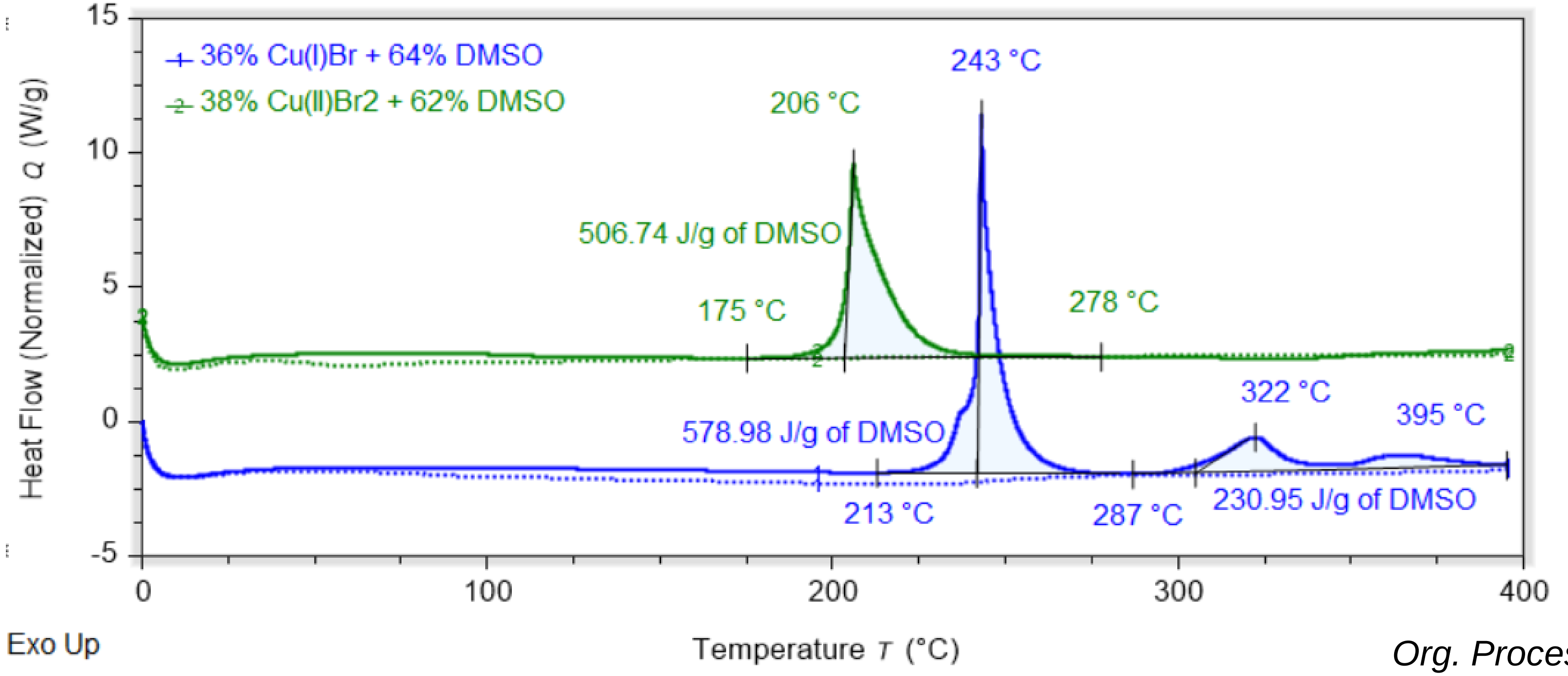
- An explosion occurred when 0.105 mol of IF_5 was added to a cold solution of 0.105 mol of DMSO in sulfolane.
- A detonation was reported when 880 g of DMSO was treated with 600 g of methyl bromide (MeBr).
- Two large scale explosions associated with the decomposition of DMSO during recovery of DMSO via distillation from mixtures containing potassium bromide (KBr) occurred in 1977 and 1979, respectively.
- DSC of KBr/DMSO and NaBr/DMSO mixtures:



Org. Process Res. Dev. **2020**, *24*, 916–939.

