Table of Contents

Introduction2
Learning Outcomes 2
Pre-required Skills2
Materials2
Example 1. Using Mogul to assess intramolecular geometry
Conclusion5
Example 2. Using Mogul to explain activity data 6
Exercise: Find these molecules in ConQuest and assess the preferred orientation 8
Conclusions9
Exercise9
Summary 10
Next Steps10
Feedback
Glossary



Introduction to Mogul Geometry Check

(MOG-001)

2022.3 CSD Release

Introduction

This tutorial will introduce you to the Mogul Geometry Check included with Mercury under the CSD-Core toolsets.

Structural chemists can use the Mogul Geometry Check tool to validate the threedimensional <u>conformation</u> of a particular molecule. The data from structures in the CSD can be used to show the most likely conformation a particular bond, angle, torsion or ring should adopt. The information obtained from a Mogul check can help identify inconsistencies within a crystal structure and can suggest values to be used for restraints during refinement. In addition, Mogul can also be run on 3D coordinates generated <u>in silico</u> as a validation of calculated structures.

Learning Outcomes

In this workshop you will learn:

- How to use the Mogul geometry to assess the geometry of a molecule.
- How to launch Mogul from Mercury.
- How to run a geometry check on specific features (for example a torsional angle) of a molecule that you load.

The exercise in this handout will take approximately **45** *minutes* to be completed. The words in <u>Blue Italic</u> in the text are reported in the <u>Glossary</u> at the end of this handout.

Pre-required Skills

The following exercises assume you have a working knowledge of the program Mercury, namely, how to display and manipulate structures from a 3D coordinates file. You can find the Visualization workshop (MER-001) in the <u>CSD-Community workshop area on our website</u>.

Materials

For this workshop we will use the file **1JR1_ligand.pdb** that you can download from <u>this link</u>.



Example of the Mogul geometry assessment interface.

Example 1. Using Mogul to assess intramolecular geometry

Mogul can provide an assessment of a given structure's <u>conformation</u> by comparing it to the data from the over one million structures already in the CSD. By using the statistical distributions of similar fragments, Mogul can confirm your 3D geometry is plausible, or flag values that are too far outside the norm.

In this example, you will see how to use Mogul to assess the geometry of a given molecule. Mogul can be run as a stand-alone application or from the Mercury or Hermes interfaces. For this tutorial, we will use Mercury to run Mogul.

- 1. Launch Mercury and type VUSDIX in the Structure Navigator toolbar.
- 2. To start a geometry analysis, click the CSD-Core menu and then click *Mogul Geometry Check* from the dropdown menu.
- 3. This brings up the *Mogul Search Settings* dialogue box. You can typically use the defaults in this window, but we can streamline our search by unticking the box for ring and ticking the boxes for *Apply Filters, Exclude Organometallics*, and *Exclude Powder structures*.
- 4. Click Search to start.
- 5. A dialogue box will pop up to warn you that you are going to check the entire molecule. Click **OK** to continue.
- 6. The search will begin to run. You can follow its progress in the *Search Progress* dialogue box.



Stop

C8 C9 C14

Search completed - 41 observations c

15 Angles 15 Torsions 40 Rings 15

Search Close

Customise fragment classification

Help

3

7. When the search is complete, your results will be displayed in the Mogul **Results Viewer.**

4

- The results are color-coded. Unusual values are flagged in orange. Please be 8. aware that the number of hits might differ based on the version of the data update. The data in this workshop were obtained with the 2022.3 version of the database.
- 9. Scroll through the results until you find the angle for C20-C21-C22. Doubleclick this line to bring up the data from the Mogul library.
- 10. The red line marks the value of the angle from your molecule (the query).
- 11. The histogram shows the data from the CSD, color coded by update. (Note, you can double-click the color swatches to change what color is shown.)
- 12. To see which structures contribute to a certain bar on the histogram, first click Deselect (all the bars will turn grey), and then click the bar directly under the red query line. This will highlight with colours that specific bar of the histogram.



