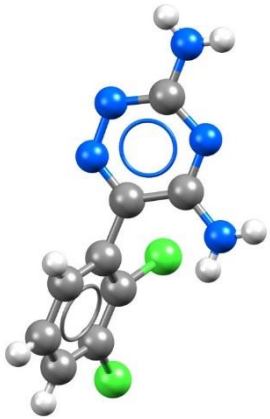
Mercury Intermediate
CCDC Virtual Workshops

2020.3 CSD Release



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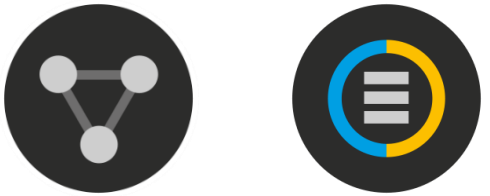
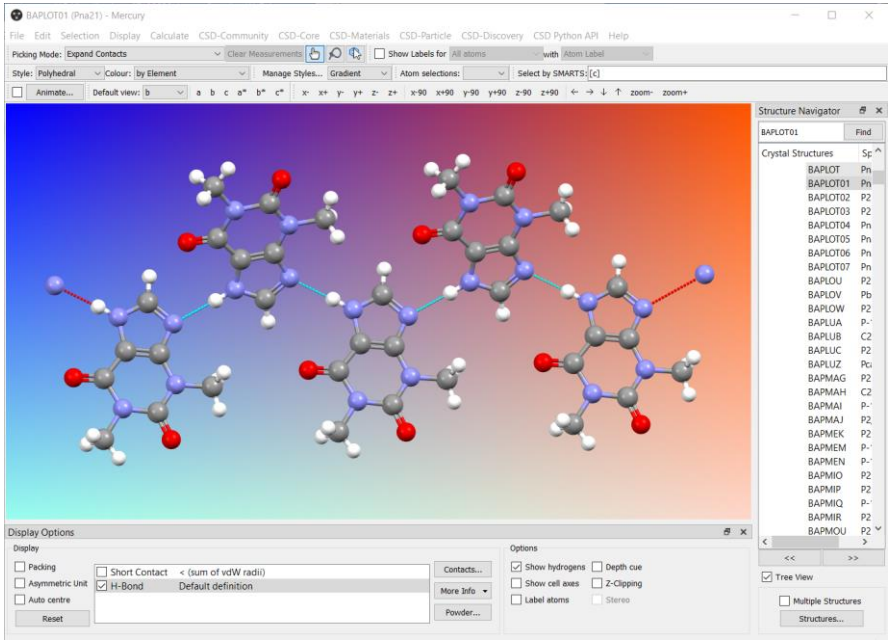
Introduction

Mercury is the visualisation and analysis software of the Cambridge Structural Database (CSD). Mercury is used in investigating and analysing crystal structures thanks to features such as packing diagrams, display and strength assessment of intermolecular interactions networks, calculation and display of voids, calculation and display of BFDH theoretical crystal morphologies and more (features availability subject to appropriate licence). With Mercury you can visualise 3D structures from the CSD as well as your own. You can also produce high-quality publication-ready images, frames for videos and 3D print files.

Before beginning this workshop, ensure that you have installed Mercury. Please contact your site administrator or workshop host for further information.





Objectives

In this workshop we will learn about analysis tools in Mercury. In particular, we will:

- Learn how to display hydrogen bonds and create an H-bonded network.
- Generate graph set views.
- Learn how to measure distances, angles, and torsions.
- Learn how to calculate and display centroids and planes.

This workshop will take approximately **25 minutes** to be completed, excluding the bonus questions and exercises.

Note: The Glossary at the end of this handout contains useful terminology for the exercises and for the demo.

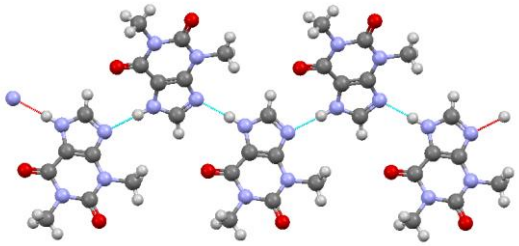
Pre-required skills

To complete this workshop, you would need to be comfortable with basics of Mercury visualization, including navigating the Mercury interface, editing styles and colours, displaying packing diagrams.

Example 1. Hydrogen Bonds

The creation of hydrogen bonds and the characteristics of the H-bonded network, as well as the formation of short contacts, can play a role in the stability of a crystal and the occurrence of polymorphism. The program Mercury contains many features to study intermolecular interactions with this purpose.

In this example, we approach the topic by learning how to visualise and analyse intermolecular interactions. We will be using entries in the Teaching Subset, however, the following methods can be applied to any entry in the CSD, or any of your own structure files.



*Hydrogen bonding network in Theophylline (refcode **BAPLOT01**)*

Displaying Intermolecular Contacts

This example will show you how to display hydrogen bonds and short contacts in a crystal structure.

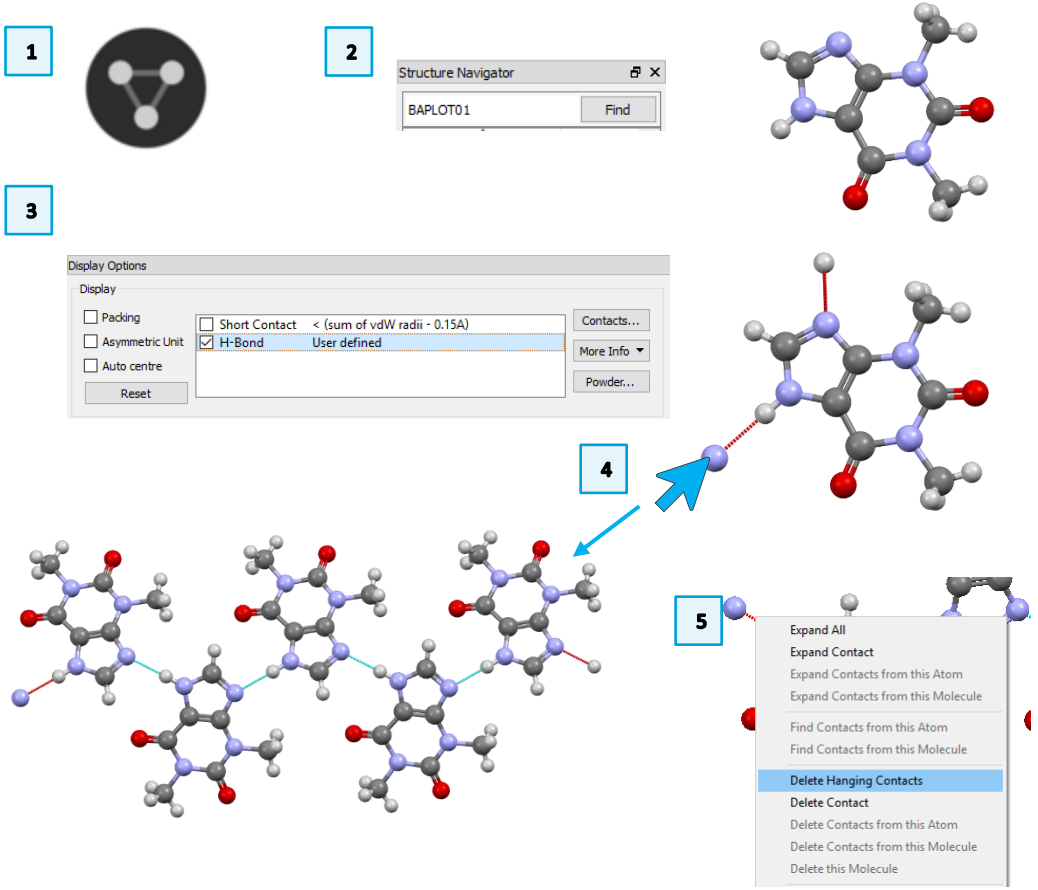
1. Open Mercury by clicking the desktop icon, or launching from the Start menu, Launchpad (macOS) or command line (Linux).

2. Type the refcode **BAPLOT01** in the **Structure Navigator** toolbar to load the structure of theophylline into the viewer.

3. To see if theophylline exhibits any hydrogen bonds, tick the box next to H-Bond in the **Display Options** toolbar. Now you will see red dashed lines indicating hydrogen bonding interactions to nearby atoms.

4. Click each atom to generate the complete molecule. Keep doing this until you have generated a network of 4 or 5 molecules.

5. Once you have a nice hydrogen-bonded chain of molecules, right click the red dashed lines and choose *Delete Hanging Contacts* to remove these dangling bonds. Click *Reset* in the bottom left corner to return to the default view.

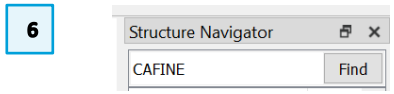


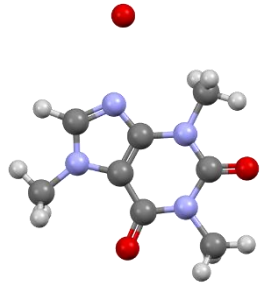
6. Now type the refcode **CAFINE** in the **Structure Navigator** toolbar. This will load caffeine hydrate in the viewer.

