

# **KnowItAll Informatics Training**

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## NMR Predictions

# Predict NMR

## How to Predict NMR Spectra

### Purpose

This exercise demonstrates how to use the KnowItAll Informatics System's PredictIt NMR application to generate a predicted NMR spectrum from a chemical structure.

### Objectives

These exercises will teach you:

- How to set database and solvent preferences
- How to open a structure in PredictIt NMR
- How to perform a prediction
- How to interpret the predicted results

### Background

The PredictIt NMR application allows the prediction of  $^1\text{H}$ ,  $^{13}\text{C}$ , and other NMR shifts for a structure by searching the database(s) for specific chemical environments. These are described by a Hierarchical Organization of Spherical Environments (HOSE) code that is used to characterize the chemical surroundings of an atom in a molecular structure.

Because the PredictIt NMR application allows you to choose from a list of common solvents, predictions can be solvent-specific, if desired.


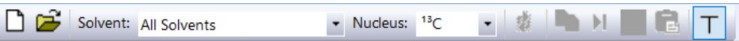
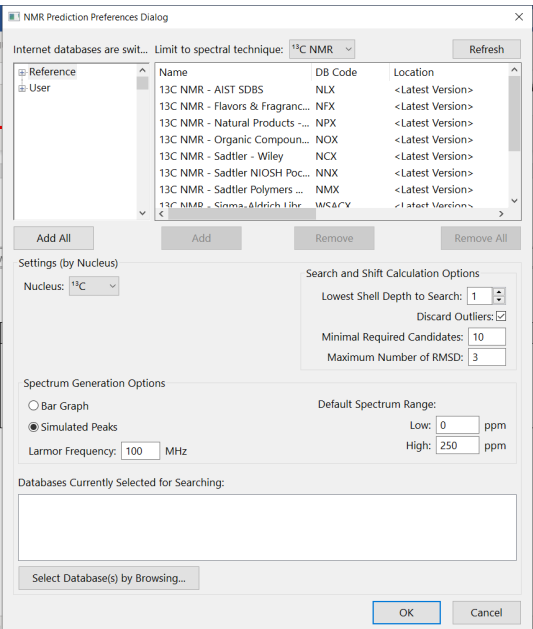
#### *Training Files Used in This Lesson*

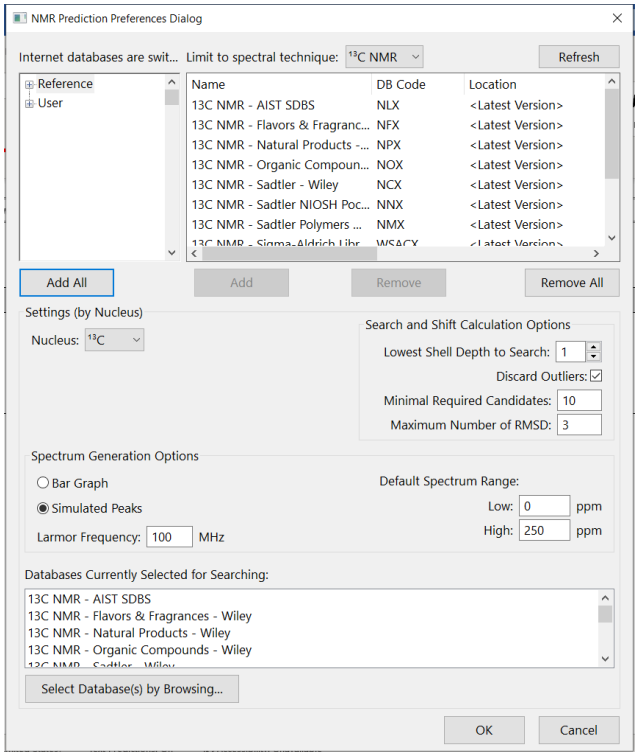
- C:\Users\Public\Public Documents\Wiley\KnowItAll\Samples\Structures\p-Methoxycarbanilic acid, 2-ethoxyethyl ester.dsf

