The Benefits of Spectral Databasing within Chemistry and Natural Products

Matthew Reid, PMAS

Introduction

- Syngenta Jealott’s Hill
- Structural Chemistry Group at Syngenta Jealott’s Hill
  - Who We Are and What We Do
  - Spectroscopic Capabilities
- Data Archiving and Prediction Training
  - What for?
  - What Software We Use and How We Do It
  - Future Developments

Syngenta Jealotts Hill

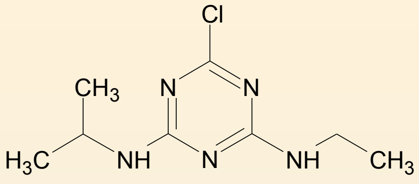
Jealott's Hill is our largest site for R&D and product support with ca.800 employees

Jealott's Hill Research Centre in the UK is our centre for Crop Protection Discovery, Bioscience, Weed Control Research, Seeds Research, bio-performance enhancement and Product Safety Research.

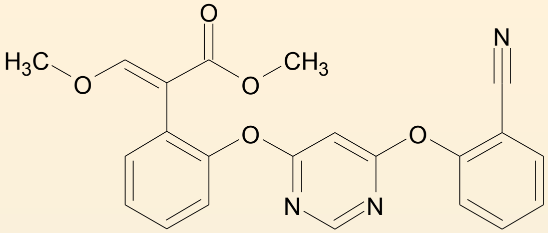
Key activities on site include research into discovery of new active ingredients (AIs), new formulation technologies to develop products from existing AIs and technical support of our product range.

Syngenta Jealotts Hill

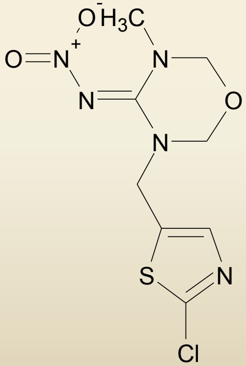
Key Products



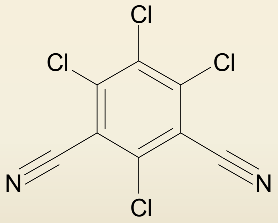
Atrazine - Herbicide



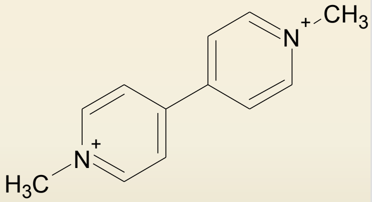
Azoxystrobin - Broad Spectrum Fungicide



Thiamethoxam - Broad Spectrum Insecticide



Chlorothalonil - Broad Spectrum Fungicide



Paraquat - Broad Spectrum Herbicide

Structural Chemistry Group at JH

Who We Are and What We Do

- The group is part of Product Metabolism and Analytical Science
- Provide qualitative and quantitative services and technical expertise to global projects in Research, Development and beyond.

NMR Spectroscopy

Structure elucidation for Research Chemistry (including natural products, impurity ID and physical chemistry),

Solid-state NMR.

Process studies, mode of action.

Competitor product analysis

Formulation studies, product safety, biochemistry (including protein NMR), quantitative NMR and Stage 1 metabolism

Mass Spectrometry

Open access LC and GC-MS support for Research Chemistry, Formulation and Process Science

Structure elucidation studies for Research Chemistry, Formulation and Process Science

Structure elucidation for Stage 1 and Stage 2 metabolism

Structural Chemistry Group at JH

- Spectroscopic Capabilities

Varian Inova 400MHz

•Routine Open Access instrument

Bruker AVANCE III 500MHz

•Research instrument - 1D/2D experiments
•Primarily used for structure elucidation

Varian Inova 600MHz

•Research instrument – high sensitivity for ^{1}H and ^{13}C
•Primarily used for structure elucidation of low level samples

2 x Waters ZQ Open Access LC-MS systems, Shimadzu GC-MS, Jeol GC-MS

- Routine Open Access instruments

LTQ Velos

- Accurate mass instrument used for structure elucidation
- Applications within Chemistry, Process Science, Metabolism, Formulation

LTQ Orbitrap XL

- Accurate mass instrument used for metabolite ID

Structural Chemistry Group at JH

- **Spectroscopic Capabilities**

Sample Throughput – 2011

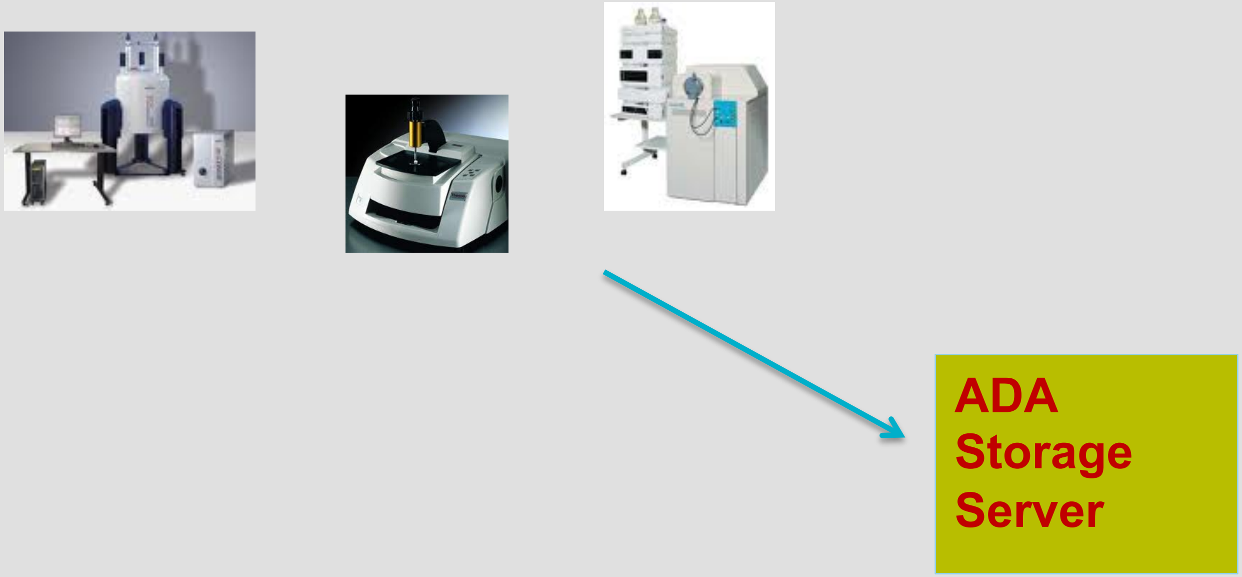
- **NMR**
  - Full Structure Elucidations – 349
  - Open Access NMR – 20639
- **MS**
  - Open Access MS – 38152

Sample Throughput – 2012 Jan - Apr

- **NMR**
  - Full Structure Elucidations – 316
  - Open Access NMR – 8930
  - Batch Analysis - 10166
- **MS**
  - Full Analysis – 62
  - Open Access MS – 11587
  - Batch Analysis - 11782

Data Archiving

The raw data acquired on our analytical instruments is archived onto a server and can be accessed by chemists and analysts for reference.



ADA Storage Server

This process is automatic and the system can be searched using a number of variables.

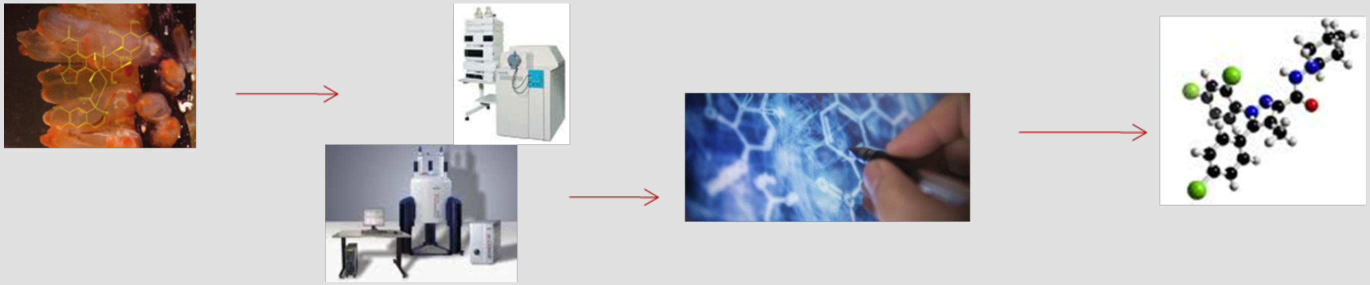
Data Archiving

•From a Spectroscopists/Analysts Point of View….