Potential Explosion Hazards of DMSO with Metals and Salts

- A runaway reaction involving the interaction of copper wool with DMSO in the presence of trichloroacetic acid.
- Violent reaction of DMSO with AgF_2 was reported in 1969.
- A reaction mixture exploded during scale up of a coordinatively linked Yb Metal–Organic Framework (MOF) involving 12 mL of DMSO.
- DSC of CuBr/DMSO and $CuBr_2$/DMSO mixtures:



Org. Process Res. Dev. **2020**, *24*, 916–939.

Potential Explosion Hazards of DMSO with Electrophiles

- DMSO reacts violently with electrophiles such as cyanuric chloride, acetyl chloride, benzoyl chloride, benzenesulfonyl chloride, thionyl chloride, phosphoryl chloride, and phosphorus trichloride.
- Mancuso et al. observed that oxalyl chloride reacted explosively with DMSO at room temperature.
- The byproducts from the reaction of DMSO with electrophiles include acids and/or chloride ion, which could further lower the onset temperature and increase the severity of DMSO decomposition to aggravate the potential safety hazards.
- Other electrophiles such as alkyl halides, sulfur trioxide (SO_3), sulfur dichloride (SCl_2), sulfur monochloride (S_2Cl_2), silicon tetrachloride ($SiCl_4$), carbonyl diisothiocyanate, and P_4O_{10}, etc. are also known to cause potential hazards associated with the thermal decomposition of DMSO.

Org. Process Res. Dev. **2020**, *24*, 916–939.

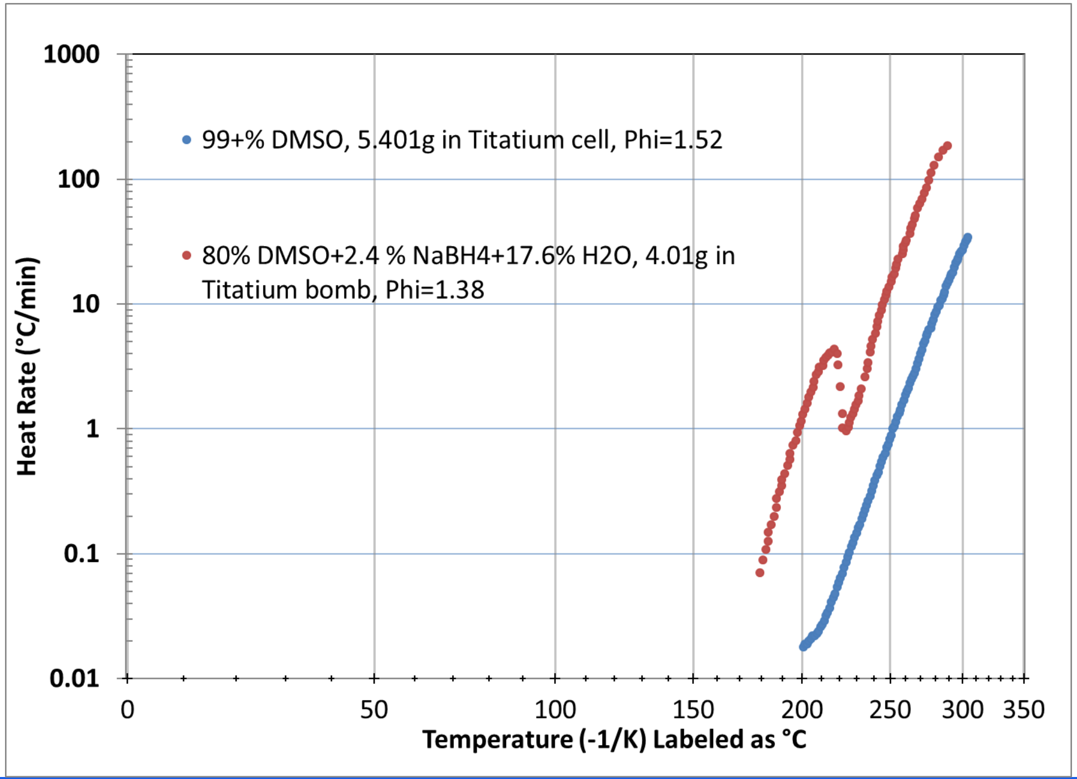
Potential Explosion Hazards of DMSO with Oxidants

