
Reactor – switching on the manual gear

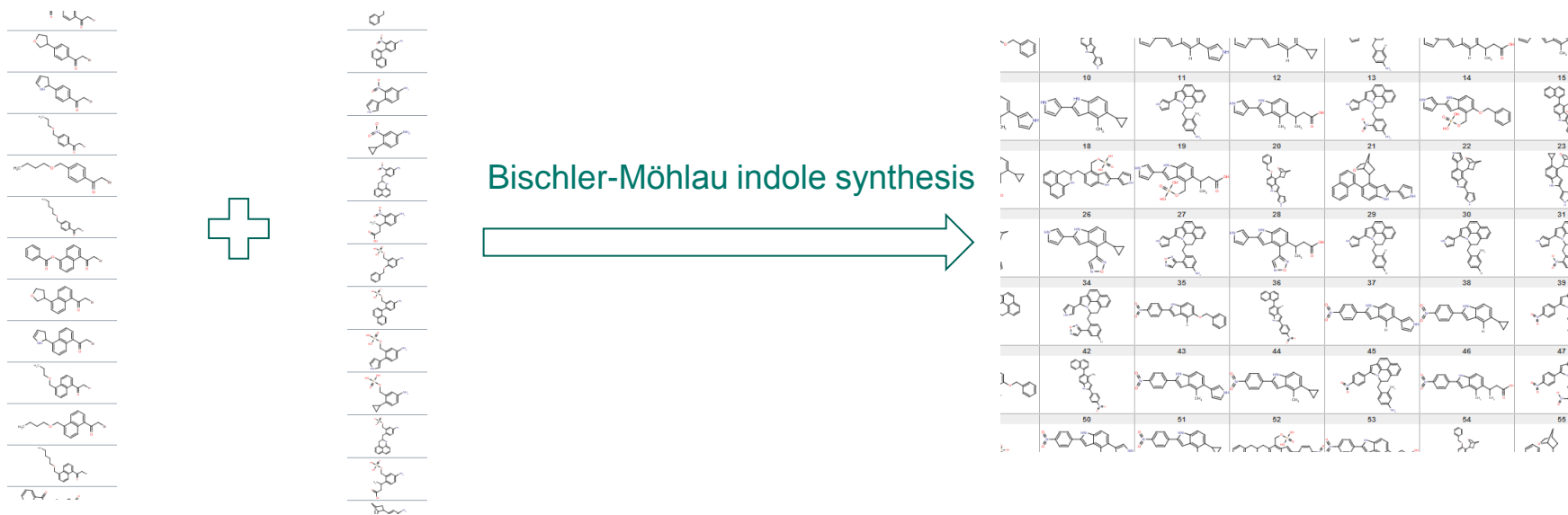
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Reactor – overview

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

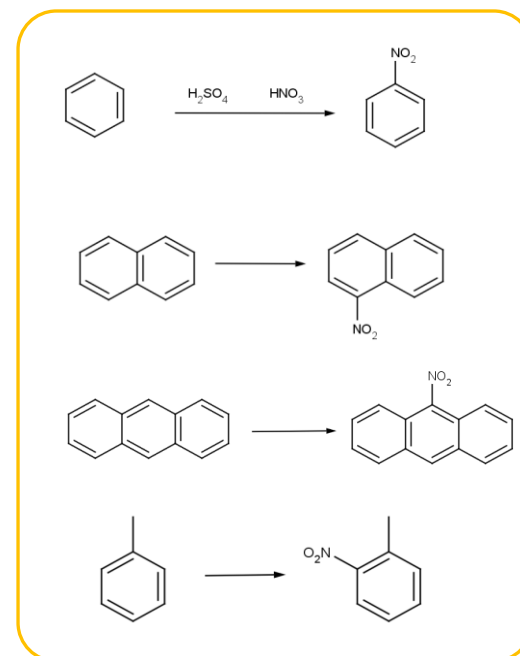
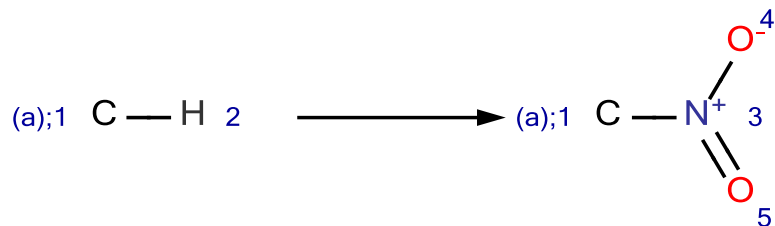


