TorsiFlex v2021.1

A program for the conformational search in flexible molecules

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The Cathedral Package

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About `TorsiFlex` License

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Contents

1. `TorsiFlex` **software**

This document is a guide to use `TorsiFlex`, a program designed to find the conformers of flexible molecules using a combination of a preconditioned variation of the torsions and a Monte Carlo search.

The example files cited along the document are listed in Chapter 8.

1.1 **About** `TorsiFlex`

- Programming language: Python 3

- Operating systems: Linux and macOS

`TorsiFlex` is an user-friendly code written in Python 3 designed to seek the conformers of a given molecule by adopting a combined low-level/high-level (LL/HL) methodology.[1,2] `TorsiFlex` is part of a bigger project where other programs of interest are included: the `Cathedral` package. We encourage the user to visit our GitHub webpage to know about the software we are developing in our group.[3]

1.2 **Terms of use**

`TorsiFlex` is free software under MIT license. We refer to the GitHub webpage for more details about the license:

> https://github.com/cathedralpkg/torsiflex

1.3 `TorsiFlex` **software contents**

The source code is located in the `src/` folder and contains the following files/sub-directories:

- `torsiflex.py`: the main executable file;

- `common/`: modules with diverse functions of general use;

- `modtorsiflex/`: modules that deal with (i) `TorsiFlex` options, (ii) electronic structure softwares, (iii) reading/writing of files.

1.4   Setting up `TorsiFlex`

`TorsiFlex` can be executed using the `python3` executable:

```
>> python3 path_to_torsiflex/torsiflex.py
```

or it can be directly executed provided that execution permissions are granted:

```
>> chmod u+x path_to_torsiflex/torsiflex.py
```

and as long as the path to the `python3` executable is `/usr/bin/python3`. If this is not the case, the user can modify the *shebang* line of `torsiflex.py` to define the path of the Python interpreter:

```
#!/usr/bin/python3
```

1.5   Electronic structure software

At this stage, `TorsiFlex` can only perform electronic structure calculations using the Gaussian software (versions 09 and 16).[4,5] The path to the Gaussian executable is read from an environment variable denoted as `GauExe`, which can be defined and exported in the `.bashrc` file. For example:

```
export GauExe="/home/programs/Gaussian/g09"
```

1.6   How to cite

The following publications must be cited in any work presenting results obtained with `TorsiFlex`:

- D. Ferro-Costas and A. Fernández-Ramos, *Front. Chem.*, 2020, **8**:16 [A Combined Systematic-Stochastic Algorithm for the Conformational Search in Flexible Acyclic Molecules].

2. The algorithm in a nutshell

This Chapter briefly describes the algorithm implemented in `TorsiFlex`, which is also schematized in the flowchart of Figure 2.1. The first part of the algorithm consists on a low-level search of conformers (section 2.1). The second part comprises a geometry re-optimization at a higher level of calculation (section 2.2). We refer to our previous works[1,2] for a more detailed explanation.
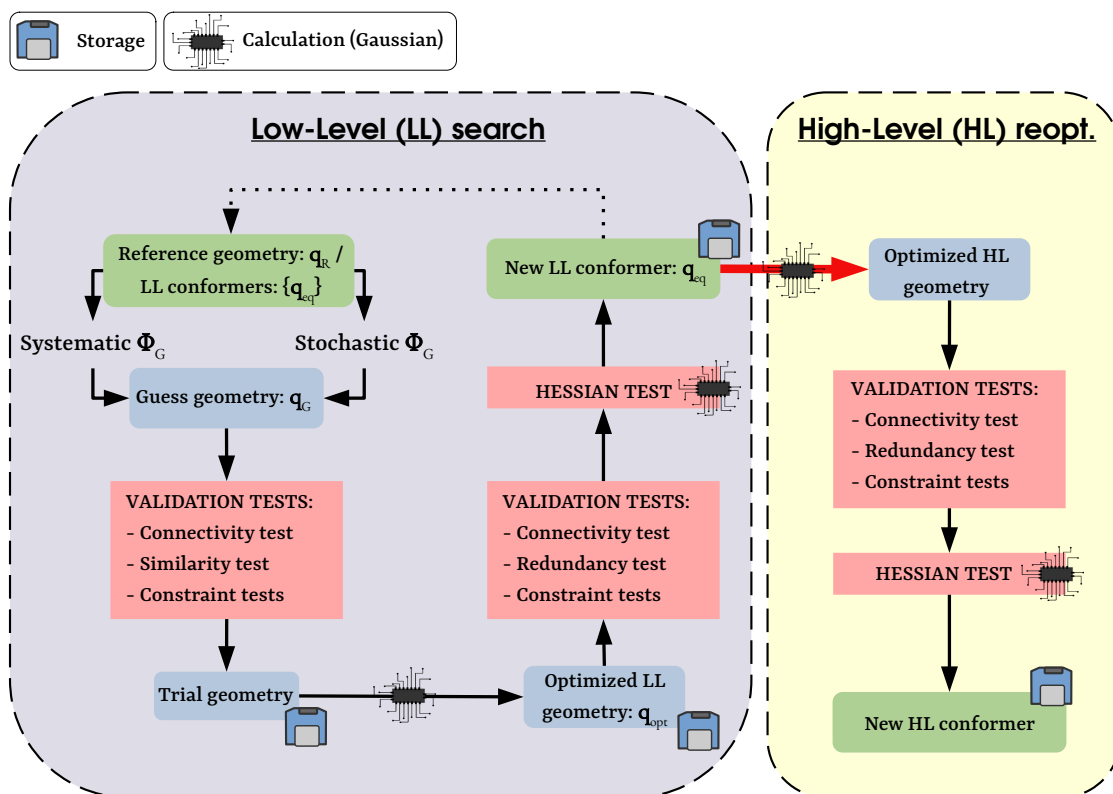

Figure 2.1: Flowchart of the search and reoptimization processes implemented in `TorsiFlex`.

2.1   The low-level search

`TorsiFlex` requires a reference geometry, $\mathbf{q}_R$, which is given in the Z-matrix format. This geometry explicitly includes the K proper torsions of interest, which can be collected into a K-dimensional torsion vector, $\boldsymbol{\Phi}^R$. The replacement of $\boldsymbol{\Phi}^R$ by a guess vector, $\boldsymbol{\Phi}^G$, renders a new configuration or guess geometry, $\mathbf{q}_G$.[*] There are two strategies for the generation of $\boldsymbol{\Phi}^G$: preconditioned or stochastic. The former is based on chemically-intuitive dihedral angles,[†] whereas the latter is based on the random generation of K integers between 0 and 360 (degrees).

Each guess Z-matrix, $\mathbf{q}_G$, is validated through a series of tests. Guess geometries that fail the tests are discarded, whereas those that pass them turn into trial structures that will be optimized geometrically. In this manner, unnecessary calculations are avoided, accelerating the search process.

The resulting optimized geometry, $\mathbf{q}_{opt}$, is validated through a new set of tests and, if all of them result positive, the Hessian matrix is calculated in order to confirm that we are dealing with a conformer of the system (Hessian test).

2.2   The high-level reoptimization

The search task described in the previous section is intended to be carried out at an inexpensive level of calculation (low-level, LL), in order to reduce the computational cost and speed up the location of conformers.

`TorsiFlex` can use the LL conformers as trial geometries for more accurate electronic structure calculations (high-level, HL). The HL optimized structures are validated by a new set of tests. If all of them result positive, the Hessian test is carried out by calculating the Hessian matrix. If this test is also positive, the HL optimized geometry corresponds to a new conformer.

2.3   The validation tests

The following tests are implemented in `TorsiFlex`:

- **The connectivity test**: positive if the connectivity of the guess/optimized structure corresponds to that of the reference Z-matrix (`i.e.` this test asserts that we are dealing with the same constitutional isomer).

---

[*]The Z-matrix of the conformers located along the search process is generally more convenient than the reference one. For this reason, whenever possible, `TorsiFlex` uses the Z-matrix of the conformer with the closest torsion vector to $\boldsymbol{\Phi}^G$ instead of resorting to the reference Z-matrix, speeding up the geometry optimization.

[†]By default, the dihedral angles for the expected gauche (60° and 300°) and anti (180°) arrangements in hydrocarbons.