- An explosion involving thermal decomposition of DMSO in the presence of $HClO_4$ was published in 1971.
- A fatality caused by explosion involving DMSO and $HClO_4$ was reported in 1991 when DMSO was accidentally in contact with residual $HClO_4$ in a titrimeter to determine bromamine acid content using $HClO_4$.
- Metal perchlorates solvated by DMSO are generally powerful explosives.
- Magnesium perchlorate [$Mg(ClO_4)_2$], a drying agent that has been frequently used for the preparation of anhydrous DMSO, caused an explosion during the distillation of DMSO over anhydrous $Mg(ClO_4)_2$.
- Other oxidants such as nitrogen dioxide (NO_2), metal chlorates, and metal permanganates, etc. have also been reported to react violently with DMSO to result in potential safety hazards.

Org. Process Res. Dev. **2020**, *24*, 916–939.

Potential Explosion Hazards of DMSO with Reductants

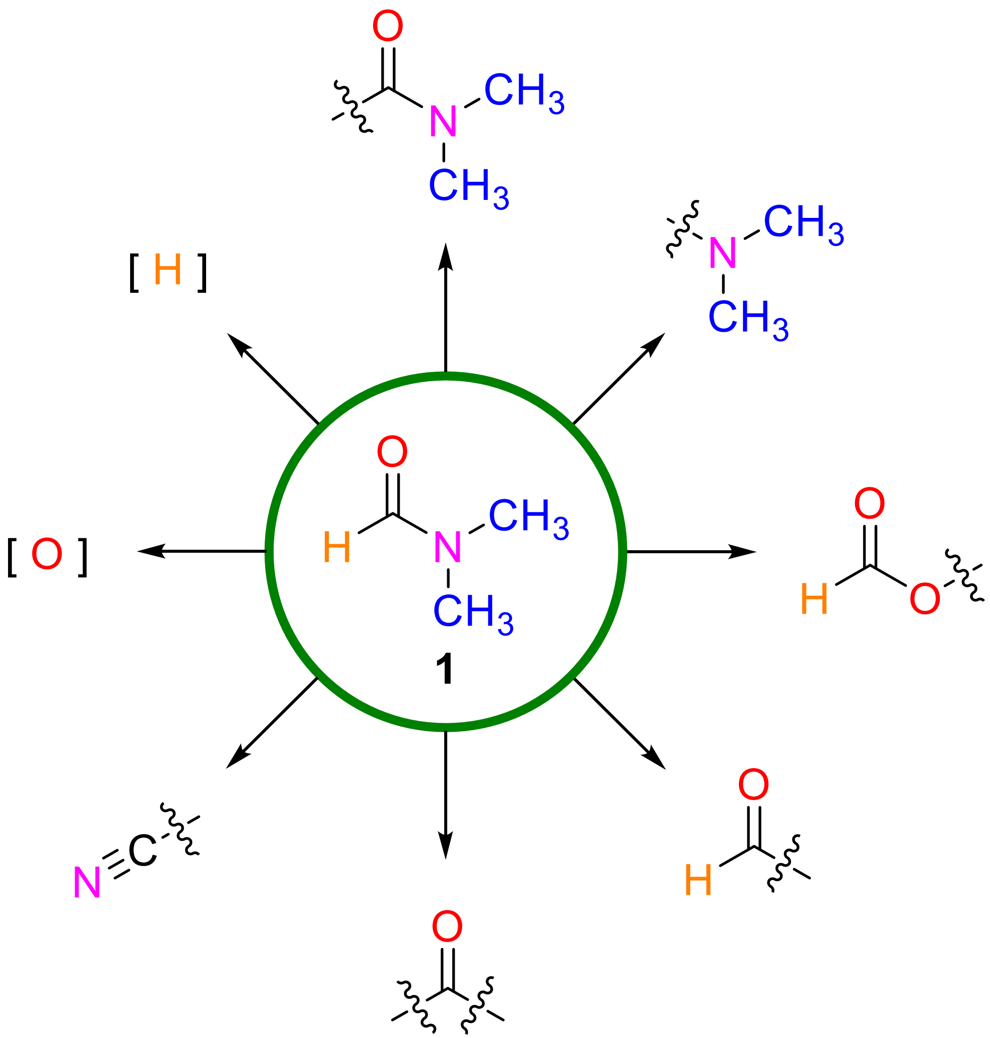
- DMSO is reduced to dimethyl sulfide by certain reductants. This reaction could be violently exothermic when strong reductants are used.
- The reductants and catalysts employed in the reactions, as well as byproducts formed during the reduction reactions could potentially lower the onset temperature and/or increase the severity of the DMSO decomposition to result in runaway scenarios or even explosions.
- ARC of $NaBH_4/H_2O/DMSO$:



