Thinking about the RDKit representation of stereochemistry

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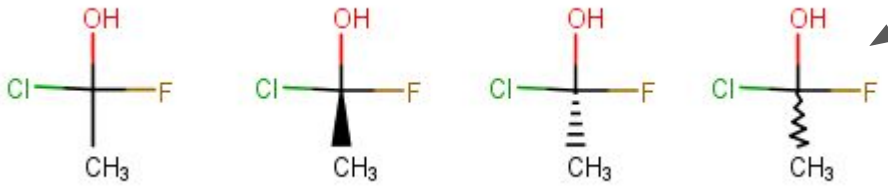
RDKit UGM 2019

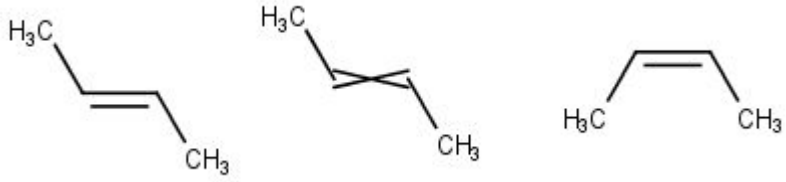
Status quo

Tetrahedral stereo



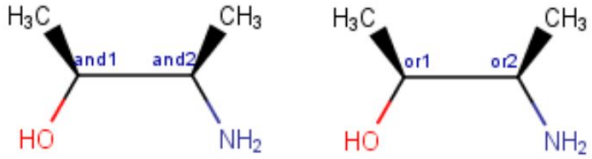
We don't really have any way to represent this

Double bond stereo



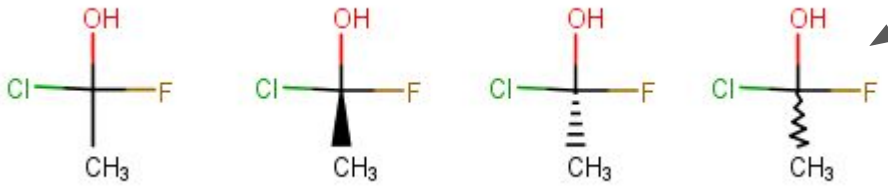
One more form you can't draw:
no information present

Stereo groups



Status quo

Tetrahedral stereo



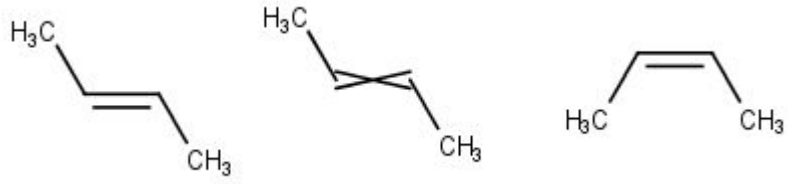
We don't currently have any way to represent this

Representation: atom attribute implicitly using the order of bonds around the atom

```
CHI_TETRAHEDRAL_CW, CHI_TETRAHEDRAL_CCW
```

Status quo

Double bond stereo



One more form you can't draw:
no information present

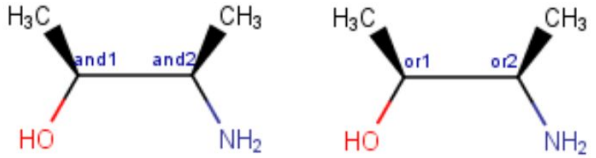
Representation: Bond attribute(s)

`STEREO_E, STEREO_Z`

`STEREO_CIS, STEREO_TRANS` (use stereoAtoms attribute)

Status quo

Stereo groups

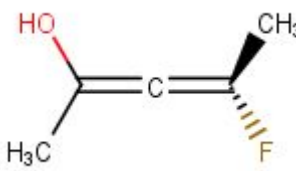


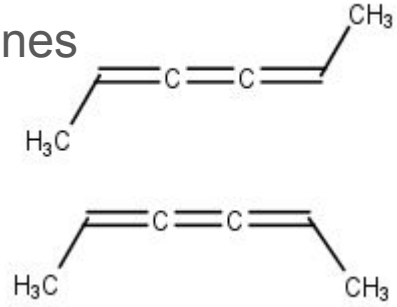
Representation: vector of `StereoGroup` objects on `ROMol`

More information in github:
https://github.com/rdkit/rdkit/blob/master/Docs/Code/EnhancedStereo.md

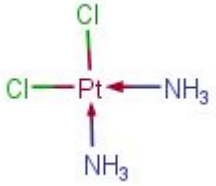
What's not handled?

