The Open Reaction Database

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RDKit UGM | 7 October 2020 | open-reaction-database.org

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Design considerations

From the documentation: "support machine learning and related efforts in reaction prediction, chemical synthesis planning, and experiment design"

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Goals:

- Provide a structured data format for chemical reaction data
- Provide an interface for easy browsing and downloading of data
- Make reaction data freely and publicly available for anyone to use
- Encourage sharing of precompetitive proprietary data, especially HTE data

Design considerations

From the documentation: "support machine learning and related efforts in reaction prediction, chemical synthesis planning, and experiment design"

Non-goals (at least initially):

- Capture reaction processes as action sequences for robotic execution
- Store processed, structured analytical data or other inputs that are not directly related to the machine learning efforts described above
- Integrate model building or other use of the data as part of the database

Primary use cases: synthetic organic chemistry

1. High-throughput experimentation
    a. Data are recorded in spreadsheet formats including only varied parameters;
    b. One template Reaction is defined to specify all aspects held constant;
    c. The Dataset is defined by iterating over the spreadsheet and creating one Reaction entry per experimental condition.
2. “Traditional” bench chemistry
    a. A chemist uses a graphical webform to define the settings and outcomes of all reactions used within a paper or project;
    b. The structured Dataset is saved, uploaded to the Open Reaction Database, and used as part of their supporting information;
    c. A list of reactions is exported from the Dataset in an SI-like text format.

Goals for the schema

- Capture the most important aspects of reactions in a *structured* format
  - Guided by our survey last winter, the focus is on single-step batch reactions
  - Structured data enables downstream ML applications
- Allow additional details in a flexible, *unstructured* format
- Match chemist expectations around structure and nomenclature
- Record what physically occurred in a chemical reaction; de-emphasize recording of a chemist's intent
  - e.g., record the actual masses and volumes that were used to create a stock solution, not the target concentration
- Be human readable

Structure of the schema

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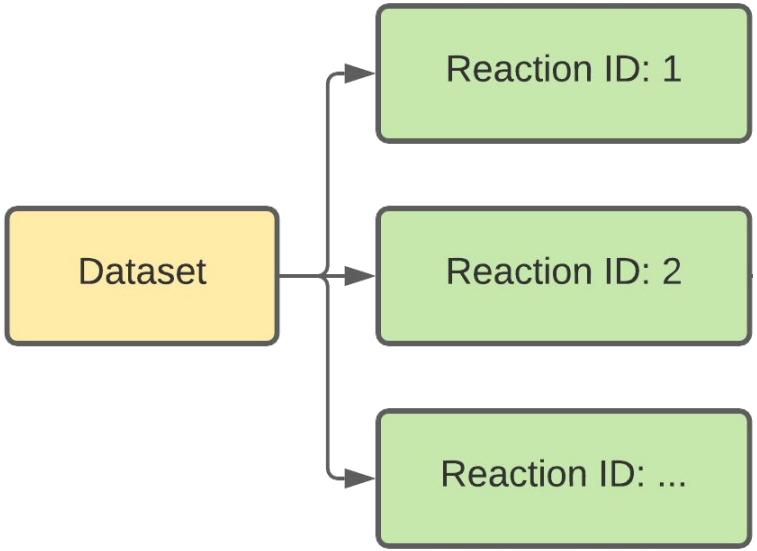
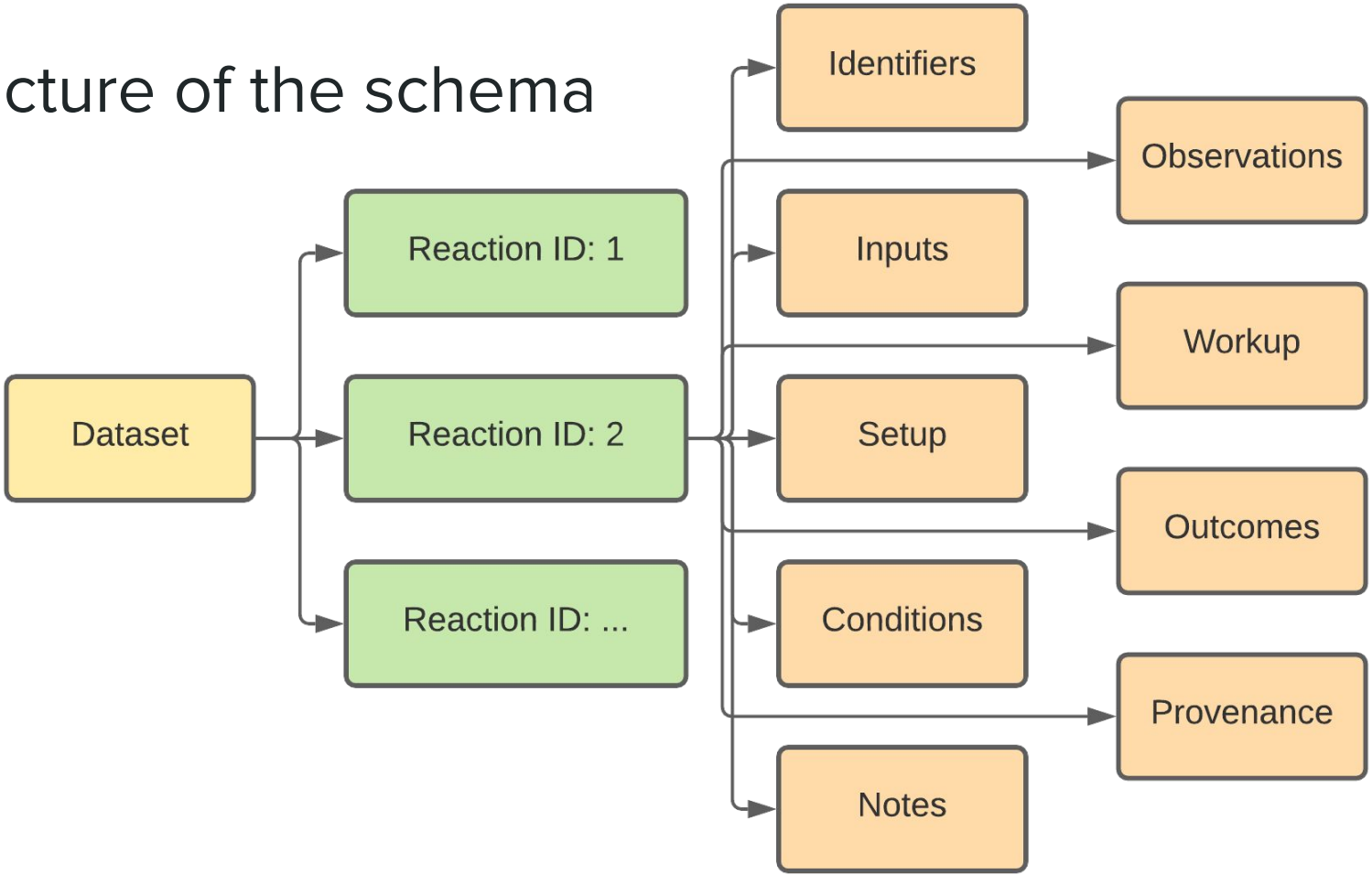