Org. Process Res. Dev. **2020**, *24*, 916–939.

N,N-Dimethylformamide (DMF)

- DMF is widely used as a polar aprotic solvent in synthetic organic chemistry to effect a broad range of chemical reactions because of its excellent dissolution property that solubilizes both organic and inorganic species
- DMF has found broad applications in a wide variety of chemical transformations



Org. Process Res. Dev. **2020**, *24*, 1586–1601.

DMF is Incompatible with a Variety of Chemicals…

- Bases
- Acids
- Halogenated reagents
- Oxidants
- Reductants
- **Please fully analyze the safety profile when DMF is used in a chemical reaction!**

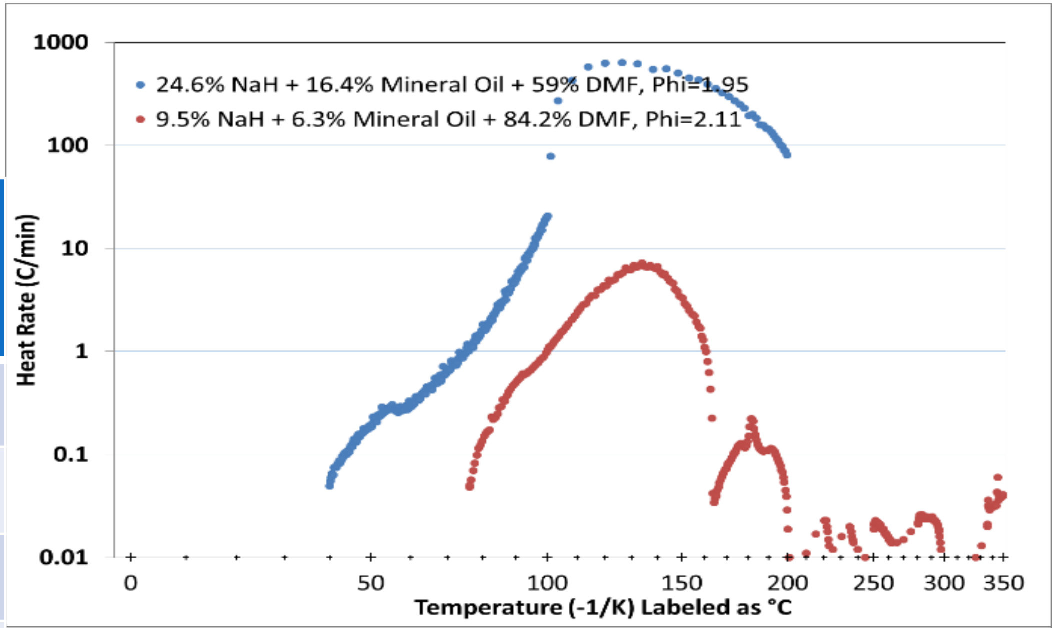
Runaways & Explosions!

