CONFLEX 7

What is CONFLEX?

CONFLEX Corporation provides conformation search and analysis software for examining the conformational space of small and large molecules. Identifying these conformers helps researchers in the selection of better quality leads during the discovery process. CONFLEX also includes algorithms for predicting IR, NMR, CD, and UV-Vis spectra.

CONFLEX also develops and licenses the CONFLEX Interface, a visualization and analysis platform especially designed for analysing CONFLEX outputs, e.g. conformational analyses, spectra output, and crystal packing, spectra, etc.

CONFLEX software products provide meaningful answers to both the expert computational chemist as well as the experimental and medicinal chemist investigating the role of molecular conformation. Designed for chemists by chemists, CONFLEX products exhibit high-accuracy, intuitive interfaces, and powerful command-line operation for interfacing with other modeling packages.

New features in CONFLEX 7 include Crystal Search and Optimization
Powder Diffraction Prediction, and the ability to run CONFLEX from ChemOffice products.

NEW IN CONFLEX 7D

- Calculate sum of interaction energies in hemispherical crystal
  CONFLEX can calculate sum of interaction energies in hemispherical crystal with respect to a molecule “in” or “on” a crystal plane specified by Miller indices. It is useful for the energy analysis regarding crystal plane such as dissolution, sublimation, and so on.
- Performance improvement for crystal structure search (Parallel CONFLEX)
  The method of parallel computation for the crystal structure search is implemented that geometry optimizations of crystal structures are distributed over multiple threads. (ONLY for Parallel CONFLEX)
  The performance of parallel computation for crystal structure search is vastly improved.
- Change the definition of crystal energy
  The definition of crystal energy is changed to improve the accuracy.
- Support for MOL2 file format
  CONFLEX now support MOL2 file format for direct CONFLEX calculation.
- Expanded torsion interaction
  CONFLEX can treat the higher order of torsion interaction term up to 6 dimensions.
- New keyword for fixed E-Z torsional configuration
  The keyword that fixed E-Z torsional configuration can be released is available during conformation search.

CONFLEX 7 Engine Enhancements In addition to all the functions and features CONFLEX 7 now includes:

- Crystal Structure Searching and optimization
- Simulation of Powder Diffraction Patterns
- Can be launched from ChemOffice products

CONFLEX 7 Interface Features -The CONFLEX 7 Interface includes all the functionality of the previous interface, BARISTA, in addition to the following improvements in managing CONFLEX engine output.

Modifying Molecules

- Gaussian checkpoint file
- GAMESS log file
- Firefly log file
- Sybyl mol2 file
- Copy & Paste from ChemDraw
- Modify bond multiplicity

Control Features

- Prepare and Run CONFLEX Calculations
- Monitor and control local machine and server processes
- Prepare and Run calculations for Gaussian, GAMESS and Firefly

Visualize Calculation Results

- Display spectra: IR, NMR, CD, UV-Visible, etc.
- Zoom-In and Out on spectra
- Save plots as textual data files
- Report absolute NMR chemical shifts and shifts relative to reference compounds
- Create surfaces for molecular orbitals and electron density

Display Formats

- 3D solid and translucent
- Color surfaces by a property
- Control surface threshold values
- Control surface transparency
- Automatically load binary cubed created by CONFLEX
- Automatically save computed cubes for future use

Conformation Search-

Conformational Search Algorithm in CONFLEX
For convenience, the structures being processed are referred to differently depending on the particular stage of the search process:

- input structure is the input at the beginning of a search
- initial structure is called from the conformer storage database at the beginning of each perturbation cycle
- starting (trial) structure is the perturbed structure before geometry-optimization
- optimized structure is the structure after geometry-optimization
- stored structure is the optimized structure that survived the redundancy test, and it is saved in the conformer storage.

The algorithms for searching conformational space or a torsional hypersurface involve repeated sampling from the vast conformational space. The process, which is illustrated below (a curved arrow indicates a looping subprocess), has the following steps:

(1) generation of an appropriate starting structure
(2) geometry-optimization of the starting structure
(3) comparison of the optimized structure with the stored conformers.

Finally, a structure passing all comparisons is added to the list of stored conformers.

Local Perturbation
If the perturbation cannot move the starting structure from the territory to which it initially belonged, subsequent geometry-optimization will return it to the same structure. The territories of similar conformers may be located in close vicinity in the conformational space, constituting a local network of local territories, and less similar conformers may be considered to belong to different localities. Therefore, the method of perturbing an initial structure to produce a new candidate conformer is also responsible for the efficiency of search.

To ensure exhaustive generation of all possible starting structures, local perturbation is applied to every flexible part in the initial structure. The following three modes of perturbation are designed to mimic the elementary process in the thermal movements of a molecule undergoing conformational change: corner flap and edge flip for endocyclic parts, and stepwise rotation for acyclic parts.

Optimization

Pre-check during optimization
The time required to perform systematic perturbations on the initial structure comprises only a few percent of the total computing time, while by far the most time-consuming step is the geometry-optimization. Therefore, the pre-check is an effective way to increase the efficiency of the conformational space search. In CONFLEX, a structure that is being geometry-optimized is frequently compared with all the stored conformers during the optimization, and that calculation is stopped as soon as the candidate structure is identified as superimposable with one of the stored structures. However, if comparison is made too often, the comparison time will take up a significant part of the total time when the number of stored structures

increases. Therefore, with this option, CONFLEX will perform the comparison at 0, 10, 20, and every 10 iterations until 200 iteration, and every 50 iterations thereafter. This strategy reduces the total computing time by 30 to 60%.

Comparison

Comparison using conformational distance

The similarity between two conformers can be quickly identified by comparing the root mean square of differences in the corresponding pair of dihedral angles, f A and f B. This method is fast and accurate. To save time, the dihedral angles of a stored conformer are retrieved for comparison rather than re-calculating those dihedral angles each time.

$$d_{conf} = \sqrt{\left(\sum_{i=1}^{N_{dihedral}} (f_i^A - f_i^B)^2 \right) / N}$$

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