Reaction schema

Generic reaction equation

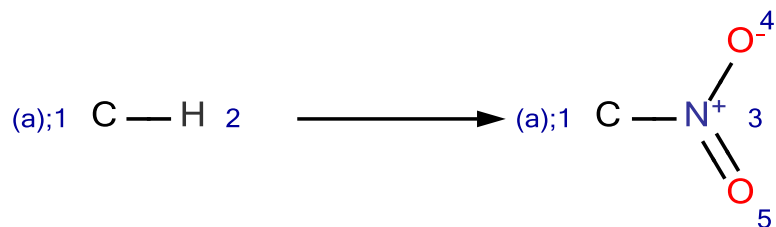
- query notation
- atom mapping on atoms involved in the reaction
- orphan atoms can be present
- implicit hydrogens not considered!

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;`

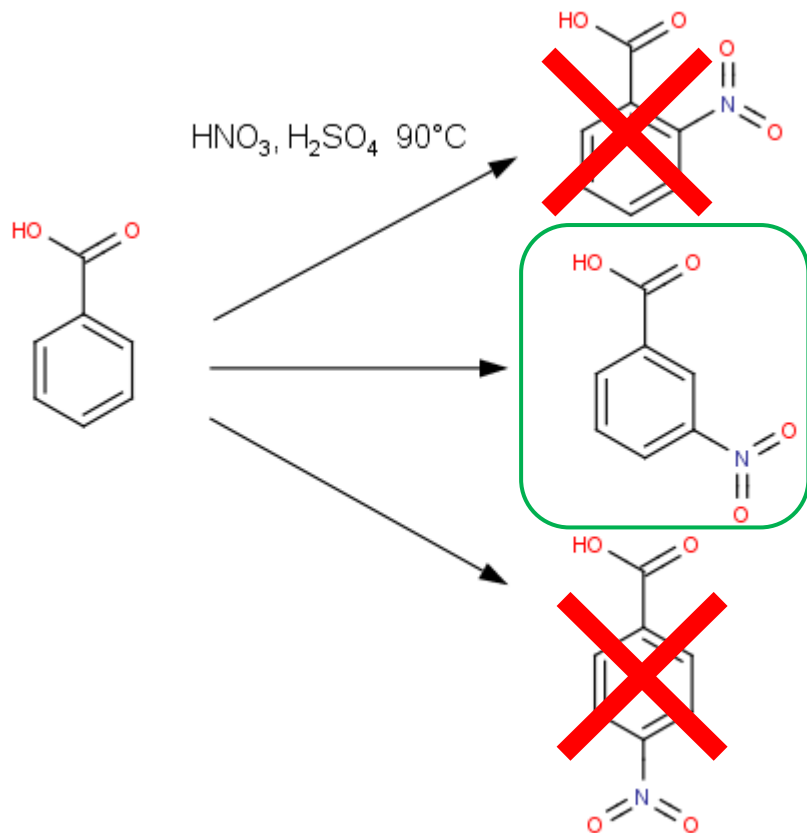
Selectivity: `-energyE(ratom(1))`

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
 - Description 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

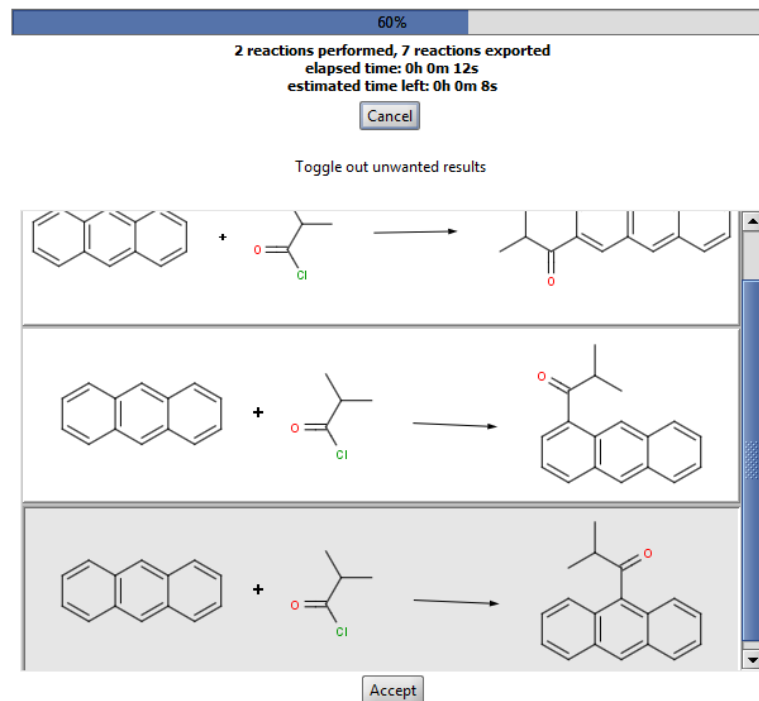
Desired process for small libraries:

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

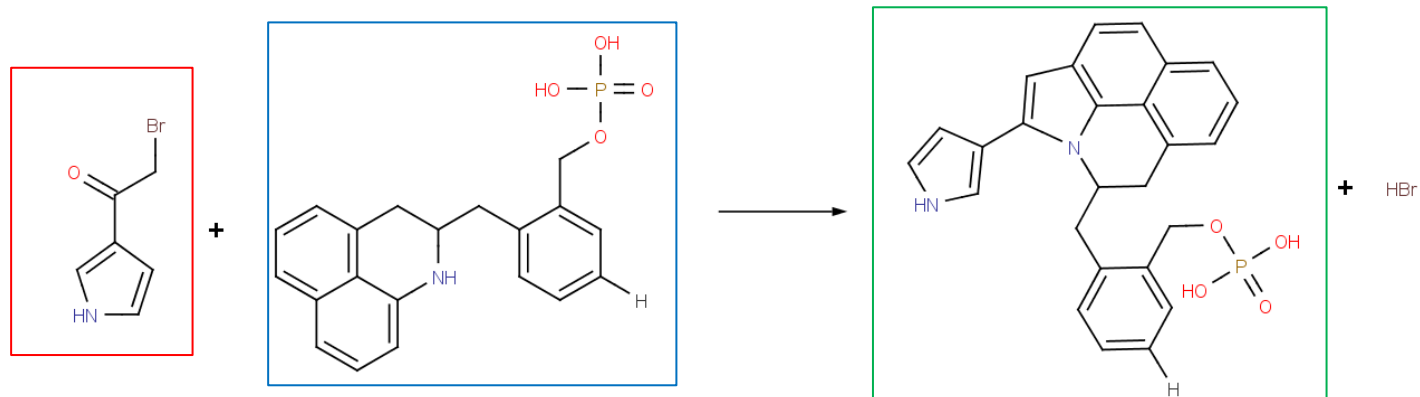
Manual in silico chemistry

Full manual control over enumeration process

- Quick and simple
- For small libraries
- *Manual drawing* of reagent input in GUI
- *Regioselectivity* 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

Solubility

Hazard

Solvent

Price

Boiling point

Melting point

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

Synthesis code:

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

Reactant information:

Reactant 1

Solubility

Hazard

Solvent

Price

Boiling point

Melting point

Reactant 2

Solubility

Hazard

Solvent

Price

Boiling 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
 - ...
- Concatenated for multi-step reactions – synthesis path definition

▲ Synthesis code options...

Generate synthesis code

Field name in schema Name

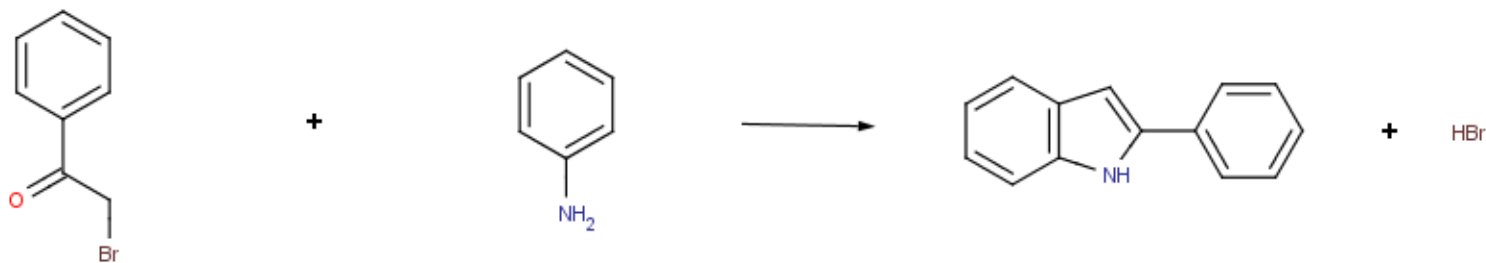
Field name in reactant 1 Compound id

Field name in reactant 2 BM-reactant1.sdf#Index
Cdid

Field name in Output Compound id

▼ Property Copy...

