Electronic Supplementary Material (ESI) for Chemical Science.

Strain Visualization for Strained Macrocycles

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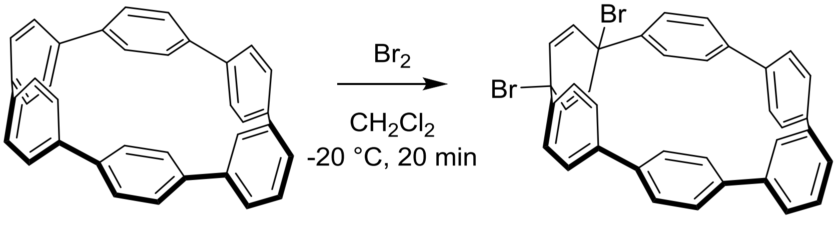
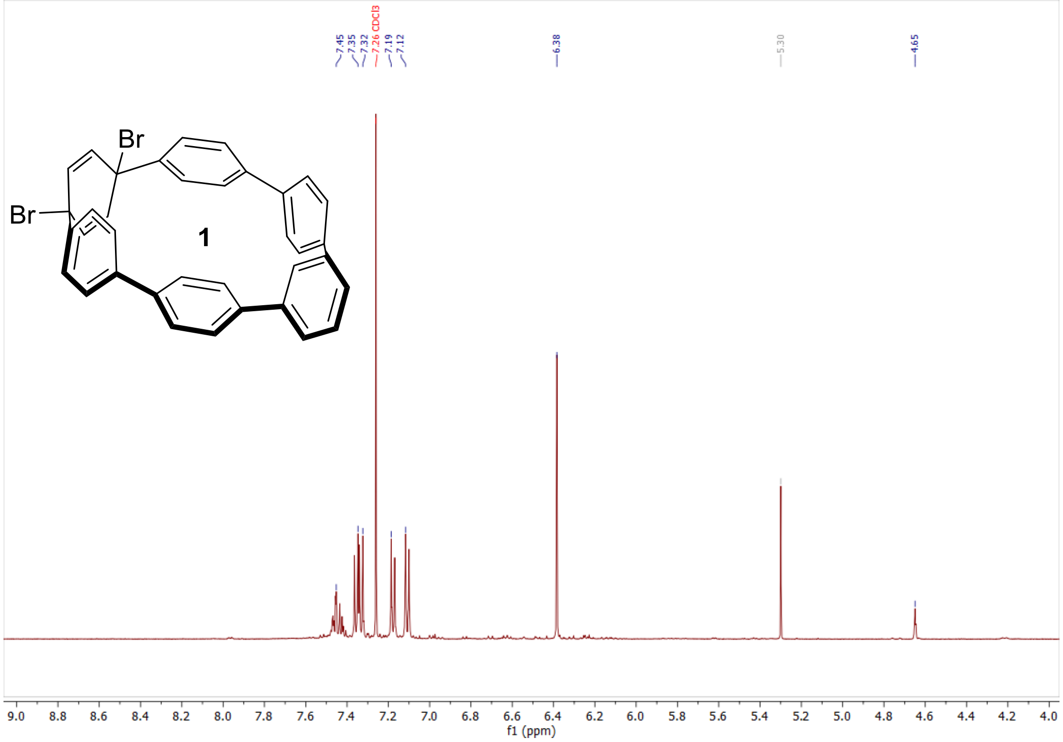
2. General experimental details

All glassware was flame dried and cooled under an inert atmosphere of nitrogen unless otherwise noted. Moisture sensitive reactions were carried out under nitrogen atmosphere using Schlenk and standard syringe/septa techniques. Dichloromethane was dried by filtration through alumina according to the methods describes by Grubbs.[1] ^{1}H NMR spectra were recorded at 500 MHz on a Bruker Advance-III-HD NMR spectrometer. ^{13}C NMR spectra were recorded at 125 MHz on a Bruker Advance-III-HD NMR spectrometer. All ^{1}H NMR spectra were taken in chloroform-*d* (referenced to TMS, δ 0.00 ppm). All ^{13}C NMR spectra were taken in chloroform-*d* (referenced to chloroform, δ 77.16 ppm). All reagents were obtained commercially unless otherwise noted. Mass spectra were obtained from the University of Illinois at Urbana-Champaign Mass Spectrometry Lab using ESI on a Micromass 70-VSE.



