Structure Searching in CrossFire Beilstein

DiscoveryGate[SM]
Version 1.4
Participant's Guide

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TABLE OF CONTENTS

STRUCTURE SEARCHING IN CROSSFIRE BEILSTEIN

REFERENCE

Structure Searching in CrossFire Beilstein

Key points

- Welcome to the *Structure Searching in CrossFire Beilstein* module.
- In this module, we will search the Beilstein database through DiscoveryGate using the MDL Database Browser.

Notes

Module objectives

- Conduct an exact structure search
- Conduct a substructure search
- Apply query features to atoms and bonds
- Use links to obtain information
- Conduct a stereochemical search
- Review the search history, save a list, and create a report

Key points

- In this module, you will learn the how to conduct an exact, substructure, and stereochemical search.
- You will learn how to apply query features to atoms and bonds.
- You will learn how to access information for the retrieved compounds using internal links.
- You will save a list of results, review the search history, and create a report.

Notes

Search scenario

Use a core structure to conduct a series of searches, in the CrossFire Beilstein database, to answer the following questions. In the process, you will learn how to use the MDL Database Browser in DiscoveryGate.

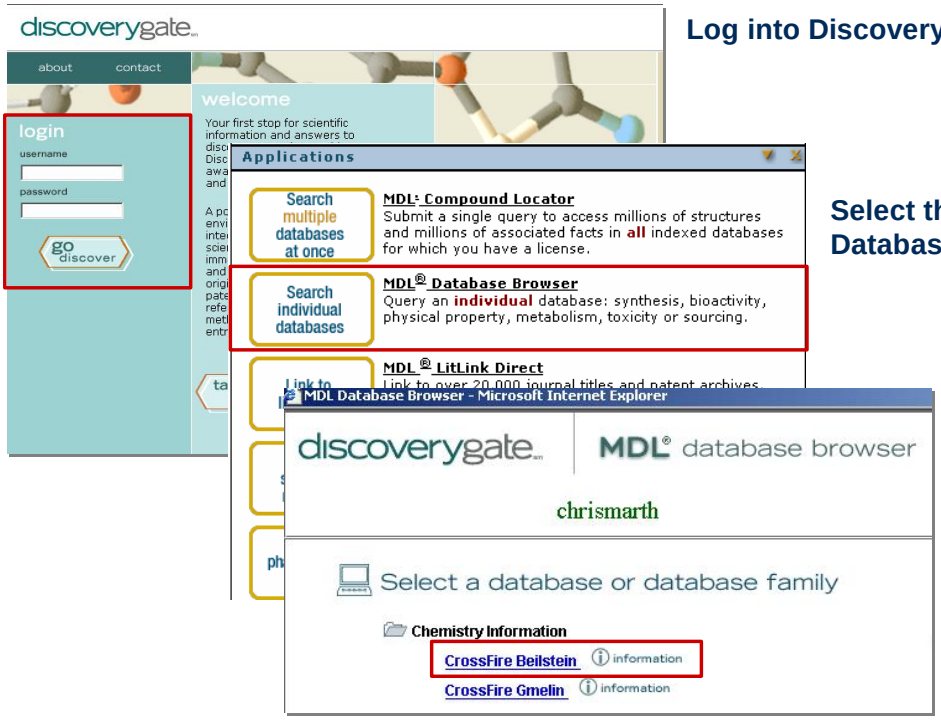
- Is this compound in the database and how do I retrieve it?
- Can I synthesize this compound?
- What other compounds contain the oxaziridine structure?
- How can I obtain any alkyl substituted oxaziridines?

Key points

- In this example, you will conduct a series of structure searches using oxaziridine as the core structure to answer the questions stated in the slide.
- Knowledge of the MDL Draw structure editor is required to successfully use this module.

Notes

Launch the application and database



Log into DiscoveryGate

Select the MDL Database Browser

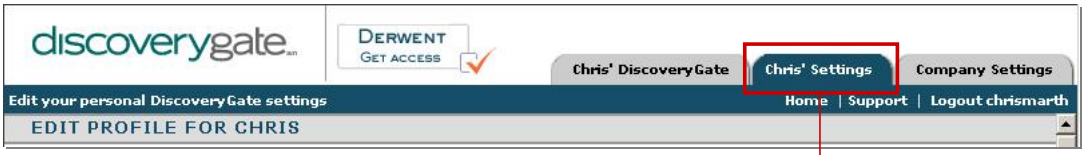
Select the CrossFire Beilstein database

Key points

- Launch the internet browser and enter the DiscoveryGate URL. To log in, enter your user name and password, and then click "go discover."
- DiscoveryGate uses the MDL Database Browser to search individual databases.
- CrossFire Beilstein is one of the individual database selections. It is an essential source of information for generating leads, planning syntheses, and determining bioactivity and physical properties.

Notes

Configure CrossFire access information



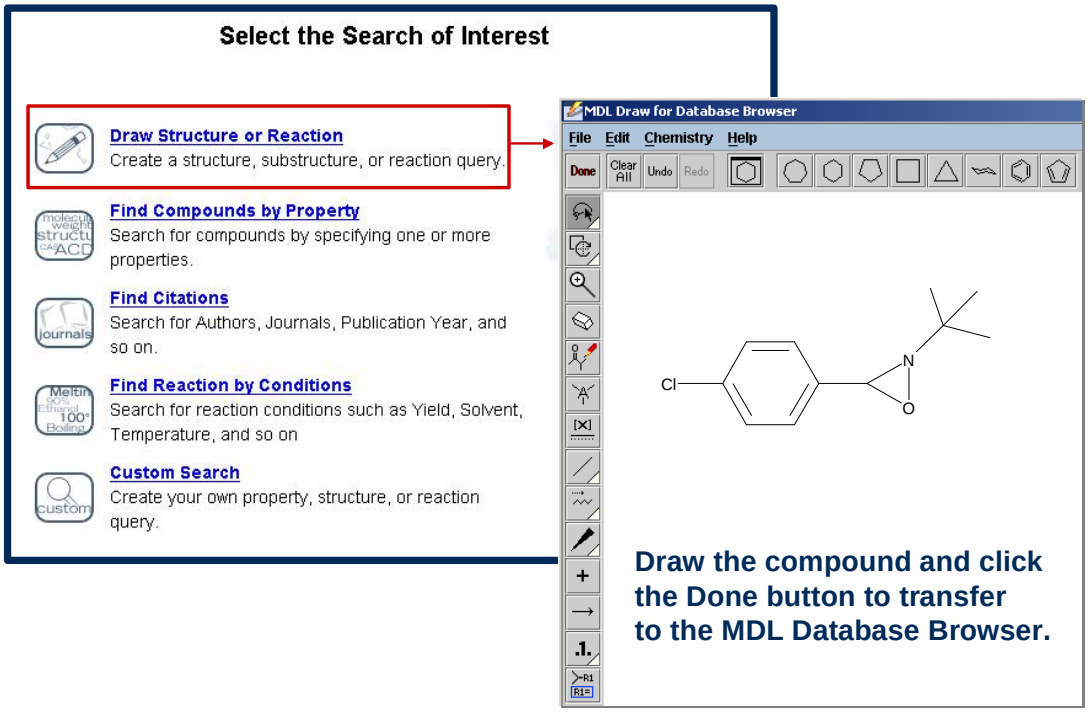
Configure the login information to access the Beilstein database.

Key points

- Prior to searching the CrossFire Beilstein database, you will need to enter the CrossFire login information.
- If this is not configured, return to the main screen and click the Settings tab. Enter your user name, password, and group for CrossFire Beilstein.

Notes

Create the structure query

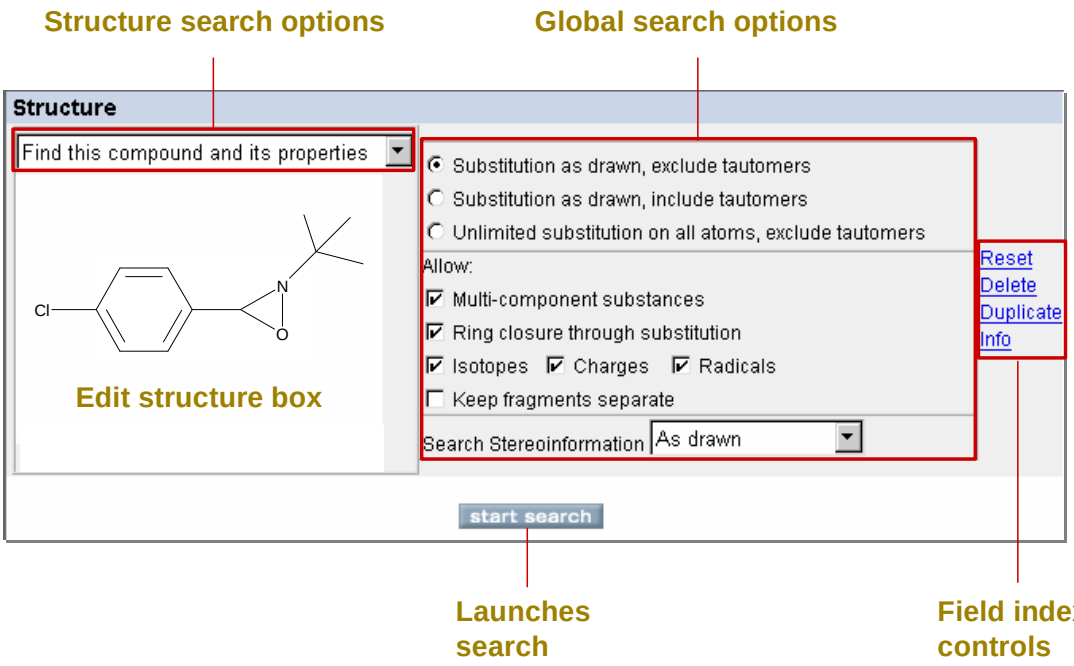


Key points

- Create your structural query using the MDL Draw structure editor.
- Drawing is not taught during this session. See the *Drawing Basics* module for complete instructions on creating structures and reactions.

Notes

Structure field index controls

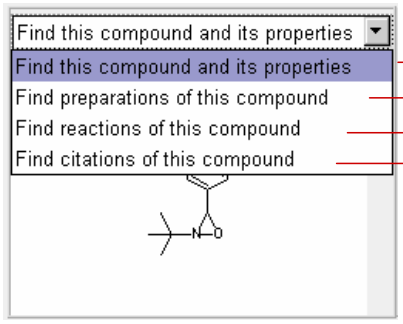


Key points

- The Structure field index has a series of structure search options and global search options that affect how the search will be conducted.
- There are structure controls that allow you to reset the default settings, delete structure or data fields and controls, duplicate data field and its controls, or access information in the help box.

Notes

Structure search options



Retrieves a list of molecules and associated properties for the compound specified.

Retrieves a list of reactions where the compound a product. Click the "Synthesize the Reactant" link for the preparation information.