- **The similarity test**: the torsion vector of a guess structure, $\mathbf{\Phi}^{\mathrm{G}}$, is compared to a pool of stored torsion vectors from previous iterations, $\{\mathbf{\Phi}^{\mathrm{st}}\}$; if $\mathbf{\Phi}^{\mathrm{G}}$ falls outside of the domain associated to each stored vector, *i.e.*:

$$\forall\ p,\ \exists\ \tau : |(\mathbf{\Phi}^{\mathrm{G}})_\tau - (\mathbf{\Phi}^{\mathrm{st}}_p)_\tau| > d \tag{2.1}$$

  then the test is positive. In the previous equation, d defines the domain of each stored point and p and τ run over all stored points and over each target torsion, respectively.

- **The redundancy test**: compares the optimized torsion vector, $\mathbf{\Phi}^{\mathrm{opt}}$, against the pool of stored conformers, $\{\mathbf{\Phi}^{\mathrm{eq}}\}$. If $\mathbf{\Phi}^{\mathrm{opt}}$ is not stored in $\{\mathbf{\Phi}^{\mathrm{eq}}\}$, *i.e.* $\mathbf{\Phi}^{\mathrm{opt}} \not\subset \{\mathbf{\Phi}^{\mathrm{eq}}\}$, the test results positive. From a practical point of view this test is positive if:

$$\forall\ p,\ \exists\ \tau : |(\mathbf{\Phi}^{\mathrm{opt}})_\tau - (\mathbf{\Phi}^{\mathrm{eq}}_p)_\tau| > \epsilon \tag{2.2}$$

  where ϵ is a threshold (not greater than 2 degrees) that accounts for numerical errors.

- **The constraint tests**. For different reasons, the user may be interested in a certain set of conformers. For such cases, `TorsiFlex` accepts the definition of constraints based on the distance between a pair of atoms, the angle between a triad of atoms and the dihedral angle between four atoms. Specifically, `TorsiFlex` differenciates between two types of constraints:

  - *hard* constraints; the test is positive if all the specific requirements for the constraints are fulfilled.

  - *soft* constraints; the test is positive if one or more of the specific requirements for the constraints are fulfilled.

- **The Hessian test**: performs a test on the Hessian matrix of the optimized geometry. If all its vibrational frequencies are real, the test is positive. When dealing with the conformers of a transition state, the test results positive when all the vibrational frequencies are real but one. Notice that the calculation of the Hessian matrix is time-demanding.

In Figure 2.1 we illustrate the tests that are used to validate trial and optimized structures.

3. `TorsiFlex` **options**

The list of available options in `TorsiFlex` can be displayed by executing:

```
>> path_to_torsiflex/torsiflex.py --help
```

or just:

```
>> path_to_torsiflex/torsiflex.py -h
```

The corresponding help message is shown below.

```
=======================
 Welcome to TORSIFLEX
=======================


Current version: TorsiFlex v2021.1 (2021-03-18)

Description:

  A program to seek the conformers of flexible molecules
  by means of a combined preconditioned-stochastic algorithm.
  The located conformers, calculated with a low-level (LL)
  electronic structure method, can be re-optimized using
  a high-level (HL) method.

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  Santiago de Compostela, Galicia, Spain

Execution:

  torsiflex.py [--help /-h]  [--version/-v]  [--inp   ]
               [--prec    ]  [--stoc       ]  [--hlopt ]
               [--msho    ]  [--mstor      ]  [--regen ]


-------------------
  Program options
-------------------

   --inp
```

```
   Generates the input file and the templates for Gaussian.


--prec [M m]

  Uses the preconditioned algorithm for the conformer location.

  In order to divide the preconditioned guesses into M groups
  and deal with the m-th group, use this option as follows:
       --hlopt M m
  For example:
       torsiflex --hlopt 10 2
  divides the guesses into 10 groups and only carries out
  the calculations associated to the 2nd group.

  --> Calculations with Gaussian are carried out <--


--stoc

  Uses the stochastic algorithm for the conformer location.

  --> Calculations with Gaussian are carried out <--


--hlopt [nocalc]

  Re-optimizes LL conformers at HL.

  When followed by 'nocalc':
       --hlopt nocalc
  it generates the gjf files (Gaussian inputs) without
  carrying out calculations.
  Useful to send the calculations on your own.

  --> Calculations with Gaussian are carried out <--


--msho [ll/hl]

  Checks the located conformers and calculates the
  multi-structure harmonic-oscillator (MS-HO) partition
  functions.

  This option can be carried out exclusively for the
  low-level (ll) or the high-level (hl) conformers if
  followed by the corresponding abbreviation:
       --msho ll
       --msho hl


--mstor [ll/hl]

  Generates the MsTor input files.
```

```
      This option can be carried out exclusively for the
      low-level (ll) or the high-level (hl) conformers if
      followed by the corresponding abbreviation:
          --mstor ll
          --mstor hl


  --regen

    Regenerates the domains.txt file using the temporal files.


  --help (also -h)

    Prints this help message.


  --version (also -v)

    Prints the program version.

--------------------
  Extra Information
--------------------

(a) Assert the path to the Gaussian executable
    is defined in your .bashrc file under the name
    'GauExe' and export it. Example:

    export GauExe='/home/programs/Gaussian/g09'

(b) Modify the Gaussian templates (in GauTemplates/),
    taking into account that:

    * [nproc], [mem], [level], [optmode], [charge],
      [multipl], [zmat], [modred], and [ffccards]
      are TorsiFlex indications.
      They should not be removed.

    * Gaussian command line must start with '#p'

    * The command line includes 'iop(99/9=1,99/14=3)'.
      This is mandatory and should not be deleted:
          99/9=1  --> rotates to z-matrix orientation first
          99/14=3 --> expresses final optimized structure
                      in terms of the input z-matrix

    * 'scf=(incore)' is recommended with Hartree-Fock
      calculations. With it, Gaussian stores the full
      integral list in memory, speeding up the calculation.

(c) We highly recommend to firstly carry out the
    preconditioned search, which should found the
    chemically-intuitive conformers.
    After it, the stochastic algorithm should be used.
```

Notice that `TorsiFlex` accepts several options. Of them, we highlight the following:

> `--inp`: generates the `TorsiFlex` standard input file;
>
> `--prec`: performs the LL-searching using the preconditioned algorithm;
>
> `--stoc`: performs the LL-searching using the stochastic algorithm;
>
> `--hltop`: carries out the HL-refinement of the LL-conformers;
>
> `--msho`: checks the list of conformers and calculates the corresponding multi-structural harmonic-oscillator (MS-HO) partition function.
>
> `--mstor`: generates the `MsTor` input files.[6,7]

3.1   Input generation and Gaussian templates

`TorsiFlex` generates a default input file by executing:

```
>> path_to_torsiflex/torsiflex.py --inp
```

This file, named `torsiflex.inp` (see Chapter 8), contains keywords that control the program. Their detailed description can be found in Chapter 5.

This execution also generates the following eight templates for the calculations with Gaussian inside the `GauTemplates/` folder:

- `min_optLL`: LL optimization of a minimum.

- `min_optHL`: HL optimization of a minimum.

- `min_frqLL`: LL frequency calculation of a minimum.

- `min_frqHL`: HL frequency calculation of a minimum.

- `ts_optLL` : LL optimization of a transition state (TS).

- `ts_optHL` : HL optimization of a TS.

- `ts_frqLL` : LL frequency calculation of a TS.

- `ts_frqHL` : HL frequency calculation of a TS.

Although the above files are templates for the calculations with Gaussian, they contain indications for `TorsiFlex` (between square brackets). The [zmat] indicator is automatically replaced with a guess Z-matrix and must not be removed under any circumstance. The rest of them, listed below, can be controlled with the keywords in the `TorsiFlex` input file (Chapter 8):

- [nproc]   - [level]   - [charge]   - [modred]
- [mem]   - [optmode]   - [multipl]   - [fccards]

3.2   Low-level search

`TorsiFlex` will carry out the preconditioned conformer localization when executed together with `--prec`:

```
>> path_to_torsiflex/torsiflex.py --prec
```

whereas the stochastic search is carried out when executed with `--stoc`:

```
>> path_to_torsiflex/torsiflex.py --stoc
```

The difference between the two procedures lies on the generation of the geometry guesses (see section 2.1). Optimum performance is achieved when the preconditioned generation precedes the stochastic one. There are two reasons for this choice. Firstly, the geometry optimizations of preconditioned guesses rarely fail. Secondly, two preconditioned guesses infrequently lead to the same conformer.

