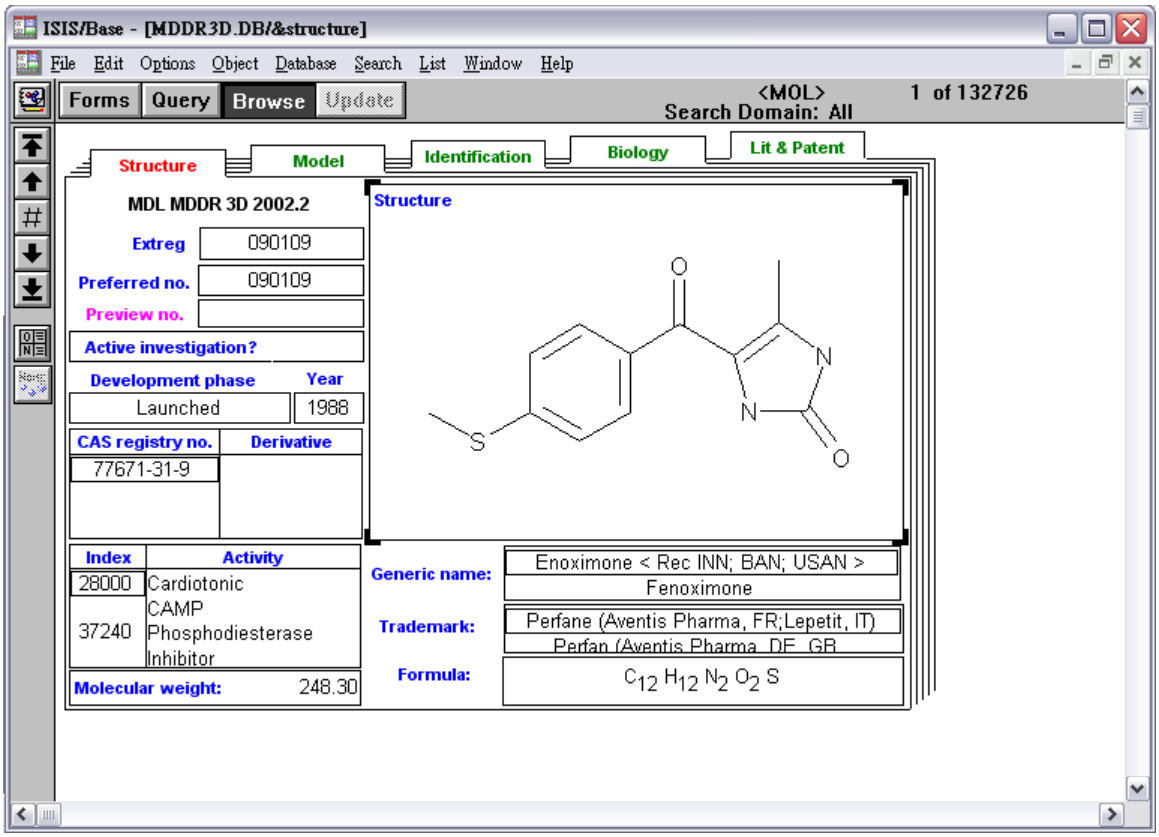
Appendix

A. Preparation of the Screening Set of DHFR: Steps and Tools

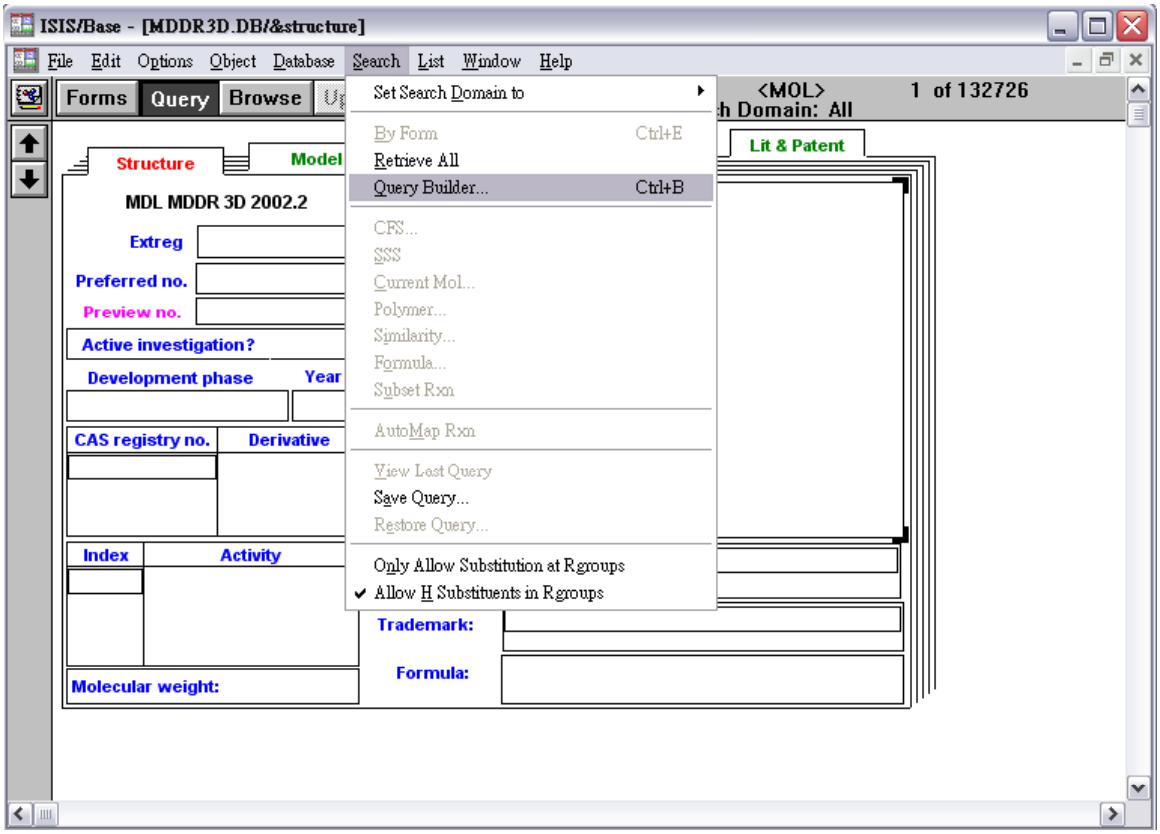
a. Tools: MDL ISIS/Base and ISIS/Draw

b. Databases: the MDDR and PDB

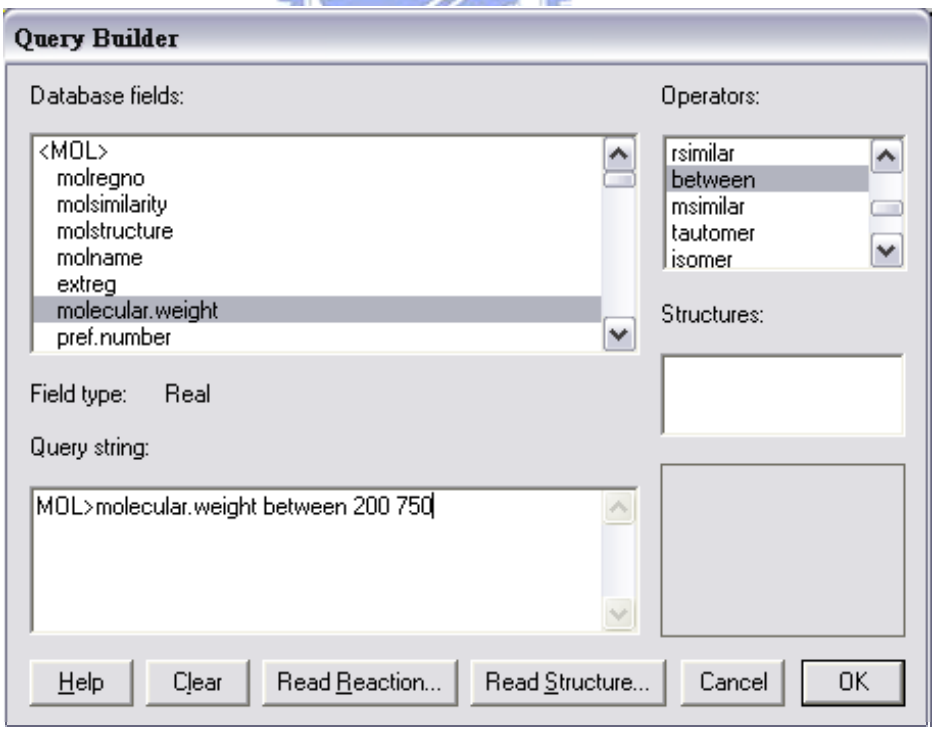
c. Steps:



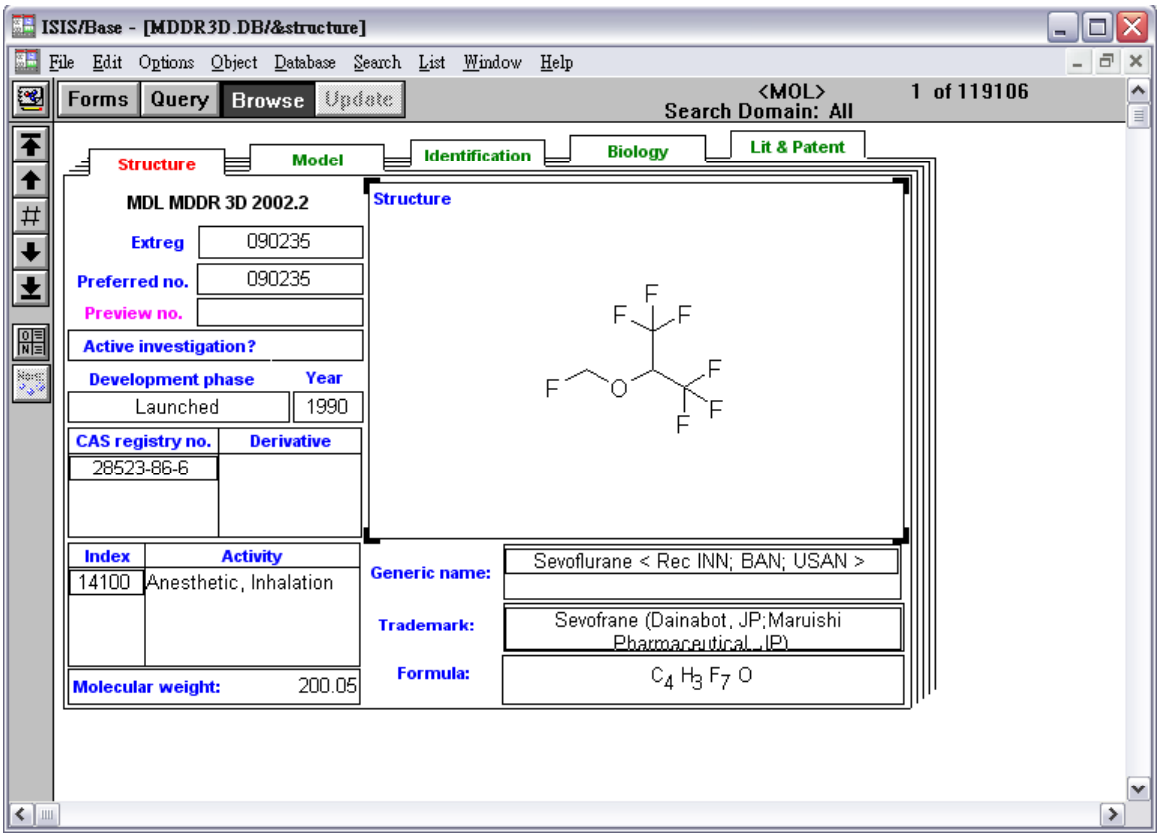
Step 1. Connect to the MDDR with ISIS/Base



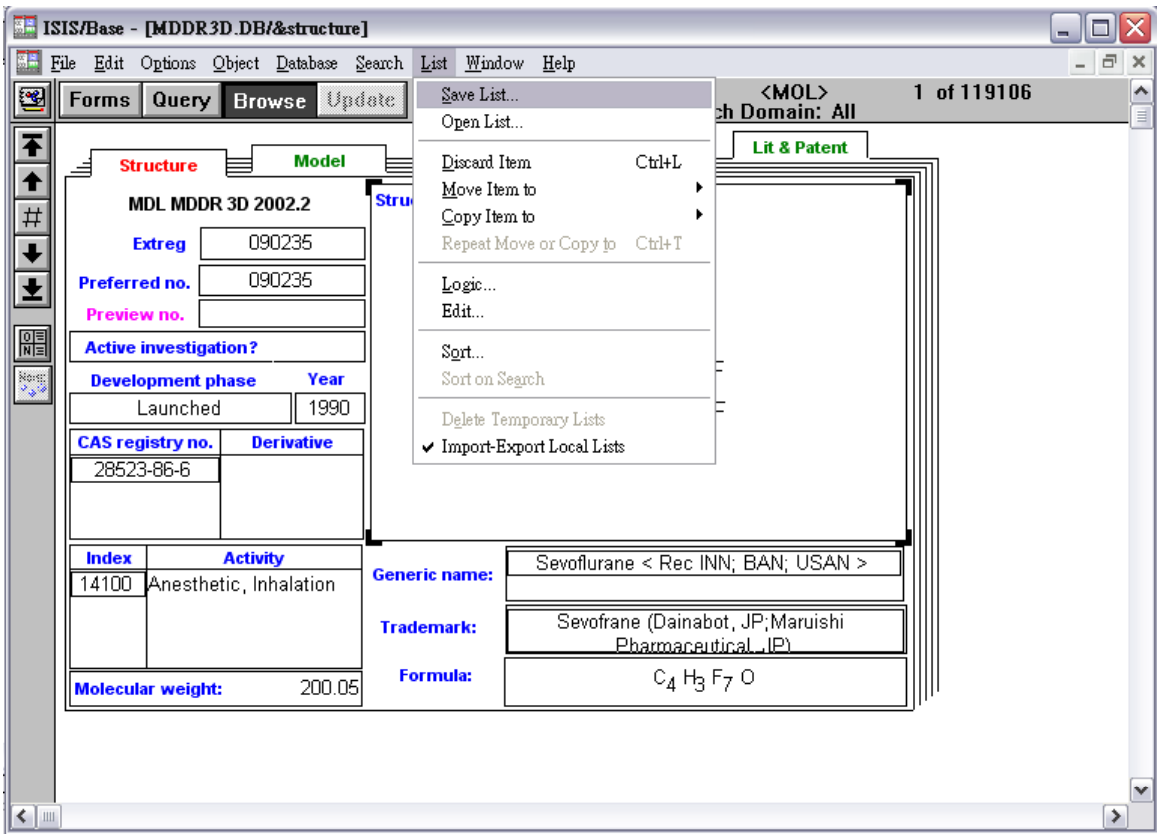
Step 2. Build a query with the query builder



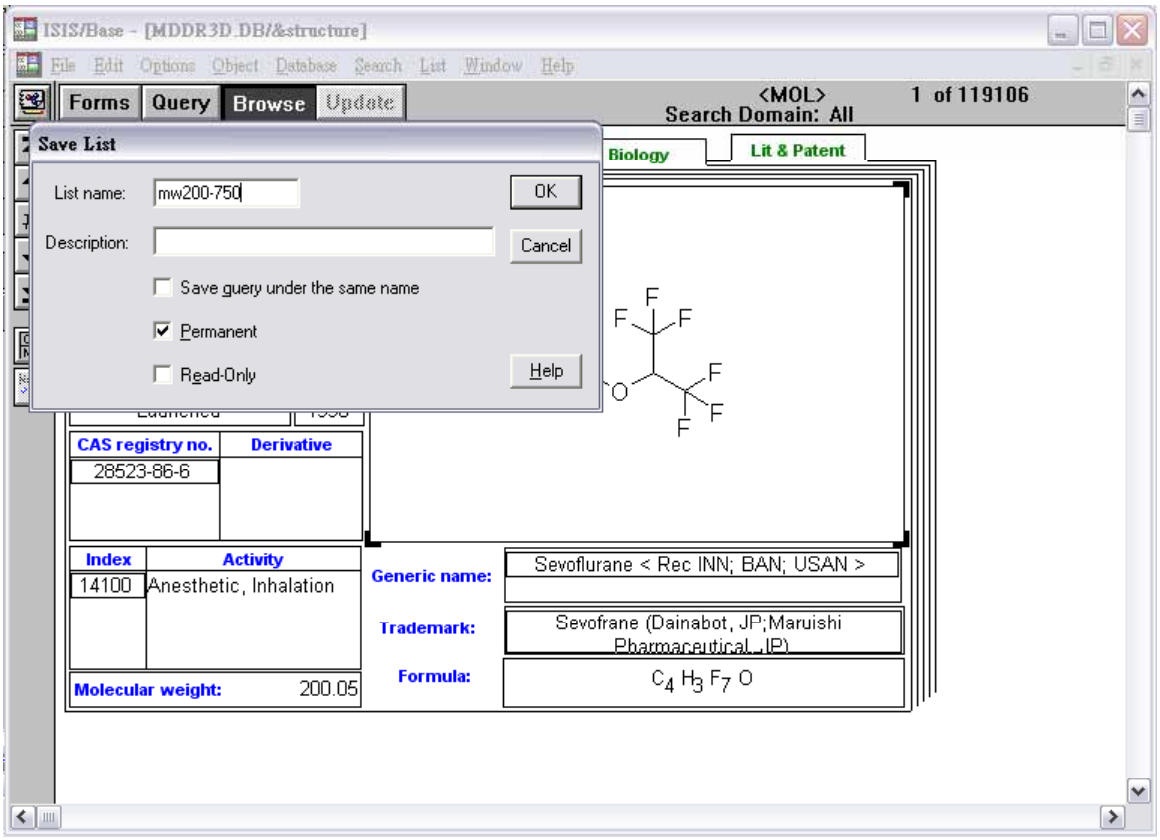
Step3. Select “molecular.weight” between 200 and 750



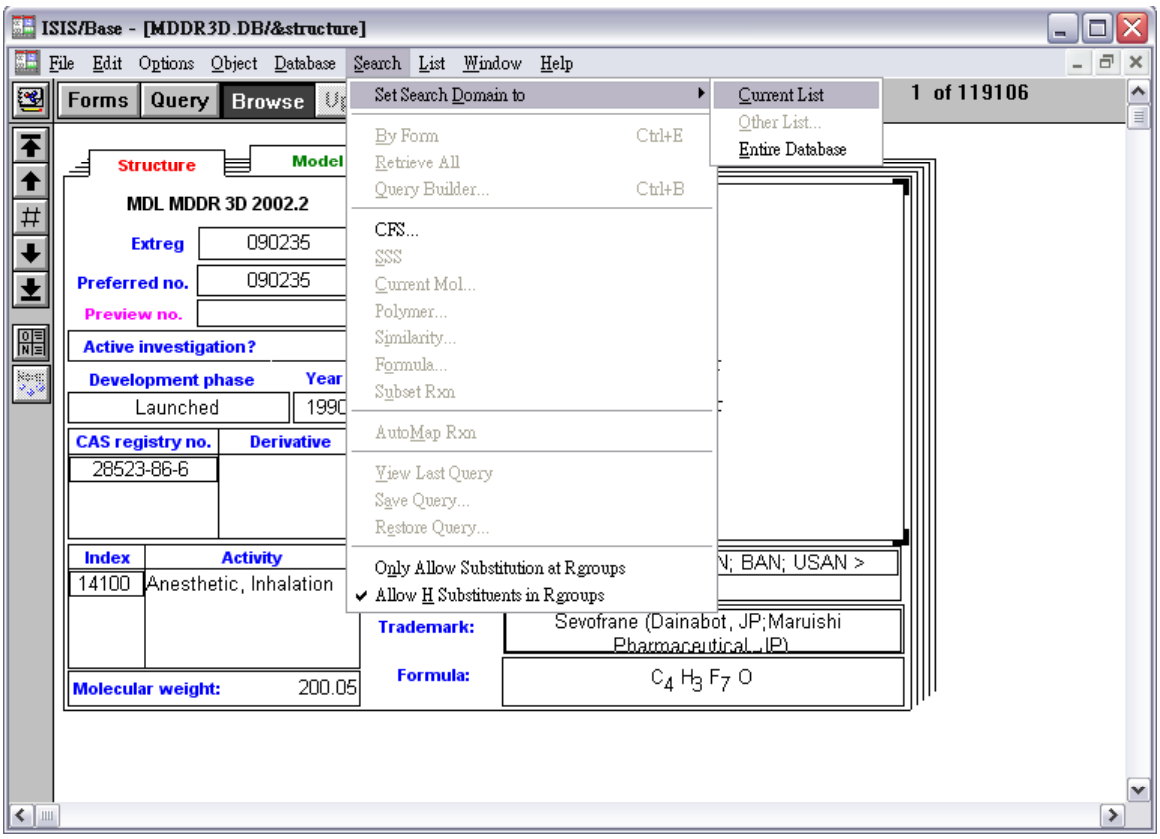
Step 4. 119106 molecules with molecular weights between 200 and 750



