NICA

IS CONFORMATIONAL ANALYSIS

MANUAL

sheets 15

2020

CONTENTS

1 INTRODUCTION

NICA is a tool for spatial molecular modeling, searching low-energy conformations (conformers).

NICA allows you to build and edit the structure of the molecule, open many file formats, can perform optimization and conformational analysis of molecule.

1.1 Glossary

Term	Description
NICA application	NICA application – NICA is Conformational Analysis.
Conformational analysis	Conformational analysis – branch of stereochemistry that explores dependence of properties of compounds in a molecule on the structure and ratio of conformations in which the molecule can theoretically exist.
Conformer	Conformer – low energy conformation of the molecule.

2 APPLICATION USAGE

To run the application, you must start the Internet browser and follow the link https://nica.icu

2.1 Main application window

The main window of the NICA application is shown in Fig. 1.

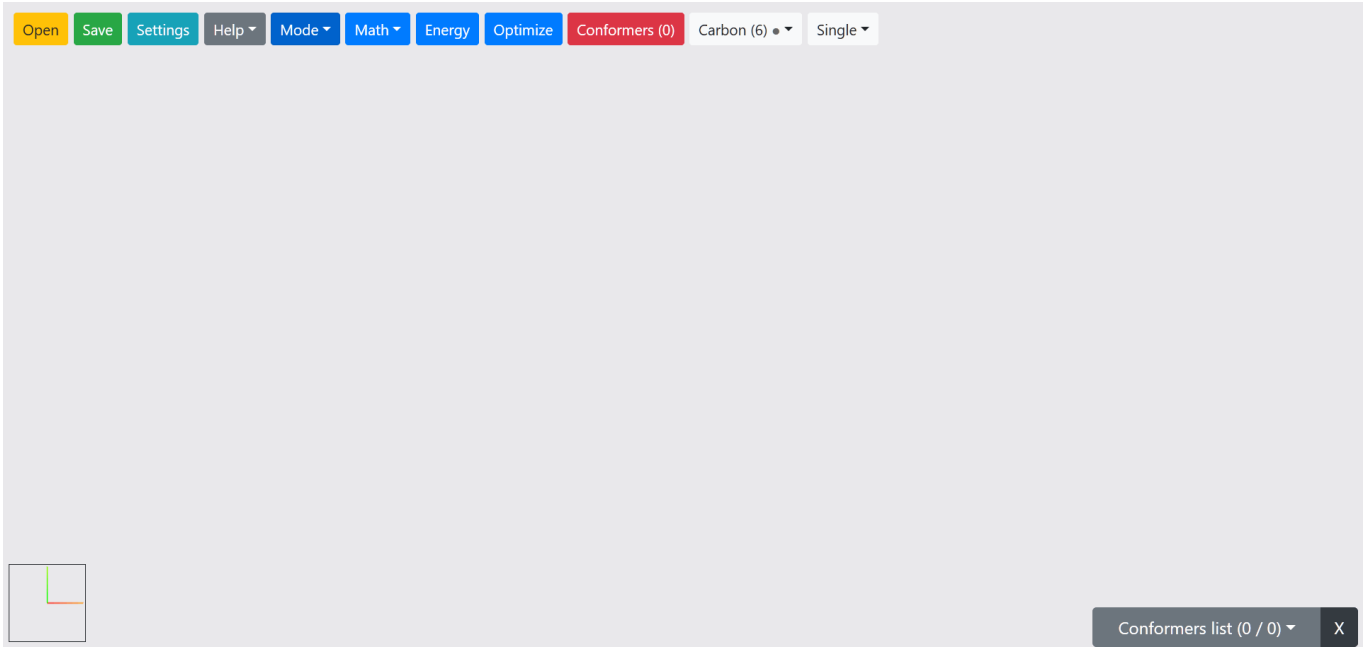

Fig. 1. Main application window

2.2 Main functions of the application

The main menu bar displays the following function buttons:

- Open
- Save
- Settings
- Mode
- Math
- Energy
- Optimize
- Conformers

2.2.1 «Open»

The first thing you will probably want to do is open a file and navigate around the molecule. To do this click «Open» button and select file or drag it to workspace. NICA supports a large number of file types, including CML, XYZ, SDF, PDB, SMI, CAN, MOP, OUT.