- A raw data or paper archive isn’t enough – we need something more specific:-
    - A spectral database that contains only what is useful and relevant
    - Something that’s searchable by variables I want to search by
    - A database that is quick, powerful and can be customised
    - Something that stops duplication – very important in not wasting time
    - A system that can accept spectral data in multiple vendor formats

Data Archiving

- **Why do I need this?**

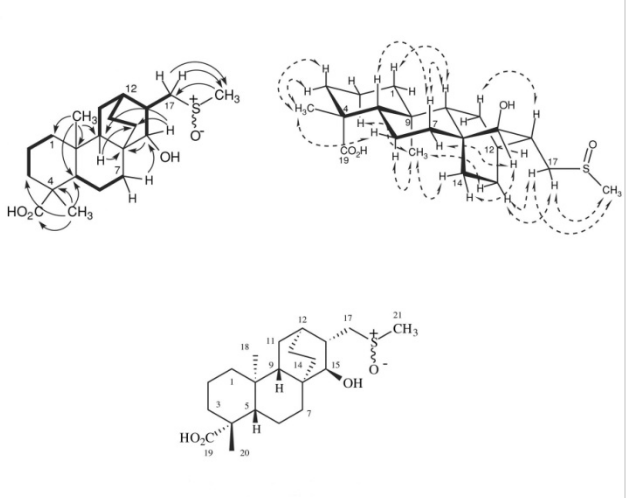


Structure elucidation takes time - everything we’ve done in the past is useful. A spectral database gives us valuable legacy data from a range compounds and projects:-

- Have we seen this compound before? If so where and when.
- What does the spectral information look like – is it similar to what we are currently working on?
- Are my raw materials the right compounds and of sufficient purity?
- Are the polymers present in my formulation similar to those in our database?

Data Archiving

- **What do we want to put in our database?**
  - **As much data from Chemistry projects as possible**
    - **The more assigned compounds we have the more it can aid in structure elucidation of compounds from the same projects**



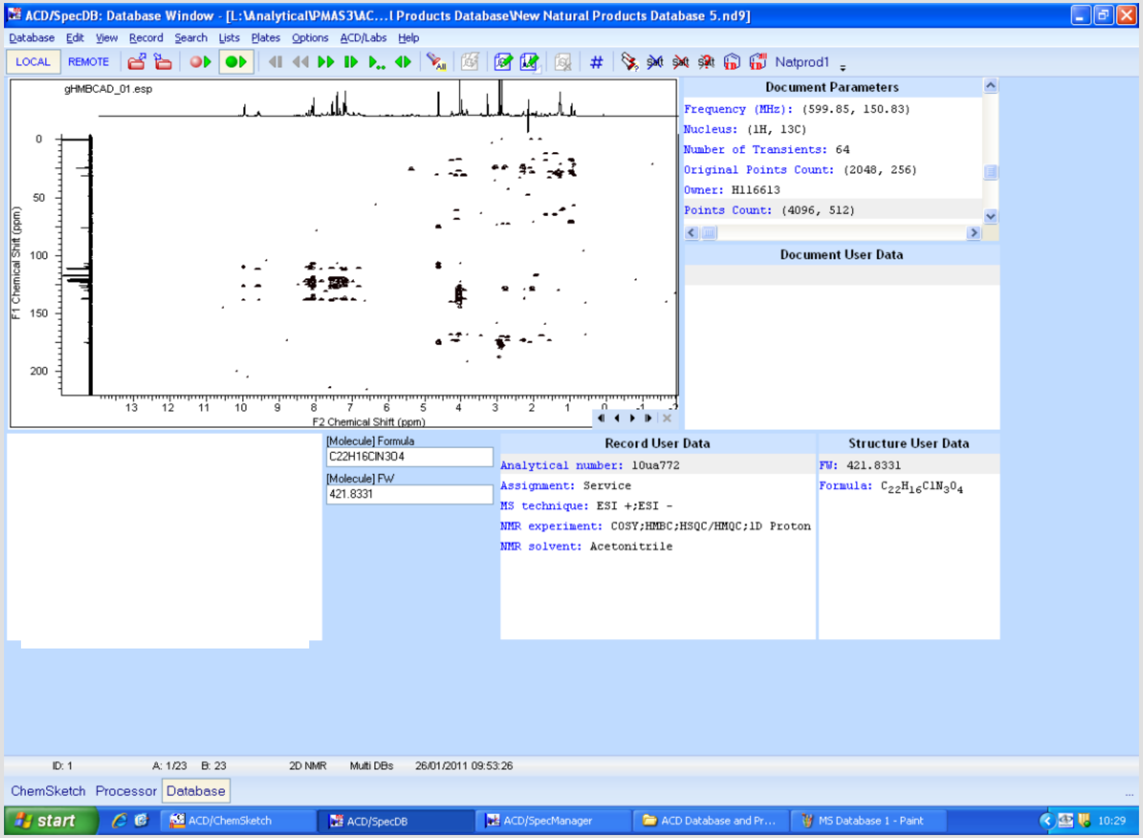
^{1}H, ^{13}C, COSY, HSQC, HMBC, NOESY, LR or HRMS

^{15}N has become very important!!!

- **For natural products in particular, a comprehensive record should be kept, especially if the compound is novel**

Data Archiving

- **The software of choice…ACD/Labs SpecDB Enterprise**



Document Parameters

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Number of Transients: 64
Original Points Count: (2048, 256)
Owner: H116613
Points Count: (4096, 512)

[Molecule] Formula
C22H16ClN3O4

[Molecule] FW
421.8331

Record User Data

Analytical number: 10ua772
Assignment: Service
MS technique: ESI +;ESI -
NMR experiment: COSY;HMBC;HSQC/HMQC;1D Proton
NMR solvent: Acetonitrile

Structure User Data

FW: 421.8331
Formula: $C_{22}H_{16}ClN_3O_4$

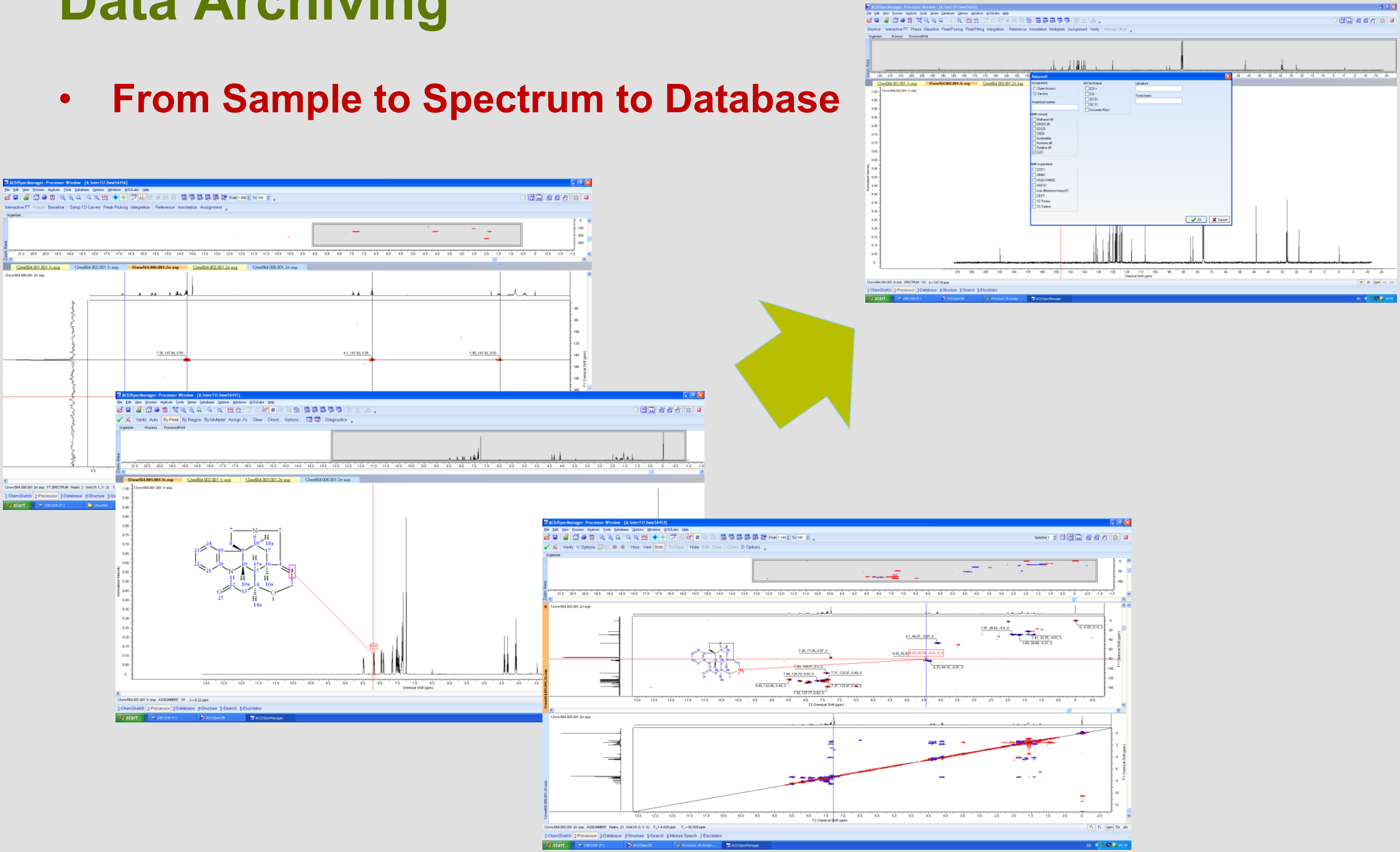
Chemistry and natural product database with fully assigned NMR and MS data – Over 300 records.