Structure of the schema



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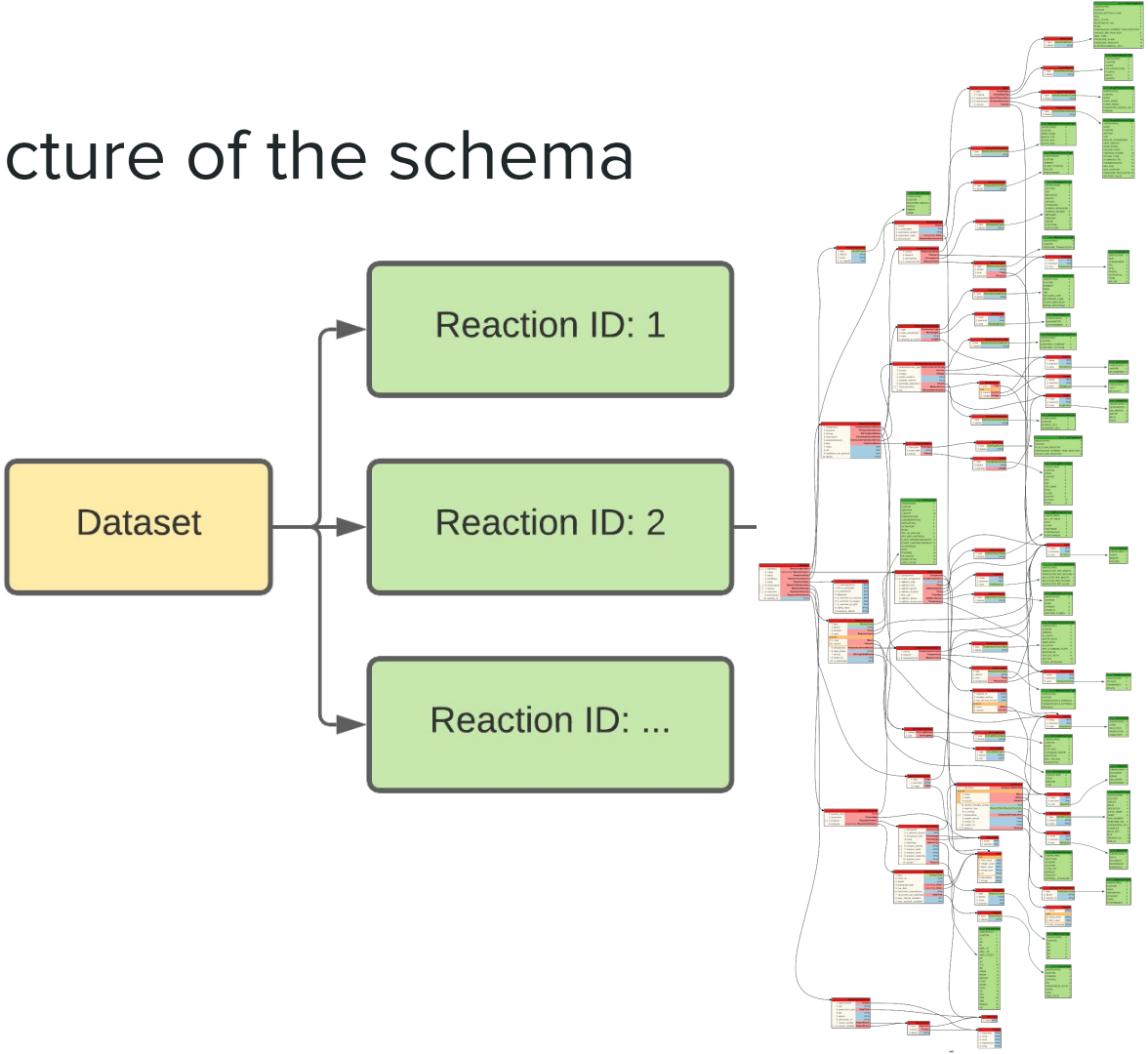

Protocol buffers

```
message Mass {
  enum MassUnit {
    UNSPECIFIED = 0;
    KILOGRAM = 1;
    GRAM = 2;
    MILLIGRAM = 3;
    MICROGRAM = 4;
  }
  float value = 1;
  // Precision of the measurement (with the same units as `value`).
  float precision = 2;
  MassUnit units = 3;
}
```

Protocol buffers

```
mass = schema.Mass(value=1.25, units='GRAM')
```

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```
mass = schema.Mass(value=1.25, units='GRAM')

resolver = units.UnitResolver()
mass = resolver.resolve('1.25 g')
```

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mass = schema.Mass(value=1.25, units='GRAM')

resolver = units.UnitResolver()
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mass_json = """{
  "value": 1.25,
  "units": "GRAM"
}"""
mass = json_format.Parse(mass_json, schema.Mass)
```

```
reaction = schema.Reaction()
reaction.identifiers.add(value=r'deoxyfluorination', type='NAME')

# Input 1a is a stock solution of alcohol in THF
reaction.inputs['alcohol in THF'].addition_order = 1
solute = reaction.inputs['alcohol in THF'].components.add()
solvent = reaction.inputs['alcohol in THF'].components.add()

solute.reaction_role = schema.Compound.ReactionRole.REACTANT
solute.identifiers.add(value=r'c1ccccc1CCC(O)C', type='SMILES')
solute.moles.CopyFrom(unit_resolver.resolve('0.1 mmol'))
solute.is_limiting = True

solvent.reaction_role = schema.Compound.ReactionRole.SOLVENT
solvent.identifiers.add(value=r'THF', type='NAME')
solvent.identifiers.add(value=r'C1CCCO1', type='SMILES')
solvent.volume.CopyFrom(unit_resolver.resolve('125 uL'))
solvent.preparations.add(type='DRIED')

...
```