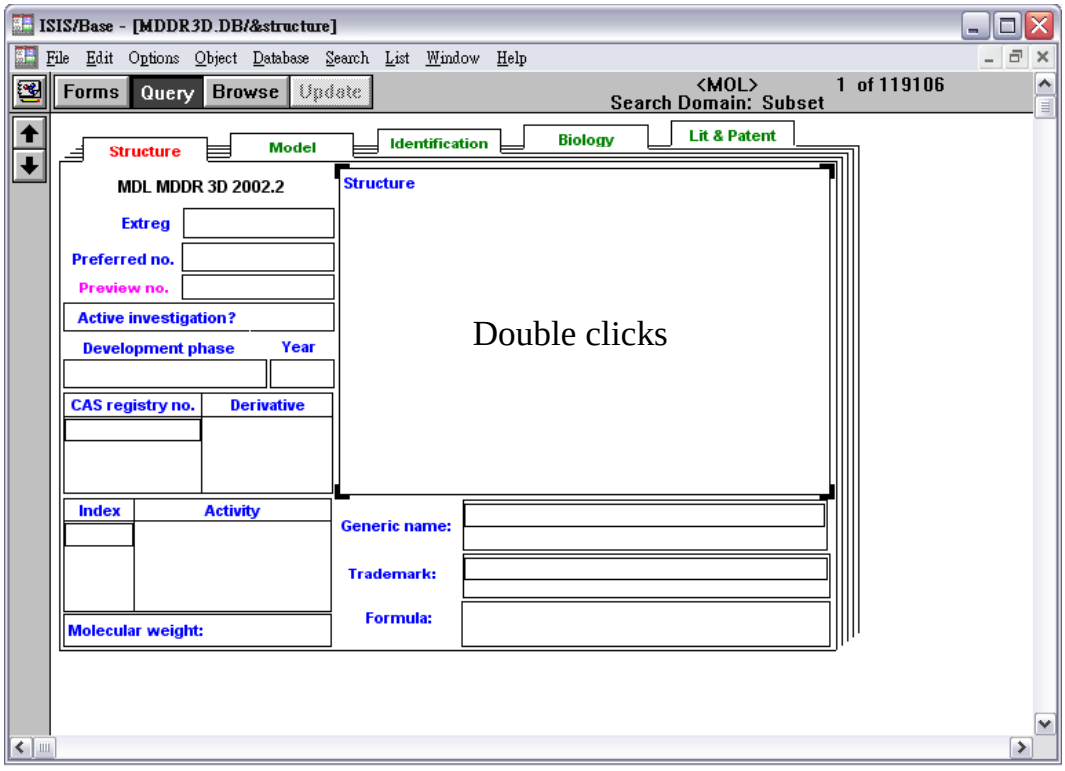
Step 5. Save the list of molecules with molecular weights between 200 and 750



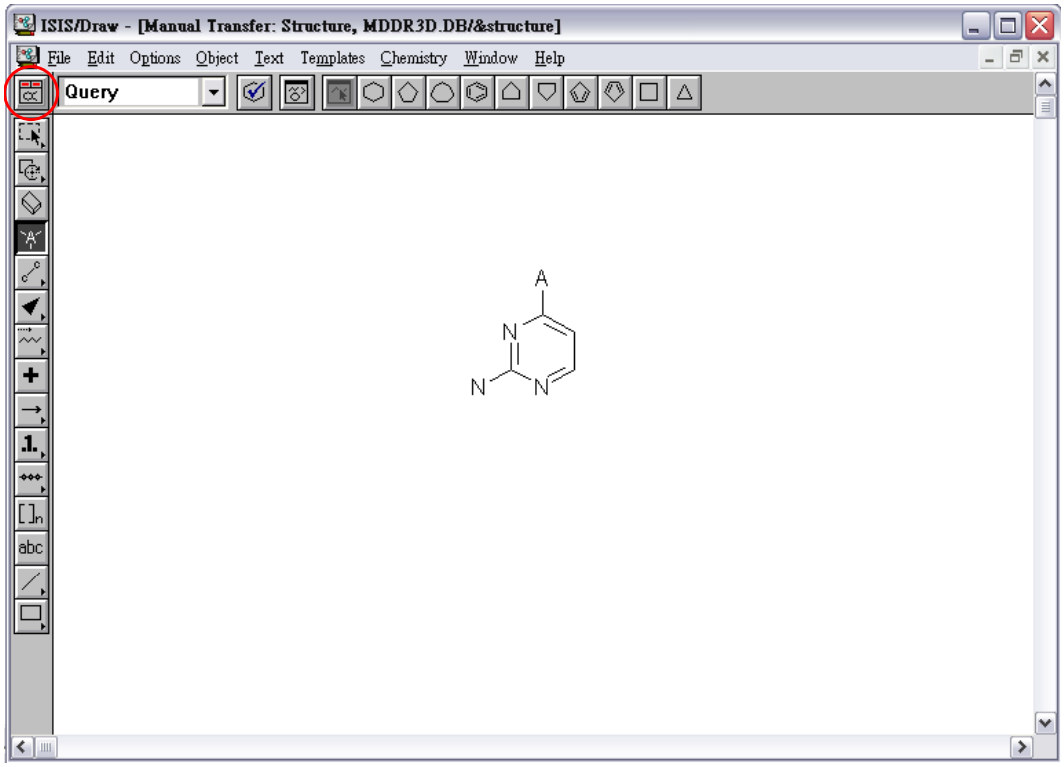
Step 6. Input the list name



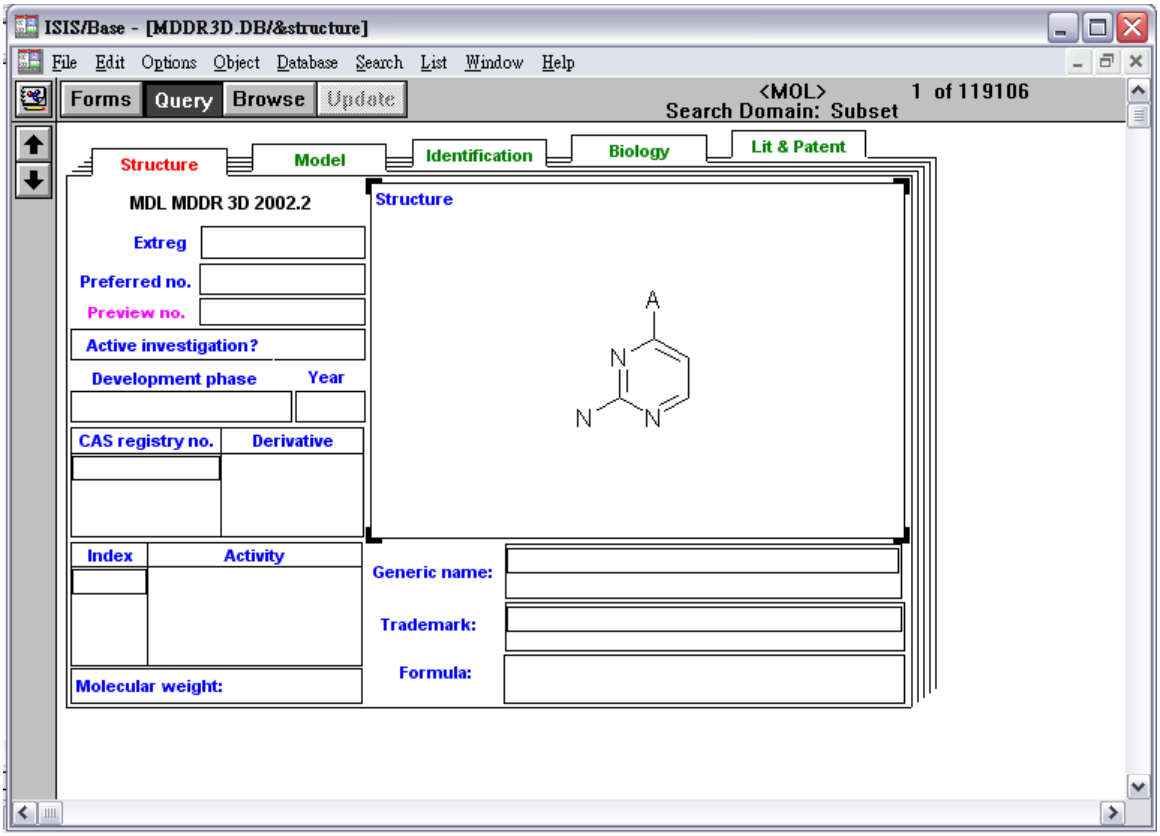
Step 7. Set search domain to the current list