Show / h	ide : Co	lumns	Fragments	Deselect all	fragments	Expo	rt										
Help	Doub	le click to v	iew result in Mog	ul													
Туре	Molecule	Fragment		Classification		No. of hits	Query value	e Mean	Std. dev.	z-score	x - mean	Minimum	Maximum	Median	d(min)	Local den	sit
× bond																	
- bond																	
~	VUSDIX																
		N1 N2	1	Not unusual (e	nough hits)	160	1.362	1.363	0.027	0.005	0.000	1.291	1.573	1.362	0.000		
		C1 N2		Not unusual (e	nouah hits)	243	1.342	1.340	0.009	0.251	0.002	1.291	1.374	1.340	0.000		
		C2 N1		Not unucual (c	nough hite)	160	1 255	1 262	0.022	0 249	0.009	1 227	1 5 2 6	1 260	0.000		
		C4 (2)		voc unusual (e	nough fills)	4204	1.000	1.302	0.022	0.349	0.000	1.007	1.520	1.300	0.000		
		C4 C3		vot unusual (e	nough hits)	4384	1.396	1.391	0.014	0.400	0.006	1.259	1.572	1.390	0.000		
		C4 C5		vot unusual (e	nough hits)	686	1.369	1.387	0.014	1.277	0.018	1.284	1.439	1.389	0.000		
		C7 C2	,	Not unusual (e	nough hits)	10526	1.407	1.394	0.013	0.996	0.013	1.225	1.560	1.394	0.000		
		C5 S1		Not unusual (e	nough hite)	1371	1 771	1 775	0.021	0 176	0.004	1 385	1 9/8	1 775	0.000		
2	Mogul Results View	ier	Unusual (e	nough nits)	1150		.423	1.333	-	= ×	0.02	9	1.240	1.004	1.	395 0.0	10
s	Help Doubl	e click to view resul	sents Deselect all free t in Mogul	enerts Export	- Mean Std. de	/ z-score x -	mean Minimum	Maximum Med	ian Id(min)I Ic	ocal density							
Fyg	e Molecule	riaginetic	000000000000000000000000000000000000000														
Fyg	e Molecule	C9 C8 S1	Not unusual (enough hits) 1	91 120,944	121.024 2.668	0.030 0.07	9 106.712	127.093 120.6	77 0.000								
Fys	be Molecule	C9 C8 S1 C13 C8 S1 C13 C8 C9	Not unusual (enough hits) 11 Not unusual (enough hits) 1. Not unusual (enough hits) 9	91 120.944 262 119.919 34 119.116	121.024 2.668 119.648 2.467 119.539 1.037	0.030 0.07 0.110 0.27 0.408 0.42	9 106.712 1 107.576 4 115.716	127.093 120.6 126.752 119.5 23.424 119.5	77 0.000 78 0.000 38 0.000								
Tys	be Molecule	C9 C8 S1 C13 C8 S1 C13 C8 C9 C10 C9 C8	Not unusual (enough hits) 1. Not unusual (enough hits) 1. Not unusual (enough hits) 9. Not unusual (enough hits) 8	91 120.944 262 119.919 84 119.116 11 117.873	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955	0.030 0.07 0.110 0.27 0.408 0.42 0.825 0.78	9 106.712 1 107.576 4 115.716 8 114.962	127.093 120.6 126.752 119.5 123.424 119.5 26.738 118.7	77 0.000 78 0.000 38 0.000 53 0.000								
Tyr	be Molecule	C9 C8 S1 C13 C8 S1 C13 C8 C9 C10 C9 C8 C8 C9 C14 C10 C9 C14	Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 90 Not unusual (enough hits) 8 Not unusual (enough hits) 8	91 120,944 262 119,919 84 119,116 71 117,873) 120,945	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140	0.030 0.07 0.110 0.27 0.408 0.42 0.825 0.78 0.259 0.55	9 106.712 1 107.576 4 115.716 8 114.962 5 119.111 4 109.049	127.093 120.6 126.752 119.5 123.424 119.5 126.738 118.7 29.145 120.8 27.955 119.7	777 0.000 78 0.000 38 0.000 53 0.000 53 0.000 52 0.000								
9	be Molecule	C9 C8 S1 C13 C8 S1 C13 C8 C9 C10 C9 C8 C8 C9 C14 C10 C9 C14 C11 C10 C9	Not unusual (enough hits) 1 Not unusual (enough hits) 1. Not unusual (enough hits) 9 Not unusual (enough hits) 6 Not unusual (enough hits) 6 Not unusual (enough hits) 2 Not unusual (enough hits) 2	91 120,944 262 119,919 84 119,116 71 117,873 0 120,945 386 121,063 1228 122,288	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.779 2.591 119.611 1.659	0.030 0.07 0.110 0.27 0.408 0.42 0.825 0.78 0.259 0.55 0.882 2.28 1.613 2.67	9 106712 1 107576 4 115716 8 114962 5 119.111 4 108.948 7 99.222	127.093 120.€ 126.752 119.5 123.424 119.5 126.738 118.7 129.145 120.8 27.885 118.7 32.186 119.7	77 0.000 78 0.000 38 0.000 53 0.000 53 0.000 85 0.000 61 0.000								