2.2.2 «Save»

You can save the current molecule or conformer by choosing from file types:

- CML, XYZ, MOP

else save all found conformers by choosing from file types:

- MultiXYZ, ZIP(CML)

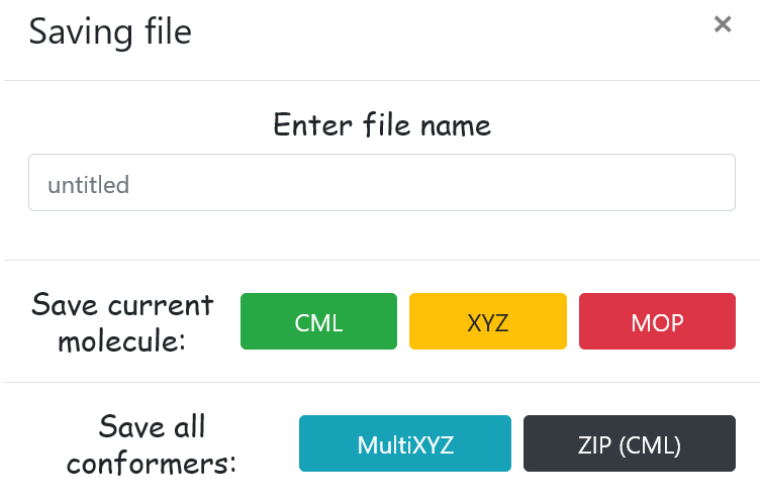

Fig. 2. Save file

2.2.3 «Settings»

The «Settings» menu item includes: general settings (General), graphics settings (Graphics), geometry optimization settings of the molecule (Geometry optimization), settings of conformational search (Conformers).

- **General:**
  1) Force field – selection of the force field for geometry optimization, conformational search, energy calculation of the molecule (MMFF94, MMFF94s, UFF, GAFF, Ghemical), or self-consistent field provides by MOPAC7 for geometry optimization and energy calculation.
  2) Dynamically change camera position – enable or disable the dynamic camera positioning feature.
  3) Torsion angle is always non-negative – enable or disable of displaying negative values of the torsion angle.
  4) Generate rough geometry for 2d structure – enable or disable generate rough geometry for 2d structure.
  5) Auto adjust hydrogens – enable or disable of automatic control of hydrogen atoms when performing geometry optimization or conformational search.

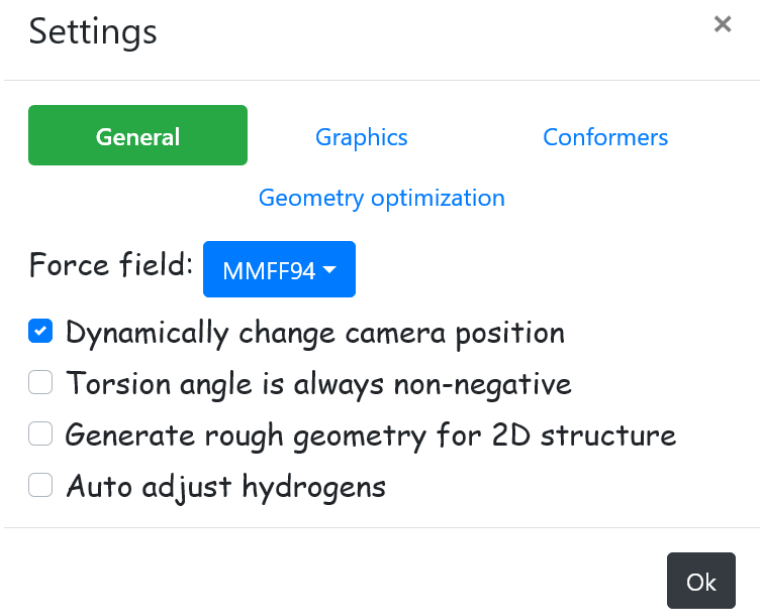

Fig. 3. Settings – General

- **Graphics:**
  1) View mode – selection of the mode of displaying the molecule (molecular model): Ball and Stick, Stick, Van der Waals Spheres.
  2) Graphic quality – selection of graphics quality settings (Low, Medium, Hight).
  3) Background color – select the background color of the workspace (White, Gray, Blue, Dark Blue, Black).
  4) Enable post-processing – enable or disable the post-processing graphics effects.
  5) Enable atom labeling – enable or disable the atom labeling.