***m*[6]CPP** **1**

1. Freshly synthesized ***m*[6]CPP**[2] (8 mg, 17.5 nmol, 1 equiv) was added to a flame dried 25 mL round bottom flask. The contents were evacuated and backfilled with nitrogen three times. Dichloromethane (6 mL) was added to the flask. This was cooled to -20 °C. A 50 mM solution of Br_2 (64.0 µL) in methylene chloride (50 mL) was prepared in a flame dried 100 mL pear shaped shaped flask. The bromine solution (385 µL, 19.3 nmol, 1.1 equiv) was added dropwise and the mixture was stirred at -20 °C for 20 min. The contents of the flask were passed through an Aura MT 0.45 µm PTFE syringe filter and evaporated under reduced pressure to obtain **1** as an orange-red solid (8.7 mg, 81%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.49 – 7.40 (m, 3H), 7.36 (d, *J* = 8.5 Hz, 4H), 7.33 (d, *J* = 8.4 Hz, 4H), 7.18 (d, *J* = 8.5 Hz, 4H), 7.11 (d, *J* = 8.4 Hz, 4H), 6.38 (s, 4H), 4.65 (t, *J* = 1.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.35, 142.82, 142.69, 141.66, 140.34, 139.15, 130.35, 130.27, 129.08, 127.32, 126.78, 121.81, 56.44, 1.17. HRMS (ESI-TOF) (m/z): $[M-HBr]^+$ calculated for $C_{36}H_{23}Br$, 534.09831; found, 534.09804.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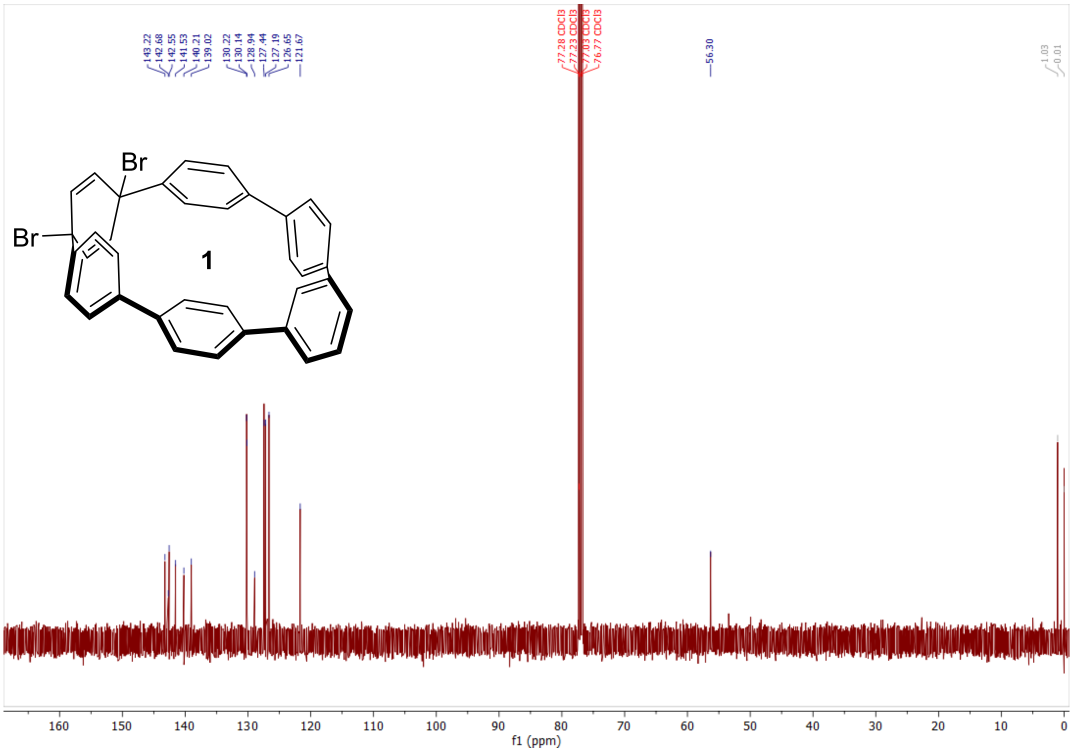
7.35
7.32
7.26 CDCl3
7.19
7.12
6.38
5.30
4.65
Br
Br
1
9.0
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
f1 (ppm)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142.68
142.55
141.53
140.21
139.02
130.22
130.14
128.94
127.44
127.19
126.65
121.67
77.28 CDCl3
77.23 CDCl3
77.03 CDCl3
76.77 CDCl3
56.30
1.03
0.01
Br
Br
1
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3. Comments on calculations