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solvent.volume.CopyFrom(unit_reso
solvent.preparations.add(type='DR

...
```
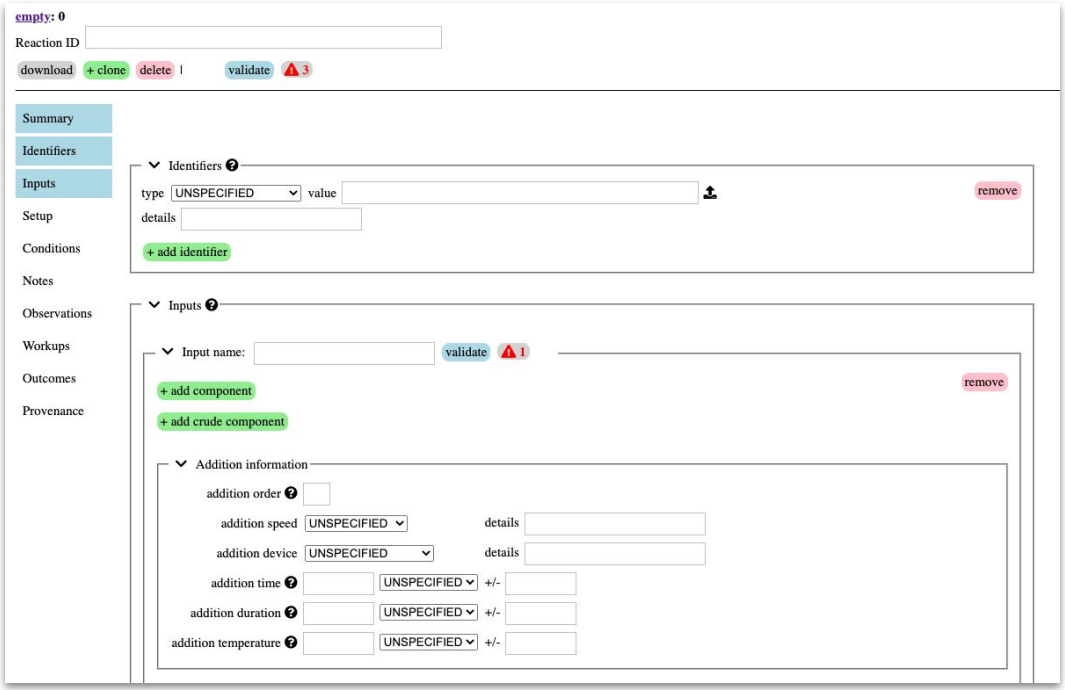

The RDKit is used in the data validation process:

- Reaction SMILES are checked for validity
- Compound structural identifiers are checked for validity and consistency

Web interface



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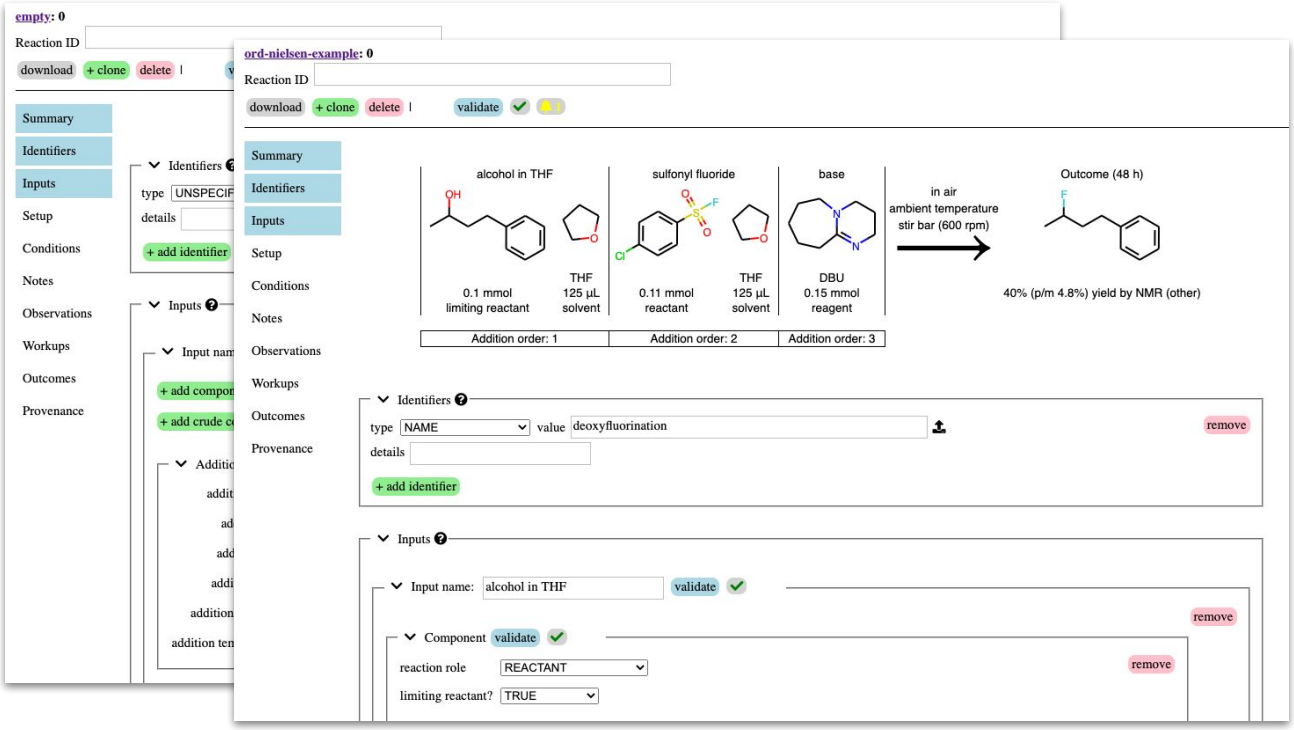