#### *KnowItAll Applications Used*

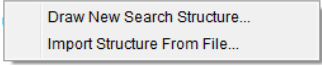
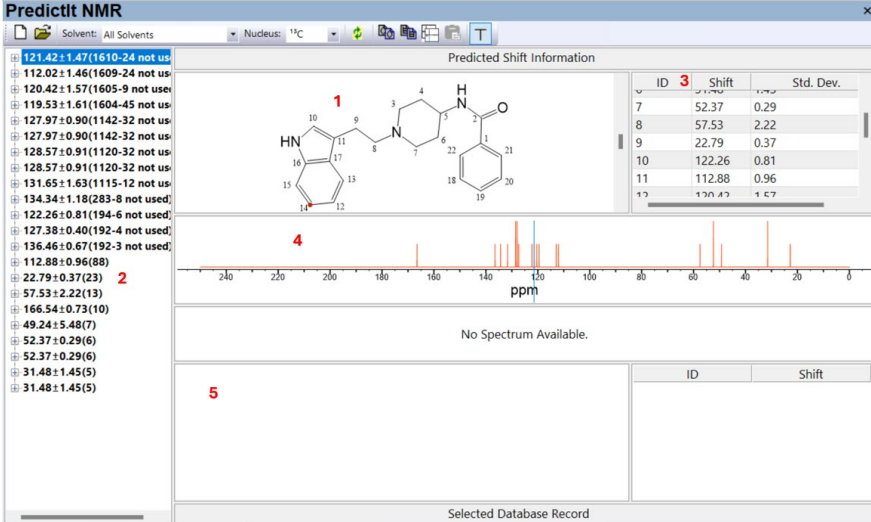
- PredictIt NMR
- ChemWindow
- Minelt

## Set PredictIt NMR preferences


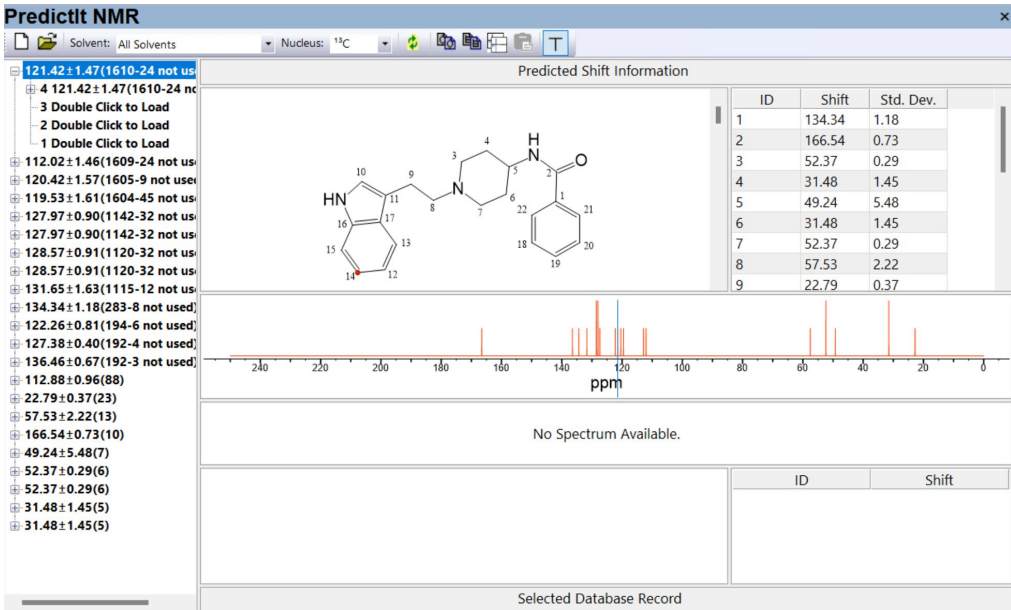
	Action	Result
1	Open the <b>PredictIt NMR</b> application by clicking its icon, typically found in the <b>Spectral Analysis</b> group.	
2	Examine the entries in the <b>Solvent</b> and <b>Nucleus</b> drop-down lists on the <b>Standard Toolbar</b> . Change the mention option to $^{13}\text{C}$ .	<p>The <b>Nucleus</b> displays <math>^{13}\text{C}</math>:</p>  <p>The <b>PredictIt NMR</b> application performs predictions for the solvent and nucleus specified using the toolbar.</p>
3	Choose <b>File &gt; Preferences</b> .	<p>The <b>PredictIt NMR Preferences Dialog</b> box opens:</p> 

