Finding Derivatives

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library.stanford.edu/depts/swain/chem130/chem130.html

Lecture Outline:

- Choosing a derivative
- Synthesizing a derivative
- Finding properties for a derivative

Choosing a Derivative

- See *Guidelines for Recommended Derivatives*
  - Organized by class of parent compound
  - IN Chem 130/132 Course Pack, Lectures, pgs 50-53
  - On the web:

library.stanford.edu/depts/swain/chem130.derivatives.html

- Examples (if you have, then make):
  - Aldehydes and Ketones
    - 2,4-DNP
    - Semicarbazone
    - Oxime
  - Primary and Secondary

Need to Know "Parent" Unknown Before Making a Derivative?

- Ideal:
  - Know exact structure of "parent" unknown compound
  - Consult "Guidelines" and choose which derivative to make
  - Find a literature reference on the synthesis of a derivative as they include physical property data and a spectral diagram
  - Locate additional property data in POC, CCD, or Beilstein
- Reality:
  - Sometimes, don't know exact structure of "parent" unknown
  - Must know compound class of "parent" unknown
  - Consult with a TA

Synthesizing a Derivative

- Print and electronic resources are available: library.stanford.edu/depts/swain/chem130/derivbibl.html
  - Print resources:
    - Usually arranged by class of compound.
    - One particularly helpful text is Vogel's Textbook of Practical Organic Chemistry
    - Other helpful texts include Pasto, Harwood, & Shriner
  - Electronic Resources:
    - Combined Chemical Dictionary via CHEMnetBASE
    - Beilstein Crossfire

Synthesizing a Derivative: Overview of Search Methods in Electronic Resources

- Use the Combined Chemical Dictionary (CCD) via CHEMnetBASE and Beilstein Crossfire
- Two search methods for finding derivatives:
  - Search by CAS Registry Number (CCD or Beilstein)
  - Search by chemical reaction (Beilstein)

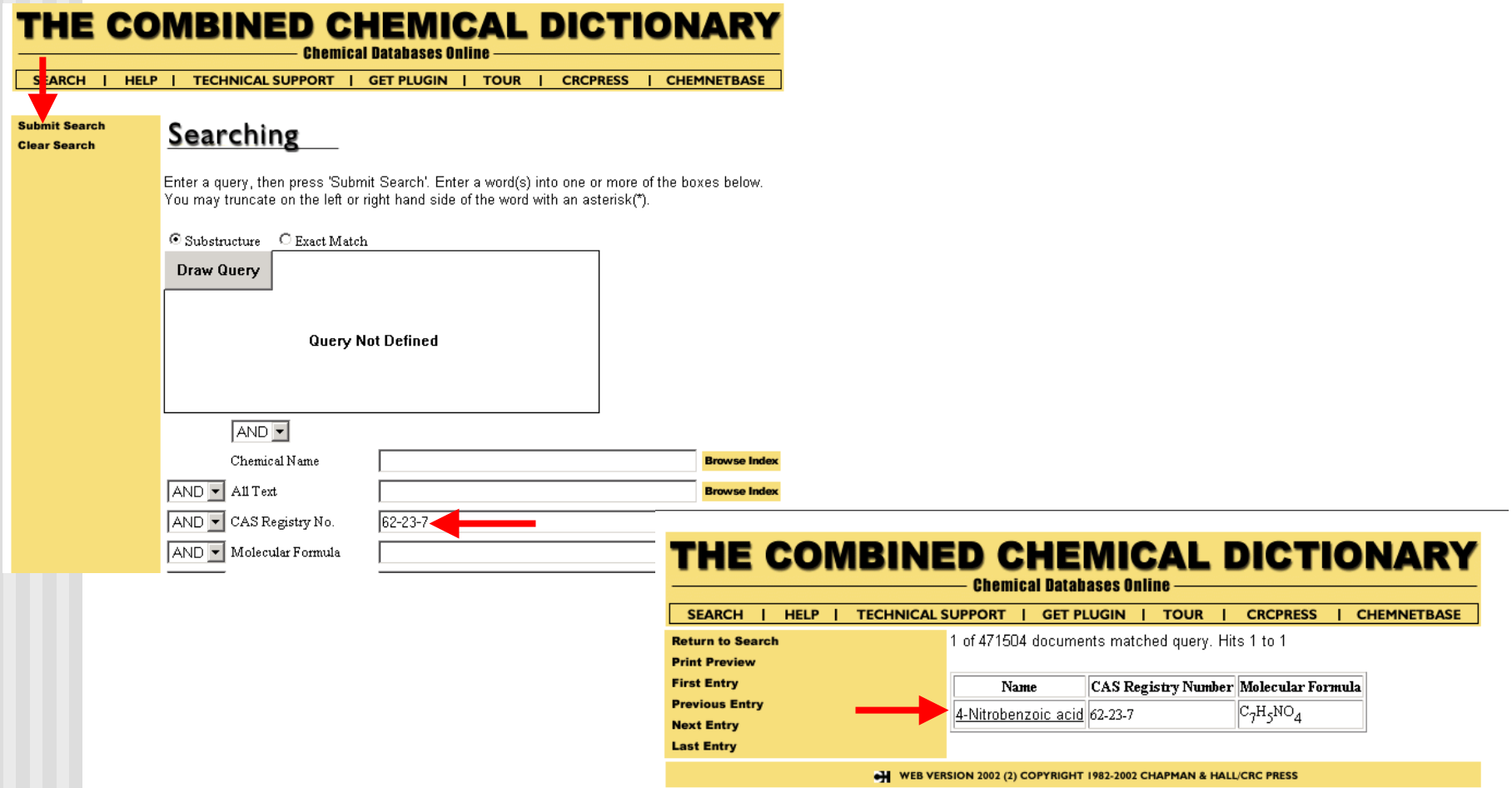
Searching by CAS Registry Number

- **CCD** and **Beilstein** include derivatives in a record for a compound.

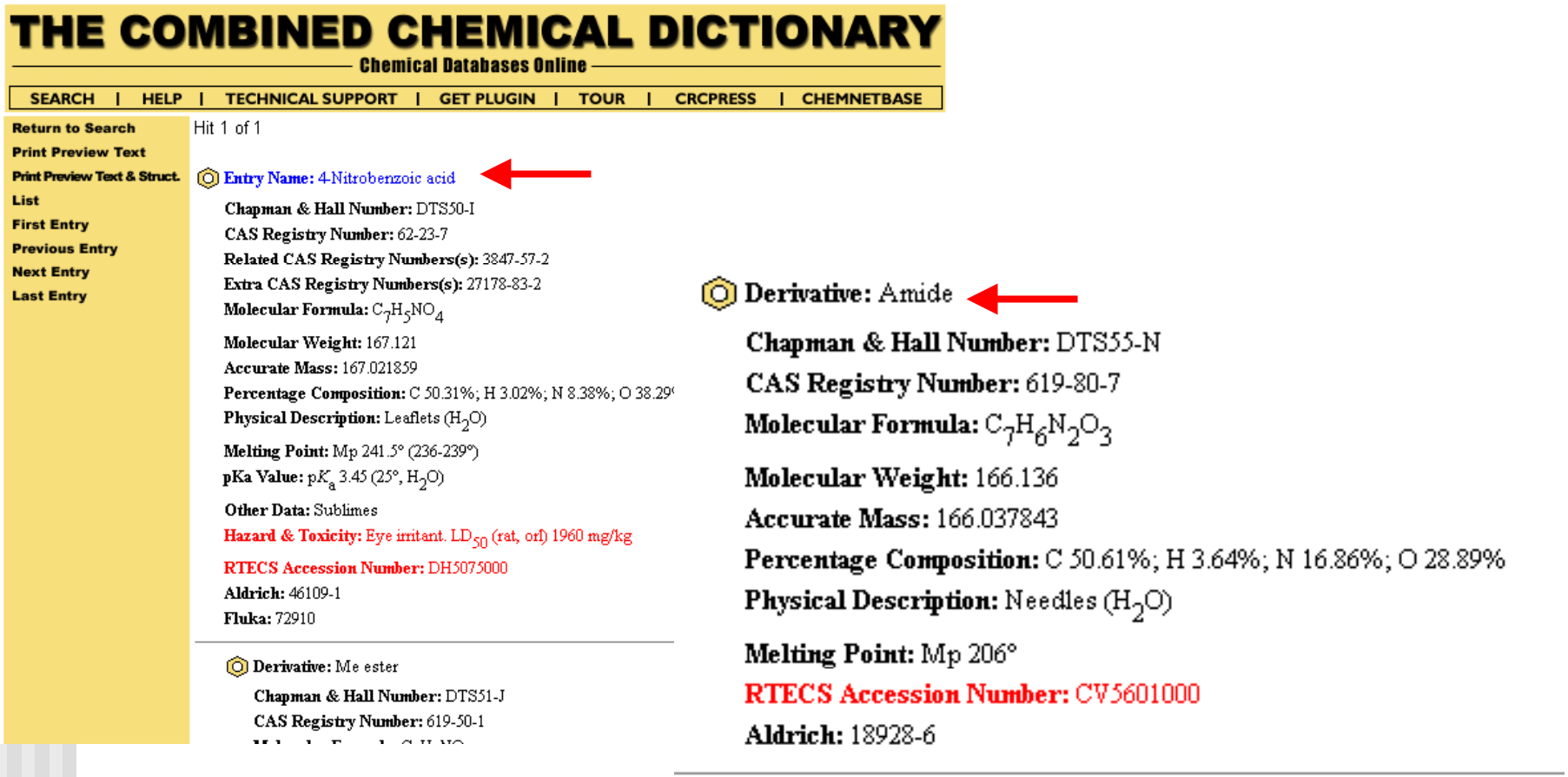
- **CCD:**
  - Use CCD ***first*** because it has a carefully chosen set of derivatives.
  - If your unknown is a "main entry" compound, then look for a recommended derivative.
  - Consult literature references labeled ""deriv" or "synth"
  - If your unknown compound is listed as a derivative in CCD, then search Beilstein Crossfire by CAS Registry Number

- **Beilstein:**
  - See Derivative field in record.
  - Note: Beilstein has a narrower definition for derivatives than is used in Chemistry 130/132.