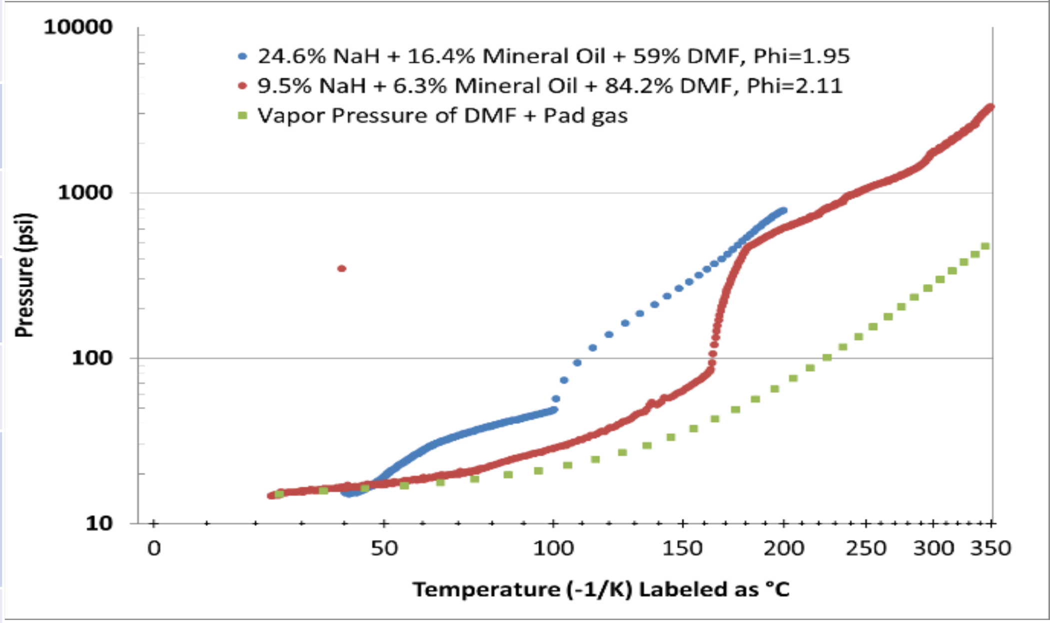
Incompatibilities of DMF with Acids, Bases, Halogenated Reagents, Oxidants, and Reductants

Org. Process Res. Dev. **2020**, *24*, 1586–1601.

