



Evaluation of reactive hazard on a production site

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EPSC Technical Meeting, 8.10.25

**Add value.
Inspire trust.**

Agenda



- Overview Methodology
- Detail of Assessment Criteria
- Project Organisation
- Use

Project

- Fine chemical company
- Multipurpose plants and equipment
- Reactors from 63 L to 16 m³
- Mostly batch and semi-batch processes

- Wide range of chemistry and process conditions
 - Grignard reactions
 - Hydrogenations
 - Ester formations
 - Cyclisations
 - Ether formation
 - Acetalization
 - Alcynation
 - Acid Chloride formation

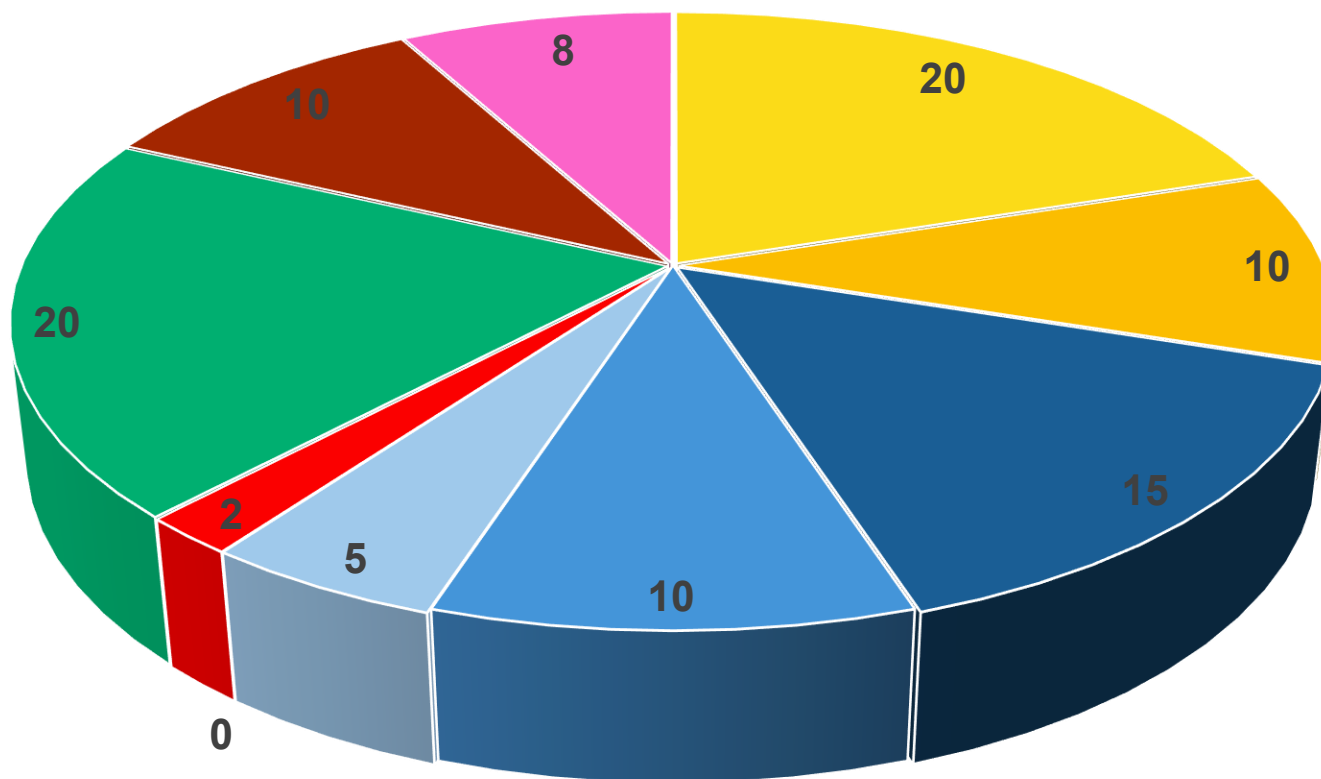
- Request: determine reactivity hazards for all synthesis reactions including first steps of work-up (dilutions, mixing etc are excluded)



AI generated image

- Alkylation
- Epoxidation
- Reductions
-

Assessment Criteria and weight



Hazard / Criteria

- Synthesis reaction
- Stability
- Gas release
- Reaction under pressure
- Process temperature
- Size
- Flammability of substances
- Toxicity of involved subst
- Accident history
- Frequency of operation