Includes 1D and 2D data for 1H, 13C and 15N.

Polymer and surfactant database – 209 compounds

Data Archiving

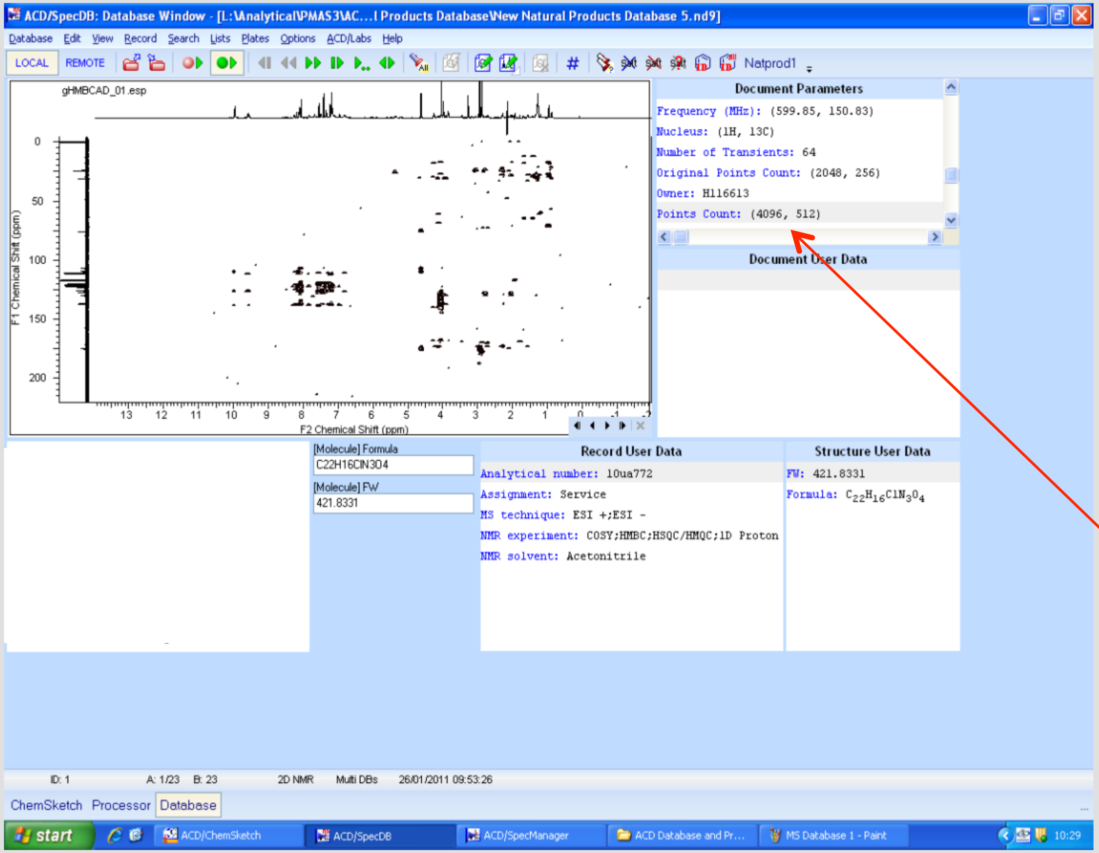
- **From Sample to Spectrum to Database**



ACD/SpecManager: Processor Window
1-ChemSketch 2-Processor 3-Database 4-Structure 5-Search 6-Elucidator
start

Data Archiving

- **The Database**



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Structure User Data

FW: 421.8331
Formula: $C_{22}H_{16}ClN_3O_4$

ID: 1 A: 1/23 B: 23 2D NMR Multi DBs 26/01/2011 09:53:26

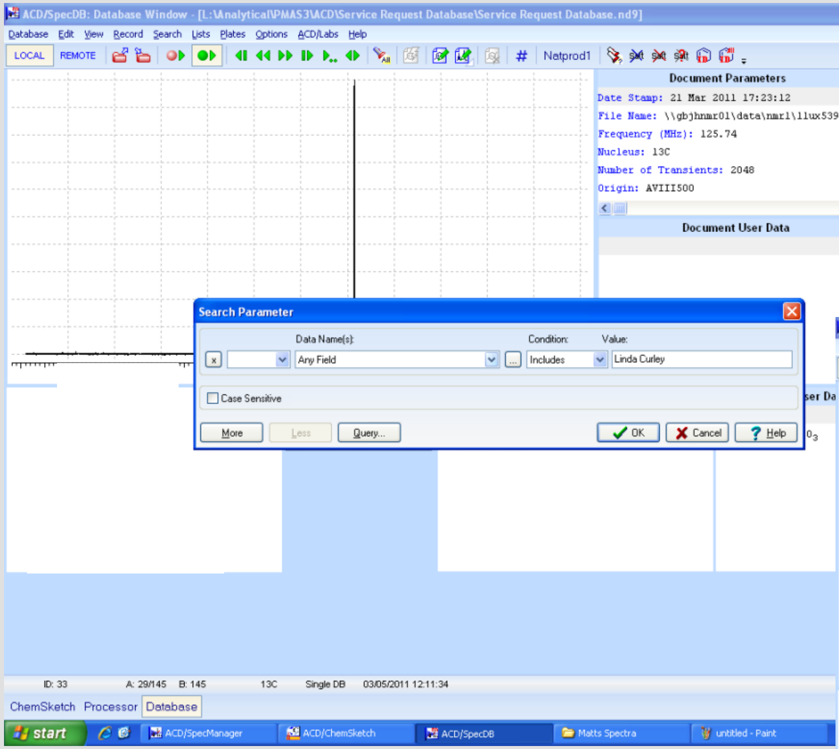
The format of the database is fully customisable. You only see what you want to see.

This customisation can be done at database creation or later on.

All the experimental/user/record data is taken from the spectrometer automatically.

