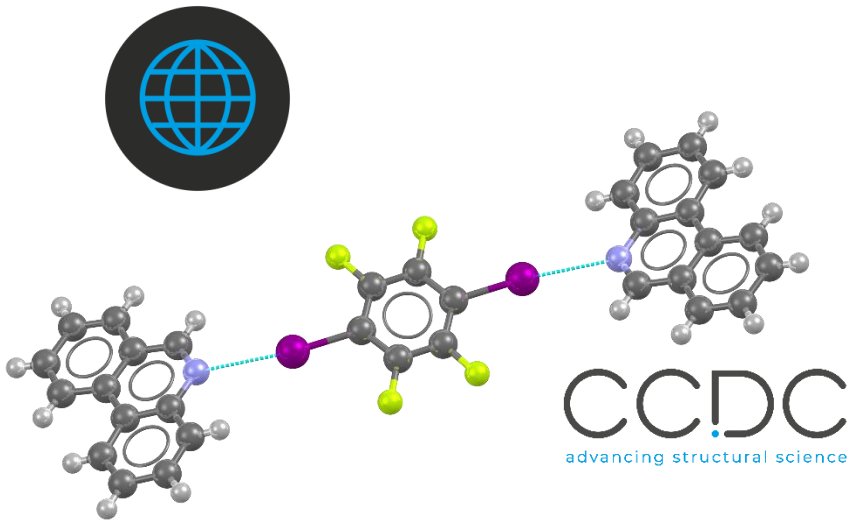
Searching the CSD 101 - Searching Structures Online with WebCSD

UTry

Developed using WebCSD version 1.9.32



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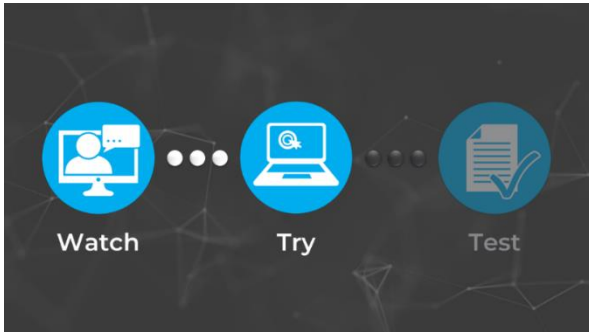


UTry – it's your turn!

In the second part of the *Searching the CSD online – WebCSD 101* module, "U Try", you will review the concepts and features presented in the first part, "U Watch", and try them out yourself. If at any time you want to rewatch the videos, you can find them from the course webpage (https://www.ccdc.cam.ac.uk/community/training-and-learning/csdu-modules/csdu-webcsd-searching-101/).

This tutorial will introduce you to how to searching using WebCSD with a focus on substructure searching and molecular similarity searching.

Learning Outcomes

You will explore the tools available for searching the CSD online using WebCSD. After completing this handout, you will be able to:

- Create substructure searches and include defined 2D and 3D parameters.
- Conduct a similarity search based on a molecular structure.
- Search for compounds based on their chemical formula.
- Use the unit cell search function to compare structures.

Example 1 will take approximately ***20*** minutes. Examples 2, 3 or 4 require each approximately ***5-10*** minutes.

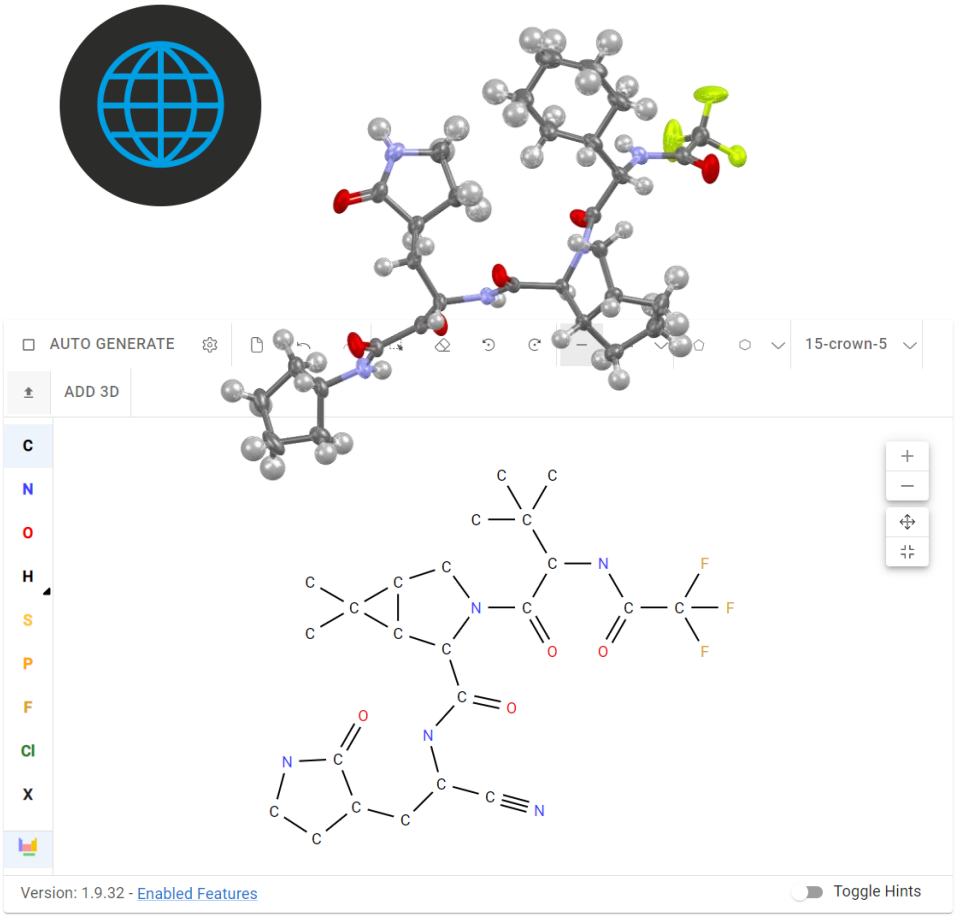
Note: The words in *Blue Italic* in the text are reported in the Glossary at the end of this handout.

Note: This workshop is for beginners; no entry skills are required.

Note: Please ensure that you are signed in to WebCSD with a user account connected to a valid CSD license (see here). Please contact your site administrator for further information.

Materials

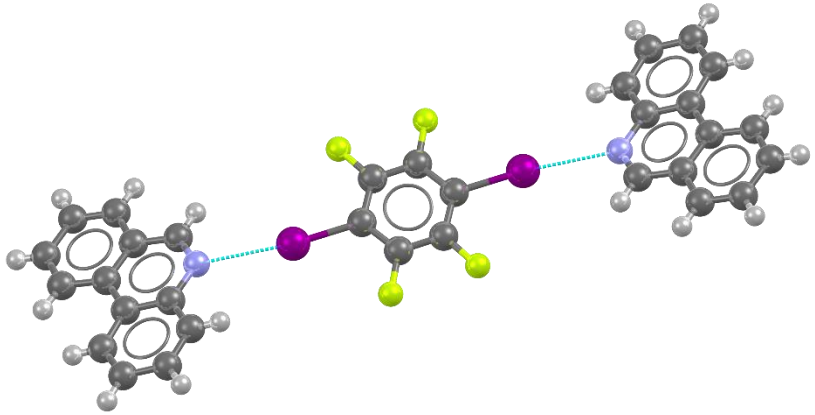
Download the MOL file for nirmatrelvir here.



Example 1. Investigating N···I interactions in the CSD using a substructure search.

The CSD can be used to help us understand what non-bonded contacts exist and what geometrical features these contacts have in the solid form. In this use case we will be using WebCSD to explore a particular type of halogen bond to help us learn about how strong the interaction is and what geometrical features are observed in these interactions.

A *halogen bond* occurs when there is evidence of a net attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another, or the same, molecular entity.[1] We will extract geometrical information about *intermolecular contact* distances and angles associated with halogen bonds in the solid state, using a *substructure* search of the CSD. Specifically, we will search for N···I interactions taking R—I to be the halogen bond donor, where R is an aromatic group, and taking sp^2 hybridised nitrogen to be the halogen bond acceptor.



CSD entry TOKFEG displaying halogen bonds between the iodine atoms of 2,3,5,6-tetrafluoro-1,4-diiodobenzene and the nitrogen atoms of the phenanthridine molecules.

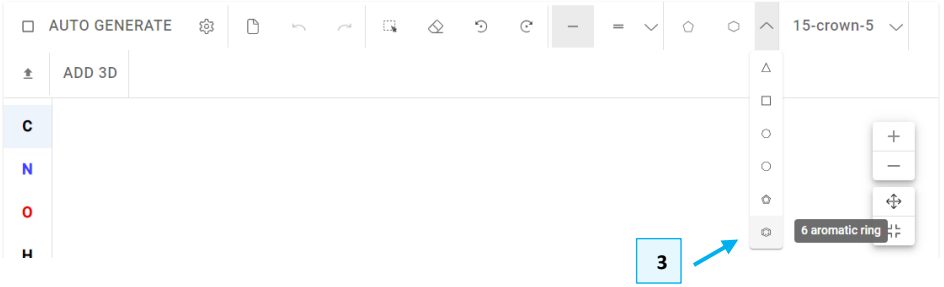
We will begin by defining our donor and acceptor groups.

1. Open a web browser and navigate to the Access Structures webpage (https://www.ccdc.cam.ac.uk/structures/).

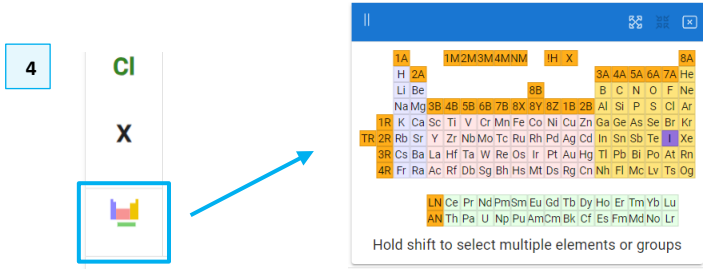
2. Click on the **Structure Search** tab to bring up the sketcher. If the periodic table is visible, you can drag it to reposition it in a convenient area or close it for the time being.

