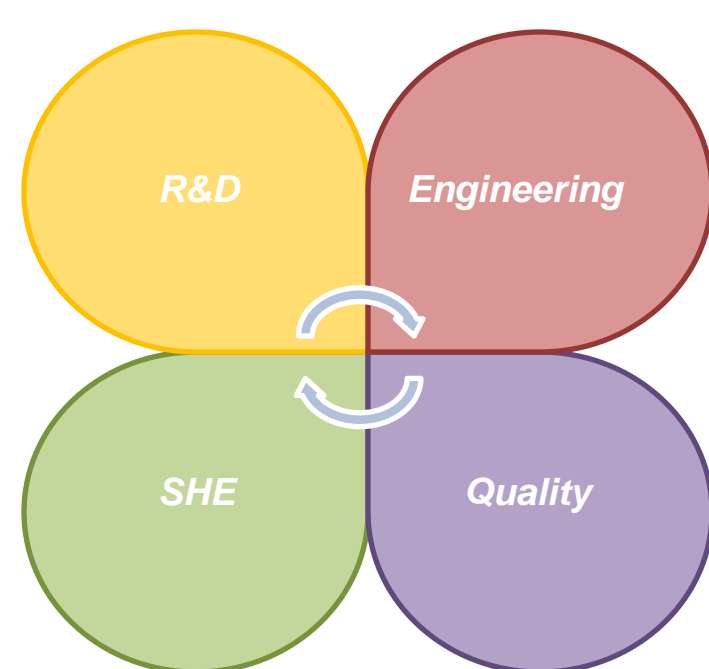


Energetic Chemistries for the Manufacturing of APIs

A Long History of Developing Hazardous Chemistries

A Balanced Approach of Chemistry and Engineering is Used for Safely Conducting Energetic Chemistry at Commercial Scale for over 70 years