Classification



Criteria		Weight %	Low	Med	High	Very high
1	Thermal data: foreseen process	8	1	2	3	
1	Thermal data: 100% acc	12	1	2	3	
2	Stability	10	1	2	3	5
3	Gas release	15	1		3	5
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6	Flammability of substances involved	2	1	2	3	
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8	Accident hist	10	1	2	3	
9	Frequency of op	8	1	2	3	

Classification



- Score calculation:

$$8\% \cdot 2 + 12\% \cdot 3 + 10\% \cdot 2 + 15\% \cdot 1 + 10\% \cdot 1 + 5\% \cdot 1 + 2\% \cdot 3 + 20\% \cdot 2 + 10\% \cdot 1 + 8\% \cdot 2 = 1.74$$

High

Overall classification of interest but score more useful

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9	Frequency of op	8	1	2	3	

	LOW	MEDIUM	HIGH	VERY HIGH
Score	< 1.3	≥ 1.3 & ≤ 1.7	> 1.7 & < 2.3	≥ 2.3

Criteria Synthesis Reaction



- Assessing foreseen accumulation and 100% accumulation

$P_{\max} > P_{\text{design}}$	MEDIUM	MEDIUM	HIGH
$P_{\text{design}} \geq P_{\max} > P_{\text{set}}$	LOW	MEDIUM	MEDIUM
$P_{\max} \leq P_{\text{set}}$	LOW	LOW	LOW
	> 48h	24-48h	<24h
	$P_{\max}$ reached in ($t_{\text{mr}_{\text{ad}}}$)		

$P_{\max}$: maximum pressure that can be reached in the reactor upon runaway of the reaction

P_{set} : set pressure emergency relief system

$t_{\text{mr}_{\text{ad}}}$: time to maximum rate under adiabatic conditions

Criteria Stability: 1. Thermal Stability



$\Delta T_{ad} > 200K$	MEDIUM	HIGH	HIGH
$50K < \Delta T_{ad} < 200K$	MEDIUM	MEDIUM	HIGH
$\Delta T_{ad} < 50 K$ and no pressure	LOW	LOW	LOW
	$t_{mr_{ad}} \text{ at } T_p \geq 24h$	$8h < t_{mr_{ad}} \text{ at } T_p < 24h$	$t_{mr_{ad}} \text{ at } T_p \leq 8h$

ΔT_{ad} : adiabatic temperature rise

$t_{mr_{ad}}$: time to maximum rate under adiabatic conditions

T_p : process temperature

Criteria Stability: 2. Reactivity



	LOW	MEDIUM	HIGH	VERY HIGH
Reactivity	None of the properties listed	Reacts strongly with acid or base, or oxidiser or reducing agent (section 10 MSDS) or May form explosive peroxides or EUH031: Contact with acids liberates toxic gas	Reacts violently with water or alcohols H260: In contact with water releases flammable gases which may ignite spontaneously H261: In contact with water releases flammable gases EUH014: Reacts violently with water EUH029: Contact with water liberates toxic gas EUH032: Contact with acids liberates very toxic gas	H200/H201/202/203/204/205: Explosive H240/241/242 Heat may cause an explosion or fire H250: Pyrophoric

Criteria Gas release and Reaction under pressure



- Gas release

	LOW	MEDIUM	HIGH	VERY HIGH
Gas release	No gas release		Yes and gas release neither flammable nor toxic	Yes, and gas released either toxic or flammable or comburant (O ₂)

- Reaction under pressure

	LOW	MEDIUM	HIGH
Reaction under pressure	Reaction done at atmospheric pressure or under vacuum	Overpressure of less than 100mbar	Reaction done under pressure (above 1,1 bar abs)

Criteria Temperature and Batch Size



- Temperature

	LOW	MEDIUM	HIGH
Temperature of Reaction Steps	25-100°C	0-25°C or 100-150°C	<0°C or >150°C

- Size

	LOW	MEDIUM	HIGH
Size	g	kg	tons

Criteria: Flammability and Toxicity



- Flammability

	LOW	MEDIUM	HIGH
Flammability of involved substances	No flammable substances involved	Flash point above room temperature but reached under process conditions	For liquids: Flash point < 60°C OR AIT < 200°C Flammable gas Or other specific flammability issues (e.g. powder with very low MIE)

- Toxicity

	LOW	MEDIUM	HIGH	VERY HIGH
Toxicity of substances involved	None of the properties listed	H311 Toxic in contact with skin H341 May cause genetic defects H351 Suspected of causing cancer H361 Suspected of damaging fertility or the unborn child	H310 Fatal in contact with skin H340 May cause genetic defects H350 May cause cancer H360 May damage fertility or the unborn child	H330 Fatal if inhaled H331 Toxic if inhaled