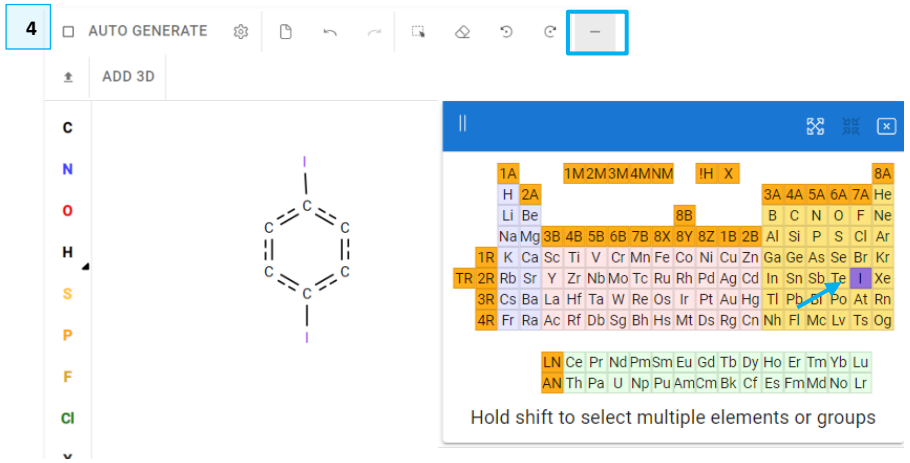
[1] G. R. Desiraju, P. S. Ho, L. Kloo, A. C. Legon, R. Marquardt, P. Metrangolo, P. Politzer, G. Resnati and K. Rissanen, *Pure Appl. Chem.*, 2013, **85**, 1711-1713.

3. From the drop-down menu next to the cyclohexane ring in the tools bar, select the *6 aromatic ring*  then **click** in the sketcher area to add an aromatic group.

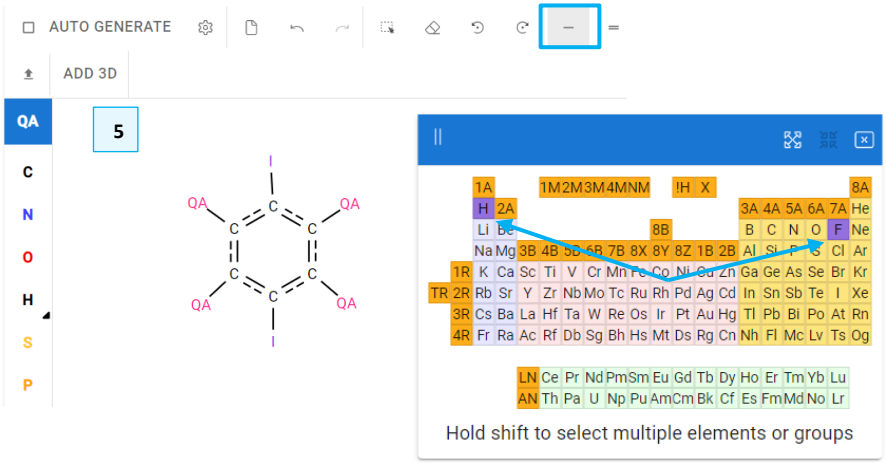


4. As the halogen bond donor molecule, we will use 1,4-diiodobenzene and fluorinated analogues, $C_6H_nF_{4-n}I_2$. If the periodic table is not visible, click the icon in the left-hand side toolbar. Click on the **single bond** symbol in the toolbar, then select iodine by clicking on the **I** symbol on the periodic table. Left-click on a carbon atom and drag to add a C—I bond. Repeat this procedure for the carbon atom in the 4-position.

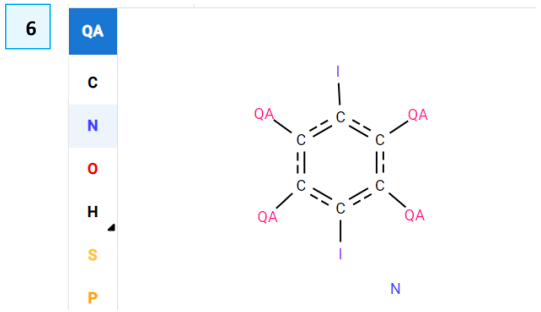




5. For the remaining substituents, we need to allow either hydrogen or fluorine. In the periodic table, click **H** then shift+left-click on **F**. Click and drag from the remaining unsubstituted carbon atoms, which will add “QA” substituents.

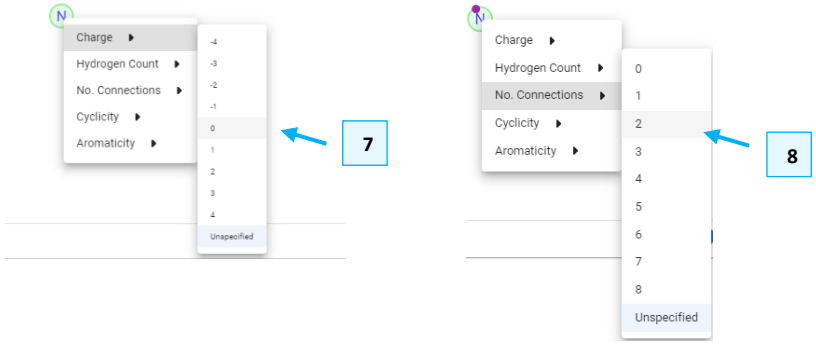


6. For the acceptor group we will add a neutral sp^2 hybridised nitrogen atom. Click **N** in the left-hand toolbar and then click near to an iodine atom in the sketcher.



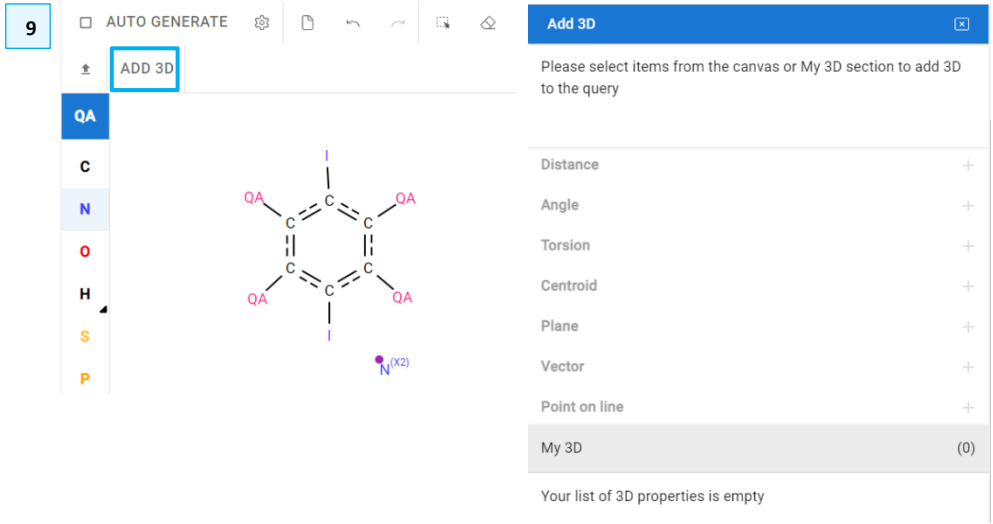
7. Right-click on **N** in the sketcher to bring up the drop-down menu. Select *Charge* and then choose *0*.

8. Right-click on **N** again and select *No. Connections* then choose *2*. The nitrogen atom should now appear as $N^{(X2)}$.

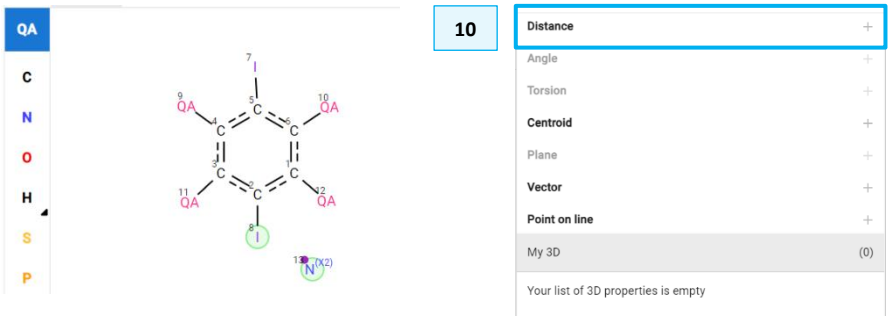


We will now define the geometric data to be extracted from the structures during the search. The three parameters that we will define are: the I···N distance, the C—I···N angle and the perpendicular distance of the N atom from the *mean plane* defined by the six carbon atoms of the aromatic ring.

9. Click the **ADD 3D** button from the top toolbar to bring up the 3D parameter options. The options will be greyed out until we have selected enough atoms to define a valid geometric parameter.



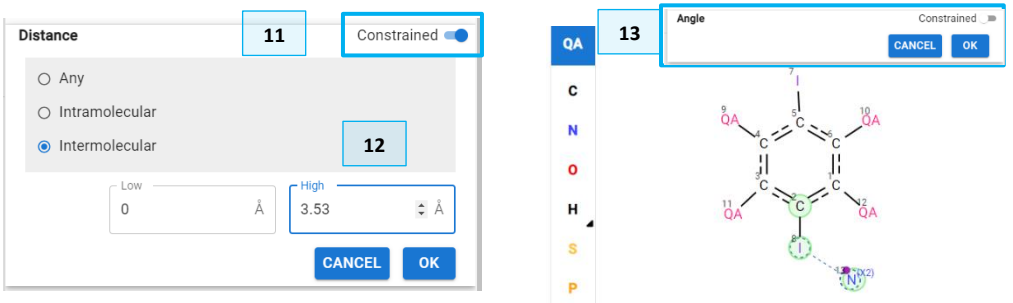
10. Shift+left-click on the **N** and **I** atoms (they will become highlighted in green); this will enable options to define a distance, centroid, vector or a point on a line. Click the **+** button next to *Distance*.



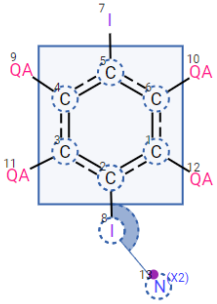
11. Move the *Constrained* slider to **on** and click the **Intermolecular** radio button.

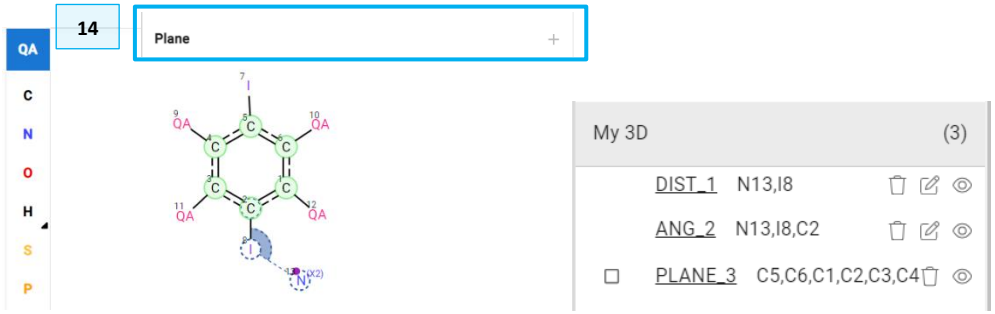
12. Leave the *low* limit as "0" and enter "3.53" in the *high* limit box. This is the sum of the *van der Waals radii* for nitrogen and iodine.[2] This will ensure only results that show definite evidence of halogen bonding are returned. Press **OK**.