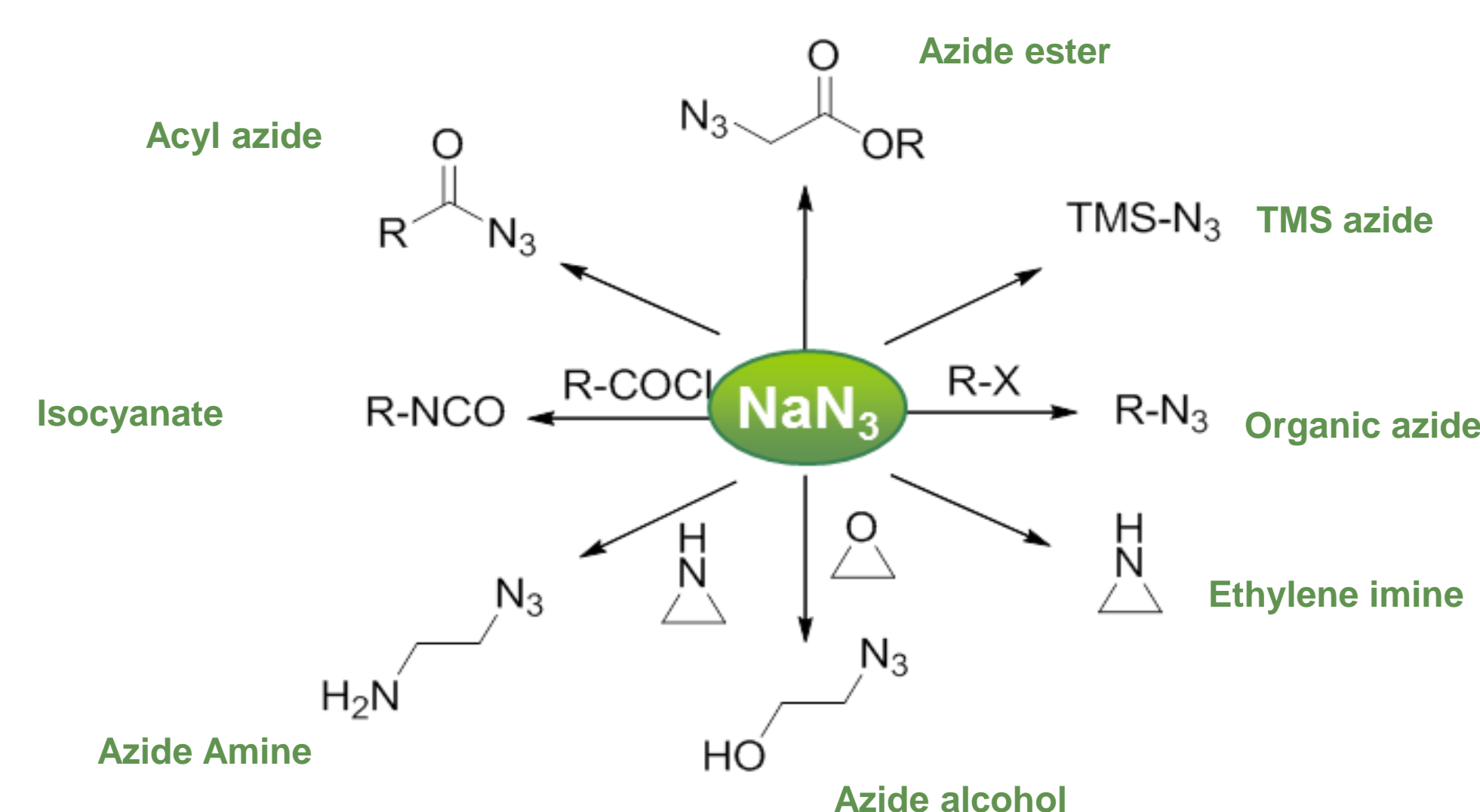


- Over 75 years of experience in commercial scale production using highly hazardous chemistries
- Proprietary technologies and know-how for safely scaling up hazardous chemistry
- Collaboration between Chemists, Chemical Engineers, SHE, and Quality personnel early in the process to ensure safe and reliable scale-up
 - Over 90 chemical engineers and chemists
- Specially engineered facilities for conducting energetic chemistry
 - Azide rated pilot facilities (100/500 gal) and five production lines (1,500/2,000 gal)
 - Dedicated continuous diazomethane generator
 - Dedicated facility for the generation of methyl isocyanate
 - Hazards evaluation laboratory: DSC, TGA, RC-1, Impact, Friction

Technology	Example
Azide	Sodium azide, hydrazoic acid
Diazo	Diazomethane, ethyl diazoacetate
Aziridines	Ethylene Imine, methyl aziridine
Nitrations	Mixed acids, acetyl nitrate
Isocyanates	Methyl isocyanate
Ozone	Continuous or batch ozonolysis
Hydrogenation	Batch and continuous
Others	Sodium cyanide, hydrazine, phosgene, halogenated solvents, benzene, Pyrophoric reagents