Contributors: Nathan Kim (MIT), Anton Kast (Google)

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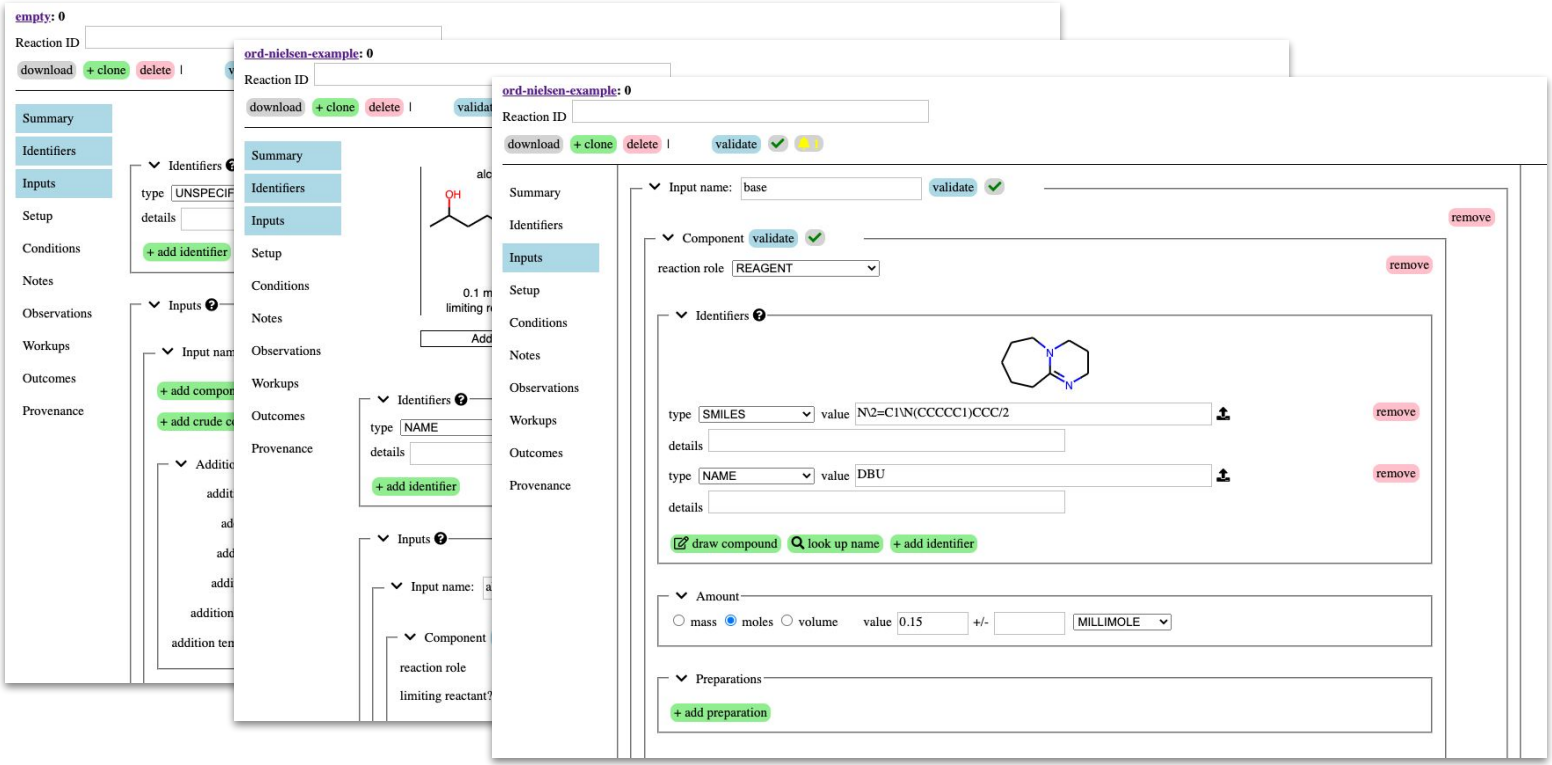

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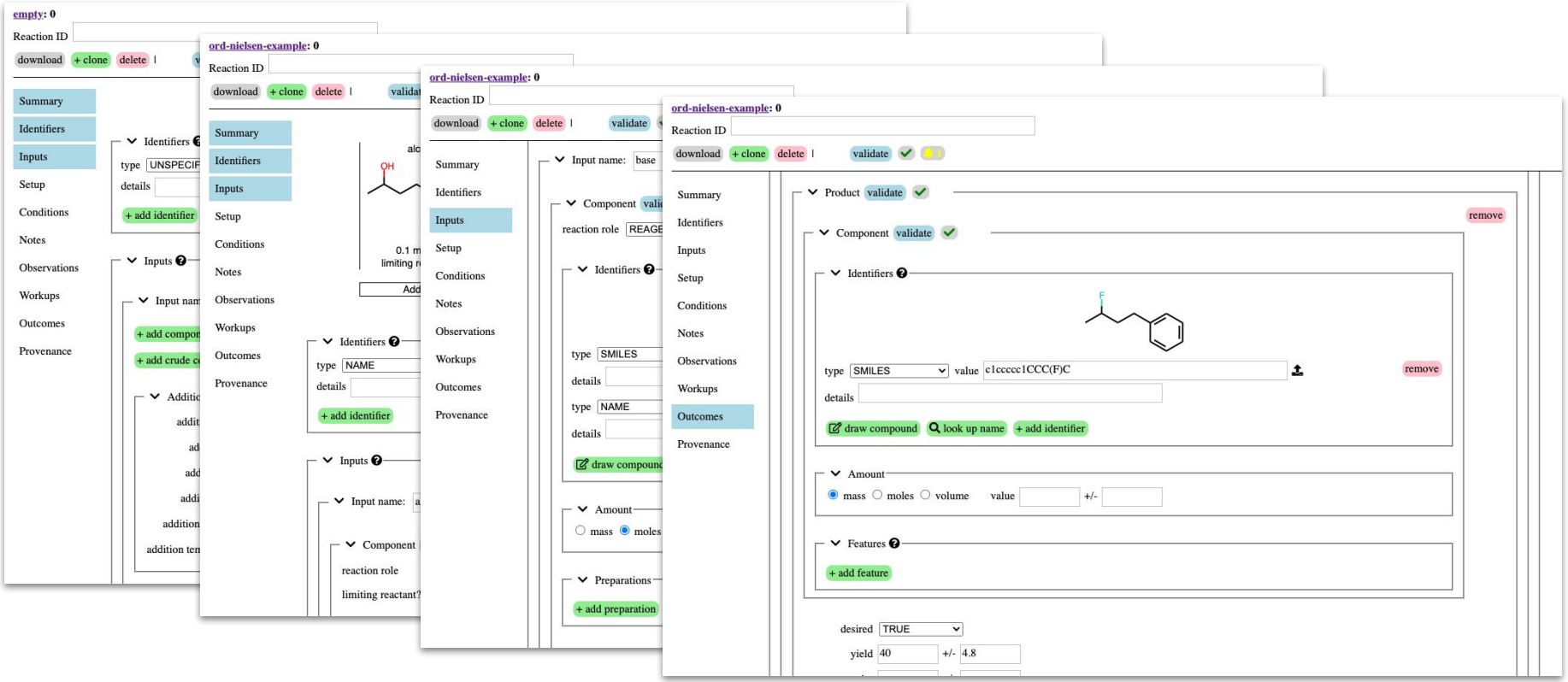

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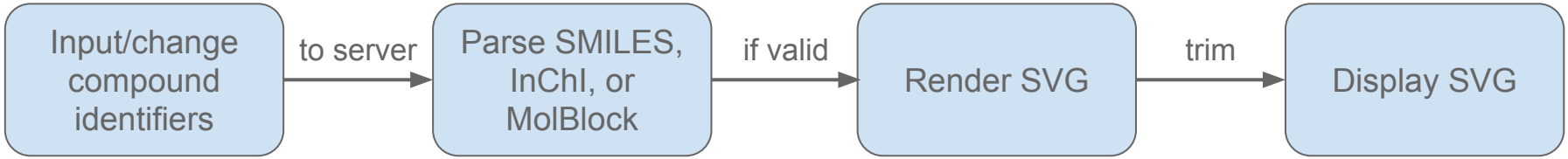
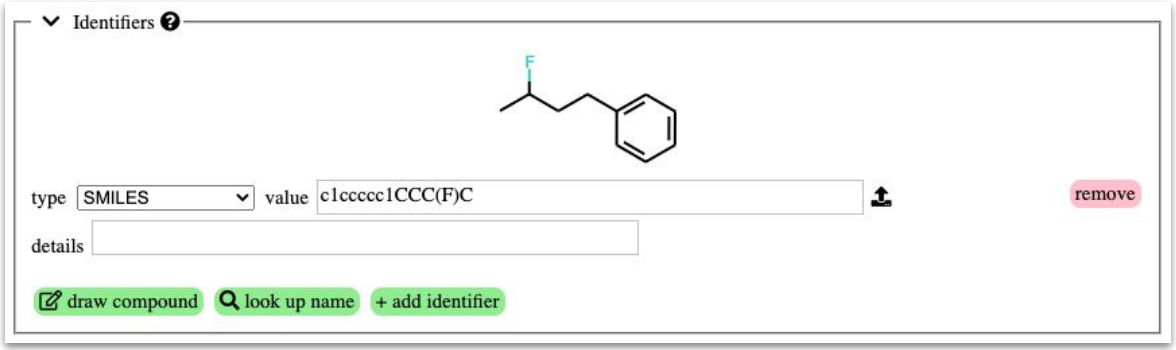
Web editor compound visualization