Retrieves a list of reactions where the compound is either a reactant or a product.

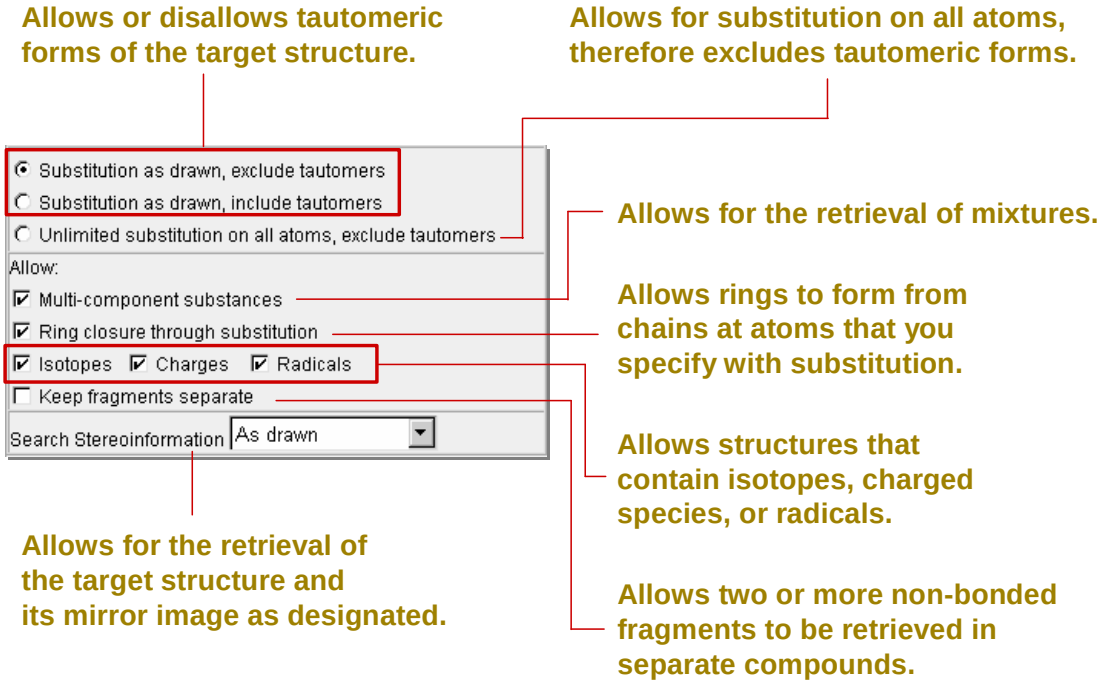
Retrieves a list of citations for the specified compound.

Key points

- "Find this compound and its properties" retrieves a list of molecules, based on the structure entered and the associated properties for that compound.
- "Find preparations of this compound" retrieves a list of reactions where the structure entered is a reactant.
- "Find reactions of this compound" retrieves a list of reactions where the structure entered is either a reactant or a product.
- "Find citations of this compound" retrieves a list of citations that reference the structure entered.

Notes

Global search options



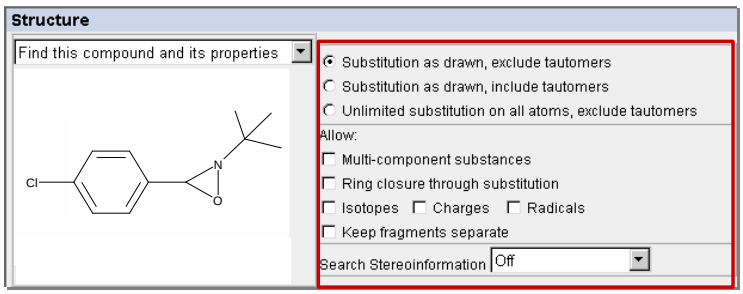
Key points

- The global search options directly alter the results of a structure search. The first two settings lock in the ability to accept substituents only at positions drawn directly onto the original structure query.
- Unlike the first two settings, the "Unlimited substitution on all atoms, exclude tautomers" setting allows for substitution on any atom that has an open valence.
- When the "Allow" boxes are checked, you allow the retrieval of structures that contain the specific designation.

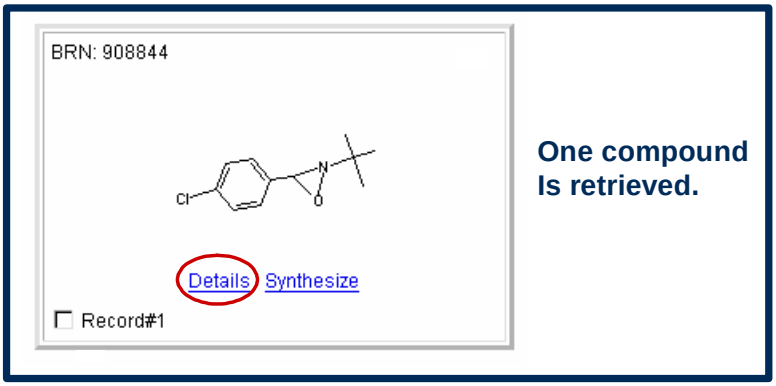
Notes

Exact match search query and results

Query:



Results:



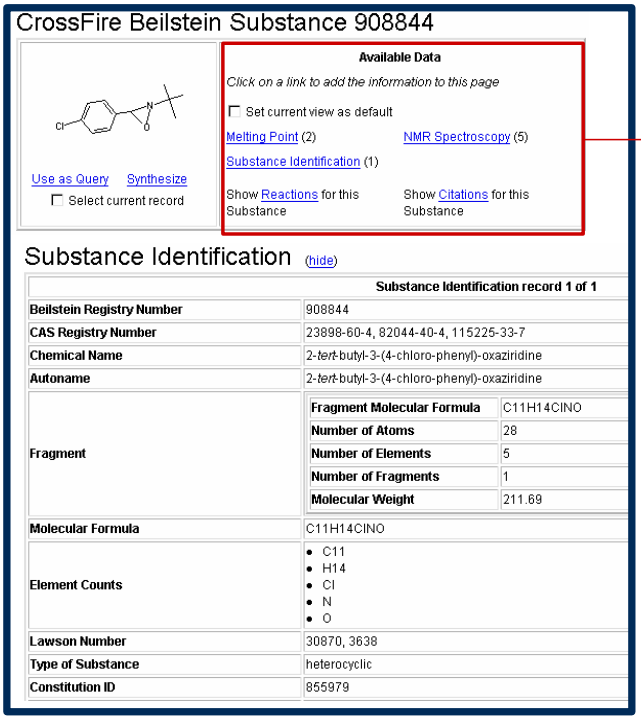
One compound Is retrieved.

Key points

- We spoke about the global search options. To retrieve an exact match of the structure, you must uncheck all the "Allow" options.
- You must also set the substitution to retrieve only what you have drawn.
- When the search is complete, you are automatically transferred to the Results form, and the search results are displayed in table format.
- To view the associated data, click the "Details" link.

Notes

Search details

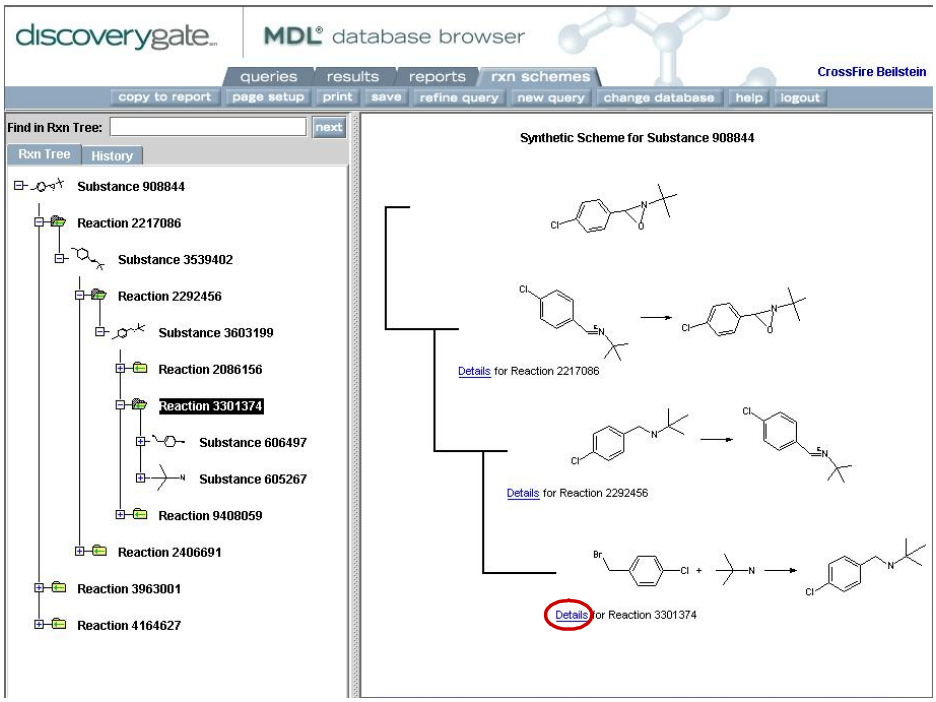


Key points

- When you click the "Details" link, the structure table is replaced with a detailed display of the data.
- The available data for the compound can be displayed by clicking the links for Substance (displayed by default), or any field found in the Available Data location. The additional information is added to the bottom of the display.

Notes

Can I synthesize the compound?

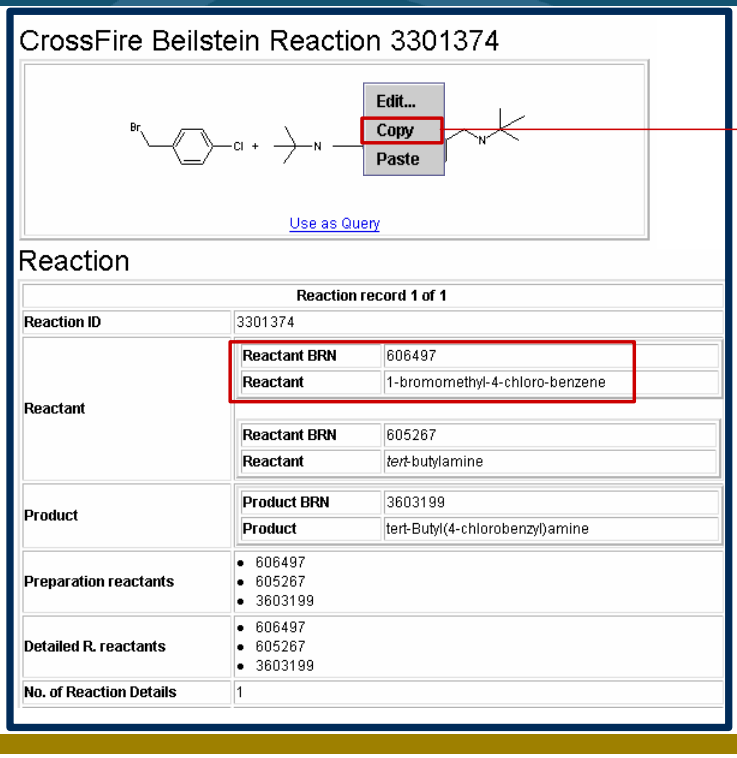


Key points

- Click the "Synthesize" link found below the structure result. This takes you to the "rxn schemes" tab.
- The "rxn schemes" tab displays a hierarchy of retrosynthetic pathways beginning with the final product.
- To expand the reaction tree, double-click a substance or a reaction folder (or click the plus sign).
- Click the "Details" link below a reaction step to view reaction conditions and citation information.

