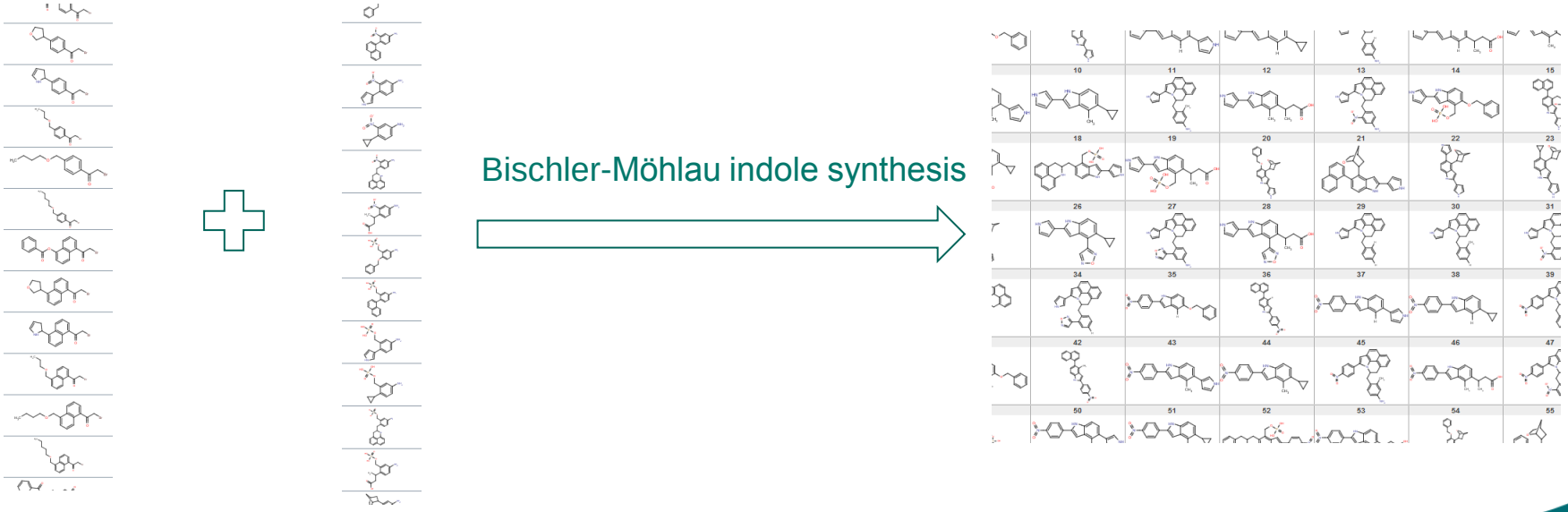
Reactor – switching on the manual gear

György Pirok, Zsolt Mohácsi, **Iván Solt**

Reactor – overview

ChemAxon's virtual reaction enumeration engine and application

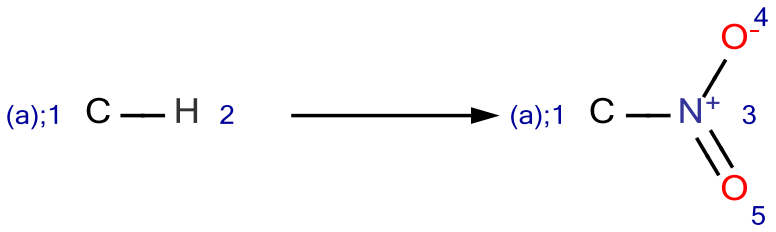
- generic reaction schemes to yield chemically feasible reaction products
- reaction library of organic chemical reactions
- reaction sketching interface
- Accessibility: application with GUI and batch mode; JChem for Excel; Instant JChem; API