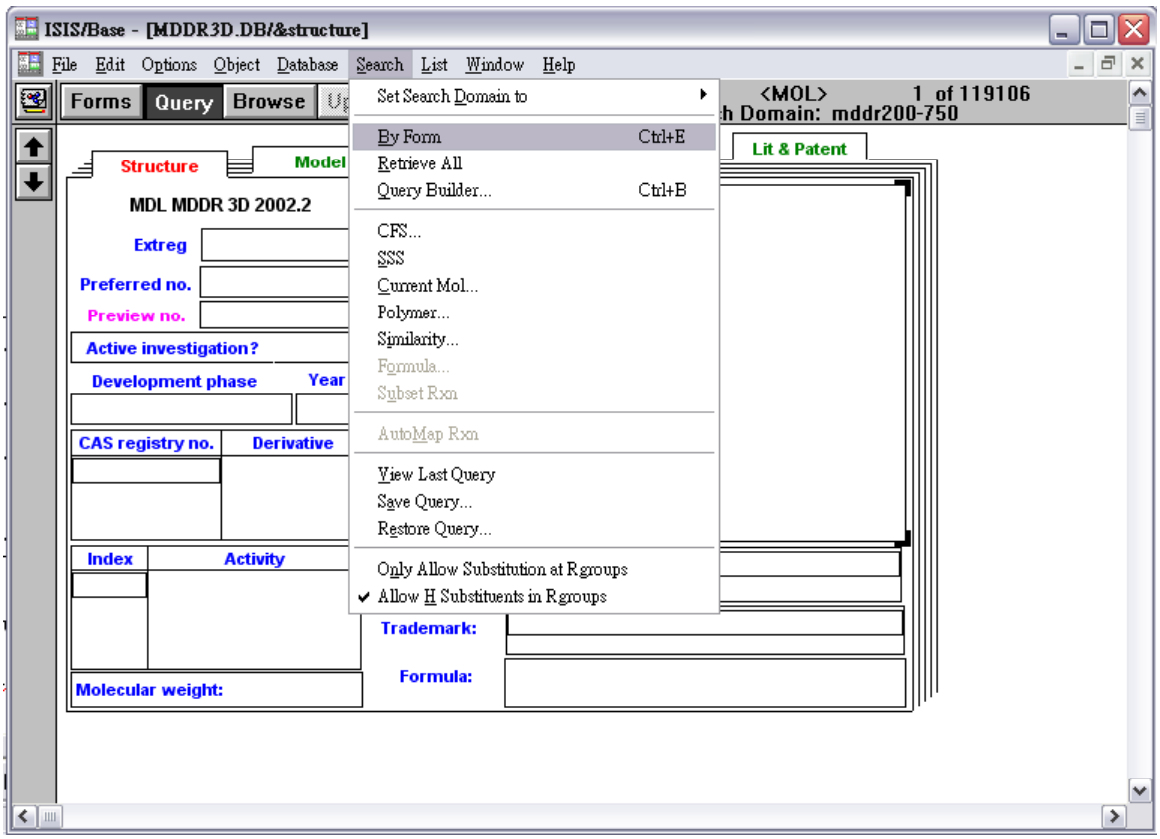
Step 8. Query the similar structures in the current list. Double clicks on the structure block



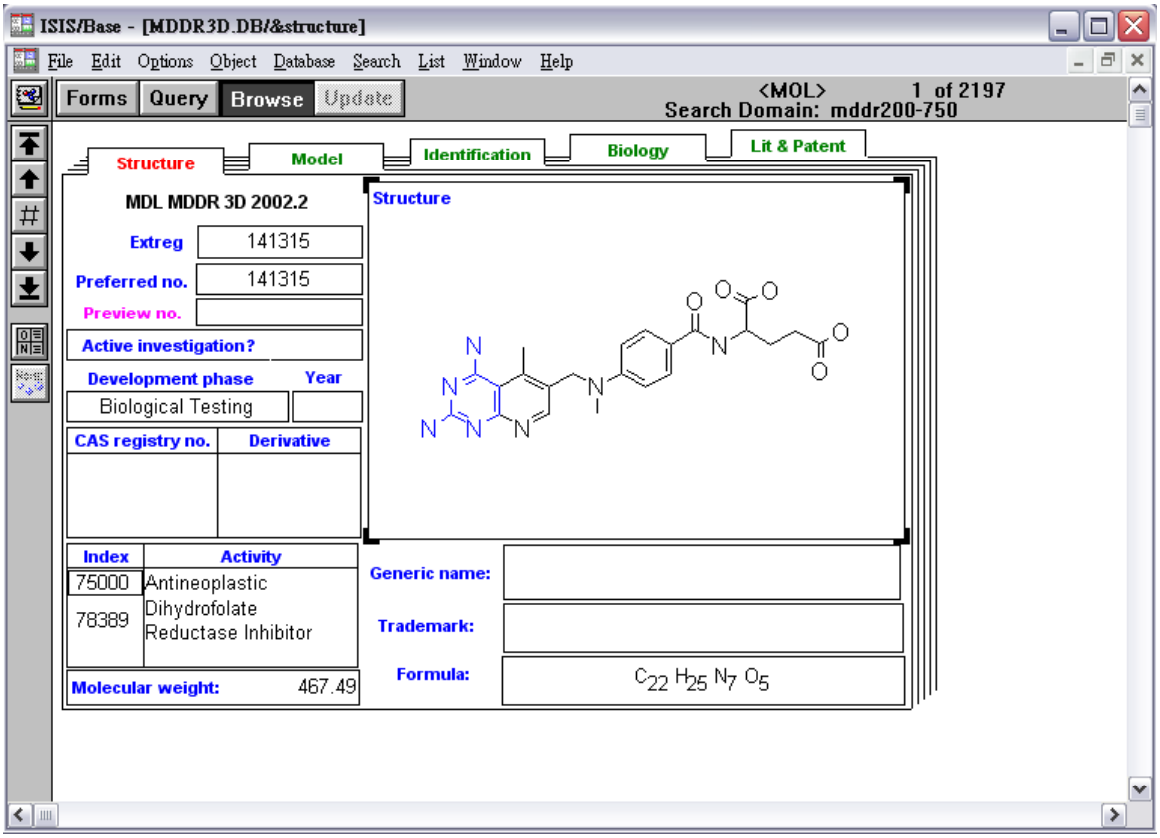
Step 9. Draw the structure that you want to query with the ISIS/Draw. Click the up-left icon (red circle) to transfer the query structure to the ISIS/Base