13. Shift+left-click on **N**, then **I**, then the **C** bonded to I, in that order. This will enable the option to define an angle. Click **+** next to *Angle*, then click **OK**. Ensure that the *Constrained* option is not enabled.



14. Select all six atoms of the aromatic ring using Shift+left-click, then click **+** next to *Plane*. The newly defined plane will be highlighted as a square in the sketcher window.



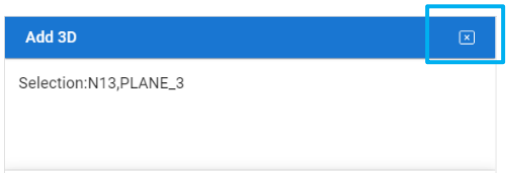


[2] M. Mantina, A. C. Chamberlain, R. Valero, C. J. Cramer and D. G. Truhlar, *J. Phys. Chem. A.*, 2009, **113**, 5806—5812.

15. Click on **N** in the sketcher and then tick the box next to *PLANE_3* in the **Add 3D** window. This will then enable the option to define the perpendicular distance between the N atom and plane of the aromatic ring.

16. Click **+** next to Distance and ensure that the *Constrained* option is NOT enabled by sliding it to the off position if necessary. Click **OK**.

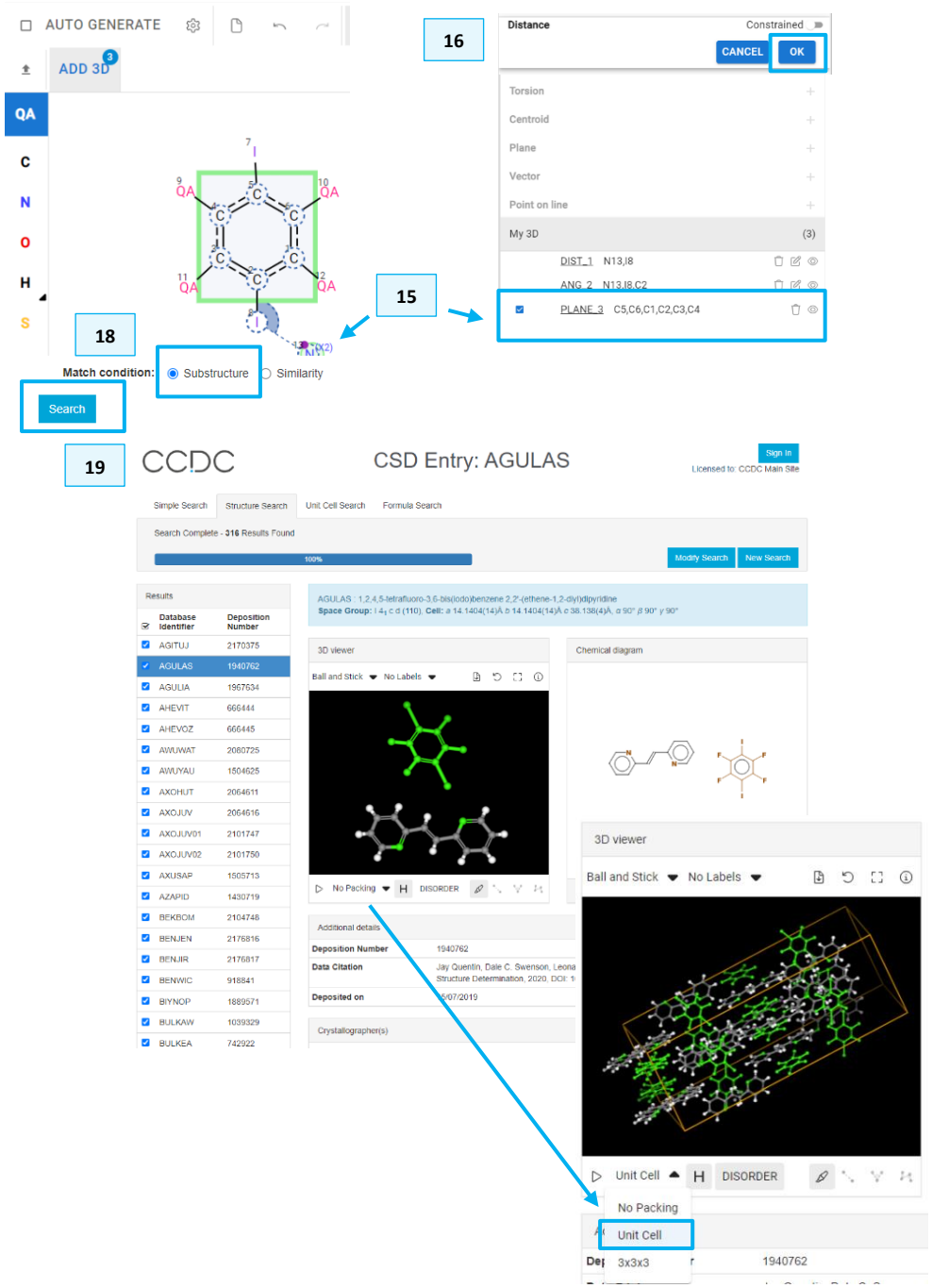
17. You should now have four defined parameters. Close the **Add 3D** window.



18. Underneath the molecule sketcher, ensure that the **Substructure** radio button is selected, then click **Search**.

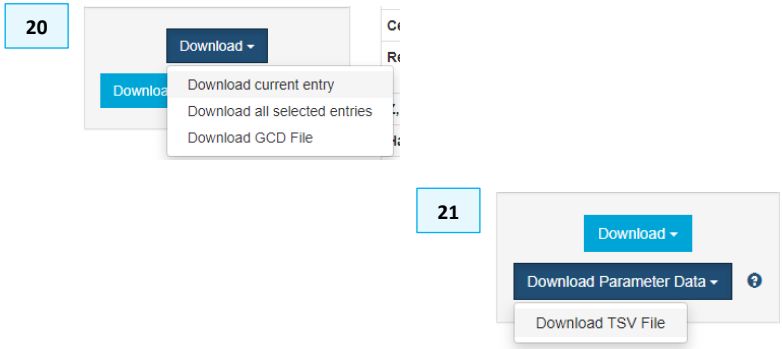
19. A new page will load showing the results, listed by refcode on the left-hand side, and information about the currently selected entry. There should be at least 318 hits (please note that your value may be larger, due to WebCSD being updated every minute). In the 3D viewer, the hit fragments are highlighted in green, while in the 2D diagram they are highlighted in brown. Scroll through the results and notice how the information and viewer are updated as you do so. As we are studying an intermolecular interaction, you may need to turn of the packing display to visualise all interactions. To do so, from the dropdown menu for the display options, select *Unit Cell.*

Tips and tricks: you can find more tips on how to get the most out of the 3D viewer here https://www.ccdc.cam.ac.uk/community/education-and-outreach/outreach/home-learning-activities/3d-visualizer-tips/



20. Click **Download** at the bottom of the results list to download entries as *CIF* files or as a *GCD* file, which allows you to load the CSD entries for the hitlist directly in Mercury. *Tip: very recent additions to the CSD may not be available through desktop applications until the next CSD data update.*

21. Click **Download Parameter Data** to download the 3D information gathered during the search as a TSV file. This can be imported into a suitable program, such as Microsoft Excel, for further investigation. *Note: 3D parameters are reported to two decimal places, and a maximum of 10 3D parameters per structure is permitted.*



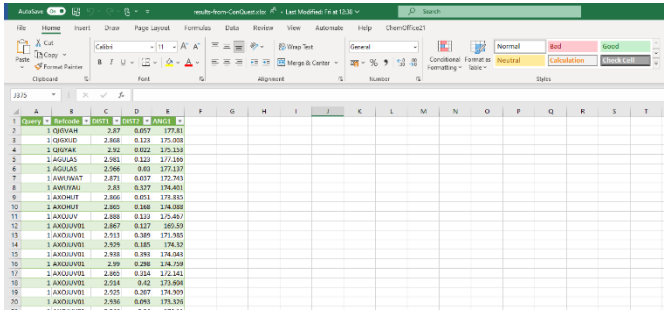
Conclusion

We have seen how to construct a substructure query using WebCSD, how to add 2D constraints to define aspects of the chemistry, and how to search for 3D data so that it can be extracted for further analysis. In this example, we have explored structural evidence for halogen bonding between aromatic iodides and non-bonded sp^2 nitrogen atoms.

Extension (optional)

1) Import the downloaded data into a suitable program, such as Microsoft Excel. Note that because there may be multiple measurement of interactions within the same structure, the number of items in the TSV file is expected to exceed the number in the list displayed in WebCSD.