Finding Derivatives: CAS Registry Number Search in CCD and Brief Display Format



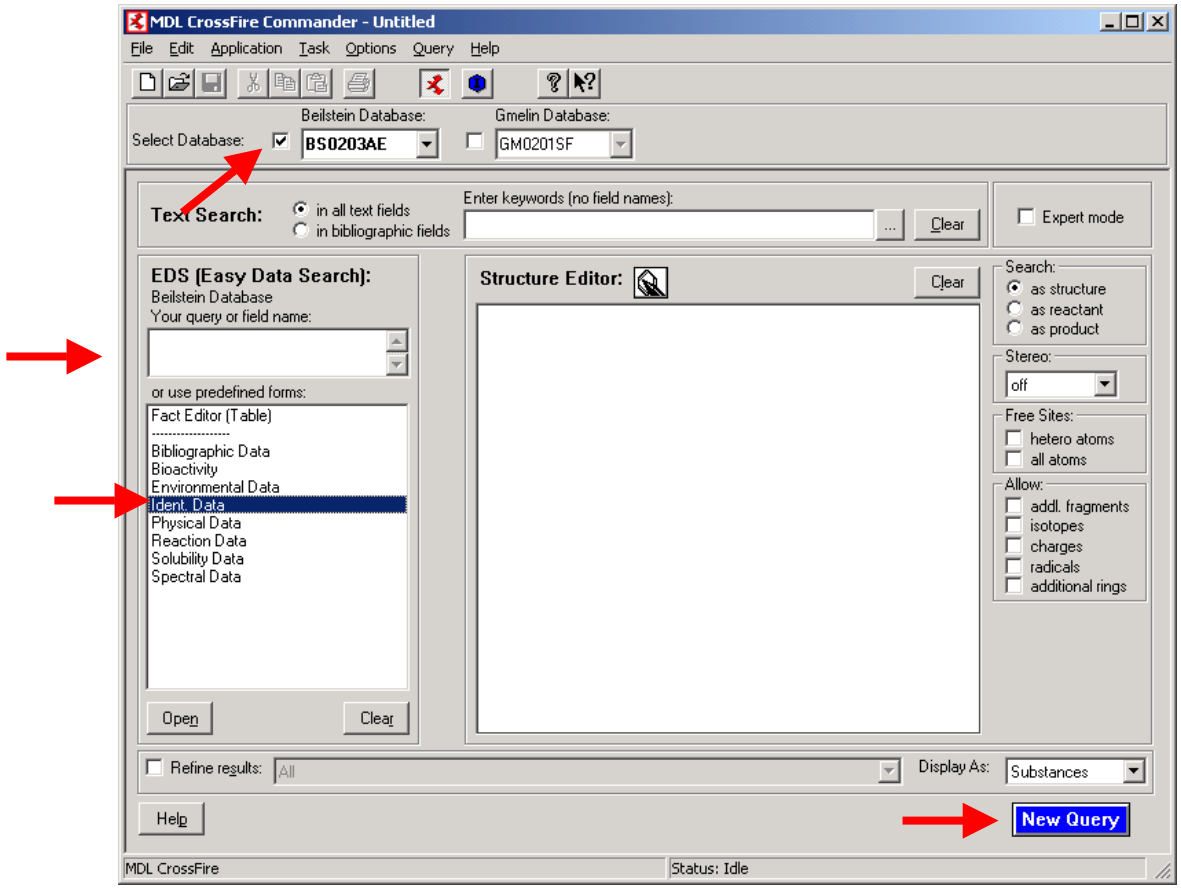
Full Display Format in CCD



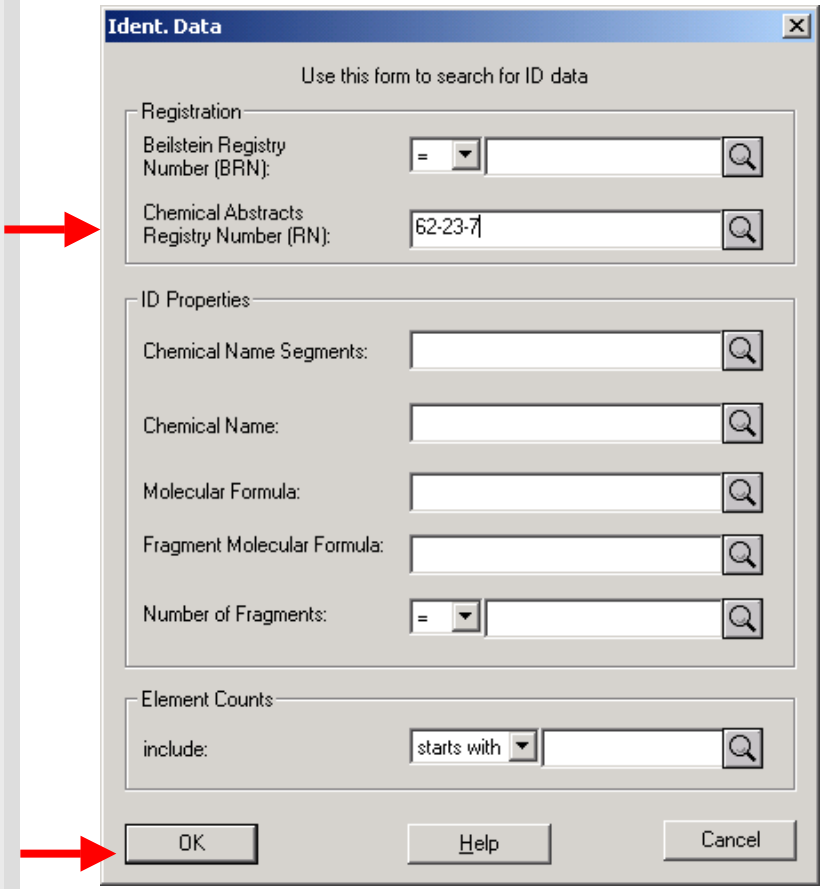
Full Display Format in CCD (Literature References)

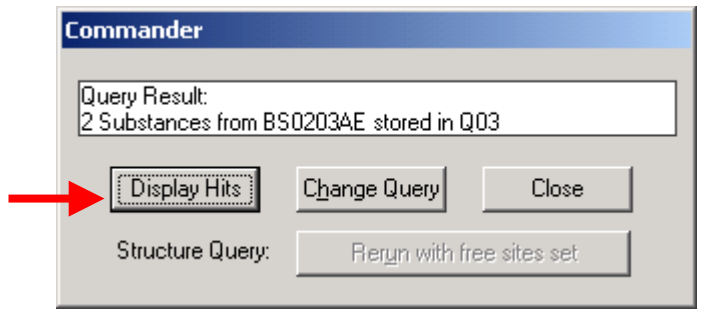
Aldrich Library of NMR Spectra, **6**, 152B, *(pmr)*
Org. Synth., Coll. Vol., 1, 1932, 392
394, *(chloride)*
Papariello, G.J. *etal.*, *Anal. Chem.*, 1964, **36**, 1028, *(use, hydrazide)*
Litvinenko, L.M., *Zh. Anal. Khim.*, 1966, **21**, 200, *(use, chloride)*
Koehergin, P.M. *etal.*, *CA*, 1967, **66**, 10702w, *(synth)*
Fieser and Fieser's Reagents for Organic Synthesis, Wiley, 1967, **1**, 736
Tavale, S.S. *etal.*, *Acta Cryst. B*, 1971, **27**, 1479, *(cryst struct)*
Tomer, K.B. *etal.*, *Org. Mass Spectrom.*, 1973, **7**, 383, *(ms)*
Kamath, B.V. *etal.*, *J. Appl. Chem. Biotechnol.*, 1975, **25**, 743, *(uv)*
Nachtmann, F. *etal.*, *J. Chromatogr.*, 1976, **122**, 293
1977, **136**, 279, *(use, chloride)*
Di Rienzo, F. *etal.*, *Acta Cryst. B*, 1977, **33**, 3854, *(cryst struct)*
Dignam, V.J. *etal.*, *J.C.S. Perkin 2*, 1977, 1457-1462, *(nitrile N-oxide)*
Kosugi, Y. *etal.*, *Tetrahedron*, 1980, **36**, 2741, *(cmr)*
Hammela, P.J. *etal.*, *Aust. J. Chem.*, 1989, **42**, 1257-1262, *(nitrile N-oxide)*
Niazi, M.S.K., *Bull. Chem. Soc. Jpn.*, 1989, **62**, 1253, *(pKa)*
Murray, R.W. *etal.*, *J.O.C.*, 1989, **54**, 5783, *(synth)*
Kocevar, M. *etal.*, *J.O.C.*, 1995, **60**, 1466, *(synth, derivs)*
Sato, K. *etal.*, *Bull. Chem. Soc. Jpn.*, 1999, **72**, 2287-2306, *(synth, pmr, cmr)*
Kong, Y.C. *etal.*, *J. Het. Chem.*, 1999, **36**, 515-523, *(Me ester)*
Sakamoto, T. *etal.*, *J.C.S. Perkin 1*, 1999, 2323-2326, *(nitrile, synth, ir, pmr)*
Bretherick, L., *Handbook of Reactive Chemical Hazards, 4th edn., Butterworths*, 1990, 2529
Luxon, S.G., *Hazards in the Chemical Laboratory, 5th edn., Royal Society of Chemistry*, 1992, 904
Lewis, R.J., *Sax's Dangerous Properties of Industrial Materials, 8th edn., Van Nostrand Reinhold*, 1992, CCI250
ENO000
MMI000
NFH000
NFK100