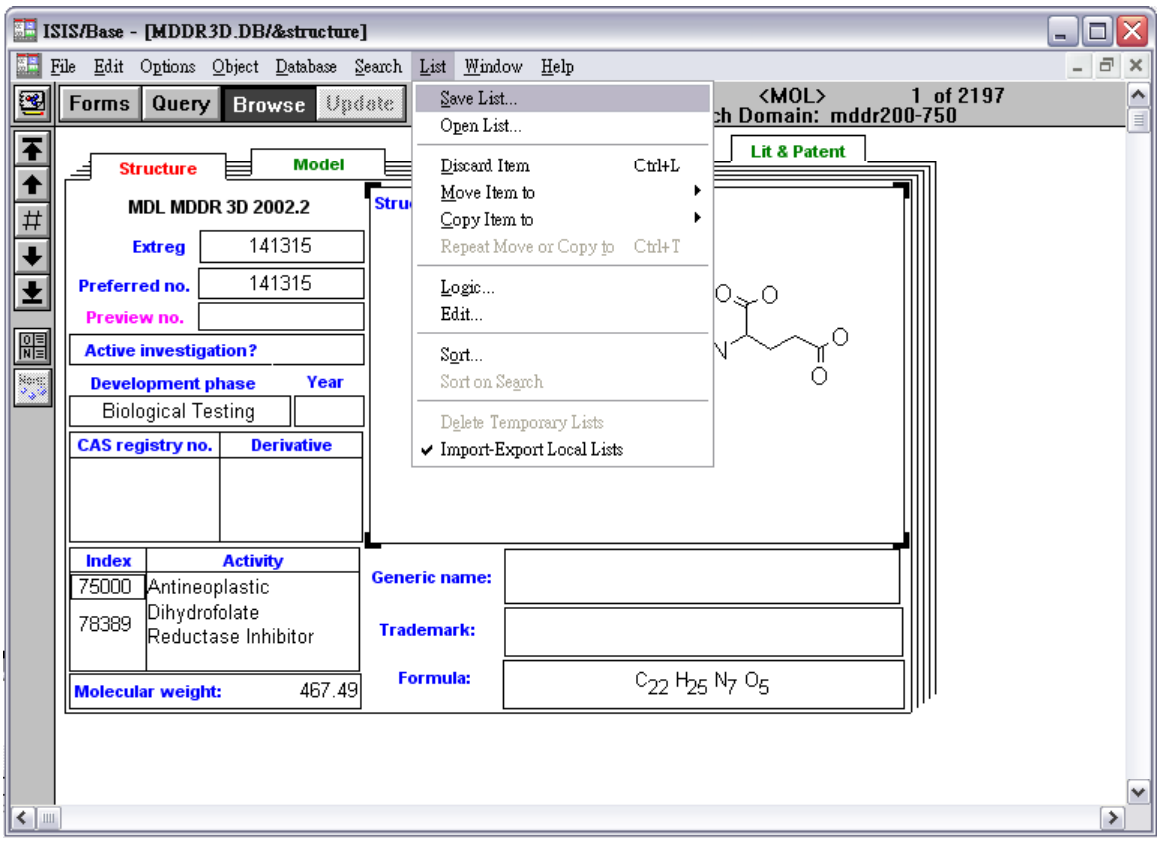
Step 10. Transfer completely



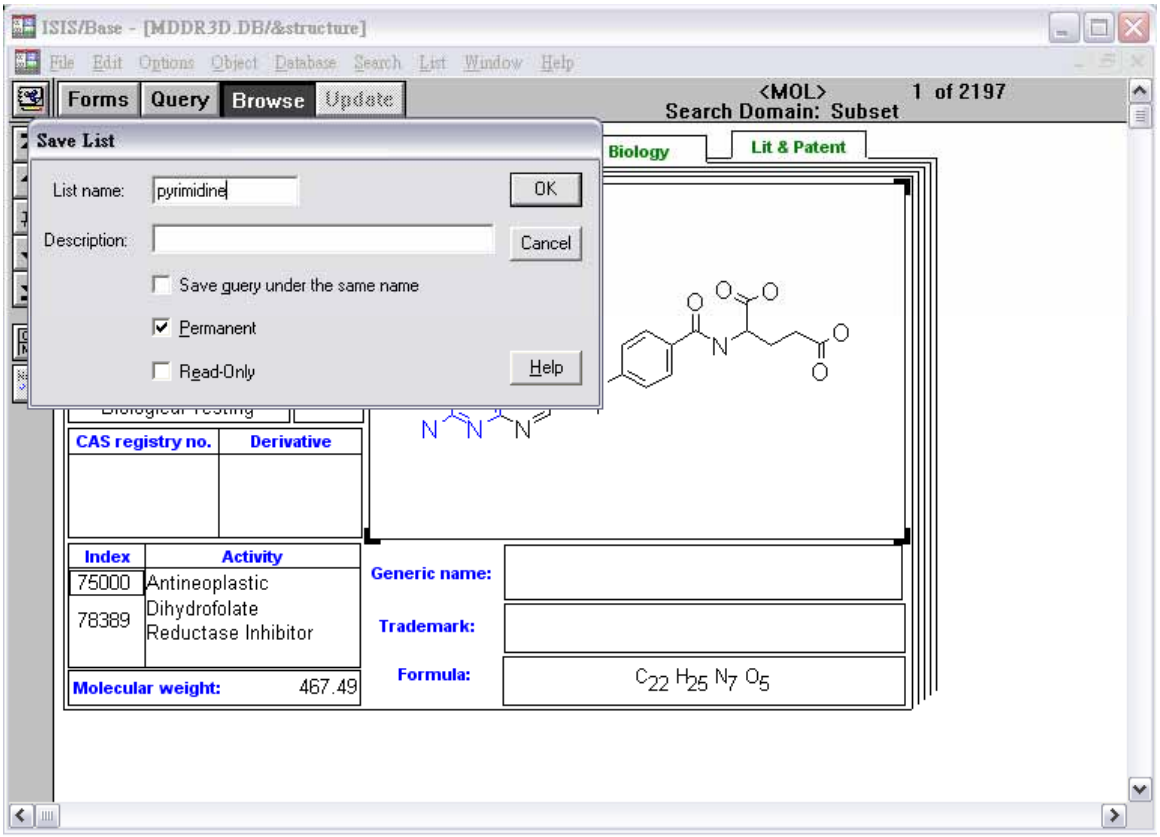
Step 11. Search by the form



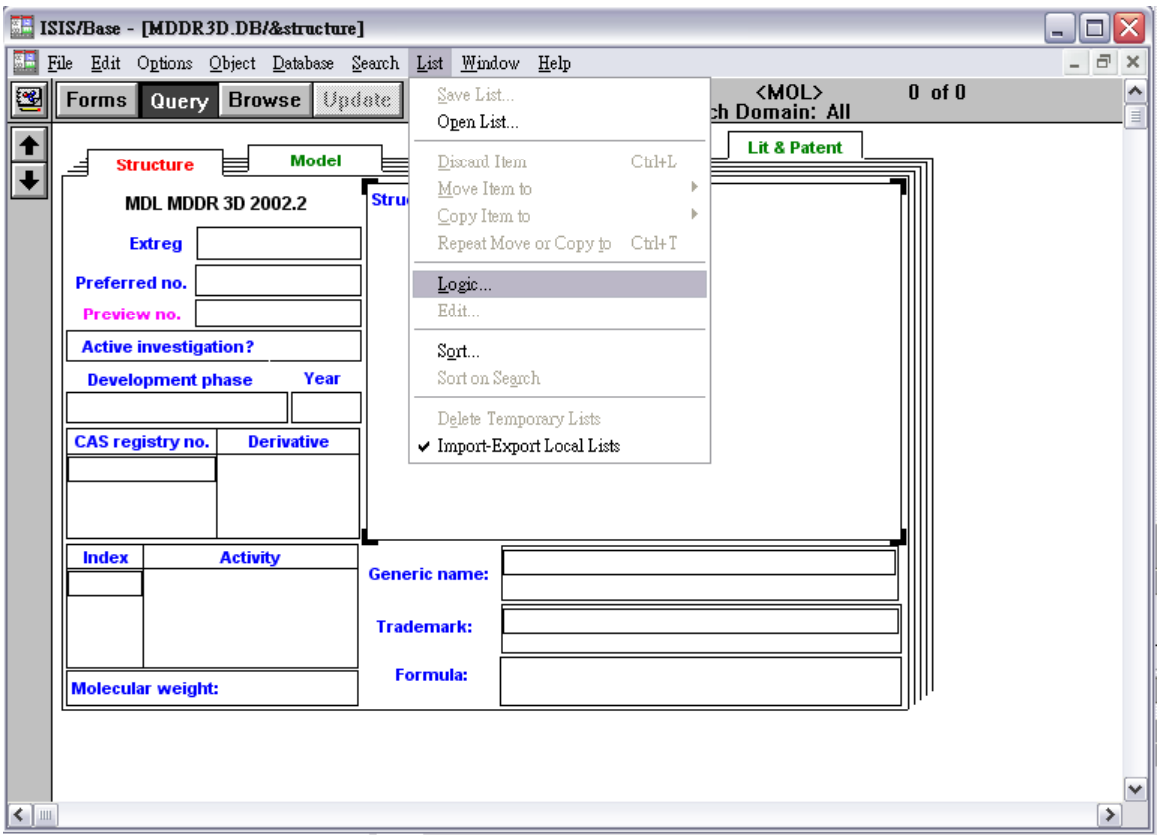
Step 12. Search result



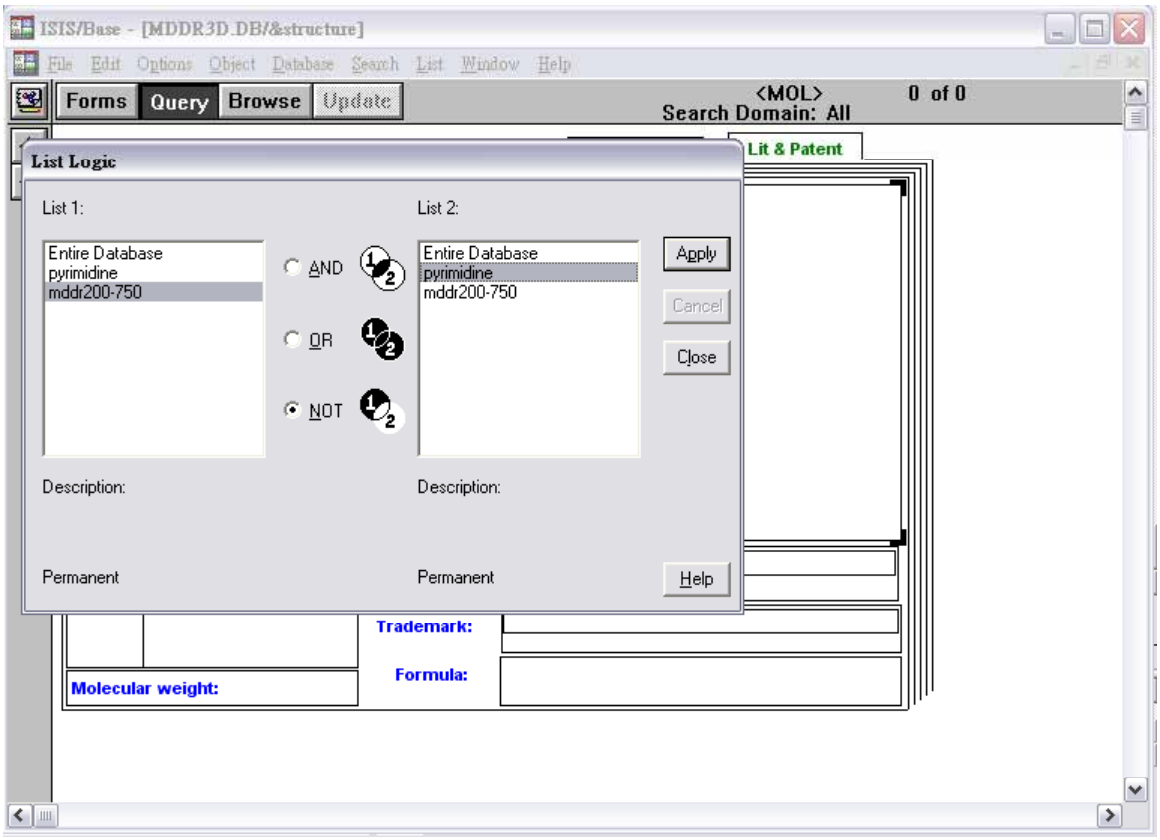
Step 13. Save the list of the search result