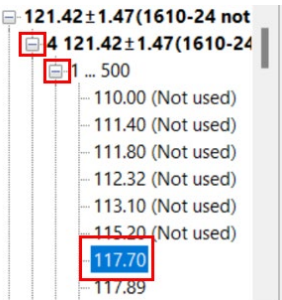
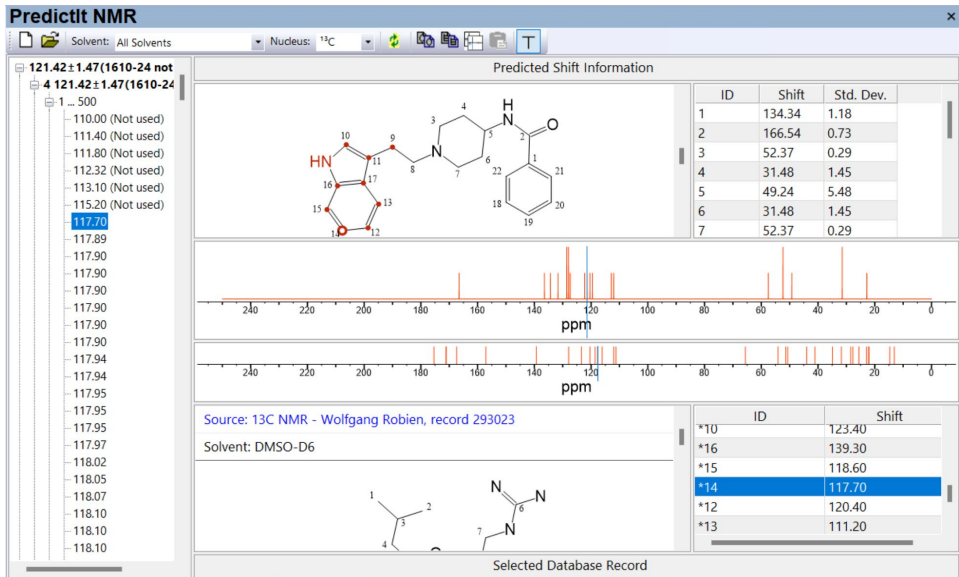
	Action	Result
4	In the <b>NMR Prediction Preferences Dialog</b> , set the <b>Settings (by Nucleus)</b> to $^{13}\text{C}$ . Under <b>Limit to spectral technique</b> , choose $^{13}\text{C}$ NMR. Click the <b>Add All</b> button followed by <b>OK</b> .	<p>The selected databases will be used when a prediction is performed. Upon clicking <b>OK</b>, the dialog box closes.</p>  <p><b>Note:</b> Specific availability of databases will depend on your package.</p>

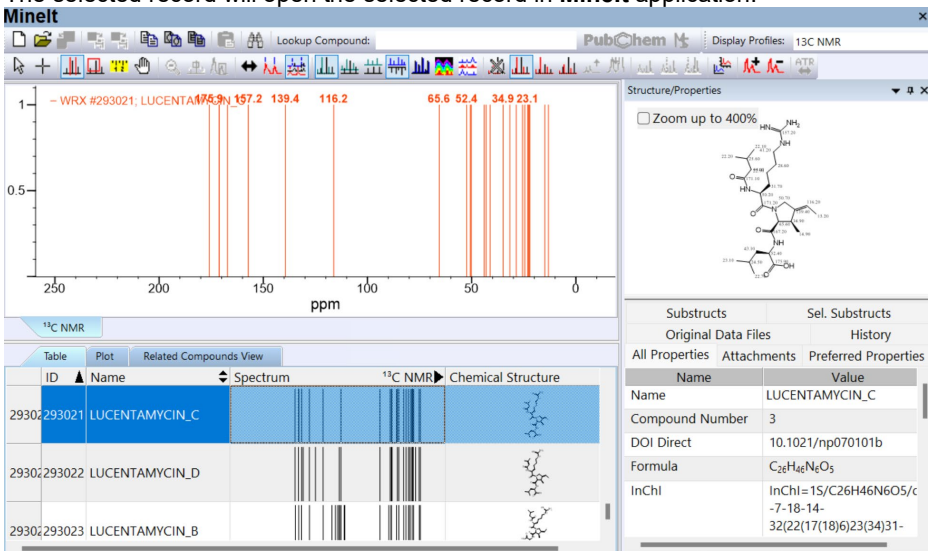
## Load a structure and perform a prediction

