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Increased process robustness for an API

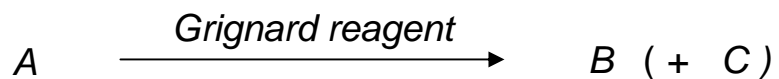
- An example of how PAT tools can be used





The API process

70% Yield



Process input:

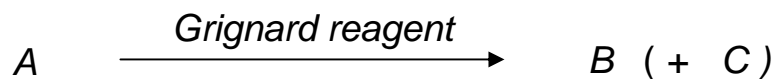
- Fixed amount of A (batch variation in quality)
- Fixed amount of grignard reagent (batch variation in grignard strength)
- Fixed process time

Process output:

- Variable yield of B
- Variable amount of impurities C



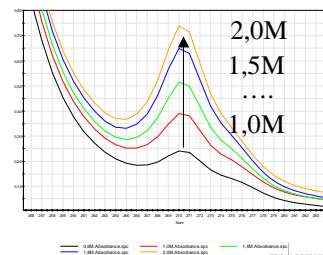
PAT tools for increased process understanding - 1



At-line NIR for grignard reagent strength determination:

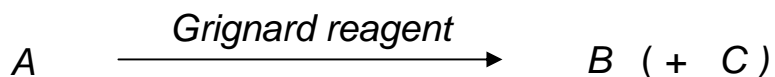


Preparation of Grignard reagent

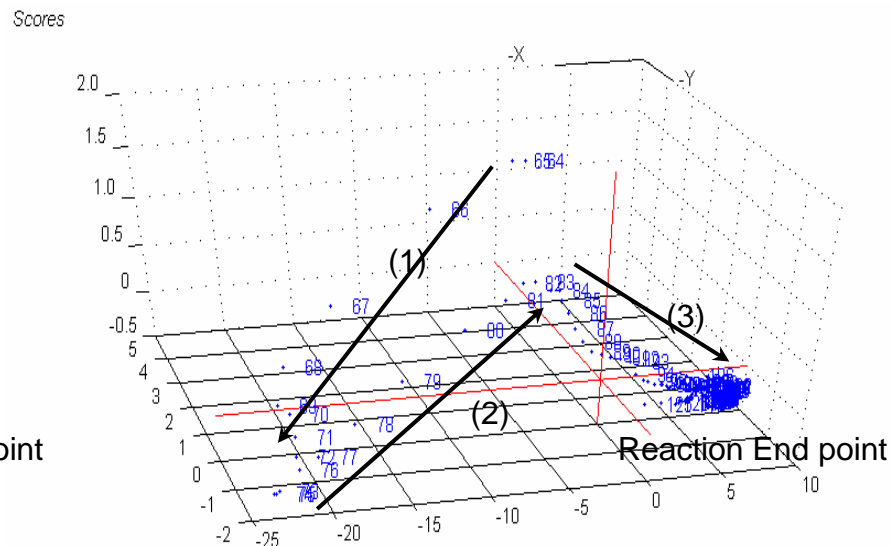
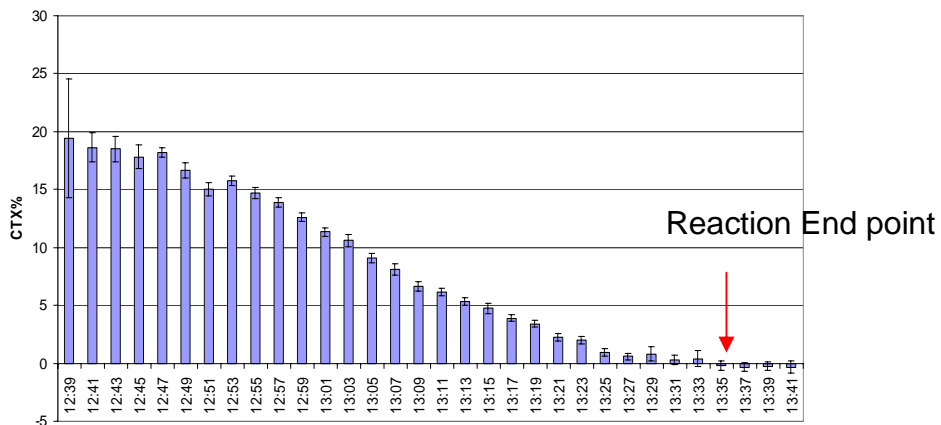




PAT tools for increased process understanding - 2



In-line NIR monitoring to understand reaction mechanism:

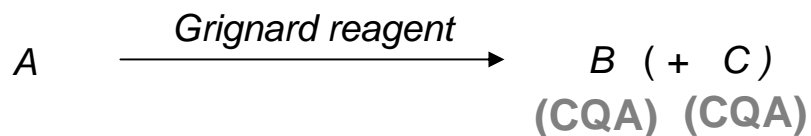


- 1) Dissolution of "A"
- 2) Consumption of "A"
- 3) Steady state reaction kinetic