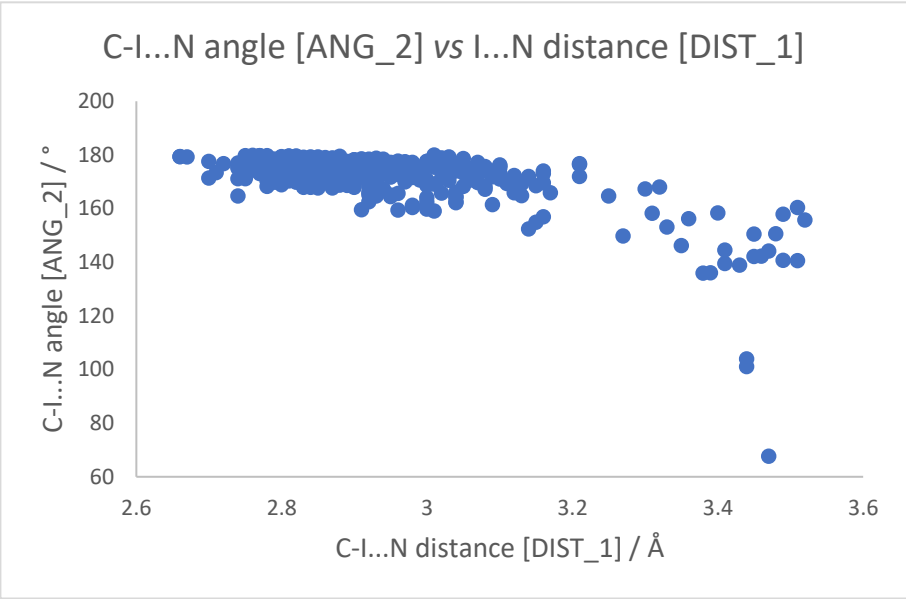
1

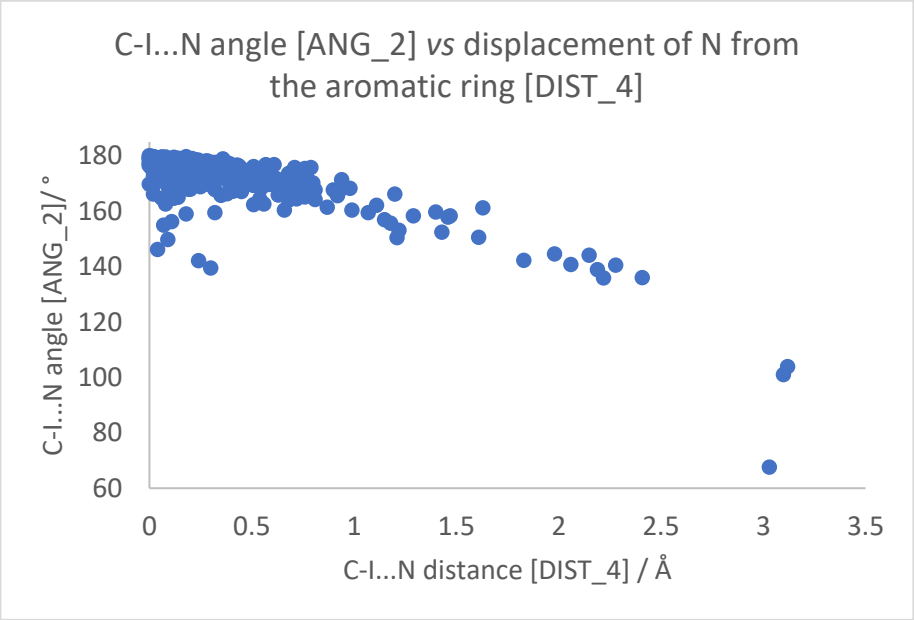


2) Investigate correlations within the data, for example by plotting the non-bonded N···I distance against the C—I···N angle. Also investigate any correlation between the displacement of N from the mean plane of the aromatic ring with the C—I···N angle. What can you conclude about the geometry of the N···I interactions?

Note: your results may look slightly different as the number of entries in the CSD changes daily.

2

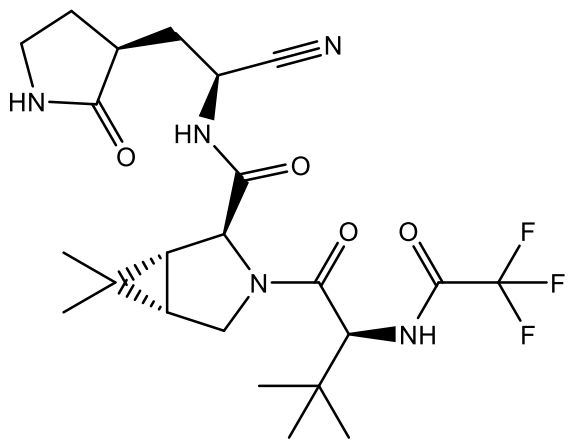




Example 2: Conducting a similarity search for pharmaceutically active molecules in the CSD

WebCSD offers the ability to conduct a *similarity search* using a molecular fingerprint generated from a structure, with the similarity evaluated based on the *Tanimoto coefficient*. Hits are returned if the Tanimoto coefficient is 0.7 or above.[3]

The drug nirmatrelvir is an orally-active C3-like protease inhibitor which is a component of Paxlovid, a combination drug developed by Pfizer for the treatment of SARS-CoV-2 infection.[4] The structure of Nirmatrelvir has recently been reported (CSD entry ZIVMEA). In this example, we will uncover structurally similar compounds which may potentially also have biological activity, using a WebCSD Similarity search.



The molecular structure of nirmatrelvir.

1. Open a web browser and navigate to the Access Structures webpage (https://www.ccdc.cam.ac.uk/structures/) if you do not already have WebCSD open. If you have already run a search, click **New Search** at the top.

2. Click on the **Structure Search** tab to bring up the sketcher. You can drag the periodic table to reposition it in a convenient area.

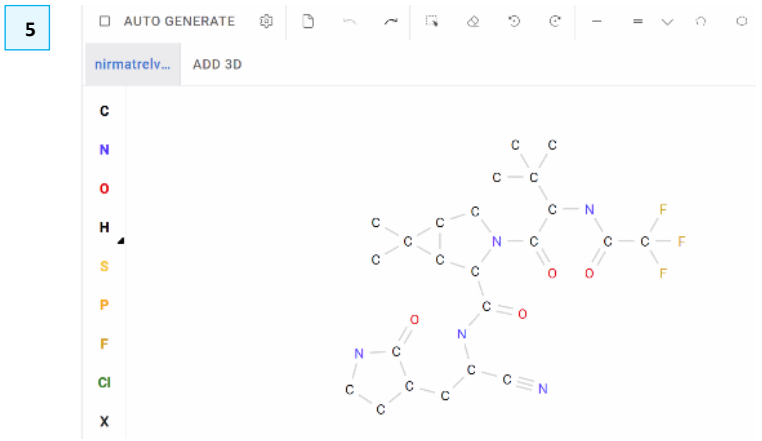
3. Rather than drawing the structure of Nirmatrelvir, we will upload a MOL file which has been prepared for this workshop using the program ChemDraw. Download the MOL file from here if you have not already done so. *Tip: If you are exporting your own file from ChemDraw, it is not necessary to explicitly draw hydrogen atoms, they will be automatically added during a similarity search.*

[3] I. R. Thomas, I. J. Bruno, J. Cole, C. F. Macrae, E. Pidcock and P. A. Wood, *J. Appl. Crystallog.*, 2010, **43**, 362 – 366.

[4] S. M. R. Hashemian, A. Sheida, M. Taghizadieh, M. Y. Memar, M. R. Hamblin, H. B. Baghi, J. S. Nahand, Z. Asemi and H. Mirzaei, *Biomed. Pharmacother.*, 2023, **162**, 11467 – 11475.

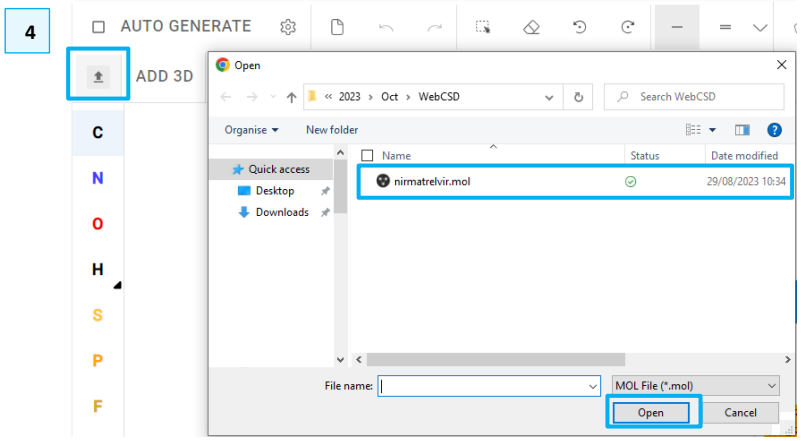
4. In the top toolbar in the sketcher window, click the upwards arrow  to launch the file explorer and select *nirmatrelvir.mol* and click **Open**.

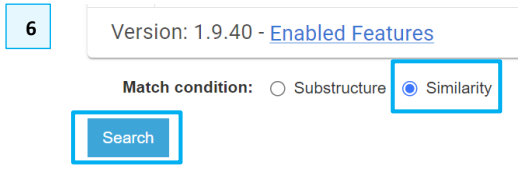
5. The cursor will now show the outline of the molecule. Move to a suitable position in the sketcher and click once to add the molecule.

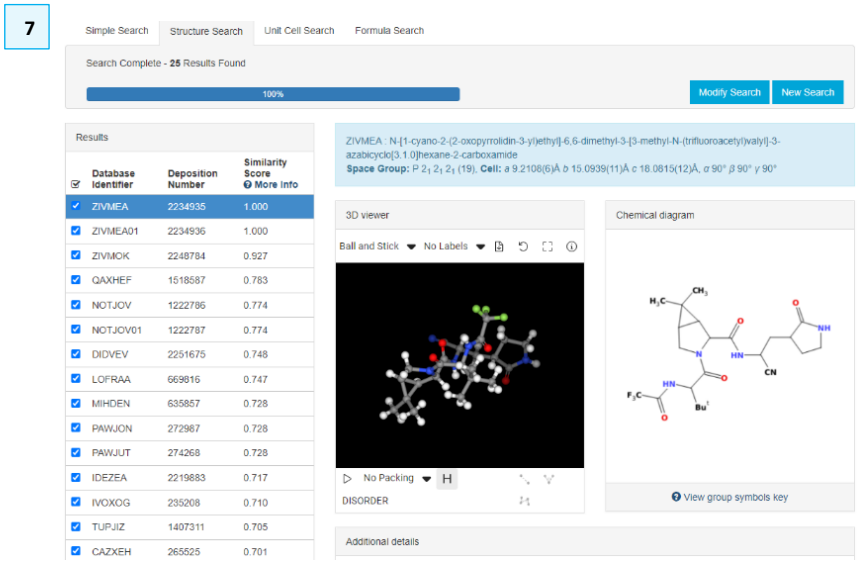


6. Ensure that the **Similarity** radio button is turned on and click **Search**.

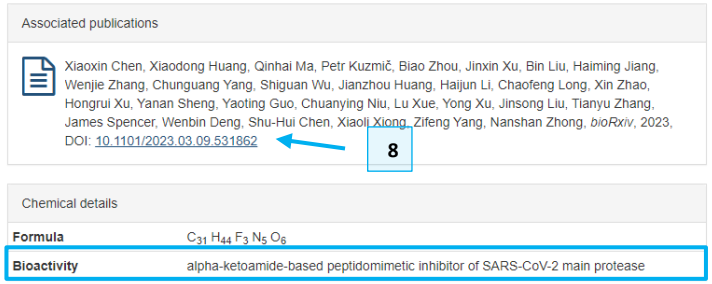
7. A new page will load showing the results, listed with their refcode and similarity score on the left-hand side, and information about the currently selected entry. Scroll through the results and notice how the information and viewer is updated as you do so.