In order to speed up the preconditioned search, `TorsiFlex` can split the set of preconditioned guesses into `G` groups and deal with each individual group separately. Thus, `TorsiFlex` manages the g-th group with ($g \leq G$):

```
>> python3 torsiflex.py --prec G g
```

For example, to split the guess vectors into `G=10` groups and take care of the second group ($g=2$) we use:

```
>> python3 torsiflex.py --prec 10 2
```

3.3   High-level re-optimization

When the LL conformers are obtained, HL refinements can be carried out by using the `--hlopt` option:

```
>> path_to_torsiflex/torsiflex.py --hlopt
```

This execution may computationally expensive. For this reason we recommend to run it in the background using either a queue system or the well-known nohup command.

3.4   Conformer analysis

Once all conformers (LL and/or HL) are obtained, the multi-structural harmonic-oscillator (MS-HO) partition function[8,9] can be calculated by:

```
>> path_to_torsiflex/torsiflex.py --msho
```

This option also classifies the located conformers by increasing energy and lists their total and Gibbs free energies. Other properties, as dipole moments and rotational constants are also listed.

3.5   Torsional anhamonicity

A more accurate method than MS-HO to evaluate the partition function can be obtained by means of the coupled torsional anharmonic approximation, MS-T(C), which incorporates couplings in the kinetic and potential energies between the torsions.[10–12] This partition function can be calculated using the `MsTor` software.[6,7]

`TorsiFlex` is able to generate the standard `MsTor` input files when executed with the `--mstor` option:

```
>> path_to_torsiflex/torsiflex.py --mstor
```

Firstly, `TorsiFlex` calculates the local periodicity parameter for each conformer (M_j for the j-th conformer) adopting a Monte Carlo approach:

$$M_j = \left(\frac{N_{\text{tot}}}{N_j} \right)^{1/K} \tag{3.1}$$

In this equation, N_{tot} is the total number of random points in the torsional space and N_j is the number of samples assigned to structure j. The number of torsions is represented by K.

The standard error of each M_j is given by:

$$\sigma_{M_j} = \frac{M_j}{K \sqrt{N_j}} \tag{3.2}$$

The program increases N_{tot} until all σ_{M_j} are smaller (or equal) than the value associated with the `sigmamj` keyword.

Once these M_j parameters are calculated, `TorsiFlex` generates the two `MsTor` input files: `mstor.dat` and `hess.dat`.

4. The reference Z-matrix

The user has to provide `TorsiFlex` with a file containing the Z-matrix of the system. We highly recommend `Molden`[13,14] to build up the molecule. `Molden` saves the Z-matrix in the correct format by selecting the "Gaussian" option and by clicking on the "Write Z-Matrix" button (see Figure 4.1).
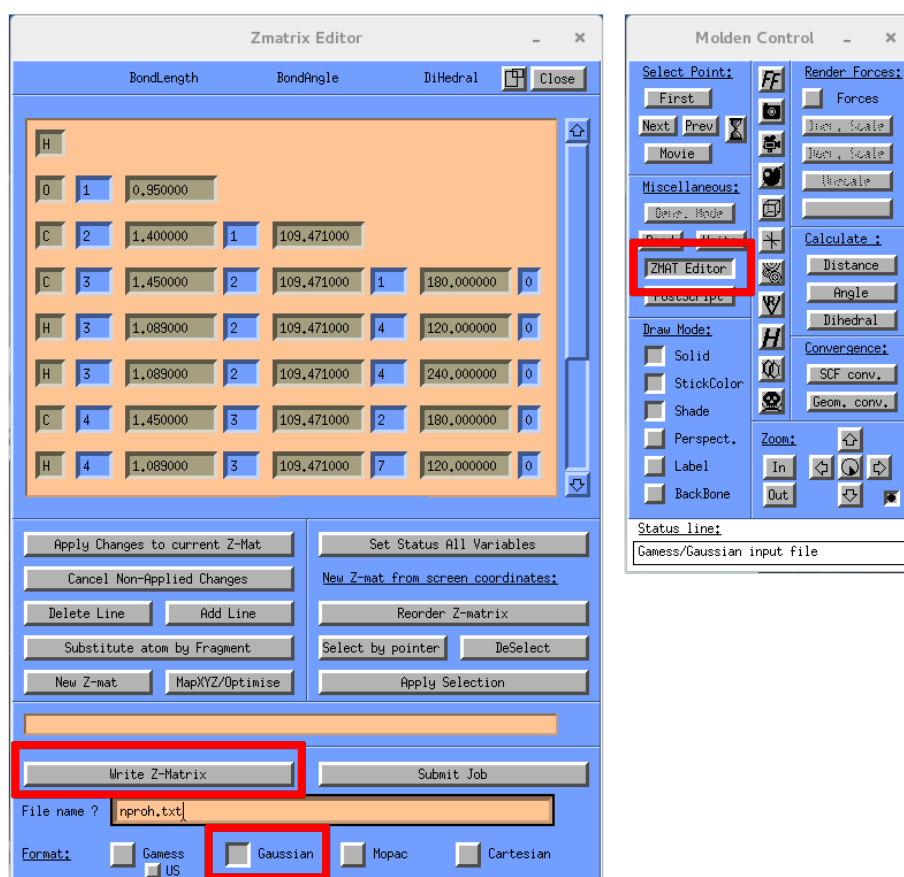

Figure 4.1: The Molden interface.

We highlight that the torsions of interest should be defined univocally: the file must contain **only one proper torsion about each torsional bond**; otherwise the `TorsiFlex` algorithm will fail.

5. The `TorsiFlex` input file

5.1 Keywords

An example of the `TorsiFlex` input file, `torsiflex.inp`, can be found in Chapter 8. This file contains different keywords, which are listed in Table 5.1. A detailed description of their meaning can be found in the following sections.

5.1.1 System-specific keywords

- `zmatfile`: the file containing the Z-matrix of the system. This file can be created with `Molden`.[13,14] See Chapter 4.

- `enantio`: `yes` if torsional enantiomers are generated upon internal rotations, `no` otherwise.

- `ts`: `yes` if a transition state (TS) structure is being studied, `no` otherwise.

- `cfactor`: a factor that control the distance criterium needed to obtain the connectivity graph of the system. For a pair of atoms, the higher the value of `cfactor`, the easiest is for the two atoms to be 'connected'. We recommend a value of 1.3 for a proper connectivity.

5.1.2 Keywords associated with the target torsions

In the keywords, `X` must be replaced by the corresponding integer.

- `torsionX`: the name of the target torsion in the Z-matrix file (`zmatfile` variable).

- `precondX`: defines the preconditioned angles of `torsionX`. By default, these values are 60, 180 and 300 degrees.

- `tdomainX`: defines the allowed domain of `torsionX`. See section 5.3 for more information on the definition of domains. By default the domain is [0,360).

- `tsigmaX`: the torsional symmetry number for `torsionX`. By default, it is set to 1.

- `pcfile`: a file containing preconditioned angles. It overrides `precondX`. See section 5.2.

5.1.3   Keywords associated with the search procedure

- `ncycles`: the number of steps in the random search of conformers (active when `TorsiFlex` is executed with the `--stoc` option).

5.1.4   Keywords associated with the HL re-optimization

- `hlcutoff`: a cutoff for HL calculations. LL conformers with relative Gibbs free energy smaller than `hlcutoff` (in kcal/mol) are re-optimized at HL. If this keyword is deactivated, all LL conformers are re-optimized.

- `tempGibbs`: temperature, in Kelvin, for the calculation of the Gibbs free energy.

