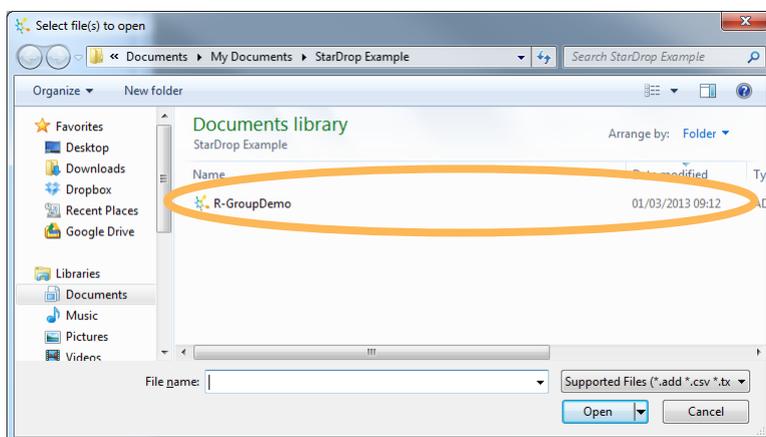


Worked Example:

R-Group Analysis

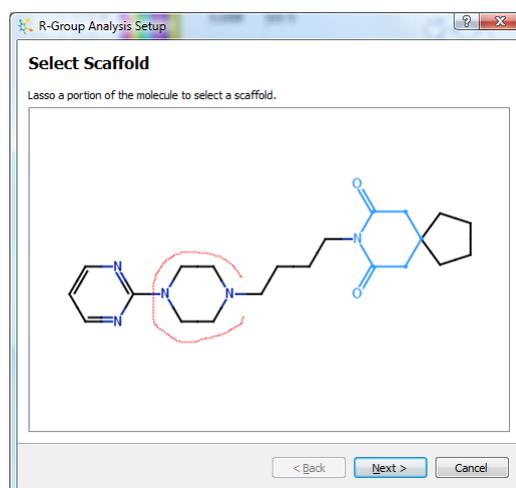
In this example we are going to take a look at an R-Group analysis of a data set containing Buspirone and some close analogues to identify functionalities which are influencing potency.

- Start StarDrop from the Start menu.
- Open the file **R-GroupDemo** by using the **File -> Open** menu option.



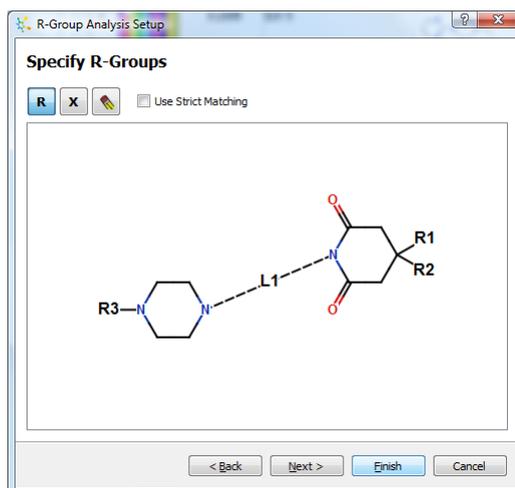
Select the first row (Buspirone) and start the R-Group analysis wizard by clicking the button on the toolbar (it is also available from the **Tools** menu).

- The selected molecule is displayed in the wizard so that you can now choose which regions of the molecule make up the scaffold.
- Select the two ring functionalities indicated in the screenshot below by drawing around them to lasso the area, holding down the **Shift** or **Ctrl** button to select a second region.



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- Click **Next** to confirm the R-Groups that will be analysed. In this example, because we selected two separate regions, the connecting functionalities will be considered to be variations in linkers.