5vr	Nolecule	C9 C8 S1 C13 C8 S1 C13 C8 S1 C13 C8 C9 C10 C9 C8 C8 C9 C14 C10 C9 C14 C10 C9 C14 C11 C10 C9 C12 C11 C10	Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 9 Not unusual (enough hits) 6 Not unusual (enough hits) 6 Not unusual (enough hits) 7 Not unusual (enough hits) 7	91 120.944 262 119.919 84 119.116 71 117.873 0 120.945 866 122.083 1228 122.288 1773 119.123	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.779 2.591 119.611 1.659 120.342 0.966	0.030 0.07 0.110 0.27 0.408 0.42 0.825 0.78 0.259 0.55 0.882 2.28 1.613 2.67 1.262 1.21	9 106.712 1 107.576 4 115.716 8 114.962 5 119.111 4 108.948 7 99.222 9 99.585	127.093 120.6 126.752 119.5 123.424 119.5 123.424 119.5 129.145 120.8 127.885 118.7 32.186 119.7 35.789 120.3	77 0.000 78 0.000 38 0.000 53 0.000 53 0.000 55 0.000 56 0.000 56 0.001								
9	>e Molecule	C9 C8 51 C13 C8 51 C13 C8 51 C13 C8 C9 C10 C9 C8 C8 C9 C14 C10 C9 C14 C10 C9 C14 C11 C10 C9 C12 C11 C10 C11 C12 C13 C13 C12 C13	Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 9 Not unusual (enough hits) 6 Not unusual (enough hits) 6 Not unusual (enough hits) 2 Not unusual (enough hits) 2 Not unusual (enough hits) 2	91 120.944 262 119.919 84 119.116 71 117.873 0 120.945 586 122.083 1228 122.288 1773 119.927 109 13.677	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.779 2.591 119.611 1.659 120.342 0.966 120.342 0.966	0.030 0.07 0.110 0.27 0.408 0.42 0.825 0.65 0.882 2.28 1.613 2.67 1.262 1.21 0.430 0.41	9 106.712 1 107.576 4 115.716 5 119.111 5 119.111 7 99.222 9 99.585 5 99.585 5 99.585	127.093 120.6 126.752 119.5 123.424 119.5 126.738 118.7 129.145 120.8 127.885 118.7 132.186 119.7 35.789 120.3 35.789 120.3	77 0.000 78 0.000 53 0.000 53 0.000 55 0.000 55 0.000 56 0.000 56 0.001 56 0.000								
9	>e Molecule	C9 C8 51 C13 C8 51 C13 C8 51 C13 C8 C9 C10 C9 C8 C8 C9 C14 C10 C9 C14 C11 C10 C9 C12 C11 C10 C11 C12 C13 C12 C13 C8 O1 C14 C9	Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 8 Not unusual (enough hits) 6 Not unusual (enough hits) 6 Not unusual (enough hits) 2 Not unusual (enough hits) 2 Not unusual (enough hits) 2 Not unusual (enough hits) 5 Not unusual (enough hits) 6	91 120.944 262 119.919 84 119.116 71 117.873 50 120.945 586 121.063 12228 122.288 7773 119.927 190 121.627 724 121.417	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.779 2.591 119.611 1.659 120.342 0.966 120.342 0.966 119.480 1.494 121.036 1.537	0.030 0.07 0.110 0.27 0.408 0.42 0.825 0.78 0.825 0.55 0.882 2.28 1.613 2.67 1.262 1.21 0.430 0.41 1.437 2.14 0.248 0.38	9 106.712 1 107.576 4 115.716 8 114.962 5 119.111 4 103.948 7 99.222 9 99.585 5 99.585 7 100.171 2 103.190	127.093 120.6 126.752 119.5 123.424 119.5 126.738 118.7 129.145 120.8 132.186 119.7 135.789 120.3 35.789 120.3 32.208 119.7 132.067 120.9	77 0.000 78 0.000 53 0.000 53 0.000 65 0.000 56 0.000 56 0.000 56 0.000 56 0.000 57 0.000 58 0.000 59 0.000 50 0.0000 50 0.00000 50 0.0000 50 0.0000 50 0.0000 50 0.00000 50 0.0000 50 0								
9	e Molecule	C13 C8 S1 C13 C8 S1 C13 C8 S1 C10 C9 C8 C10 C9 C8 C10 C9 C4 C10 C9 C14 C11 C10 C9 C12 C11 C10 C11 C12 C13 C12 C13 C8 O1 C14 C9 C19 C14 N3	Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 9 Not unusual (enough hits) 8 Not unusual (enough hits) 8 Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 3 Not unusual (enough hits) 3 Not unusual (enough hits) 3	91 120.944 262 119.919 84 119.116 71 117.873 0 120.945 586 121.063 1228 122.288 7773 119.927 190 121.627 190 121.627 192 121.417 16 116.855	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.779 2.591 119.611 1.659 120.342 0.966 120.342 0.966 119.480 1.494 121.036 1.537 116.903 1.444	0.030 0.07 0.110 0.27 0.408 0.42 0.825 0.78 0.259 0.55 0.882 2.28 1.613 2.67 1.262 1.21 0.430 0.41 1.437 2.14 0.248 0.38 0.033 0.04	9 106.712 1 107.576 4 115.716 8 114.962 5 119.111 4 103.948 7 99.222 9 99.585 5 99.585 7 100.171 2 103.190 8 112.973	127.093 120.6 126.752 119.5 123.424 119.5 126.738 116.7 129.145 120.0 132.7885 118.7 132.186 119.7 132.7895 120.3 135.789 120.3 32.208 119.7 21.216 116.6	77 0.000 778 0.000 38 0.000 53 0.000 55 0.000 55 0.000 56 0.000 56 0.000 57 0.000 57 0.000 51 0.000								