Formula
Location
Mol weight
New chemical terms
New chemical terms 2



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

Manual product selection

Ignore errors

▼ Advanced options...

▼ Synthesis code options...

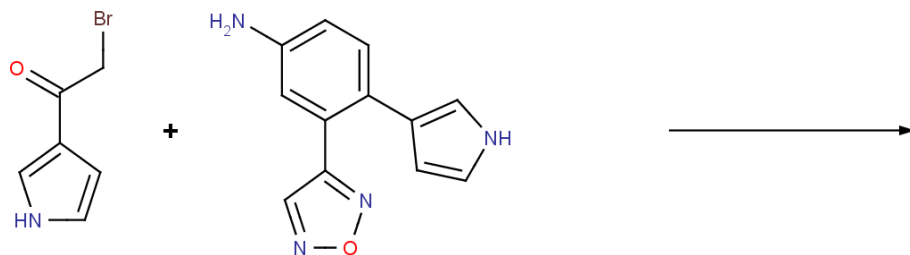
▲ Property Copy...

Copy from	Property name	Copy as
Reactant 1	IUPAC Name	IUPAC Name R1
Reactant 1	Major microspecies distr at pH 5.2	Major microspecies distr at pH 5.2...
Reactant 1	<div style="border: 1px solid gray; padding: 2px;">▼ Mol Weight Formula CdId LogP Chiral atoms Major microspecies distr at pH 5.2 Strongest acidic pKa Major microspecies at pH 5.2 ▼</div>	

New features

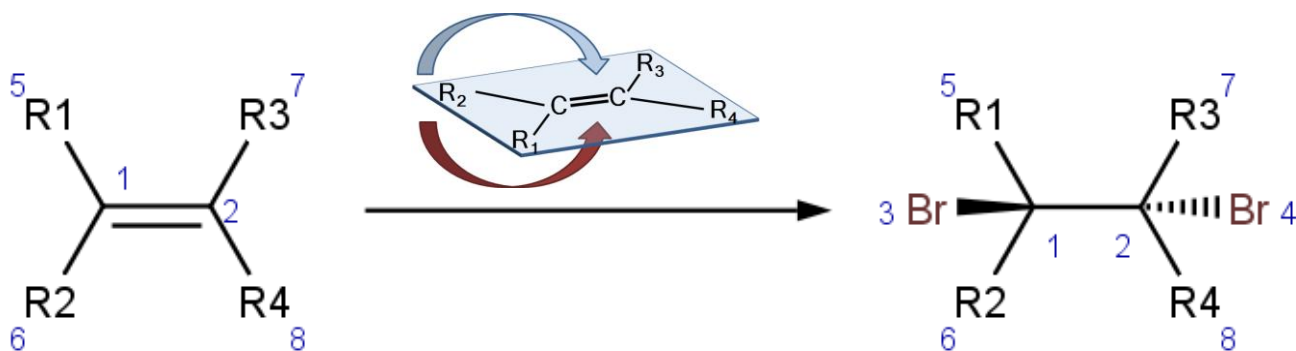
- Unsuccessful reactions

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

The screenshot displays the Reactor interface in Instant JChem. The main window shows the reaction: CC(=O)C + Nc1ccccc1 >> C1=CNc2ccccc12. The reaction is titled "Bischler-Mohrlau indole synthesis". The interface includes a sidebar on the left with "and queries" and "les" tabs. The main area has a "Reaction" section with a chemical structure diagram. Below the diagram are fields for "Reactant 1" (localdb/BM-reactant1), "Reactant 2" (localdb/BM-reactant2), "Copied Fields" (Compound ID, Index 1, Index 2), and "Output" (localdb/bm Results). The "Mode" is set to "Combinatorial" and "Products" is set to "Reaction". There are "Advanced options" including "Ratio" (1:1), "Generate Unsuccessful Reactions" (unchecked), "Unambiguous Only" (unchecked), and "Ignore Reaction Rules" (Reactivity and exclude, Selectivity, Tolerance, all unchecked). Buttons for "Save", "Reset", "Execute", "Select Reaction", and "Reaction Rules" are visible.

Reactor in JChem for Excel

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

	A	B	C	D	E	F	G
	Reaction	Reagent A	Reagent B	Product	Acidic pKa	Aromatic Ring Count	Chemical Structure
1					14,69369817	0	
2					15,04352706	1	
3					14,97291514	3	
4					9,504288847	2	
5							

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



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