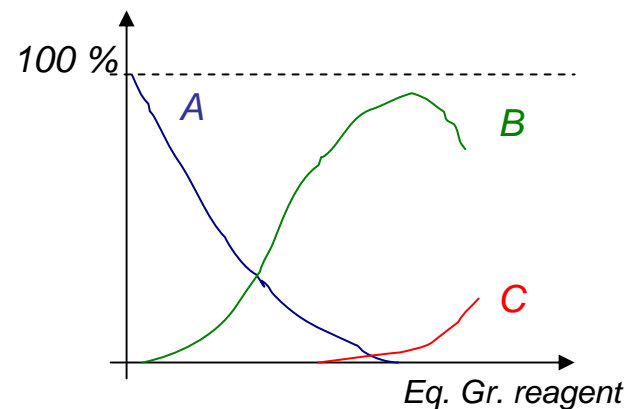
Process Understanding

Results



Critical process parameters:

- Water content in solvents
- Grignard strength (eq. added)

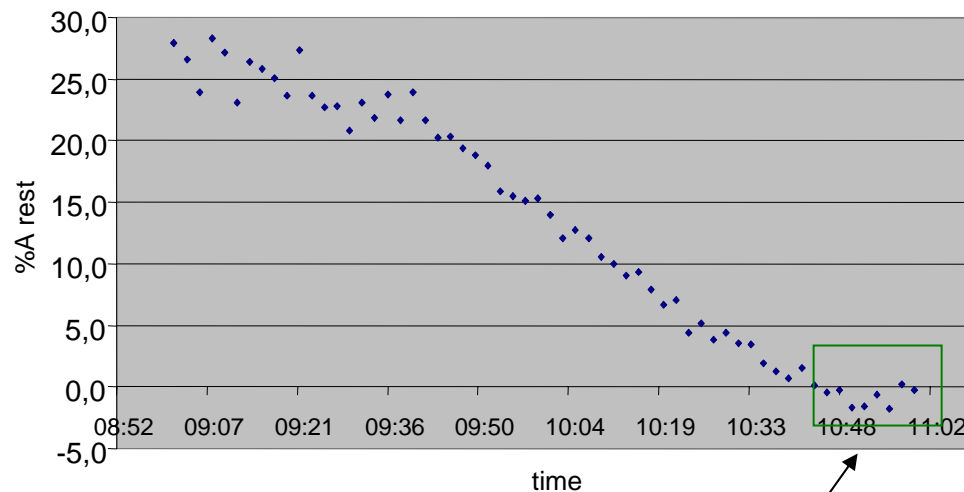




Full scale implementation



In-line NIR (prediction) monitoring
Grignard reaction



Reaction end-point!!
(%A rest ~ 0)



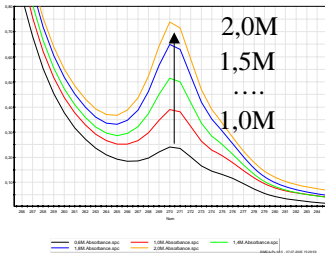


The improved process

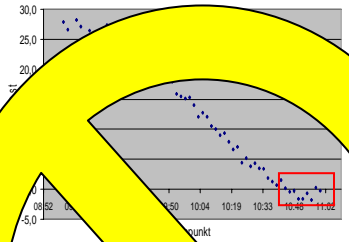
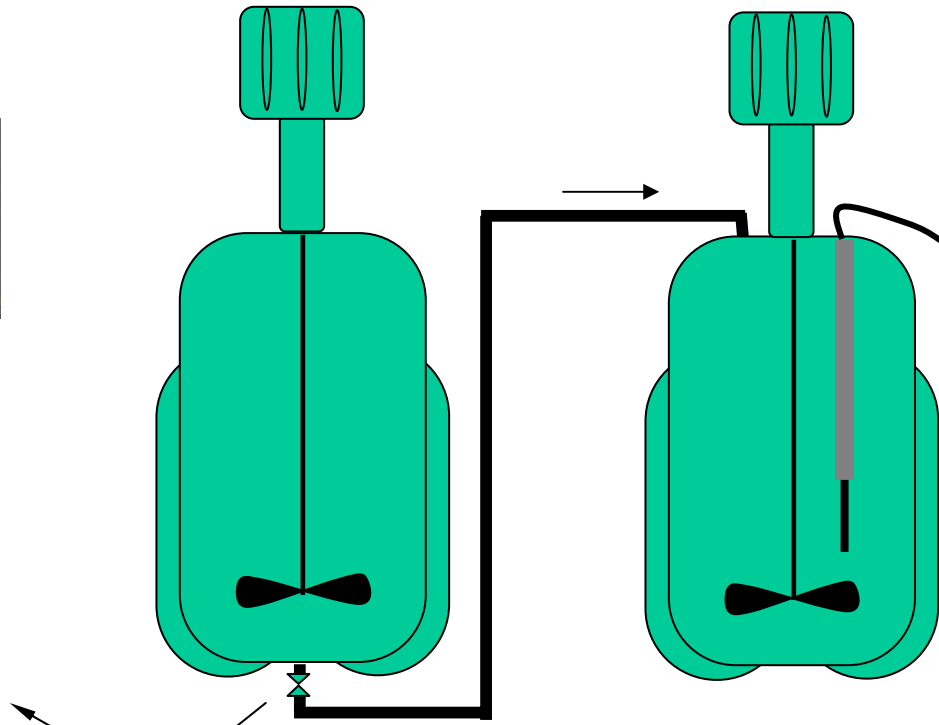
96% Yield

Syntese af Grignard reagens

Grignard reaktion:



At-line NIR analyse af Grignard reagens



In-proces prøve