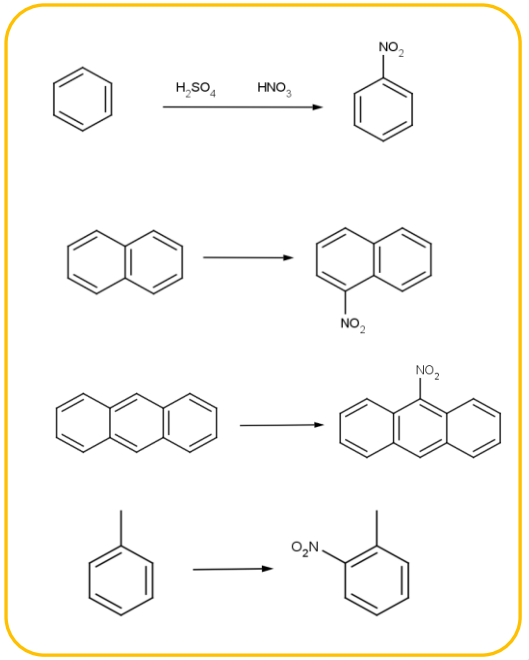


Reaction schema

Generic reaction equation
- query notation
- atom mapping on atoms involved in the reaction
- orphan atoms can be present
- implicit hydrogens not considered!

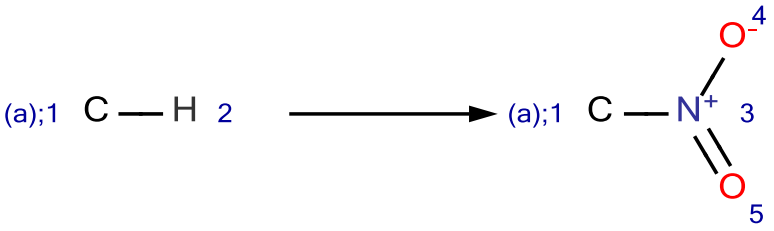
Example: nitration of aromatic hydrocarbons:





Highly automated enumeration

- Reagents loaded from structure files
- Chemical intelligence by reaction rules
- Rules evaluated by calculated or imported properties (Chemical Terms)
- Fine-tuning of the automatic enumeration process



Reactivity: `electronDensity(ratom(1))>0.75;`

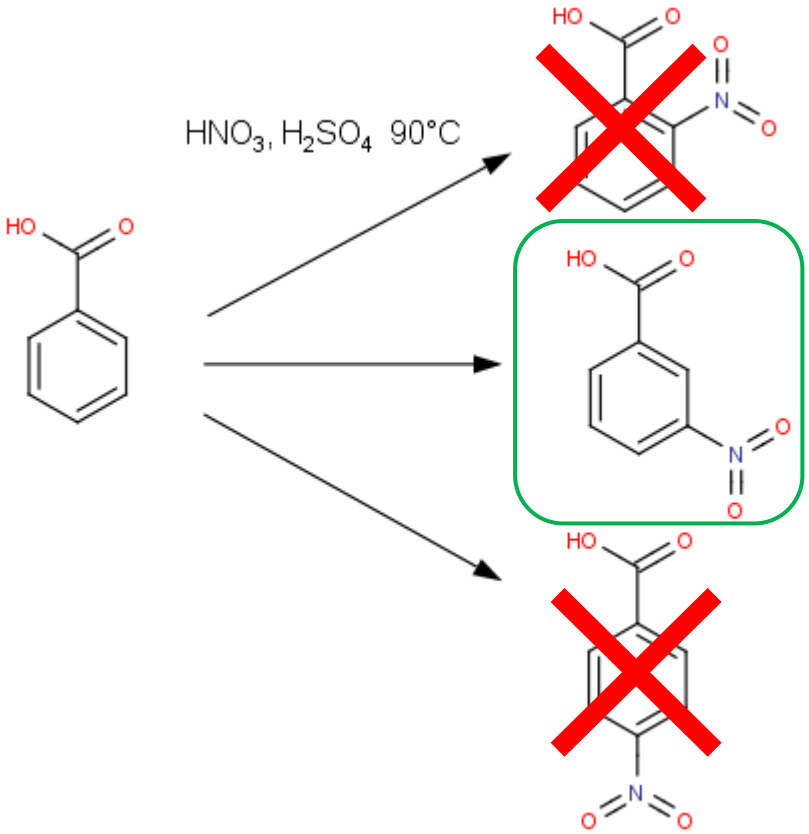
Selectivity: `-energyE(ratom(1))`

Exclude:
```
match(reactant(0),"[#6]C(=O)OC([#6])=O")  or
match(reactant(0),
      "[#6]-[#5,#12,#15,#16,#25,#26,#29,#33,#47,#50,#51,#80,#82,#83]")
```