Thermal Stability of NaH in DMF

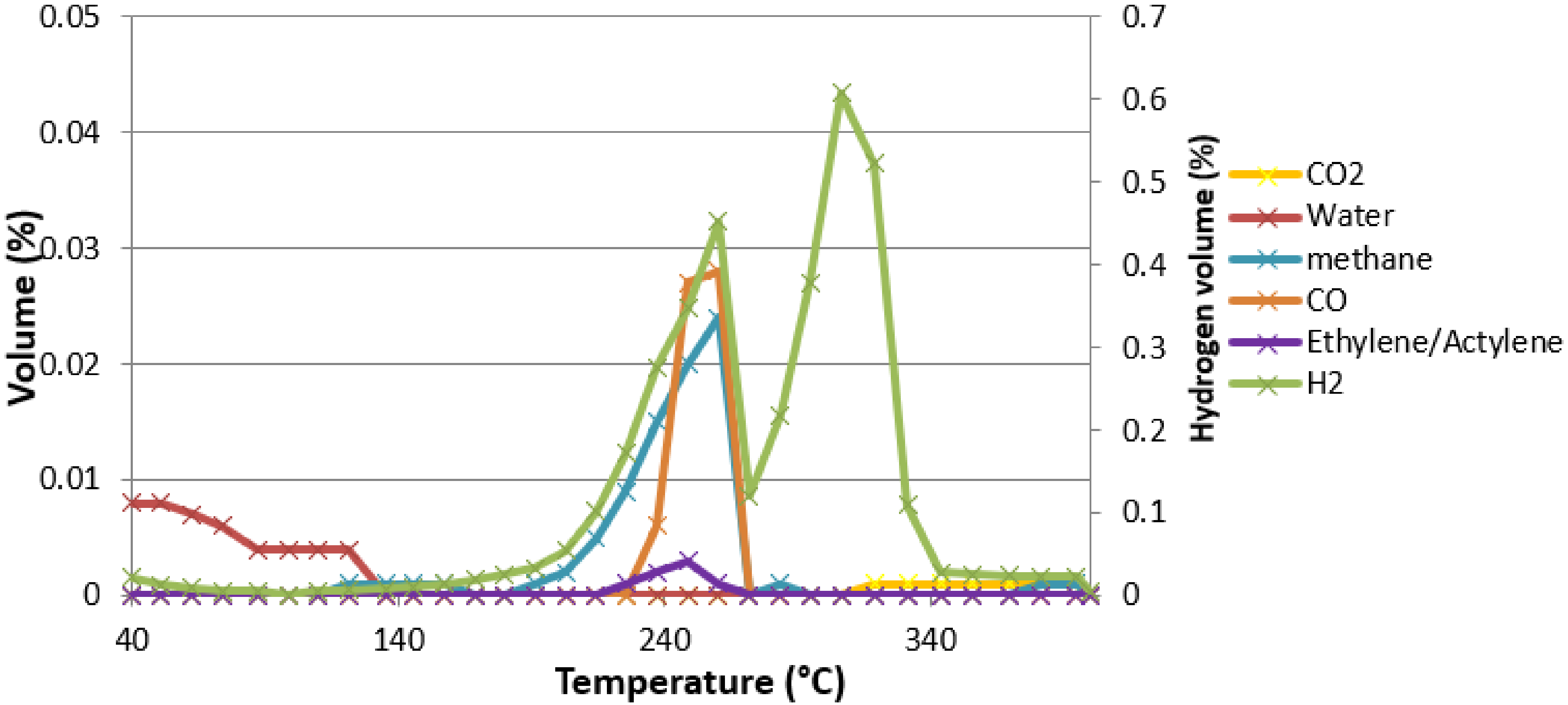
Sample Description	9.5% NaH + 6.3% mineral oil + 84.2% DMF	24.6% NaH + 16.4% mineral oil + 59% DMF
Total sample mass (g)	4.1234	3.3896
Cp of sample (J/g/°C)	2.010	1.930
ARC cell mass (g)	21.8926	14.8079
Set end Temperature (°C)	350	200
Phi	2.11	1.95
Onset Temperature (°C)	76.1	39.8
Peak Temperature (°C)	133.8	126.2
End Temperature (°C)	200.7	>199.7
Max self-heating rate (°C/min)	7.23	634.7
Total heat output (J/g)	–528.4	>–601.8





Org. Process Res. Dev. **2019**, *23*, 2210–2217.