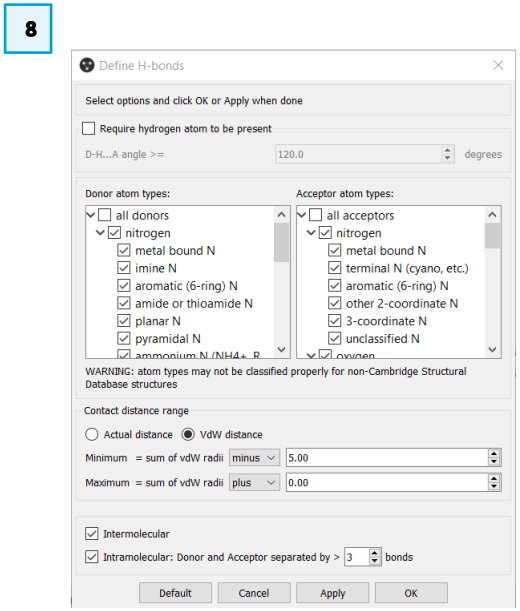
7. We want to know if there are hydrogen bonding interactions to the water molecule, but this crystal structure does not include the hydrogen atoms on this water. Tick the box next to H-Bond and contacts might not appear.

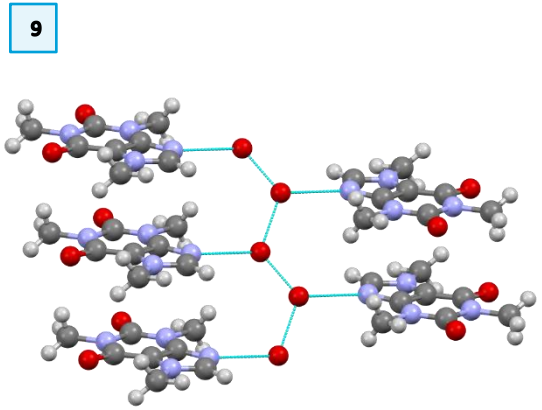
8. To see hydrogen bonding contacts without hydrogen atoms present, double click the row for H-Bond to access the *Define H-Bonds* dialog window. Make sure the box next to "Require hydrogen atoms to be present" is unticked and then click **OK** to exit the window.

9. Now you will see hydrogen interactions between the caffeine and water molecules. Follow steps 3 and 4 above to generate the hydrogen bonding network.









Generating a Graph Set View

Graph set analysis of hydrogen-bonding patterns is based on a set of descriptors which specify the type of pattern along with the numbers of hydrogen-bond donors and acceptors, written as $G^a_d(n)$. **G** represents the type of pattern (**C** for chain, **S** for intramolecular hydrogen bonds, **R** for ring, **D** for discrete), **a** is the number of acceptors, **d** is the number of donors and **n** the number of atoms in the pattern. This example will show you how to calculate the graph set notation and display hydrogen bonding patterns in Mercury.

10. In Mercury, type the refcode **GLYCIN** in the **Structure Navigator** toolbar to load the structure of glycine into the viewer. This simple molecule has many available hydrogen bonding patterns. Click **Reset** to restore the view to the default (i.e., no packing) arrangement.

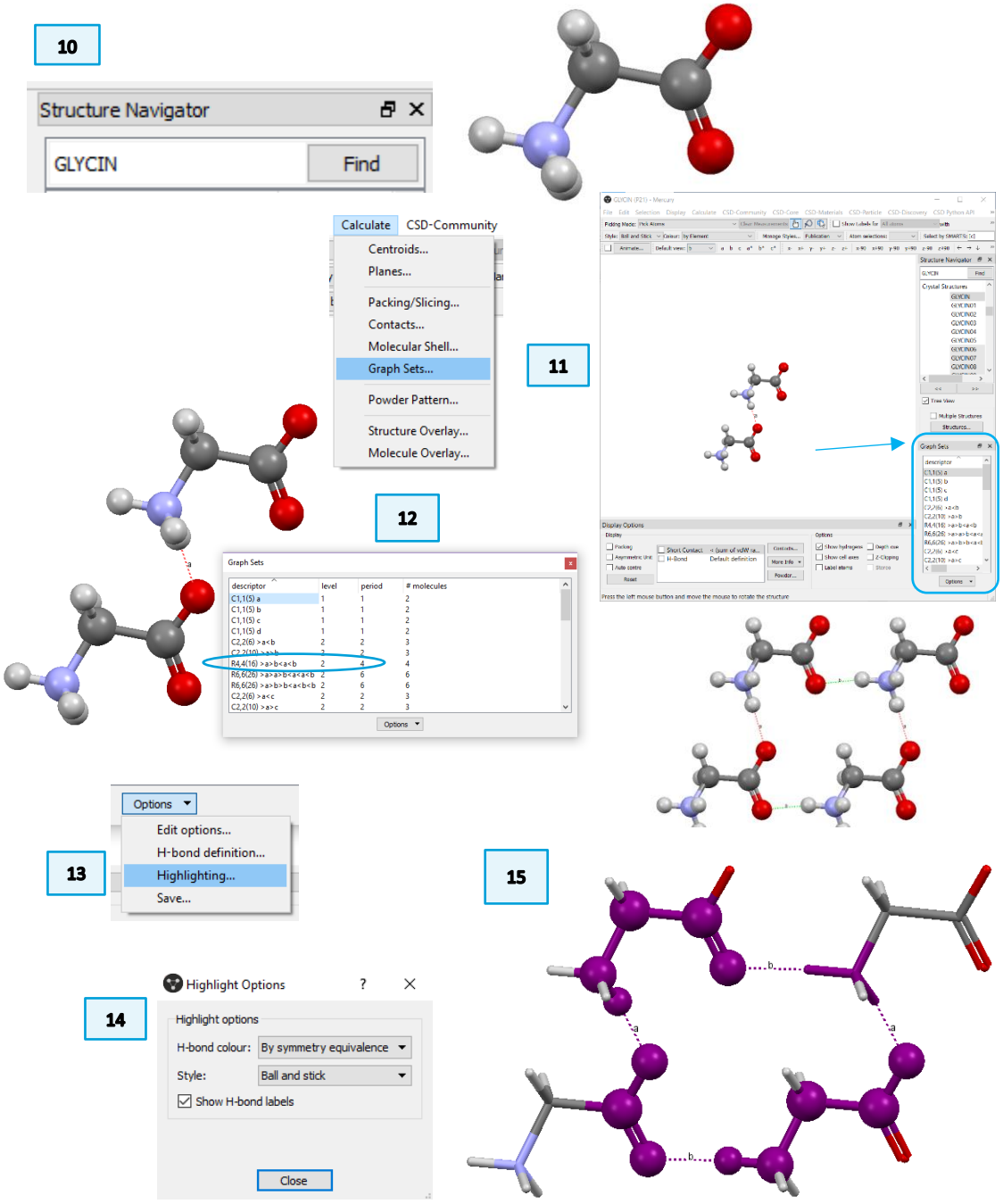
11. From the top menu choose *Calculate* > *Graph Sets…* which will launch the **Graph Sets** window. This may appear as a separate window, or as a tab hidden behind the **Structure Navigator** toolbar.

12. Click on any of the descriptors to see the corresponding motif. To generate a nice view, click on the **R4,4(16) >a>b<a<b** motif. This will bring up a view of four glycine molecules in a ring.

13. The *Options* drop-down menu includes features to *Edit* the type of motif that is displayed in the list, define the geometry of hydrogen bonds and donor/acceptor atom types (*H-bond definition…*), change the *Highlighting* of motifs, and *Save* the list of graph set descriptors. Choose *Highlighting…*

14. The H-bond colour should be set to “By symmetry equivalence” and the Style should be set to “Ball and stick.” Click these dropdown menus to change colours and see different styles, but ultimately remain with “Ball and stick.” In the *Style* dropdown in the main Mercury window, choose *Capped Sticks*.

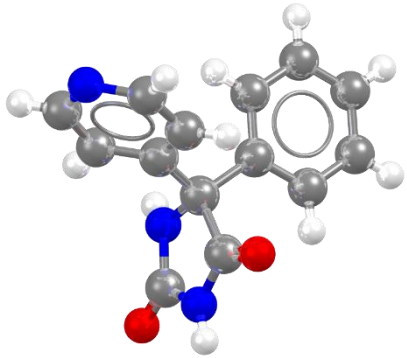
15. Select the atoms in Ball and Stick mode – the ones involved in the motif – and right-click to change their colour to highlight the motif even more.



Example 2. Measuring and Calculating Objects

Mercury's analysis features include the possibility measure distances, angles, and torsions among atoms and other user-defined objects, such as centroids and plane.

In the following exercises, we will learn how to measure distances, angles, and torsions among bonded and non-bonded atoms, how to calculate and display centroids and planes, and how to use them for measurements.



*High-resolution image of 5-(4-Pyridyl)-5-phenylhydantoin (refcode: **GODRAS**).*

Measuring Distances, Angles, and Torsions

This example will show you how to measure distances, angles, and torsions for a molecule in Mercury.