Notes

Copy the reaction



Right-click and choose Copy.

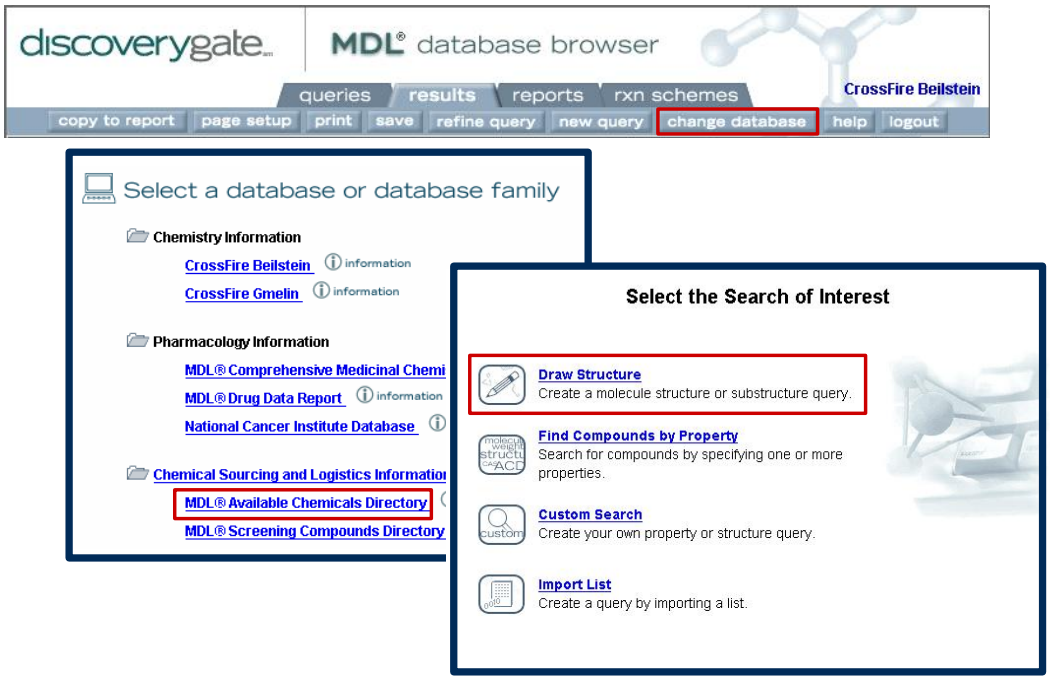
We will search for the commercial availability of 1-bromomethyl-4-chloro-benzene.

Key points

- When you the "Details" link below a reaction step, the reaction and its conditions and references are displayed.
- To see details about the reactants and products for the reaction, click the "Substances" link found at the bottom of the page.
- To see details about the citations related to this reaction, click the "Citations" link found at the bottom of the page.
- To copy a structure or reaction, right-click and choose Copy.

Notes

Change database

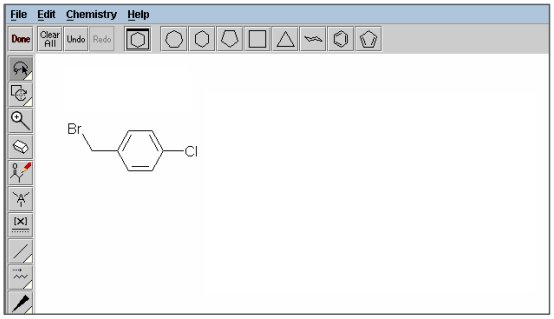


Key points

- We will switch to the Available Chemicals Directory (ACD) database to find information about the commercial availability of 1-bromomethyl-4-chloro-benzene.
- Click the "change database" button to switch to a new database. Then, click the link for the MDL Available Chemicals Directory.
- Finally, click the "Draw Structure" link in order to create a structure query.

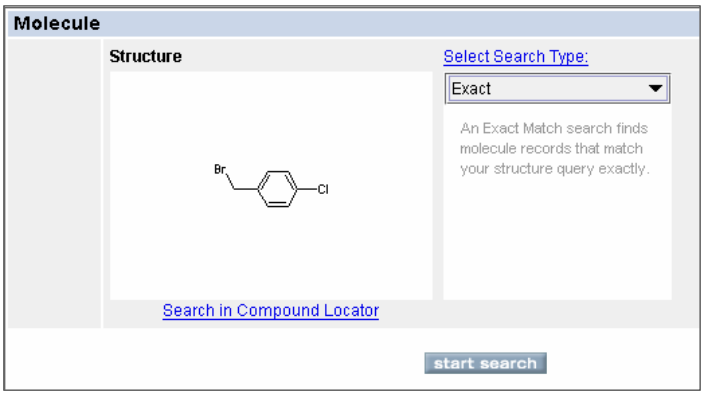
Notes

Retrieve commercial availability data



- **Right-click and choose Paste.**
- **Delete all but the desired reactant.**

- **Transfer to ACD and perform an exact search.**

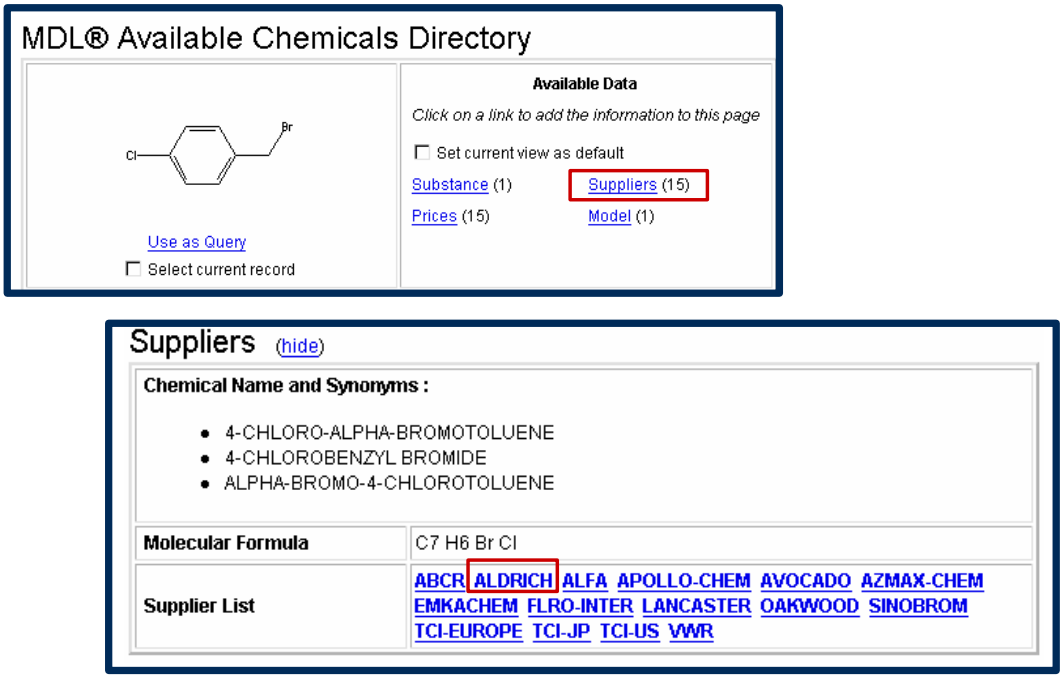


Key points

- To paste the reaction query into MDL Draw, right-click in the drawing area and choose Paste.
- Delete all but the starting material of interest, and transfer back into the MDL Database Browser.
- Create an exact match search in the ACD database and view the retrieved information.

Notes

Commercial availability

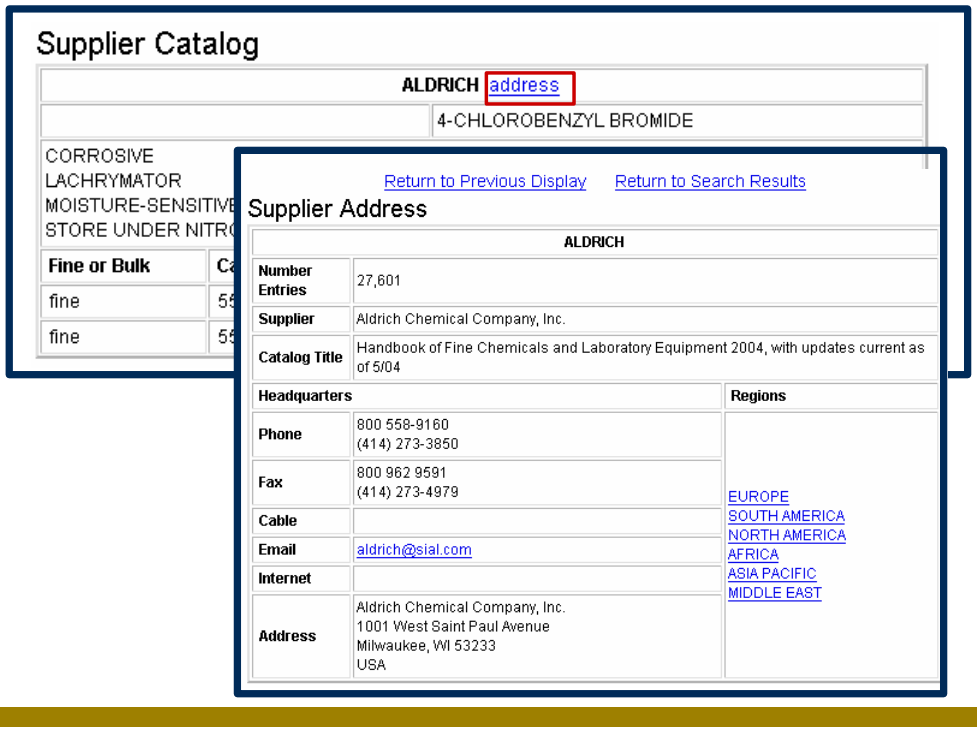


Key points

- The results from the ACD search indicate that this compound can be obtained from several suppliers.
- When you click Suppliers, the suppliers for the compound appear in the display area.
- To view pricing information and the available quantities, click the link associated with the supplier of interest.
- The Available Chemicals Directory includes information on product purities, forms, grades, available quantities, and prices, along with supplier and distributor contact information.