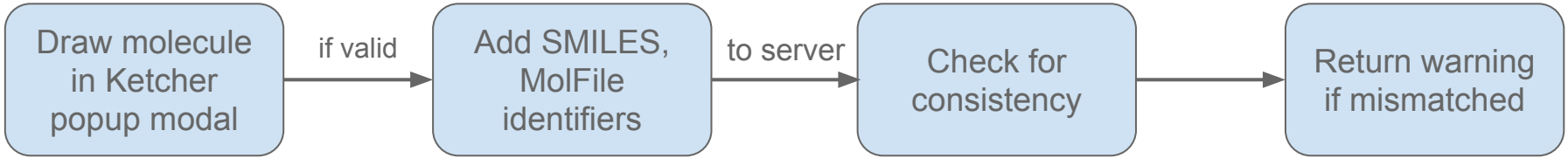
When viewing/editing a Reaction record, it's much easier to look at a chemical rendering than a SMILES or InChI string:

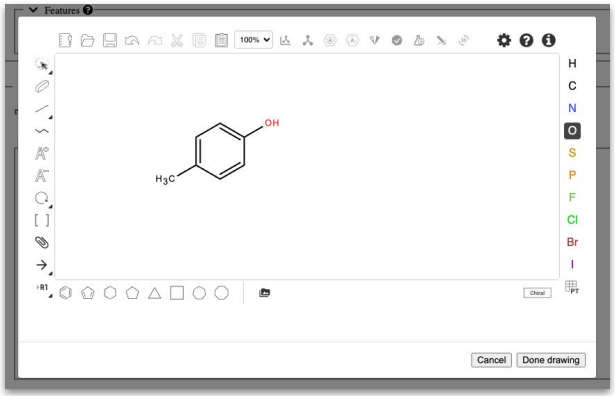


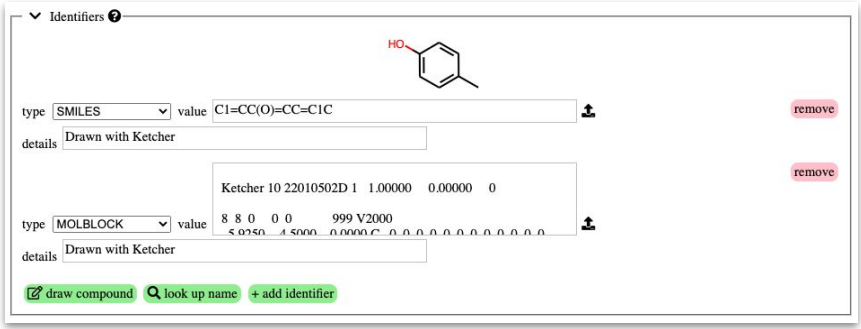


Web editor Ketcher integration

When defining a new molecule, it is handy to have an embedded drawing tool; we use Ketcher.