1. Open Mercury by clicking the desktop icon, or launching from the Start menu, Launchpad (macOS) or command line (Linux).

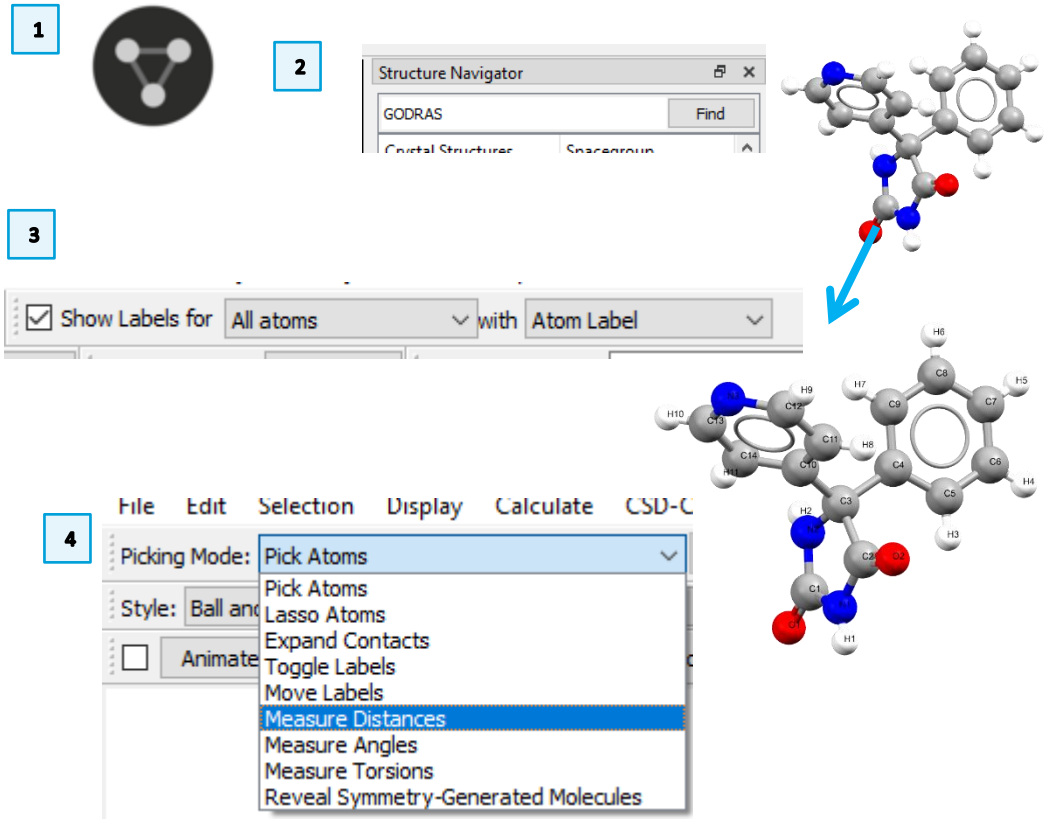
2. Type the refcode **GODRAS** in the **Structure Navigator** toolbar to load the structure of theophylline into the viewer.

3. To better identify atoms, you can add labels by ticking *Show Labels for* at the top right of the Mercury window. Adjust the options as needed.

4. To measure distances, we need to change Picking Mode (top left) to *Measure Distances*. You will notice that the cursor has now a "plus"-shape.

5. You can now measure the length of a bond by clicking on two bonded atoms. In this example we click on atom C3 and then atom C4. You can see the value of the length appearing on the bond. The unit is Angstrom. The distance between C3 and C4 in GODRAS is 1.533 Å.

6. You can measure more bonds lengths by repeating **Step 5** on other pairs of bonded atoms.



7. You can measure the distance between any two atoms by clicking on them as in **Step 5**. In this example, we measure the distance between C4 and C10. The measurement, in this case, appears above a dotted line. The distance between C4 and C10 is 2.551 Å.

8. To measure the distance between other pairs of non-bonded atoms, simply repeat **Step 5**.

9. To remove these measurements, right click on a measurement and select *Clear All Measurements*.

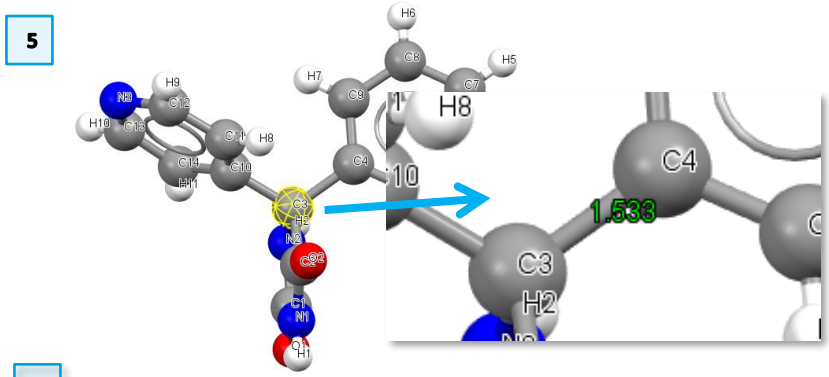
10. We will now move to measuring angles. To do so, from *Picking Mode* select *Measure Angles*.

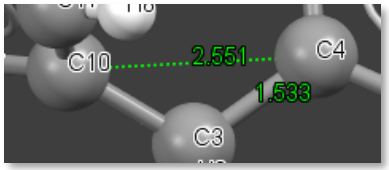
11. To measure an angle between bonded atoms, click on three consecutive atoms. In this example, we measure the C10-C3-C2 angle by clicking on them in this order. The angle's value appears in green over the central atom, and the angle is highlighted with a dotted arch. The unit is degrees. The value of the C10-C3-C2 is 108.07°.

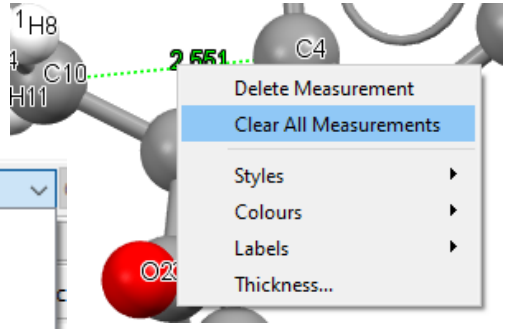
12. As for measuring distances, you can measure angles also among non-bonded atoms. To do so, simply select three atoms in the appropriate order. In this example, we measure the C2-N2-C10 angle by clicking on the atoms in this order. The value of the angle is 62.32°.

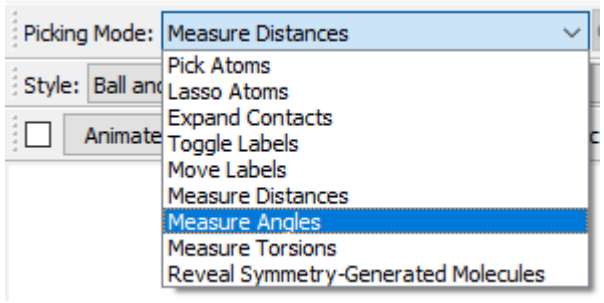
13. You can measure more angles by repeating **Step 11** on other groups of three bonded atoms.

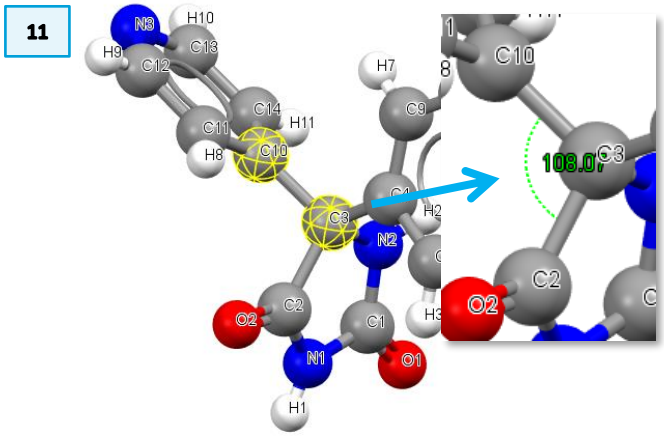
14. To delete all measurements, repeat **Step 9**.

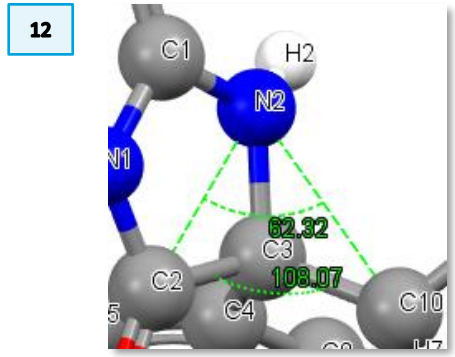












15. Next, we are going to measure torsional angles. To measure dihedrals, or torsional angles, we need to change *Picking Mode* to *Measure Torsions*.

16. In this case, we will need to select four atoms in the correct order. Also in this case, this operation is possible for both bonded and not bonded atoms. We will see an example for each case. To measure the torsion between atoms N2, C3, C4, C5, select them in this order. The two planes employed for the calculations are represented by green squares and the measurement appears in green. Units are degrees. The N2-C3-C4-C5 torsion is -76.03°.