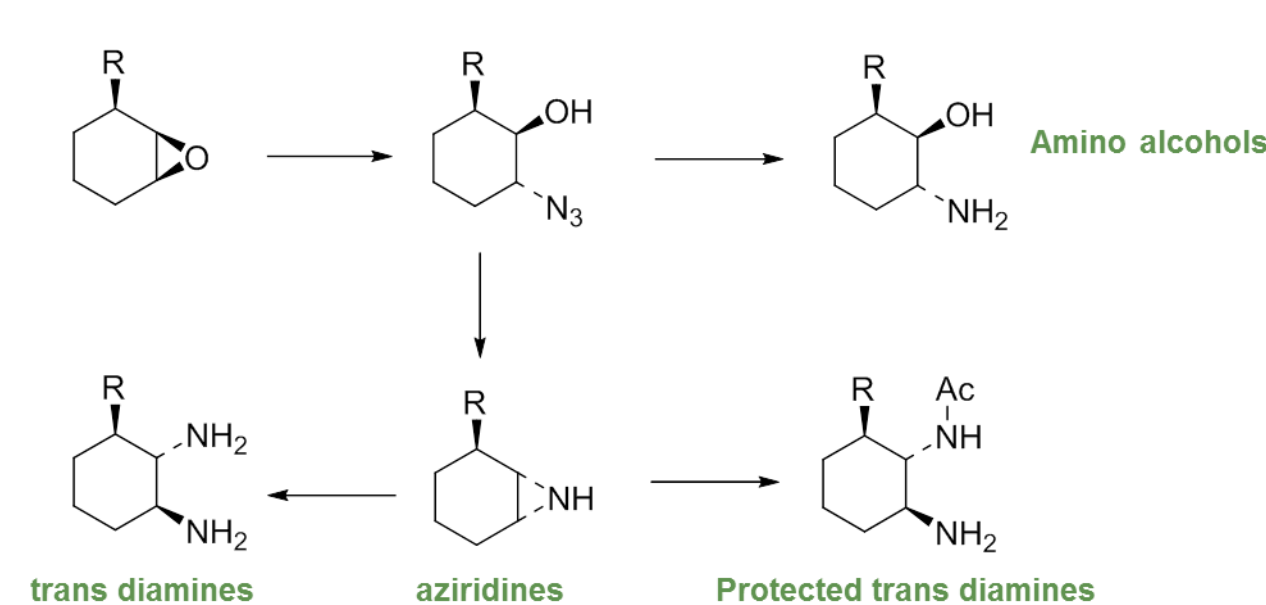
Energetic Chemistries Provide Clean, High Yielding Routes

Sodium Azide



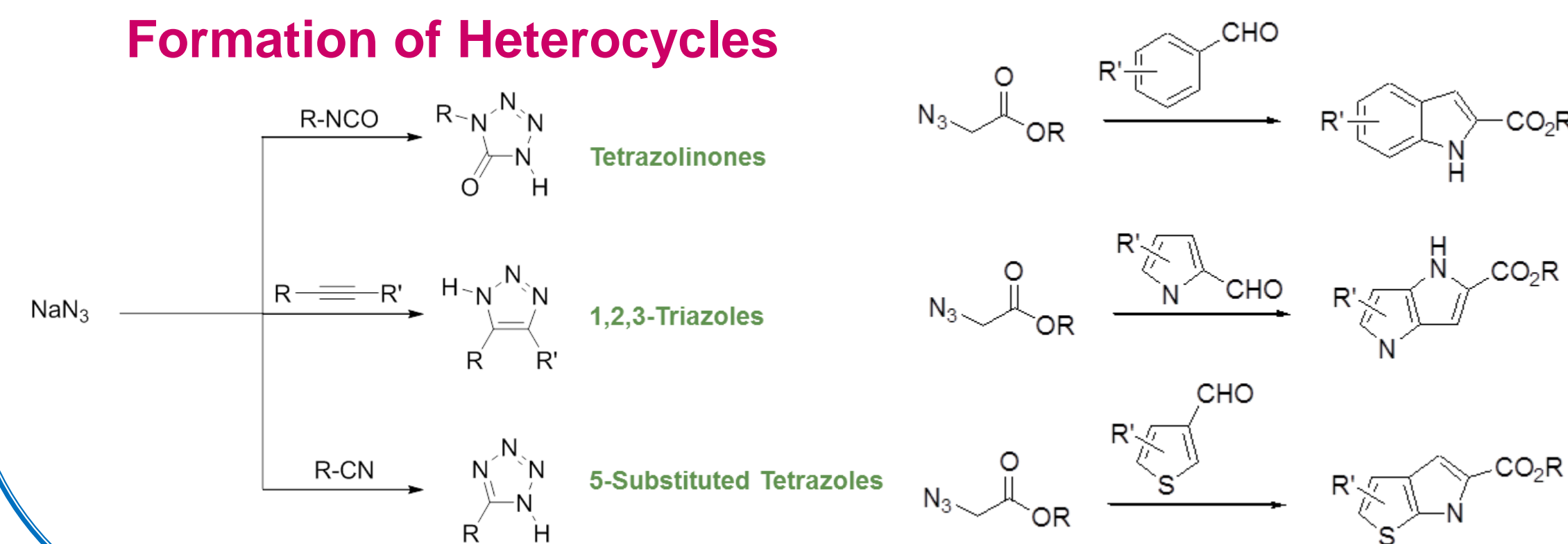
- Preferred route to primary amines, azido acetates, isocyanates, amino alcohols, aziridines
- AFC has many decades of experience in commercial scale production of organic azides and derivatives