Notes

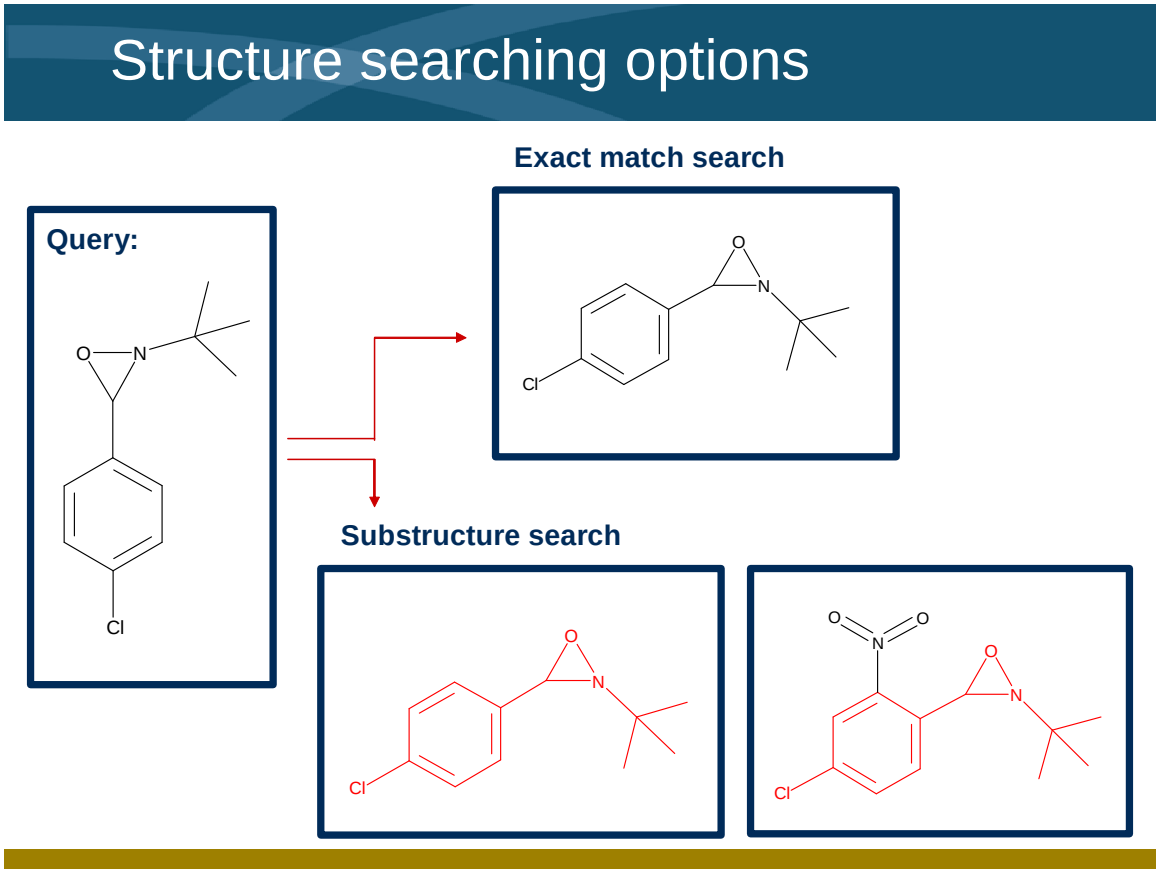
Catalog information



Key points

- Aldrich supplies this compound in fine quantities only.
- Click the Address link to view the contact information. This supplier offers services in various regions.

Notes



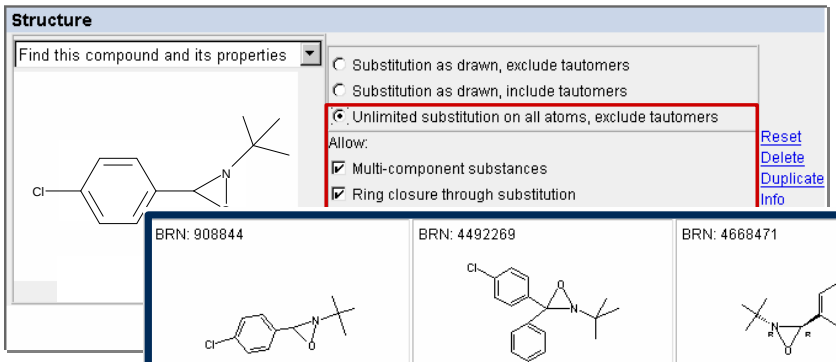
Key points

- An exact match retrieves the structure you entered.
- The rules of a substructure search are: the core structure must be embedded in all hits retrieved, and substitution can occur at any open valence.

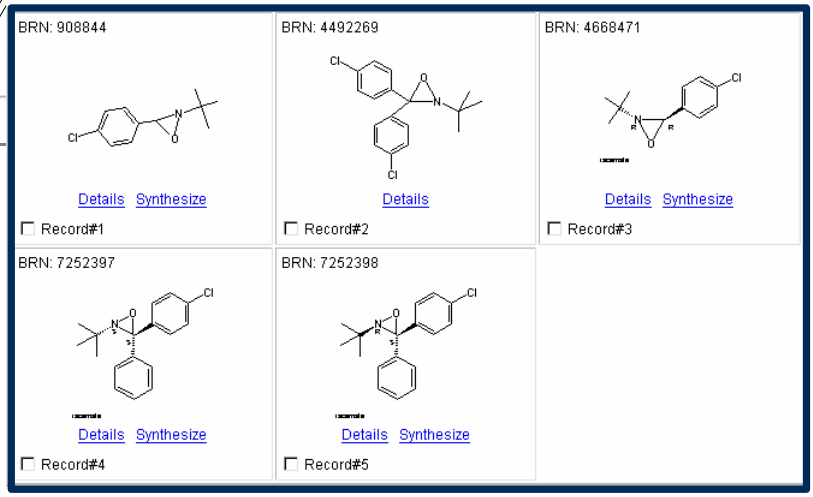
Notes

Substructure search query and results

Query:



Results:



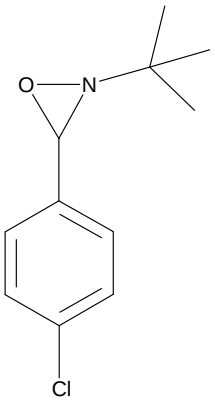
Key points

- The substructure search retrieved more hits than the previous exact match search. This is expected because you are opening the possibility of substitution at all the atom sites.

Notes

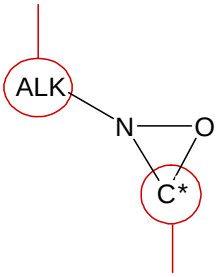
Generalize a query

Original substructure query



Generalized substructure query

Predefined generic group



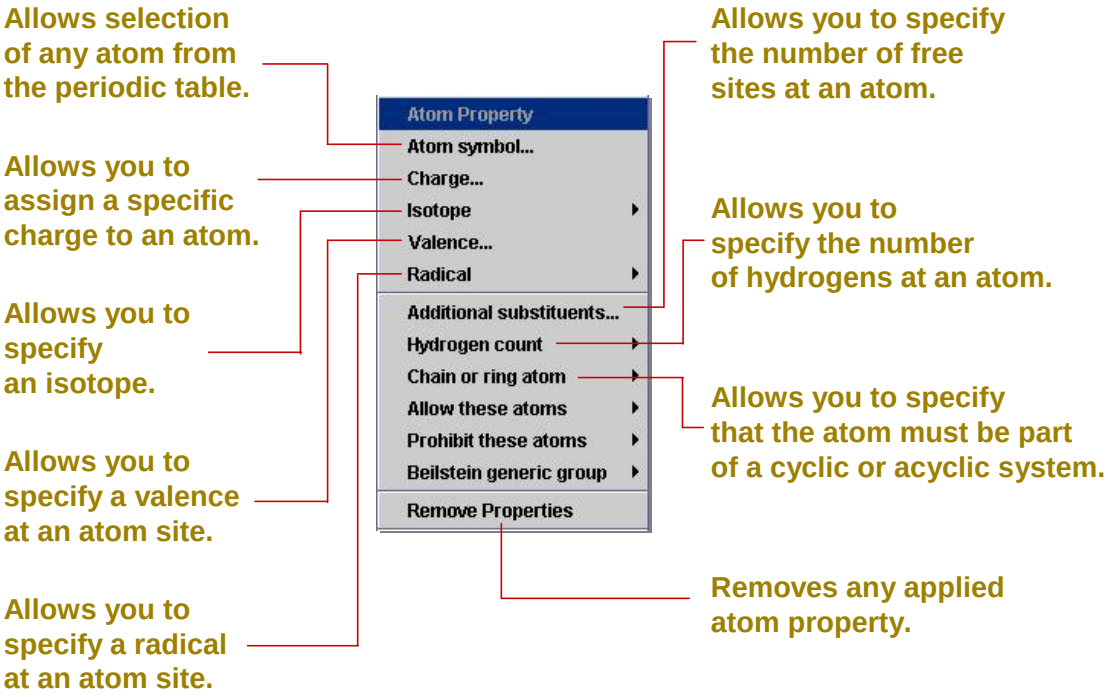
Substitution query feature

Key points

- You want to modify the structure to retrieve any alkyl-substituted oxaziridines.
- When you generalize a query, you draw only those portions that are required. You will use query features to introduce flexibility or to make the search more focused.
- You will apply a substitution feature and a predefined generic group on our modified structure.

Notes

Atom query features

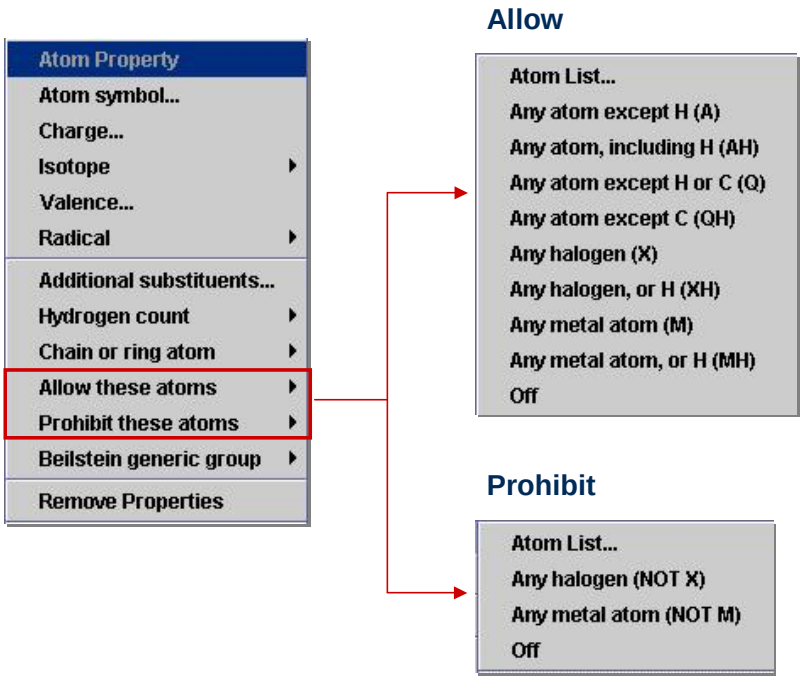


Key points

- The first grouping of atom features allows you to select any atom from the periodic table, assign a specific charge, specify an isotope, specify a valence, and specify a radical at an atom site.
- The second grouping of atom features allows you to specify the number of free atoms or the number of hydrogens at an atom site.
- There is also a feature that allows you to specify whether the atom must be part of a cyclic or acyclic system.
- The Remove Properties selection removes any features previously placed on the structure.