8. There should be at least 25 hits retrieved. Note that hits are only returned when the similarity score is 0.7 or above. CSD entries ZIVMEA and ZIVMEA01 have perfect scores of 1.000 because they are identical to the query. Scroll through the results and study the *Chemical details* section to look for *Bioactivity* information. You should find that a couple of results are flagged as bioactive; one of them, CSD entry DIVDEV, is in fact another SARS-CoV-2 protease inhibitor. You can click the DOI link in the *Associated publications* section to explore this result further.



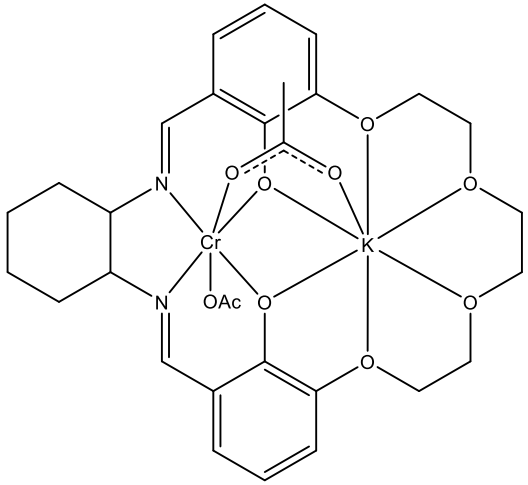
Conclusion

Similarity searching is a useful way to search the CSD for compounds which are likely to have related properties and is available exclusively via WebCSD. In this example we have uncovered an example of a compound in the CSD with similar pharmacological activity to a currently marketed SARS-CoV-2 treatment drug by conducting a similarity search.

Example 3. Discovering catalysts using a formula search

A WebCSD formula search offers a quick way to find compounds with a specific chemical composition, as well as to discover related compounds containing specific elements. The latter is particularly useful for transition metal complexes where related structures may have different ligands despite containing common metal atoms or ions.

A *bimetallic* catalyst was reported to selectively deliver poly(dithiocarbonates) from CS_2 and oxetanes.[5] However, the crystal structure of the catalyst was not determined. We will search for potential structural motifs for the catalyst in the CSD based on formula.



2D structure of the polymerisation catalyst reported in reference 5.

We will search for bimetallic compounds which contain at least one chromium and one potassium atom.

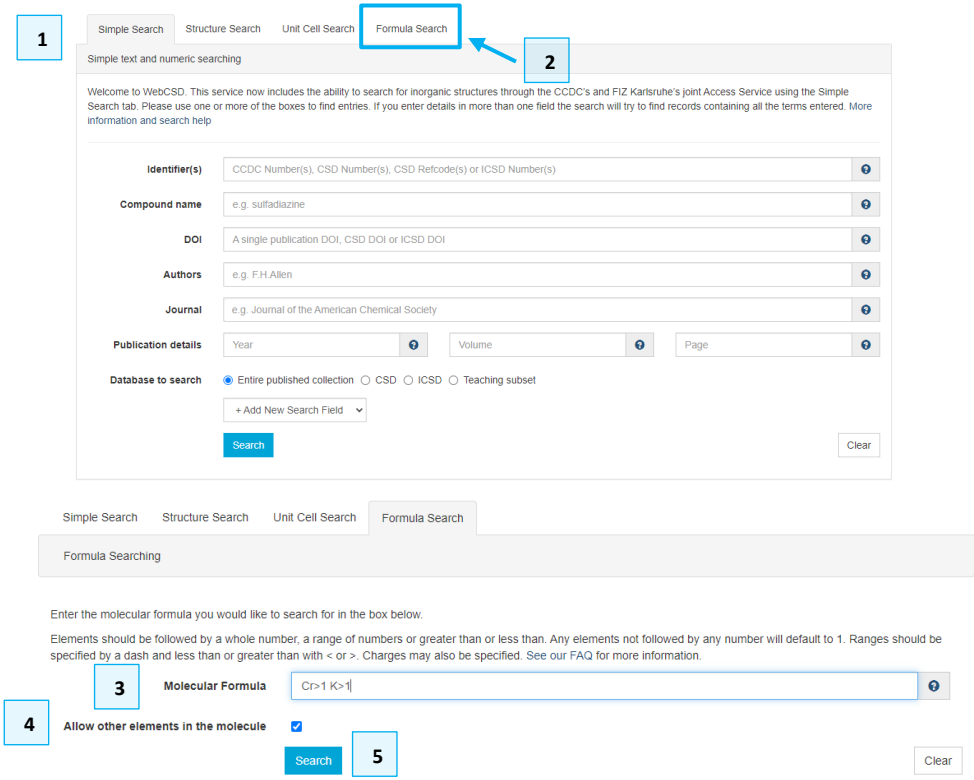
1. Open a web browser and navigate to the Access Structures webpage (https://www.ccdc.cam.ac.uk/structures/) if you do not already have WebCSD open. If you have already run a search, click **New Search** at the top.

2. Select the **Formula Search** tab.

3. In the *Molecular formula* box type "Cr>1 K>1". This specifies that there will be at least two chromium atoms and two potassium atoms in the curated molecular *formula unit*. Make sure there are no spaces between the element symbol, inequality sign and the number.

4. Tick *Allow other elements in the molecule*. This allows for any of the remaining elements that may be present in the ligand(s).

5. Click **Search**.



[5] C. Fornacon-Wood, B. R. Manjunatha, M. R. Stühler, C. Gallizioli, C. Müller, P. Pröhm and A. J. Plajer, *Nat. Commun.*, 2023, **14**, No. 4525.

6. A new page will load showing the results (the refcodes are listed on the left-hand side) and information about the currently selected entry. There should be at least 25 records returned. Scroll through the results and notice how the information and viewer is updated as you do so. You should notice that there are at least four entries with similar structures to the complex on the previous page.

7. You can explore these results further by following the DOI link in the *Associated publications* section. For example, CSD RIPCUS is an earlier structure reported by the same research group.

8. Click **Modify Search** or **New Search**.

9. In the *Molecular Formula* box, enter "Cr1 K1-2". This tells WebCSD to look for complexes which contain one chromium and one to two potassium atoms per formula unit.

10. Click **Search**.

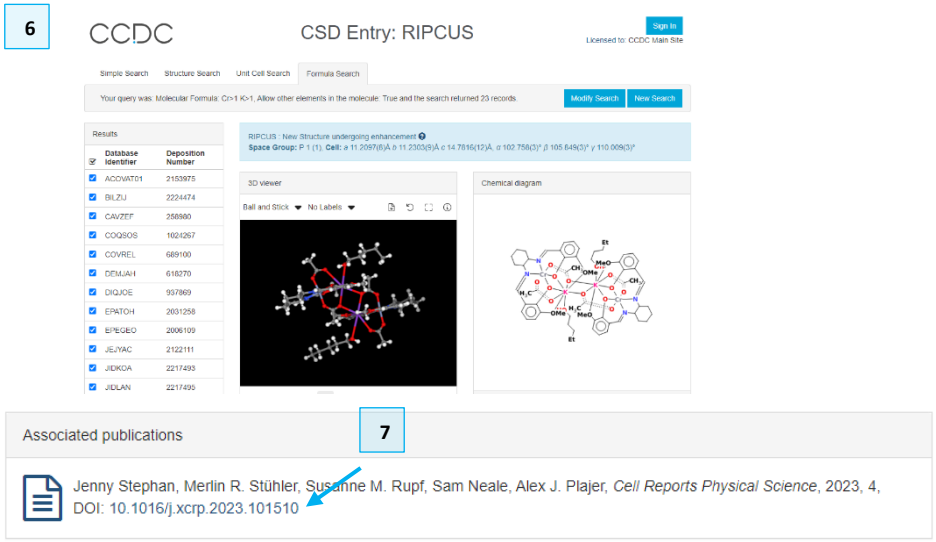
11. You should find at least 88 search records returned. Browse through these to compare them with previous results.

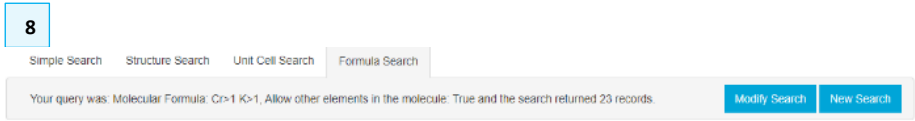
Conclusion

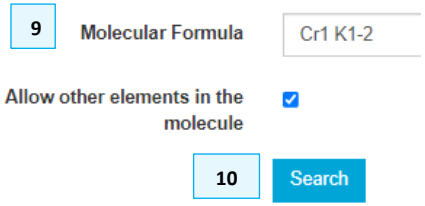
In this example, we have seen how to make use of several options for formula searching in WebCSD to uncover bimetallic complexes which may be of interest for catalytic applications by specifying elements that must be present and placing constraints on their occurrence in the molecular formula.

Extension (optional)

Use the formula search to explore other bimetallic complexes where potassium is switched for other alkali metals.



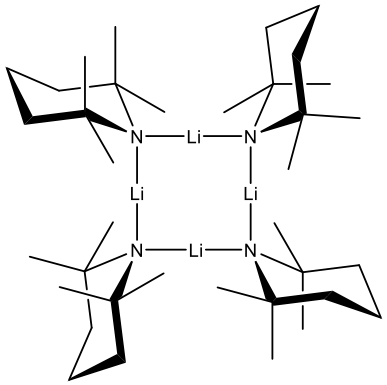




Example 4. Unit cell searching with WebCSD

In an X-ray diffraction experiment, a *unit cell* search is often a convenient way of checking whether a data set has been published before the full experiment is undertaken, potentially saving time and resources. In this example, we will see how the WebCSD Unit Cell search feature can be used to confirm that a lithium-containing structure has already been published in the CSD. Lithium-containing by-products are common in many reactions; therefore, it is usually advisable to screen for these before devoting resources to a full experiment.

Lattice centring may not always be reliably determined prior to data collection therefore it is advisable to search for a *reduced cell*.



Putative amidolithium compound, CSD entry BUXNUD.

