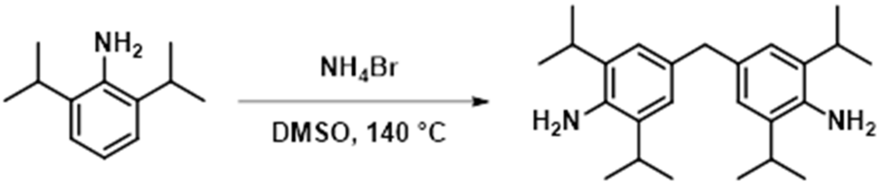
Safety Bulletin – Decomposition of Dimethyl Sulfoxide

1. Overview of Incident

Researchers were attempting to produce compound **2** by modifying a known literature procedure. The reaction involved heating a mixture of 2,6-di-isopropyl aniline (**1**) and ammonium bromide in dimethyl sulfoxide (DMSO) to 140 °C in a sealed, heavy-walled glass vessel behind a safety shield. Formation of **2** requires formaldehyde that is generated through the decomposition of DMSO.



1 2

Overnight, sufficient pressure developed to cause the glass vessel to fail. The pressure release was energetic enough to break the safety shield and destroy the glass baffle at the rear of the fume cupboard. A mercury bubbler was broken leading to the release of liquid mercury. Loose syringes being quenched at the rear of the fume cupboard were scattered during the event resulting in unsheathed needles being present in the debris.

2. Lessons Learned

During the accident investigation, several lessons were identified.

2.1 Explosion Hazards Associated with the Thermal Decomposition of DMSO

Dimethyl sulfoxide is widely used as a solvent for chemical reactions, however, the explosion hazards associated with the thermal decomposition of DMSO are still underappreciated. A wide range of substances exacerbate the thermal decomposition of DMSO. Examples include:

- Acids including HBr and H_2SO_4
- Bases including sodium hydride and potassium *tert*-butoxide
- Halides including KBr
- Metals and metal salts including AgF_2 and copper
- Electrophiles such acetyl chloride and trifluoroacetic anhydride
- Oxidants such as periodic acid and perchloric acid

A comprehensive overview of the potential explosion hazards associated with DMSO has been published by Yang and co-workers (Org. Process Res. Dev. 2020, 24, 916−939).

Whilst the examples listed above relate to the thermal decomposition of DMSO, one report by Whiting describes an unexpected exothermic reaction between thioacetic acid and DMSO in which "the reaction exotherms from room temperature to a reflux of 98 °C in 6 s" (Org. Process Res. Dev. 2006, 10, 4, 846).

Key Lesson: If you plan to conduct an experiment that involves DMSO, it is worth checking its compatibility with components of the reaction mixture, especially if you plan to heat the reaction to a high temperature.

2.2 Reaction Scale

The literature procedure was performed on a small scale (174 mg of ammonium iodide), whereas the "in-house" reaction was performed using 3 g of ammonium bromide.

Key Lesson: Scale is often a major contributor to the overall risk posed by a reaction. If you are scaling a reaction from the literature, give proper consideration to the safety implications of performing the reaction on a larger scale.

2.3 Use of Alternative Synthetic Methods:

A classical approach for the formation of the desired product (**2**) involves treating aniline with formaldehyde. This approach did not require the use of high temperatures or a sealed reaction vessel.

Key Lesson: It is good practice to exhaust safer alternatives before attempting more hazardous procedures.