Notes

Allow and Prohibit atom features



Key points

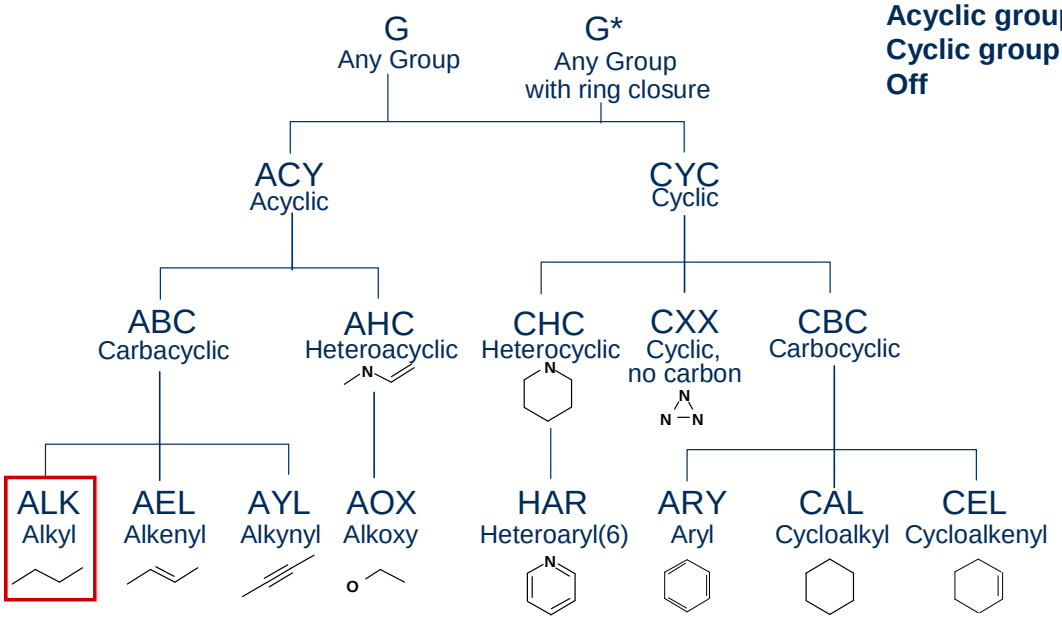
- There are two additional selections that allow or prohibit atom types from being retrieved when they are used.
- Under "Allow these atoms," you will find the generic atoms A, Q, X, and M. A is any atom except hydrogen. Q is any atom except carbon or hydrogen. X is any halogen. M is any metal.
- Under the "Prohibit these atoms," you will find Atom List, NOT X, NOT M, and Off. The Atom List allows you to select any atoms from the periodic table to exclude from the search. The NOT X excludes any halogens and the NOT M excludes any metal atom.

Notes

Predefined generic groups

MDL Draw for Database Browser > Atom Property > Beilstein generic group >

Any
Acyclic group
Cyclic group
Off



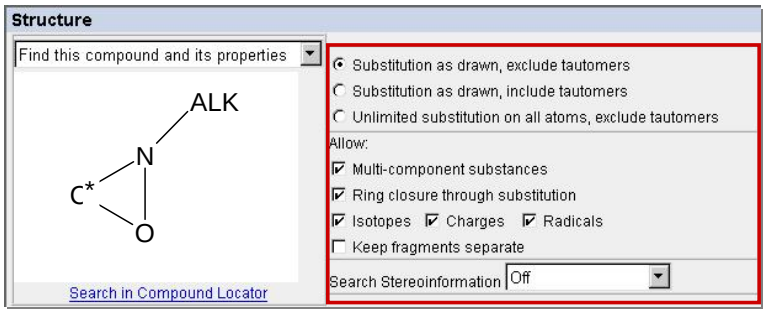
Key points

- The last atom feature introduces the Beilstein generic groups. They are shown in this slide.
- You will use the ALK generic group for the query to represent alkyl substitution.

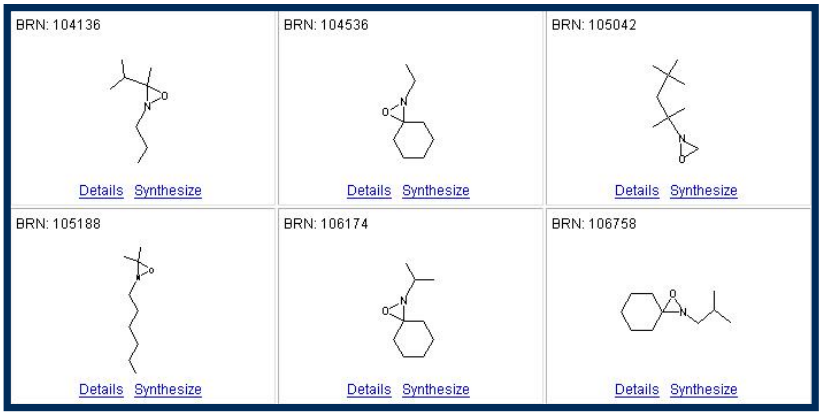
Notes

Generalized search query and results

Query:



Results:

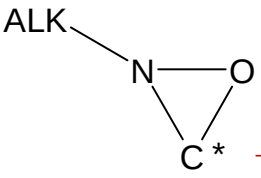


Key points

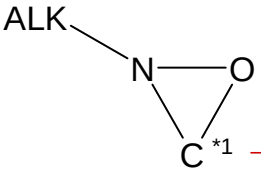
- The global search options are set to allow substitution as drawn. This allows substitution at the designated carbon atom only.
- All compounds retrieved contain the oxaziridine substructure and any alkyl group.

Notes

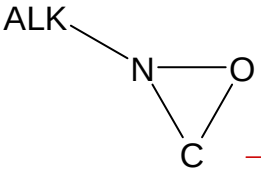
Vary the amount of substitution



Any number of additional substituents (455 records retrieved)



Up to that number of substituents (291 records retrieved)



No additional substituents, as drawn (4 records retrieved)

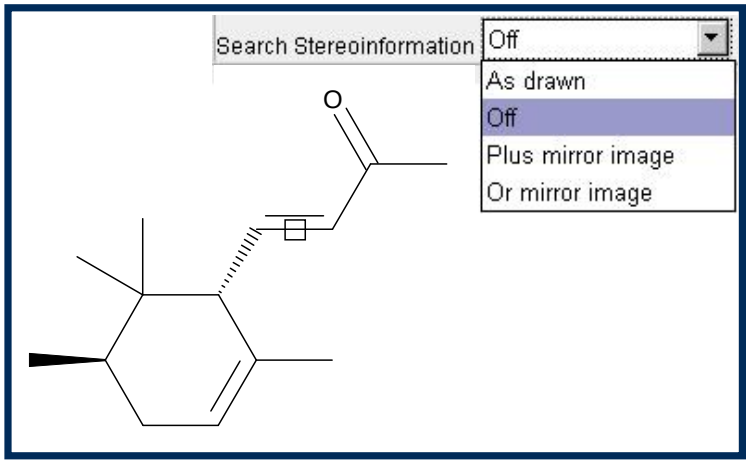
Key points

- Placing explicit substituents allows substitution only at the sites you specify.
- When you apply a specific number, the search retrieves compounds having up to that number of additional substituents at that site.
- When you specify Any # at an atom, the number of additional substituents is limited only by its valence.

Notes

Search scenario

Search the Beilstein database, using the MDL Database Browser, to retrieve isocyclic compounds where the asymmetric or chiral centers are defined.

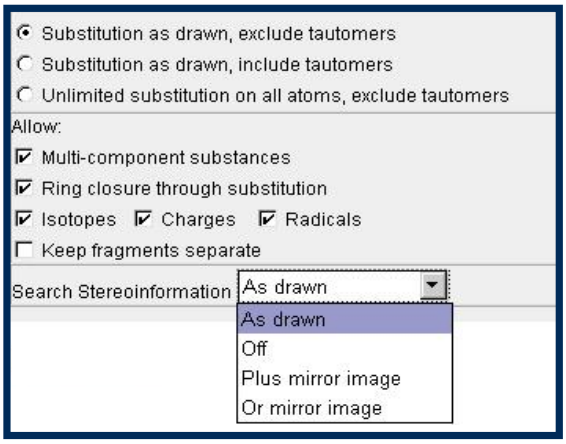


Key points

- In this example, you will search using a structure with defined asymmetric or chiral centers.
- Alter the Search Stereoinformation settings and compare the results.

Notes

Stereochemical considerations



As drawn – retrieves compounds with the absolute stereochemical representation.

Off – retrieves all stereochemical representations.

Plus mirror image – retrieves racemic compounds.

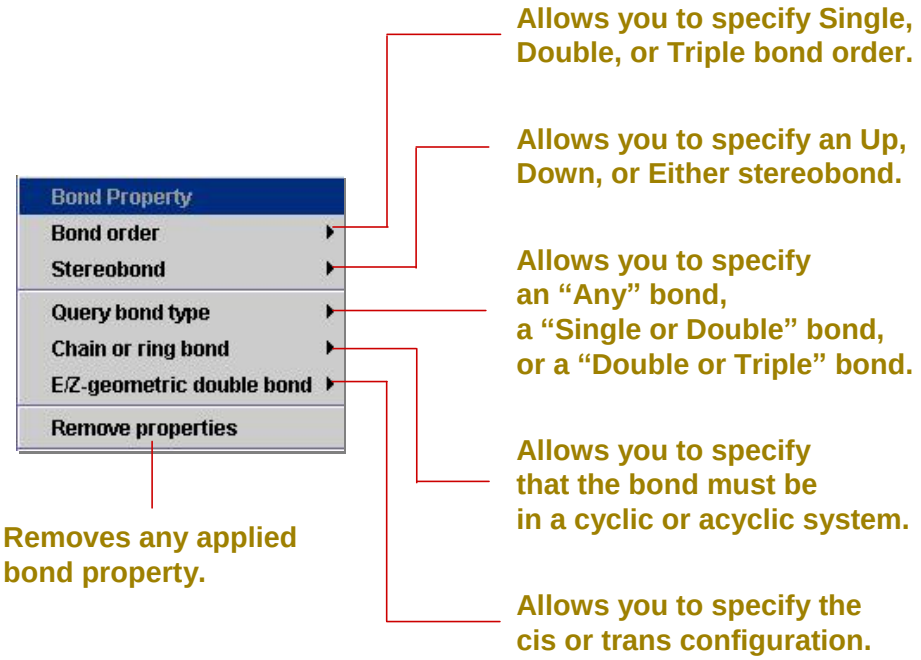
Or mirror image – retrieves compounds with the relative stereochemical representation.