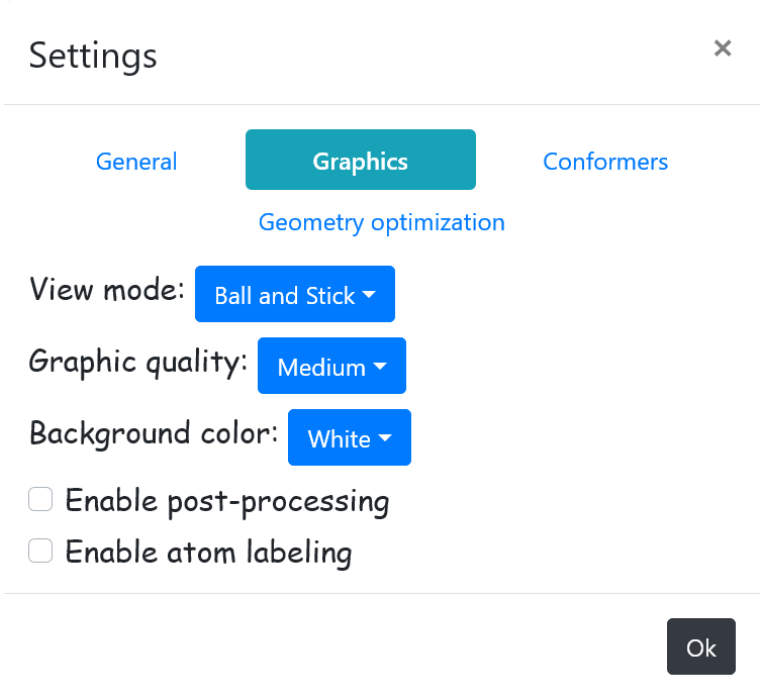

Fig. 4. Settings – Graphics

- **Conformers:**

Settings of conformational search:

1) RMSD cutoff – setting minimum heavy-atoms root-mean-square deviation relative to conformers already stored.
2) Energy cutoff – setting upper limit of energy range of conformers.
3) Max number of conformers to test – setting the maximum number of conformers to test.
4) Rearrange bonds – enable or disable of rearranging bond in the original structure of the molecule.
5) Optimize conformers – enable or disable geometry optimization of the obtained conformers using molecular mechanics methods or semi-empirical methods of quantum chemistry.

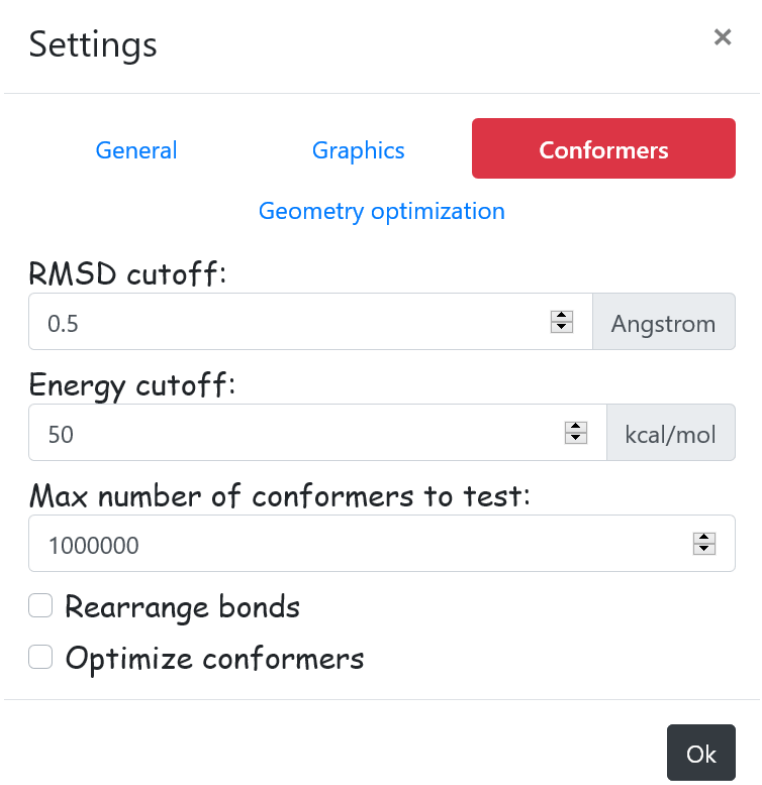

Fig. 5. Settings – Conformers

- **Geometry optimization:**

For all “Force field” values:

1) Algorithm – selection of geometry optimization algorithm of the molecule from the list: [Steepest Descent, Conjugate Gradients].
2) Number of steps – setting number of steps for geometry optimization.
3) Convergence – setting convergence value for geometry optimization.