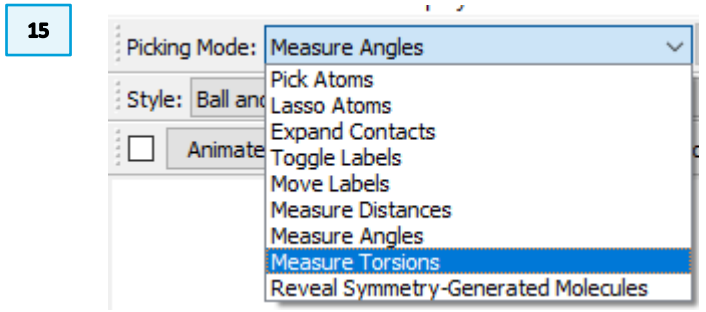
17. Repeat the procedure in **Step 16** for a group including non-bonded molecules, for example C1-N1-C3-C5. The C1-N1-C3-C5 torsion is -98.55°.

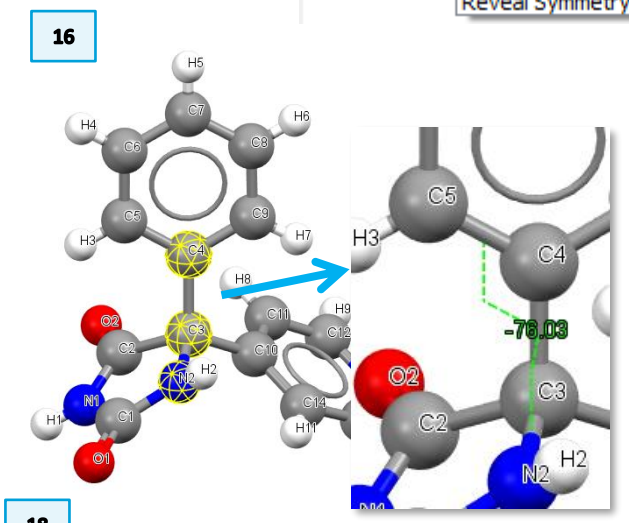
18. To view these measurements in a table, click on *More Info > Torsions List…* at the bottom of the Mercury window. In the pop-up window you can see the measured torsions, and save them as a document (.tsv, .csv, and .txt formats available).

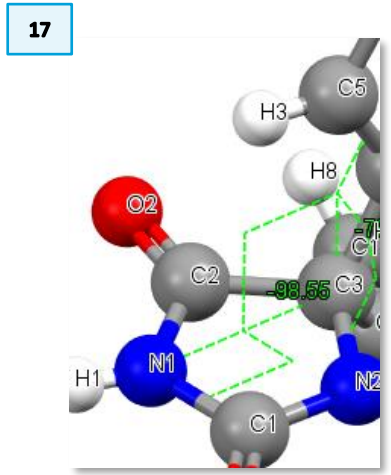
19. In this window you can click on *Distances* or *Angles* to visualise and save measurements of distances and angles. If you have cleared measurements along the way of this exercise, these tables will be empty.

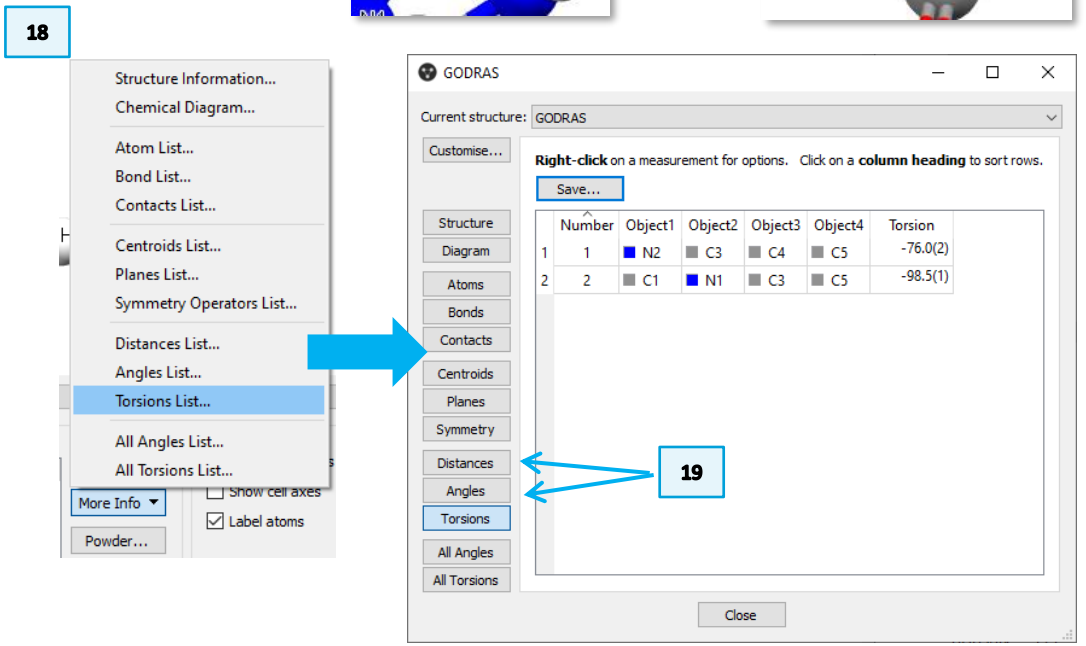
Bonus Exercise

You can measure distances, angles, and torsions also for atoms not belonging to the same molecule. To try this, you will need to visualise more molecules. You can do so for example by ticking *Packing* in *Display*. You can now repeat **Steps 4&5, 10&11,** and **15&16** for atoms belonging to different molecules.









Calculating Centroids and Planes

In this example we will see how to calculate and display centroids and planes in Mercury and how it is possible to use them to measure distances, angles, and torsions.

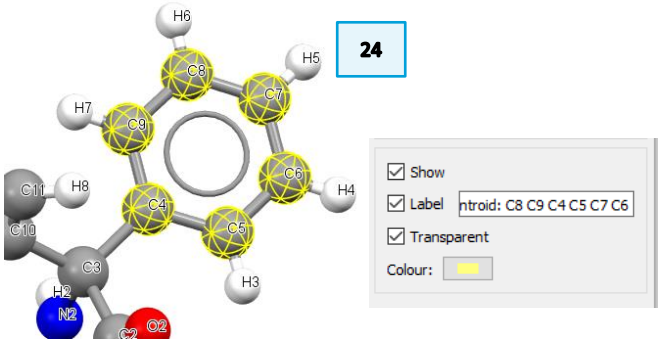
20. For this second part of exercise 2, we will be using the same molecule as the first part, i.e., **GODRAS**. Before proceeding with the rest of the exercise, make sure you clear all measurements following the directions in **Step 9** of the previous part, and go back to the view as in **Step 3** above. In *Picking Mode* select *Pick Atoms*.

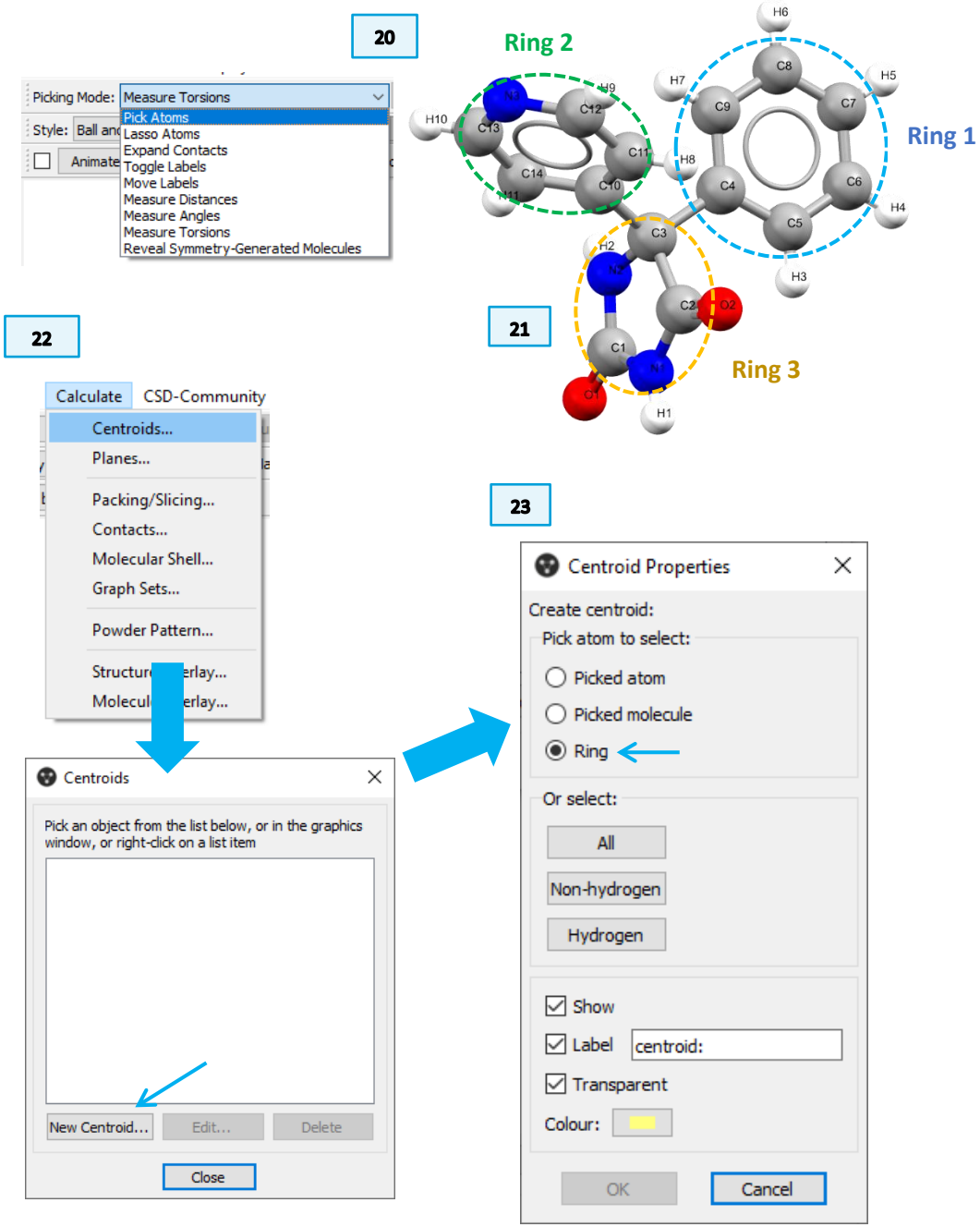
21. In this exercise, when referring to the three rings in this molecule, we will identify them as **Ring 1** = C4, C5, C6, C7, C8, C9; **Ring 2** = C10, C11, C12, N3, C13, C14; **Ring 3** = C1, N1, C2, C3, N2.

