

Isomer- and Diamutamer-Enumeration with *MATHEMATICA***

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Abstract

We introduce the *MATHEMATICA*[1] package `Isomers.m[2]`, which is the implementation of an efficient isomer and diamutamer enumeration algorithm[3] based on Pölyas theorem[4]. The computer algebra package enables the user to generate and to classify point groups describing the symmetry of a compound. `Isomers.m` can enumerate the diamutamers with one or more types of achiral ligands of specified, unspecified, and partially specified multiplicity. The handling of the software is demonstrated with an example calculation.

Chemical compounds that exhibit identical molecular formulae but differ in constitution are called isomers. Molecules, that exhibit the same central skeleton but differ in the arrangement of ligands, are called *diamutamers* [5].

We are going to take the reader step by step through an isomer and diamutamer enumeration with `Isomers.m`. The initial step is the loading of the package into *MATHEMATICA*.

```
In[1] := << Isomers`Isomers`
```

Biphenyl in its twisted conformation as depicted in Figure 1 will serve as a central skeleton example. The two rings of *biphenyl* are rotated along the *a* axis by 90° with respect to each other. This twisted conformation is energetically favorable compared to the planar conformation, in which both rings are aligned in parallel¹. We assume that *biphenyl* can flip 180° around the σ -bond connecting the two rings. Such a 180° twist amounts to a conformational transformation that permutes the substitutions sites. Other permutation of substitution sites occurs when rotating the entire molecule around axes *a* or *b*, or when considering a reflection across a plane. These site permutations define the symmetry and the isomeric equivalence relations of

^{*}*MATHEMATICA* is a registered trademark of Wolfram Research Inc., www.wolfram.com.

¹Our model of the *Biphenyl* skeleton is kept simple. We do not consider a locked up twist between 0°-90° that would render the central skeleton chiral.

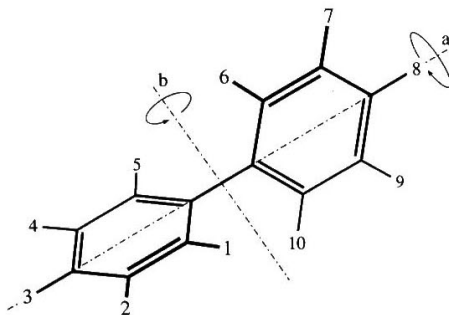


Figure 1: The twisted *biphenyl* skeleton with its ten substitution sites and two symmetry axes.

the central skeleton. We provide the permutations together with a compound name in the first step of our isomer enumeration.

```
In[2]:= DefineParentCompound[
  BiphenylTwisted,
  {R[5, 4, 3, 2, 1, 10, 9, 8, 7, 6], R[10, 9, 8, 7, 6, 5, 4, 3, 2, 1],
   Rσ[1, 2, 3, 4, 5, 10, 9, 8, 7, 6], Rc[1, 2, 3, 4, 5, 10, 9, 8, 7, 6]}
]
```

The input $R_c[1, 2, 3, 4, 5, 10, 9, 8, 7, 6]$ above describes the site permutation of the conformational transformation as indicated by the c-subscript. The permutation due to a reflection is denoted by the σ -subscript. The two other permutations are the result of spatial rotations around the *a* and *b* axes.

To verify our input we let `Isomers.m` determine all point groups that may generate the same site permutations. In most cases, there is only one point group that fits this requirement. For *biphenyl* in its twisted confirmation we find D_{2d} , the Schoenflies symbol[6] for the dihedral group with diagonal reflection and 2-folded rotation axes. The structure of permutation cycles is an additional criteria to screen for false input.

```
In[3]:= PointGroupReport[BiphenylTwisted]

The group cycles of the point group are:
{{(6)}, (2 C2), (2 σ), (C22), (σC4, σC43)}

The corresponding point groups are: D2d.

The group cycles including conformational transformations are:
{{(6)}, (2 C2), (2 C2'), (σ), (σ'), (2 σ), (2 σ'), (C4, C43), (σC4, σC43)}

Such a group cycle structure would correspond to: D4h.
```