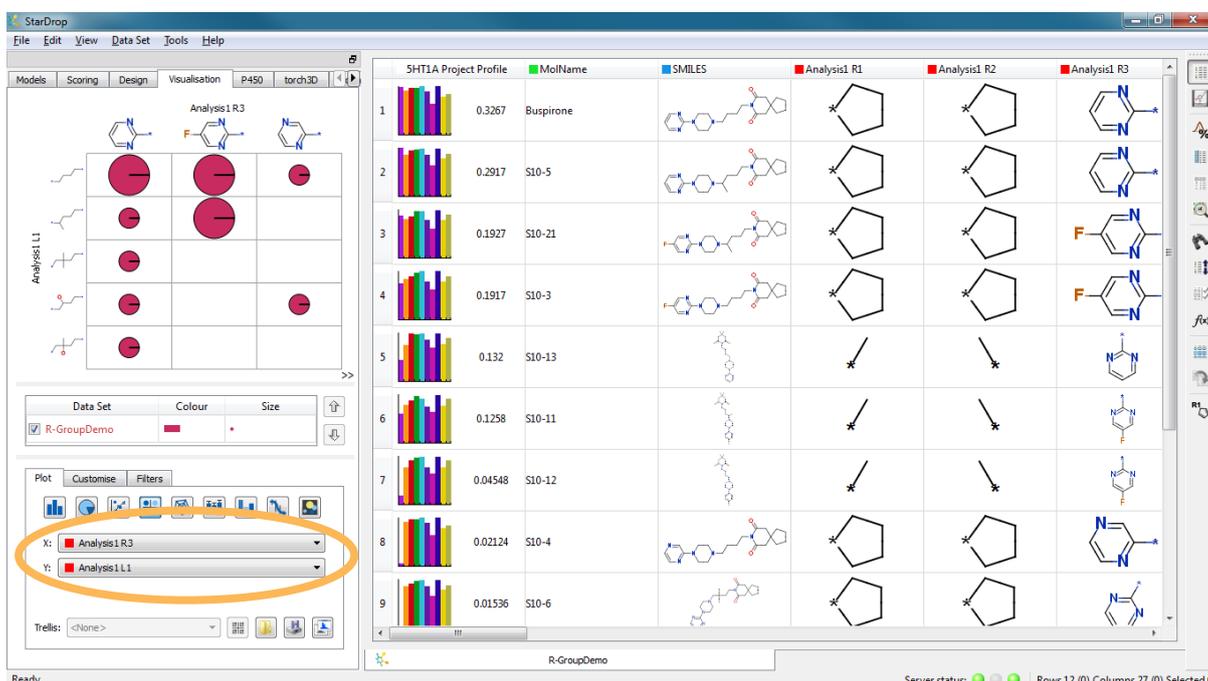


Please note that you can add R-Groups by clicking the  button and then clicking at the point on the scaffold where they should be analysed. If you wish to specify variable atoms or fragments, click the  button and then select atoms on the scaffold which may vary between the compounds being analysed. In this case, no additional R-groups, variable atoms or fragments are required.

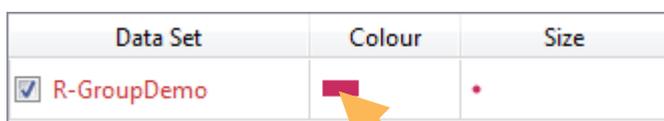
- Click the **Finish** button and new columns will be added to the data set indicating the R-Groups and linkers that have been found for each compound.

5HT1A Project Profile	MolName	SMILES	Analysis1 R1	Analysis1 R2	Analysis1 R3
1	0.3267	Buspirone			
2	0.2917	SI0-5			
3	0.1927	SI0-21			
4	0.1917	SI0-3			
5	0.132	SI0-13			
6	0.1258	SI0-11			
7	0.04548	SI0-12			
8	0.02124	SI0-4			
9	0.01536	SI0-6			

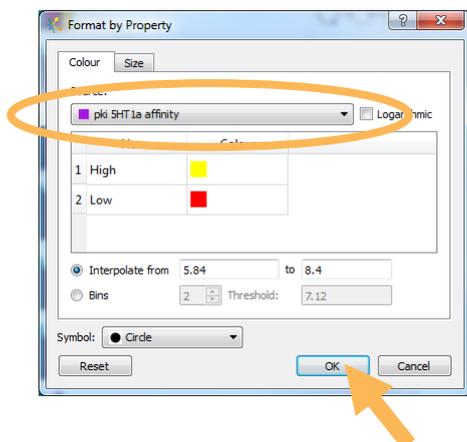
- Hover over any of the R-Groups to see a pop-up of the scaffold. To keep a scaffold window open, right-click on the R-Group column header and choose **View Scaffold**. This window can be docked in the tabbed area and if you have more than one analysis in your data set the displayed scaffold will change to show the scaffold associated with the selected R-Group column at any given time.
- You can visualise the SAR in the series using the visualisation tools in StarDrop. Change to the **Visualisation** tab, select a SAR plot by clicking the  button and choose **Analysis1 R3** from the **X:** drop-down menu and **Analysis1 L1** from the **Y:** drop-down menu. This will display an SAR table of R3 against L1 as shown below:



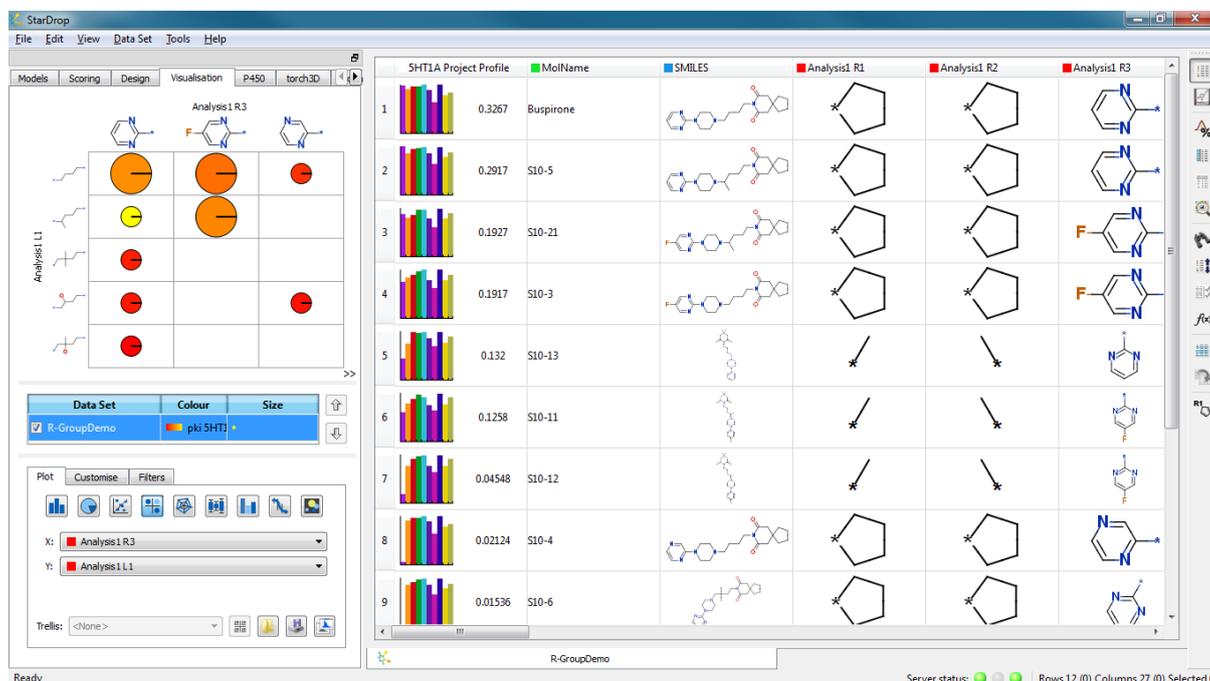
- You can colour the SAR plot by different properties. For example, to colour the plot by the **pKi 5HT1a affinity** values in the data set, click on the block of colour next to the 'R-GroupDemo' in the key, as shown below, to bring up the **Format by Property** dialogue.



- In the resulting dialogue, change the **Source** for the colour to **pki 5HT1a affinity** and click **OK**.

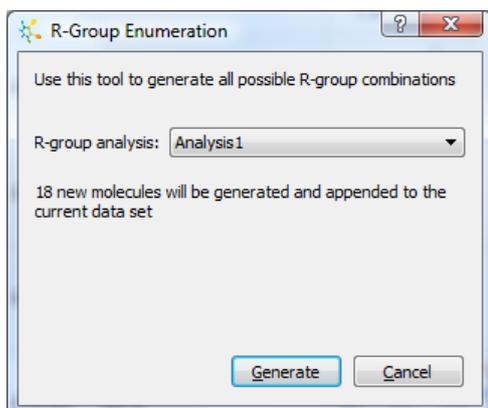


- The compounds with the highest pK_i s will be highlighted yellow, the lowest red. The size of the circles indicates the number of compounds which contain those groups.



- You can also change the size of the circles according to another property by clicking on the circle under **Size** in the key and there are many other ways to view your data, for example by plotting pie charts, histograms or radar plots in the SAR table. Click on **Customise** to see some of these options.
- Other visualisations can be plotted by selecting an R-Group column on its own or in combination with a property. Feel free to explore!
- Finally, StarDrop can 'fill in' the missing combinations of R-groups and linkers that are not present in the series, helping to explore other, potentially interesting, compounds. To do

this, right-click on one of the R-Group column headers to choose **R-Group Enumeration...** from the menu



This will estimate the number of new compounds that will be generated

- Click **Generate** and the new compounds will be added to the data set and their predicted properties automatically calculated.