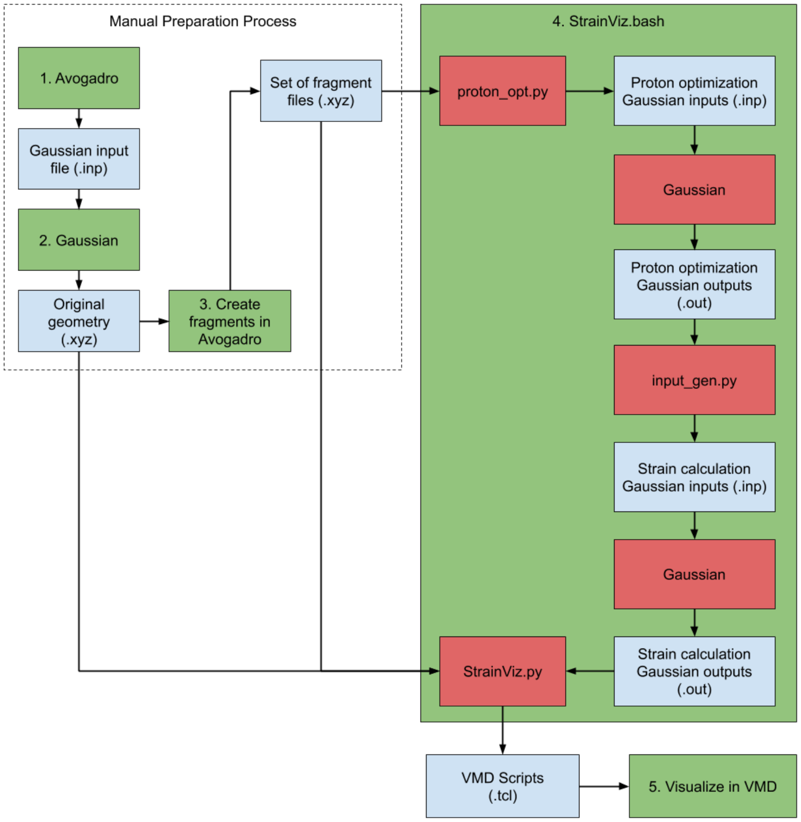
Throughout the development of this program when fragments were clearly able to relax into perfectly flat aromatic hydrocarbons (fragments of CPPs or cyclophenacenes) the program worked best. This appears to be due to a clear and obvious trajectory on a potential energy surface between the strained and unstrained states and a finite end with a single conformation. When the trajectory is not so clear, as in the case of fragments with little strain (~10 kcal/mol or less) or alkyl chains (cyclophanes), more oversight by the user is required to acquire accurate results. There are two optimization errors that often lead to poor quality results. Non-converging optimizations where small changes in energy add up over many non-convergent cycles and instances where the algorithm takes a step into a high energy state. The program alerts the user if problems like this occur. This led to the use of the quasi-Newton rational function optimization algorithm for optimization, however, using this algorithm does not always solve these issues. When necessary, calculating frequencies at each step does solve this problem in every instance tested, however, at a higher computational expense.

4. Instructions for running StrainViz

All details for running calculations can be found at https://github.com/CurtisColwell/StrainViz

The following is an excerpt from the README.md file that details running a calculation

Use the following block diagram as a reference for the instructions below. All manual steps are shown in green, all automated steps are shown in red, and all intermediate files are shown in blue. The proton optimization files are deleted after being used.



1. Model the strained compound in Avogadro and create a Gaussian input file to optimize the geometry.

2. Use Gaussian to create an optimized geometry output file. Open this file in Avogadro and save it in the input/ directory with the .xyz file extension. Create a directory with the same name.

3. Create fragments by symmetrically deleting portions of the molecule that will allow the molecule to release its strain in Avogadro and save them as .xyz files in the directory named after the original molecule. Make sure that when a piece of the molecule is removed, protons are added to the empty bonding sites by drawing them at every severed bond. For an example, see the input/ folder where example-molecule.xyz is [5]CPP and five fragment .xyz files are in the related folder.