Data Archiving

The searching options within the database are too numerous to mention. Examples are to search by username or by NMR chemical shift and coupling constant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Database Edit View Record Search Lists Plates Options ACD/Labs Help
LOCAL REMOTE Natprod1

Document Parameters
```
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File Name: \\gbjhnmr01\data\nmr1\1lux539\2\
Frequency (MHz): 125.74
Nucleus: 13C
Number of Transients: 2048
Origin: AVIII500
```
Document User Data

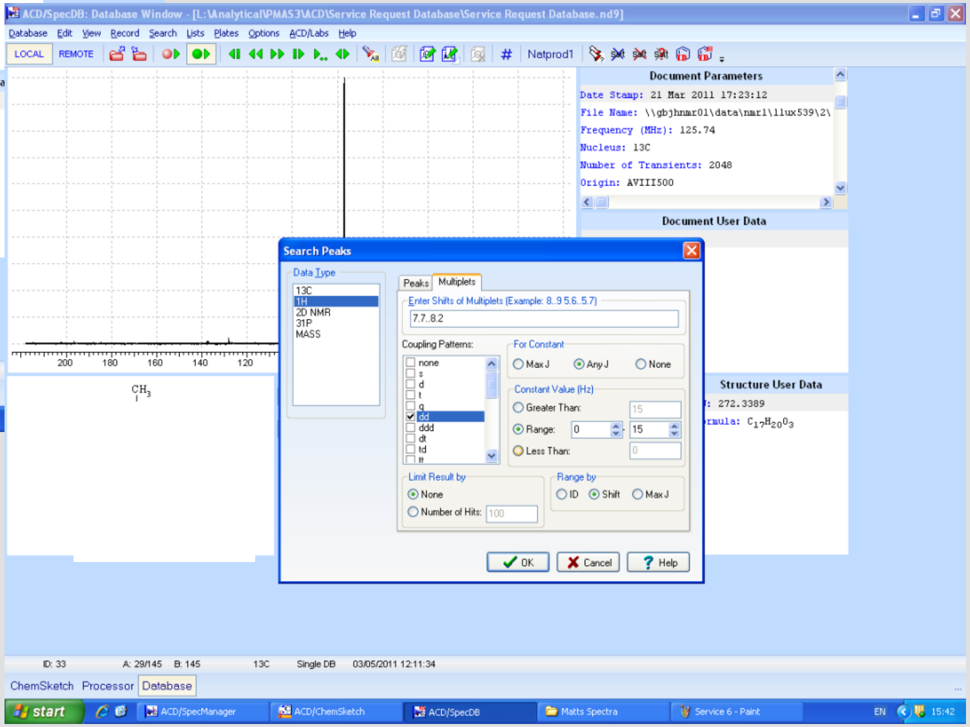
Search Parameter

Data Name(s):	Condition:	Value:
Any Field	Includes	Linda Curley

□ Case Sensitive

ID: 33 A: 29/145 B: 145 13C Single DB 03/05/2011 12:11:34

ChemSketch Processor Database
start ACD/SpecManager ACD/ChemSketch ACD/SpecDB Matts Spectra untitled - Paint


ACD/SpecDB: Database Window - [L:\Analytical\PMAS3\ACD\Service Request Database\Service Request Database.nd9]

Database Edit View Record Search Lists Plates Options ACD/Labs Help
LOCAL REMOTE Natprod1
200 180 160 140 120

Document Parameters
```
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File Name: \\gbjhnmr01\data\nmr1\1lux539\2\
Frequency (MHz): 125.74
Nucleus: 13C
Number of Transients: 2048
Origin: AVIII500
```
Document User Data

Structure User Data
```
: 272.3389
rmula: C17H20O3
```

Search Peaks

Data Type: 13C, **1H** (selected), 2D NMR, 31P, MASS

Peaks | Multiplets

Enter Shifts of Multiplets (Example: 8..9 5.6..5.7): 7.7..8.2

Coupling Patterns:
- □ none
- □ s
- □ d
- □ t
- □ q
- ☑ dd
- □ ddd
- □ dt
- □ td
- □ tt

For Constant: ○ Max J ● Any J ○ None

Constant Value (Hz):
- ○ Greater Than: 15
- ● Range: 0 - 15
- ○ Less Than: 0

Limit Result by: ● None ○ Number of Hits: 100

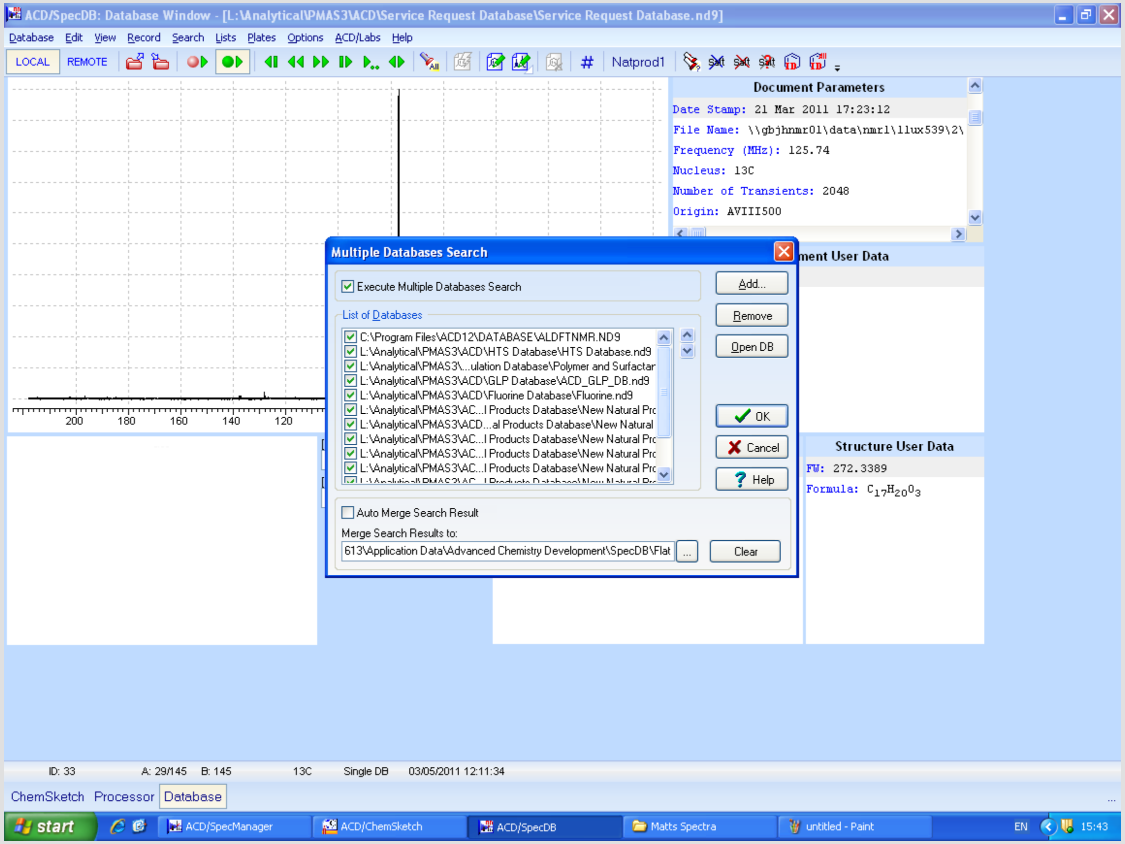
Range by: ○ ID ● Shift ○ Max J

ID: 33 A: 29/145 B: 145 13C Single DB 03/05/2011 12:11:34

ChemSketch Processor Database
start ACD/SpecManager ACD/ChemSketch ACD/SpecDB Matts Spectra Service 6 - Paint EN 15:42

Data Archiving

- **The Database**



ACD/SpecDB: Database Window - [L:\Analytical\PMAS3\ACD\Service Request Database\Service Request Database.nd9]

Database Edit View Record Search Lists Plates Options ACD/Labs Help
LOCAL
REMOTE
Natprod1
200
180
160
140
120

Document Parameters

Date Stamp: 21 Mar 2011 17:23:12
File Name: \\gbjhnmr01\data\nmr1\llux539\2\
Frequency (MHz): 125.74
Nucleus: 13C
Number of Transients: 2048
Origin: AVIII500

Multiple Databases Search

☑ Execute Multiple Databases Search

List of Databases

☑ C:\Program Files\ACD12\DATABASE\ALDFTNMR.ND9
☑ L:\Analytical\PMAS3\ACD\HTS Database\HTS Database.nd9
☑ L:\Analytical\PMAS3\...ulation Database\Polymer and Surfactar
☑ L:\Analytical\PMAS3\ACD\GLP Database\ACD_GLP_DB.nd9
☑ L:\Analytical\PMAS3\ACD\Fluorine Database\Fluorine.nd9
☑ L:\Analytical\PMAS3\AC...l Products Database\New Natural Prc
☑ L:\Analytical\PMAS3\ACD...al Products Database\New Natural
☑ L:\Analytical\PMAS3\AC...l Products Database\New Natural Prc
☑ L:\Analytical\PMAS3\AC...l Products Database\New Natural Prc
☑ L:\Analytical\PMAS3\AC...l Products Database\New Natural Prc

□ Auto Merge Search Result

Merge Search Results to: 613\Application Data\Advanced Chemistry Development\SpecDB\Flat

ment User Data

Structure User Data

FW: 272.3389
Formula: $C_{17}H_{20}O_3$

ID: 33 A: 29/145 B: 145 13C Single DB 03/05/2011 12:11:34

Saving time…search multiple databases at once

Search for a structure, m/z, NMR chemical shift a range of database

Select the database you wish to search

Data Archiving

•Conclusions

❑ACD/Labs database software allows us to archive all our data From MS/NMR/UV/IR instrumentation.