9	e Molecule	Programmers C13 C8 S1 C13 C8 S1 C13 C8 S1 C13 C8 C9 C10 C9 C8 C8 C9 C14 C10 C9 C14 C10 C9 C14 C11 C10 C9 C12 C11 C10 C12 C13 C8 C12 C13 C8 C13 C9 C14 C13 C9 C14 C13 C9 C14 C13 C9 C14 C13 C9 C14 C13 C9 C14 C13 C8 C13 C13 C8 C13 C13 C8 C13 C13 C8 C13 C13 C8 C13 C13 C9 C14 C13 C9 C14 C13 C13 C14 C13 C14 C13 C14 C13 C14 C13 C14 C13 C14 C14 C13 C14	Advantage (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 9 Not unusual (enough hits) 8 Not unusual (enough hits) 2 Not unusual (enough hits) 2 Not unusual (enough hits) 2 Not unusual (enough hits) 2 Not unusual (enough hits) 3 Not unusual (enough hits) 3 Not unusual (enough hits) 3 Not unusual (enough hits) 3 Not unusual (enough hits) 3	91 120.944 262 119.919 84 119.116 71 117.873 3 120.945 586 121.063 1228 122.288 1273 119.223 1773 119.227 190 121.627 190 121.627 190 121.625 81 121.673 81 121.675 81 121.675 81 121.675 81 121.675 81 121.675 81 121.675 81 121.675 81 121.6	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.6779 2.591 119.611 1.659 120.342 0.966 120.342 0.966 120.342 0.966 121.036 1.537 116.903 1.444 122.090 1.472	0.030 0.07 0.110 0.27 0.408 0.42 0.825 0.78 0.825 0.78 0.825 0.78 1.613 267 1.622 1.21 0.430 0.41 1.437 2.14 0.430 0.43 0.248 0.33 0.033 0.04 0.691 1.01	9 106.712 1 107.576 4 115.716 8 114.962 5 119.111 7 99.222 9 99.585 7 100.171 2 103.190 8 112.973 8 119.381	127.093 120.6 126.752 119.5 123.424 119.5 126.753 118.7 126.758 118.7 132.185 118.7 132.185 118.7 132.185 119.7 132.285 119.7 132.285 119.7 132.2067 120.9 132.2068 119.7 132.067 120.9	77 0.000 78 0.000 38 0.000 53 0.000 53 0.000 55 0.000 55 0.000 56 0.000 56 0.000 57 0.000 57 0.000 53 0.000 53 0.000 59 0.000 59 0.000								
9	e Molecule	Programmers C13 (26 S1 C13 (26 S1 C13 (26 S1 C13 (26 S1 C13 (26 S1 C13 (26 C3 C10 (27 C4 C10 (27 C4 C10 (27 C4 C11 (210 C3 C12 (213 (26 C4 C11 (210 C3 C12 (213 (26 C4 C12 (214 C3 C12 (214 C12 C12 (214 C12	Advanced (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 9 Not unusual (enough hits) 9 Not unusual (enough hits) 6 Not unusual (enough hits) 7 Not u	91 120,544 262 119,919 84 119,116 71 117,873 0 120,945 886 121,063 1228 122,288 7773 119,927 773 119,927 724 121,427 724 121,417 16 116,855 11 121,537 11 121,537 12 121,537	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.779 2.591 119.611 1.659 120.342 0.966 119.480 1.494 120.36 1.537 116.903 1.444 122.690 1.472 123.91 1.344 1.251 384 1.277	0.030 007 0.110 027 0.408 042 0.825 078 0.825 078 0.822 228 1.613 2.67 1.262 121 0.430 041 1.437 2.14 0.430 041 1.437 2.14 0.430 041 1.437 2.14 0.430 041 1.437 2.14 0.430 041 1.437 2.14 0.430 041 0.431 044 0.431 044 0.431 044 0.432 044 0.430 044 0.432 044 0.430 044 0.432 044 0.430 044 0.440 044 0.440 044 0.440 044 0.440 044 0.440 044 0.440 044 0.440 044 0.440 044 0.440	9 106.712 1 107.576 8 114.962 5 119.111 7 99.222 9 99.585 7 100.171 2 103.190 8 112.973 8 112.973 8 119.381 3 111.842 9 122.277	127.093 120.6 126.752 119.5 123.424 119.5 126.753 118.7 123.424 119.5 126.738 118.7 132.186 119.7 132.186 119.7 132.186 119.7 132.208 119.7 132.020 119.7 132.020 12.216 116.6 34.433 122.6 28.528 121.9 27.903 125.9	77 0.000 78 0.000 38 0.000 53 0.000 55 0.000 65 0.000 66 0.000 66 0.000 66 0.000 67 0.000 69 0.000 60 0.0000 60 0.00000 60 0.0000 60 0.00000 60 0.00000 60 0.0000								
^{Tys}	Nolecule	Programmers C13 C8 S1 C13 C8 S1 C13 C8 C9 C10 C9 C8 C8 C9 C14 C10 C9 C14 C10 C9 C14 C11 C10 C9 C12 C13 C8 O1 C14 C9 C12 C13 C8 O1 C14 A3 C15 N3 C14 C17 C16 C1 C18 C17 C16	Advanced (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 9 Not unusual (enough hits) 8 Not unusual (enough hits) 6 Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 1 Not unusual (enough hits) 6 Not unusual (enough hits) 6 Not unusual (enough hits) 1 Not unusual (enough hits) 1	91 120,944 262 119,919 84 119,116 71 117,873 9 120,945 966 121,063 122,80 122,045 90 122,045 910 121,623 9173 119,123 9173 119,123 9173 119,123 9174 121,417 95 11,625 911 121,627 911 121,537 91 127,643 