Criteria: Accident history and Frequency of operation



- Accident history

	LOW	MEDIUM	HIGH
Accident history	No accident nor near miss reported	Near miss reported	Accident, incident process-related already occurred

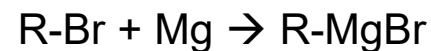
- Frequency of operation

	LOW	MEDIUM	HIGH
Frequency of operation	Very rare production (1-2 batches per year)	Regular production	Top 10 products of the site

Example



- Grignard reagent synthesis:



- Initiation: 3% of total bromide reactant at 50°C
 - Reaction energy: initiation 40 kJ/kg
 - Decomposition energy not relevant
- Full batch: process T 66°C (boiling point THF)
 - Reaction energy: 890 kJ/kg
 - Accumulation 10%
 - T_{D24} reaction mass 150°C, decomposition energy 150 kJ/kg
- Solvent THF (Bp 66°C), c'p 2 kJ/(kg·K)

Example



- Criteria 1 initiation batch: MTSR: 72.5°C, Pvap: 1.2 bara
 - Criteria 1 reaction: semi-batch: MTSR: 111°C, Pvap: 3.6 bara, MTSR < T_{D24} , Tfinal: 186°C Pvap >> 6 barg
 - Criteria 1 reaction: batch: MTSR: 511, Pvap >> 6 barg
-
- 6 barg design pressure, 2 barg Pset

Criteria Synthesis Reaction



- Assessing foreseen accumulation

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Classification – Grignard reagent synthesis



- Overall score : $8\% \cdot 2 + 12\% \cdot 3 + 10\% \cdot 3 + 15\% \cdot 1 + 10\% \cdot 1 + 5\% \cdot 1 + 2\% \cdot 3 + 20\% \cdot 2 + 10\% \cdot 2 + 8\% \cdot 2 = 1.94$