4. Run StrainViz to run multiple Gaussian jobs on each fragment and analyze the results. Specify the variable "molecule-name" so that it matches the geometry .xyz file and fragment folder, "processors-for-Gaussian" to be the number of processor for the Gaussian jobs, "level-of-theory" as a string that is the level of theory and basis set. This script creates .tcl files for the bond, angle and dihedral strain for each fragment and the combination of the fragments.

```
bash StrainViz.bash molecule-name processors-for-Gaussian level-of-theory
```

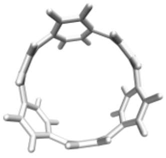
5. In VMD, open the "Tk Console" found under "Extensions", navigate to the output/molecule-name/ folder, and visualize the strain using the following command while replacing "example.tcl" for the .tcl file you would like to visualize:

```
source example.tcl
```

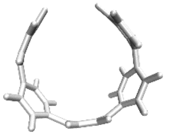
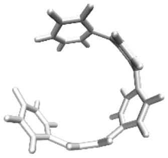
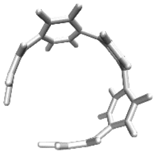
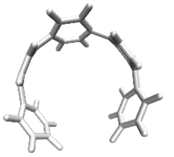
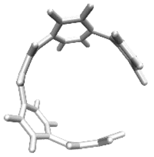
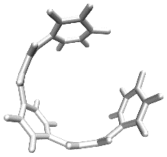
5. Specific Example

Below is a worked through example using [6]CPP. All files are from the attached Computational Results.

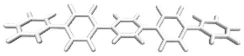
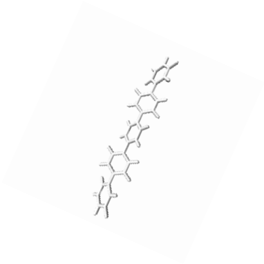
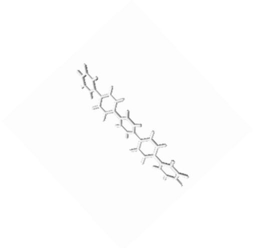
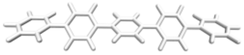
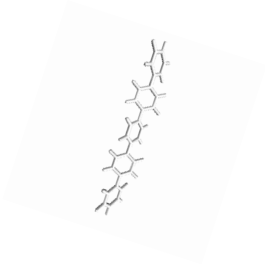
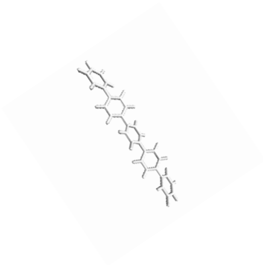
First, the molecule is optimized using Gaussian to generate an optimized geometry for the molecule.



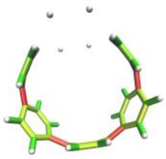
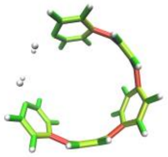
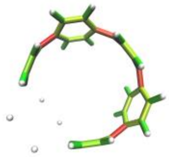
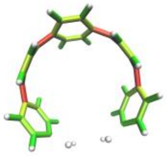
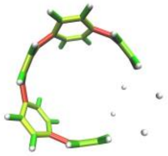
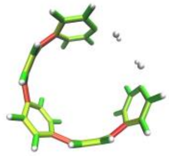
Then the molecule is split into six fragments.

 1	 2	 3
 4	 5	 6

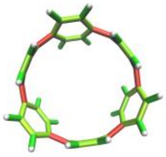
These six geometries are then submitted to StrainViz where they are optimized to find the following geometries and the strain released is determined.

 1	 2	 3
 4	 5	 6

This strain is then mapped back on to the original geometry. In the output folder, there are three files generated per fragment: an angle, bond, and dihedral strain map. The dihedral map is shown here.

 1	 2	 3
 4	 5	 6

Finally, the strain is averaged over all fragments by the script and combined into a total picture for the entire molecule. This appears in the output folder as total_force.tcl



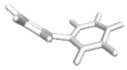
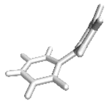
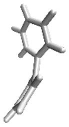
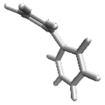
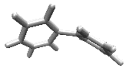
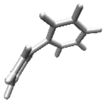
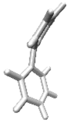
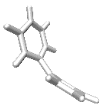
The scale bar can then be generated by opening total_force.tcl in a text editor. The first two lines are the minimum and maximum energies in kcal/mol.

6. Fragments used for strain calculations

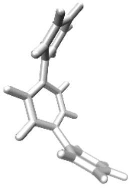
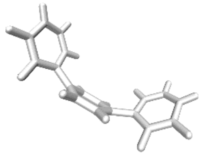
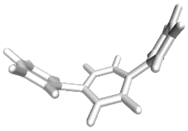
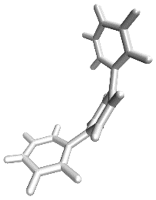
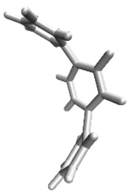
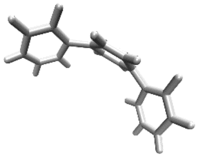
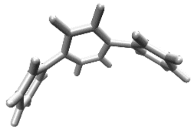
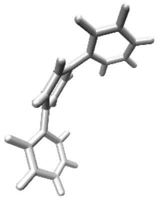
All input files, fragment geometries, and output files are available for download. Fragment geometries are shown below and in .xyz format.