5.1.5   Keywords associated with the validation tests

- `testsG`: controls which tests are carried out on a **Guess geometry**. This keyword must be followed by four integers, each one controlling one test. These tests are the connectivity, similarity, hard-constraint and soft-constraint tests (given in this order). Use 1 to activate a test and 0 to switch it off. By default, its value is:

```
testsG 1 1 1 1
```

  For example, the connectivity test for the guess geometry is deactivated with the following line:

```
testsG 0 1 1 1
```

- `testsO`: controls which tests are carried out on a **Optimized geometry**. This keyword must be followed by four integers, each one controlling one test. These tests are the connectivity, redundancy, hard-constraint and soft-constraint tests (given in this order). Use 1 to activate a test and 0 to switch it off. By default, its value is:

```
testsO 1 1 1 1
```

- `dist1D`: the domain about a torsional angle (in degrees). An angle ϕ_i belongs to the domain of another angle ϕ_j if their difference is within `dist1D` (d):

$$\phi_i \in \text{Dom}(\phi_j) \text{ if } |\phi_i - \phi_j| < d$$

  This variable defines the threshold in the **similarity test**.

- epsdeg: a criterium to decide whether two angles are equal or not (in degrees). Two angles, ϕ_i and ϕ_j, are considered identical if their difference is within epsdeg (ϵ):

$$\phi_i = \phi_j \text{ if } |\phi_i - \phi_j| < \epsilon$$

  This variable defines the threshold in the **redundancy test**.

- hconstr: defines a *hard* constraint (one per line). The argument of a hconstr line consists of an internal coordinate (a distance, an angle or a torsional angle) and a domain:

```
hconstr icoord domain
```

  The coordinates are defined by listing the involved atoms. Thus, 1-2-3 refers to the angle defined by the atoms labelled as 1, 2 and 3. The definition of domains can be found below, in section 5.3. We notice that all hard-constraints are mandatory and a guess/optimized geometry is **discarded** if **a single** hard constraint is **not fulfilled**.

- sconstr: defines a *soft* constraint (one per line) using the same format as in hconstr:

```
sconstr icoord domain
```

  In this case, a guess/optimized geometry is **discarded** if **all** the soft constraints are **not fulfilled**.

5.1.6 Keywords associated with the calculations with Gaussian

- optmode: defines the arguments of the opt keyword in the Gaussian input file (it replaces the [optmode] string in the template). It can be:

  - 0: to use opt(z-matrix)
  - 1: to use opt(modreduntant).

- fccards: when set to yes, the LL Hessian matrix is used in the HL optimization. This keyword will also modify the [optmode] string in the template by adding the fccards argument:

  - opt(z-matrix,fccards)
  - opt(modreduntant,fccards).

- charge: the charge of the system (it replaces the [charge] string in the Gaussian templates).

- multipl: the spin multiplicity of the system (it replaces the [multipl] string in the Gaussian templates).

- lowlevel: the low-level to be inserted in the Gaussian template. This keyword replaces the [level] string in the Gaussian template.

- `highlevel`: same as `lowlevel` but to define the level of calculation in the HL templates.

- `nproc`: number of threads for Gaussian calculations. This keyword replaces the [nproc] string in the Gaussian template.

- `mem`: dynamic memory for Gaussian calculations. This keyword replaces the [mem] string in the Gaussian template.

5.1.7 Keywords associated with the partition functions

- `tempsPF`: temperatures, in Kelvin, for the calculation of partition functions. Each line can contain several temperatures. More than one line can be used.

- `freqscalLL`: a scaling factor for the harmonic frequencies of the LL conformers, if needed. By default, frequencies are not scaled (i.e. `freqscalLL` is set to 1).

- `freqscalHL`: a scaling factor for the harmonic frequencies of the HL conformers, if needed. By default, frequencies are not scaled (i.e. `freqscalHL` is set to 1).

- `sigmamj`: the standard error in the calculation of the local periodicity parameters for MsTor (see section 3.5). This value must be $\geq 10^{-2}$.

5.1.8 Keywords associated with the storage of conformers

- `dirll`: the folder where the LL conformers are stored.

- `dirhl`: the folder where the HL conformers are stored.

- `tmpll`: the folder where the temporal LL Gaussian files are stored. By default this folder is set to `/scratch/user/LL_xxxxx/` where `user` is the name of the user and `xxxxx` is a random sequence of characters. The folder `LL_xxxxx/` is automatically created by the program when executed. If the creation fails, the program will let the user know that the folder must be created by themselves.

- `tmphl`: the folder where the temporal HL Gaussian files are stored. See also `tmpll`.

Table 5.1: Available keywords in the `TorsiFlex` input file.

Keyword	(Type of) value	More info
zmatfile	string	path to Z-matrix file
enantio	yes, no	are there torsional enantiomers?
ts	yes, no	is the system a transition state?
cfactor	float	controls system connectivity
torsionX	string	the coordinate name of the X-th torsion
		in the Z-matrix file; replace X with integer;
precondX	a list of integers	preconditioned angles for `torsionX`;
		replace X with integer;
		e.g. precond1 0 180
tdomainX	a domain	domain for `torsionX`; replace X with integer;
		e.g. tdomain1 (-60,60)
tsigmaX	integer	torsional symmetry number of `torsionX`;
		replace X with integer
pcfile	string	path to file with preconditioned angles
ncycles	integer	number of cycles in stochastic search;
		for `--stoc`
hlcutoff	float (kcal/mol)	Gibbs free energy cutoff for HL re-optimizations
tempGibbs	float (Kelvin)	temperature for the calculation of Gibbs free energy
testsG	four integers (0's or 1's)	selected validation tests for Guess geometries
testsO	four integers (0's or 1's)	selected validation tests for Optimized geometries
dist1D	integer (in degrees)	≥ 2.0; domain about an angle
epsdeg	integer (in degrees)	≤ 2.0; max. difference between equal angles
hconstr	internal coord. and domain	one line per hard constraint
sconstr	internal coord. and domain	one line per soft constraint
optmode	0,1	defines the argument of the `opt` Gaussian keyword
fccards	yes,no	use LL Hessian in HL optimization
charge	integer (in a.u.)	charge of the system
multipl	integer	spin multiplicity of the system
lowlevel	string	low-level methodology
highlevel	string	high-level methodology
nproc	integer	number of threads in Gaussian template (e.g. 2)
mem	string	dynamic memory in Gaussian template (e.g. 2GB)
tempsPF	list of floats (Kelvin)	temperatures for the partition functions
freqscalLL	float	scale factor for harmonic frequencies (LL conformers)
freqscalHL	float	scale factor for harmonic frequencies (HL conformers)
sigmamj	float	≥ 0.01; for `--mstor`
dirll	string	folder for storing LL conformers
dirhl	string	folder for storing HL conformers
tmpll	string	folder for LL Gaussian calculations
tmphl	string	folder for HL Gaussian calculations

5.2   The file with preconditioned angles: `pcfile`

The preconditioned angles can be also introduced as plain text using the `pcfile` keyword. Different combinations are possible for the selected torsions.

The first line in this file consists of the target torsions, whereas the rest of the lines define their corresponding values (separated by blank spaces or by an underscore). For example, the next file:

```
  1     3
100_100
200_300
```

defines two combinations:

- $(\texttt{torsion1}, \texttt{torsion3}) = (100, 100)$

- $(\texttt{torsion1}, \texttt{torsion3}) = (200, 300)$

The value of the disregarded torsions, if any, will be defined according to the default angles, *i.e.* the (60,180,300) triad or those defined through `precondX`. In this manner, if the system contains three torsions (`torsion1`,`torsion2`,`torsion3`), the previous lines would lead to the next points:

- (100,60,100)   - (200,60,300)

- (100,180,100)   - (200,180,300)

- (100,300,100)   - (200,300,300)

5.3   Specifying a domain

Keywords `hconstr`, `sconstr` and `tdomainX` require the definition of a domain. An interval can be defined with the format (a,b), where a and b are the limits of the interval (a<b). Several intervals can be used to define a given domain through their union (denoted by a capital U). For example, (a,b)U(c,d), where a<b<c<d.

In the case of `tdomainX`, the domain corresponds to a torsion angle (in degrees). However, `hconstr` or `sconstr` can be specified to restrict the domain of a distance (in Angstrom) or of an angle (in degrees).

6. Some tips

6.1 Low-level calculations at the HF level

If Hartree-Fock (HF) is the LL method of choice for the searching algorithm, we highly recommend to modify the Gaussian template and include the argument `incore` in the `scf` Gaussian keyword:

```
scf =( verytight , incore )
```

In this manner, the full integral list will be stored in memory along the self-consistent field method (SCF). This should speed up the calculation. Obviously, if `incore` is used, enough memory should be available.