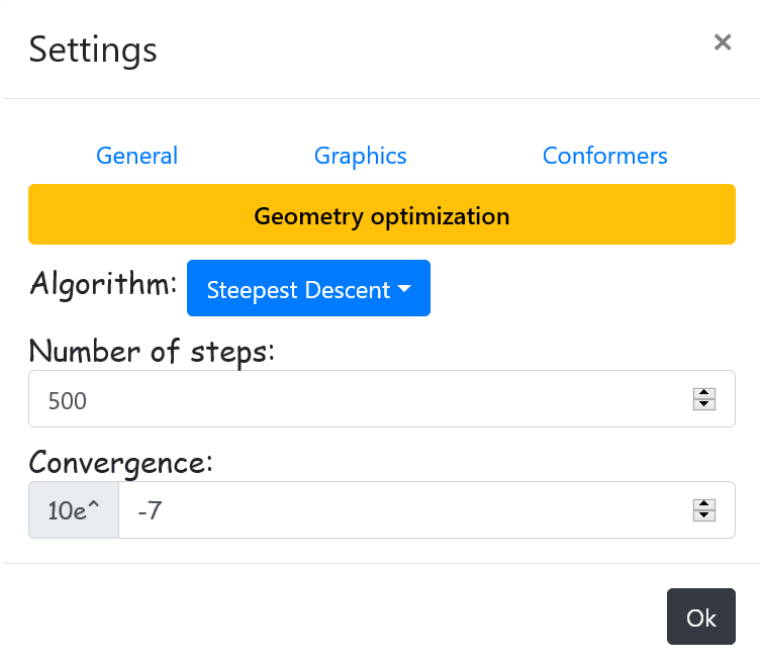

Fig. 6. Settings – Geometry optimization

For MOPAC7:

1) Semi-empirical method – selection of semi-empirical optimization method from the list: [PM3, MNDO, MINDO/3, AM1].
2) Max number of SCF iterations – setting max number of SCF iterations for geometry optimization.
3) Pulay converger – enable or disable the Pulay converger.
4) Camp-King converger – enable or disable Camp-King converger.

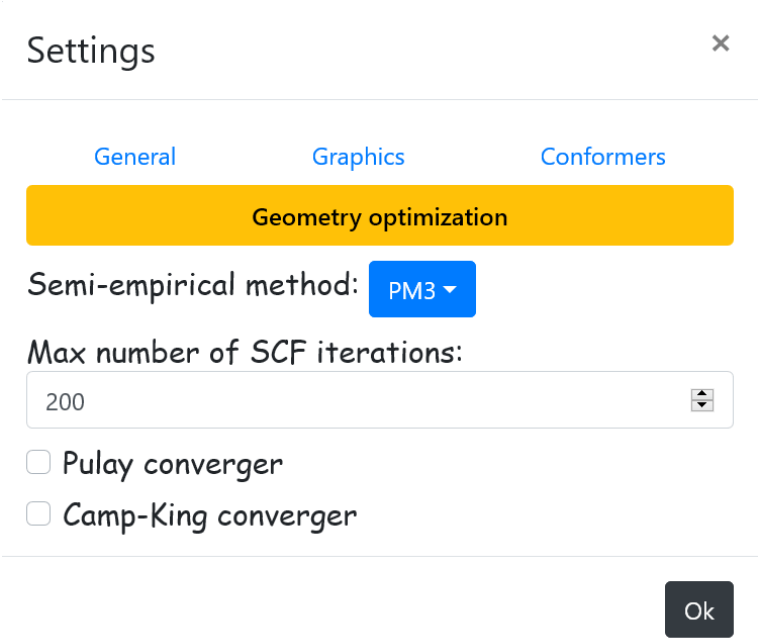

Fig. 7. Settings – Geometry optimization (MOPAC7)

2.2.4 «Mode»

The Mode menu contains several functions which are listed below (Fig. 8).

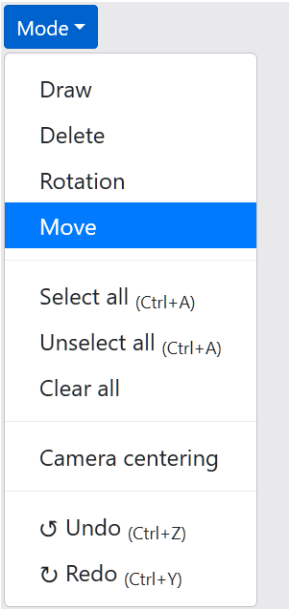

Fig. 8. Mode

- **Draw:** When choosing this mode of operation, two additional function buttons pop up on the main menu panel for selecting an element and the order of bond between atoms.

The structure of molecule is entered by pressing the left mouse button on workspace: it creates an atom corresponding to the value of the «Element» field from list of chemical elements of periodic table (the second right button on main menu bar).