91 127,633 91 127,637	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.779 2.591 119.611 1.659 120.342 0.966 119.480 1.494 120.36 1.537 116.503 1.444 122.590 1.472 122.590 1.472 122.590 1.472 122.591 1.344	0.030 007 0.110 027 0.408 042 0.825 078 0.825 078 0.822 228 1.613 2.67 1.262 121 0.450 021 0.450 021 0.450 021 0.450 033 004 1.437 2.14 0.248 0.33 0.059 1.101 0.271 0.33 1.842 2.255 0.591 0.51 0.591 0.591 0.51 0.591	9 106712 1 107376 4 115716 8 114962 5 119111 4 108948 7 99222 9 99385 5 99385 5 99385 5 99385 5 99385 8 112973 8 112973 8 111842 9 122277 9 122277	127.093 120.6 126.752 119.5 123.424 119.5 123.424 119.5 123.424 119.5 123.425 118.7 129.145 120.8 127.865 118.7 132.769 120.3 135.769 120.3 135.769 120.3 132.208 119.7 132.007 120.9 121.216 116.6 28.528 121.9 27.863 125.4	77 0.000 78 0.000 38 0.000 53 0.000 65 0.000 65 0.000 66 0.000 67 0.000 441 0.000 457 0.000 464 0.000 464 0.000 464 0.000 464 0.000 464 0.000 464 0.000 464 0.000								
9	Nolecule	Programmers (1) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2	Not ansual (enough hits) 1 Not ansual (enough hits) 1 Not ansual (enough hits) 9 Not ansual (enough hits) 9 Not ansual (enough hits) 6 Not ansual (enough hits) 6 Not ansual (enough hits) 1 Not ansual (enough hits) 1	91 120,944 262 119,919 944 119,116 71 117,873 93 92,0945 94 121,036 91 121,037 92 122,038 93 119,927 910 121,627 92 121,627 92 121,627 93 119,927 94 121,537 91 121,627 91 121,627 92 122,537 91 125,537 91 125,537 92 126,700 94 113,361	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.779 2.591 119.611 1.659 120.342 0.966 120.342 0.966 120.342 0.966 121.030 1.444 122.030 1.537 116.503 1.444 122.590 1.472 121.501 1.344 125.591 3.223 117.355 3.559	0.030 007 0.110 027 0.408 042 0.825 078 0.852 028 0.862 228 1.613 267 1.262 121 0.450 041 1.457 214 0.450 041 1.457 214 0.248 038 0.033 004 0.691 101 1.842 225 0.856 199	9 106.712 1 107.576 4 115.776 8 114.962 5 119.111 4 108.946 9 99.585 5 99.585 5 99.585 5 99.585 5 103.190 8 112.973 8 112.973 8 112.277 9 122.277 4 102.335	127.093 120.6 126.752 119.5 123.424 119.5 123.424 119.5 123.424 119.5 123.424 119.5 128.455 118.7 129.145 120.8 112.785 118.7 132.789 120.3 135.789 120.3 135.789 120.3 132.208 119.7 132.067 120.9 121.216 116.6 28.528 121.9 27.663 125.4 28.528 121.9 27.663 125.4 31.028 117.7	77 0.000 78 0.000 53 0.000 53 0.000 53 0.000 53 0.000 55 0.000 56 0.000 56 0.000 56 0.000 57 0.000 58 0.000 58 0.000 57 0.000 31 0.000 44 0.000 56 0.000 45 0.000								
9	Notecule	Programmers (1) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2	Not answare (ensugh hits) 1 Not answare (ensugh hits) 1 Not answare (ensugh hits) 1 Not answare (ensugh hits) 8 Not answare (ensugh hits) 8 Not answare (ensugh hits) 8 Not answare (ensugh hits) 2 Not answare (ensugh hits) 2	91 120,944 22 119,919 84 119,116 71 117,873 90 120,965 122,88 122,288 9773 119,927 9190 121,653 91224 121,417 95 112,633 91 121,633 91 12,1633 91 12,1633 91 12,1633 91 12,1633 91 12,1633 91 12,1633 91 12,1633 91 12,1633 91 12,1633 91 12,1633 91 12,1633 91 12,1633 92 12,1470	121/24/2668 119.648/2.467 119.648/2.467 118.661/0.955 121.500/2.140 118.779/2.591 120.342/0.966 120.342/0.966 120.342/0.966 120.342/0.966 120.342/0.966 139.401/1.454 121.901/1.454 122.1901/1.424 121.901	0.030 007 0.110 027 0.408 042 0.259 078 0.259 078 0.82 228 0.420 045 0.430 041 1.437 2.14 0.430 041 1.437 2.14 0.430 041 0.430 041 0.431 036 0.033 004 0.651 101 0.221 036 0.221	9 106712 1 107576 4 115776 8 114962 5 119.111 4 108.946 9 99.585 5 99.585 5 99.585 5 99.585 5 99.585 8 112.973 8 112.973 8 112.973 8 112.973 9 122.277 3 121.372 11.1436 11.14	127.093 120.6 126.752 119.5 126.752 119.5 126.738 110.7 129.145 120.8 120.738 110.7 129.145 120.8 120.785 110.7 135.789 120.3 135.789 120.3 132.067 120.9 121.216 116.6 134.433 122.6 134.433 122.6 124.528 121.9 27.653 125.5 37.604 125.7 37.604 125.7 37.655 120.6 127.793 125.5 120.6 127.795 125.5 120.6 127.755 125.5 120.5 127.755 125.5 120.5 127.555 125.5 120.5 127.555 125.5 120.5 127.555 125.5 120.555 125.5	77 0.000 78 0.000 53 0.000 53 0.000 55 0.000 55 0.000 56 0.000 56 0.000 56 0.000 57 0.000 58 0.000 59 0.000 51 0.000 53 0.000 54 0.000 56 0.000 56 0.000 56 0.000 56 0.000 56 0.000 56 0.000 56 0.000 56 0.000 56 0.000 57 0.000 580 0.000 597 0.000								