Finding Derivatives: CAS Registry Number Search in Beilstein Crossfire

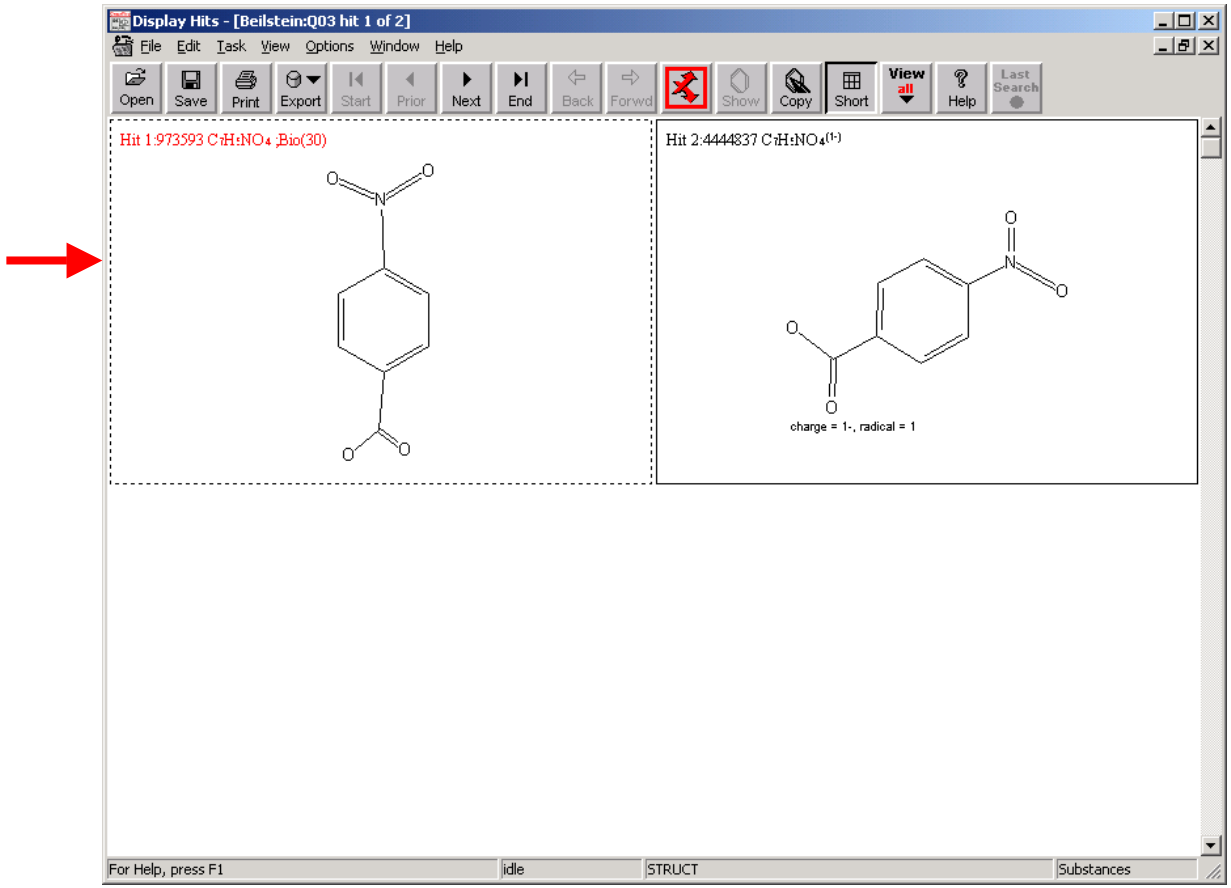


Finding Derivatives: Using Beilstein Crossfire continued

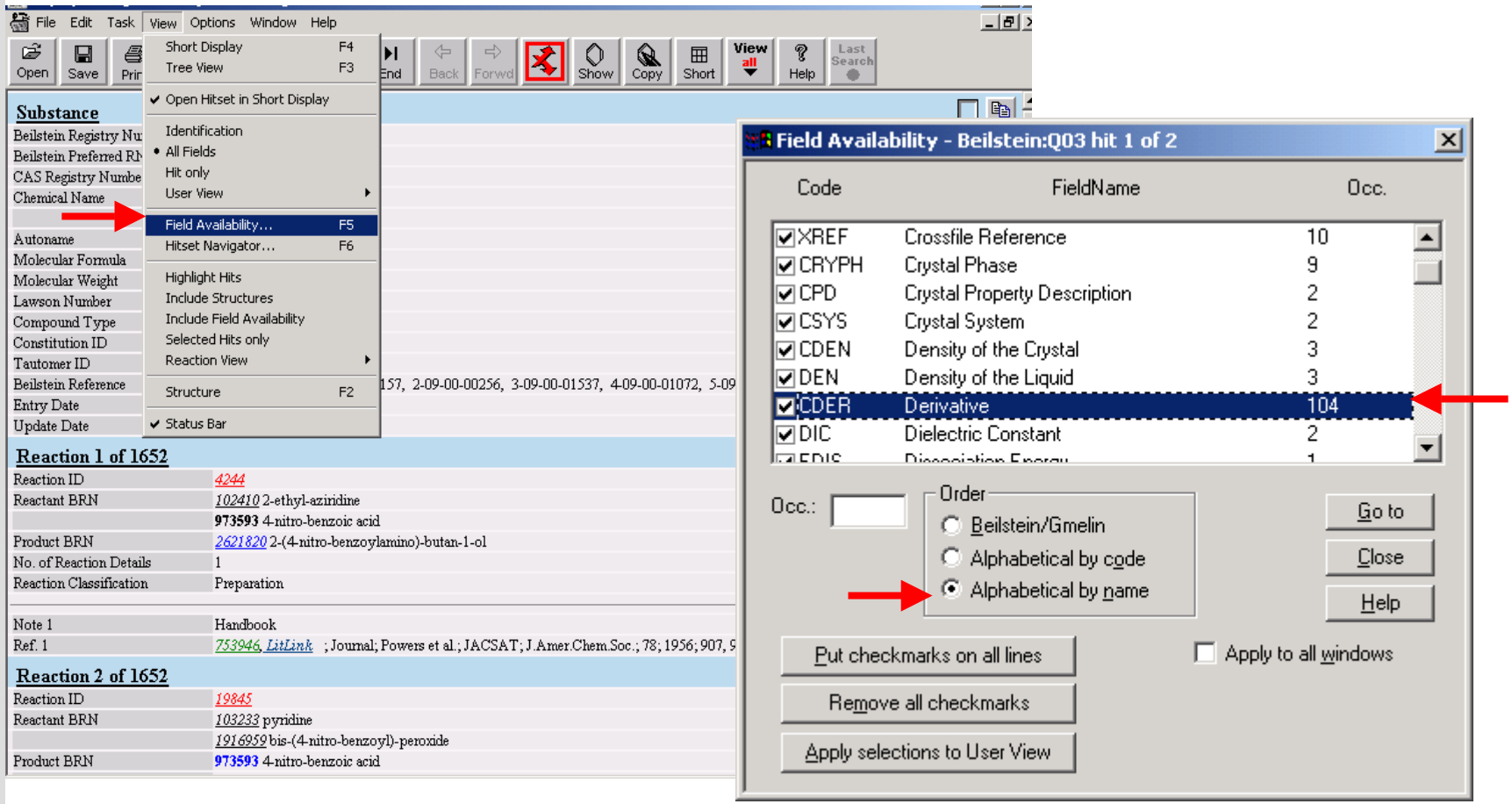




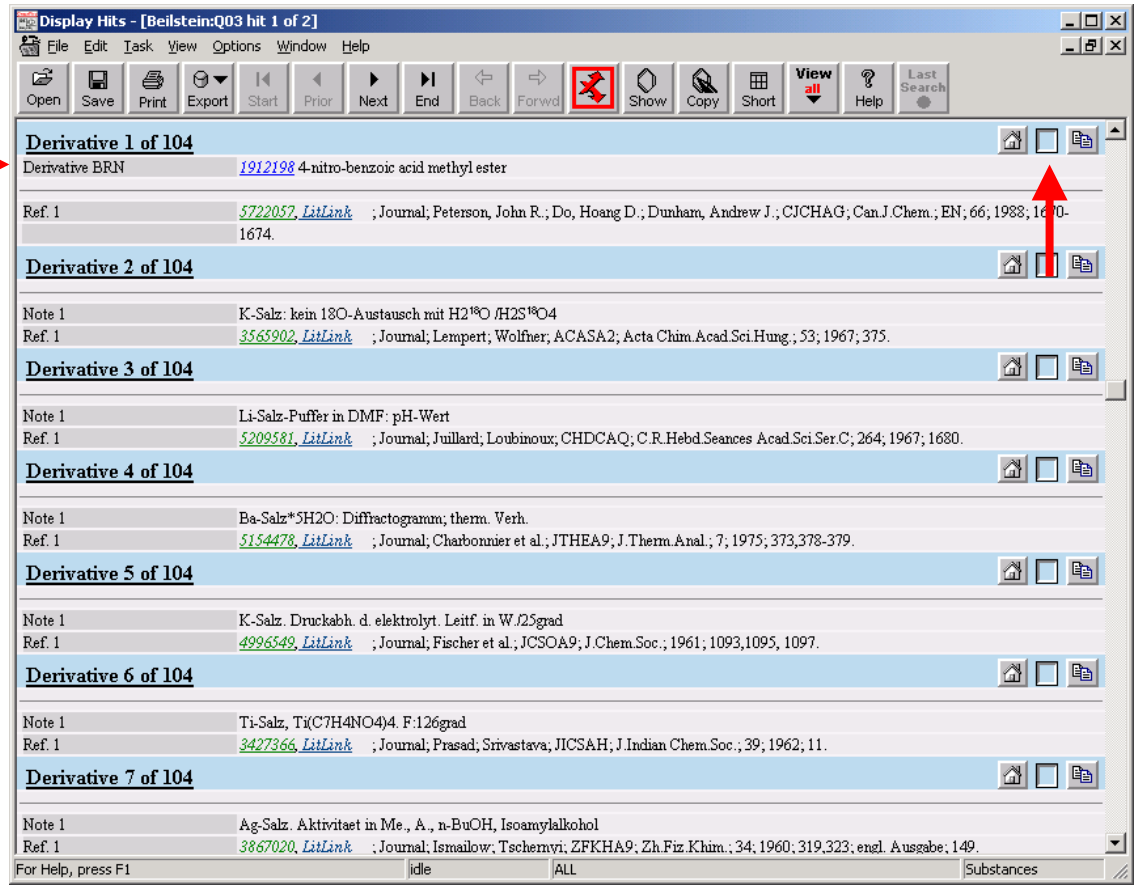
Finding Derivatives: Using Beilstein Crossfire continued



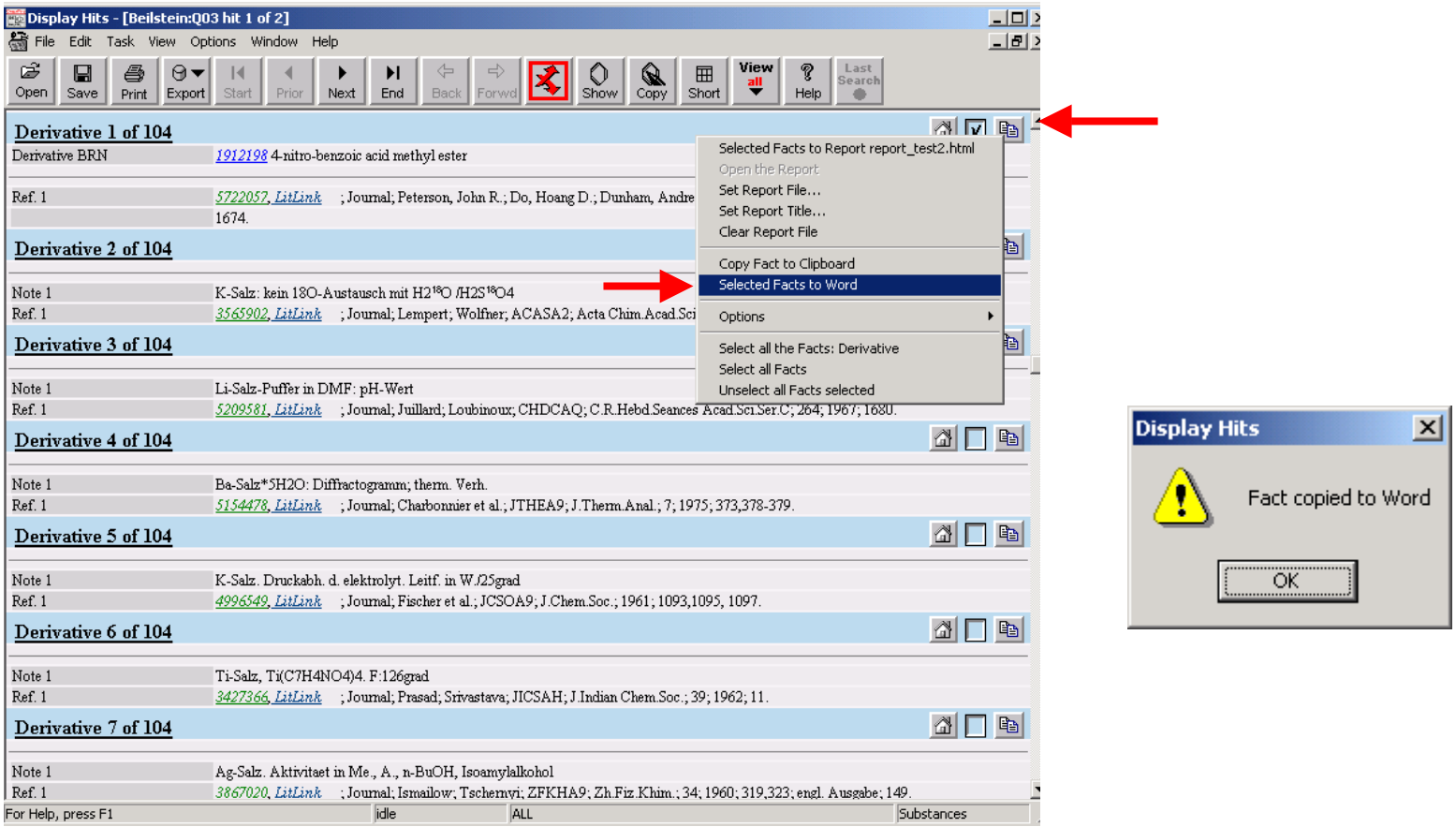
Finding Derivatives: Using Beilstein Crossfire continued



Finding Derivatives: Using Beilstein Crossfire continued



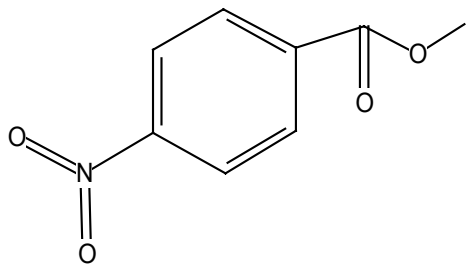
Finding Derivatives: Using Beilstein Crossfire continued



Finding Derivatives: Using Beilstein Crossfire continued

Derivative 1 of 104 (BS0203AE:Substances:Q03 hit 1, BRN 973593)

