# Analysis of a Wolff-Kishner reaction

Table E-1, E-2

| Synthesis Step | | | Relevant SWIF Categories | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| What-If Scenario | Consequence(s) | Safeguard(s) | | C | F | R | Recommendation(s) |
| **In a suitable fume hood set up a nitrogen purged multi-neck flask** | |  | | SWIF Category: 6 | | | |
| N2 is lost during this step? | Possible air ingress to flask; possible flammable atmosphere (FL ATM) | None at present | | 4 | 3 | MJ | Consider adding no-flow alarm on N2 line for continuous inserting; consider measuring O2 conc. in head space after one-time inserting |
| **Add an agitator to the flask** | |  | | SWIF Category: 1, 2, 3, 4, and 6 | | | |
| Stirrer assembly detaches from mountings? | Probably break glass vessel; loss of containment; possible fire | Monthly inspection of agitator mounting | | 4 | 2 | MD | No additional recommendations |
| Unstable motion of the agitator shaft/paddle? | Possibly break glass vessel; possible loss of containment | Agitator motion checked before starting reaction | | 3 | 3 | MD | No additional recommendations |
| Agitation rate is too fast or too slow? | Wrong reaction rate | Chemist monitors reaction regularly | | 2 | 4 | MD | No additional recommendations |
| Electric motor is an ignition source | Fire/Explosion if FL ATM forms in hood? | None at present | | 5 | 2 | MD | Electric motor must be explosion proof |
| **Add a reflux condense** | |  | | SWIF Category: 1 and 6 | | | |
| Condenser water is not cold enough? | Failure to condenser volatiles; possible FL ATM in hood; possible fire/explosion | Chemist monitors reaction regularly | | 3 | 3 | MD | Consider high T alarm placed in vapor space above condenser |
| Water flow to condenser decreases or stops? | Failure to condenser volatiles; possible FL ATM in hood | Chemist monitors reaction regularly | | 3 | 4 | MJ | Consider installing an alarm for No/Low Flow of water |
| The loss of cooling water is not noticed by chemist? | Possible FL ATM in hood; possible fire/explosion | None at present | | 5 | 2 | MJ | Shut down reactor heating system on No Flow of water |
| **Add a Dean Stark trap to the flask** | |  | | SWIF Category: 1 and 5 | | | |
| Water from the Dean Stark trap back-flows into the reactor? | Flash evaporation of water if reaction T > 125C; possible loss of containment; possible fire | Chemist monitors reaction regularly | | 4 | 2 | MD | Match size of Dean Stark trap with expected volume of water from reaction |
| **Install and set a temperature controller for reactor** | |  | | SWIF Category: 2 and 3 | | | |
| Temperature controller incorrectly set up or fails | Failure to control reaction temperature; possible runaway reaction; possible loss of containment | Chemist monitors reaction regularly | | 4 | 3 | MJ | Determine if runaway is possible; consider using redundant T controller if true |
| Runaway reaction occurs before evasive action can be taken? | Probable loss of containment; possible fire/explosion | None at present | | 5 | 3 | S | Determine if runaway is possible; consider using redundant T controller if true; do not perform overnight runs for this reaction |

Note: Risk rank categories are S–severe; MJ–major; MD–moderate; MR–minor; ML–minimal (*Source:* Leggett17).

| **Table E-2** | | | | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Synthesis Step Relevant SWIF Categories | | | | | | | | | | | | | | |
| Deviation | Deviation/Upset | Consequence | Safeguards | C | F | | R | Recommendation(s) | | | | | | |
| **Install and set a temperature controller** | | | | | | | | | | | | | | |
| Other than Step | The set-point for the T controller incorrectly set | The reaction T exceeds set point T; possible runaway reaction; possible loss of containment | Chemist monitors reaction regularly | 4 | | 3 | MJ | | Determine if runaway is possible; consider using redundant T controller if runaway can occur; do not perform overnight runs for this reaction | | | | | |
| Higher temperature | Temperature controller fails | The reaction T exceeds set point T; possible runaway reaction; possible loss of containment | Chemist monitors reaction regularly | 4 | | 3 | MJ | |  | | | | | |
| More reaction | A runaway reaction occurs before evasive action can be taken | Probable loss of containment; possible fire/explosion | None at present | 5 | | 3 | S | |  | | | | | |
| **Suspend the ketone (85 g) in diethylene glycol (2 L)** | | | | | | | | | | | | | | |
| Less PPE | The chemist is exposed to diethylene glycol | Low toxicity LD50 (rat) = 12,000 mg/kg (data from Chemical Hazard Review form) | Standard PPE | 2 | | 3 | MR | | |  | | |
|  | The chemist is exposed to ketone | No data available; assume toxic by ingestion | Standard PPE | 2 | | 3 | MR | | | |  | | | |
| **Place the flask in a room temperature oil bath then add KOH (70 g)** | | | | | | | | | | | | | | |
| Less PPE | The chemist is exposed to KOH | Moderately toxic LD50 (rat) = 273 mg/kg.(data from Chemical Hazard Review form) | Standard PPE + lab safety goggles | 3 | | 3 | MD | | | |  | | |
| As well as reaction | There is a high heat of solution between NaOH solid and EG | Possible unexpected heating of glycol–no concern | Standard PPE+ lab safety goggles | 3 | | 3 | MD | |  | | |
| **Gradually add 80% solution of hydrazine hydrate (65 mL)** | | | | | | | | | | | | | | |
| Less PPE | The chemist is exposed to these reagents | Extremely hazardous and highly toxic LD50 (rat) 60 mg/kg; IDLH 50 ppm (data from Chemical Hazard Review form) | Standard PPE + lab safety goggles | 5 | | 3 | S | | | Require use of full face respirator when handling N2H4 | | | | |
| More reaction | The addition rate of 80% hydrazine is too high | Higher reaction rate than expected; possible to exceed heat removal capacity | None at present | 3 | 2 | | MR | | | Consider using small scale reaction to determine impact of higher concentration or addition rate of N2H4 Consider adding flow restrictor in N2H4 line | | | | |
| Other than flow | Control of the hydrazine flow is lost | Higher reaction rate than expected; possible runaway reaction if all N2H4 is added at once | None at present | 4 | 2 | | MD | | |  | | | | |
| **Heat the reaction mixture slowly heated to 200 8C over about 3–4 h allowing water to collect in the Dean–Stark trap** | | | | | | | | | | | | | | |
| Reverse flow | Water from the Dean Stark trap back-flows into the reactor | Flash evaporation of water if reaction T > 125 8C; possible loss of containment; possible fire | Chemist monitors reaction regularly | 4 | 2 | | MD | | | Ensure capacity of trap matches expected volume of water | | | | |

Note: Risk rank categories are S–severe; MJ–major; MD–moderate; MR–minor; ML–minimal (*Source:* Leggett17).

This file is excerpted from “Identifying and Evaluating Hazards in Research Laboratories: Guidelines developed by the Hazard Identification and Evaluation Task Force of the American Chemical Society’s Committee on Chemical Safety”.

© Copyright 2015 American Chemical Society