❑The software is vendor neutral so has no bias to any particular data format

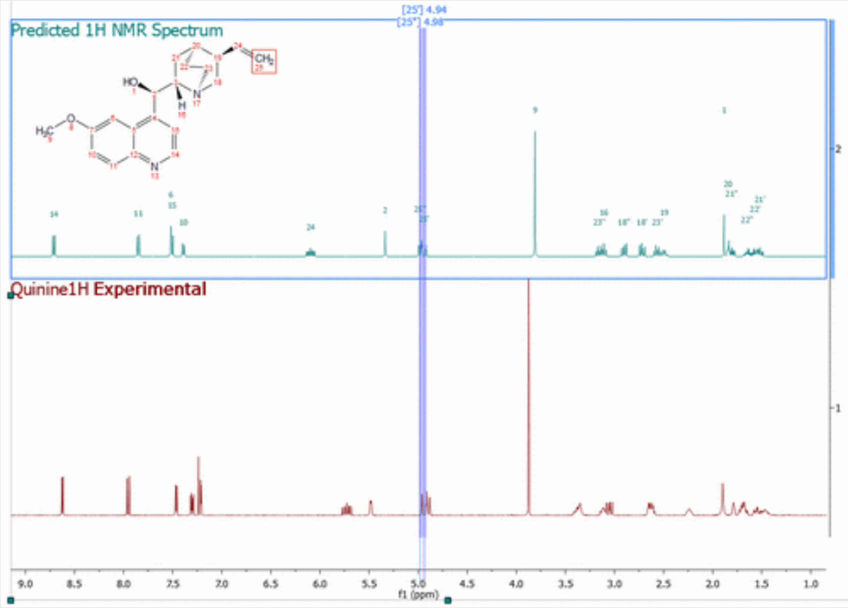
❑The databases are searchable in a huge number of ways and each database can be presented as the user sees fit

❑The data is only as good as the user inputs – careful consideration should be given as to what is submitted

NMR Prediction

The ability to predict what the NMR spectrum of a small organic molecule may look like is a valuable tool for the organic chemist and analyst.

It allows the chemist to gain some idea as to whether they have synthesised the correct compound by comparison of experimental and calculated ^1H and ^{13}C spectra.



This can save the chemist valuable time - giving the confidence the right compound had been made - they can move on to the next stage of synthesis

NMR Prediction

There are a number of key software vendors who offer NMR chemical shift prediction packages:

ACD/Labs For both ^{1}H and ^{13}C NMR use a combination of HOSE code and neural works. Prediction training is possible with HOSE code, hence the value mental chemical shift databases

Modgraph ^{1}H NMR uses additivity rules (all the substituents have a contribution to the shift of the atom in question) and partial atomic charges and steric effects.

^{13}C NMR uses HOSE code/NN – dependent on the quality of shift database

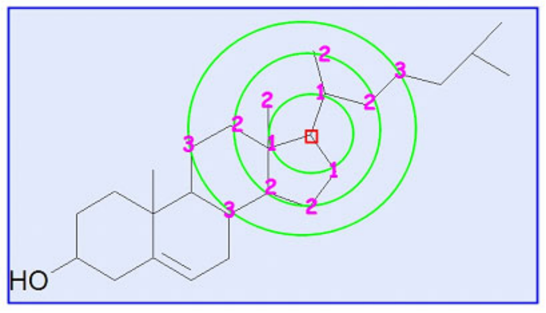
Perch Deterministic methods – high computational time to determine c ions

Quantum Chemistry Predictors (e.g. Gaussian)

Predicted from first principals – computationally very heavy

NMR Prediction

The software uses the HOSE code approach in its prediction (Hierarchical Organisation of Spherical Environments).



The HOSE starts at the atom whose shift is to be predicted.

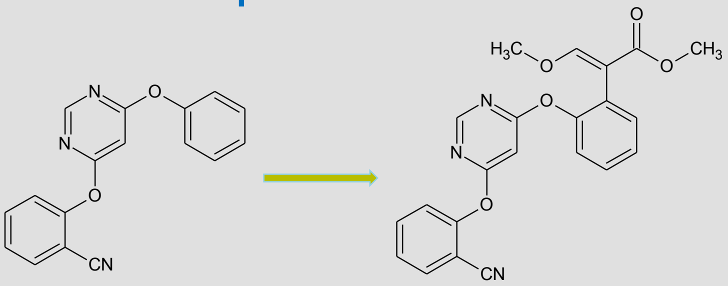
•It looks one bond away from the atom and tries to find this environment in its database.

•If it is successful it moves two bonds away, tries again and so on until it comes across something not represented in the database, reaches the boundary of the molecule or the HOSE code limits.

NMR Prediction

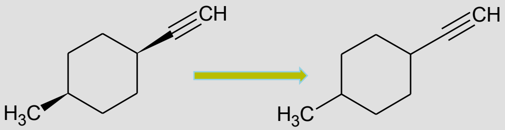
HOSE Code works well if:-

- Structures are well represented in the reference collection.
- If atoms can be predicted to three spheres or more.



HOSE Code doesn’t work well if:-

- Query structure is not well represented in the database
- The atom in question can only be predicted to one or two spheres.

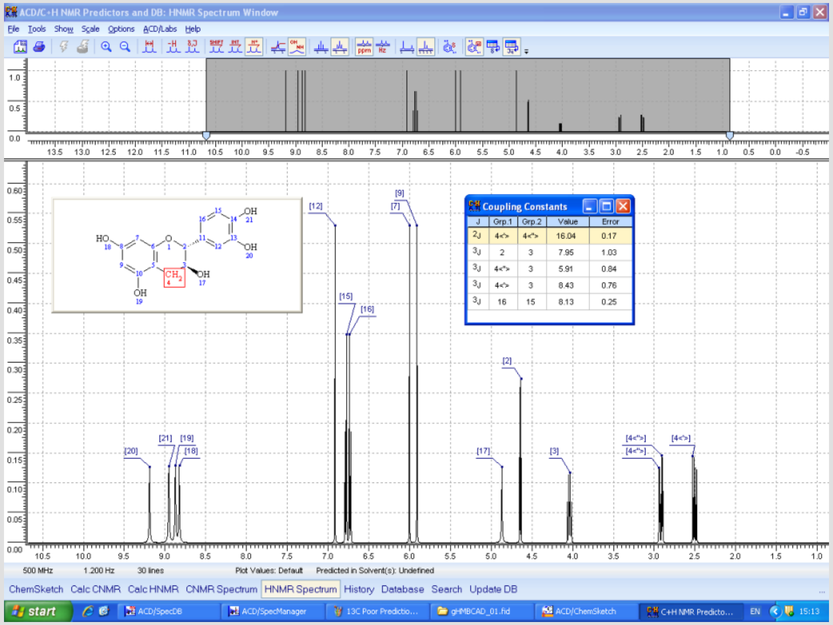


HOSE code approach exactly reproduces the contents of the reference database including every error within the reference database.

NMR Prediction

So how do we use the predictors?