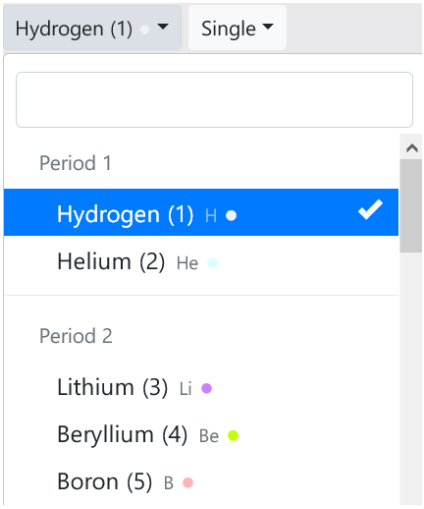

Fig. 9. Draw – Chemical elements

Bond between two atoms is created by clicking on them sequentially with the left mouse button. Bond order corresponds to selected value of field «Bond order» (the button is located at right side of main menu bar).

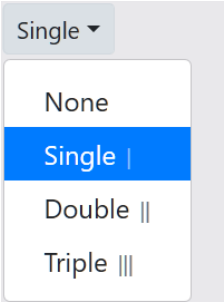

Fig. 10. Draw – Bond order

In the drawing mode of molecule, you can replace one atom with another. To do this select a new value in the «Element» field and pressing right mouse button on selected atom.

- **Delete:** erase atoms or bonds.

- **Rotation:** rotation and movement of camera and molecule on the screen.
  - Camera rotation is performed by simultaneously pressing left mouse button and turning the molecule in the desired direction relative to center of mass.
  - Camera movement is performed by simultaneously pressing right mouse button and moving the molecule in desired direction.
  - Rotation around bond is performed by sequentially selecting atoms of molecule (press Ctrl + clicking on the atoms) and moving slider[1] in the range from -180 to +180 degrees. First two atoms form a bond around which all other selected atoms rotate. If only two atoms are selected, then the rotating atoms are searched automatically.
  - Rotation of molecule in plane of camera around center of mass is performed by selecting all atoms and moving slider in the range from -180 to +180 degrees.
- **Move:** moving atoms or group of atoms in the screen plane by dragging and dropping.
  - Changing coordinates (X, Y, Z) of an atom is also done by double-clicking on it and setting new values in the «Changing coordinates» window that opens (Fig. 11).

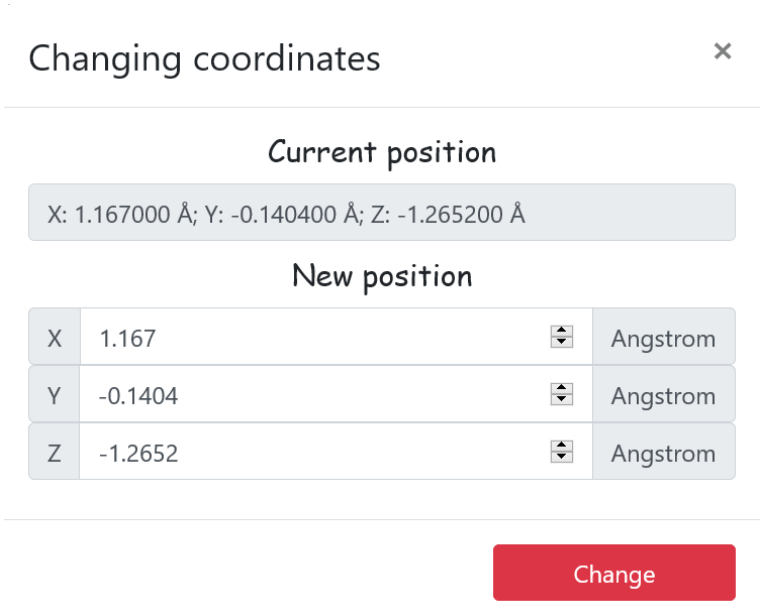

Fig. 11. Move – Changing coordinates

- **Clear all:** erase current molecule.
- **Select all** (while holding **Ctrl+A**)**:** selects all atoms of molecule. If current mode is different from «Delete» or «Rotation» it will change to «Move».
- **Unselect all** (while holding **Ctrl+A**)**:** removes selection from all atoms of molecule.
- **Camera centering:** move camera to center position.
- **Undo** (while holding **Ctrl+Z**)**:** undo your recent changes.
- **Redo** (while holding **Ctrl+Y**)**:** redo your recent changes.

[1] Slider is located at bottom left of the screen.

2.2.5 «Math»

The Math menu contains several functions which are listed below (Fig. 12).

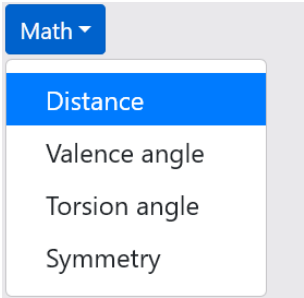

Fig. 12. Math

- **Distance:**

Measurement and changing of the distance between any two atomic nuclei in the molecule (in Angstroms). To do this, simply select this mode and left-click on the selected atoms of the molecule. At the bottom of the screen appears a field with the information received.