Key points

- You can use the Search Stereoinformation drop-down list to search for the compound shown in the structure box and its mirror image as follows:
  - As drawn
  - Off (stereoinformation is not important)
  - Plus mirror image (racemic mixture)
  - Or mirror image (relative search, for isomer as drawn or its enantiomer)

Notes

Bond query features

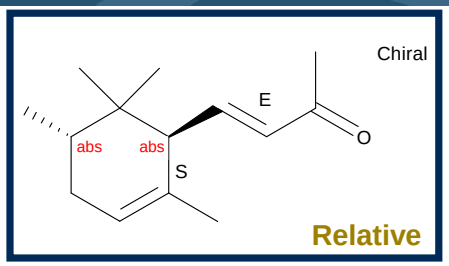


Key points

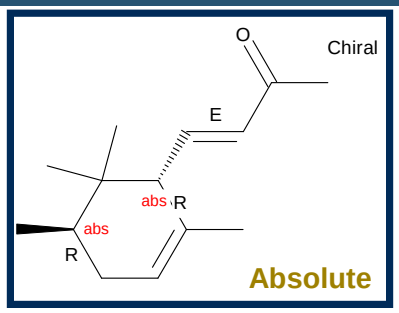
- There are a series of bond features that can be used when conducting a structure search that will make the query more flexible or more focused.

Notes

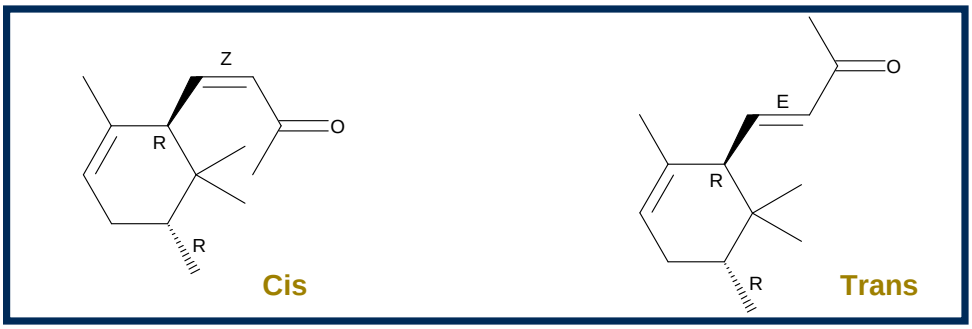
Search results



“Off”, “Plus mirror image”, or “Or mirror image” search



“As drawn” search



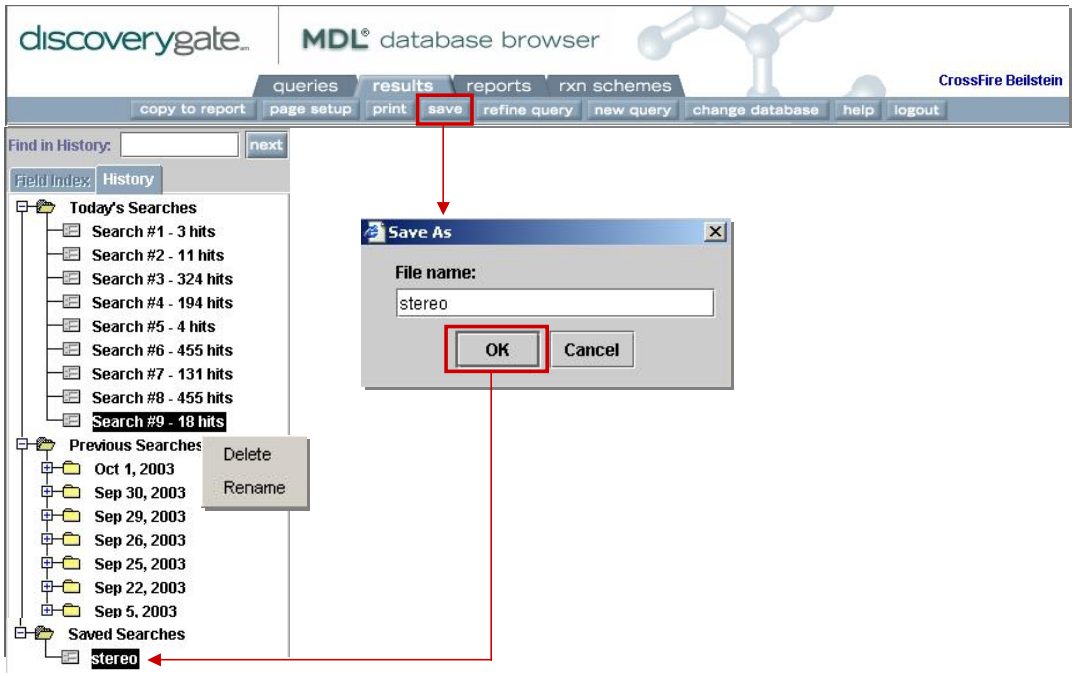
“Off” search

Key points

- You can see the variation in the retrieved results when you alter the Search Stereoinformation settings and use specific stereochemical tools on the structure.

Notes

Search History and saving a list

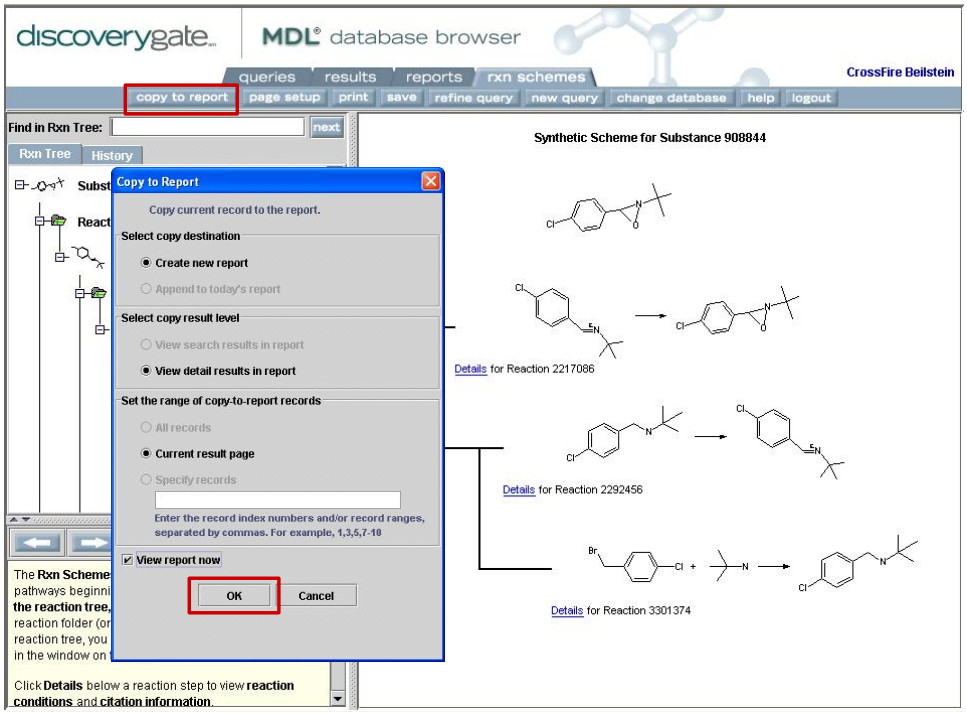


Key points

- The History tab acts as a visual history of your searches, shown as documents within folders.
- All searches from the current day are saved in Today's Searches. All searches older than one day are moved into Previous Searches.
- Right-click on a search to delete or rename it.
- To save a search, click the save button on the top menu bar. Saved searches are placed in the Saved Searches folder and stored permanently.

Notes

Create a report



Key points

- You can copy your search results to a report that can be printed or exported. To retrieve previous search results, double-click the item on the History tab.
- To create a report, click "copy to report" on the menu bar.
- Depending upon what data is currently displayed, you have control over the result level and range of records to copy to the report.
- You have the option of creating a new report or appending the data to an existing report. If you want to view the report immediately, check the box.

Notes

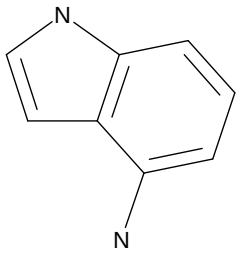
Exercise descriptions

The following descriptions explain the goal of each exercise. If you like to figure things out on your own, use the descriptions to conduct the exercises. If you prefer step-by-step instructions, go to the page listed below the description.

Exercise 1

Conduct an exact structure and substructure search for 4-amino-indole.

- Conduct an exact structure search.



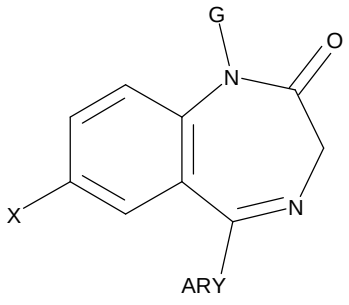
- Use the Synthesize link to view preparation data.
- Conduct a substructure search.

For a step-by-step solution, see page 1-33.

Exercise 2

Conduct a substructure search.

- Search for benzodiazepine derivatives. Use predefined generic groups and an X halogen atom to generalize the query. View all fields.

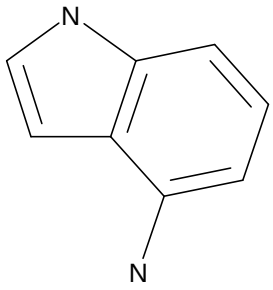


For a step-by-step solution, see page 1-36.

Conduct a series of structure searches for 4-amino-indole

Exercise 1

Conduct a structure search for 4-amino-indole. View the preparation methods. Then conduct a substructure search on the same structure.



Start DiscoveryGate

1. If you have already started the application, go to Step 3. Launch your internet browser and enter the DiscoveryGate URL (www.discoverygate.com).