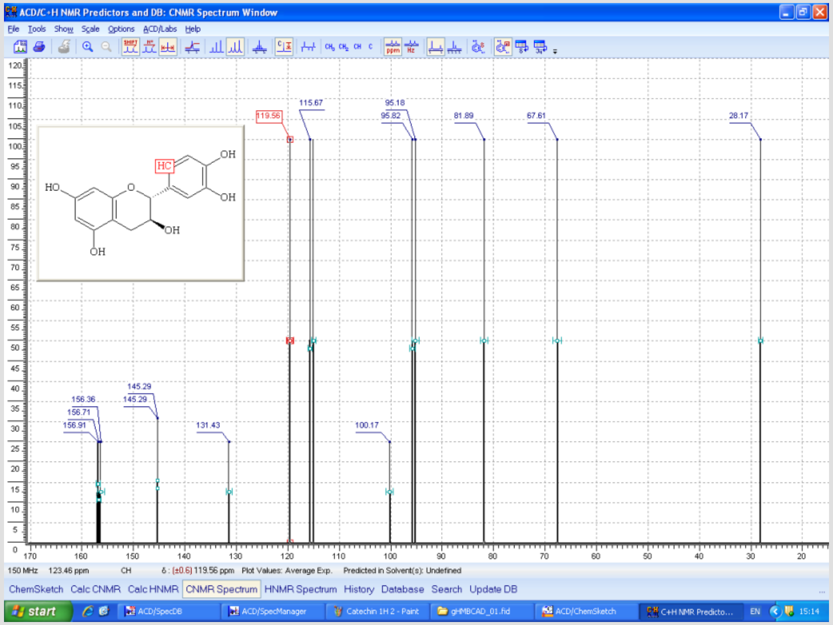
Very simply - just draw the structure and predict the $^{1}H/^{13}C$ spectrum. The structure atoms and spectrum peaks will be correlated and peaks will light up when atoms are hovered over with the mouse and vice versa.



Coupling Constants

J	Grp.1	Grp.2	Value	Error
^{2}J	4<'>	4<">	16.04	0.17
^{3}J	2	3	7.95	1.03
^{3}J	4<">	3	5.91	0.84
^{3}J	4<'>	3	8.43	0.76
^{3}J	16	15	8.13	0.25

500 MHz 1.200 Hz 30 lines Plot Values: Default Predicted in Solvent(s): Undefined

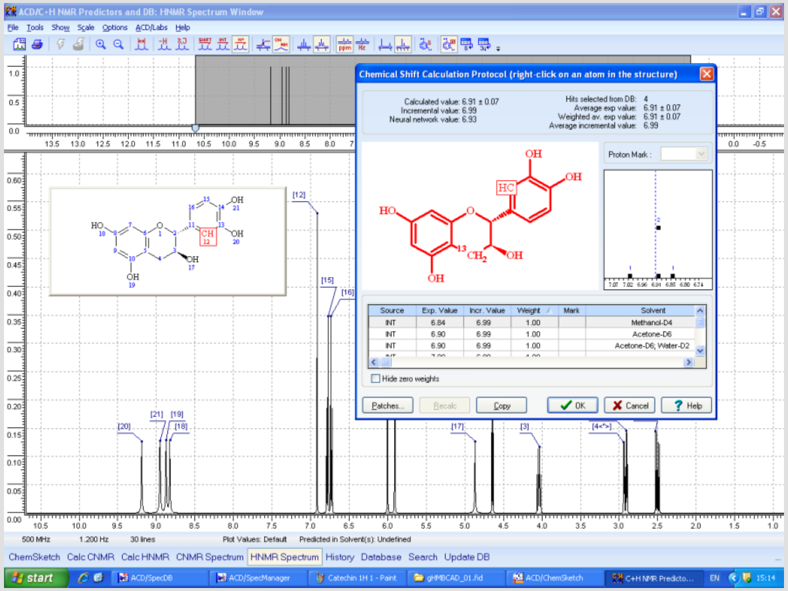


150 MHz 123.46 ppm CH 6 : [±0.6] 119.56 ppm Plot Values: Average Exp. Predicted in Solvent(s): Undefined

Tables of chemical shifts, coupling constants and confidence limits can be displayed and couplings to other atoms/exchangeable protons can also be turned on or off.

NMR Prediction

By right clicking on an appropriate atom on the structure, its possible to see if this structure has good representation in the internal chemical shift database that the HOSE code uses.
Within the ^{1}H database are over 210,700 structures and within the ^{13}C database over 200,100 structures.


ACD/C+H NMR Predictors and DB: HNMR Spectrum Window
File Tools Show Scale Options ACD/Labs Help
ChemSketch Calc CNMR Calc HNMR CNMR Spectrum HNMR Spectrum History Database Search Update DB
500 MHz 1.200 Hz 30 lines Plot Values: Default Predicted in Solvent(s): Undefined
[12] [15] [16] [17] [3] [4<*>] [18] [19] [20] [21]
start ACD/SpecDB ACD/SpecManager Catechin 1H 1 - Paint gHMBCAD_01.fid ACD/ChemSketch C+H NMR Predicto... EN 15:14

Chemical Shift Calculation Protocol (right-click on an atom in the structure)

Calculated value: 6.91 ± 0.07
Incremental value: 6.99
Neural network value: 6.93

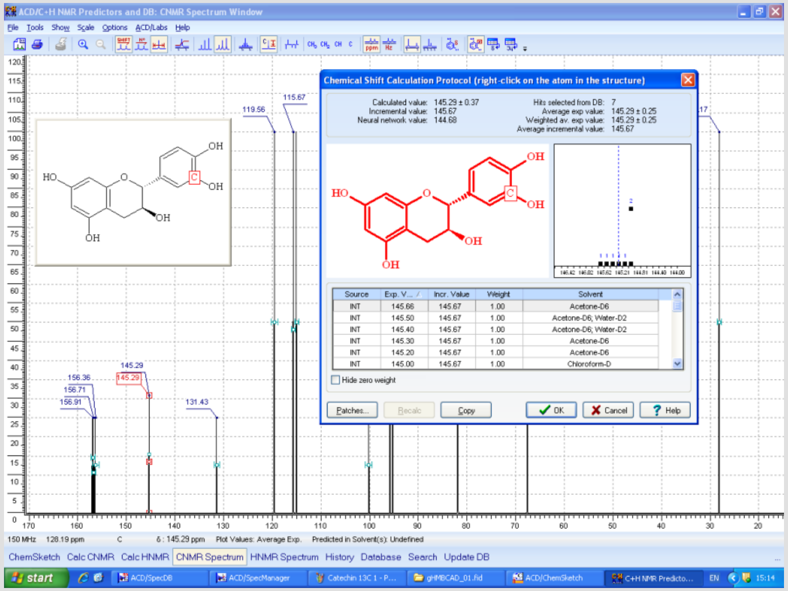
Hits selected from DB: 4
Average exp value: 6.91 ± 0.07
Weighted av. exp value: 6.91 ± 0.07
Average incremental value: 6.99

Proton Mark :

Source	Exp. Value	Incr. Value	Weight	Mark	Solvent
INT	6.84	6.99	1.00		Methanol-D4
INT	6.90	6.99	1.00		Acetone-D6
INT	6.90	6.99	1.00		Acetone-D6; Water-D2

☐ Hide zero weights

Patches... Recalc Copy OK Cancel Help


ACD/C+H NMR Predictors and DB: CNMR Spectrum Window
File Tools Show Scale Options ACD/Labs Help
ChemSketch Calc CNMR Calc HNMR CNMR Spectrum HNMR Spectrum History Database Search Update DB
150 MHz 128.19 ppm C 6 : 145.29 ppm Plot Values: Average Exp. Predicted in Solvent(s): Undefined
115.67 119.56 156.36 156.71 156.91 145.29 131.43
start ACD/SpecDB ACD/SpecManager Catechin 13C 1 - P... gHMBCAD_01.fid ACD/ChemSketch C+H NMR Predicto... EN 15:14

Chemical Shift Calculation Protocol (right-click on the atom in the structure)

Calculated value: 145.29 ± 0.37
Incremental value: 145.67
Neural network value: 144.68

Hits selected from DB: 7
Average exp value: 145.29 ± 0.25
Weighted av. exp value: 145.29 ± 0.25
Average incremental value: 145.67

Source	Exp. V...	Incr. Value	Weight	Solvent
INT	145.66	145.67	1.00	Acetone-D6
INT	145.50	145.67	1.00	Acetone-D6; Water-D2
INT	145.40	145.67	1.00	Acetone-D6; Water-D2
INT	145.30	145.67	1.00	Acetone-D6
INT	145.20	145.67	1.00	Acetone-D6
INT	145.00	145.67	1.00	Chloroform-D