6.2 Systems with many LL conformers

The HL re-optimizations are carried out sequentially, which may not be convenient for systems with a big number of conformers. In such a cases, we recommend to execute `TorsiFlex` as follows:

```
>> path_to_torsiflex/torsiflex.py --hlopt nocalc
```

This will generate the Gaussian input files for the HL re-optimization of all the LL conformers. In this manner, the user can execute all Gaussian jobs at the same time if desired (i.e. the calculations are managed by the user and not by `TorsiFlex`). Once the optimizations are complete, the corresponding Gaussian input files for the frequency calculations can be also generated by executing `TorsiFlex` again:

```
>> path_to_torsiflex/torsiflex.py --hlopt nocalc
```

When all optimization and frequency calculations are finished, `TorsiFlex` can be executed normally and will automatically read the generated output files:

```
>> path_to_torsiflex/torsiflex.py --hlopt
```

6.3 Focusing on low energy conformers

The user may also be interested into re-optimize only the most stable conformers. In such cases, we recommend to use the `hlcutoff` keyword. Only those LL con-

formers whose Gibbs free energy is below the value associated to `hlcutoff` are optimized at HL.

For example, in order to optimize at HL those conformers whose relative Gibbs free energy is smaller than 3 kcal/mol at 300 K, we need the following line in the input file:

```
hlcutoff      3.0 300.0
```

The first argument of `hlcutoff` defines the cutoff for the Gibbs free energy, whereas the second argument defines the temperature for the calculation of such an energy. If not indicated, the default temperature is 300 K.

6.4   Dealing with similar molecules

When performing conformational studies, it may occur that we have to deal with two molecules with common fragments. For the sake of simplicity, let us name these two molecules as AM and BM, both containing the M moiety. In such cases, it is very likely for the conformations of the M moiety in A and in B to be similar. If we have performed a full study on AM, it would be very convenient to use the conformations of its M moiety as a guess for BM. This may be achieved by defining the pre-conditioned angles through `pcfile` instead of with the `precondX` keyword.

For instance, let us assume that molecule AM consists of three torsions, `torsion1` to `torsion3`, the last two torsions being located in the M fragment, whereas BM consists of four torsions, `torsion1` to `torsion4`, the last two corresponding to M. TorsiFlex can initialize `torsion3` and `torsion4` of BM according to the values of `torsion2` and `torsion3` of AM. The procedure is as follows:

(a) Go to the working directory of AM and enter in the folder where conformers are stored.

(b) List the angles using:

```
>> ls *log | awk -F. '{print $2}'
```

The output would look like:

```
069_284_314
071_172_060
071_182_301
072_268_179
073_080_304
075_093_192
075_280_051
```

(c) As we are only interested in the second and third columns of this list (`torsion2` and `torsion3`), the first column should be eliminated. This can be achieved with a slight modification of the command:

```
>> ls *log | awk -F. '{print $2}' | \
   awk -F"_" '{print $2, $3}'
```

leading to:

```
284 314
172 060
182 301
268 179
080 304
093 192
280 051
```

(d) Save these lines in a new file and use it for BM through the `pcfile` keyword. A first line, indicating the target torsions, must be added to this file:

```
  3   4
284 314
172 060
182 301
268 179
080 304
093 192
280 051
```

(e) Now, the initial angles for torsions `torsion3` and `torsion4` of BM are set to those in AM, whereas starting values for `torsion1` and `torsion2` are defined by the default triad, (60,180,300).

An example of this situation may be found when studying the amino acids. For example, alanine and valine, or cysteine and methionine, et cetera.

Finally, we notice that (i) `precondX` defines preconditioned values for individual torsions whereas (ii) `pcfile` defines preconditioned (sub)vectors in the torsional space.

7. Worked examples

This Chapter contains the following step-by-steps examples:

- WE1: n-butanol

- WE2: L-alanine

- WE3: L-proline

- WE4: Transition state for the H abstraction from n-butanol at the C$-\alpha$ atom by the H radical

The level of calculation for the search procedure is set to HF/3-21G (low-level, LL), whereas B3LYP/6-31G is employed as the accurate high-level (HL) for the re-optimizations.

Torsions of interest

Torsions for WE1:

- dih4 (H1-O2-C3-C4)

- dih7 (O2-C3-C4-C7)

- dih10 (C3-C4-C7-H9)

Torsions for WE3:

- dih4 (C1-C2-C3-C4)

- dih5 (C2-C3-C4-N5)

- dih17 (C3-C4-N5-H17)

- dih7 (C2-C1-C6-O7)

- dih8 (C1-C6-O7-H8)

Torsions for WE2:

- dih4 (H1-O2-C3-O4)

- dih6 (O2-C3-C5-N6)

- dih9 (C3-C5-N6-H9)

Torsions for WE4:

- dih9 (C9-C8-C5-C1)

- dih12 (O12-C9-C8-C5)

- dih15 (H15-O12-C9-C8)

7.1 WE1: conformers of n-butanol

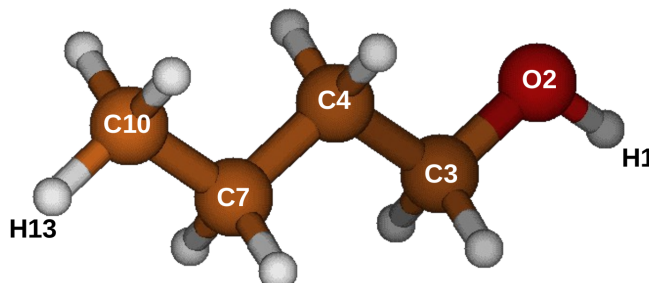In this worked example, we find the conformers of n-butanol (Figure 7.1)

Figure 7.1: Labeling for n-butanol.

How to proceed

- Assert that the `GauExe` variable with the path to your Gaussian version is exported in the `.bashrc` file.

- Create the folder `WE1/` and enter to it.

```
>> mkdir WE1/
>> cd WE1/
```

- Copy the corresponding Z-matrix file (`we1.zmat`, see Chapter 8) from the `tests/` folder to the current directory (or create it with the help of `Molden`).

- Create the input file and the templates for the Gaussian calculations:

```
>> path_to_torsiflex/torsiflex.py --inp
```

- Modify/add the following keywords in the input file:

```
zmatfile    we1.zmat            torsion1    dih4
enantio     yes                 torsion2    dih7
ncycles     20                  torsion3    dih10
lowlevel    hf/3-21g
```

Keyword `tmpll` may be also modified.

- In principle, it is not necessary to modify the templates for Gaussian. However, the `incore` argument could be included in the `scf` Gaussian option to speed-up the LL calculations (`min_optLL` file inside `GauTemplates/`).

- Execute `TorsiFlex` with the `--prec` option:

```
>> path_to_torsiflex/torsiflex.py --prec
```

In a few minutes, the program finds the conformers from the preconditioned guesses at the HF/3-21g level. A total of 14 conformers should be found.

- Execute `TorsiFlex` with the `--stoc` option:

```
>> path_to_torsiflex/torsiflex.py --stoc
```

In this case, `TorsiFlex` considers random angles to find new conformers. Execute `TorsiFlex` as many times as needed. A new conformer should be found in this random search (086_305_086 or 274_055_274).

- A total of 15 LL conformers should be found (14+1). Notice that there exists an enantiomer for any of the conformers, but the one with Cs symmetry. Consequently, there are 29 conformers for n-butanol ($14 \cdot 2 + 1$).

- List your LL conformers and calculate the corresponding MS-HO partition functions using `--msho`:

```
>> path_to_torsiflex/torsiflex.py --msho ll
```

- Modify again the input file to indicate the high-level of calculation:

```
highlevel  b3lyp/6-31g
```

Keyword `tmphl` may be also modified.

- Execute `TorsiFlex` to carry out the HL optimizations based on the LL structures:

```
>> path_to_torsiflex/torsiflex.py --hlopt
```

This execution may take a few minutes.