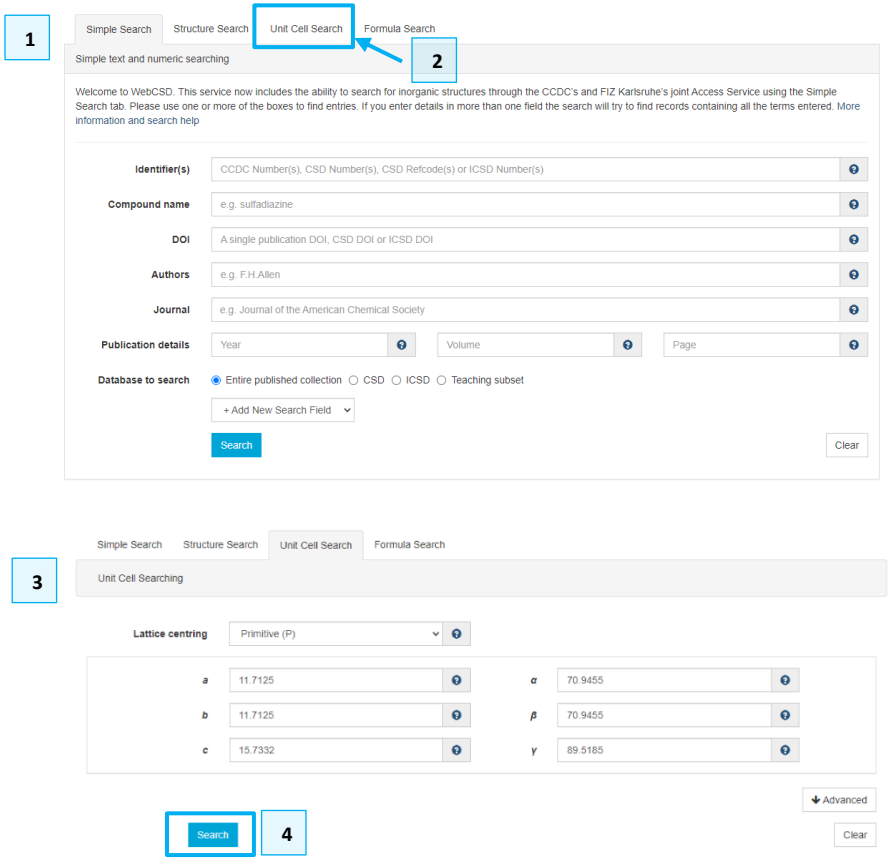
---

1) Open a web browser and navigate to the Access Structures webpage (https://www.ccdc.cam.ac.uk/structures/) if you do not already have WebCSD open. If you have already run a search, click **New Search** at the top.

2) Navigate to the **Unit Cell Search** tab.

3) The reduced cell for the putative lithium compound is *a* = 11.7125, *b* = 11.7125, *c* = 15.7332; α = 70.9455, β = 70.9455, γ = 89.5185. Enter these values in the relevant boxes and select the lattice centring as primitive (P).

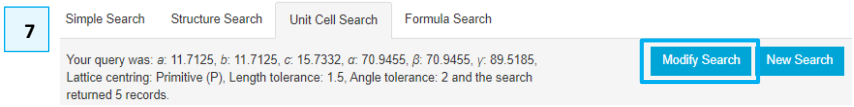
4) Press **Search**.



5) A new page will load showing the results (refcode listed on the left-hand side) and information about the currently selected entry. There should be at least 5 records returned. Scroll through the results and notice how the information and viewer is updated as you do so. The refcode family BUXNUD corresponds to the putative structure. Notice that CSD entry JUJCOI is an isostructural compound with copper in place of lithium.

6) Scroll down to the *Chemical details* and *Crystal details* to confirm that the physical and chemical properties match those expected for the target compound.

7) We can refine the results further by decreasing *Length tolerance* and *Angle tolerance* in the search. Click **Modify search** to return to the search setup.



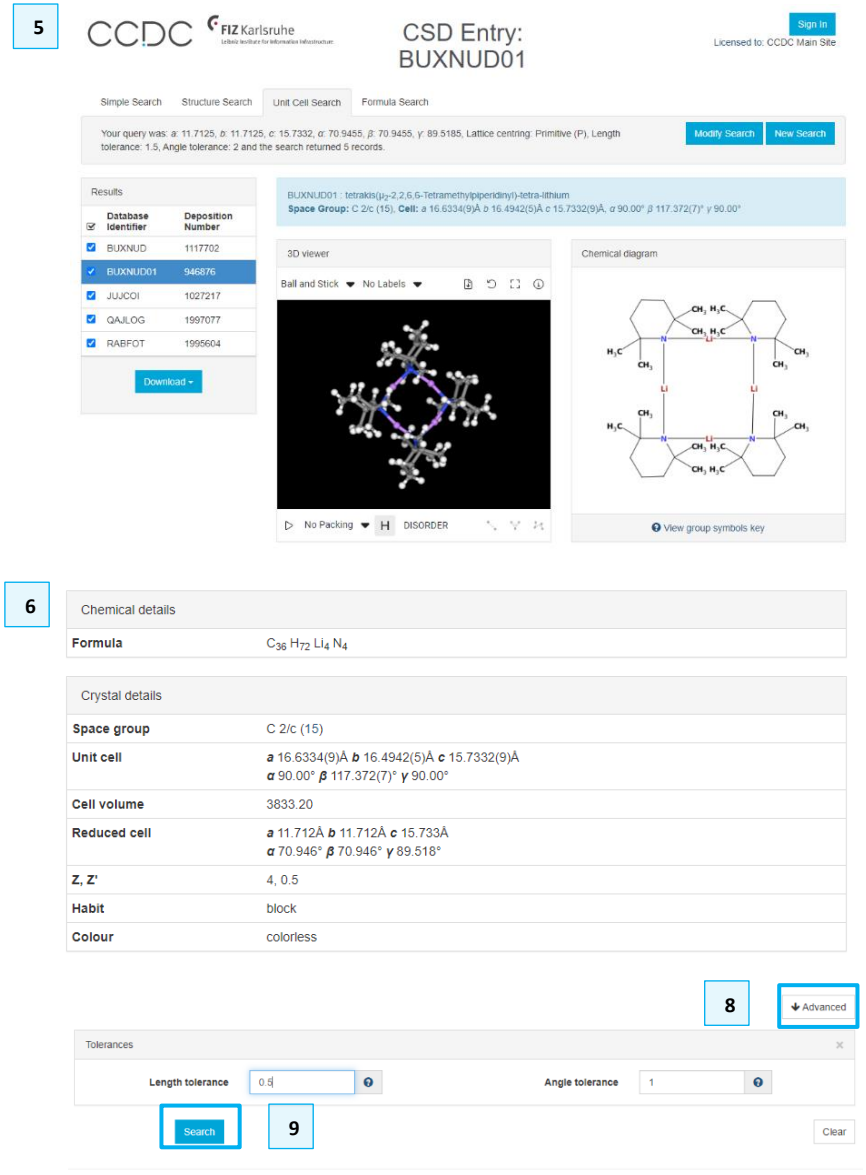
8) Click on the **Advanced** button to bring up the *Tolerances* options. Reduce the *Length tolerance* to "0.5" and the *Angle tolerance* to "1". Hover over the symbol ? to reveal the units.

9) Click **Search**.

10) This time, a single result, only BUXNUD01 is returned. You may wish to experiment with the *Tolerances* to find the optimum number of results.

Conclusion

This example demonstrated that the unit cell searching feature in WebCSD is a fast and convenient way to retrieve crystallographic information, and particularly to screen a putative crystal structure which may already be published. The search can be customised to allow for the precision of the determined unit cell.



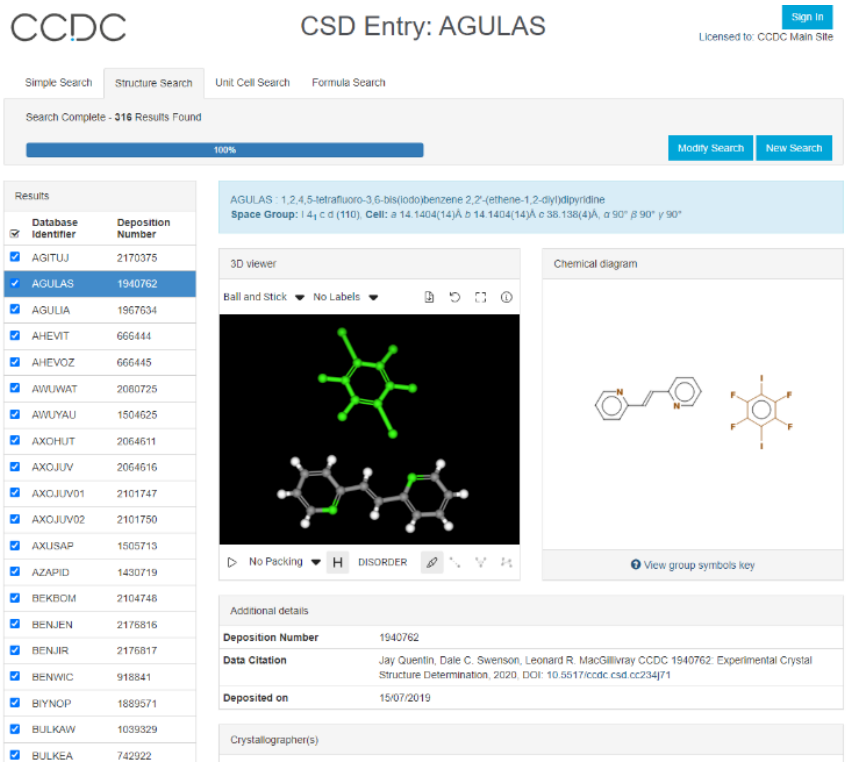
Summary

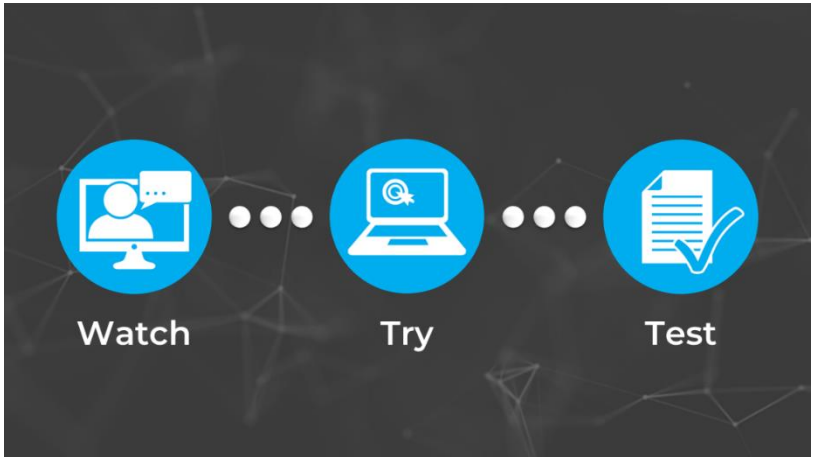
In this workshop you have explored the search options that are available with WebCSD. You should now be confident in:

- Creating substructure and similarity searches.
- Defining 2D and 3D search parameters.
- Searching for compounds by chemical formula, including defining variable atom counts.
- Conducting a unit cell search, including customising the tolerances of the metric parameters.