22. To calculate centroids, go to *Calculate > Centroids…* . In the *Centroids* window that appears click *New Centroid* to calculate our first centroid. This brings up another window with the *Centroids Properties*.

23. Our first centroid will be for **Ring 1**. In *Centroid Properties*, under *Create Centroid: Pick atom to select:* tick *Ring*. In this way by selecting one atom belonging to the ring we will be able to select the entire ring.

24. Now, on the Mercury interface, select one atom (any atom) belonging to Ring 1. You will see that the entire ring has indeed been selected. The *Label* in *Centroid Properties* now includes the labels of the atoms in Ring 1.





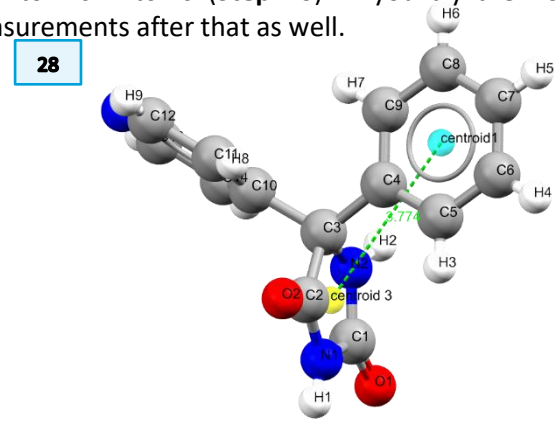
25. For clarity, change the *Label* in *Centroid Properties* to "*centroid 1*", and the *Colour* to blue (clicking on it, selecting the new colour, and then *OK*). When you are done, click *OK* to create the new centroid.

26. Centroid 1 has now been calculated and represented on the molecule. You can also find it listed in the window.

27. To calculate and display the centroid of **Ring 3**, repeat **Steps 22 to 25** selecting this time an atom from Ring 3. Edit the *Label* to *"centroid 3"* and the *Colour* to yellow.

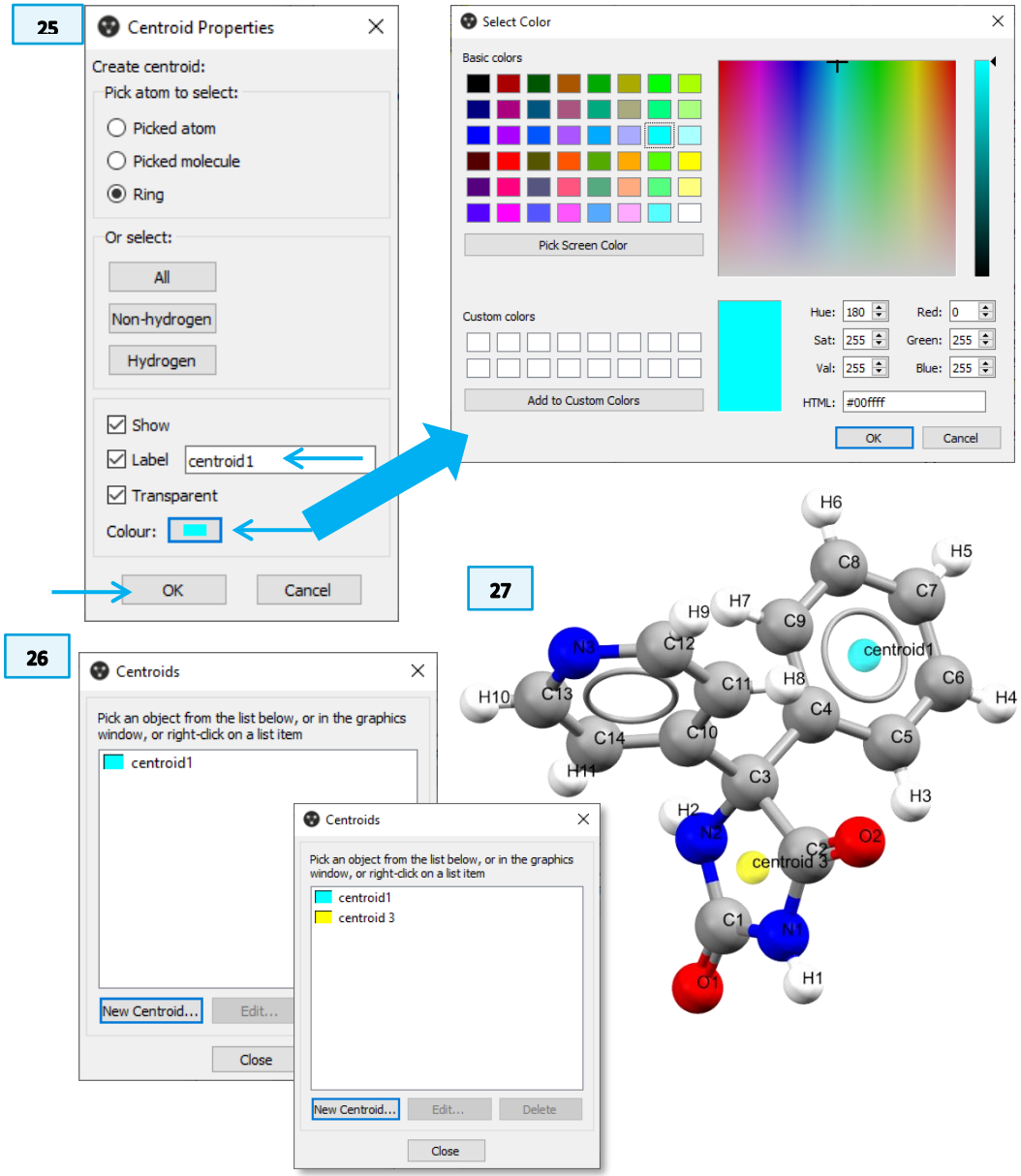
28. Centroids can be used for calculations of distances, angles, and torsions with other atoms. First, we measure the distance between *centroid 1* and *centroid 3*. To do so, repeat **Steps 4&5** from the first part of Exercise 2, selecting this time the two centroids we have just calculated. The distance between centroids 1 and 3 is 3.774Å.

29. For clarity, clear all measurements (**Step 9**) and change the *Picking Mode* back to *Pick Atoms* (**Step 20**). If you try the Bonus Questions, clear measurements after that as well.



Bonus Questions

- What is the distance between centroid 1 and N3?
- Try and measure angles and torsions using these centroids and other atoms of your choice. To do so, follow **Steps 10&11,** and **15&16** from the previous part.



30. We will now move to calculating planes. You will notice that the procedure is very similar to what we have just done to calculate centroids. Go to *Calculate* > *Planes…* . In the *Planes* window that appears click *New Plane* to calculate our first plane. This brings up another window with the *Plane Properties*.

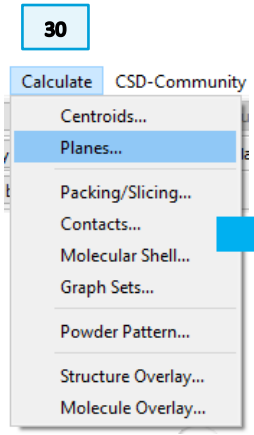
31. Our first plane will be for **Ring 3**. In *Plane Properties*, in the *Mean Plane* tab, under *Pick atom to select:* tick *Ring*.