- List your HL conformers and calculate the corresponding MS-HO partition function using the `--msho` option:

```
>> path_to_torsiflex/torsiflex.py --msho hl
```

List of low-level conformers

1. (065,056,184)
2. (184,060,183)
3. (064,054,070)
4. (063,064,287)
5. (064,177,180)
6. (183,058,070)
7. (075,298,181)
8. (180,180,180)
9. (182,067,282)
10. (063,179,291)
11. (065,174,069)
12. (077,302,295)
13. (179,177,068)
14. (274,055,274)
15. (068,276,061)

List of high-level conformers

1. (063,059,183)
2. (062,177,180)
3. (069,295,181)
4. (184,063,181)
5. (180,180,180)
6. (062,057,067)
7. (183,061,066)
8. (060,179,294)
9. (060,064,287)
10. (068,296,294)
11. (063,174,067)
12. (178,177,066)
13. (181,070,285)
14. (067,279,062)
15. (283,063,274)

7.2 WE2: conformers of L-alanine

In this example, we find the conformers of L-alanine (see Figure 7.2).
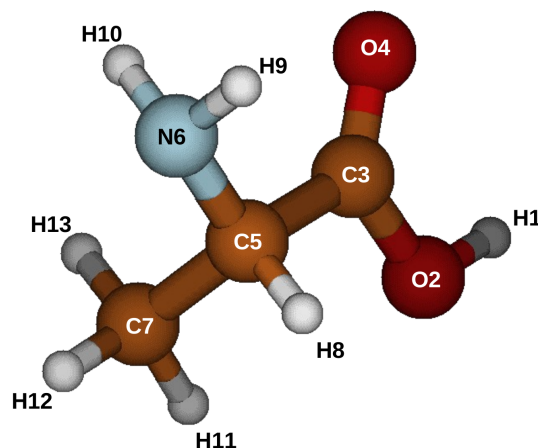

Figure 7.2: Labeling for Alanine.

How to proceed

- Assert that the `GauExe` variable with the path to your Gaussian version is exported in the `.bashrc` file.

- Create the folder `WE2/` and enter to it.

```
>> mkdir WE2/
>> cd WE2/
```

- Copy the corresponding Z-matrix file (`we2.zmat`, see Chapter 8) from the `tests/` folder to the current directory (or create it with the help of `Molden`).

- Create the input file and the templates for the Gaussian calculations:

```
>> path_to_torsiflex/torsiflex.py --inp
```

- Modify/add the following keywords in the input file:

zmatfile	we2.zmat	torsion1	dih4
ncycles	20	torsion2	dih6
hconstr	5-6-9-10 (0,180)	torsion3	dih9
lowlevel	hf/3-21g	precond1	0 180

Notice that keyword `precond1` is used to set the preconditioned angles for the carboxyl group to 0 and 180 degrees. Keyword `hconstr` adds a constraint to the C-H-H-N improper torsion, in order to exclude conformations

where the NH$_2$ umbrella inversion has taken place. Keywords `tmpll` and `tmphl` may be also modified.

- In principle, it is not necessary to modify the templates for Gaussian. However, the `incore` argument could be included in the `scf` Gaussian option to speed-up the LL calculations (`min_optLL` file inside `GauTemplates/`).

- Execute `TorsiFlex` with the `--prec` option:

```
>> path_to_torsiflex/torsiflex.py --prec
```

In a few minutes, the program finds the conformers at the HF/3-21g level from the preconditioned guesses. A total of 11 conformers should be found.

- Execute `TorsiFlex` with the `--stoc` option:

```
>> path_to_torsiflex/torsiflex.py --stoc
```

In this case, `TorsiFlex` considers random angles to find new conformers. This execution may take some time, depending on the value of the `ncycles` keyword. No new conformers are found for this system.

- List your LL conformers and calculate the corresponding MS-HO partition function using `--msho`:

```
>> path_to_torsiflex/torsiflex.py --msho ll
```

- Modify again the input file to perform the HL calculations:

```
highlevel   b3lyp/6-31g
```

- Execute `TorsiFlex` to carry out the HL optimizations based on the LL structures:

```
>> path_to_torsiflex/torsiflex.py --hltopt
```

This execution may take a few minutes.

- List your HL conformers and calculate the corresponding MS-HO partition function using the `--msho` option:

```
>> path_to_torsiflex/torsiflex.py --msho hl
```

The number of conformers should have been reduced to 10.

List of low-level conformers

1. (000,176,294)
2. (175,020,088)
3. (000,038,304)
4. (000,314,288)
5. (000,167,033)
6. (359,187,197)
7. (003,052,174)
8. (357,305,059)
9. (177,173,290)
10. (174,167,023)
11. (192,065,174)

List of high-level conformers

1. (178,012,097)
2. (000,170,295)
3. (000,074,295)
4. (000,313,290)
5. (000,164,027)
6. (000,185,196)
7. (002,044,175)
8. (357,310,058)
9. (179,170,294)
10. (177,166,016)

7.3   WE3: conformers of proline

In this example, we find the conformers of L-proline (see Figure 7.4).
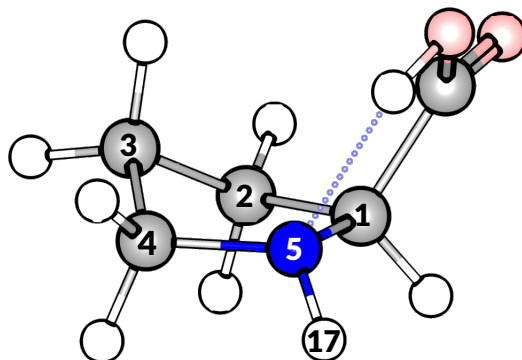

Figure 7.3: Cycle numeration in Pro. C in grey, O in red, N in blue and H in white.

We notice that L-proline is the only proteinogenic amino acid containing a flexible ring in its structure. `TorsiFlex` is not specially optimized for dealing with ring puckering, but it can still be used to find the corresponding conformers. If we consider the numbering shown in Figure 7.3, the ring configurations arise from the following torsions: (i) C_1-C_2-C_3-C_4, (ii) C_2-C_3-C_4-N_5 and (iii) C_3-C_4-N_5-H_{17}. In order to avoid huge distortions in the five-member ring, the domains of these torsions are limited to a small interval. Moreover, since the connectivity of the ring may be compromised in the guess structure, the connectivity test for guess structures should be deactivated.

How to proceed

- Assert that the `GauExe` variable with the path to your Gaussian version is exported in the `.bashrc` file.

- Create the folder `WE2/` and enter to it.
  ```
  >> mkdir WE3/
  >> cd WE3/
  ```

- Copy the corresponding Z-matrix file (`we3.zmat`, see Chapter 8) from the `tests/` folder to the current directory (or create it with the help of `Molden`).

- Create the input file and the templates for the Gaussian calculations:
  ```
  >> path_to_torsiflex/torsiflex.py --inp
  ```

- Modify/add the following keywords in the input file:

```
zmatfile    we3.zmat            tdomain1    (-70,70)
testsG      0 1 1 1             tdomain2    (-70,70)
lowlevel    hf/3-21g            tdomain3    (60,300)
torsion1    dih4                precond1     -35  +35
torsion2    dih5                precond2     -35  +35
torsion3    dih17               precond3    -120 +120
torsion4    dih7                precond5       0  180
torsion5    dih8
```

Notice that we have reduced the interval for dih4 and dih5 to (-70,70), in order to generate structures where the five-member ring is "conserved". Similarly, the interval for dih17 should account for the two arrangements in the umbrella inversion (in this case, this conformational effect leads to different conformers). The preconditional angles for these torsions were also modified, in order to fit the previous defined intervals. As in WE2, `precond5` account for the two expected conformations of the carboxylic acid group. The first argument of `testsG` is set to 0 to deactivate the connectivity test on the guess structures.

- Execute `TorsiFlex` with the `--prec` option:

```
>> path_to_torsiflex/torsiflex.py --prec
```

In a few minutes, the program finds the conformers at the HF/3-21g level from the preconditioned guesses. A total of 17 conformers should be found.

- Execute `TorsiFlex` with the `--stoc` option:

```
>> path_to_torsiflex/torsiflex.py --stoc
```

In this case, `TorsiFlex` considers random angles to find new conformers. This execution may take some time, depending on the value of the `ncycles` keyword. A total of 3 new conformers should be found.

- List your LL conformers and calculate the corresponding MS-HO partition function using `--msho`:

```
>> path_to_torsiflex/torsiflex.py --msho ll
```

- Modify again the input file to perform the HL calculations:

```
highlevel   b3lyp/6-31g
```

- Execute `TorsiFlex` to carry out the HL optimizations based on the LL structures:

```
>> path_to_torsiflex/torsiflex.py --hltopt
```

This execution may take a few minutes.