Next steps

Now that you have completed the Try part of this CSDU module, you can head to the final part: the quiz! Go back to the module webpage (https://www.ccdc.cam.ac.uk/community/training-and-learning/csdu-modules/csdu-webcsd-searching-101/) and follow the instructions to complete the final test and earn a completion certificate.





Glossary

Bimetallic
A bimetallic complex contains two metal centres which may be of the same type or different (heterobimetallic).

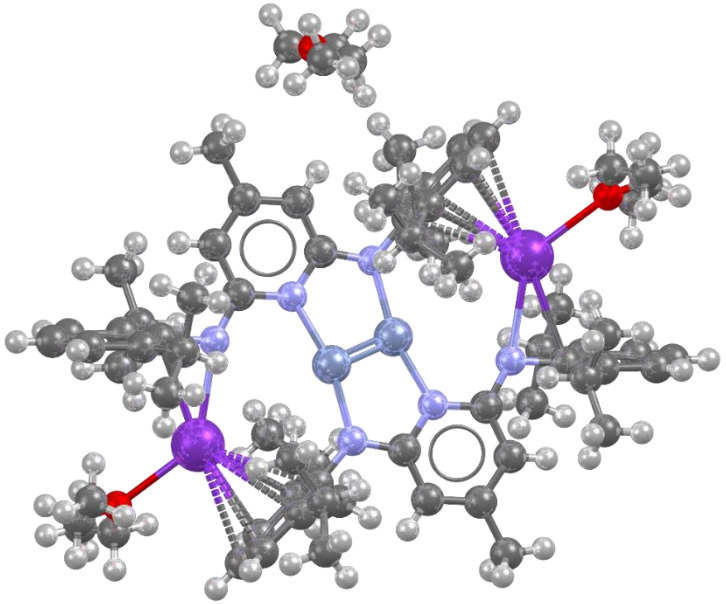
CIF
A Crystallographic Information File. This is the standard file format for crystallographic data. Further information about this format can be obtained from the IUCr website here (https://www.iucr.org/resources/cif) and from the CCDC website here (https://www.ccdc.cam.ac.uk/community/access-deposit-structures/deposit-a-structure/guide-to-cifs/).

Formula unit
In WebCSD, a formula unit refers to an individual molecule or ion within a structure.

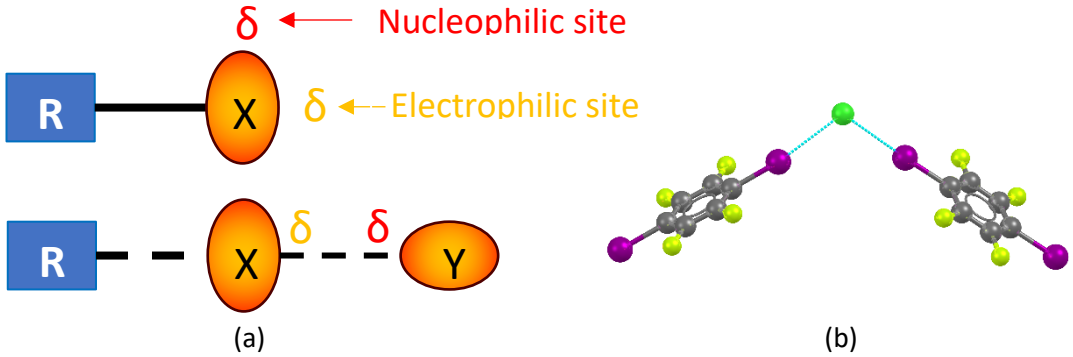
GCD
A GCD file contains a refcode list which can be read into programs such as Mercury and ConQuest.

Halogen bond
A halogen bond occurs when there is evidence of a net attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another, or the same, molecular entity. [IUPAC definition, *Pure Appl. Chem.*, 2013, **85**, 1711–1713].

Schematically, the halogen bond can be represented as R—X···Y, where the entity R—X, where X is any halogen atom with an electrophilic region, is designated the halogen bond donor, whilst Y, the entity with the nucleophilic groups, is called the halogen bond acceptor.



A bimetallic (or strictly, heterobimetallic) species from CSD Entry TIFPAB.



(a) Schematic illustration of a halogen bond involving donor group R—X and acceptor group Y. (b) Halogen bond between an aromatic C-I group and Cl^- in CSD Entry OHOVUD.

In a typical halogen-bonded complex, R—X···Y, the interatomic distance X···Y tends to be less than the sum of the van der Waals radii, the R—X bond is usually extended relative to unbonded R—X, and the R—X···Y angle tends to be close to 180°.

Intermolecular contact

An intermolecular contact is simply a contact between two different molecules. Usually, it connotes non-covalent interations, such as intermolecular hydrogen or halogen bonding interactions.

Lattice centring

When the unit cell does not reflect the symmetry of the lattice, it is usual to refer to a 'conventional', non-primitive basis instead of a primitive basis. This is done by adding lattice nodes at the centre of the unit cell or one of the three faces. The conventional lattice centrings are primitive (*P*), A-face centred (*A)*, B-face centred (*B*), C-face centred (*C*), body centred (*I*), all-face centred (*F*) and rhobohedrally centred (*R*).

Mean plane

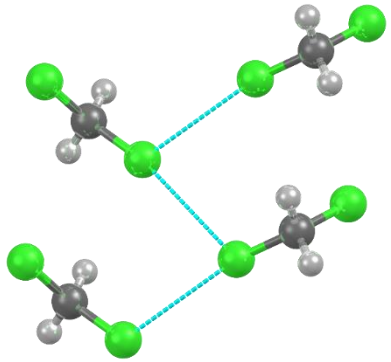
A plane in which the average squared radial distance of the atoms to the plane is minimised.

MOL

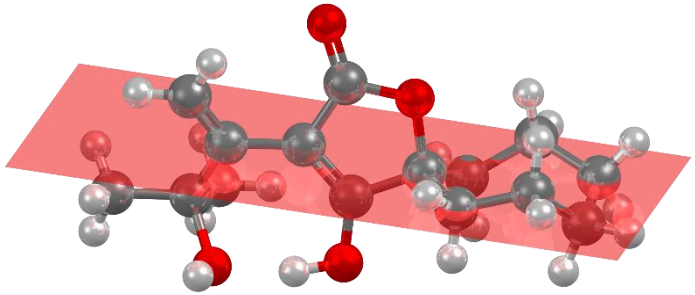
A MDL Molfile (.mol) is a file format for holding information about the atoms, bonds, connectivity and coordinates of a molecule.

Reduced cell

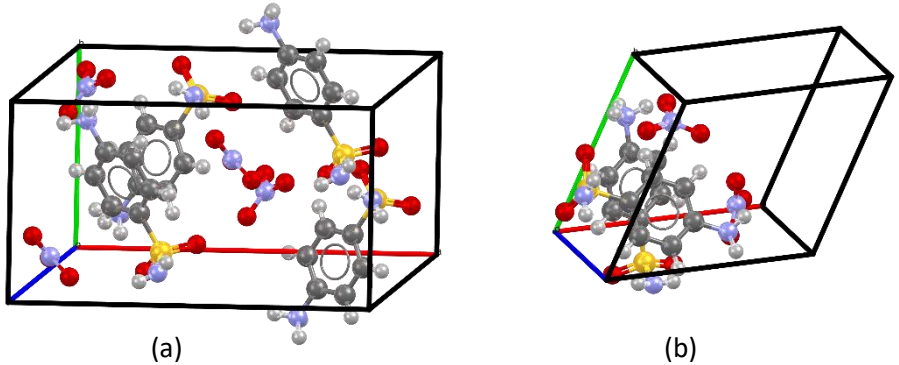
A parallelepiped whose sides are the reduced basis vectors (**a**, **b** and **c**). It is a primitive cell; there can be no lattice vectors shorter than **a**; of those not directed along **a**, none is shorter than **b**; and of those not lying in the ab plane, none is shorter than **c**. The angles between the vectors are either all acute or all obtuse. See https://dictionary.iucr.org/Reduced_cell for further information.



The solid-state structure of dichloromethane (CSD Entry DCLMET10) displaying intermolecular Cl···Cl



The mean plane defined by the seven carbon atoms of the cycloheptane ring in CSD Entry VODDUN.



(a) (b)

(a) The conventional C-centred monoclinic unit cell of CSD Entry ABADOY and (b) the reduced unit cell of the same structure.

Similarity search

A search based on the calculation of similarity between molecules in two dimensions determined by chemical features including atom types, bond types, and bonded paths through the molecule referred to as a 'fingerprint'. The fingerprint is compared with all the unique connectivities in the CSD and the similarity is evaluated with a similarity coefficient. See also *Tanimoto coefficient*.

Substructure

A substructure is a part or section of a whole molecule.

Tanimoto coefficient

In a *similarity search*, the Tanimoto coefficient is the ratio of the number of features common to both molecules to the total number of features, i.e.

$$T(A,B) = (A \cap B)/(A + B - (A \cap B))$$

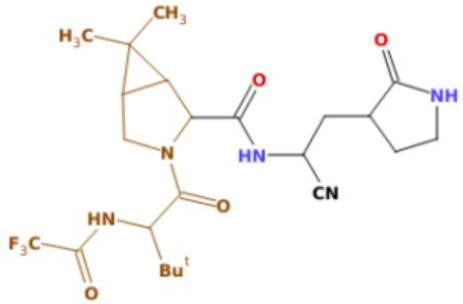
where *A* and *B* are the number of attributes of object *a* and *b*, respectively.

Unit cell

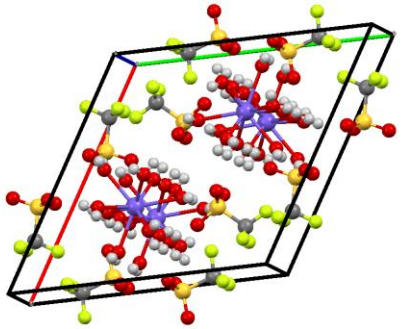
The unit cell is the basic building block of a crystal, repeated infinitely in three dimensions.

Van der Waals radius

The van der Waals radius of an element is one half of the distance between the closest approach of two non-bonded atoms of a given element.



Nirmatrelvir, CSD Entry ZIVMAE, with a substructure highlighted in brown.