Trans-Diamines and Amino Alcohols

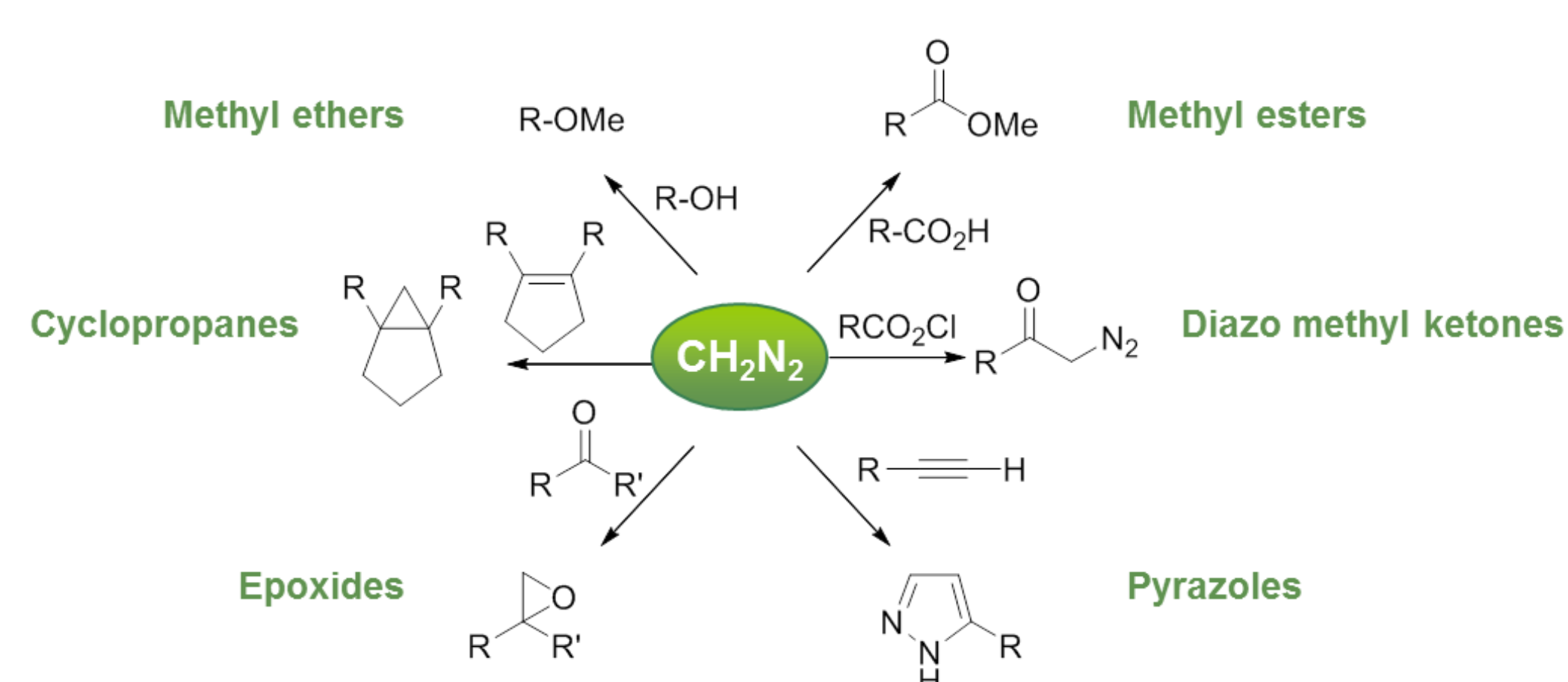


- Commercial trans-diamine produced at 2,000 gal scale