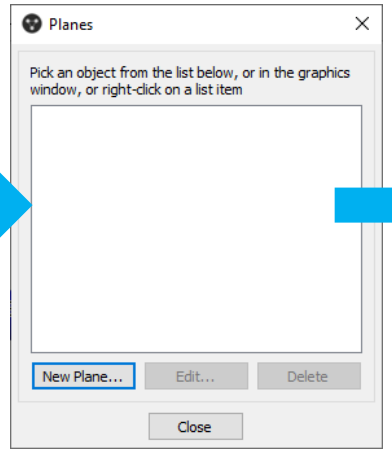
32. On the Mercury interface, select one atom (any atom) belonging to Ring 3. As for centroids, you will see that the entire ring selected. The *Label* in *Plane Properties* now includes the labels of the atoms in Ring 3.

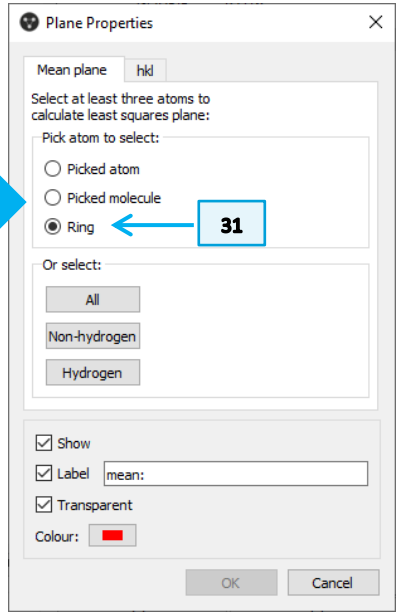
33. Change the *Label* in *Plane Properties* to "*plane* 3", and the *Colour* to orange (see **Step 25**). When you are done, click *OK* to create the new plane.

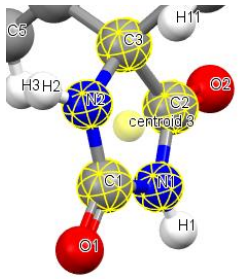
34. Plane 3 has now been calculated and represented on the molecule. You can also find it listed in the window.

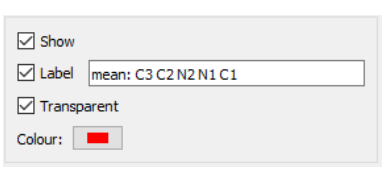
35. Next, we define the plane on which atoms C3, C4, and C10 lay. Please note that you could calculate a mean plane for more than three atoms, but for this example we will use these three. To calculate a new plane, in the *Planes* window click again *New Plane*. This time in *Plane Properties*, in the *Mean Plane* tab, under *Pick atom to select:* tick *Picked atom*.

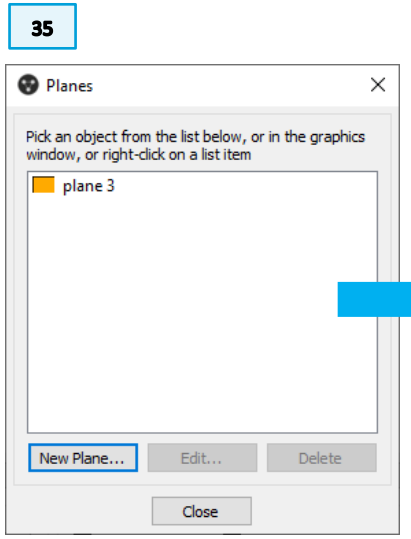


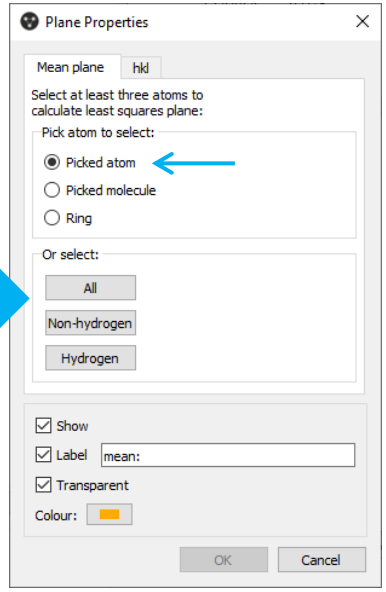


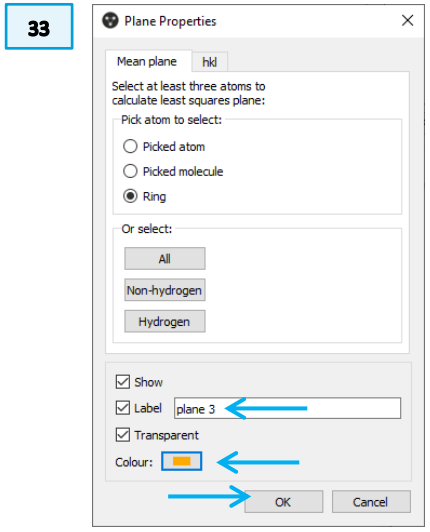


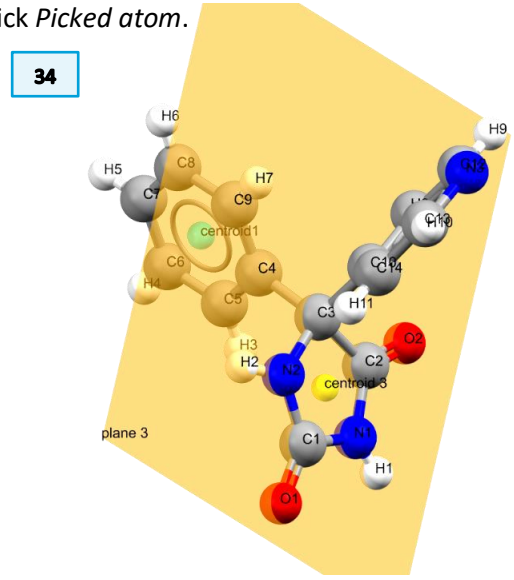








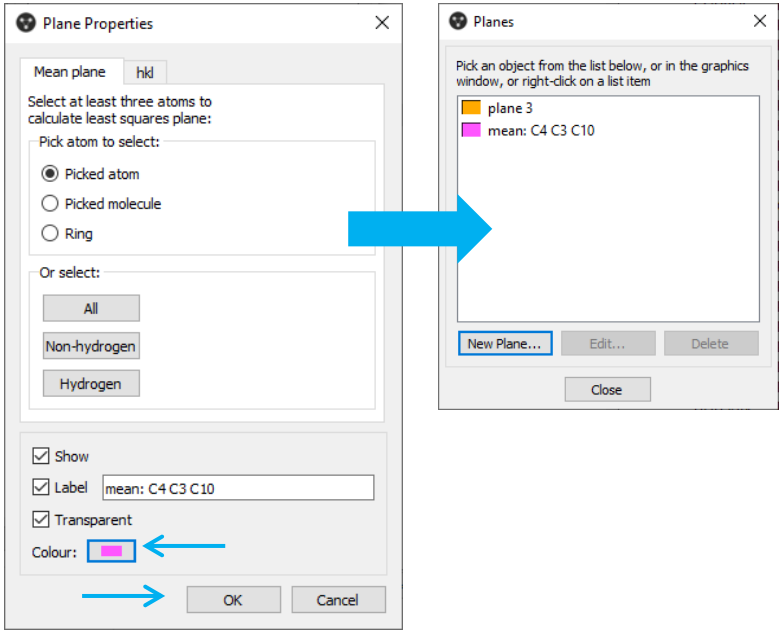




36. On the Mercury interface, select the three atoms of interest: **C3, C4, and C10**. The *Label* in *Plane Properties* is now *"mean: C4 C3 C10"*.

37. In *Plane Properties* change only the *Colour* to pink (see **Step 25**). When you are done, click *OK* to create the new plane.

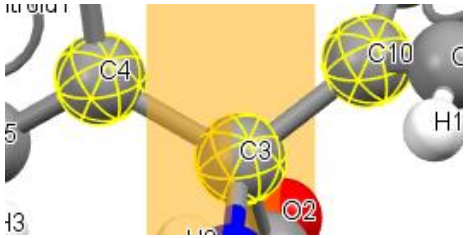
37

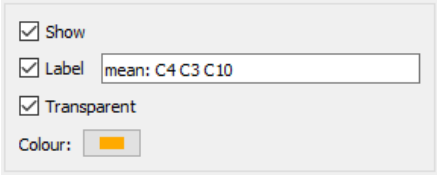


38. So far, we have calculated two centroids (centroid 1 and centroid 3) and two planes (plane 3 and mean: C4 C3 C10). We will now use them for measuring distances, angles, and torsions.

39. To measure the distance between centroid 1 and plane 3, first under *Picking Mode* select *Measure Distances* (see **Step 4** above). Then click on centroid 1 and on one (any) point on plane 3. Please note: the point on plane 3 does not need to be the closest to centroid 1. The value of the distance appears, as before, in correspondence of a dotted line. The distance between centroid 1 and plane 3 is 2.438 Å.