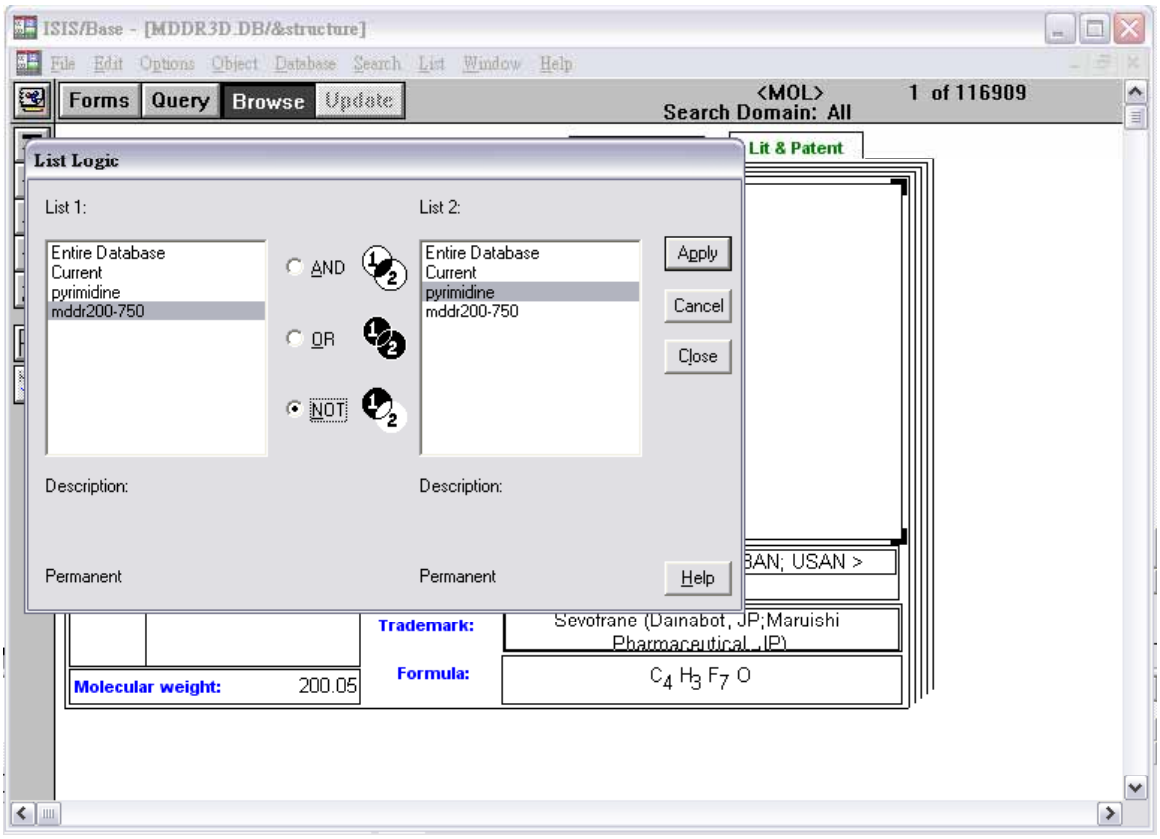
Step 14. Input the list name



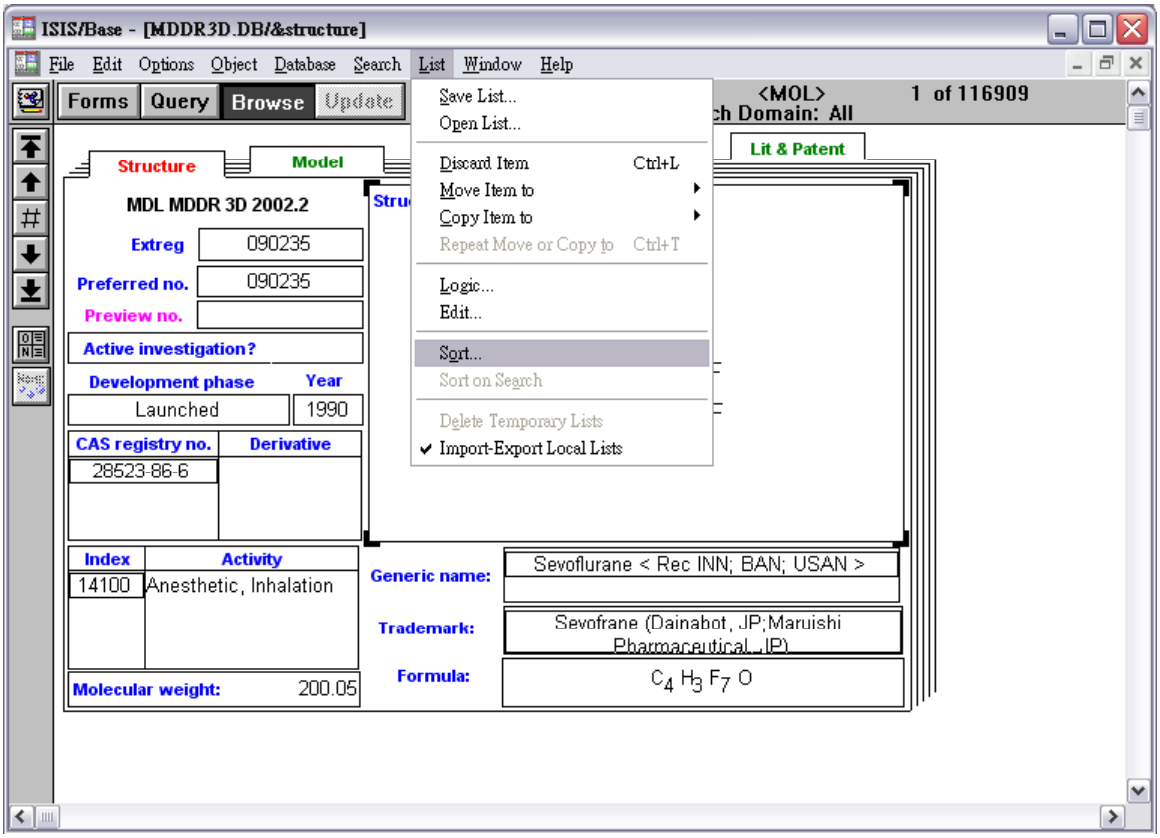
Step 15. Start logic combination of the two lists



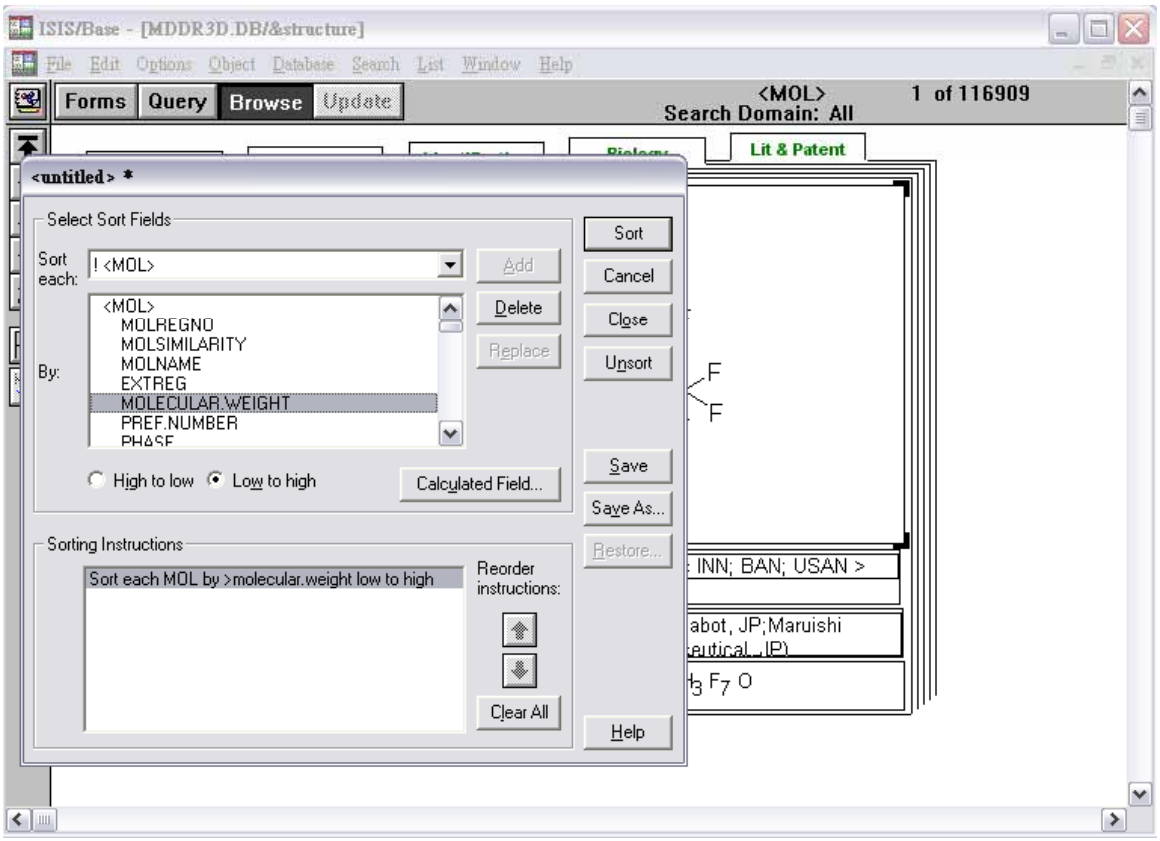
Step 16. The logic combination is “mw200-750” not “pyrimidine”



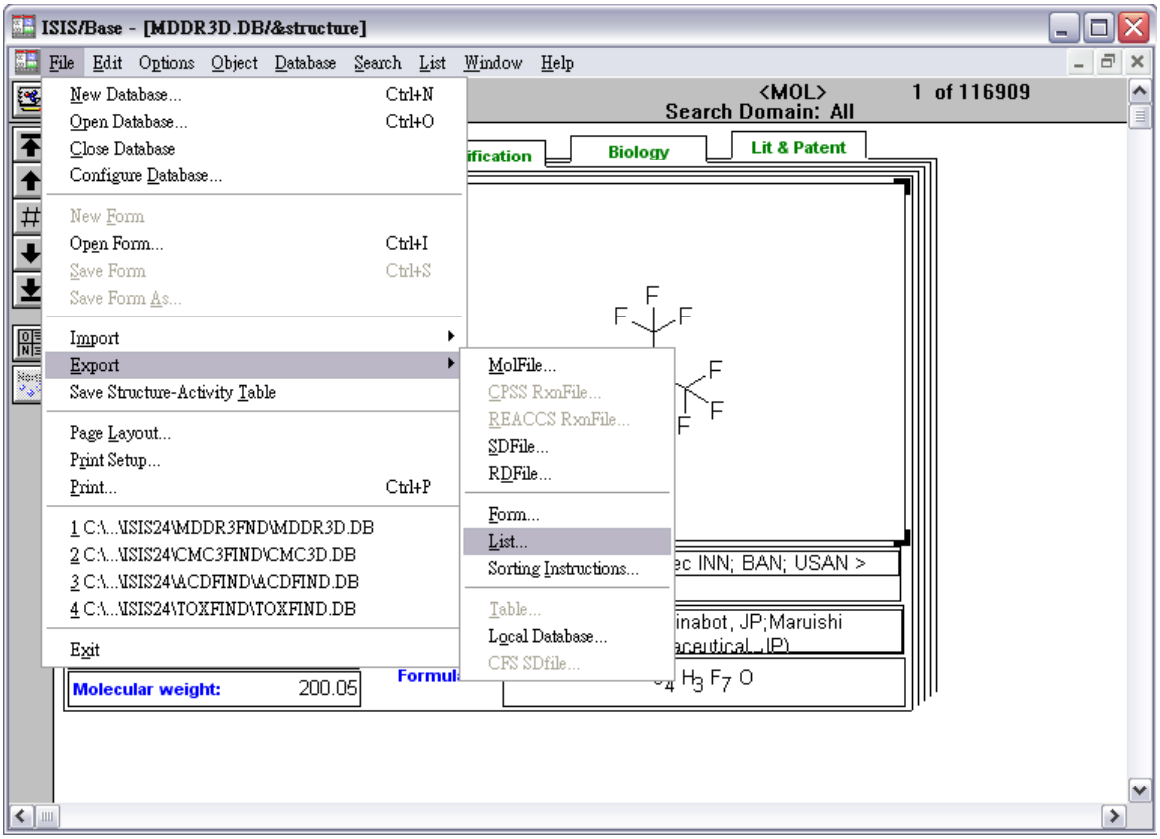
Step 17. Apply the logic combination and the result contains 1169090 molecules