9	Notecule	1130/0000000000000000000000000000000000	Supervised (encough http:) 1 Mot unsuaid (encough http:) Mot unsuaid (encough http:)	91 120044 22 119019 24 119019 94 119116 0 120345 0 120345 128 12228 12228 12228 19173 119927 1910 121827 192 121637 31 121637 31 121633 31 121633 31 121537 10 122,820 11 123,189 12 121,453 12 123,189 12 121,4531	121/24/2668 119.648/2.467 119.539/1.037 118.661/0.955 121.500/2.140 118.779/2.591 119.611/1.659 120.342/0.966 120.342/0.966 120.342/0.966 120.342/0.966 120.342/0.966 120.342/0.966 120.342/0.966 122.342/0.142 122.590/1.472 122.590/1.472 125.384/1.227 125.713/2.23 177.33/2.359 177.33/2.359 177.34/1.093	0.030 0077 0.110 027 0.408 042 0.255 078 0.259 055 0.862 228 1.613 267 1.262 121 0.430 041 1.437 2.144 0.248 038 044 0.033 040 0.691 101 0.271 036 0.691 101 0.271 036 0.560 199 0.703 224 0.668 070 777	9 105712 1 07576 4 115716 8 114362 5 119111 4 108348 7 99322 9 99385 5 99385 7 100171 8 112978 8 119381 3 111842 9 122277 9 122277 9 122277 9 122277 1 12227 1 1227 1 127 1 127	127.093 120.6 126.752 1195 126.752 1195 126.738 118.7 128.424 119.5 126.738 118.7 129.145 120.6 127.885 118.7 132.186 119.7 132.085 118.7 132.085 119.7 132.085 120.6 132.208 119.7 132.087 120.9 121.216 116.6 128.528 121.9 127.853 125.4 37.865 120.6 127.839 122.2 127.853 126.6 127.855 120.6 127.855 1	77 0.000 78 0.000 38 0.000 53 0.000 85 0.000 85 0.000 85 0.000 85 0.000 86 0.000 87 0.000 89 0.000 89 0.000 80 0.000 80 0.000 80 0.000 82 0.000 84 0.000 85 0.000 86 0.000 76 0.000 76 0.000 76 0.000 76 0.000 76 0.000 77 0.000 79 0.000 75 0.000								
9	Molecule	Programmers C13 (26 851) C13 (26 851) C10 (26 851) C10 (29 (26) C10 (29 (26) C10 (29 (26) C10 (29 (26) C11 (210 (26) C11 (210 (26) C12 (213 (26) C12 (213 (26) C12 (213 (26) C12 (213 (26) C15 (213 (26) C15 (213 (26) C15 (27) C15	Not compare (encorp) this 1 Not compare (encorp) this 1 Not compare (encorp) this 1 Not compare (encorp) this 0 Not compare (encorp) this 2 Not compare (encorp) this 2 Not compare (encorp) this 2 Not compare (encorp) this 2 Not compare (encorp) this 1 Not compare (encorp) this 1	91 120,944 220 19,919 84 119,116 71 117,873 0 120,945 120,945 122,045 120,85 122,045 120,81 122,826 121,827 121,417 1900 121,627 1924 121,417 35 121,633 31 121,637 31 121,537 2 12,7643 2 12,7643 2 12,643 11 123,361 11 123,361 12 14,455 13 12,13361 14 113,361 11 122,1430 12 12,1450 13 116,553 14 113,361 11 122,1430 167 125,041	121.024 2.668 119.648 2.467 119.539 1.037 118.661 0.955 121.500 2.140 118.779 2.591 120.342 0.966 119.440 1.494 121.036 1.537 116.903 1.444 122.1501 1.344 122.1501 1.344 125.344 1.227 126.713 2.23 117.355 3.559 120.342 2.3196 122.151 1.153 117.304 1.039 123.629 1.244	0.030 007 0.110 027 0.480 042 0.825 078 0.825 078 0.822 288 1.613 267 1.262 121 0.430 041 1.437 2.14 0.430 041 0.430 044 0.431 004 0.631 101 0.560 190 0.560 190 0.570	9 105.712 1 107.576 4 115.716 8 114.962 5 119.111 7 99.222 9 99.245 5 99.545 5 99.545 5 99.545 8 119.381 3 111.842 9 112.277 3 122.177 3 122.177 4 102.335 7 103.368 3 10.347 1 114.396 3 2 100.583 ************************************	127.093 122.6 127.093 126.7 126.752 1195 126.752 1195 127.842 1195 128.145 120.6 127.165 118.7 128.145 120.6 132.166 119.7 132.166 119.7 132.070 120.9 121.216 116.6 124.433 122.6 127.863 125.4 13.028 127.4 13.028 127.4 13.028 127.4 13.028 117.7 31.028 17.7 31.028 17.7 31.028 117.7 31.028 117.7 31.028 117.7 31.028 117.7 31.028 12.2 117.2 32.937 32.937 12.37	77 0.000 78 0.000 38 0.000 53 0.000 85 0.000 85 0.000 86 0.000 86 0.000 86 0.000 87 0.000 83 0.000 83 0.000 84 0.000 82 0.000 82 0.000 83 0.000 83 0.000								