	Action	Result
5	Right-click in the box that reads <b>Right click to add structure.</b>	A pop-up menu opens: 
6	Select <b>Import Structure From File.</b>	A standard Windows <b>Open</b> dialog box appears.
7	<p>Navigate to  <b>C:\Users\Public\Public Documents\Wiley\KnowItAll\Samples\Structures.</b></p> <p>Select <b>"N-[1-(2-Indol-3-ylethyl)(4-piperidyl)]benzamide.mol"</b>.</p> <p>Click <b>Open.</b></p>	<p>After calculating, the results are displayed in <b>PredictIt NMR</b>:</p>  <p>The screenshot shows the PredictIt NMR window with the following components:</p> <ul style="list-style-type: none"> <li><b>Tree Control:</b> A list of chemical shifts and their standard deviations. Row 3 is highlighted in red.</li> <li><b>Chemical Structure:</b> The structure of N-[1-(2-Indol-3-ylethyl)(4-piperidyl)]benzamide is shown with a red tag '1' on the selected atom.</li> <li><b>Shift Table:</b> A table showing the computed chemical shifts and standard deviations for the selected atom.</li> <li><b>Spectrum:</b> A line spectrum plot showing the computed spectrum.</li> <li><b>Database Record:</b> A table showing the selected database record for the selected atom.</li> </ul>

- 1: The structure is displayed with a red tag on the selected atom. Click to select another atom.
- 2: The corresponding row is highlighted in the **Tree Control**.
- 3: The computed chemical shifts are displayed in the **Shift Table**.
- 4: A line spectrum is generated for the computed spectrum.
- 5: When a lower level row is selected in the **Tree Control**, a database record that participated in the computation for the selected atom will display in this region. More on this below.