36





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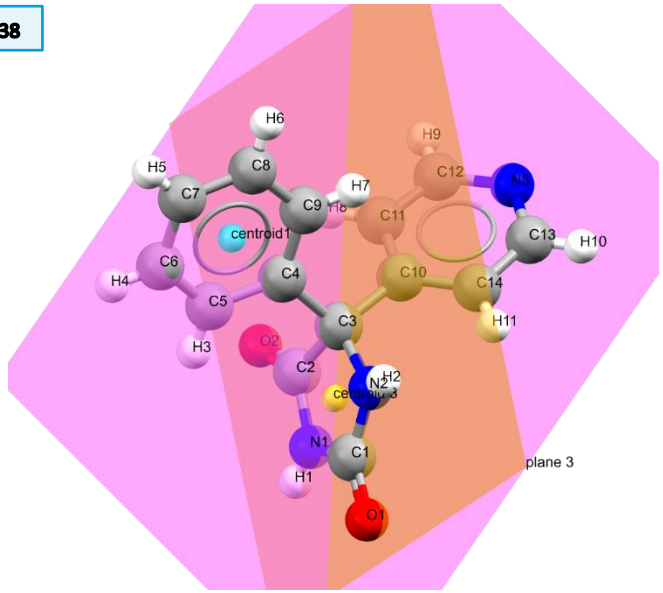

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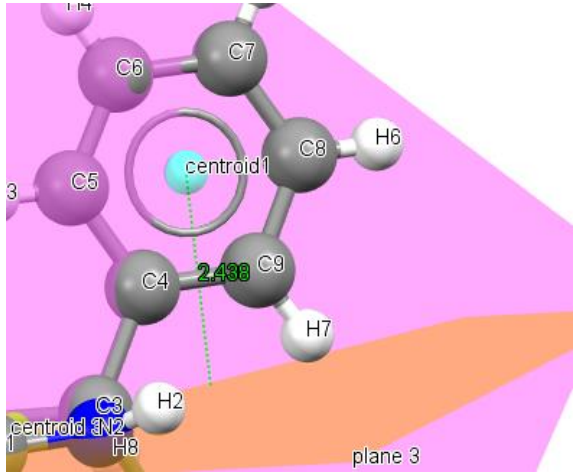
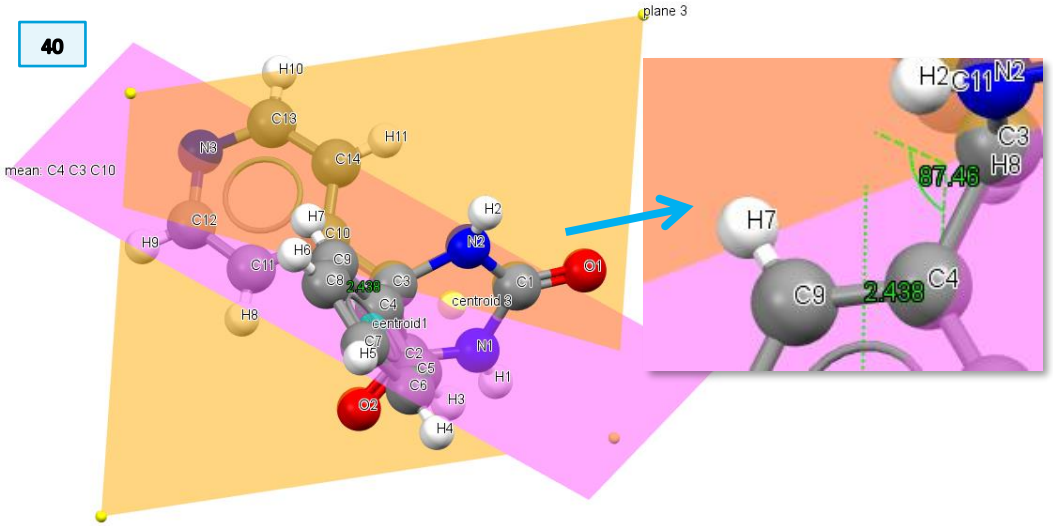


40. To measure the angle between the two planes that we calculated, under *Picking Mode* select *Measure Angles* (see **Step 10** above). Then click on plane 3 and on mean: C4 C3 C10. The angle is represented with a dotted arch as before and its value is 87.46°.

41. You can view the centroids and planes details listed in a table. Click on *More Info > Centroids List…* at the bottom of the Mercury window. In the pop-up window you can see the calculated centroids, and save them as a document (.tsv, .csv, and .txt formats available).

42. In this window you can click *Planes* to view and save the planes calculated.

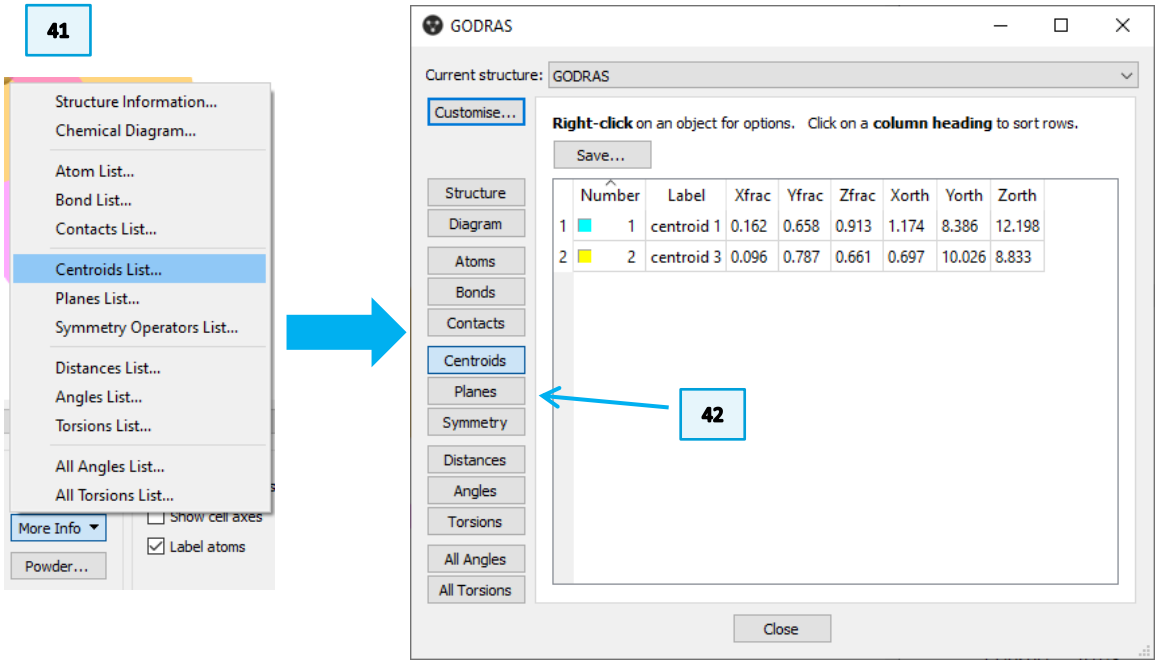


Bonus Questions

- What happens if you measure the distance between these planes?

Bonus Exercise

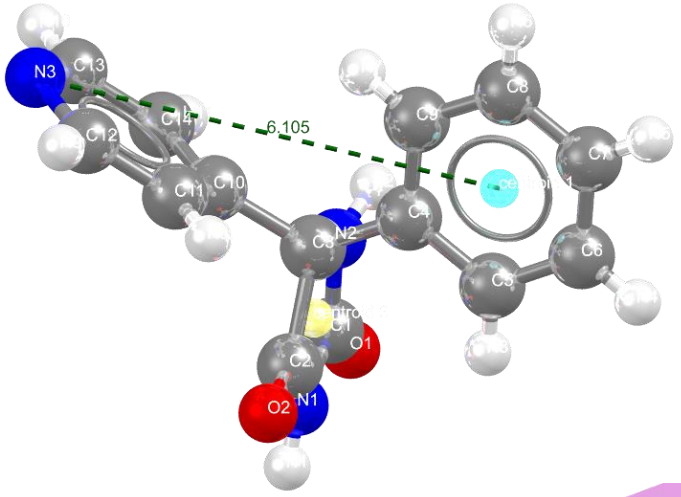
You can calculate centroids and planes for any selected group of atoms.
You can try and investigate what happens if you define a plane using 4 or more atoms.
With the packing visualisation on, define the centroid for each entire molecule and use them to explore distances, angles, and torsions.



Conclusions

In this workshop we used analysed Mercury to analyse crystal structures. You should now be familiar with:

- Displaying hydrogen bonds and edit the definition.
- Expanding and visualising the hydrogen bonds network.
- Visualising and interpreting graph sets.
- Measuring distances, angles, and torsions.
- Calculating centroids and planes.
- Viewing measurements and calculated objects from the More Info window.