Fragments used for Figure 4

Fragment size 2

 1	 2	 3	 4
 5	 6	 7	 8

Fragment size 3

 1	 2	 3	 4
 5	 6	 7	 8

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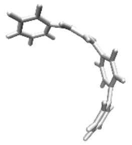
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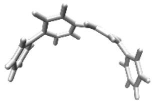
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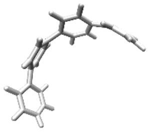
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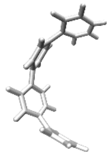
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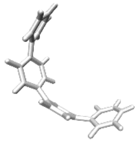
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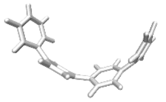
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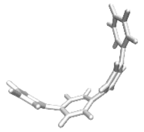
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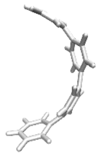
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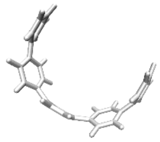
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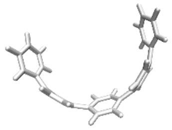
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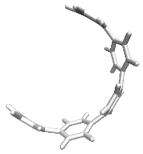
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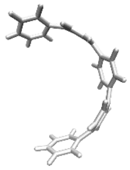
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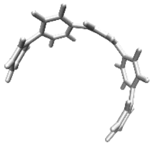
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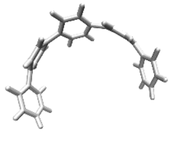
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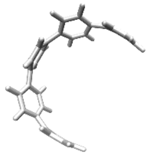
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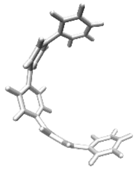
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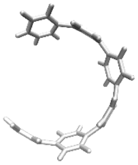
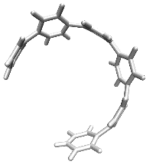
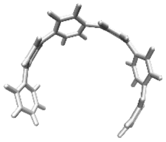
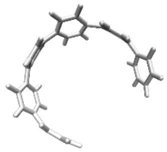
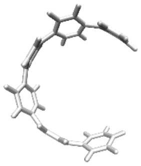
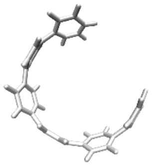
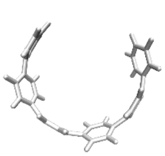
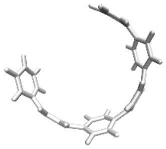
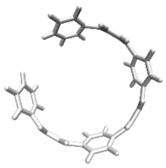
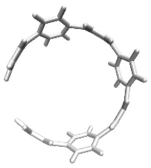
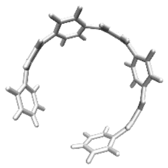
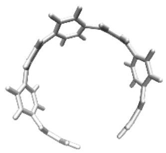
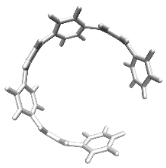
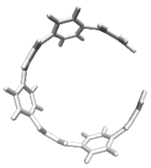
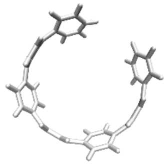
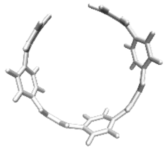
Fragment size 6

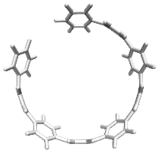
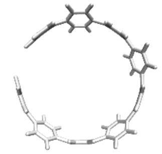
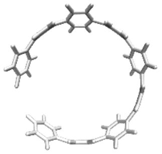
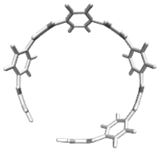
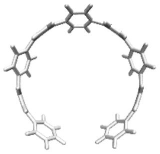
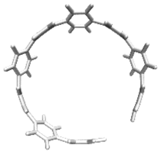
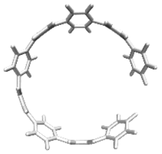
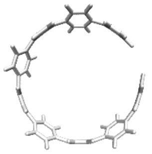
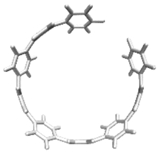
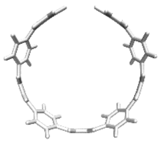
 1	 2	 3	 4
 5	 6	 7	 8