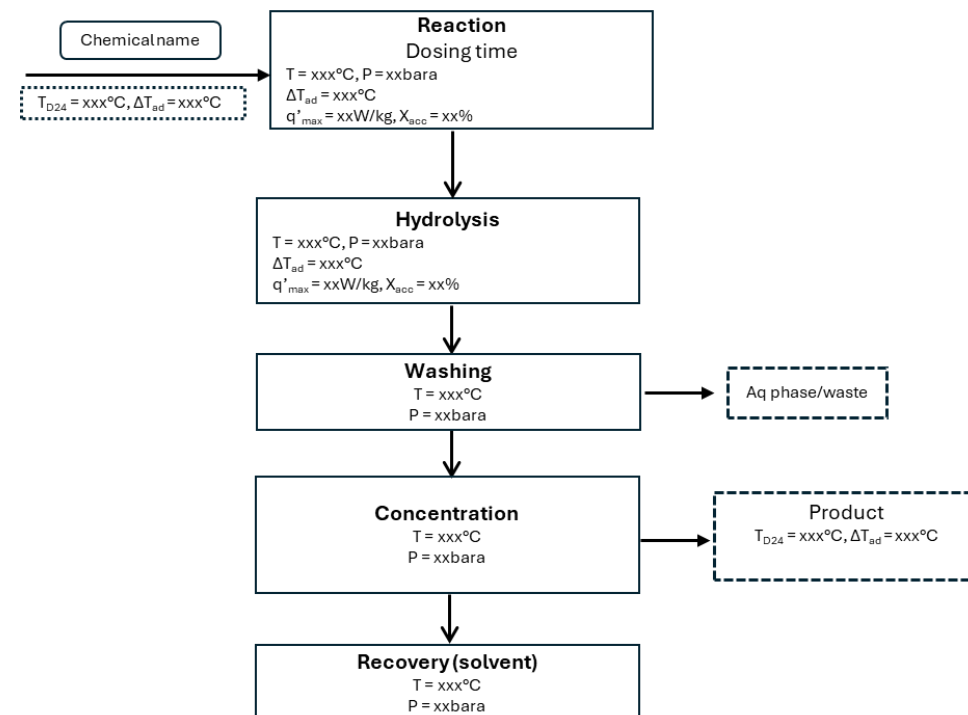
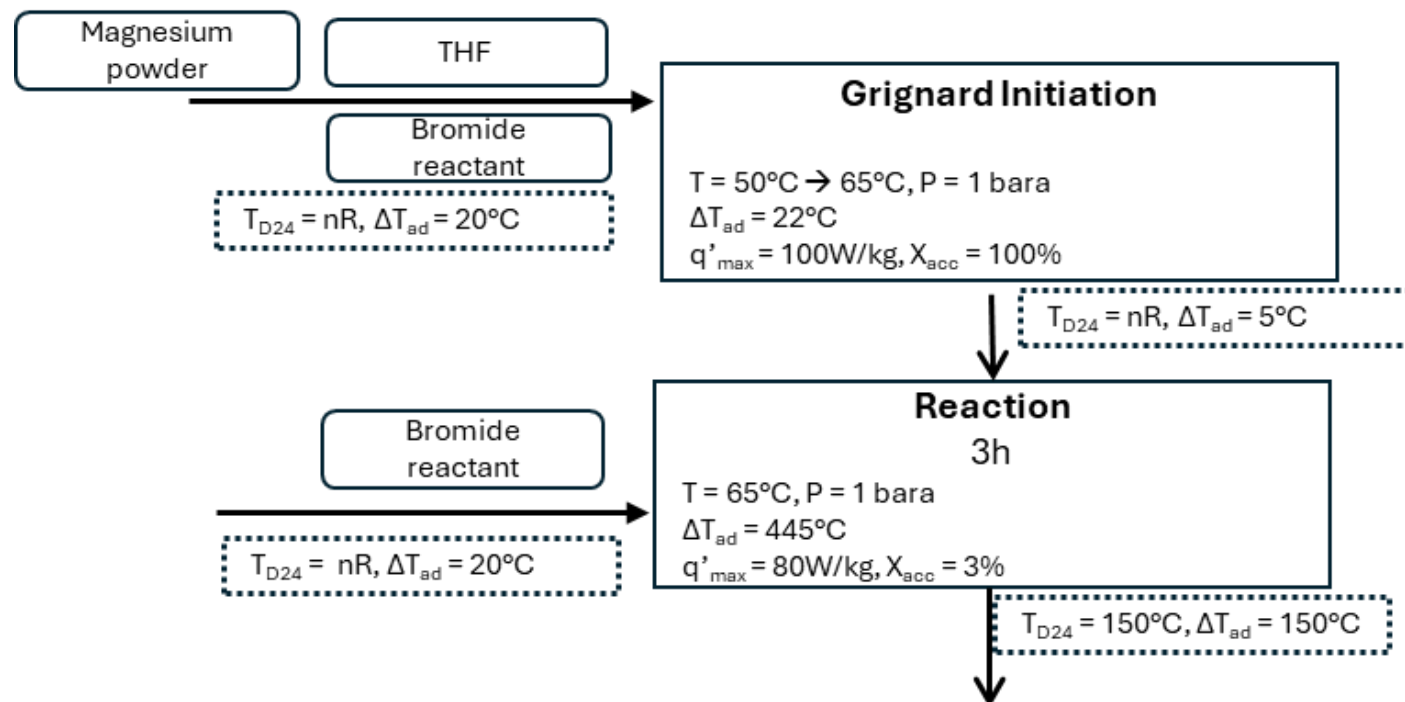
	LOW	MEDIUM	HIGH	VERY HIGH
Score	< 1.3	$\geq 1.3 \ \& \ \leq 1.7$	$> 1.7 \ \& \ < 2.3$	≥ 2.3

Required data and Tool



- Required data
 - SOP
 - Reaction scheme
 - CLP classification of reactants, intermediates, products and wastes
 - Safety lab reports (Reactivity data, stability data)
 - Technical data (Reactor size, Pset, Pdesign)
 - Accidentology
 - Number of campaigns
- Tool
 - Compile all data
 - Interpretation of reactivity and stability data
 - Calculations
 - Comments etc
 - Block flow (to be able to quickly remember what had been done)

Grignard Reaction



Project organisation



- Proof of concept (10 SOP)
 - Check criteria
 - Development of tools to perform assessment
 - Data gathering
 - Set-up of team (5 full time employees)
- Analysis of 250 SOPs
 - QM: review/discussing each evaluation
 - Regular discussion with site to obtain required data and discuss specific points
- Start-up ~ 1 month
- Project 2.5 months

Use of study



- Site overview of reactivity (mapping)
- Prioritization
 - Reaction Calorimetry and Thermal stability Measurements
 - Risk Analysis
 - Audits
 - Increase of reliability of risk reducing measures
- Research and Development
 - Criteria for improving inherent safety of processes
- Compilation and summary of data: owner onsite to add new processes and update existing one with new data