ChemAxon's Reaction Library

- A collection of named, commonly used organic chemical reactions (145)
  - Schema
  - Rules
  - Descreption with references and preparation instructions
  - Examples (test cases)
- New development: constantly evolving collection of reactions (appr. 100)
  - Systematic, based on functional groups (e.g. reactions of amines)
- Extendable

Rules vs. chemical intuition on the fly



Defining rules: can be long and complicated

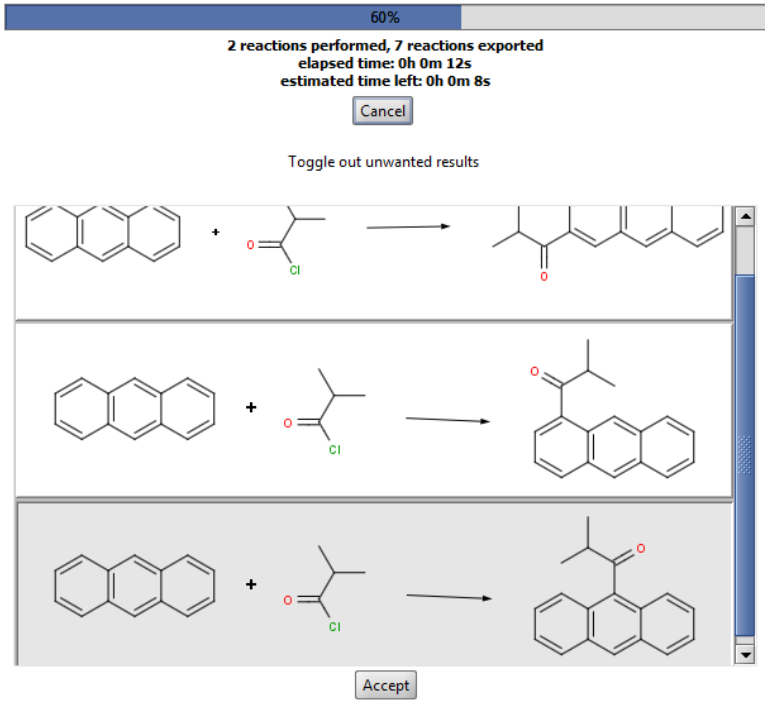
Desired process for small libraries:

1. *draw schema*
2. *draw reactants*
3. *select products based on my chemical intelligence*

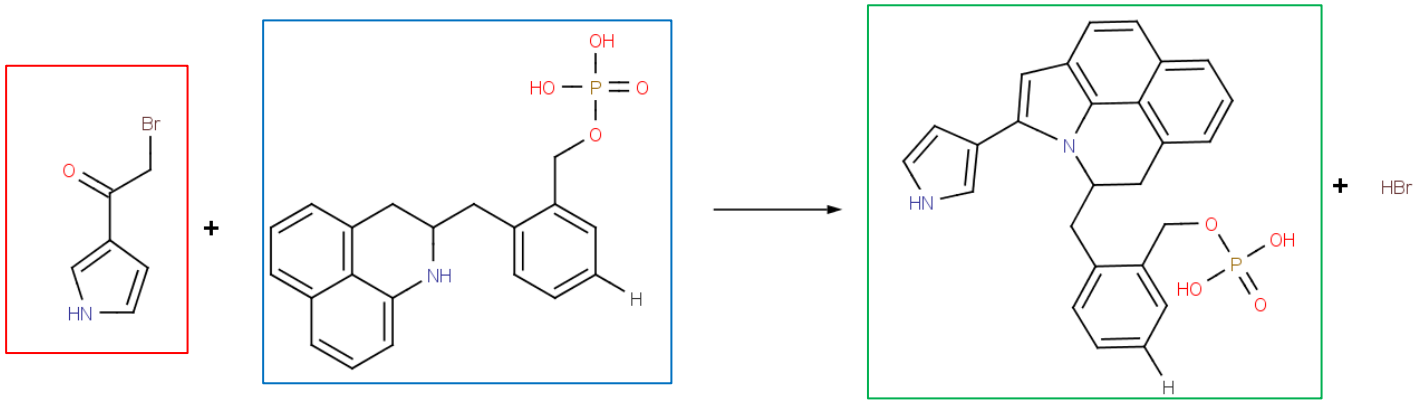
Manual in silico chemistry

Full manual control over enumeration process

- Quick and simple
- For small libraries
- *Manual drawing* of reagent input in GUI
- *Regeioselectivity* by manual product selection