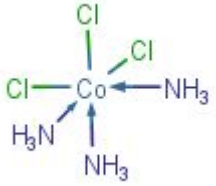
Allenes/cumulenes

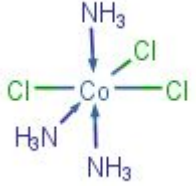




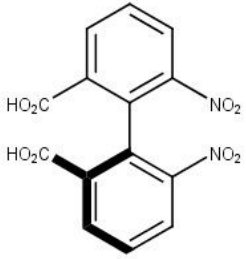
Non-tetrahedral atomic stereochemistry

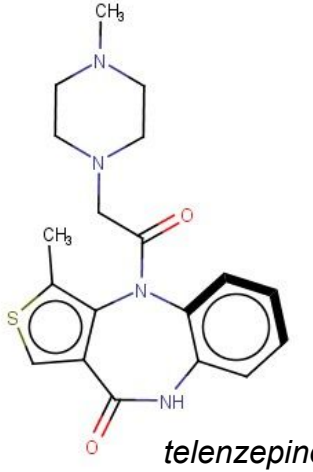






Atropisomers





telenzepine

Helicenes, etc.

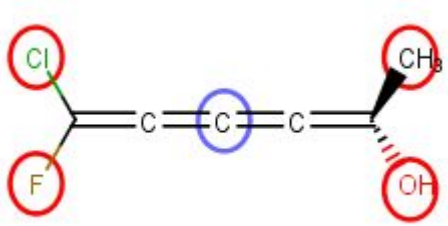
Things to think about

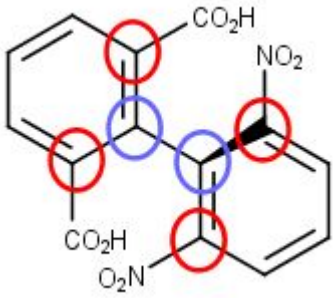
- What the input looks like: how do we know how to interpret the input correctly?
- What the internal representation is: how do we store it? At what level of granularity? Atom/bond property? Stored at the molecule level?
- Can we canonicalize it? How?
- What the public API is: how can client code interrogate/use stereochemistry?
- When it matters: when do we use the stereochemistry info? Just I/O? Drawing? Conformer generation? Substructure search? Fingerprints/descriptors? Elsewhere?
- How do we make clear the difference between when information has not been provided and when it is explicitly marked as unknown?

Simplifying the implementation

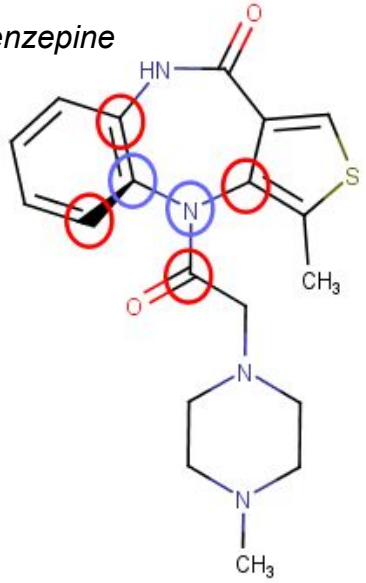
- Switch to using an explicit internal representation:
  - Directly store the atom order around a generalized stereocenter
  - Always store the atoms determining the stereochemistry of a double bond (currently done for cis/trans only)
  - ”generalized stereocenter”: an atom, set of atoms (position is defined by the mean if it’s a set of atoms), or bond
- Store stereo information on the molecule instead of on atoms/bonds
  - Still provide API functionality to retrieve whatever stereo info is present about atoms/bonds
  -

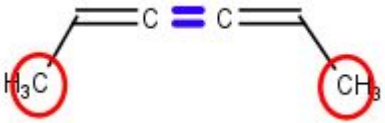
“Generalized stereocenters”





telenzepine





This isn’t really a generalized stereocenter. It’s a bond whose stereochemistry is determined by non-adjacent atoms