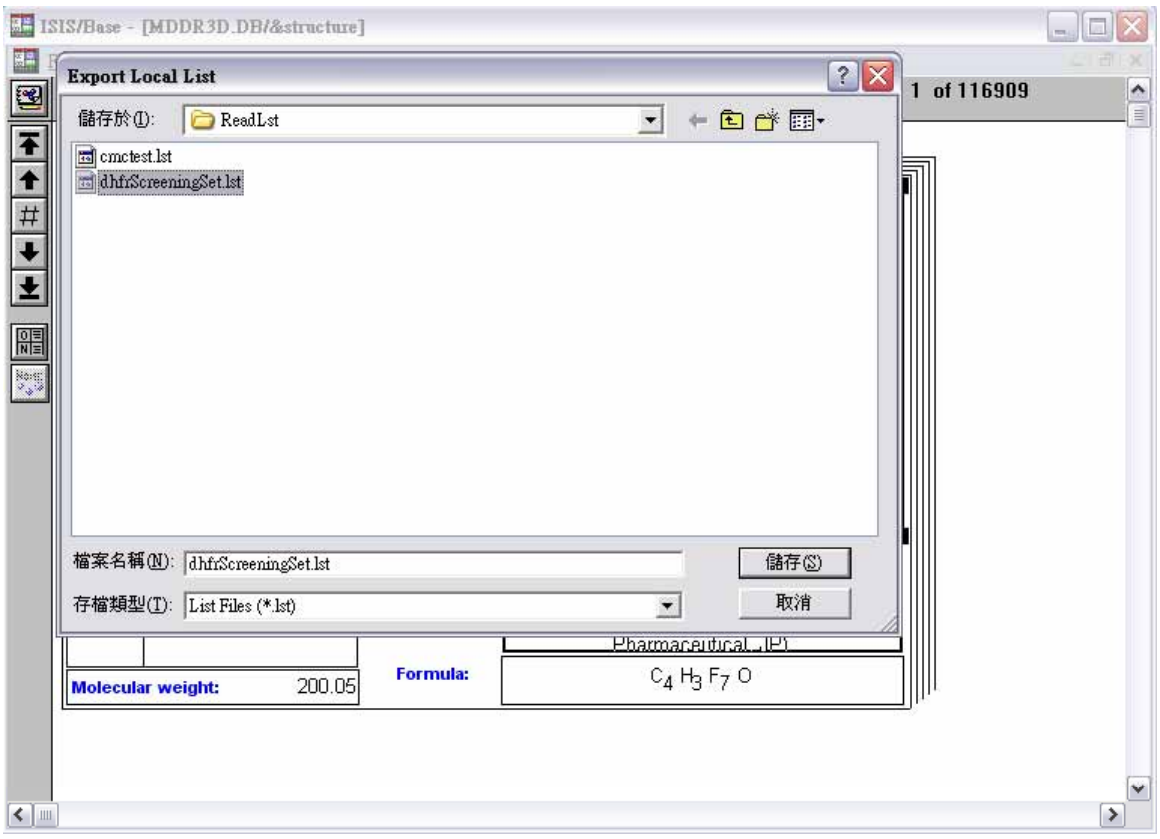
Step 18. Sort the list by the molecular weight



Step 19. Select the sort fields “molecular.weight” and “low to high”



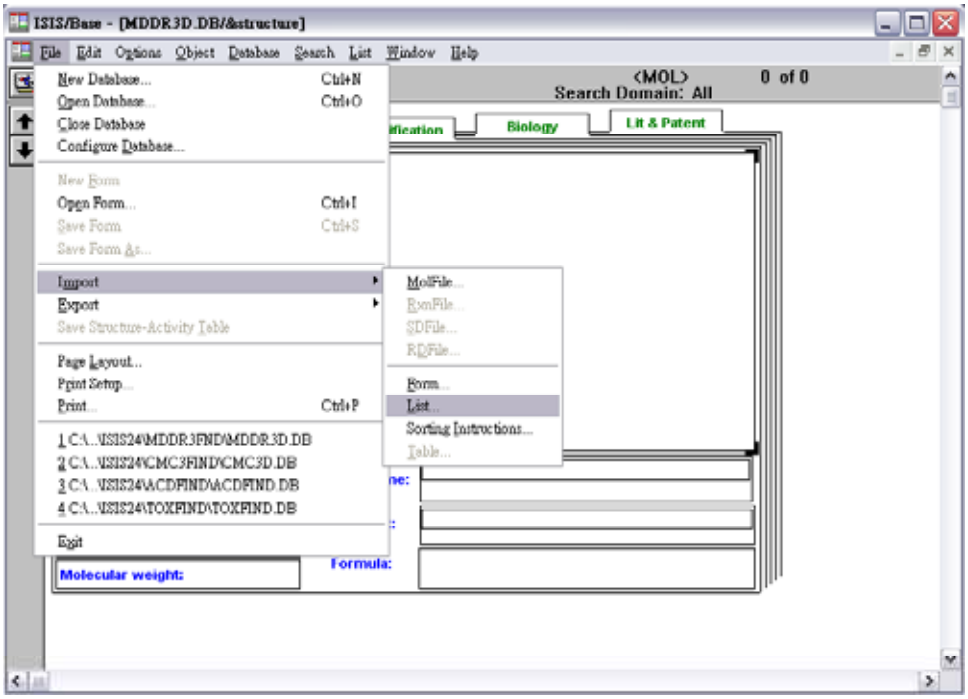
Step 20. Export the current list



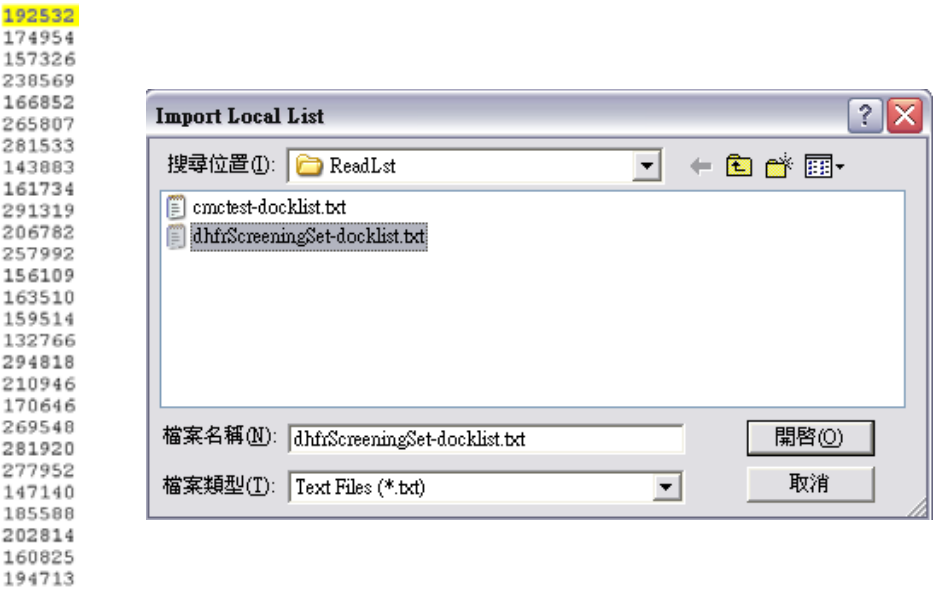
Step 21. Input the local path and the list name

Step 22. Read the list and output the list (InputFile-dockinglist.txt) for docking:

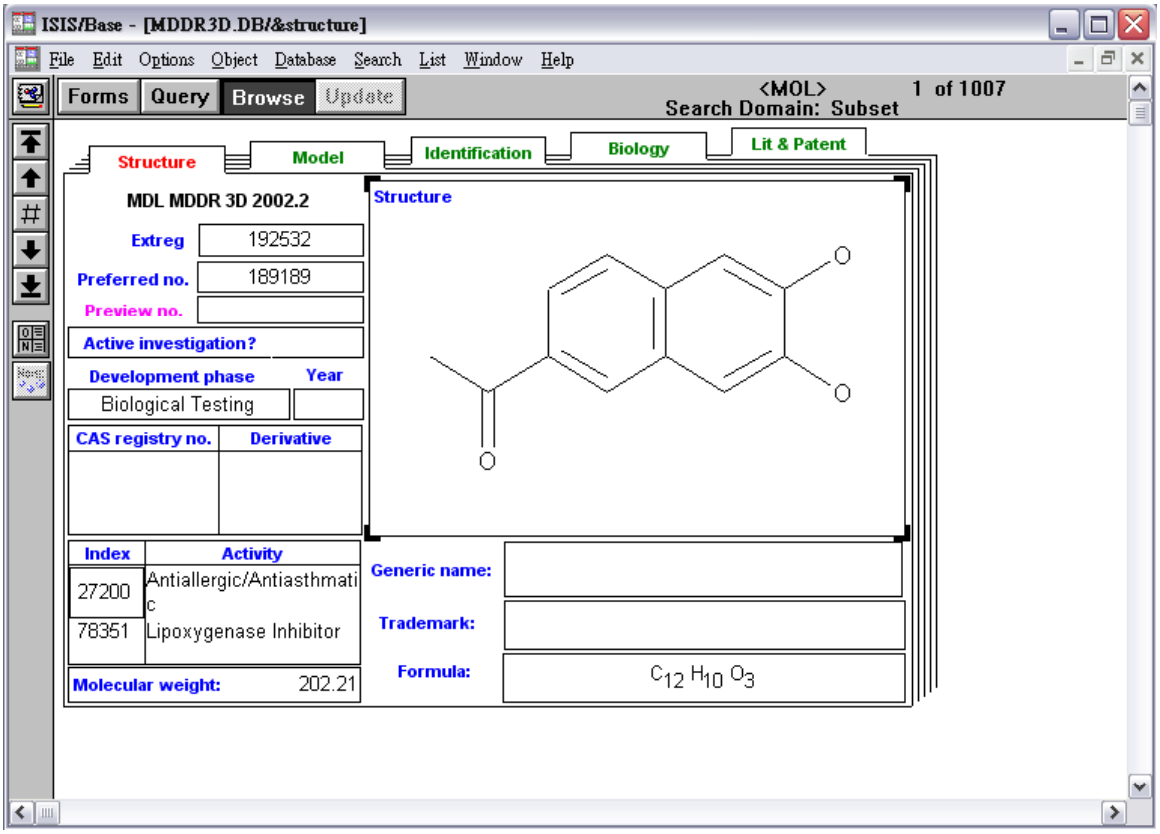
ReadLst dhfrScreeningSet.lst [the number of molecules in the docking list]