Advanced synthesis information handling



Cpd ID: CXN12768373

Location:R12/Sh3/A5

Name: 2-bromo-1-(1H-pyrrol-3-yl)ethan-1-one

Cpd ID: CXN2763123

Location: R2/Sh5/A1

Name: {[2-(2,3-dihydro-1H-perimidin-2-ylmethyl)phenyl]methoxy}phosphonic acid

Solubility
Hazard
Solvent
Price
Boiling point
Melting point

Solubility
Hazard
Solvent
Price
Boiling point
Melting point

Synthesis code:

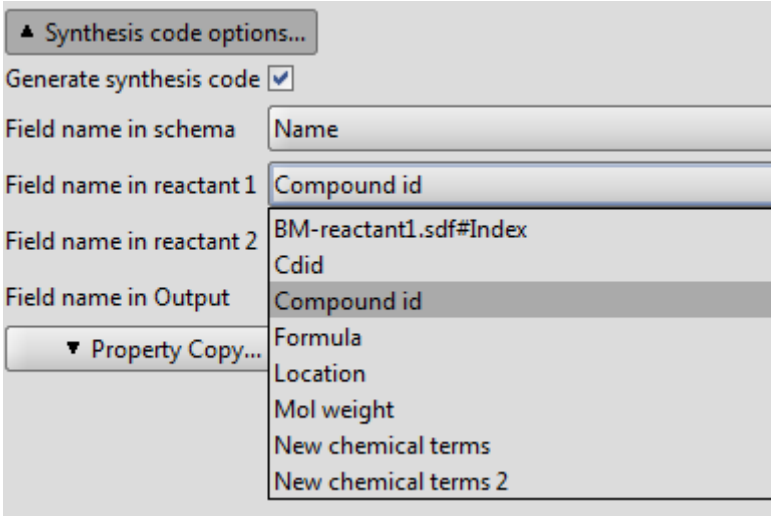
Bischler-Mohlau indole synthesis(CXN13367281, CXN18734652):1/1

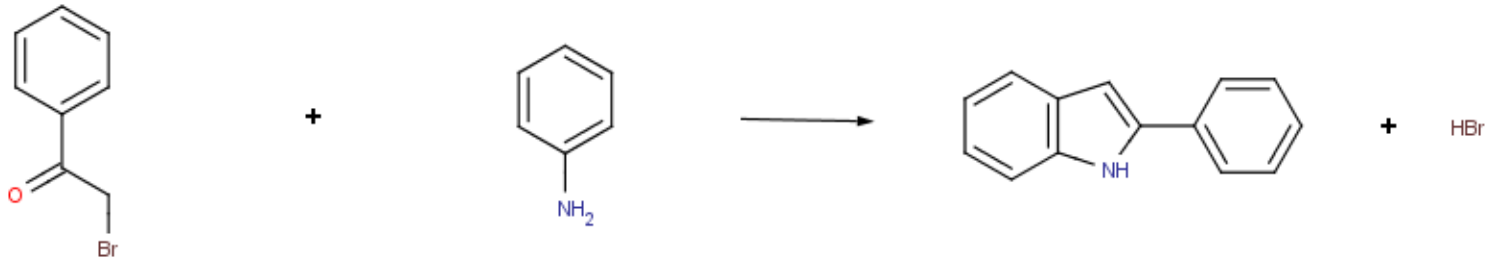
Reactant information:

Reacant 1	***Reactant 2***
Solubility	Solubility
Hazard	Hazard
Solvent	Solvent
Price	Price
Boiling point	Boiling point
Melting point	Melting point

Info dump – synthesis code

- Unique string for all enumerated products
- Contains synthesis definition information
  - reaction identifier
  - IUPAC name
  - company registration code
  - location of reagent
  - ...
- Concatenatenated for multi-step reactions – synthesis path definition