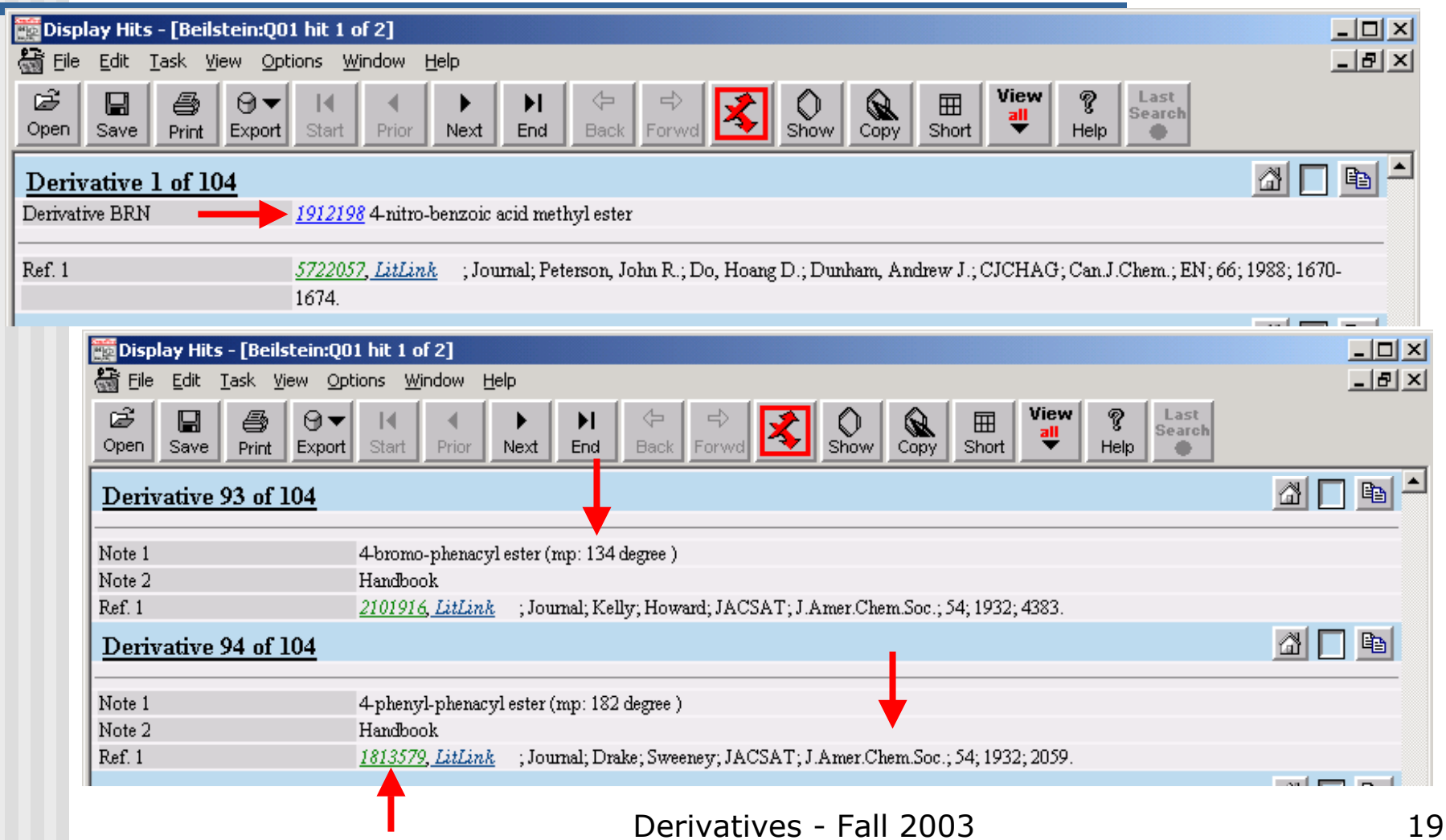
Derivative BRN	1912198 4-nitro-benzoic acid methyl ester
Ref. 1	5722057;LitLink; Journal; Peterson, John R.; Do, Hoang D.; Dunham, Andrew J.; CJCHAG; Can.J.Chem.; EN; 66; 1988; 1670-1674.



Derivative Entries in Beilstein

- Information varies but commonly includes the name of the derivative, MP/BP, and literature reference where derivative was synthesized.
- For more information about a derivative, try
  - **BRN** link (medium blue) next to name of derivative (if one exists)
  - **Citation** link (green) for literature reference
  - If neither option yields results, then do a **structure search** of the derivative in Beilstein.
- Sometimes, the full-text for a journal article indicates that the derivative you plan to make is an intermediate compound in a multi-step reaction. As long as there is physical property data for the derivative of interest, it is okay to use this reference for your lab report.

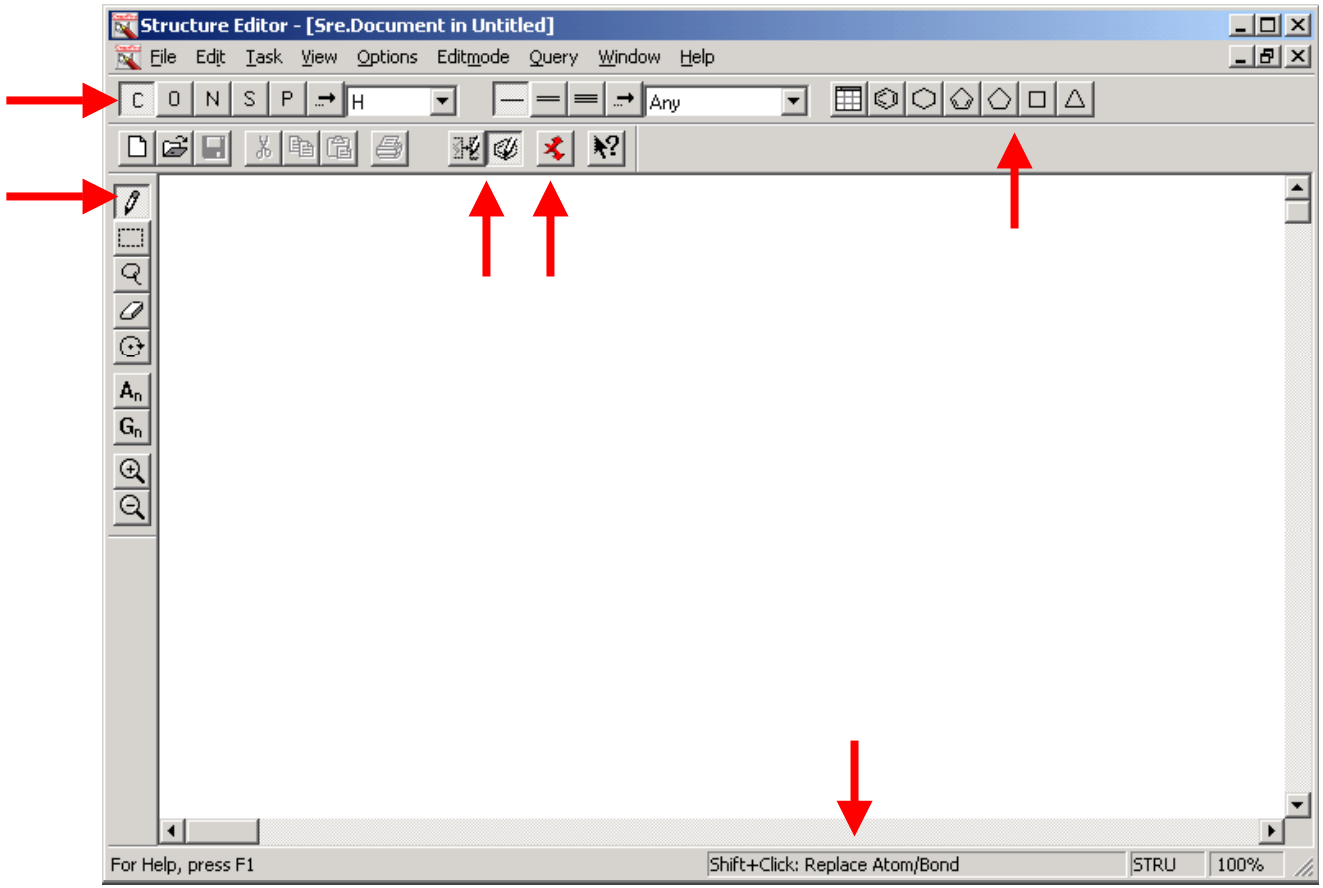
Displaying Derivative Entries in Beilstein and Using Hyperlinks Within Entries



Finding Derivatives in Beilstein Crossfire: Doing a Chemical Reaction Search

- After consulting Guidelines to determine what derivative you want to make, you can perform a reaction search two ways:
  - Unknown is a reactant and the derivative is a product
  - Unknown is a reactant and complete structure of derivative is not known
    - For example, product can be as small as a functional group. Define the point of attachment for the structural fragment of the derivative as an open site (see slide 25).

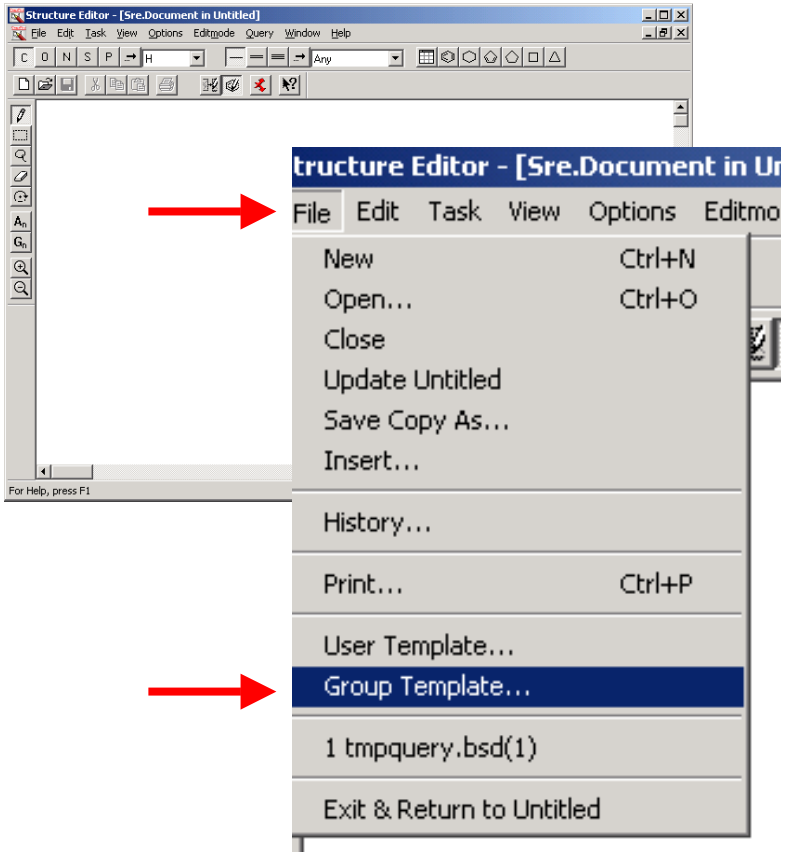
Beilstein Crossfire Structure Editor

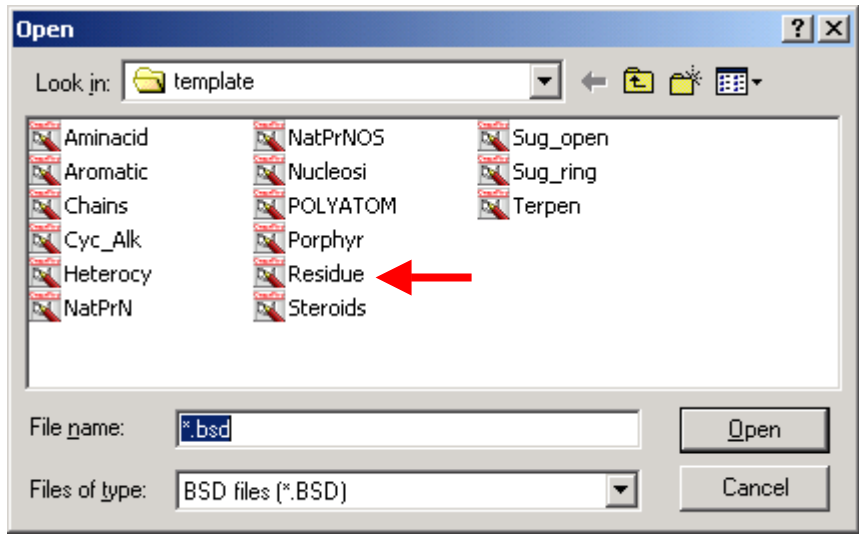


Structure Drawing Tips for Atoms, Bonds, and Functional Groups in Beilstein Crossfire