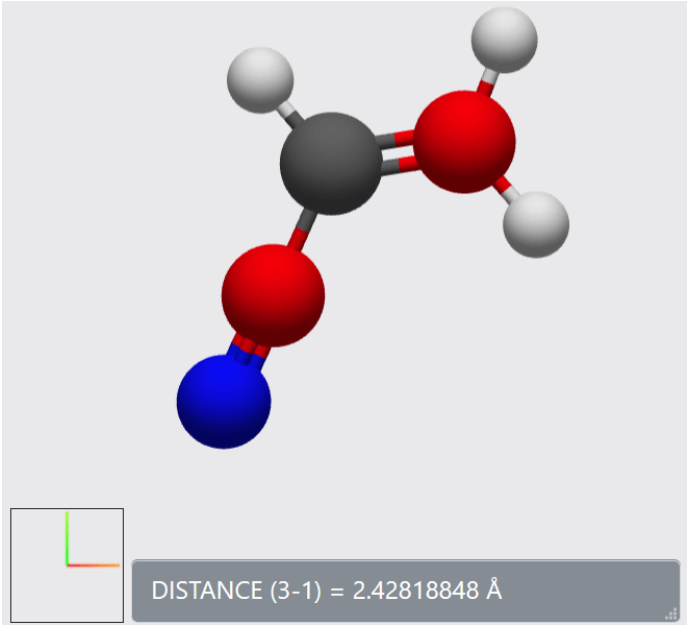

Fig. 13. Math – Distance between any two atoms

Changing the received value of distance is done by clicking on the distance field and setting a new value in the «Changing geometry» window that opens (Fig. 14).

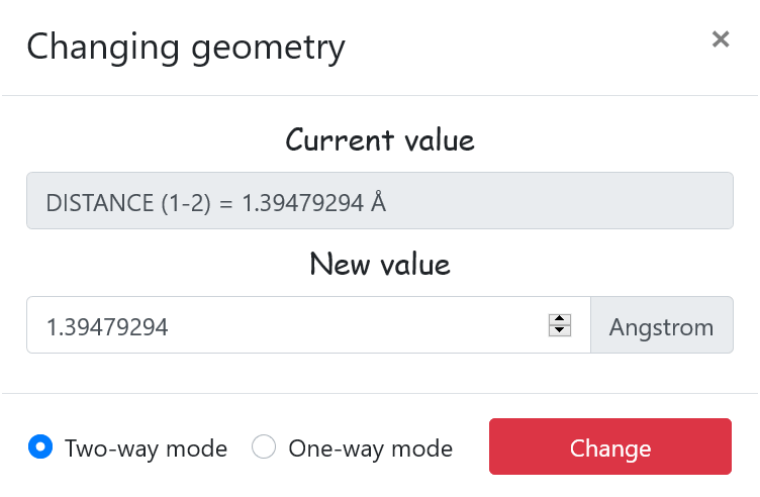

Fig. 14. Math – Changing geometry

By default, the distance between two atoms is changed in two directions «Two-way mode». To change the mode is done by clicking «One-way mode». You can set a new value in the «New value» field and click the «Change» button.

Information about the distance between two bonded atoms is also displayed when you hover the cursor over the corresponding bond (Fig. 15).

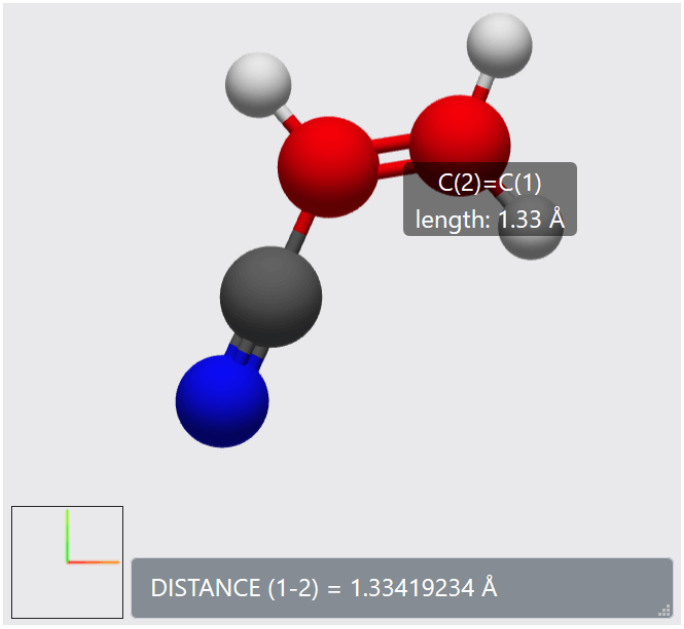

Fig. 15. Math – Distance between two bonded atoms

- **Valence angle:**

Measurement and changing of the valence angle between any three atoms in the molecule.