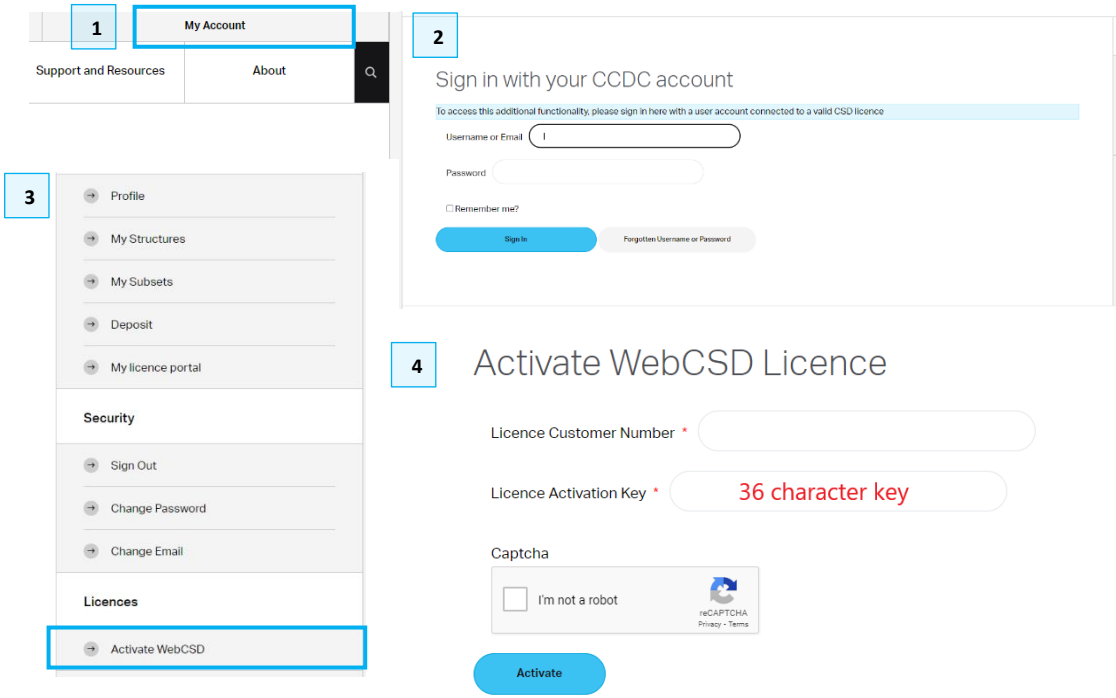
The unit cell of CSD entry YEVROH (with contents).

Activating WebCSD

To access the advanced WebCSD searching options, such as structure search and unit cell search, within the CSD web interface you will need to sign in to the site and connect a valid CSD licence. You can connect a CSD licence by either of the following methods:

- Accessing the CSD web interface from an IPv4 address registered to a CSD campus licence (we are unable to support IPv6).
- By entering a valid CCDC customer number and activation key once signed in. To do this you will need to:
  1. Go to My Account.
  2. Sign In or Register if necessary.
  3. Select "Activate WebCSD" under Licences on the right-hand side of the page.
  4. Enter your CCDC customer number and activation key.

The campus licence holder at your institution should be able to provide you with the CCDC customer number and activation key for your institution or they can provide us with the relevant IP addresses. If you are unsure of who this is or you are unsure if your institution has a licence then please contact us using our [enquiry pages (https://www.ccdc.cam.ac.uk/contact-us/)](https://www.ccdc.cam.ac.uk/contact-us/).



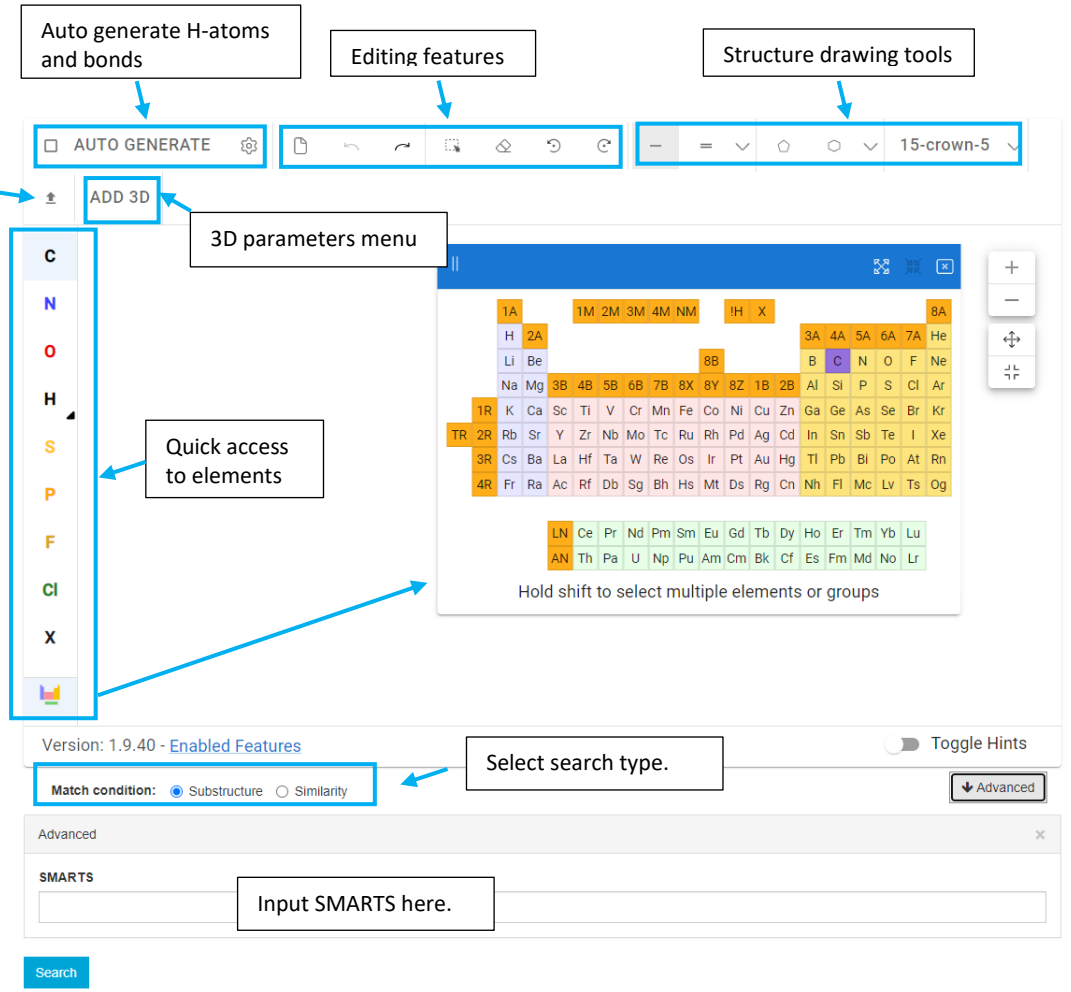
Basics of the WebCSD Sketcher

The WebCSD sketcher is the interface for creating substructure and similarity searches in WebCSD.

In the following we will see some of the basics of using the sketcher to create search queries.

In the WebCSD sketcher, we find:

1.
   - **Top left**: tools for automatic hydrogen and connection generation.
   - **Top middle**: tools to create new sketches, to edit and select parts of existing sketches and options to undo/redo operations.
   - **Top right**: tools to select bond types, simple ring drawing templates, and advanced templates.
2.
   - **Second line from the top**: button to upload a structure from a MOL file directly into the sketcher, and button to access the 3D parameters menu.
3.
   - **Left hand side toolbar**: quick access to elements and options for hydrogen placement, button to show/hide periodic the table. *Note: the periodic table is floating and can be repositioned using* **||**
4.
   - **Main window**: click here to add structure components (atoms and bonds) and click on atoms to select them to define 3D parameters.
5.
   - **Below sketcher**: options to select substructure or similarity search.
   - **Below sketcher**: options: advanced options – input SMARTS here.



Explanation of 3D parameters

3D parameter options are accessed from **ADD 3D**. To define a 3D parameter, you must select atoms. Shift + left mouse click to select multiple atoms.

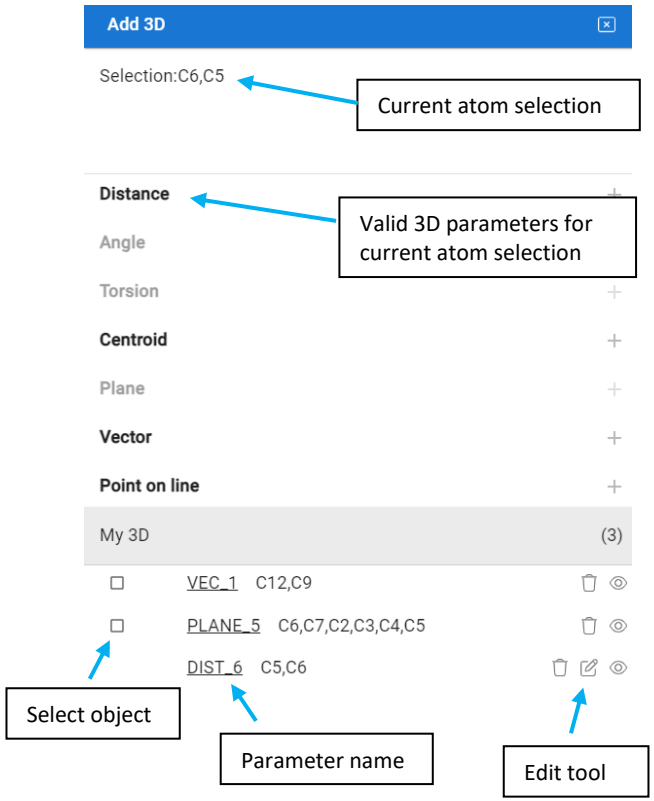
- Distances require exactly two atoms.
- Angles require exactly three atoms, in the correct sequence.
- Torsions require exactly four atoms, in the correct sequence.
- Planes require a minimum of three atoms (the sequence does not matter).
- Centroids require a minimum of two atoms.
- Vectors and points on lines require two atoms (and the point on the line requires a distance of extension from the tip of the vector defining the line).

It is possible to define 3D parameters involving other defined geometric objects. For example, with a vector and a plane defined, the angle between them may also be defined.

The Add 3D menu consists of:

1. Currently selected atoms.
2. Choice of 3D parameters to define. Valid parameters for the atoms selected are in black; non-valid ones are greyed out.
3. List of defined parameters and geometric objects, which may be edited by selecting the pen tool (geometric objects may be selected using the tick box).

To add a parameter, click the **+** icon next to a valid option.



Certain 3D parameters may be constrained:

- Distances may be constrained to be intramolecular or intermolecular, or any type, within a specified range.
- Angles and torsions may be constrained within a specified range.

To add a constraint, move the slider to constrained and enter the desired values.