Once the symmetry of *biphenyl* is added to the `Isomers.m` database we can start the isomer enumeration. Traditionally this is done by expanding the Pölya polynomial and extracting its coefficients. The Pölya polynomial for *biphenyl* with just H and Cl ligands would be

```
In[4] := PolyPolynomial[BiphenylTwisted, {H, Cl}]
```

$$\text{Out[4]} = \frac{1}{8} \left((Cl + H)^{10} + 2 (Cl + H)^8 (Cl^2 + H^2)^2 + (Cl + H)^2 (Cl^2 + H^2)^4 + 2 (Cl^2 + H^2)^5 + 2 (Cl^2 + H^2) (Cl^4 + H^4)^2 \right)$$

MATHEMATICA's `Expand`-command can expand the above polynomial. This may, however, become an enormous task for polynomials exhibiting large exponents. A faster alternative is the following command that extracts particular coefficients. Here we determine the coefficient of H^3Cl^7 or H^7Cl^3 and thus obtain the number of isomers with 3H and 7Cl ligands, or vice versa.

```
In[5] := NumberOfIsomers[BiphenylTwisted, {3, 7}]
```

```
Out[5] = 24
```

We now proceed to diamutamer enumerations. Instead of specifying the exact number of ligands for each ligand type we simply specify the total number of ligands and the number of different ligand types available. `Isomers.m` can render not just numeric but also symbolic results for such an enumeration. Here we ask for the number of diamutamers with 4 attached ligands of up to n different ligand types.

```
In[6] := NumberOfIsomers[BiphenylTwisted, 4, n]
```

$$\text{Out[6]} = \frac{1}{2} n (1 + 7n + 16n^2 + 60n^3)$$

We can also consider *biphenyl* without conformational transformations. Neglecting the 180° twist around the central σ -bond it is possible to differentiate *biphenyl* diamutamers and their mirror image. Hence, the number of diamutamers increases

```
In[7] := NumberOfIsomers[BiphenylTwisted, 4, n, Conformations -> False]
```

$$\text{Out[7]} = \frac{1}{2} n^2 (13 + 2n + 105n^2)$$

and we can find enantiomeric pairs.

```
In[8] := NumberOfEnantiomericPairs[BiphenylTwisted, 4, n, Conformations -> False]
```

$$\text{Out[8]} = \frac{1}{2} n (-1 + 6n - 14n^2 + 45n^3)$$

Consequently, not every diamutamer is automatically an achiral molecule.

```
In[9] := NumberOfAchiralIsomers[BiphenylTwisted, 4, n, Conformations -> False]
```

$$\text{Out[9]} = \frac{1}{2} n (2 + n + 30n^2 + 15n^3)$$

This has been a short and hence incomplete introduction to `Isomers.m`. Further explanations can be found in the help files and the luxurious interface of the package as shown in Figure 2. For academic use `Isomers.m` is freely available[2]. However, the user needs to have access to *MATHEMATICA* to run the package. A more technical description of the implemented algorithms has been published in [3] and an article with a collection of enumeration results can be found in [7]. We hope this software will be of use for many of you.

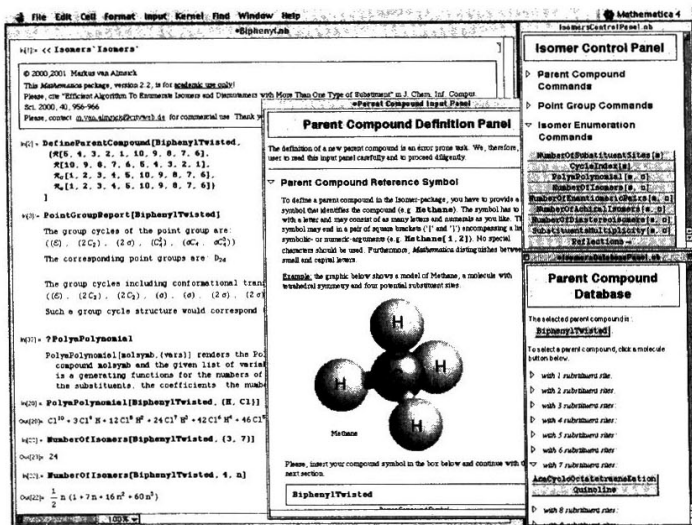


Figure 2: A screen shot of a MATHEMATICA session on a Macintosh.

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