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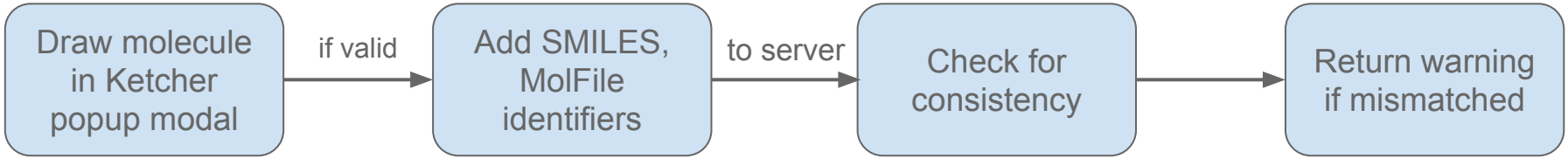
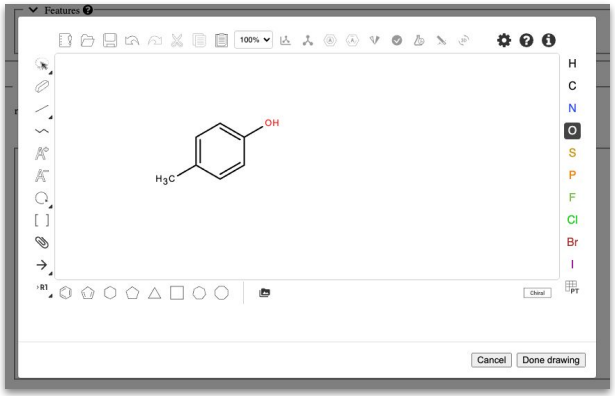
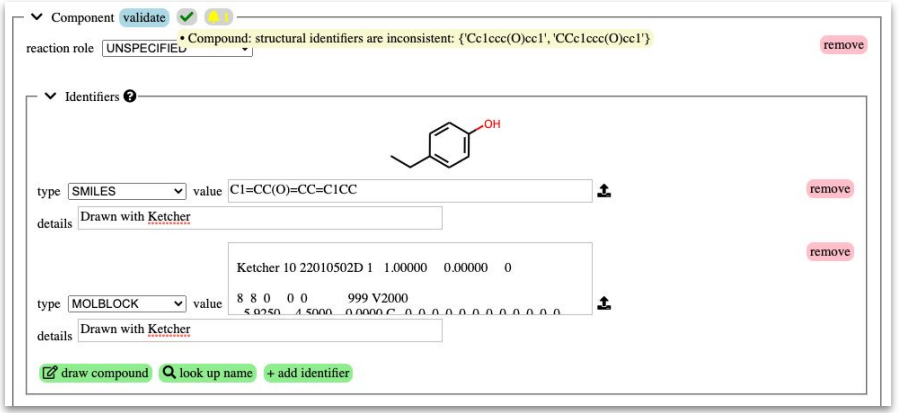




change SMILES

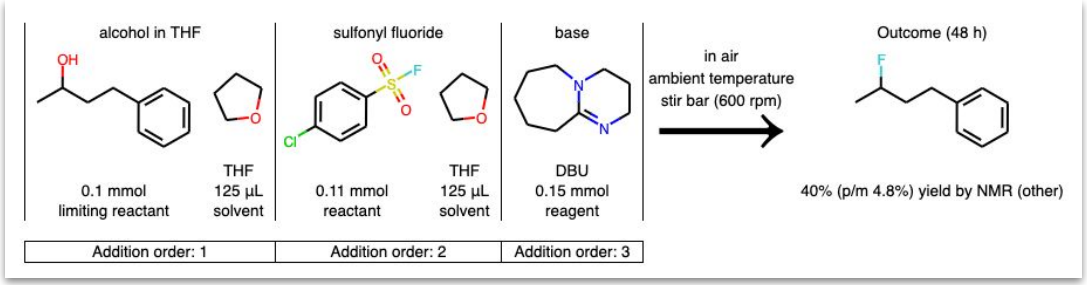


Web editor reaction visualization

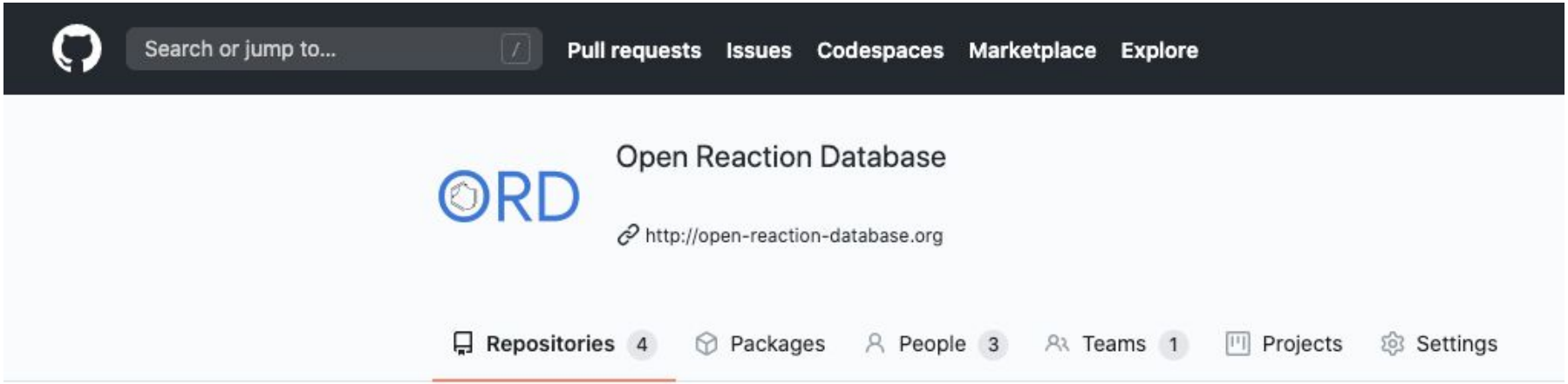
A tabular view of the overall reaction provides a concise summary. This is an HTML table produced using a Jinja2 template and RDKit-generated SVGs.