139.098

122.341

117.454

133.747 1.974 **2.711**

120.342 0.966 **2.989**

0.000 0.441

120.328 0.904 **2.226** 2.013

5.352

2.888

127.016 139.098

111.052 131.071

135.789

99.585

133.350 0.000

120.291 0.000

120.306 0.003

 117.304
 1.093
 0.707

 123.629
 1.244
 1.136

 118.446
 1.246
 0.328

 119.700
 1.051
 0.778

132

116.531 125.041 118.854 120,616

Unusual (enough hits) 5705

Unusual (enough hits) 20773

Unusual (enough hits)

167.907

C7 C2 C1

C7 C6 C5

C20 C21 C22

C9 C8 S1 C5 Not unusual (enough hits) 338

CCDC Mogul 2022.3.0: VUSDIX (P21\c) - e Searches Databases Help ild query Results and analysis View st	Mercury 13					-					
esults Navigator	Mogul search - Bond angle - C20 C21 C22										
Il hits: 20773 ccepted hits: 20773 -factor: Any Heaviest Element: Any xclude: Organometallics, Powder structures	13040		Valu	ue in query: 117.454°							
Relevance Number Contribution I.00 20773 100.0%	10432										
	97824 6 9 5 5216										
View diagrams More hits	2608	12									
Statistics	0 95 100	105 110	115	120 125	130	135	14				
Total : 20773 Selected : 83 Mean : 117.020°	Click to (de)select	pars; click and drag to (de)select a rang	Bond angle								
Standard deviation : 0.316° Minimum : 116.427° Lower quartile : 116.762° Median : 117.049° Upper quartile : 117.297° Maximum : 117.497° I - scrore I : 1.327	Histogram display Displayed hits: 20773	Select all hits in histogram	Data lit CS CS CS	braries 5D 5.43	Filters		Cluster				
	Selected hits: 83	Deselect all hits in histogram	⊡ cs	5D Sep22 update							

- 13. Now click the *View structures* tab, near the top of the window, to see a list of refcodes included in this bin. The default view for this window is the 2D diagram. Scroll through the refcodes on the right side of the window to view different structures. You will see that the fragment of interest is drawn in red and its value at the top right.
- 14. Click the **Information** button on the left to see further details about the structure.
- 15. Click the **3D Visualiser** button to see a 3D rotatable view of the structure. The fragment of the molecule used for comparison will be highlighted with the value displayed in green.
- 16. Continue to investigate other unusual parameters. You can always return to view the structure in Mercury to see which parameter you are querying.

Conclusion

In this exercise we have performed a Mogul Geometry Check on a molecule from the CSD. We have learnt how to run a Mogul Geometry Check from the CSD-Core menu in Mercury and how to read and analyse the results. Mogul provides information on values that are usual or unusual, however, it is recommended that you review the individual values to gain insight into their classification.





Example 2. Using Mogul to explain activity data

Mycophenolic acid (A) is an immunosuppressant that binds to inosine monophosphate dehydrogenase (IMPDH) with an IC_{50} of 0.02μ M. There are two close analogues (B and C) which are less active, with C much less so. How can Mogul help explain this decrease in activity?

In this example you will see how to use Mogul to correlate improved activity with geometric preferences. You will need the file <code>ljRl_ligand.pdb</code> for this example (downloadable from <u>Materials section</u>).

A successful target molecule will be able to form two favourable <u>hydrogen bonds</u> in the protein binding site, as shown. The angle of the allylic torsion angle should be in the range between 110-115° for this interaction to be achieved. We know that molecule A is a successful target but molecules B and C are not. What does Mogul have to say about these structures?

- 1. Launch Mogul (*via* the desktop icon or *via* Mercury). We will first conduct a torsion search on the ligand as it appears in the protein crystal structure.
- Click Load... and select the file 1JR1_ligand.pdb (provided for you along with this example). When the file is imported, Mogul will prompt you to edit the structure to assign bond types and add hydrogen atoms if necessary. Click OK to accept these changes.
- 3. Click to select the four carbon atoms that define the C2=C3-C4-C5 torsion angle. These will appear in the *Current Selection* box as you click. You can tick Show Labels as an aid to identify the four atoms. **Note**: the order of selection is important when defining a torsion angle. In this case, follow the order as they are bonded together.
- 4. Click **Search** when all atoms are selected.





- 5. The resulting histogram shows that the query value (114.654°) falls in a highly populated region of the histogram.
- 6. Now let's investigate the other two molecules and compare them to the ligand just seen. We can do this by editing the ligand structure in the Mogul interface.
- In the *Build query* tab, click Edit... This will launch the *Edit Structure* dialogue box. At the bottom of this box, under "Remove" click Atoms & Bonds. Then click on the <u>methyl</u> group atoms (C and 3H) to delete them from the structure.
- 8. Once the atoms are deleted, at the top of the *Edit Structure* dialogue box under "Add" click **Hydrogen Atoms**. Make sure the value is set to 1 and then click the carbon atom from which you just deleted the CH₃. This will add an idealized hydrogen at this position. Click **Close** when you are finished.
- 9. As in step 3 above, select the four carbon atoms of the C=C-C-C group, and then click **Search** to start Mogul running.
- 10. You will see the resulting histogram has shifted slightly, indicating the change in *chemistry* of the query fragment (<u>des-methyl</u> vs. <u>methyl</u>). However, the query value stays the same because we did nothing to alter the geometry of our query fragment. This shift in the predicted geometry indicates a slight loss of predicted potency in this target molecule (B, above).