Fragment size 7

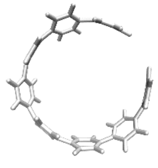
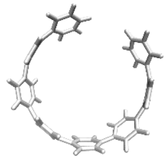
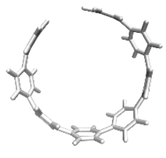
 1	 2	 3	 4
 5	 6	 7	 8

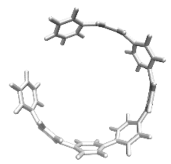
Fragments used for Figure 5

[10]CPP

 1	 2	 3	 4
 5	 6	 7	 8
 9	 10		

[9]CPP

 1	 2	 3



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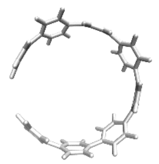

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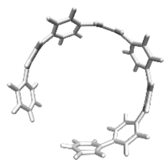

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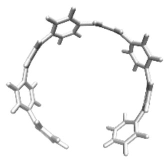

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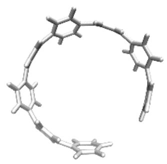

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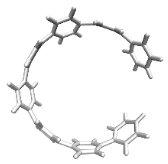

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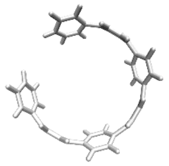
[8]CPP



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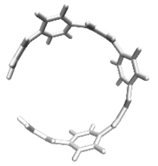

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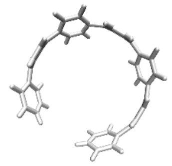

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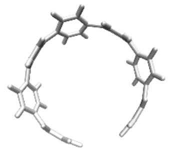

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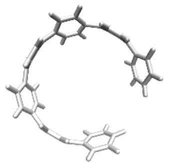

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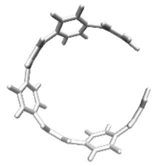

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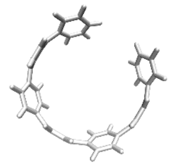

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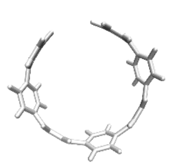

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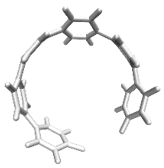
[7]CPP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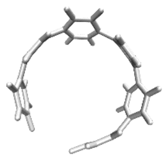
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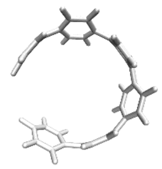
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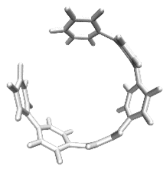
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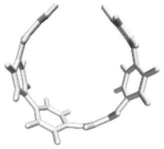
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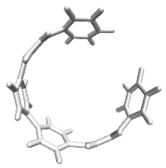
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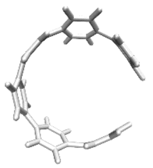
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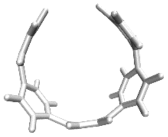
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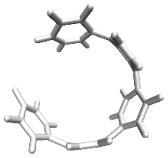
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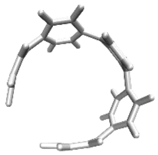
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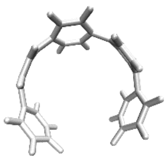
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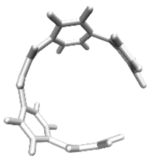
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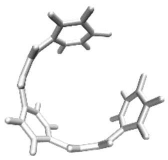
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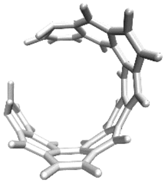
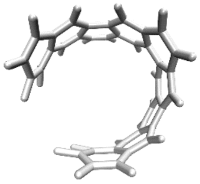
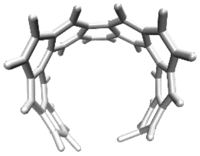
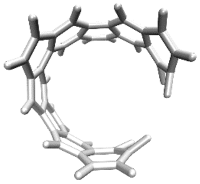
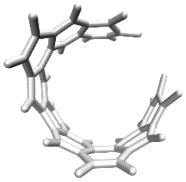
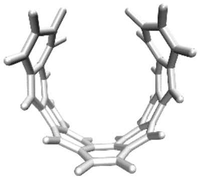
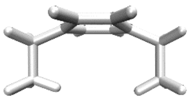
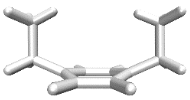
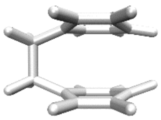
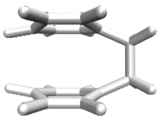
[6]cyclophenacene