Formation of Heterocycles

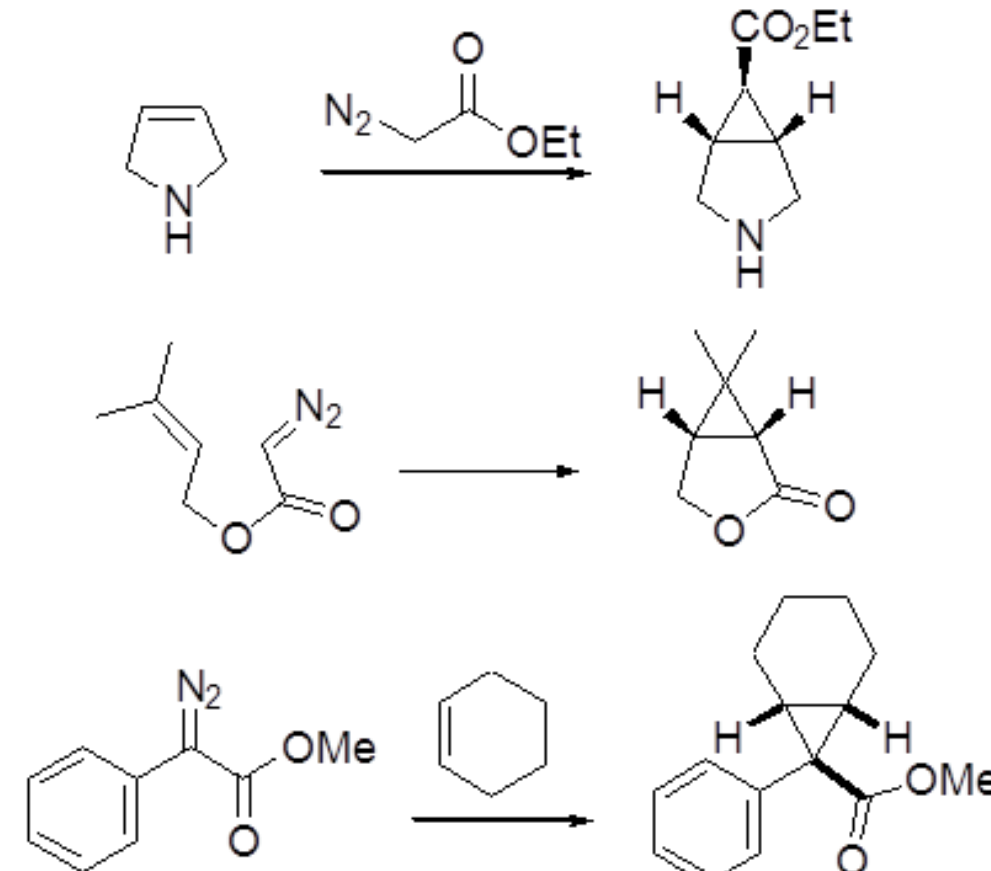


Diazomethane



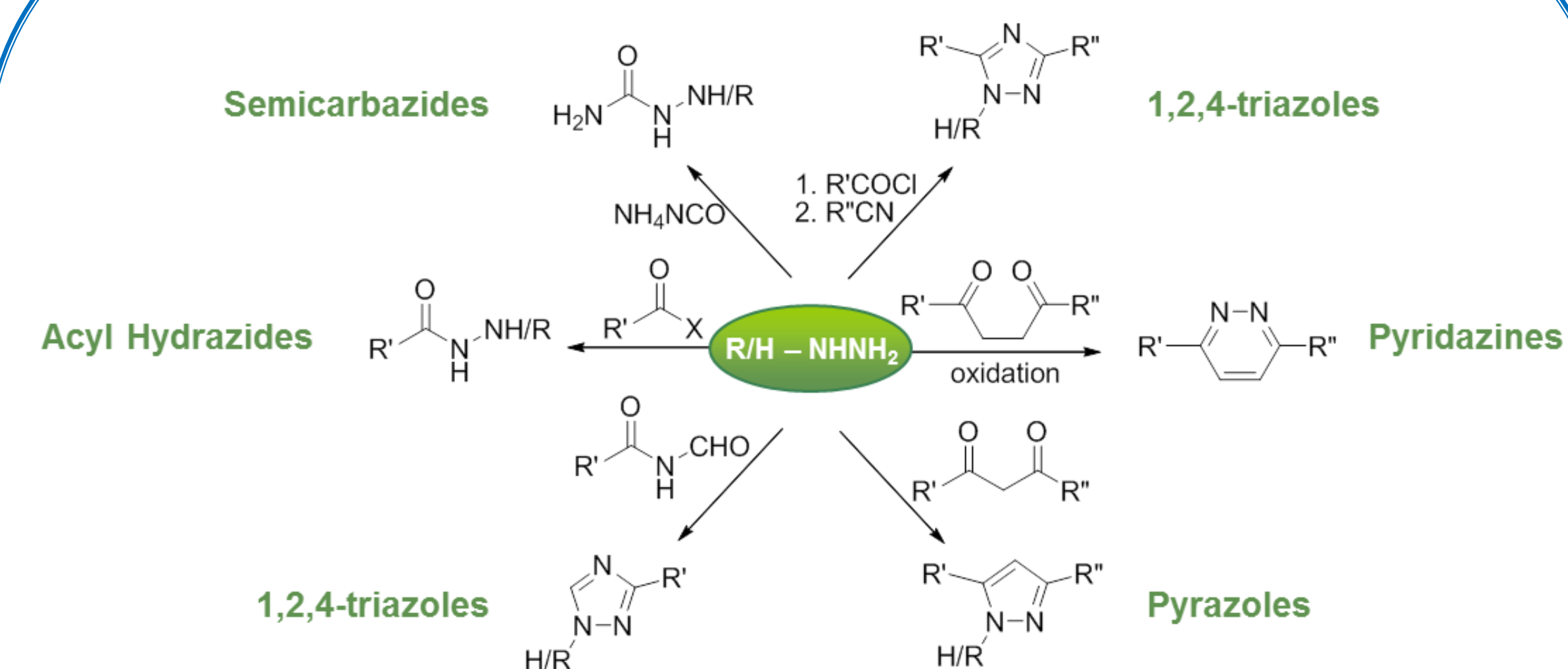
- Diazomethane allows for high yielding, very clean reactions
- AFC has produced 100s of metric tons of products via *in-situ* continuous process for diazomethane