```
…
{% for key, input in reaction.inputs|sort_addition_order %}
    {% for compound, border in input.components|get_input_borders %}
        <td class="{{ border }}">{{ compound|compound_svg }}</td>
    {% endfor %}
{% endfor %}
…
```

```
mol = message_helpers.mol_from_compound(compound)
if mol:
    return drawing.mol_to_svg(mol)
```



Where does the ORD live?



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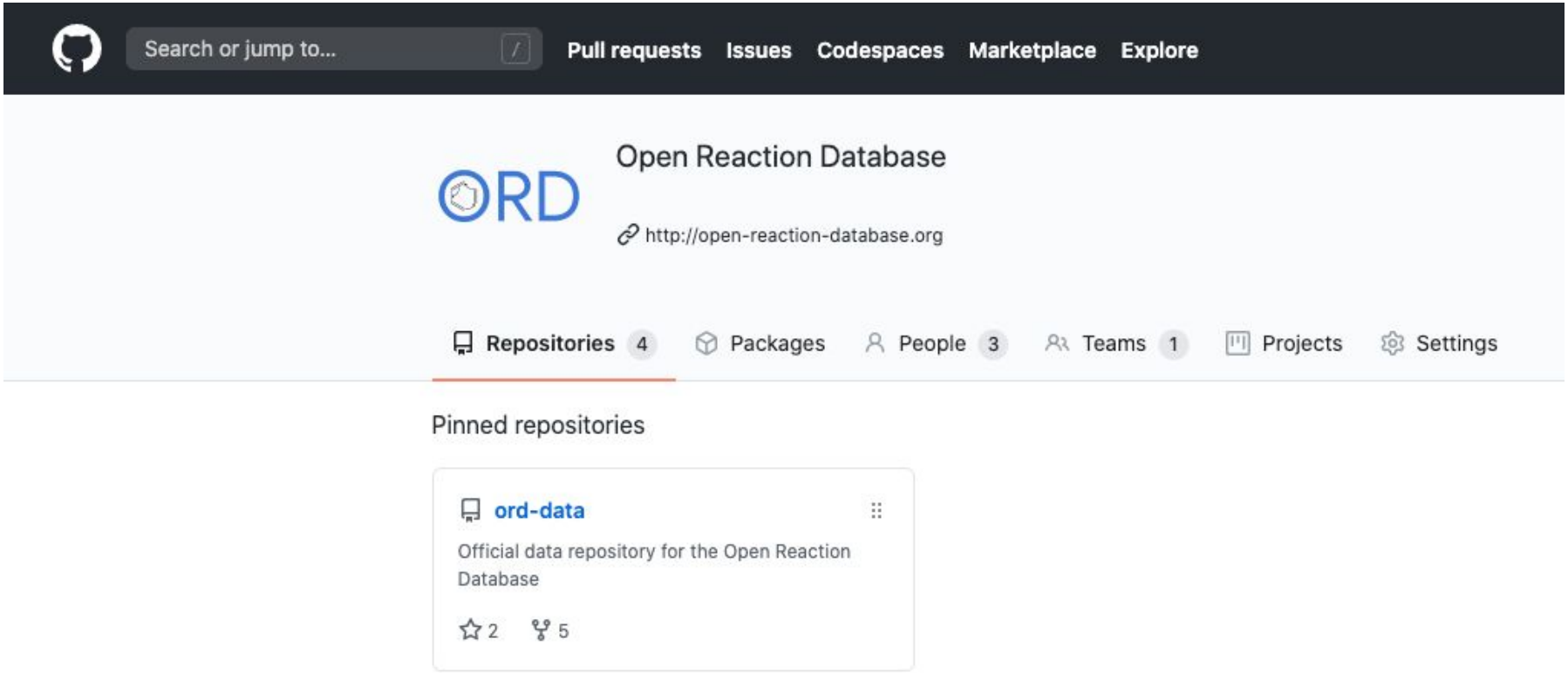

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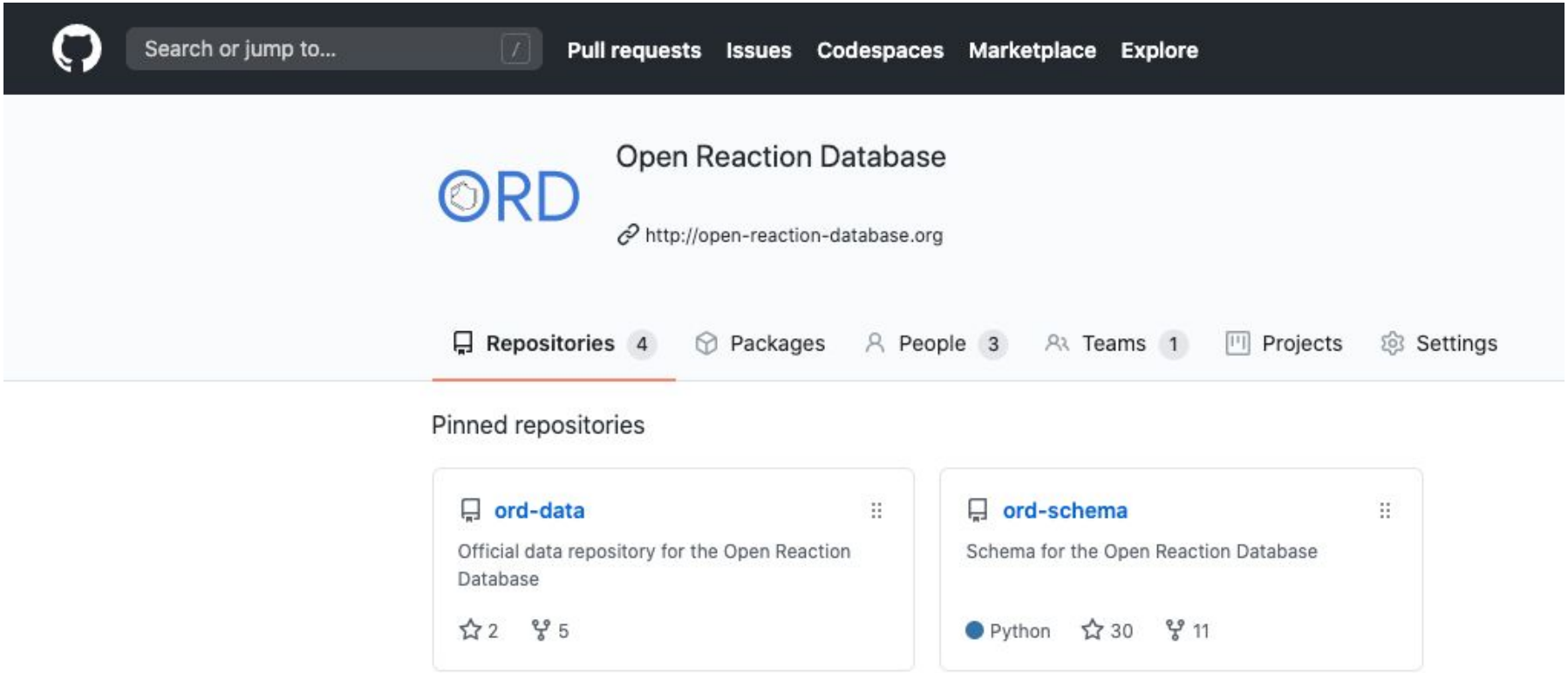
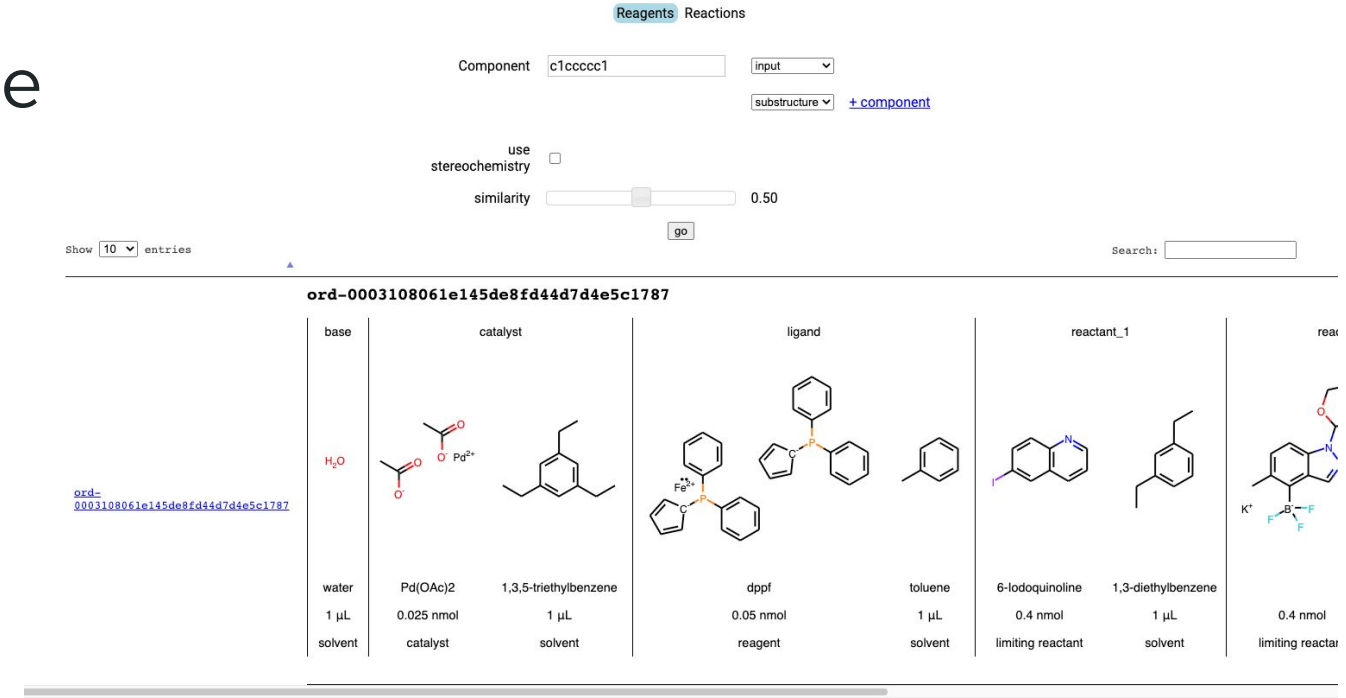


Search interface

Coming soon!



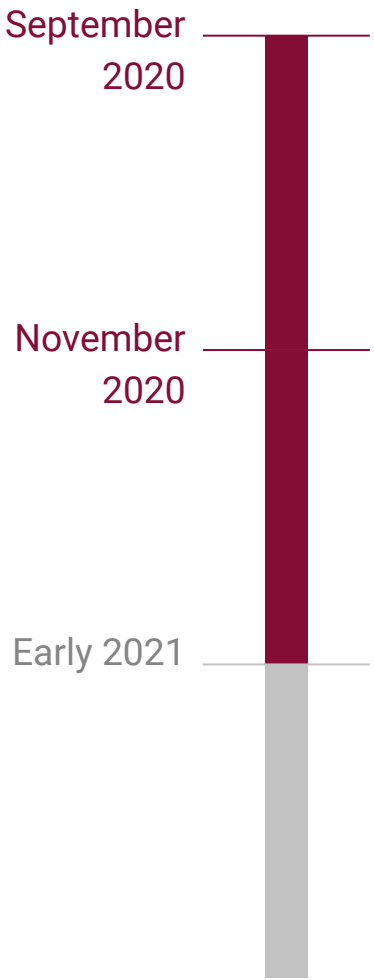
The interface makes heavy use of the RDKit postgres extension for compound and reaction searching by identity, substructure, and similarity.

Legal considerations