- List your HL conformers and calculate the corresponding MS-HO partition function using the `--msho` option:

```
>> path_to_torsiflex/torsiflex.py --msho hl
```

The number of conformers should have been reduced to 14.

List of low-level conformers

1. (320,037,211,121,358)
2. (321,029,123,294,180)
3. (016,325,171,298,181)
4. (012,330,274,139,354)
5. (323,022,136,159,179)
6. (013,327,171,157,179)
7. (322,039,195,186,186)
8. (040,330,239,098,007)
9. (323,038,198,043,176)
10. (037,335,225,181,184)
11. (031,319,171,074,182)
12. (025,322,272,204,186)
13. (027,322,271,052,175)
14. (037,337,206,299,180)
15. (007,017,081,158,355)
16. (320,031,117,291,354)
17. (022,321,170,298,357)
18. (029,319,169,182,012)
19. (331,010,246,283,352)
20. (356,342,172,038,352)

List of high-level conformers

1. (323,036,209,117,359)
2. (027,324,266,127,357)
3. (324,028,123,294,181)
4. (033,322,163,296,181)
5. (325,023,136,145,177)
6. (017,326,173,151,178)
7. (326,036,190,188,185)
8. (035,330,234,195,185)
9. (326,034,195,040,176)
10. (031,325,255,049,175)
11. (007,017,082,156,356)
12. (033,322,162,297,001)
13. (324,030,118,292,359)
14. (029,321,171,196,009)

7.4 WE4: conformers of a transition state

In this example, we find the conformers of the transition state associated to the H abstraction by H in the α position of n-BuOH (see Figure 7.4).
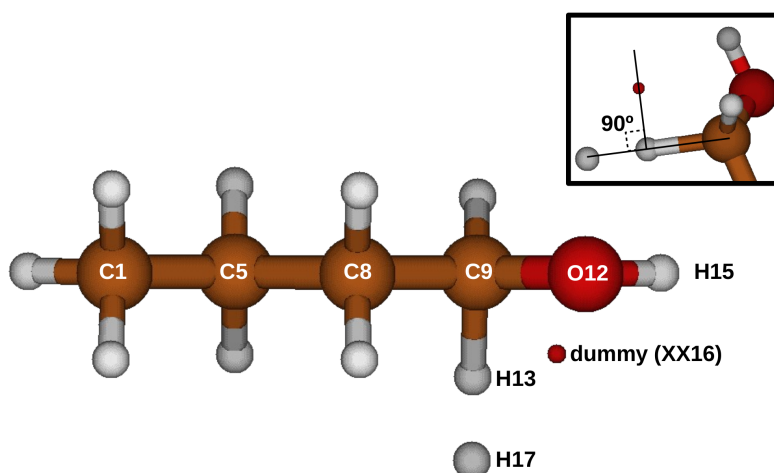
Figure 7.4: Labeling for the H-abstraction transition state. The definition of the dummy atom is also shown from another point of view.

How to proceed

- Assert that the GauExe variable with the path to your Gaussian version is exported in the .bashrc file.

- Create the folder WE4/ and enter to it.
```
>> mkdir WE4/
>> cd WE4/
```

- Copy the corresponding Z-matrix file (we4.zmat, see Chapter 8) from the tests/ folder to the current directory (or create it with the help of Molden).

- Create the input file and the templates for the Gaussian calculations:
```
>> path_to_torsiflex/torsiflex.py --inp
```

- Modify/add the following keywords in the input file:

```
zmatfile   zmat_we4.txt          torsion1    dih9
ts         yes                   torsion2    dih12
multipl    2                     torsion3    dih15
lowlevel   hf/3-21g
```

Notice that setting ts to yes indicates that we are dealing with a transition state (different Gaussian templates are selected), whereas multipl defines the spin multiplicity of the system.

- Execute `TorsiFlex` with the `--prec` option:

```
>> path_to_torsiflex/torsiflex.py --prec
```

  In a few minutes, the program finds the conformers at the HF/3-21g level from the preconditioned guesses. A total of 22 conformers should be found.

- Execute `TorsiFlex` with the `--stoc` option:

```
>> path_to_torsiflex/torsiflex.py --stoc
```

  In this case, `TorsiFlex` considers random angles to find new conformers. This execution may take some time, depending on the value of the `ncycles` keyword. A total of 3 new conformers should be found.

- List your LL conformers and calculate the corresponding MS-HO partition function using `--msho`:

```
>> path_to_torsiflex/torsiflex.py --msho ll
```

  This also lists the imaginary frequency of each transition state conformer. A total of 25 LL conformers should be listed.

- Modify again the input file to perform the HL calculations:

```
highlevel   b3lyp/6-31g
```

- Execute `TorsiFlex` to carry out the HL optimizations based on the LL structures:

```
>> path_to_torsiflex/torsiflex.py --hltopt
```

  This execution may take a few minutes.

- List your HL conformers and calculate the corresponding MS-HO partition function using the `--msho` option:

```
>> path_to_torsiflex/torsiflex.py --msho hl
```

  The number of conformers should be reduced to 19.

List of low-level conformers

1. (184,058,056)
2. (177,306,176)
3. (183,062,182)
4. (290,068,055)
5. (069,055,056)
6. (180,176,054)
7. (068,059,181)
8. (180,179,178)
9. (285,071,180)
10. (182,304,061)
11. (081,304,178)
12. (299,321,179)
13. (290,177,053)
14. (290,181,179)
15. (296,315,063)
16. (067,168,176)
17. (067,166,056)
18. (084,314,072)
19. (176,311,286)
20. (059,278,051)
21. (180,184,290)
22. (074,304,287)
23. (300,326,285)
24. (289,185,287)
25. (067,174,294)

List of high-level conformers

1. (182,062,051)
2. (181,066,186)
3. (179,178,049)
4. (179,302,183)
5. (180,180,184)
6. (182,300,052)
7. (065,060,050)
8. (290,068,048)
9. (066,064,186)
10. (293,180,048)
11. (287,074,185)
12. (294,183,184)
13. (294,311,184)
14. (296,308,051)
15. (077,297,184)
16. (069,170,050)
17. (068,171,181)
18. (060,282,048)
19. (087,306,057)

8. Example files

Example of file with preconditioned angles (`pcfile` keyword).

```
 1          3          4
068        174        063
068        183        300
071        298        299
075        291        175
172        306        296
175        300        174
179        298        070
180        176        062
180        180        180
286        307        297
292        182        182
293        301        073
299        082        295
```

Gaussian template for optimization.

```
%nproc=[nproc]
%mem=[mem]
#p [level]
scf=(verytight)
iop(99/9=1,99/14=3)
opt=([optmode],maxcyc=99)

--Optimization of minimum--

[charge],[multipl]
[zmat]
[modred]
[fccards]
```

Gaussian template for frequency calculation.

```
%nproc=[nproc]
%mem=[mem]
#p [level]
scf=(verytight)
iop(99/9=1,99/14=3)
freq=noraman

--Frequency calculation--

[charge],[multipl]
[zmat]
```