 1	 2	 3
 4	 5	 6

[2.2]paracyclophane

 1	 2	 3	 4

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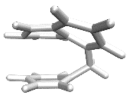
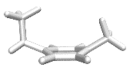
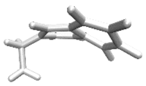
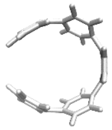
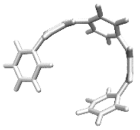
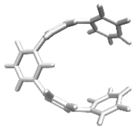
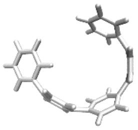
 1	 2	 3

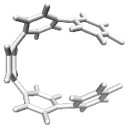
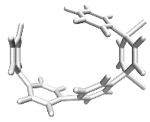
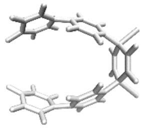
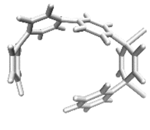
Fragments used for Figure 6

m[6]CPP

 1	 2	 3	 4

Fragments used for Figure 7

dibromo[6]CPP

 1	 2	 3	 4

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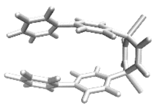
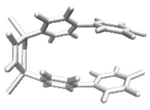
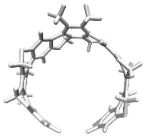
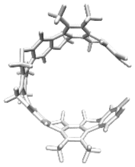
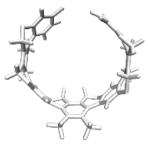
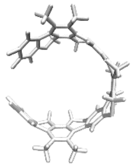
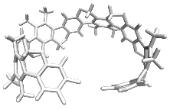
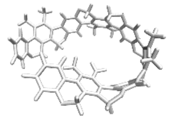
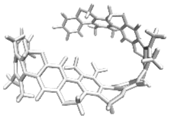
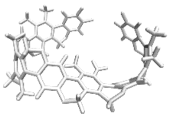
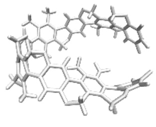
 1	 2

Fragments used for Figure 8

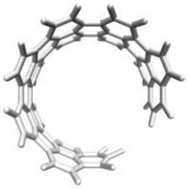
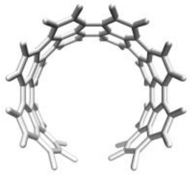
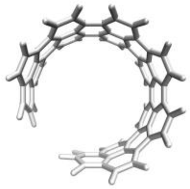
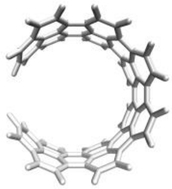
Tanaka Belt

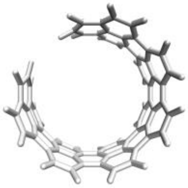
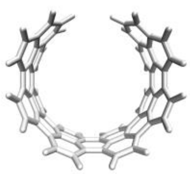
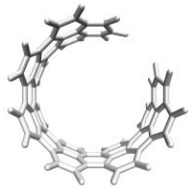
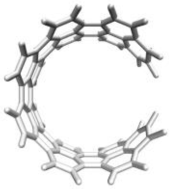
 1	 2	 3	 4

Möbius Tanaka Belt

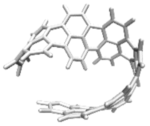
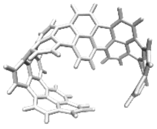
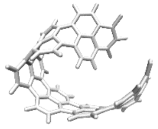
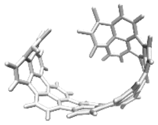
 1	 2	 3
 4	 5	

Vögtle Belt

 1	 2	 3	 4

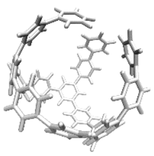
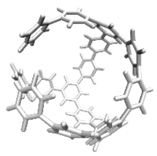
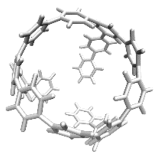
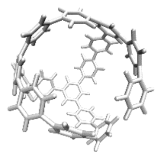
 5	 6	 7	 8

Vögtle Möbius

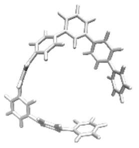
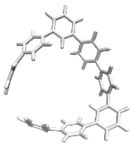
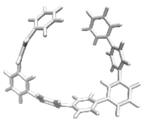
 1	 2	 3	 4