☐ Hide zero weight

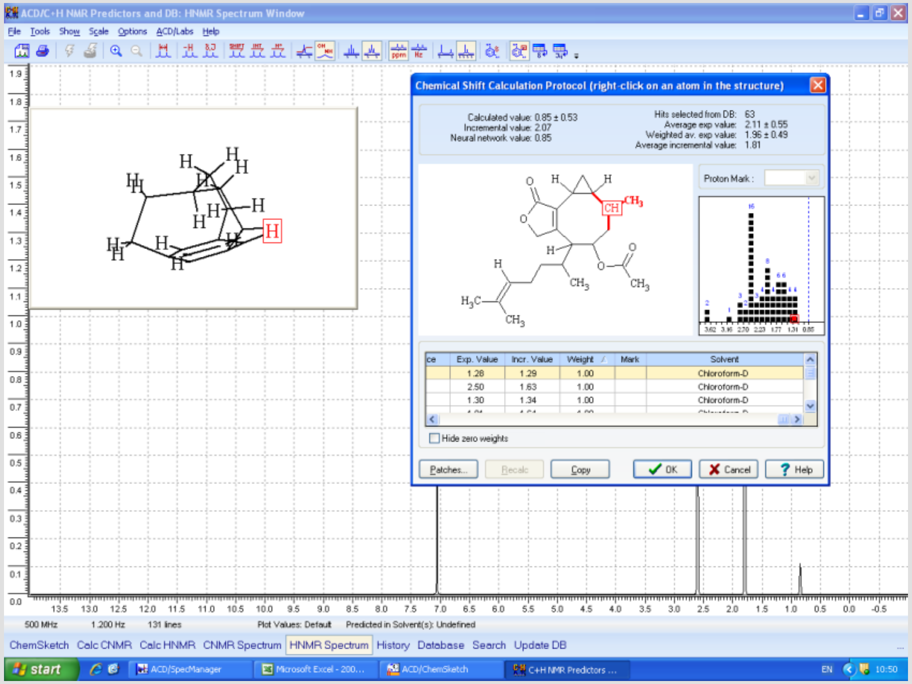
The predictions can also be solvent specific so if you recorded your spectrum in $CDCl_3$ then use only database compound shift recorded in $CDCl_3$.

NMR Prediction

The problem with HOSE code....

Because we work with novel chemical entities, they are not represented well in the internal ACD databases. When this is the case the predictions can fall down.

A primary example is [10] cyclophane:



ACD/C+H NMR Predictors and DB: HNMR Spectrum Window

Chemical Shift Calculation Protocol (right-click on an atom in the structure)

Calculated value: 0.85 ± 0.53
Incremental value: 2.07
Neural network value: 0.85

Hits selected from DB: 63
Average exp value: 2.11 ± 0.55
Weighted av. exp value: 1.96 ± 0.49
Average incremental value: 1.81

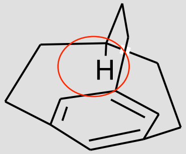
Proton Mark :

ce	Exp. Value	Incr. Value	Weight	Mark	Solvent
	1.28	1.29	1.00		Chloroform-D
	2.50	1.63	1.00		Chloroform-D
	1.30	1.34	1.00		Chloroform-D

□ Hide zero weights

500 MHz 1 200 Hz 131 lines Plot Values: Default Predicted in Solvent(s): Undefined

File Tools Show Scale Options ACD/Labs Help
Patches... Recalc Copy OK Cancel Help
ChemSketch Calc CNMR Calc HNMR CNMR Spectrum HNMR Spectrum History Database Search Update DB
start ACD/SpecManager Microsoft Excel - 200... ACD/ChemSketch C+H NMR Predictors ...
EN 10:50
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
3.62 3.16 2.70 2.23 1.77 1.31 0.85
16
8
6 6
4 4
3
2
1



The proton highlighted resonates at ~-4ppm. The best ACD can do is ~0.7ppm for the proton highlighted.

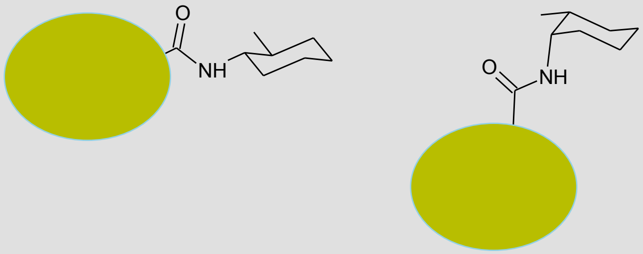
This is because there are no similar structures at all in the internal database.

NMR Prediction

How do we overcome this problem?

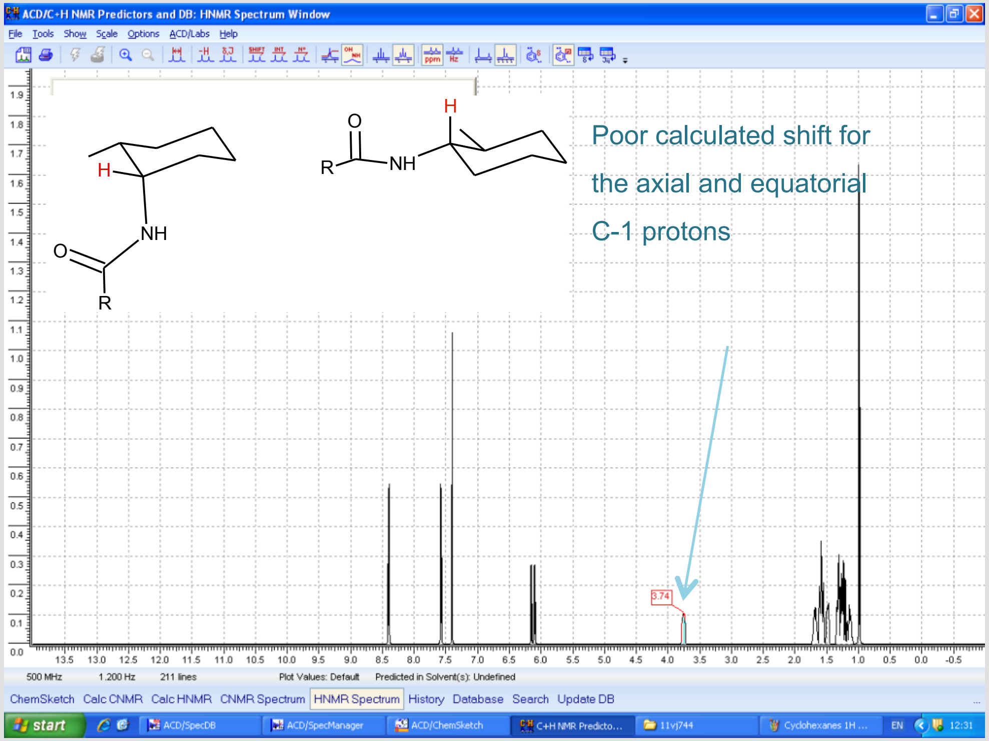
To overcome the problem of poor representation in ACD's internal databases is to simply add the experimental data yourself and ask the software to use it. We train the predictor.

A good example is for the cyclohexanes below:-



The ^{1}H prediction for these two molecules is poor and they cannot be differentiated.

By creating a ACD User HNMRDB we can add this experimental data in as we have recorded the ^{1}H and ^{13}C spectra ourselves.