2. Enter your user name and password. If necessary, enter your company id. Click **go discover**.

3. Under Applications, click **Search individual databases**.

Open the CrossFire Beilstein database

4. Under Chemistry Information, click **CrossFire Beilstein**.

5. Click the **Draw Structure or Reaction** link. Draw 4-amino-indole. Click **Done**.

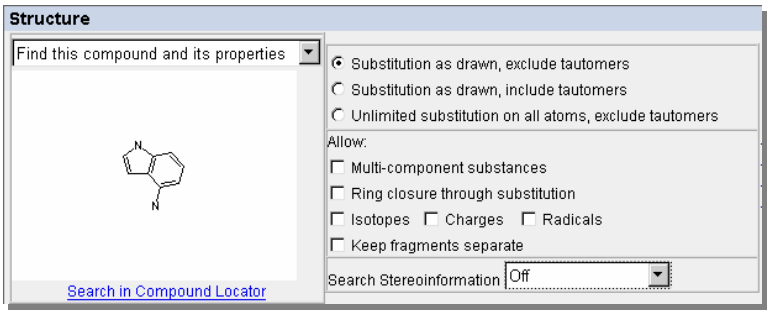
Set the Structure search options

6. In the Structure search option area, select **Find this compound and its properties**.

Set the Global search options

7. Under the Global search options, select **Substitution as drawn, exclude tautomers**. Uncheck all other options.

8. Under Search Stereoinformation, select **Off**.



start search

9. Click **start search**.

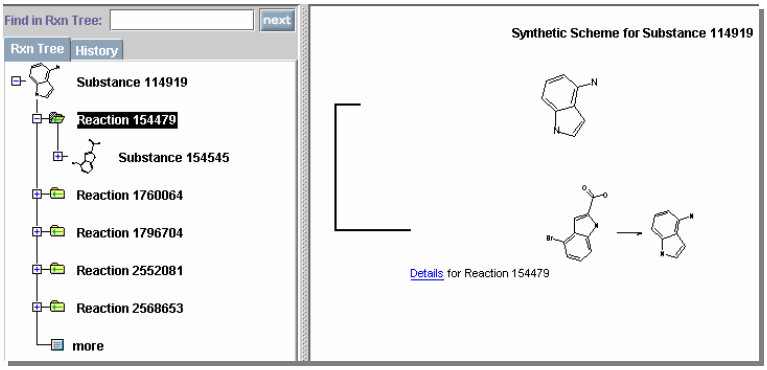
10. Click the **Details** link.

View the preparative methods

11. Click the **Synthesize** link.

12. Click the plus sign next to **Substance 114919**.

13. Click the plus sign next to **Reaction 154479**.



14. Under the reaction graphic, click the **Details** for Reaction link.

refine query

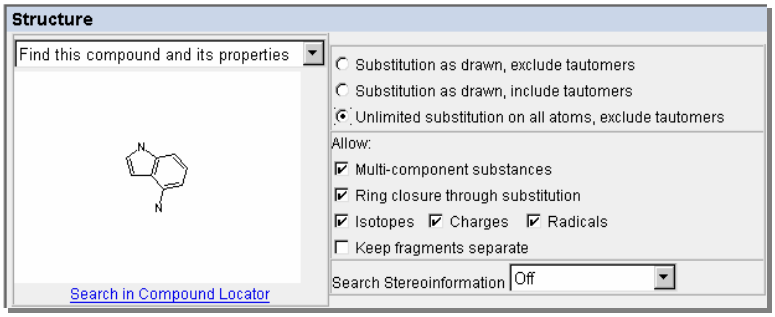
15. Click the **refine query** button.

Conduct the substructure search

16. In the MDL Database Browser select:

    - **Find this compound and its properties**

- **Unlimited substitution on all atoms, exclude tautomers**
- Under Allow, check **Multi-component substances**, **Ring closure through substitution**, **Isotopes**, **Charges**, and **Radicals**.
- Search Stereoinformation, select **Off**

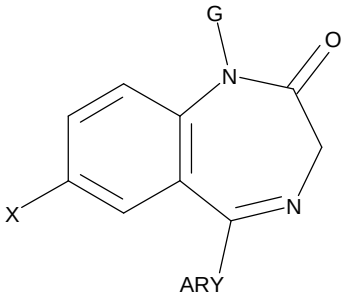


17. Click **start search** and view the results.

Retrieve benzodiazepine derivatives

Exercise 2

Conduct a substructure search for benzodiazepine derivatives. Use predefined generic groups and an X halogen atom to generalize the query. G is the abbreviation for any group. ARY is the abbreviation for aryl groups.



Prepare for a new search

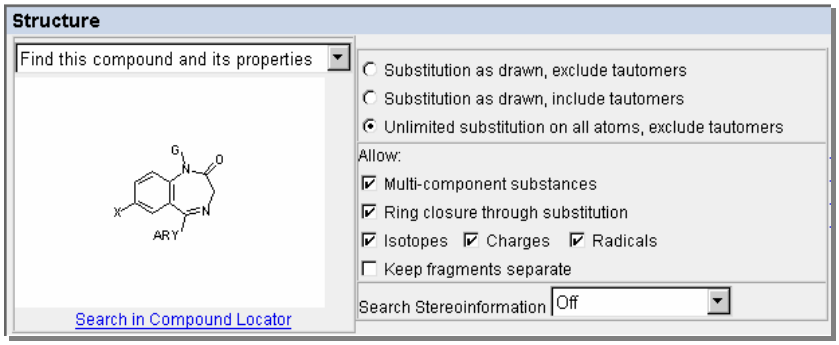
1. Click the **new query** button.

2. Click the **Draw Structure or Reaction** link. Draw the generalized benzodiazepine structure.

3. To place the ARY designation, right-click the atom, and then choose **Beilstein generic group > Cyclic group > Carbon atoms only > ARY**. Click to select the terminal carbon atom on the C-C single bond. Type **X** and press **Enter**. Right-click the terminal carbon atom on the C-N single bond. Choose **Beilstein generic group > Any group > G**. Click **Done**.

4. In the MDL Database Browser select:

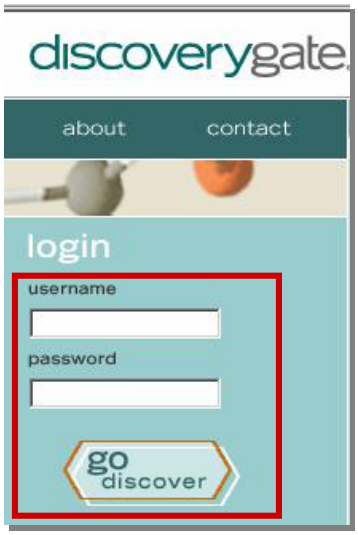
   - **Find this compound and its properties**
   - **Unlimited substitution on all atoms, exclude tautomers**
   - Under Allow, check **Multi-component substances**, **Ring closure through substitution**, **Isotopes**, **Charges**, and **Radicals**.
   - Search Stereoinformation, select **Off**



5. Click **start search** and view the results.

To launch the DiscoveryGate application

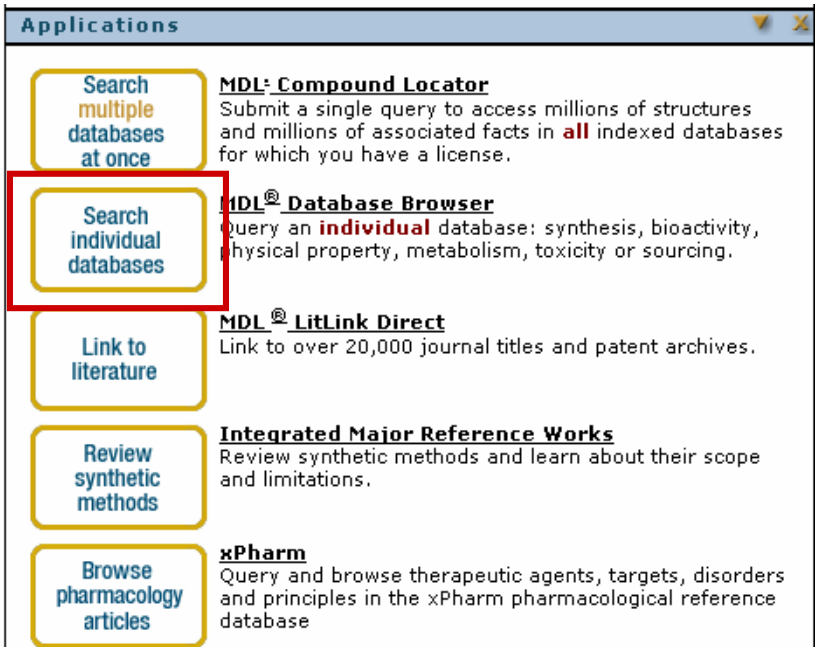
1. Launch your internet browser and enter the DiscoveryGate URL (www.discoverygate.com).
2. Enter your user name and password.
3. If necessary, enter your company ID.



4. Click **go discover**.

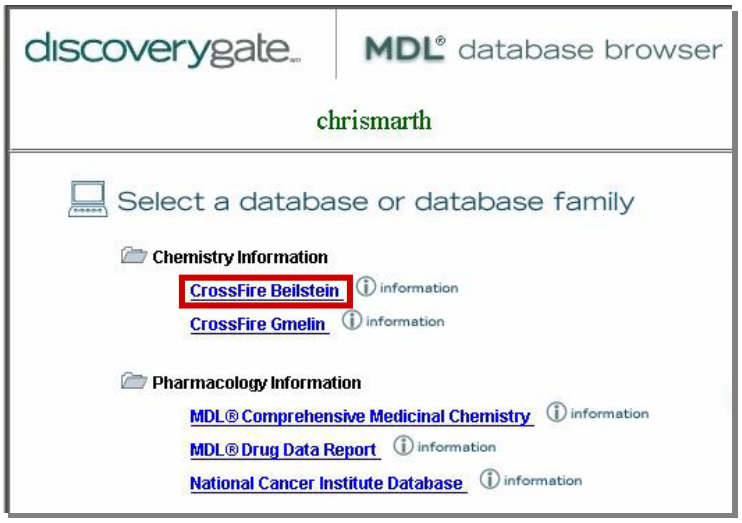
To select an individual database

1. Under Applications, click **Search individual databases**.



To select CrossFire Beilstein

1. Under Chemistry Information, click **CrossFire Beilstein**.



To configure CrossFire

1. Click the personal **Settings** tab.
2. In the My CrossFire Login Information box, enter your **User Name**, **Password**, **Confirm Password**, **Group**, and **Confirm Group** information.

3. Click **Update**.

To create a structure or reaction

1. In the Select the Search of Interest window, click **Draw Structure or Reaction**.

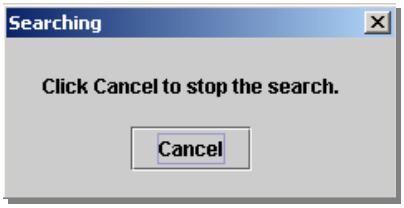
2. Use the MDL drawing tools.
3. Click the **Done** icon.

To start a search

1. Enter a query into the structure field.
2. Set structure search and/or global search options.
3. Click **start search**.