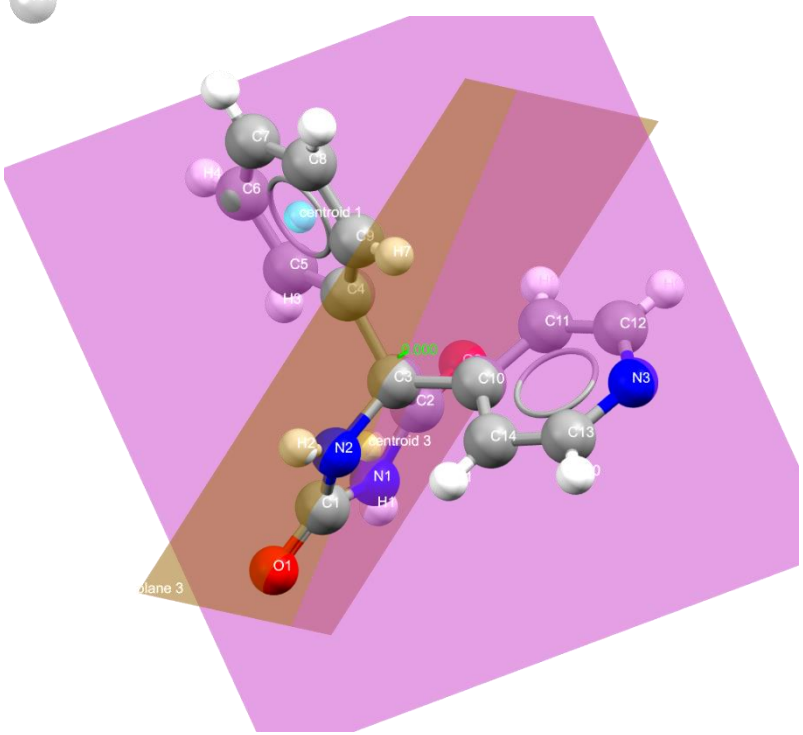


Next steps

If you finished the exercises early, you could head to the bonus exercises. Otherwise, ask the workshop tutors for new challenges!

Feedback

We hope this workshop improved your understanding of Mercury and you found it useful for your work. As we aim at continuously improving our training materials, we would love to get your feedback. We will be sharing a link for a feedback survey with you at the end of the session to fill in. It will take only **5** minutes to complete. The feedback is anonymous. Thank you!



Glossary

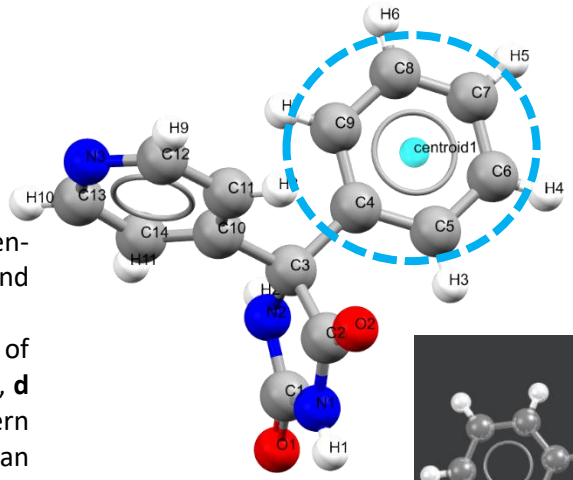
Centroid
In Mercury, the centroid is the geometric centre of a group of selected atoms.

Graph Sets
Graph set analysis of hydrogen-bonding describes the pattern of the hydrogen-bond chains or motif and includes the numbers of hydrogen-bond donors and acceptors.
A graph-set descriptor is written as $\mathbf{G^a_d(n)}$, in which **G** represents the type of pattern, **a** is the number of hydrogen bond acceptors involved in that pattern, **d** is the number of donors and **n** the number of atoms in the pattern. The pattern type, G, can be one of four different options: C for an infinite chain, S for an intramolecular hydrogen bonding pattern, R for an intermolecular ring and D for a discrete, finite hydrogen-bonding pattern.
Relevant bibliographic references:

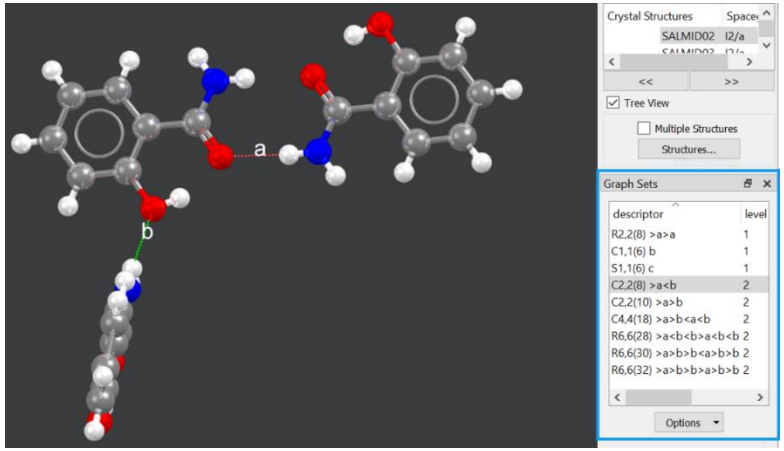
- M. C. Etter, Acc. Chem. Res., 23, 120, 1990
- J. Bernstein, R. E. Davis, L. Shimoni and N.-L. Chang, Angew. Chem. Int. Ed., 34, 1555, 1995
- W. D. S. Motherwell, G. P. Shields and F. H. Allen, Acta. Cryst. B56, 466, 2000

Intermolecular Interactions: Van der Waals, Aromatic Interactions and Hydrogen Bonds

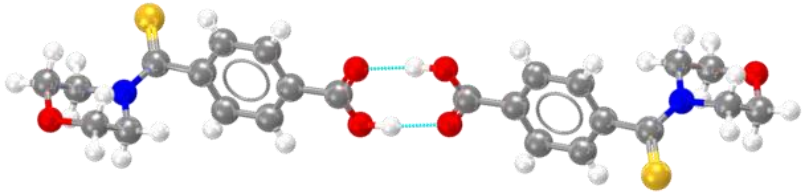
- **Hydrogen Bonding** occurs between donor-acceptor interactions precisely involving hydrogen atoms. The H-bonds interactions are classified as: strong (mostly covalent), moderate (mostly electrostatic) and weak (electrostatic).
  Their strength is observed to be between 12 and 30 kJ/mol.
- **Aromatic Interactions** are noncovalent interactions formed between aromatic rings. These interactions are important in material science since they will contribute to the overall crystal structure stability. The orientation of the aromatic ring can vary from parallel to T-shape, and we found during our DFT calculations that the T-shape interactions are very



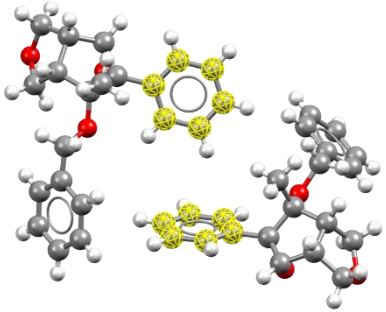
Centroid for atoms C4, C5, C6, C7, C8, C9 of structure GODRAS

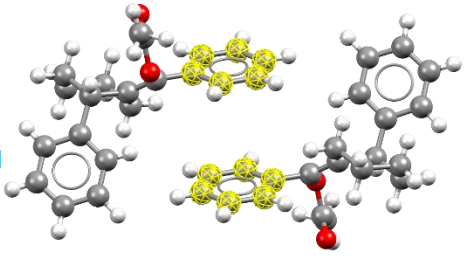


Example of Graph Sets display for structure SALMID01



Hydrogen Bonds in structure MULWIC





Aromatic interactions in structure PAGBUX (left, aromatic rings in T-shape orientation) and in structure AACMHX10 (right, aromatic rings in parallel displacement).

close in strength to the parallel displaced ones. Their strength is found between 0 and 16 kJ/mol based on DFT calculations.

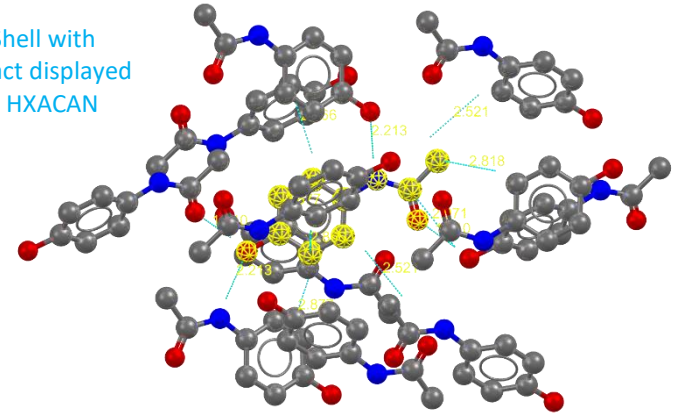
- **Van der Waals** forces are formed between atoms or molecules that are in each other's close proximity and are driven by induced electrical interaction. They are the weakest of all type of intermolecular attractions between molecules. However, with a lot of Van der Waals forces interacting between two molecules, the interaction can be very strong.

Interaction type	*Strength (kJ/mol)*
Van der Waals	**0.4-4.0**
Aromatics	**0-16**
Hydrogen Bonds	**12-30**

Molecular Shell

A molecular shell in Mercury will display all molecules within a specified distance of a selected atom or atoms. In some fields this would be referred to as a "*coordination sphere*".

Molecular Shell with Short Contact displayed in structure HXACAN



Short Non-Bonded Contacts

In Mercury, all contacts between atoms of any type that are shorter than a specified van der Waals corrected distance.