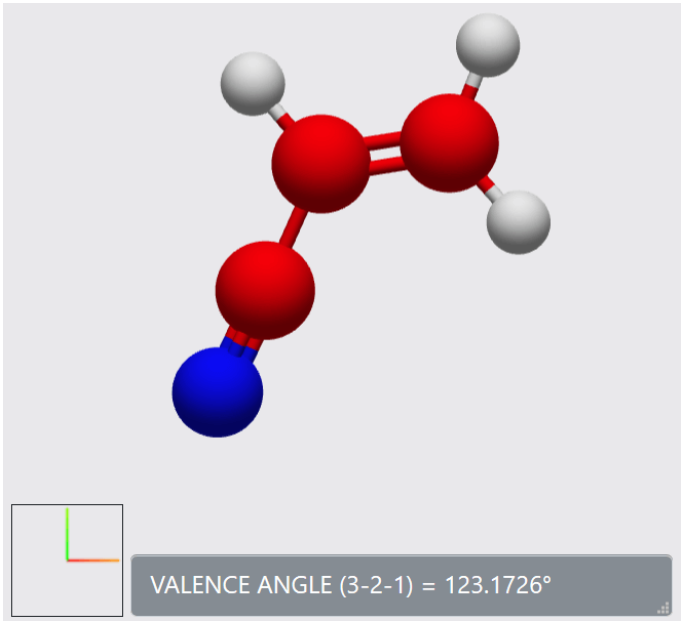

Fig. 16. Math – Valence angle

Changing the received value of valence angle is done by clicking on the valence angle field and setting a new value in the «Changing geometry» window that opens (Fig. 14).

- **Torsion angle:**

Measurement and changing of the torsion (dihedral) angle between any four atoms in the molecule.

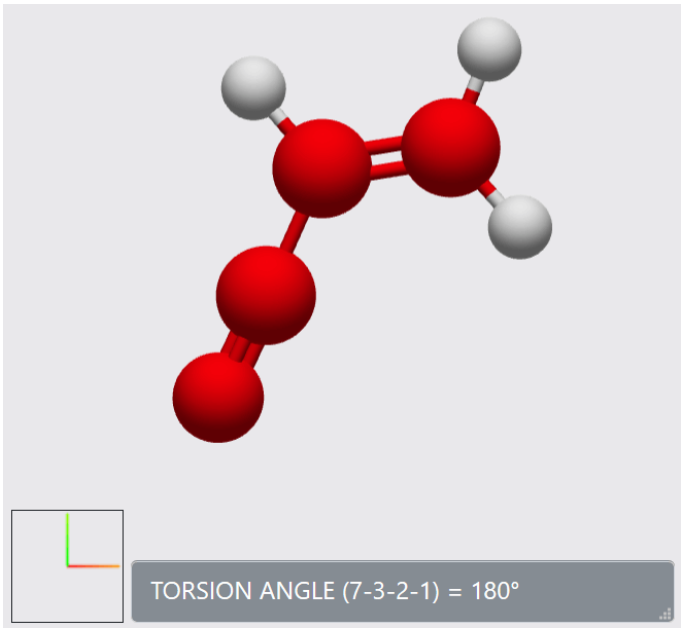

Fig. 17. Math – Torsion angle

Changing the received value of torsion angle is done by clicking on the torsion angle field and setting a new value in the «Changing geometry» window that opens (Fig. 14).

- **Symmetry:**

Determination of the symmetry of the molecule relative to axis of symmetry. The axis is set by selecting two atoms.

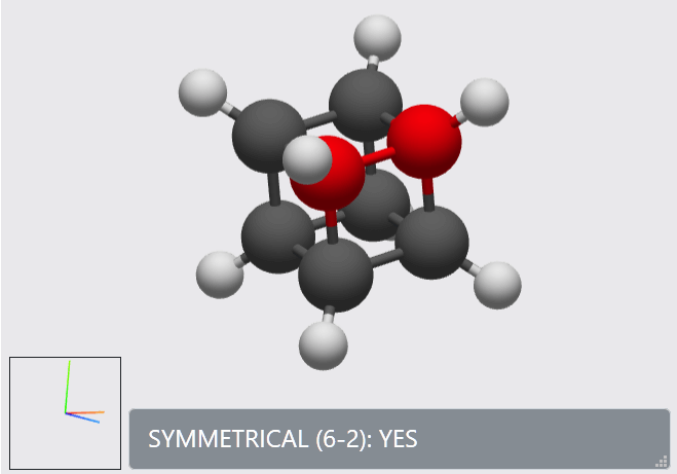

Fig. 18. Math – Symmetry

2.2.6 «Energy»

Calculate energy of the molecule in the selected force field which is displayed as a hint when the mouse cursor hovers over the «Energy» button.