Cpd ID: CXN13367281

Location: R12/Sh10/A2

Name: 2-bromo-1-phenylethan-1-one

Cpd ID: CXN18734652

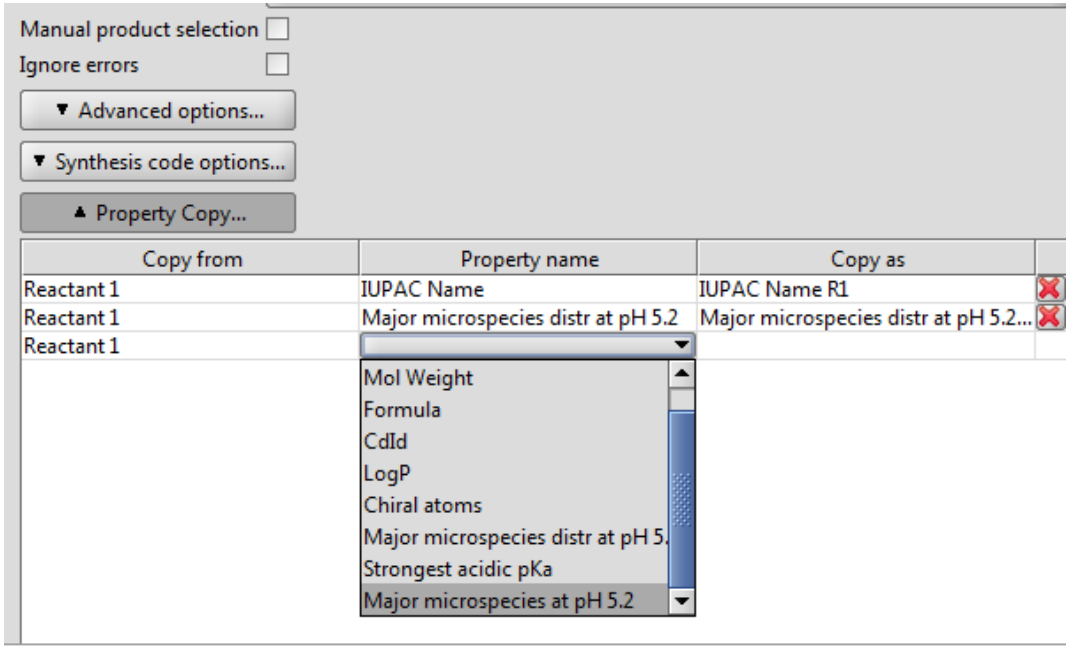
Location: R3/Sh3/A1

Name: aniline

Bischler-Mohlau indole synthesis(CXN13367281, CXN18734652):1/1

Info dump – reactant information

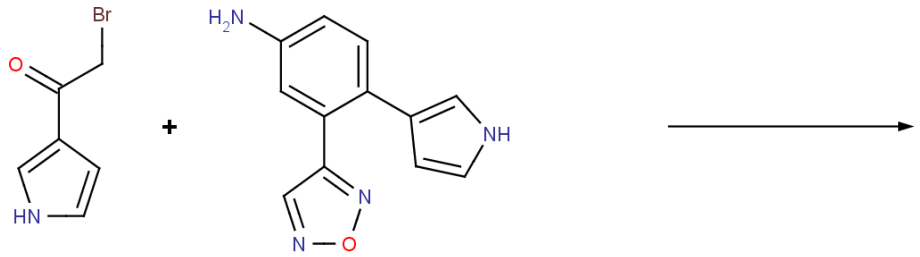
- Arbitrary fields can be copied from the input structure files to the output
  - ✓ solubility
  - ✓ toxicity
  - ✓ availability
  - ✓ price
  - ✓ microspecies information
  - ✓ ...
- Reaction databases stored with reactant information
- Reaction queries based on reactants