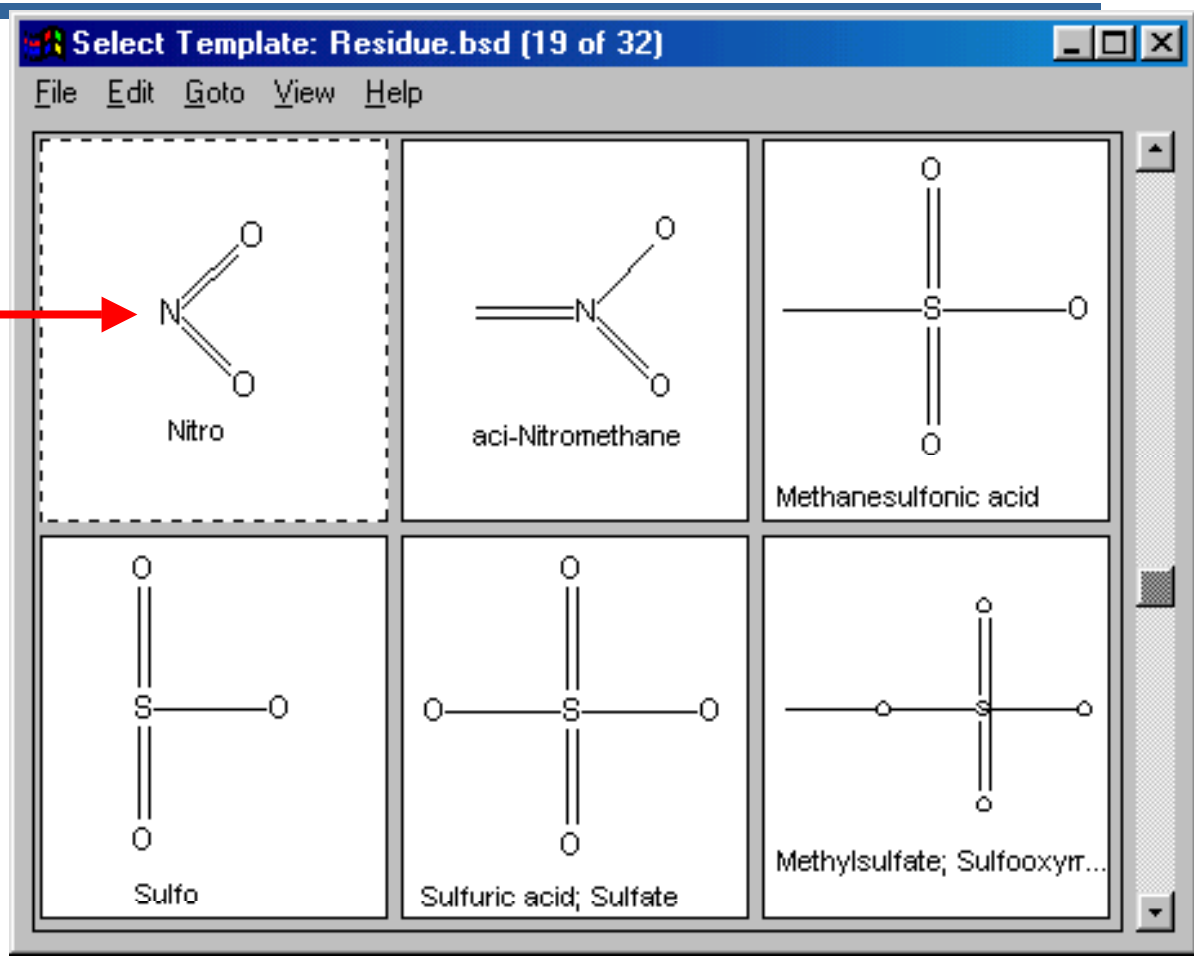
- Use Pencil and ring icons for drawing.
  - A = cursor positioned on an atom
  - B = cursor positioned on a bond
- Hold down **shift key** to change change **atoms** and **bonds**.
- To draw functional groups*:*
  - **File** menu bar > **Group Template** > **Residue** > double click to select desired item
  - Note all functional groups are drawn as if they were electrically neutral in Beilstein (e.g. a nitro group has double bonds to both Oxygen atoms)
- Don't need to draw Hydrogen atoms as Hydrogen saturation is assumed when search is run.

Using Group Templates in Beilstein Crossfire



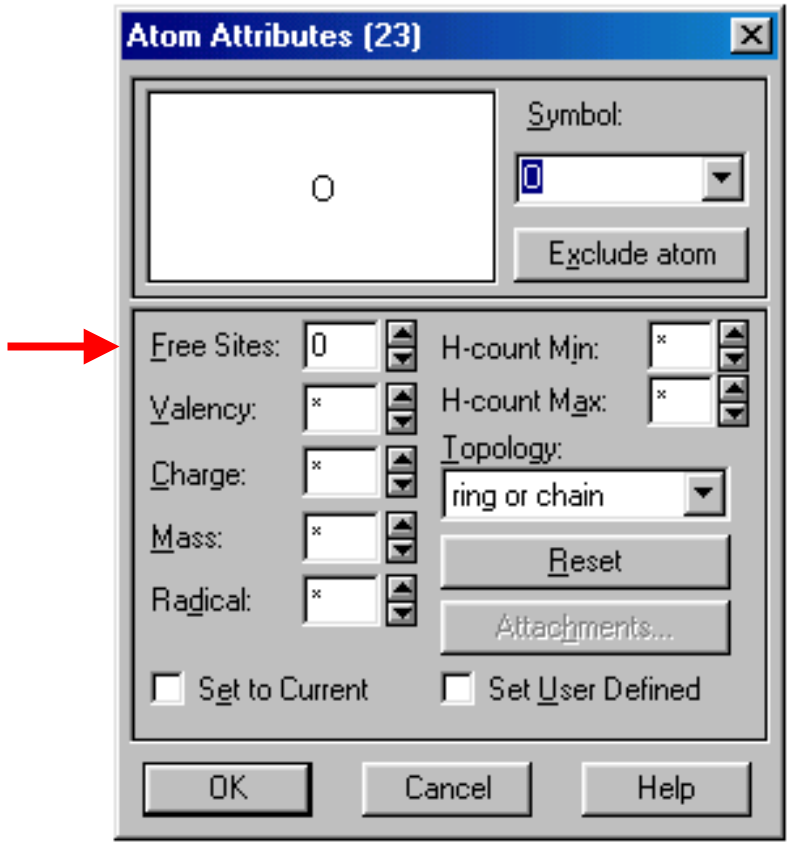


“Residues” or Functional Groups are Drawn Electrically Neutral in Beilstein Crossfire



Drawing Tip on How to Leave a Atom Position Open in Beilstein Crossfire

- If you need to leave a position open in a structure
  - Using Pencil tool, click once on an atom without holding the shift key down
  - A dialog box will open automatically. Set **Free Sites** to **Maximum** by clicking once on **Down Arrow**. Or, click on Up Arrow to indicate a specific number of connections at this position in the structure.



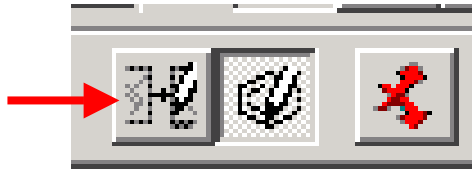
Copying Structures From Records to Structure Editor to Save Time in Beilstein

- Reduce the amount of drawing you need to do by copying the structure of your unknown into Structure Editor.
  - View full record for parent compound. If you do not see structure of compound, press F2. Highlight structure by clicking once on it.
  - Go to **Edit** menu bar and select **Copy Stucture to SE** (Structure Editor).
  - Structure will now appear in **Structure Editor** window.

Duplicating Structures Within the Structure Editor in Beilstein Crossfire

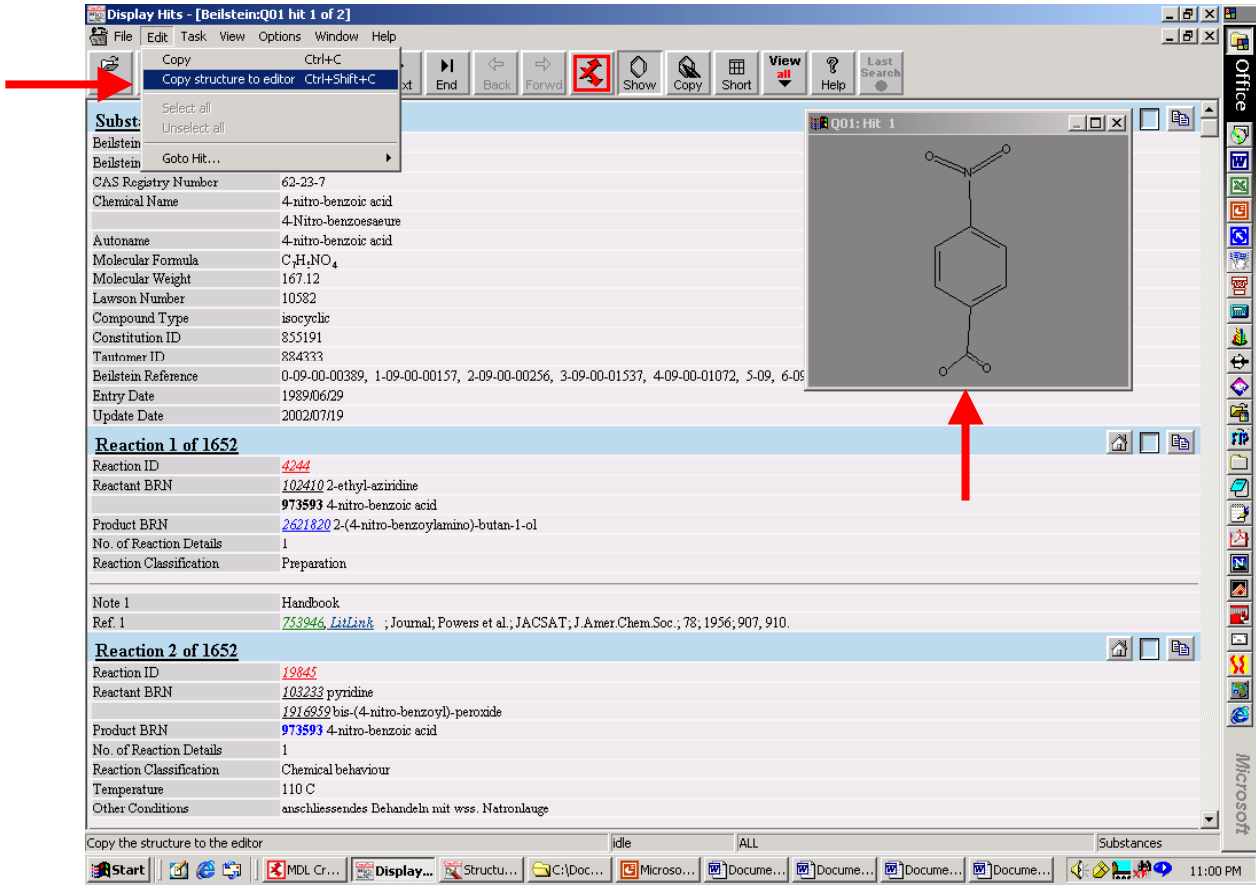
- Instead of drawing out the derivative or product you want to search, copy and modify the reactant (your parent unknown).
  - Highlight unknown with **Highlighter** tool (rectangle located directly below pencil tool).
  - Hold down **shift key** and **drag structure** to copy it.
  - Modify copied structure.
  - Make sure both structures are visible in structure drawing workspace on your screen.