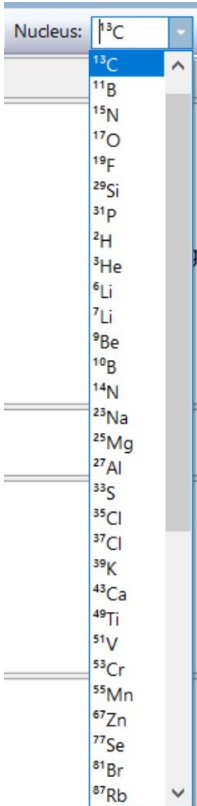
	Action	Result																														
8	Click on the plus icon (  ) in the <b>Tree Control</b> to expand it.	<p>Upon clicking the first plus box, a series of rows is expanded below in the <b>Tree Control</b>:</p>  <p><b>PredictIt NMR</b></p> <p>Solvent: All Solvents    Nucleus: <math>^{13}\text{C}</math></p> <p><b>Tree Control:</b></p> <ul style="list-style-type: none"> <li>121.42 ± 1.47 (1610-24 not used)</li> <li>4 121.42 ± 1.47 (1610-24 not used)</li> <li>3 Double Click to Load</li> <li>2 Double Click to Load</li> <li>1 Double Click to Load</li> <li>112.02 ± 1.46 (1609-24 not used)</li> <li>120.42 ± 1.57 (1605-9 not used)</li> <li>119.53 ± 1.61 (1604-45 not used)</li> <li>127.97 ± 0.90 (1142-32 not used)</li> <li>127.97 ± 0.90 (1142-32 not used)</li> <li>128.57 ± 0.91 (1120-32 not used)</li> <li>128.57 ± 0.91 (1120-32 not used)</li> <li>131.65 ± 1.63 (1115-12 not used)</li> <li>134.34 ± 1.18 (283-8 not used)</li> <li>122.26 ± 0.81 (194-6 not used)</li> <li>127.38 ± 0.40 (192-4 not used)</li> <li>136.46 ± 0.67 (192-3 not used)</li> <li>112.88 ± 0.96 (88)</li> <li>22.79 ± 0.37 (23)</li> <li>57.53 ± 2.22 (13)</li> <li>166.54 ± 0.73 (10)</li> <li>49.24 ± 5.48 (7)</li> <li>52.37 ± 0.29 (6)</li> <li>52.37 ± 0.29 (6)</li> <li>31.48 ± 1.45 (5)</li> <li>31.48 ± 1.45 (5)</li> </ul> <p><b>Predicted Shift Information:</b></p> <table border="1"> <thead> <tr> <th>ID</th><th>Shift</th><th>Std. Dev.</th></tr> </thead> <tbody> <tr><td>1</td><td>134.34</td><td>1.18</td></tr> <tr><td>2</td><td>166.54</td><td>0.73</td></tr> <tr><td>3</td><td>52.37</td><td>0.29</td></tr> <tr><td>4</td><td>31.48</td><td>1.45</td></tr> <tr><td>5</td><td>49.24</td><td>5.48</td></tr> <tr><td>6</td><td>31.48</td><td>1.45</td></tr> <tr><td>7</td><td>52.37</td><td>0.29</td></tr> <tr><td>8</td><td>57.53</td><td>2.22</td></tr> <tr><td>9</td><td>22.79</td><td>0.37</td></tr> </tbody> </table> <p>The screenshot also shows a chemical structure with atoms numbered 1 through 21, a spectrum plot (ppm vs intensity), and a table of predicted shift information.</p> <p>To compute a prediction, the program searches the database(s) for specific chemical environments, which are described by <b>HOSE (Hierarchically Ordered Spherical description of Environment)</b> code - a topology code used to describe the chemical surroundings of an atom in a molecular structure. See "W. Bremser, "HOSE - A Novel Substructure Code," <i>Anal. Chim. Acta</i> (1978), 103:355-365".</p>	ID	Shift	Std. Dev.	1	134.34	1.18	2	166.54	0.73	3	52.37	0.29	4	31.48	1.45	5	49.24	5.48	6	31.48	1.45	7	52.37	0.29	8	57.53	2.22	9	22.79	0.37
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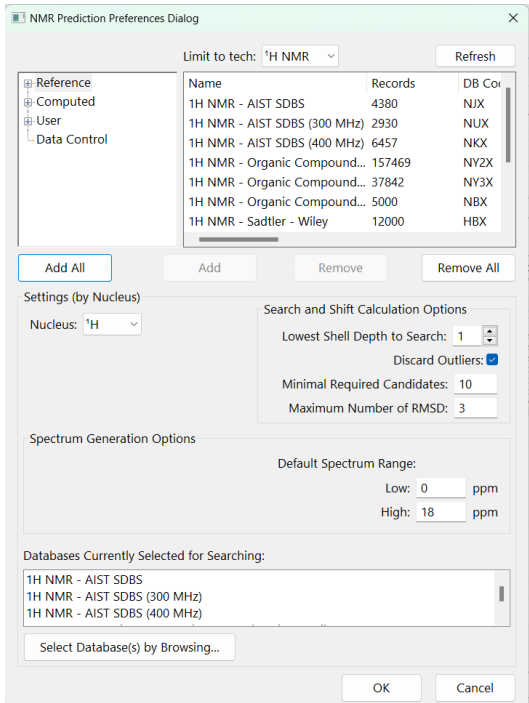