The default `TorsiFlex` **input file**

```
# This is a torsiflex input file

#----------------------#
#         System       #
#----------------------#
zmatfile     zmat.txt    # Z-matrix file
enantio      no          # yes if torsional enantioners , no otherwise
ts           no          # yes if transition state, no otherwise
cfactor      1.3         # controls the connectivity criterium


#----------------------#
#    Target torsions   #
#----------------------#
torsion1     --          # name of 1st target torsion in the Z-matrix file
#precond1   60 180 300   # precond angles for torsion1
#tdomain1   (0,360)      # domain for torsion1
#tsigma1     1           # symmetry number for torsion1
#pcfile      precond.txt # file with precond. angles


#----------------------#
#   Search  Procedure  #
#----------------------#
ncycles      200         # number of steps of stochastic algorithm


#----------------------#
#   HL reoptimization  #
#----------------------#
#hlcutoff    5.0         # Gibbs energy cutoff (kcal/mol)
tempGibbs   298.15       # Temperature (K) for Gibbs free energy


#----------------------#
#   Validation   tests #
#----------------------#
testsG       1 1 1 1     # for Guess geom (Conn, Simil, Hard, Soft)
testsO       1 1 1 1     # for Opt   geom (Conn, Redun, Hard, Soft)
dist1D       15          # domain size about each point (degrees)
epsdeg       2           # max diff between two identical angles (degrees)
#hconstr    ic domain    # hard constraint (see manual)
#sconstr    ic domain    # soft constraint (see manual)


#----------------------#
# Gaussian calculations #
#----------------------#
optmode      1           # 0:opt(z-matrix) , 1:opt(modredundant)
fccards      no          # Use LL Hessian in HL opt (yes/no)
charge       0           # charge of the system
multipl      1           # multiplicity of the system
lowlevel     hf    3-21g # low-level of calculation
highlevel    b3lyp 6-31G # high-level of calculation
nproc        1           # Number of threads
mem          1GB         # dynamic memory


#----------------------#
#  Partition functions #
#----------------------#
tempsPF      100    200  # temperatures (K) for part. functions
tempsPF      298.15      # temperatures (K) for part. functions
tempsPF      300    500  # temperatures (K) for part. functions
tempsPF      750   1000  # temperatures (K) for part. functions
tempsPF      2000  2500  # temperatures (K) for part. functions
freqscalLL   1.0         # freq. scaling factor (LL)
freqscalHL   1.0         # freq. scaling factor (HL)
sigmamj      0.02        # max value for sigma(Mj); >= 0.01


#----------------------#
#        Storage       #
#----------------------#
dirll        files_LL/   # folder to store LL conformers
dirhl        files_HL/   # folder to store HL conformers
tmpll        /scratch/user/LL_iFPph/ # folder for LL temporal files
tmphl        /scratch/user/HL_iFPph/ # folder for HL temporal files
```

Reference Z-matrix file for n-BuOH (WE1).

```
h
o     1  oh2
c     2  co3         1  coh3
c     3  cc4         2  cco4          1  dih4
h     3  hc5         2  hco5          4  dih5
h     3  hc6         2  hco6          4  dih6
c     4  cc7         3  ccc7          2  dih7
h     4  hc8         3  hcc8          7  dih8
h     4  hc9         3  hcc9          7  dih9
c     7  cc10        4  ccc10         3  dih10
h     7  hc11        4  hcc11        10  dih11
h     7  hc12        4  hcc12        10  dih12
h    10  hc13        7  hcc13         4  dih13
h    10  hc14        7  hcc14        13  dih14
h    10  hc15        7  hcc15        13  dih15


oh2        0.950
co3        1.400
coh3     109.471
cc4        1.450
cco4     109.471
dih4     180.000
hc5        1.089
hco5     109.471
dih5     120.000
hc6        1.089
hco6     109.471
dih6     240.000
cc7        1.450
ccc7     109.471
dih7     180.000
hc8        1.089
hcc8     109.471
dih8     120.000
hc9        1.089
hcc9     109.471
dih9     240.000
cc10       1.450
ccc10    109.471
dih10    180.000
hc11       1.089
hcc11    109.471
dih11    120.000
hc12       1.089
hcc12    109.471
dih12    240.000
hc13       1.089
hcc13    109.471
dih13    180.000
hc14       1.089
hcc14    109.471
dih14    120.000
hc15       1.089
hcc15    109.471
dih15    240.000
```

Reference Z-matrix file for L-alanine (WE2).

```
 h
 o     1  oh2
 c     2  co3          1  coh3
 o     3  oc4          2  oco4          1  dih4
 c     3  cc5          4  cco5          2  dih5
 n     5  nc6          3  ncc6          2  dih6
 c     5  cc7          3  ccc7          6  dih7
 h     5  hc8          3  hcc8          6  dih8
 h     6  hn9          5  hnc9          3  dih9
 h     6  hn10         5  hnc10         9  dih10
 h     7  hc11         5  hcc11         3  dih11
 h     7  hc12         5  hcc12        11  dih12
 h     7  hc13         5  hcc13        11  dih13

 oh2          0.947
 co3          1.400
 coh3       109.471
 oc4          1.220
 oco4       120.000
 dih4       180.000
 cc5          1.450
 cco5       120.000
 dih5       180.000
 nc6          1.440
 ncc6       109.471
 dih6         0.000
 cc7          1.450
 ccc7       109.471
 dih7       120.000
 hc8          1.089
 hcc8       109.471
 dih8       240.000
 hn9          1.008
 hnc9       109.471
 dih9       180.000
 hn10         1.008
 hnc10      109.471
 dih10      120.000
 hc11         1.089
 hcc11      109.471
 dih11      180.000
 hc12         1.089
 hcc12      109.471
 dih12      120.000
 hc13         1.089
 hcc13      109.471
 dih13      240.000
```

Reference Z-matrix file for proline (WE3).

```
c
c    1 cc2
c    2 cc3        1 ccc3
c    3 cc4        2 ccc4        1 dih4
n    4 nc5        3 ncc5        2 dih5
c    1 cc6        2 ccc6        5 dih6
o    6 oc7        1 occ7        2 dih7
h    7 ho8        6 hoc8        1 dih8
o    6 oc9        1 occ9        7 dih9
h    1 hc10       2 hcc10       5 dih10
h    2 hc11       1 hcc11       3 dih11
h    2 hc12       1 hcc12       3 dih12
h    3 hc13       2 hcc13       4 dih13
h    3 hc14       2 hcc14       4 dih14
h    4 hc15       3 hcc15       5 dih15
h    4 hc16       3 hcc16       5 dih16
h    5 hn17       4 hnc17       3 dih17

cc2            1.500
cc3            1.500
ccc3         109.471
cc4            1.500
ccc4         109.471
dih4           0.000
nc5            1.500
ncc5         109.471
dih5           0.000
cc6            1.500
ccc6         109.471
dih6        -120.000
oc7            1.500
occ7         109.471
dih7         180.000
ho8            1.070
hoc8         109.471
dih8         180.000
oc9            1.380
occ9         109.471
dih9         180.000
hc10           1.070
hcc10        109.471
dih10        120.000
hc11           1.070
hcc11        109.471
dih11        120.000
hc12           1.070
hcc12        109.471
dih12        240.000
hc13           1.070
hcc13        109.471
dih13        120.000
hc14           1.070
hcc14        109.471
dih14        240.000
hc15           1.070
hcc15        109.471
dih15        120.000
hc16           1.070
hcc16        109.471
dih16        240.000
hn17           1.030
hnc17        109.471
dih17        240.000
```

Reference Z-matrix file for the H$_\alpha$-abstraction by H in n-BuOH (WE4).

```
C
H  1 hc2
H  1 hc3     2 hch3
H  1 hc4     2 hch4    3 dih4
C  1 cc5     2 cch5    3 dih5
H  5 hc6     1 hcc6    2 dih6
H  5 hc7     1 hcc7    6 dih7
C  5 cc8     1 ccc8    4 dih8
C  8 cc9     5 ccc9    1 dih9
H  8 hc10    5 hcc10   9 dih10
H  8 hc11    5 hcc11   9 dih11
O  9 oc12    8 occ12   5 dih12
H  9 hc13    8 hcc13  12 dih13
H  9 hc14    8 hcc14  12 dih14
H 12 ho15    9 hoc15   8 dih15
X 13 1.0     9 90.0    8 180.0
H 13 hh17   16 hhxx17  9 dih17


hc2          1.0885
hc3          1.0883
hch3       107.5745
hc4          1.0871
hch4       107.7557
dih4       115.9003
cc5          1.5150
cch5       111.1295
dih5      -121.7304
hc6          1.0900
hcc6       109.70311
dih6       181.51880
hc7          1.0909
hcc7       109.52564
dih7       116.33407
cc8          1.5165
ccc8       112.41217
dih8       179.88719
cc9          1.4941
ccc9       112.66874
dih9       180.000
hc10         1.0927
hcc10      110.1648
dih10      121.5553
hc11         1.0904
hcc11      110.3031
dih11      238.7453
oc12         1.3754
occ12      111.1484
dih12      180.000
hc13         1.2882
hcc13      105.6461
dih13      117.8854
hc14         1.0920
hcc14      114.0850
dih14      230.0875
ho15         0.9544
hoc15      110.2999
dih15      180.000
hh17         0.9930
hhxx17      90.5885
dih17      183.134
```

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