Running a Reaction Search in Beilstein - Overview

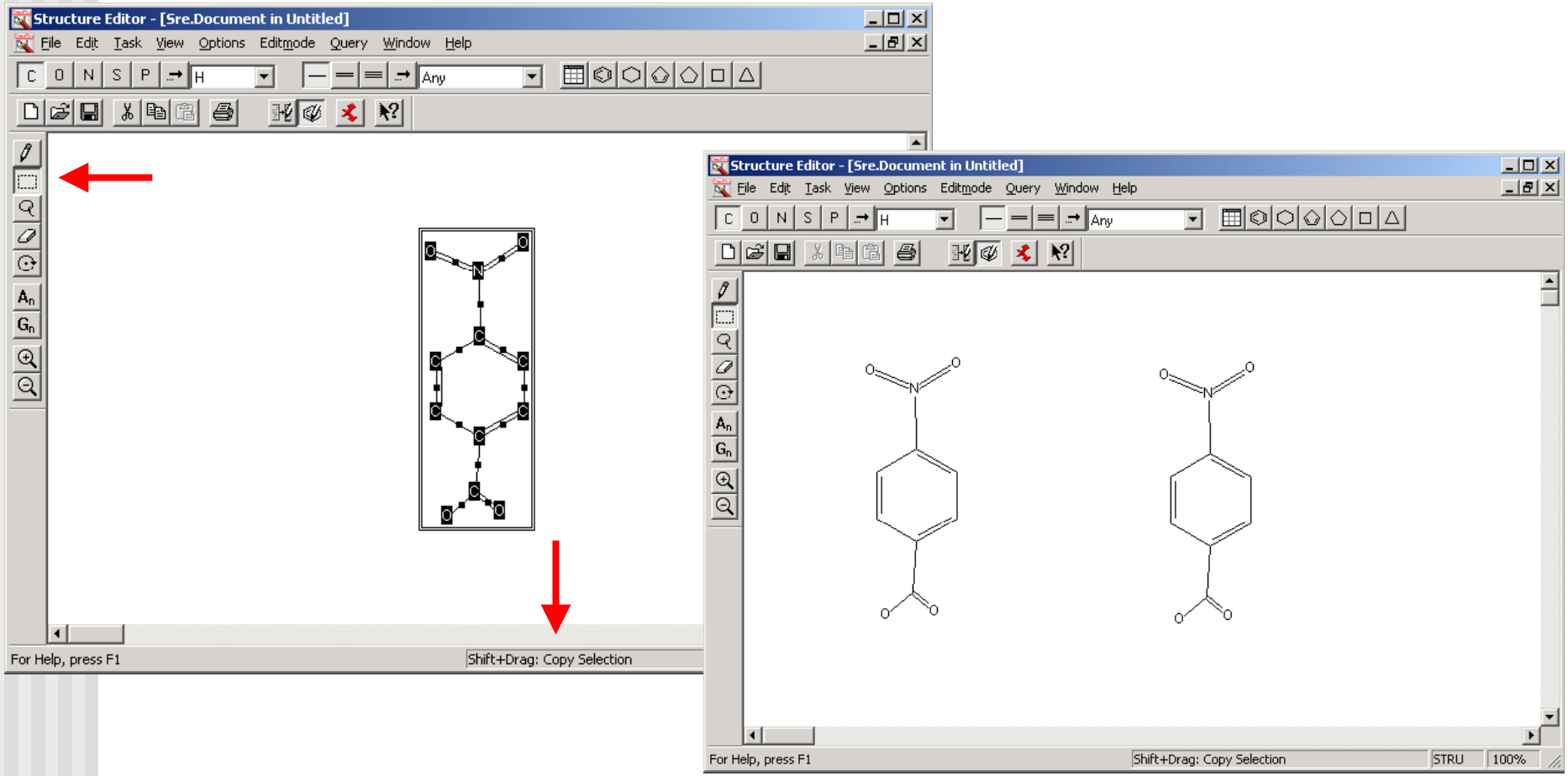


- After structures are drawn, click on **Reaction Attribute** Icon.
- Highlight each structure and label as reactant or product.
- Press Red Crosses icon to return to the main interface. Run search and view results in short display format.
- Note: if you need to modify a structure, you must do this in the **Structure Editor**.

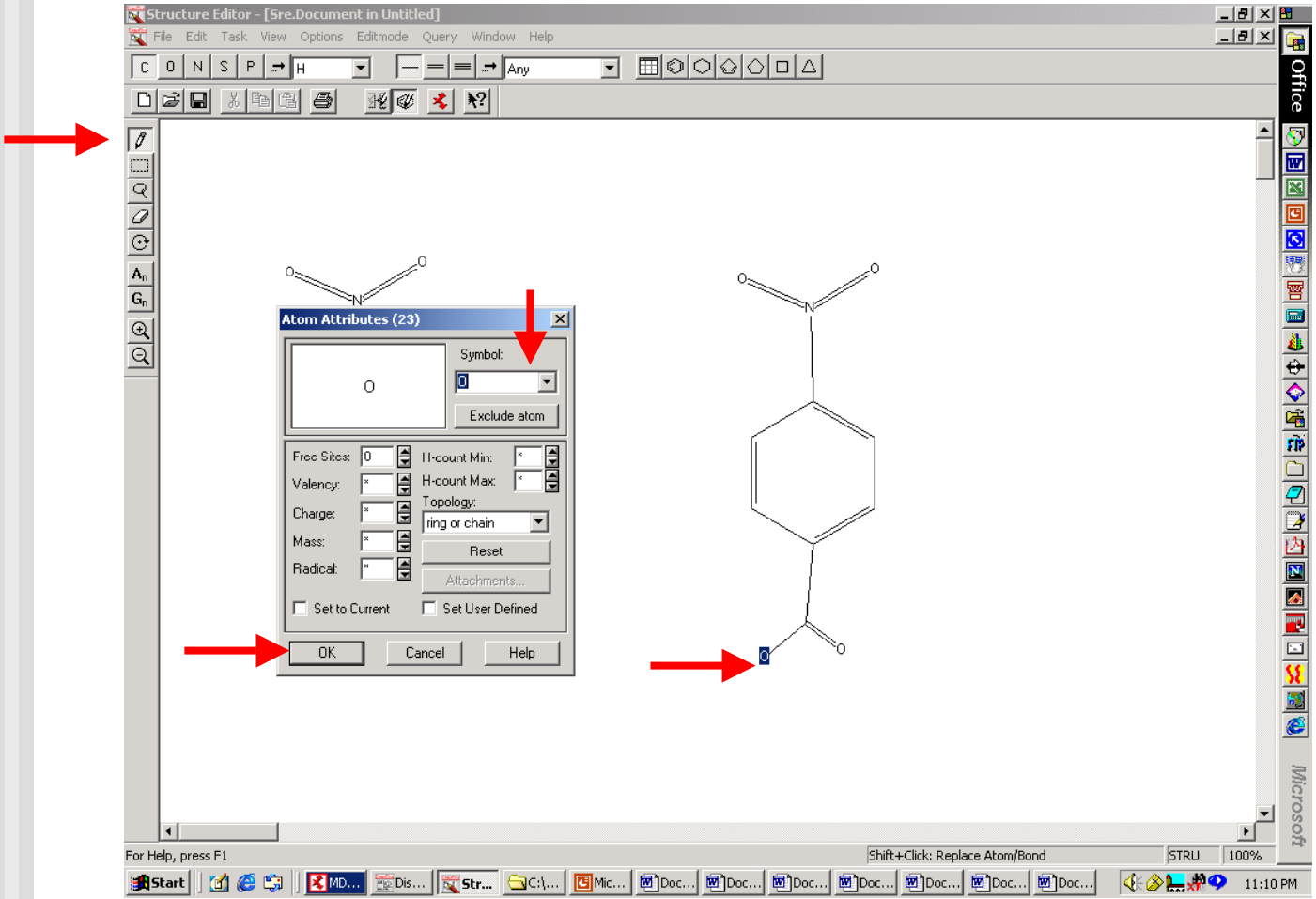
Copying structure to Structure Editor - Sample Search in Beilstein Crossfire



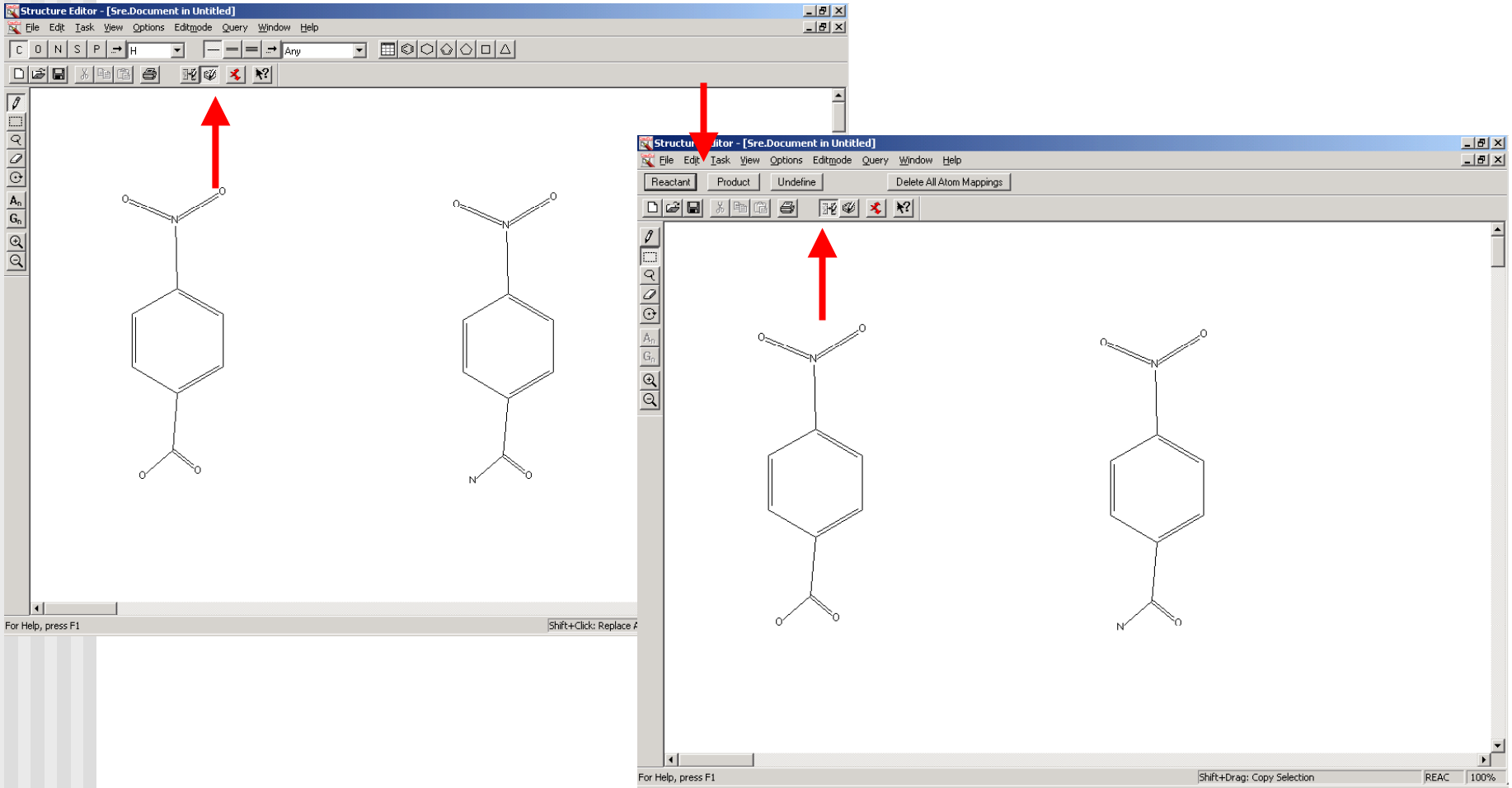
Making 2nd Copy of Structure Within Structure Editor in Beilstein Crossfire