- Code is available under the Apache 2.0 license
- Data is available under the CC-BY-SA 4.0 license
- Terms of Use (drafted in kind by Google lawyers)

More info

Roadmap



Alpha testing

- Proof of concept for record creation and submission workflows
- Small group of invited contributors

Beta testing / pre-launch expansion

- Expand the database prior to public launch
- Refine review and maintenance procedures
- Larger group of invited contributors

Public launch

- Open submissions to all contributors
- Invite specific contributions from industry and academia
- Solicit downstream use in ML and other applications

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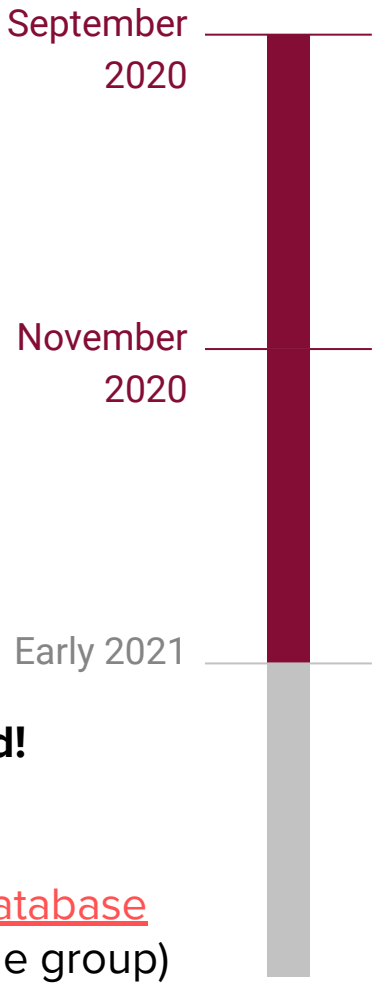

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Stay tuned!

Join the
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mailing list (Google group)

ORD