New features

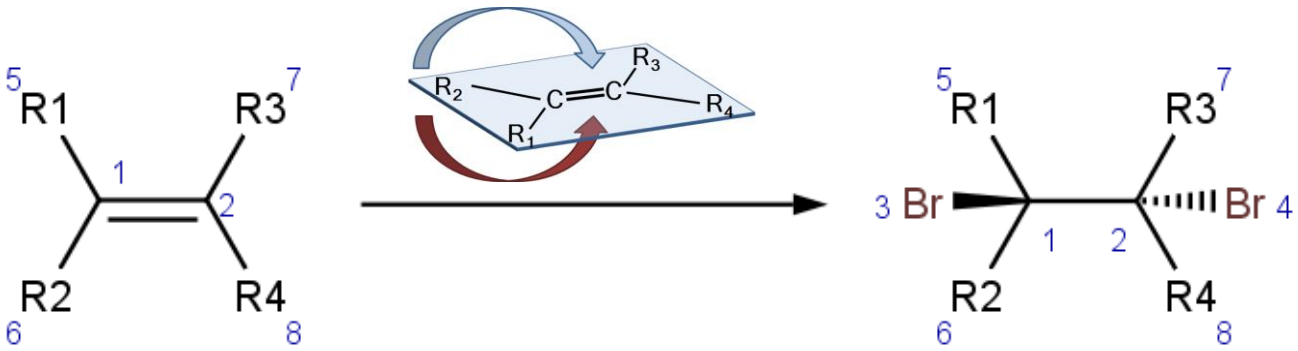
- Unsuccessful reactions

  include reactions in the output that yield no products



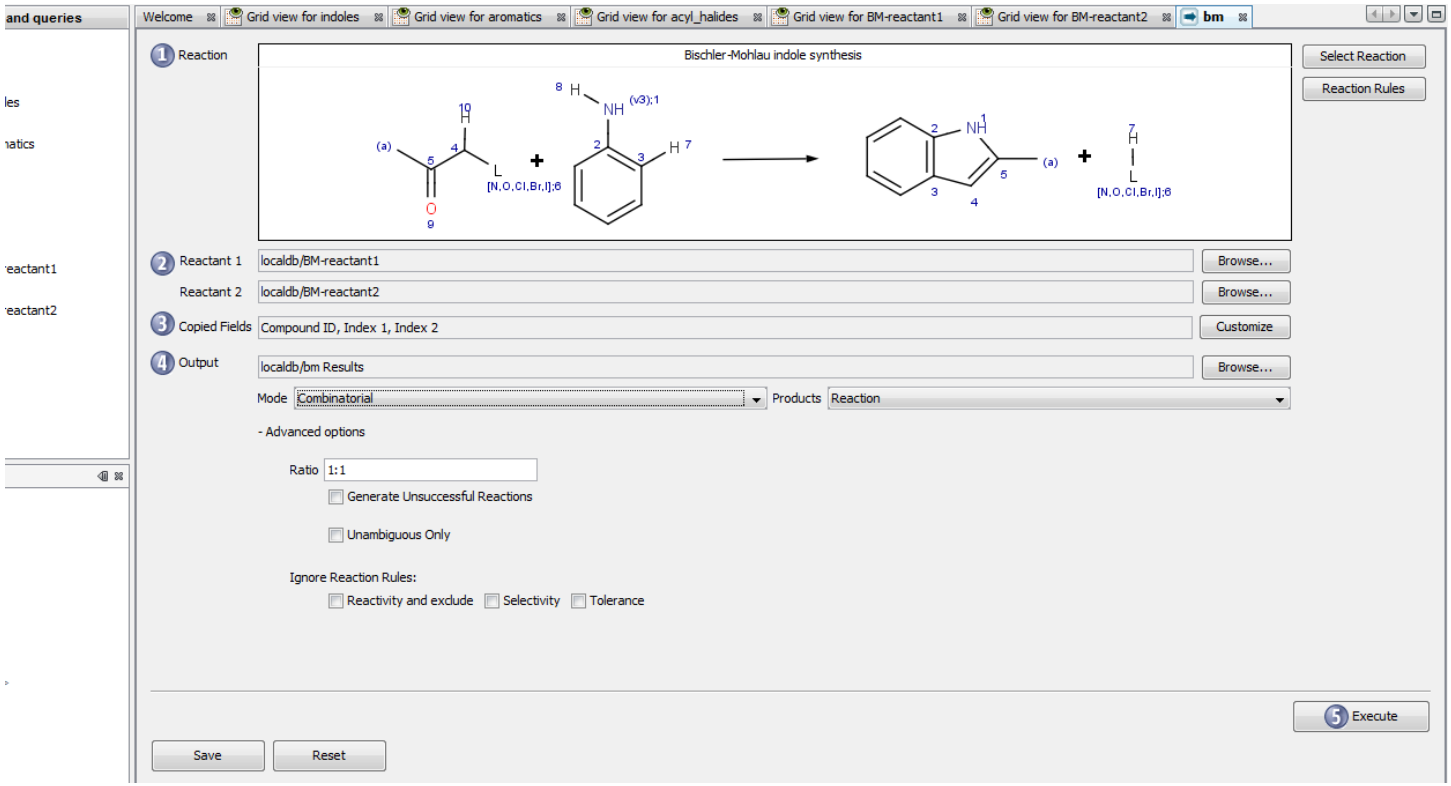
- Prochiral reactions

  syn/anti addition support on double bonds



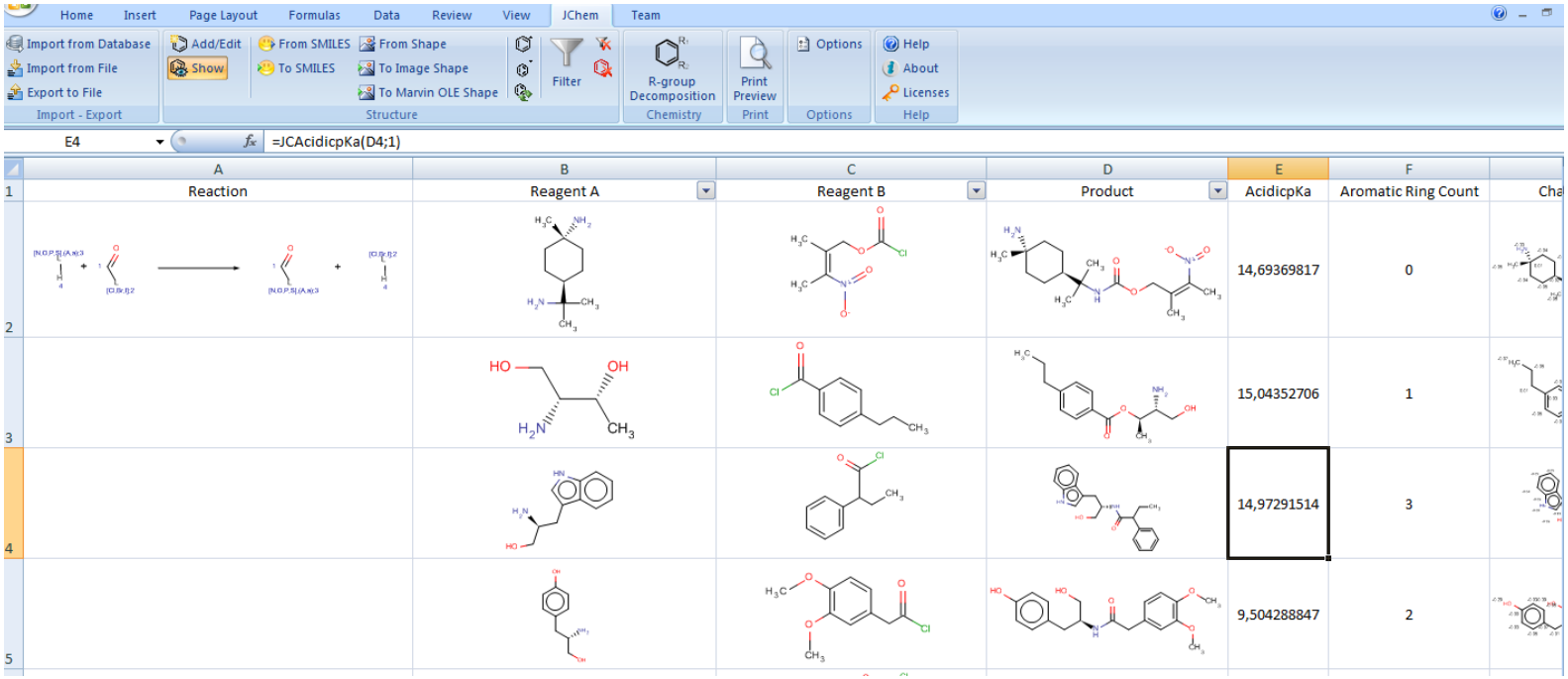
Reactor in Instant JChem

- Instant JChem integration
- Easy direct access to chemical databases for Reactor
- Straightforward post-processing and visualization



Reactor in JChem for Excel

- Smoothly integrated into Microsoft Excel environment
- Sequential and combinatorial enumeration available
- Direct post-processing of products



Future plans

- Extend systematic reaction library

  - *To cover most possible of organic chemistry*

- Custom synthesis identifier generation

  - *Combining field copy with synthesis code to have customizable identifiers for products and synthesis paths*

- Improved prochiral reaction support

Thank you

Zsolt Mohácsi

György Pirok

Anna Tomin

Attila Szabó

István Rábel

Nóra Máté