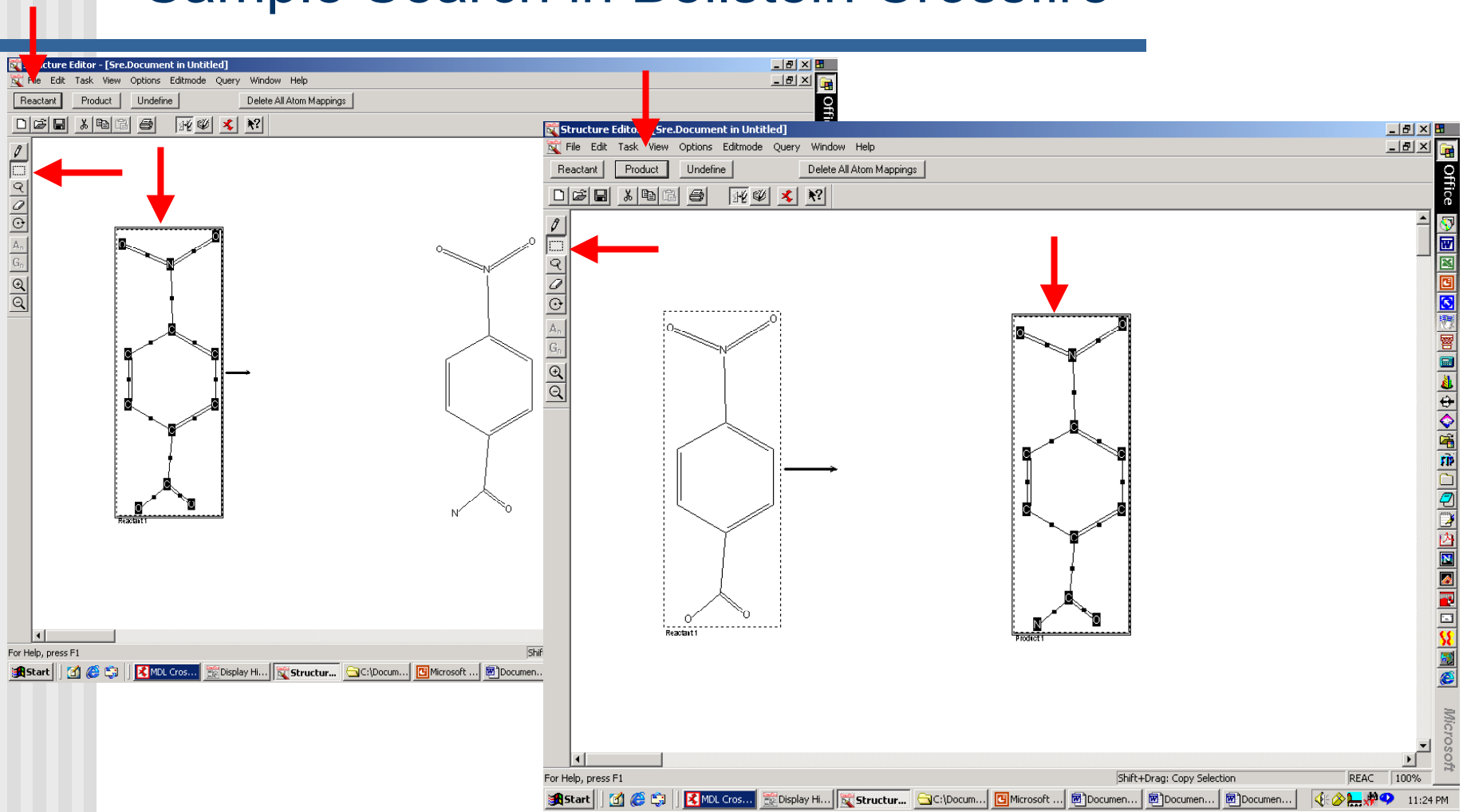
Changing an Atom Value of a Structure in Beilstein Crossfire



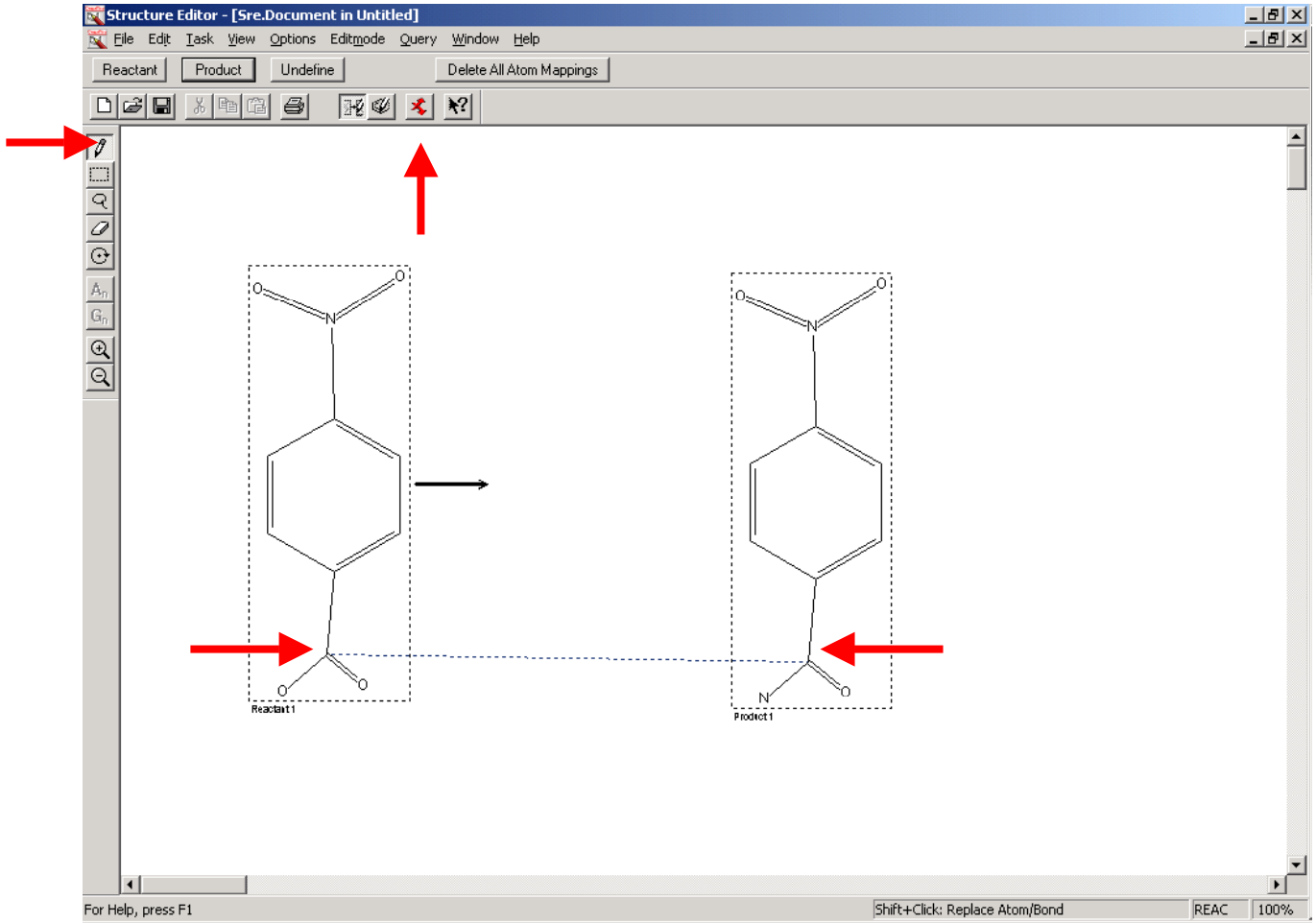
Structure Editor and Reaction Mode in Beilstein Crossfire



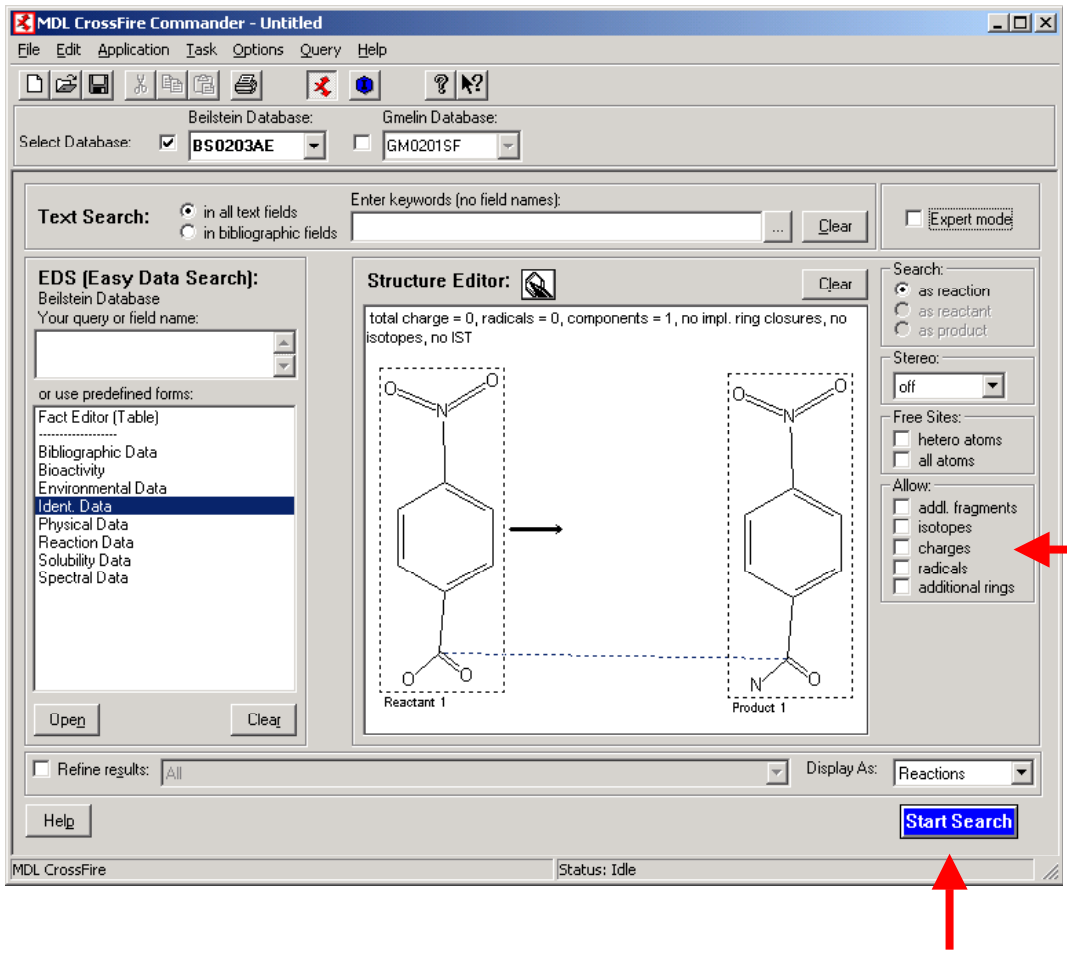
Specifying Reactant and Product of a Reaction - Sample Search in Beilstein Crossfire



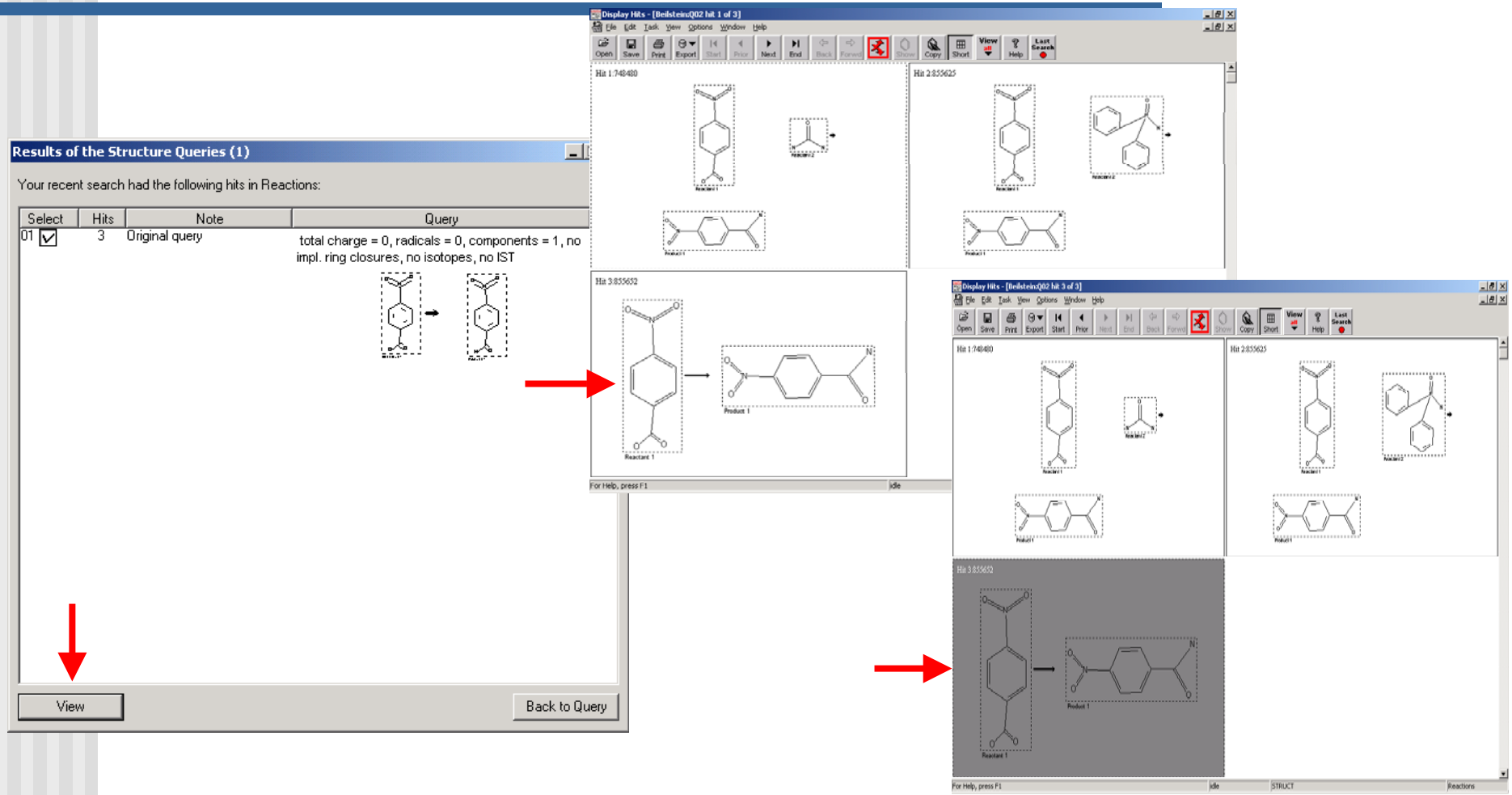
Mapping Atoms to Make a Reaction Search More Precise in Beilstein Crossfire



