Schrödinger

# Torsion Scan in LiveDesign

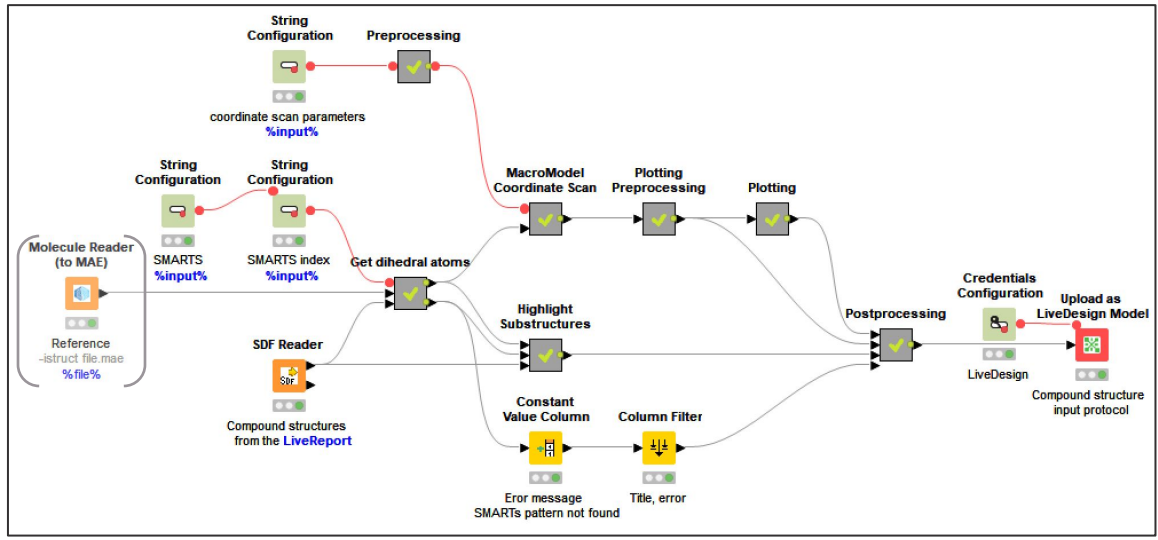
August 2022

# Currently available implementation

- KNIME based workflow
- Uses MacroModel Coordinate Scan
- Although the plotting is done differently in model,

  the respective workflow in Maestro would be to use

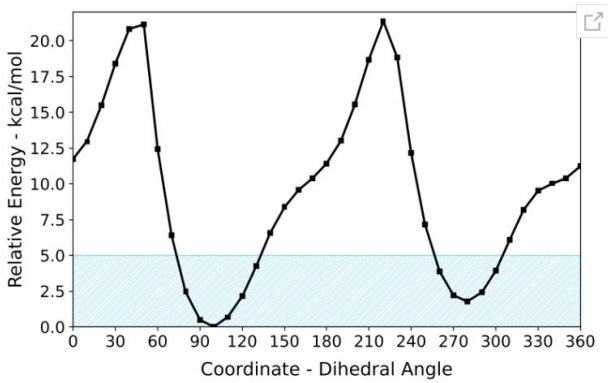
  “Coordinate Scan” + “Plot Coordinate Scan”
- MacroModel Coordinate Scan offers
  - more accurate energetics
  - more rigorous minimization protocols
  - variety of forcefields available

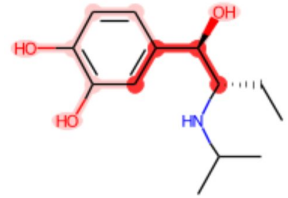



- Compared to Rapid Torsion Scan, MacroModel Coordinate Scan is considered the more accurate, but the relevance of this distinction depends on the application and chemical structure
- Of note, MacroModel Coordinate Scan using KNIME in LiveDesign is substantially slower than Rapid Torsion Scan in Maestro

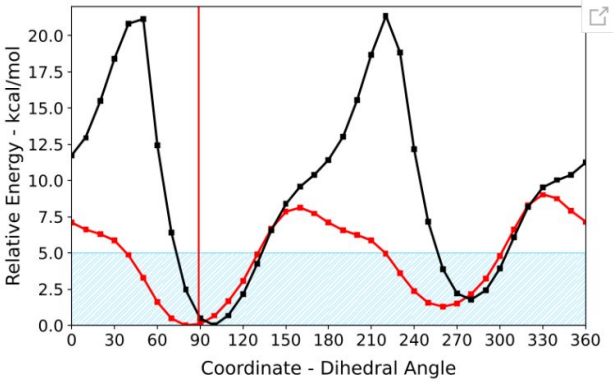
# Different setups of KNIME workflow

- **1 Compound**
  - Input:
    - 2D structure from LiveReport
  - Output:
    - Plot of relative energy for dihedral
    - 2D structure with highlighted SMARTS and dihedral