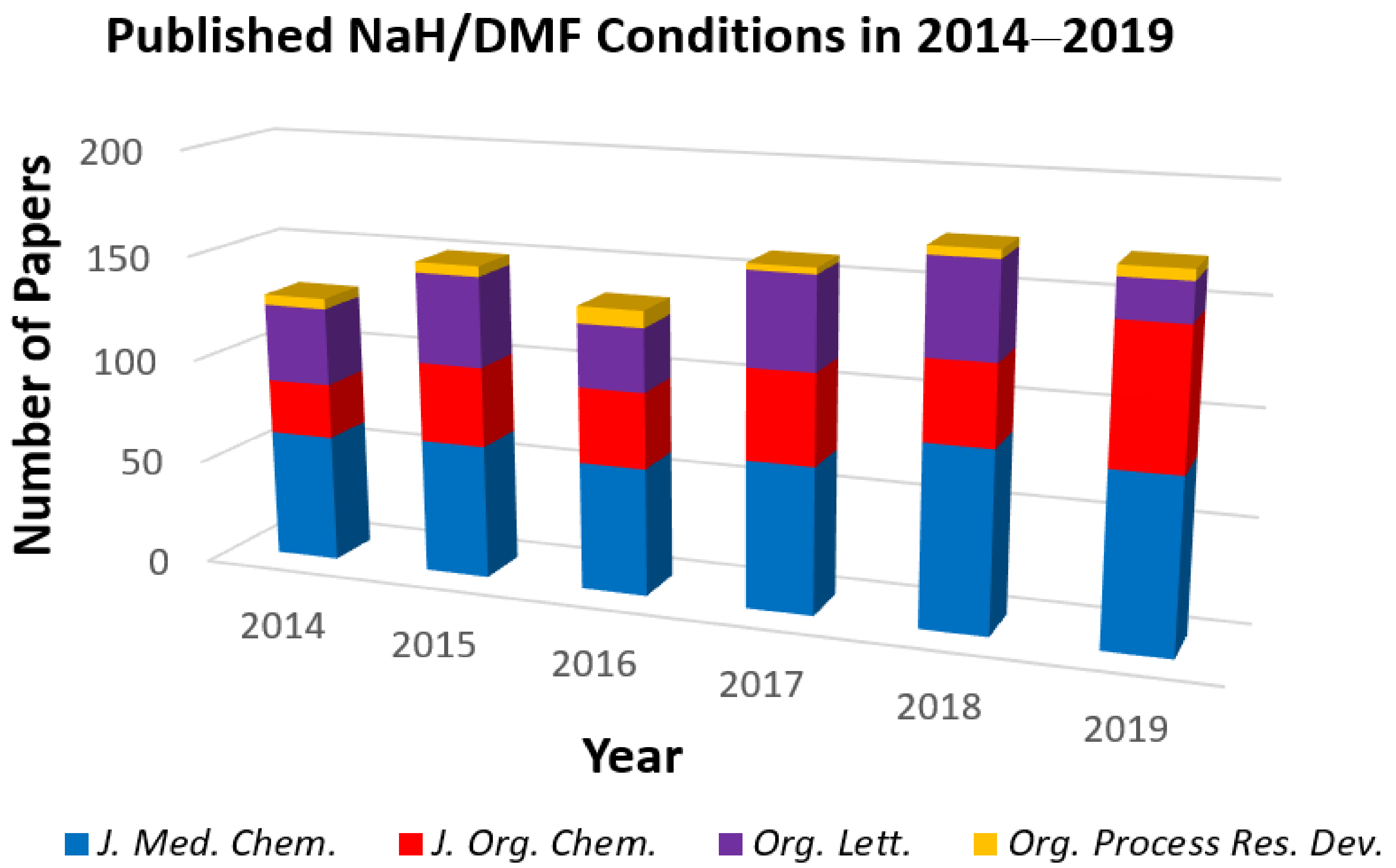
Thermal Stability of NaH in DMF



- EGA Micro-GC analysis revealed the presence of CO_2, water, methane, CO, ethylene (CH_2=CH_2)/acetylene, and H_2 in the decomposition products, indicating potential radical decomposition pathways.
- **Similar exothermic decomposition behavior was observed with NaH/DMAc mixtures.**

Org. Process Res. Dev. **2019**, *23*, 2210–2217.

NaH/DMF Combination Is Still Very Popular



Org. Process Res. Dev. **2019**, *23*, 1586–1601.