CCDC Mogul 2022.3.0: C:\training\1JR1_ligand.pdb File Searches Databases Help

Build query Results and analysis View structures



7

7

- 11. Finally, to investigate molecule C above, we need to make one more change. This molecule lacks the double bond that is present in molecules A and B.
- 12. Once again, return to the Build query tab and click Edit...
- 13. This time in the *Edit Structure* dialogue box click **Set Bond Type to** and choose *Single* from the drop-down menu beside it. Then click on the double bond (C2=C3) to change it to a single bond.
- 14. Now, as in step 8 above, in the "Add" section, click **Hydrogen Atoms** and make sure the value is set to 1. Click the two carbon atoms on either side of what had been the double bond, to ensure they are fully saturated. Click **Close** to exit the dialogue box.
- 15. Once again, click to select the same four carbon atoms (as in steps 3 and 9) and then click **Search** to start Mogul running.
- 16. Now you will see the resulting histogram for this alkyl chain has shifted far away from the query value for mycophenolic acid. This means that this chemical change will not satisfy the necessary orientation for effective binding and explains the observed loss of potency in molecule C.

Exercise: Find these molecules in ConQuest and assess the preferred orientation

- 17. Launch ConQuest and click on the Name/Class query type.
- 18. In the box for Compound Name type "mycophenol" and then click Add.
- 19. Click Search and then Start Search for the Search Setup dialogue box.







8

- 9
- 20. The search should return 8 results. MYCPHA and MYCPHA01 are the neutral species. KIWQUC is a sodium salt. WAJYUC is a neutral derivative. The others are co-crystals.
- 21. Use the *3D Visualiser* tab to view the MYCPHA and KIWQUC structures noting the different conformations. Based on what we have learnt from Mogul, which one is the preferred orientation?





KIWQUC

МҮСРНА

Conclusions

The skewed conformation for the crucial torsion in mycophenolic acid is the preferred orientation, although the neutral form of the molecule itself adopts a planar conformation for this torsion in the small molecule crystal structure. An analysis of conformational preferences rationalized the observed activity data for similar compounds.

Mogul can be an effective tool in explaining pharmacophore activity in relation to changes in substituents and bonding patterns. You should now be able to use Mogul to make changes to your own structures to see what functional groups can be altered in order to produce desired conformations or geometries.

Exercise

• Use Mogul to investigate subtle changes to your own molecules, or others that you find in the CSD.





1JR1 ligand skewed conformation

Summary

After this workshop you will be able to assess the geometry of a molecule of interest using Mogul in Mercury. In particular, you will:

- Know how to access Mogul and the Mogul Geometry Check from Mercury.
- Know how to run the Mogul Geometry Check on a molecule of interest.
- Be able to explain the results of the Mogul Geometry Check analysis, in particular the colour code of the tables and the histograms.
- Know how to load a file in Mogul and run a geometry check on specific features (for example a torsional angle) of a molecule.
- Know how to edit a molecule in Mogul to assess the geometry for different groups.

Next Steps

After this workshop, you can explore more exercises in the self-guided workshops available in the <u>CSD-Materials workshops area</u> on our website. We suggest trying the Full Interactions Maps workshop, which complement the Mogul geometry Check in the assessing of stability.

https://www.ccdc.cam.ac.uk/community/training-and-learning/workshopmaterials/csd-materials-workshops/

Feedback

We hope this workshop improved your understanding of Mogul Geometry Checks and you found it useful for your work. As we aim to continuously improve our training materials, we would love to get your feedback. Click on <u>this link</u> to a survey (link also available from workshops webpage), it will take less than 5 minutes to complete. The feedback is anonymous. You will be asked to insert the workshop code, which for this self-guided workshop is MOG-001. Thank you!



Glossary

Conformation

The shape, or more precisely, the spatial arrangement of a molecule is called conformation. The same molecule can present different conformations (different shapes).

Des-methyl

When a *methyl* group is removed from a structure, the adjective des-methyl is used for such structure.

Hydrogen Bonds

Hydrogen bonding occurs between donor-acceptor interactions involving hydrogen atoms. The H-bonds interactions are classified as: strong (mostly covalent), moderate (mostly electrostatic) and weak (electrostatic). Their strength is observed to be between 12 and 30 kJ/mol.

IC₅₀

 IC_{50} is a measure of the inhibition power of the substance. The lower the value the better, as less of the substance is needed to inhibit the process by 50%.

In silico

The expression *in silico* is used to refer to values that are generated via computer calculations or simulations.

Methyl

The methyl group is composed of a carbon atom linked to three hydrogen atoms. Its formula is CH₃.





In light blue, example of hydrogen bonds for refcode MULWIC.



Example of methyl group shown