	Action	Result
9	<p>For the first row in the <b>Tree Control</b>, click on the plus icons (+) for the lower two levels to display records which participated in the calculation. Click on one of the bottom rows, such as "117.70".</p>  <p><b>Note:</b> Specific row values will depend on the selected databases that participated in the computation.</p>	<p>Upon selecting a record in the <b>Tree Control</b>, a record that was involved in the calculation of the chemical shift is displayed:</p>  <ul style="list-style-type: none"> <li>Each row in the <b>Tree Control</b> represents a record that participated in the computation for the highlighted atom.</li> <li>The <b>Tree Control</b> gives you access to the structures, spectra, and chemical shifts from the database records upon which the predictions are based to give you confidence in the accuracy of the prediction.</li> <li>At the top level of the predicted values in the <b>Tree Control</b>, a coefficient of value <b>4, 3, 2</b> or <b>1</b> is provided, which represents the number of shells shared between the computed structure and the database record. <b>KnowItAll</b> averages the database records which match the atom environment to the 4th shell, 3rd shell, etc.</li> <li>If an exact match(es) are found in the databases for the computed structure, then these NMR shifts will be listed first before shells from similar structures.</li> <li>When a record row reads "Not used", it represents a database value that is determined to be an <b>Outlier</b>. This feature is controlled in the <b>Preferences</b> dialog (<b>File &gt; Preferences</b>).</li> </ul>

	Action	Result
10	<p>For any record, click on the <b>record ID</b> shown in blue text as "Source: 13C NMR."</p> <p>Source: 13C NMR - Wolfgang Robien, record 293023</p> <p>Solvent: DMSO-D6</p> <p>Return to <b>PredictIt NMR</b>.</p>	<p>The selected record will open the selected record in <b>Minelt</b> application:</p>  <p>This allows for further investigation of the NMR database record which participated in the computation.</p>
11	<p>Filter the prediction according to a specific solvent by using the <b>Solvent</b> dropdown menu.</p> <p>Solvent: All Solvents</p>	<p>Upon filtering the solvent, the calculation will be repeated using data only for the selected solvent.</p>



**Perform a prediction for other nuclei**

	Action	Result
12	The above example is for $^{13}\text{C}$ NMR predictions. To predict for another nuclei, change the selection in the <b>Nucleus</b> drop down menu.	 A screenshot of a software interface showing a dropdown menu for selecting a nucleus. The menu is titled "Nucleus:" and currently has $^{13}\text{C}$ selected. The dropdown list is open, showing a scrollable list of isotopes: $^{13}\text{C}$ , $^{11}\text{B}$ , $^{15}\text{N}$ , $^{17}\text{O}$ , $^{19}\text{F}$ , $^{29}\text{Si}$ , $^{31}\text{P}$ , $^2\text{H}$ , $^3\text{He}$ , $^6\text{Li}$ , $^7\text{Li}$ , $^9\text{Be}$ , $^{10}\text{B}$ , $^{14}\text{N}$ , $^{23}\text{Na}$ , $^{25}\text{Mg}$ , $^{27}\text{Al}$ , $^{33}\text{S}$ , $^{35}\text{Cl}$ , $^{37}\text{Cl}$ , $^{39}\text{K}$ , $^{43}\text{Ca}$ , $^{49}\text{Ti}$ , $^{51}\text{V}$ , $^{53}\text{Cr}$ , $^{55}\text{Mn}$ , $^{67}\text{Zn}$ , $^{77}\text{Se}$ , $^{81}\text{Br}$ , and $^{87}\text{Rb}$ . The list is scrollable, with $^{13}\text{C}$ at the top and $^{87}\text{Rb}$ at the bottom.

	Action	Result
13	<p><b>Note:</b> The databases must be updated for the selected technique.</p> <p>Choose <b>File &gt; Preferences</b>. Click <b>Remove All</b> to remove existing databases used for the prediction. Modify the selection for <b>Limit spectral technique</b> to the desired nucleus, and click <b>Add All</b> to add the related databases.</p>	<p>The <b>NMR Prediction Preferences Dialog</b> opens. In the example below, the <math>^1\text{H}</math> NMR databases were added:</p> 
14	<p>With the previous prediction opened, select <b>Edit &gt; Repeat Prediction</b> or click the <b>Repeat Prediction</b> icon on the <b>Standard Toolbar</b>.</p> 	<p>The prediction is recalculated for the selected nucleus.</p>