Explosion Hazards of DMF Mixtures

With Acids:

- Hydrolysis of DMF in the presence of acids, especially strong acids, can be hazardous because the hydrolysis product, HCO_2H, can further decompose to release noncondensable and flammable gases.
- A bottle of SO_3/DMF complex exploded during storage. it was suspected that SO_3 reacted with moisture to form sulfuric acid (H_2SO_4), which subsequently decomposed DMF.
- DSC of a sample of SO_3/DMF complex indicated two significant exothermic events at 114 °C and 228 °C with energy release of –254 J/g and –646 J/g, respectively when conducted under air in the headspace.

With halogenated reagents:

- A runaway incident involving DMF/$SOCl_2$ mixture was reported in 1977 by Spitulnik at Eastman Kodak.
- Sudden exotherm and pressure rise caused by spontaneous decomposition occurred in a 400-L reactor during vacuum distillation of a $SOCl_2$/DMF mixture to remove SO_2.
- Violent decomposition during distillation to remove sulfur dioxide (SO_2) from a $SOCl_2$/DMF mixture was also reported by Cardillo in 1992.

Org. Process Res. Dev. **2019**, *23*, 1586–1601.

Explosion Hazards of DMF Mixtures

With Oxidants:

- A flame suddenly flashed from the surface of the DMF solution and sprayed the solution all over the inside of the hood when CrO_3 was added to the reaction mixture in DMF.
- A laboratory explosion involving $KMnO_4$ and DMF was reported in 1980 by Finlay at E. I. du Pont de Nemours & Co.
- Kubota and Takeuchi at Fujisawa Pharmaceuticals Co. Ltd. reported an explosion involving a mixture of DMF with *m*-CPBA.

With Reductants:

- A violent explosion occurred from a solution of saturated solution of 13 kg of $NaBH_4$ in 70 kg of DMF at 17 °C at a plant and caused a spontaneous ignition of flammable gases released from the explosion.

With other Substances:

- Methylene diisocyanate, triethylaluminium, potassium methylselenide, and phosphorus pentoxide (P_4O_{10}) have also been reported to react exothermically with DMF.

Org. Process Res. Dev. **2019**, *23*, 1586–1601.

Summary

- The explosion hazards with using DMSO and DMF in chemical reactions have been well-documented in the literature.
- The dangers still remain underappreciated and poorly communicated.
- The data and examples confirm that mixtures involving DMSO and DMF undergo exothermic decomposition at relatively low temperatures, with the generation of non-condensable gases.
- **Please help promote awareness of these safety hazards and encourage the chemistry community to identify safer alternatives!**

Acknowledgements

David E. Ejah
James Henkelis
Leo Huang
Xiaoyong Li
Ming Sheng
Siyu Tu
Craig Tucker
Suhelen Vásquez-Céspedes
Nicola Webb
Eric Wiensch
Gregory T. Whiteker
Honglu Zhang
Yiqun Zhang
Jing Yu

Support of the Corteva Product & Process Technology R&D Leadership

Thank you for your attention!

Call for Submission to a Joint Virtual Special Issue

"Process Safety from Bench to Pilot to Plant" by *ACS Chem. Health Saf.*, *Org. Process Res. Dev.*, and *J. Loss Prevent. Proc.*

- Chemical safety research and information that informs fundamental chemical safety knowledge
- Effective chemical hygiene practices, equipment and procedure design, and qualitative or quantitative risk assessment tools
- Research that addresses human and organizational factors as well as technical engineering controls
- Classical organic process safety studies to evaluate the parameters needed to scale-up organic chemistry such as in preparation for application in multi-purpose pilot and commercial facilities
- Consequence of fire, explosion and toxic release in the process industries
- Use of bench-scale and pilot-plant data for process safety assurance in industrial plant

S. Camille Peres	Qingsheng (Sam) Wang	Qiang Yang	Ashok Dastidar
ACS CHAS Guest Editor	ACS CHAS Guest Editor	OPR&D Guest Editor	JLPPI Guest Editor
peres@tamu.edu	qwang@tamu.edu	qiang.yang@corteva.com	dastidar@fauske.com