Other Diazo chemistries



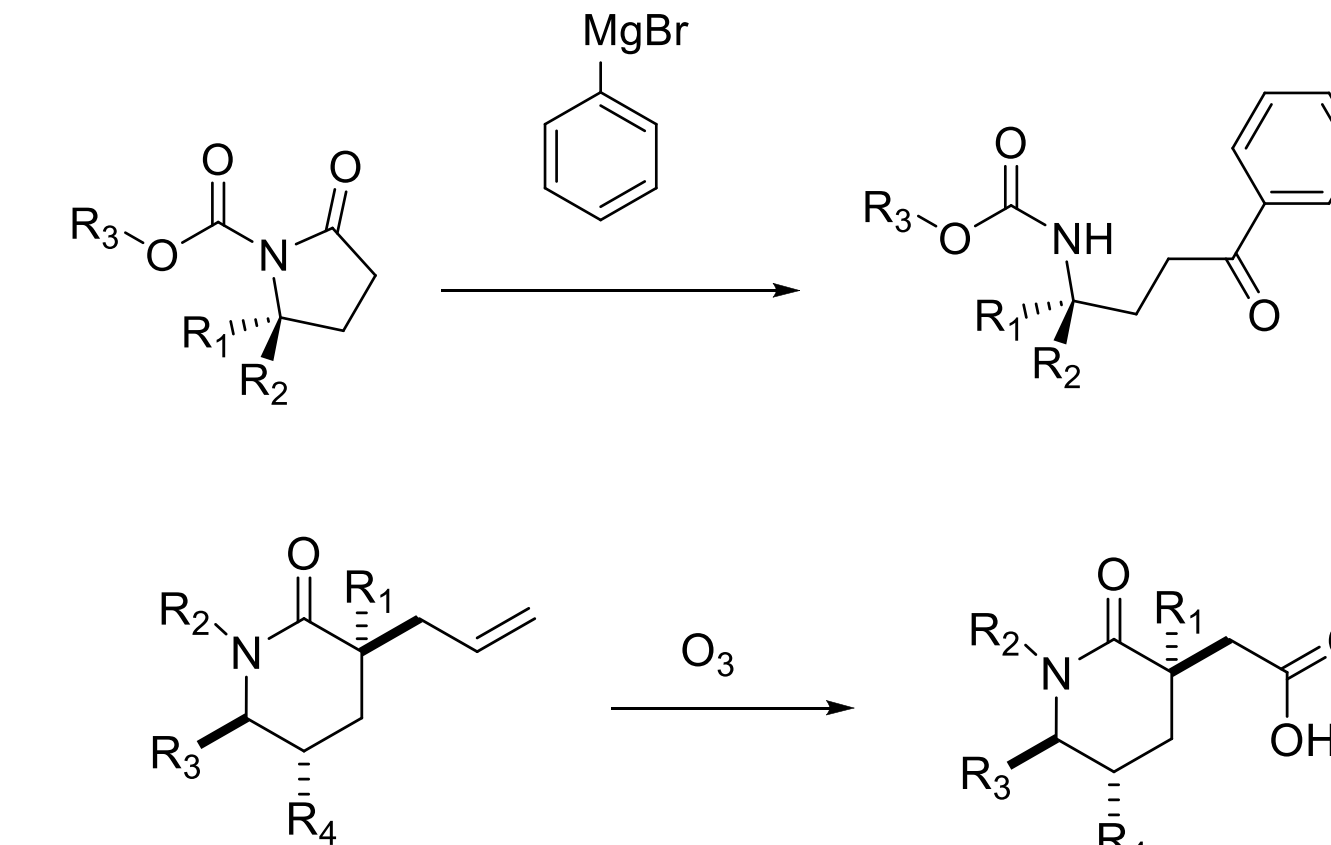
- EDA is a commercially useful reagent for cyclopropanations and ring expansions
- Various diazo precursors can be prepared through diazo transfer
- Reaction of alkenes with diazo compounds followed by SMB provides an efficient preparation of chirally pure cyclopropyl compounds

Hydrazine



- Approved user of anhydrous hydrazine (controlled by US DoD)
- Useful for preparation of substituted hydrazines, semicarbazides, and heterocycles

Continuous Processing increases capabilities



- AFC has used various types of continuous equipment to control hazardous reactions, increase selectivity, and control impurities
- AFC has expertise in designing and building continuous equipment
- AFC uses fixed equipment in conjunction with continuous skids to perform various unit operations.

AFC Equipment – Dedicated Facilities Designed to Develop and Handle Hazardous Chemistries

Process Hazard Evaluation

- A balanced approach of technologies to safely run hazardous reactions
 - Ranging tests performed to determine safe processing control limits
 - Process hazard analysis performed prior to the scale-up of each project



- DSC/TGA, RC-1, Friction, Other...