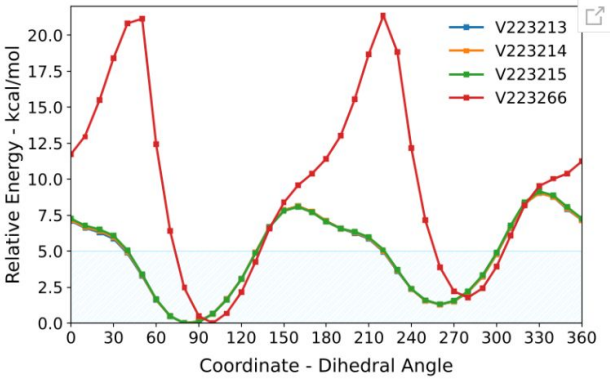



- **1 Compound + reference molecule**
  - Input:
    - 2D structure from LiveReport
    - Reference molecule as .MAE added during model configuration
  - Output:
    - Plot of relative energy for dihedral
      - overlayed with energy profile of reference compound
      - marker for dihedral value of input reference conformation
    - 2D structure with highlighted SMARTS and dihedral

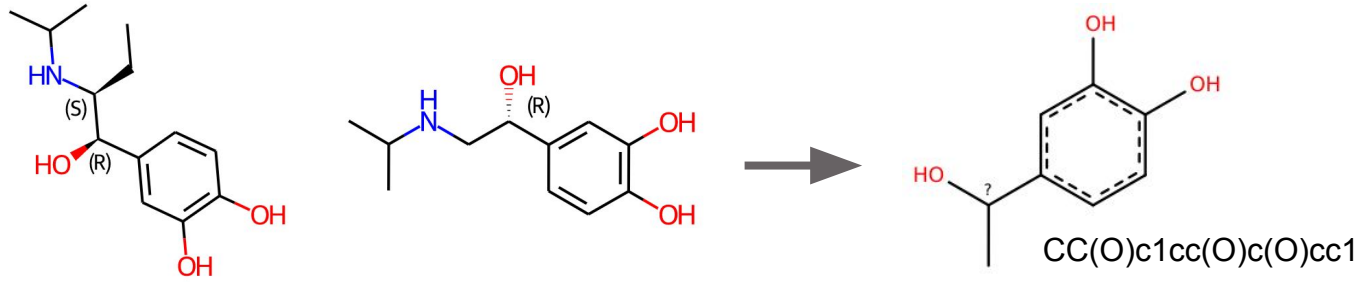



- **> 1 Compound**
  - Input:
    - 2D structures from LiveReport
  - Output:
    - Overlay of relative energy for dihedral of all compounds included in LiveDesign task (controlled by the batch size of actual calculation)
    - 2D structure with highlighted SMARTS and dihedral



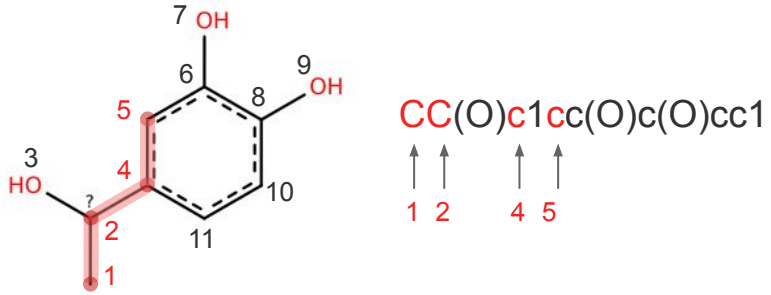
# Definition of dihedral

- Dihedral specified by SMARTS pattern + SMARTS index
- SMARTS pattern used to define common substructure that must included the 4 atoms defining dihedral
- E.g.,




  - LD model argument: -smarts 'CC(O)c1cc(O)c(O)cc1'

- SMARTS index identifies the 4 atoms within pattern that define the dihedral
- E.g.,




  - LD model argument: -index '5,4,2,1'

- "SMARTS Index Identifier" panel in Maestro is recommended to identify index of dihedral forming atoms
  - Load example molecule that includes the respective SMARTS patter into Maestro, and paste pattern into panel
  - Selecting an atom in the Workspace, will highlighted the atom in the pattern and display the index number

# Additional Information

- SMARTS pattern and SMARTS index are intended to be set by the user when adding model to a LiveReport
- Will create a parametrized model for every SMARTS pattern and SMARTS index combination

- In the returned 2D image of the structure, the used SMARTS pattern and the scanned dihedral are highlighted as a sanity check and documentation of what torsion was scanned in that calculation
- The Coordinate Scan step size and angle range is set as parameter on the model level
  e.g., -coordinate_scan_settings '0,360,10', for a scan from 0° to 360° with a step size of 10°
- If the SMARTS patter is not part of a molecule, the model will return a message that the pattern was not found
- The Y-axis of the relative energy plot is normalized to the maximum energy value (+1) of all compounds included in the specific LiveDesign task
  □ depending on the energy difference between compounds, this ensures a certain level of comparison between compounds
- In analogy to the Rapid Torsion Scan, the 5 kcal/mol range, which is considered the general area of free rotation in solution, is highlighted in the relative energy plot

# Model configuration and example LiveReport