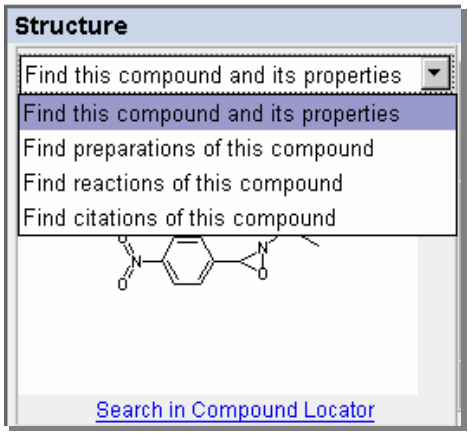
To stop a search

1. After a query is launched, click **Cancel**.



To set structure search options

1. In the Structure box, click the arrow to display the drop-down list.



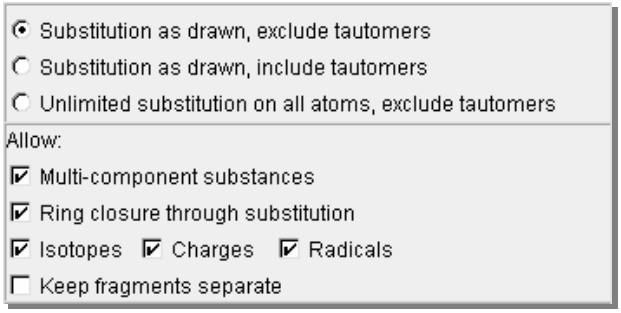
2. Choose one of the selections.

Selection	Action
Find this compound and its properties	Retrieves a list of molecule(s) and associated properties.
Find preparations of this	Retrieves a list of reactions

Selection	Action
compound	where the compound is found as a reactant. Click the "Synthesize the Reactant" link for the preparation information.
Find reactions of this compound	Retrieves a list of reactions where the compound is either the reactant or the product.
Find citations of this compound	Retrieves a list of citations for the specific compound.

To set global search options

1. In the Structure field index, click the radio button or check box next to the appropriate selections.

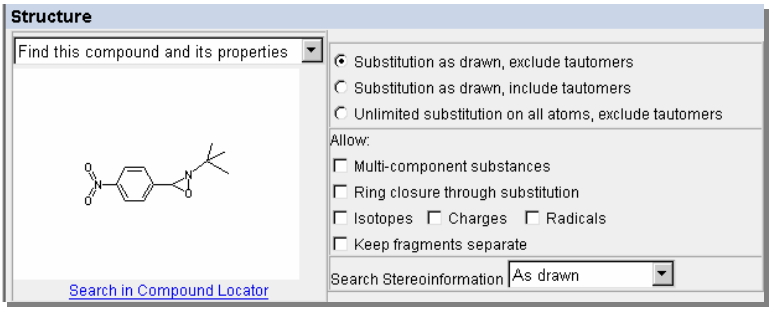


Selection	Action
Substitution as drawn, exclude tautomers	Excludes substitution where it is not explicitly specified and the retrieval of tautomers.
Substitution as drawn, include tautomers	Excludes substitution where it is not explicitly specified, but does include the retrieval of tautomers.
Unlimited substitution on	Allows for substitution on

Selection	Action
all atoms, exclude tautomers	all atoms and excludes the retrieval of tautomers.
Multi-component substances	Allows for the retrieval of mixtures.
Ring closure through substitution	Allows rings to form from chains on the atoms you assign with substitution.
Isotopes	Allows the retrieval of isotopes.
Charges	Allows the retrieval of charged species.
Radicals	Allows the retrieval of radicals.
Keep fragments separate	Allows two or more non-bonded fragments to be retrieved in separate compounds.

To conduct an exact structure search

1. Place a structure in the Structure box.
2. Under Structure search options, select **Find this compound and its properties**.
3. Under Global search options, select **Substitution as drawn, exclude tautomers**.
4. Under Allow, uncheck all selections.



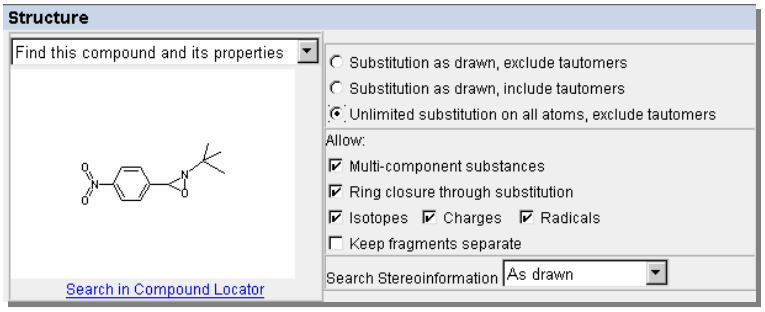
5. Click **start search**.

To modify a search query

1. At the top of the results, reports, or rxn schemes tabs, click the **refine query** button.

To conduct a substructure search

1. Place a structure in the Structure box.
2. Under Structure search options, select **Find this compound and its properties**.
3. Under Global search options, select **Unlimited substitution on all atoms, exclude tautomers**.
4. Under Allow, check **Multi-component substances**, **Ring closure through substitution**, **Isotopes**, **Charges**, and **Radicals**.



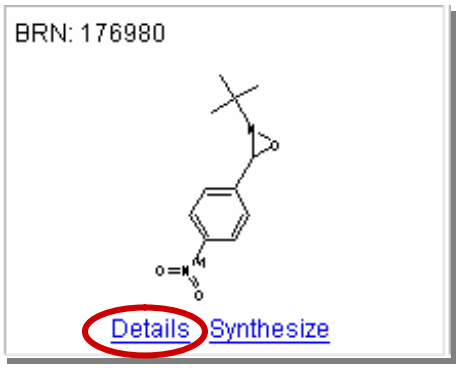
5. Click **start search**.

To view search results

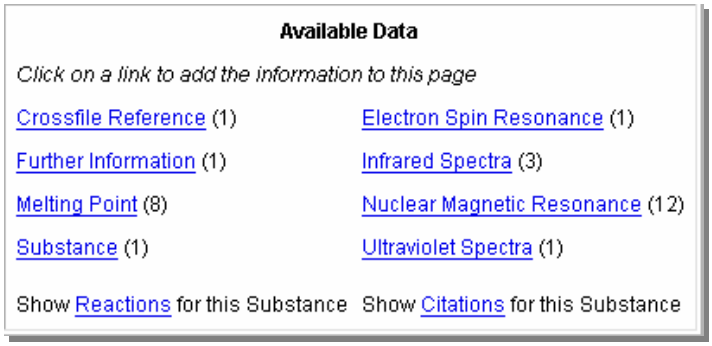
1. When the search is complete, the system automatically displays the results tab.
2. If necessary, click the **results** tab at the top of the window.
3. On the History tab, double-click to open the **Today's Searches** folder.
4. Double-click to open a **Search**.

To view details of a retrieved structure

1. On the results tab, click the **Details** link found under the structure.



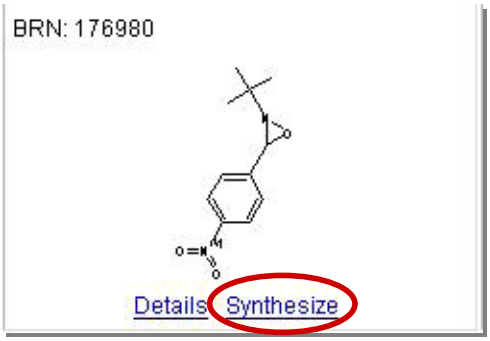
2. In the **Available Data** box, click a link to view the specific data.



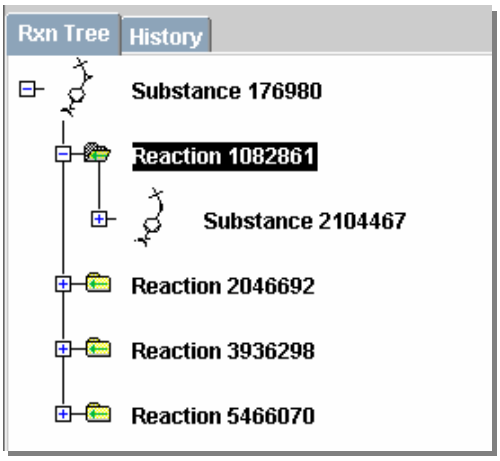
3. Click the **Top of Page** link and repeat Step 2 to view more data.

To view the synthesis of a retrieved compound

1. On the results tab or in the Details window, click the **Synthesize** link.



2. On the Rxn Tree tab, click the plus sign next to **Substance xxxxxx**.
3. Click the plus sign next to **Reaction xxxxxx**.



4. View the reaction.

To view the reaction scheme details of a retrieved compound

1. On the rxn schemes tab, click the **Details for Reaction** link found under the reaction.
2. Scroll down and view the data.

To add a substitution query feature

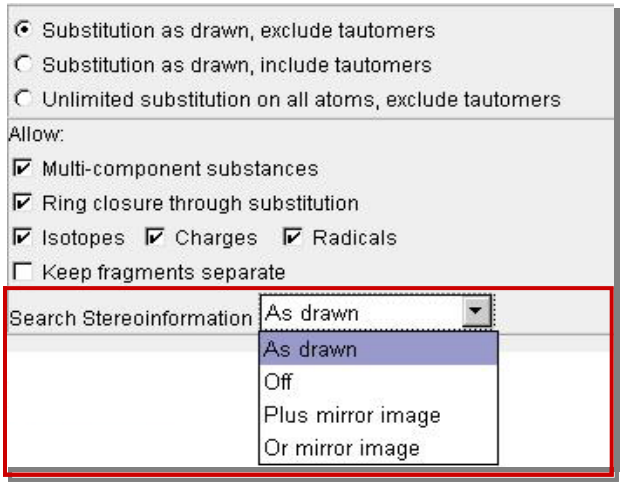
1. Transfer the structure to MDL Draw.
2. Using the All-Purpose tool, right-click an atom and select the desired substitution query feature.
3. Click the **Done** transfer icon.

To add a predefined generic group

1. Transfer the structure to MDL Draw.
2. Using the All-Purpose tool, right-click an atom and select **Beilstein generic group**, and then select the desired group.
3. Click the **Done** transfer icon.

To conduct a stereochemical structure search

1. Place a structure in the Structure box. If necessary for the query, add stereo bonds using MDL Draw.
2. Set the Structure search options and the Global search options based on what you want to retrieve.
3. Under Search Stereoinformation, click the arrow to display the drop-down list.



4. Choose one of the selections.

Selection	Action
As drawn	Retrieves compounds with the absolute stereochemical representation.
Off	Retrieves all stereochemical representations.
Plus mirror image	Retrieves racemic compounds.
Or mirror image	Retrieves compounds with the relative stereochemical representation.

To add a stereochemical bond

1. Transfer the structure to MDL Draw.
2. Using the **All-Purpose Drawing** tool, right-click on a bond and choose one of the bond options.
3. Click the **Done** transfer icon.

To add an E/Z geometric bond

1. Transfer the structure to MDL Draw.

2. Using the All-Purpose tool, right-click on a double bond and choose **E/Z-geometric double bond > As drawn (E or Z only)**.
3. Click the **Done** transfer icon.

To save search results

1. At the top of the results tab, click the **save** button.
2. Type a name into the Save As box and click **OK**.