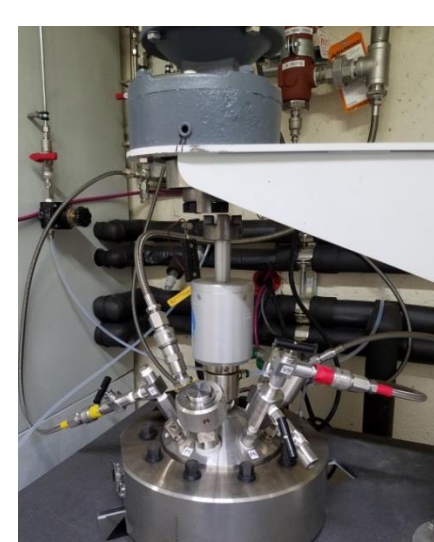


Process Development – kilo Scale

- R&D non GMP facility
- Development bays with remote controls
- Batch, CSTR or Tube Reactor demonstration
- Kg scale batch hydrogenation



High Pressure Tube Reactor



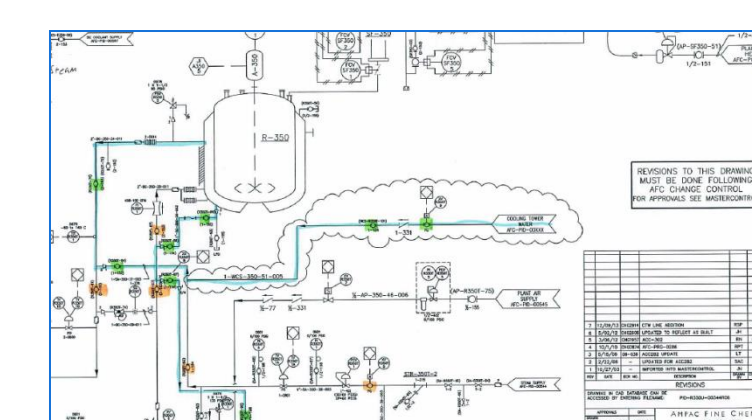
PARR Batch H₂ reactor



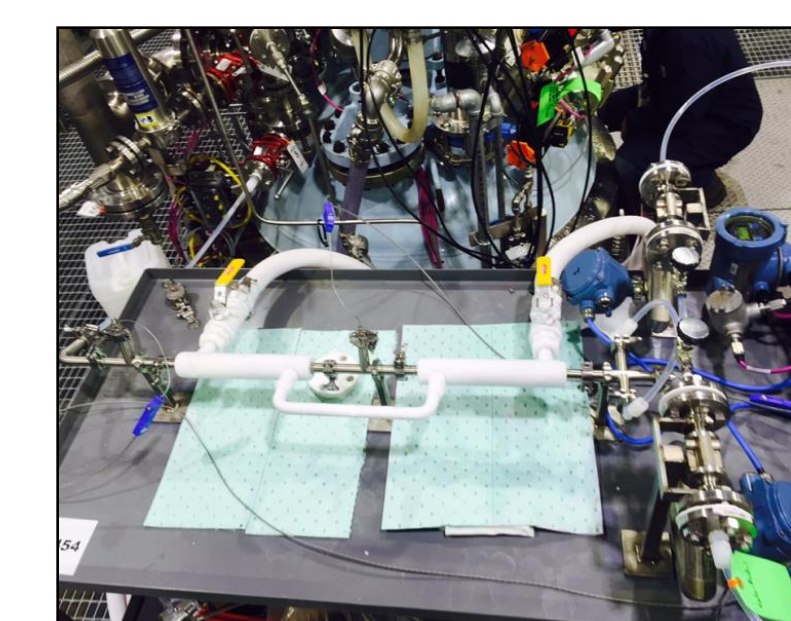
Kg scale CSTR

Batch Manufacturing at Commercial Scale

- Multiple c-GMP facilities
- Azide rated units
 - 100 - 500 gal pilot
 - 1,500/2,000 gal production
- Temperature controlled
- Engineering controls



Continuous Reactions For Hazardous Processes



Continuous Diazomethane Generator

- Safe production of over 1,600 batches of cGMP diazomethane in a 750 gallon scale multi-product facility
- Production capacity over 100's of MTA

Continuous Modular Tube Reactor

- Grignard reactions
- Static mixer and flow control
- Over 100 kg in 24 h
- Variable configuration