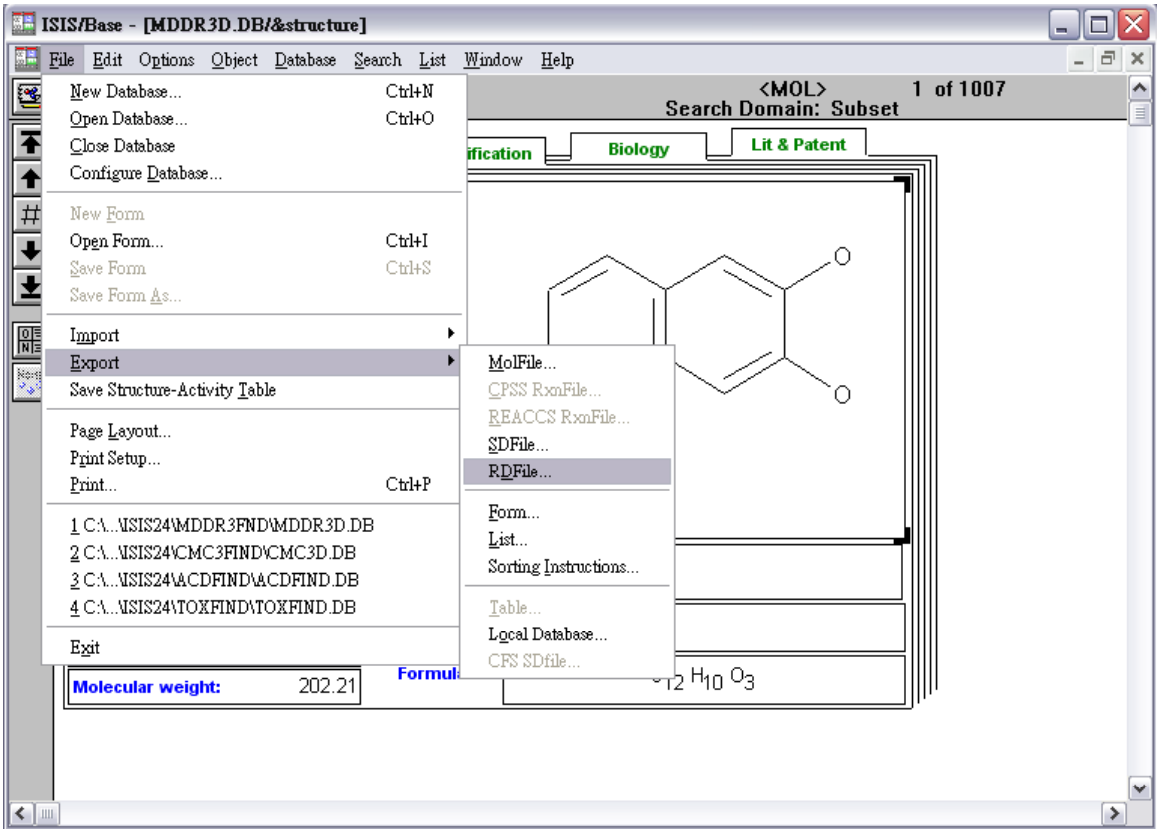
Step 23. Import the docking list (dhfrScreeningSet-dockinglist.txt) to download the coordinates of compounds



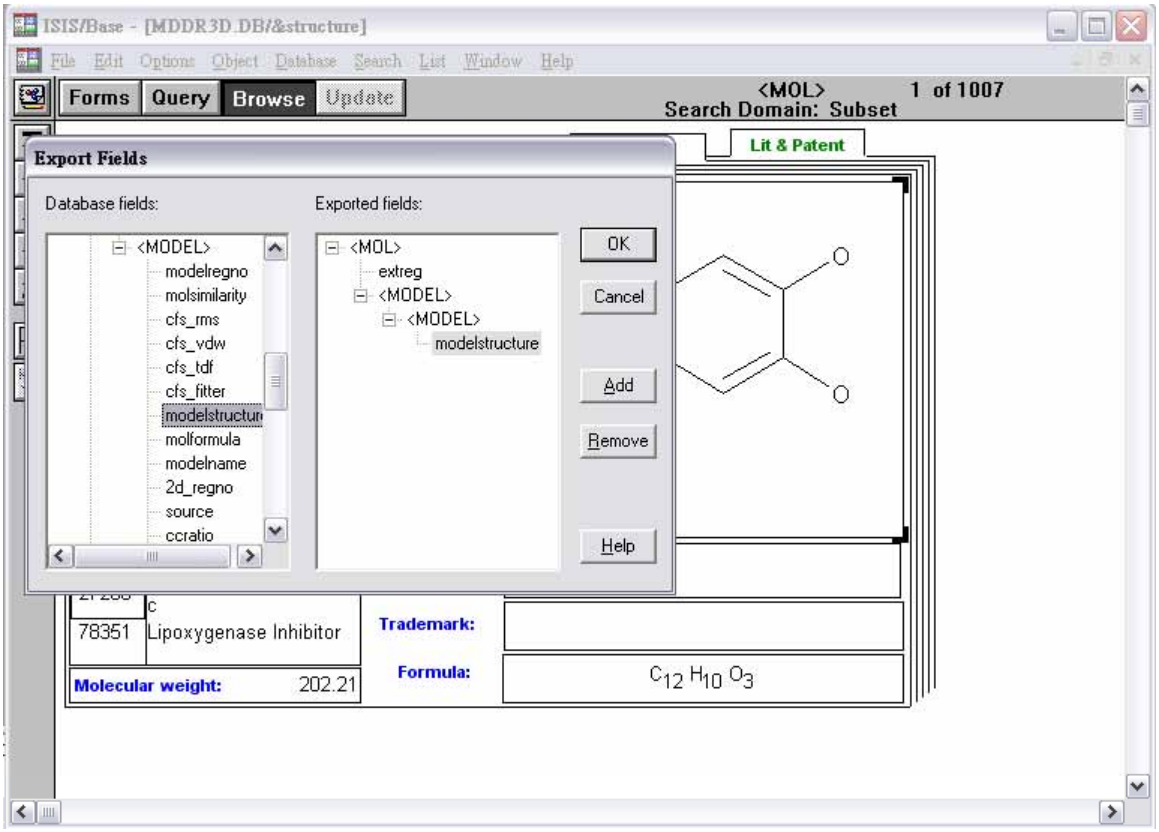
Step 24. Select the docking list



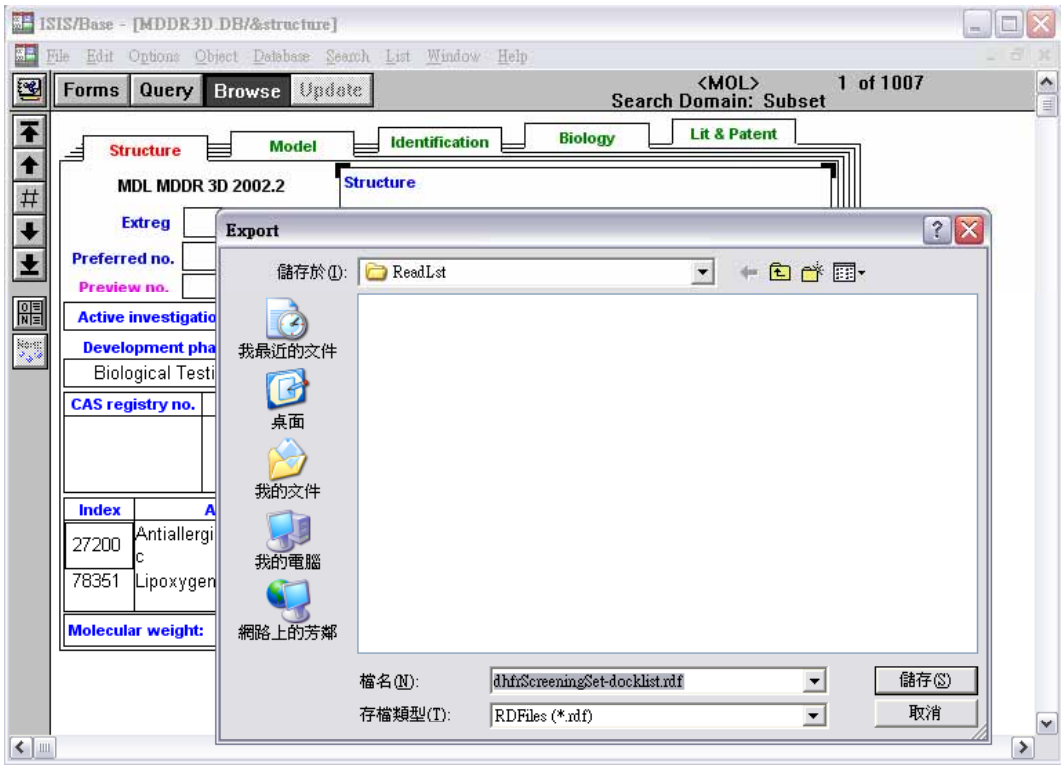
Step 25. The compounds in the docking list



Step 26. Export the reaction data file (RDFile) of the docking list



Step 27. Specify the items included in the RDFile. It have to contain two items “extreg” and “modelstructure”



Step 28. Input the RDFile name

Step 29. Copy corina.exe to same directory

Step 30. Remove small fragments from the RDFile with CORINA3.0:

corina -i t=rdf -o t=rdf -d rs dhfrScreeningSet-docklist.rdf mdhfrScreeningSet-docklist.rdf

Step 31. Split the RDFile to separated single-structure files:

splitRDF mdhfrScreeningSet-docklist.rdf

Step 32. The docking list is finished and each structure of the molecule in the docking list is prepared.