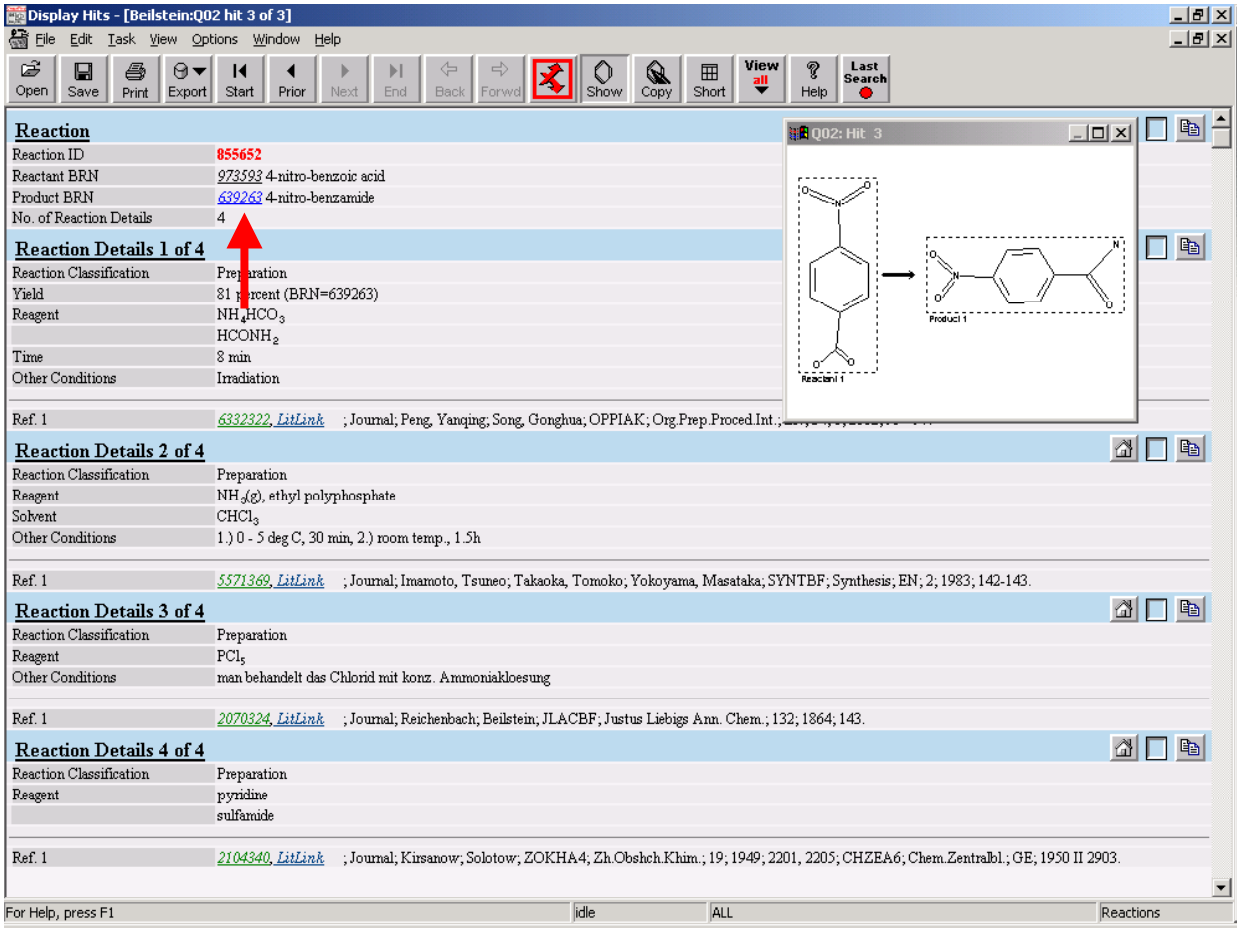
Performing a Reaction Search in Beilstein Crossfire



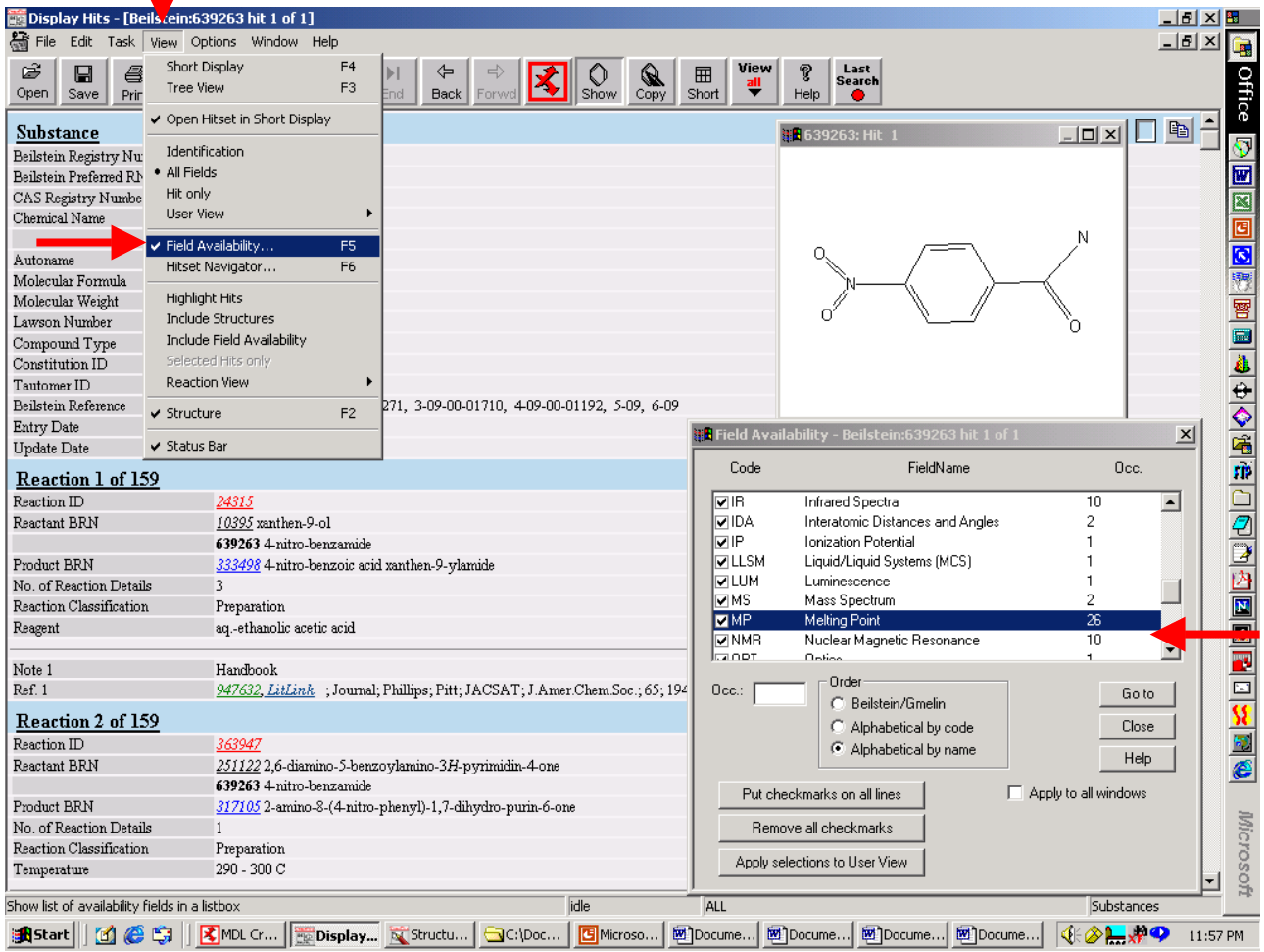
Viewing Results of Reaction Search in the Short Display Format in Beilstein Crossfire



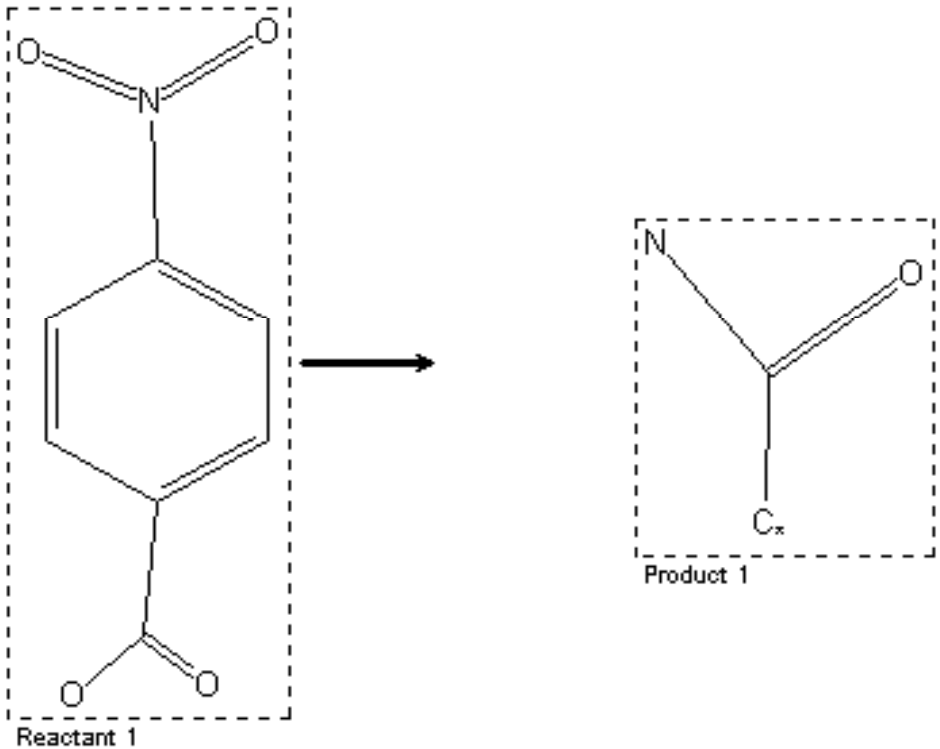
Viewing Reaction Entries and Clicking on Substance Hyperlink in Beilstein Crossfire



Finding Physical Properties for a Derivative in Beilstein Crossfire



Search Tip: Reaction Search in Beilstein Where Product is a Substructure Because you Don't Know What Complete Structure Looks Like



Finding Physical Properties for a Derivative in Beilstein

- Options for finding physical property data for a derivative:
  - View Derivative field usually includes MP/BP data.
  - View citation link as it may include a Substance link for the derivative.
  - Perform a structure search of the derivative and view compiled data.
  - After doing a reaction search, click on the Beilstein Registry Number (BRN) link of derivative to see data.

Finding Physical Properties for a Derivative in CCD, POC, Merck, & Preparation Papers

- Using a CAS Registry Number, molecular formula, or chemical name, it is also possible to search CCD, POC, or Merck to see what physical property data has been compiled for a derivative.

- Preparation or synthesis papers for substances usually contain complete descriptions, including physical properties, of compounds.

Help

- Please consult a TA if you need help selecting a derivative or interpreting lab data.
- Consult with librarians if you need help with “mechanics” of doing searches.
- Good luck and have fun searching!