Fig. 19. Energy

2.2.7 «Optimize»

Optimization geometry of the molecule in the selected force field which is displayed as a hint when the mouse cursor hovers over the «Optimize» button.

2.2.8 «Conformers»

Search of conformers of the molecule in the selected force field which is displayed as a hint when the mouse cursor hovers over the «Conformers» button.

Information about the obtained conformers with an indication of the energy for each (with the difference from the energy of the original molecule) are displayed as a list in the lower right corner of the screen. Moving through the list, current conformer is visualized on the screen.

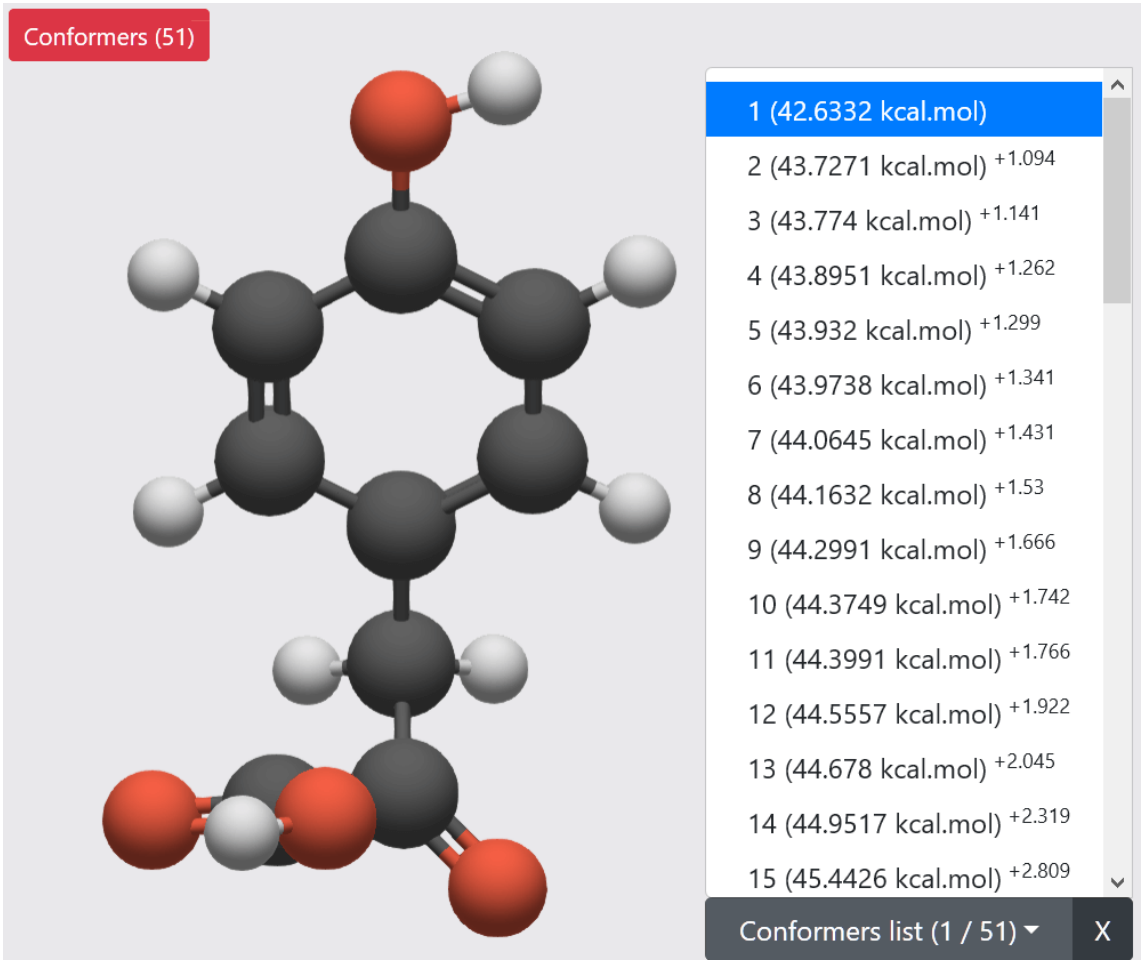

Fig. 20. Conformers

Button 

– serves to remove the current conformer from the list of received conformers. You can delete everything except first conformer.

2.2.9 «Demo»

View molecule in demo mode (autorotate). To start this mode, you must select mode «Rotation» and click on the camera field  , displayed in the lower left corner of the screen.