Fragments used for Figure 9

Ball

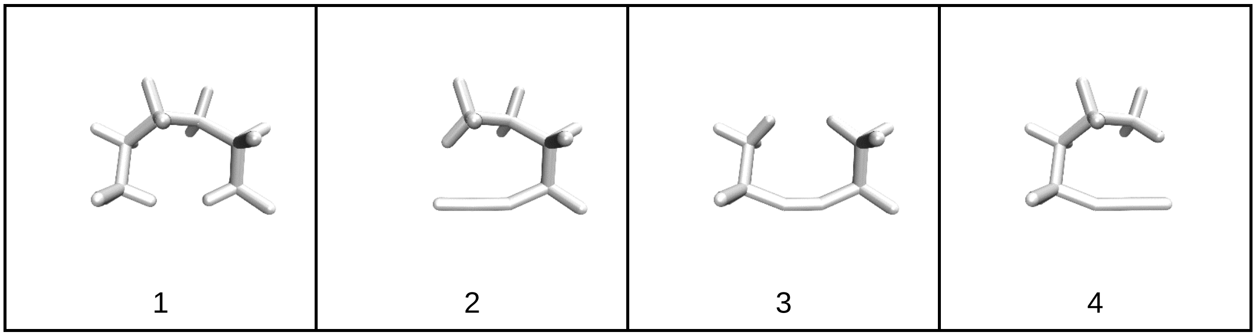
 1	 2	 3	 4

Panel

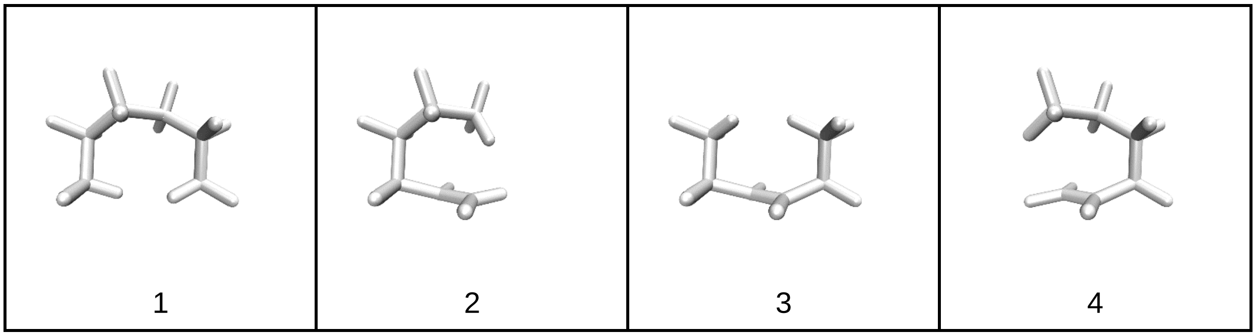
 1	 2	 3

Fragments used for Figure 10

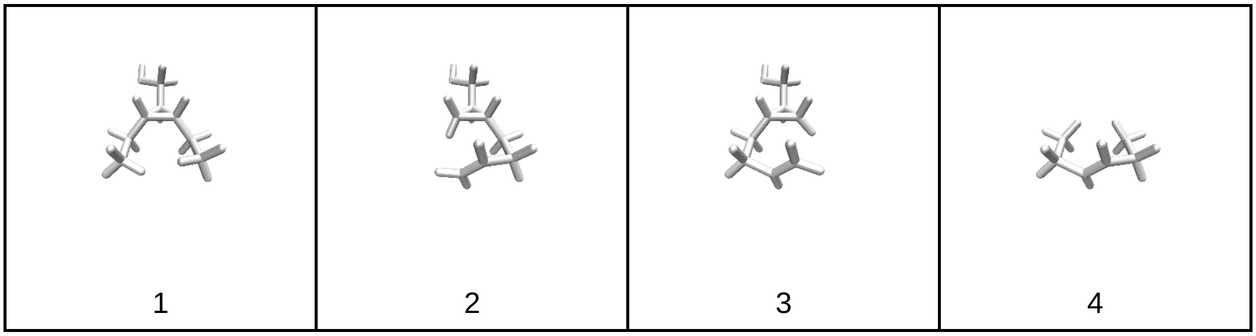
Cyclooctyne



trans-cyclooctene



trans-bicyclo[6.1.0]nonene



7. References

(1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Safe and Convenient Procedure for Solvent Purification. *Organometallics* **1996**, *15*, 1518–1520.

(2) Lovell, T. C.; Colwell, C. E.; Zakharov, L. N.; Jasti, R. Symmetry Breaking and the Turn-on Fluorescence of Small, Highly Strained Carbon Nanohoops. *Chem. Sci.* **2019**, *10*, 3786–3790.