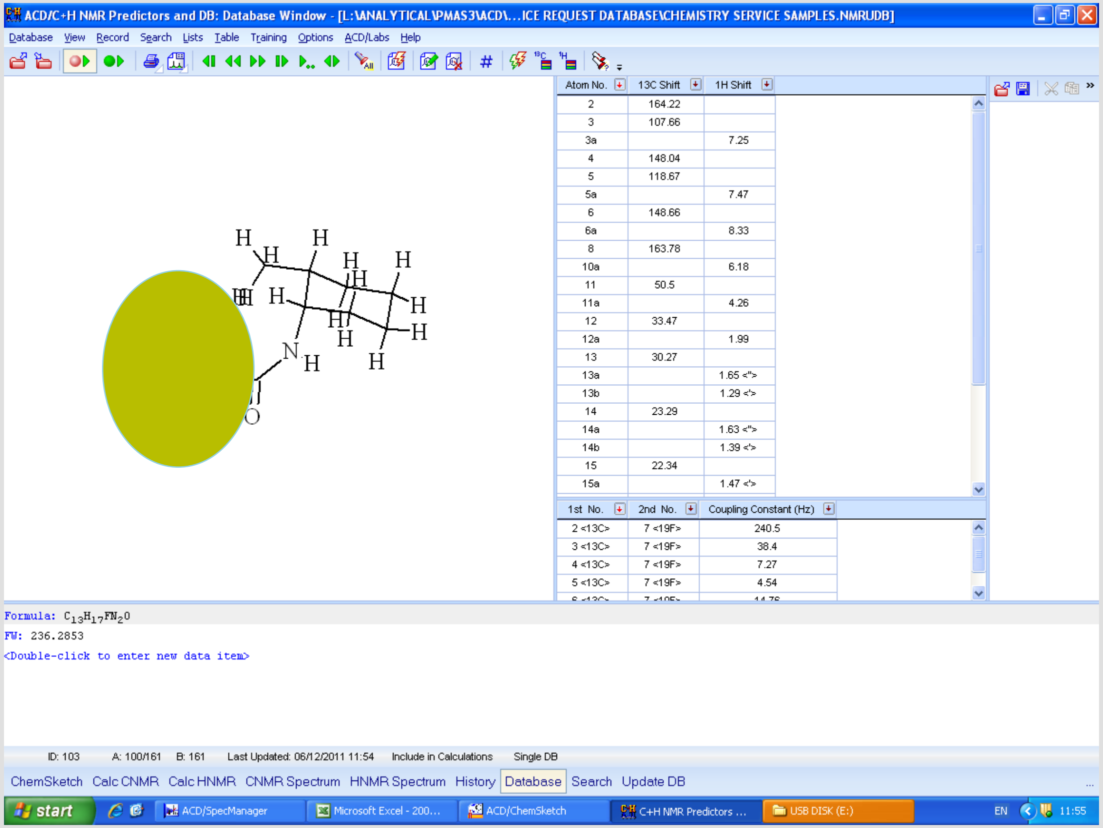

ACD/C+H NMR Predictors and DB: HNMR Spectrum Window
File Tools Show Scale Options ACD/Labs Help
H
NH
O
R
O
R
NH
H
1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 0.1 0.0
3.74
13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
500 MHz 1.200 Hz 211 lines Plot Values: Default Predicted in Solvent(s): Undefined
ChemSketch Calc CNMR Calc HNMR CNMR Spectrum HNMR Spectrum History Database Search Update DB
start ACD/SpecDB ACD/SpecManager ACD/ChemSketch C+H NMR Predicto... 11vj744 Cyclohexanes 1H ... EN 12:31

Poor calculated shift for the axial and equatorial C-1 protons

NMR Prediction

How do we overcome this problem?

We assign our experimental spectra and push these chemical shifts to the HNMRDB



ACD/C+H NMR Predictors and DB: Database Window - [L:\ANALYTICAL\PMAS3\ACD\...ICE REQUEST DATABASE\CHEMISTRY SERVICE SAMPLES.NMRUDB]

Database View Record Search Lists Table Training Options ACD/Labs Help
H H H H H H H H H H H H N H O

Atom No.	13C Shift	1H Shift
2	164.22	
3	107.66	
3a		7.25
4	148.04	
5	118.67	
5a		7.47
6	148.66	
6a		8.33
8	163.78	
10a		6.18
11	50.5	
11a		4.26
12	33.47	
12a		1.99
13	30.27	
13a		1.65 <''>
13b		1.29 <'>
14	23.29	
14a		1.63 <''>
14b		1.39 <'>
15	22.34	
15a		1.47 <'>

1st No.	2nd No.	Coupling Constant (Hz)
2 <13C>	7 <19F>	240.5
3 <13C>	7 <19F>	38.4
4 <13C>	7 <19F>	7.27
5 <13C>	7 <19F>	4.54
6 <13C>	7 <19F>	14.76

Formula: $C_{13}H_{17}FN_2O$
FW: 236.2853
<Double-click to enter new data item>

ID: 103 A: 100/161 B: 161 Last Updated: 06/12/2011 11:54 Include in Calculations Single DB

The database contains all the assignments/coupling constants we measured

Same navigation and search functions as a spectral database described earlier.

We can also:

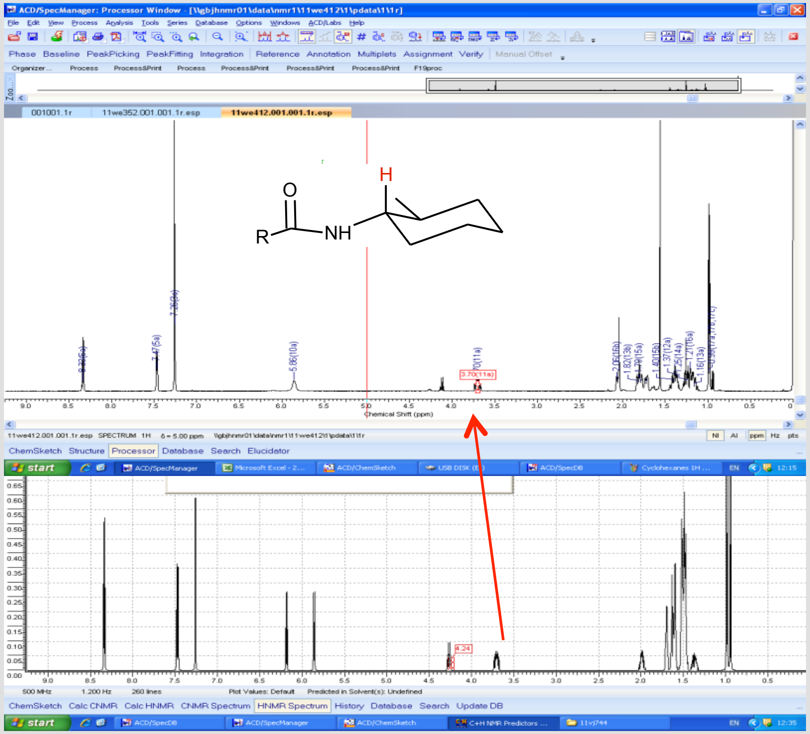
- •Use multiple databases for prediction training.
- •Edit shifts at any time
- •Set the HOSE code depth to what we want – loose or tight

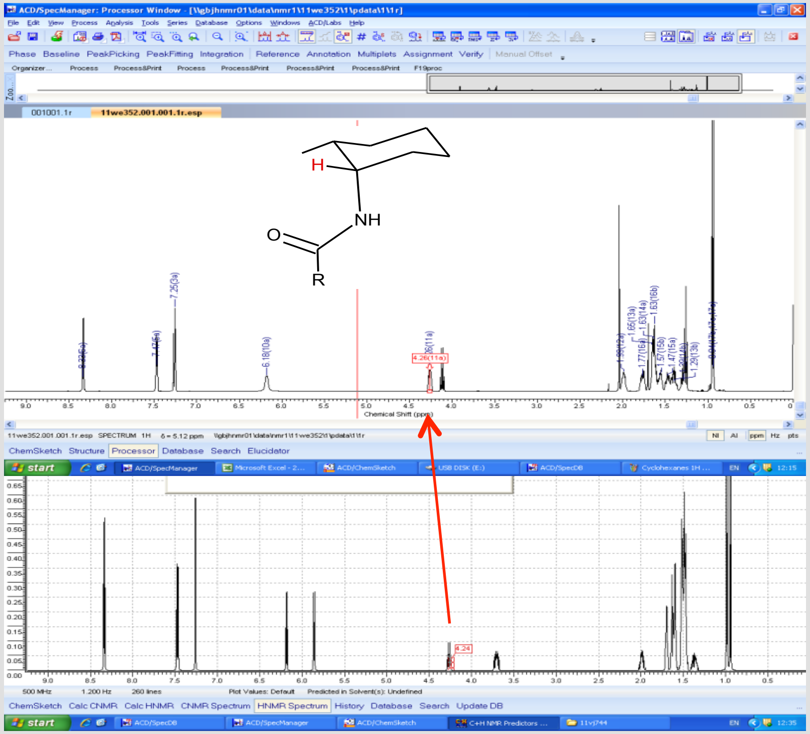
NMR Prediction

The result...

We predict again and now obtain a accurate prediction. We force the software to use our own chemical shift database - the predictions below should be a 100% match with the experimental data.

The value we get is further down the line when we predict spectra for similar compounds – we now have a representative compound in our user HNMRDB.

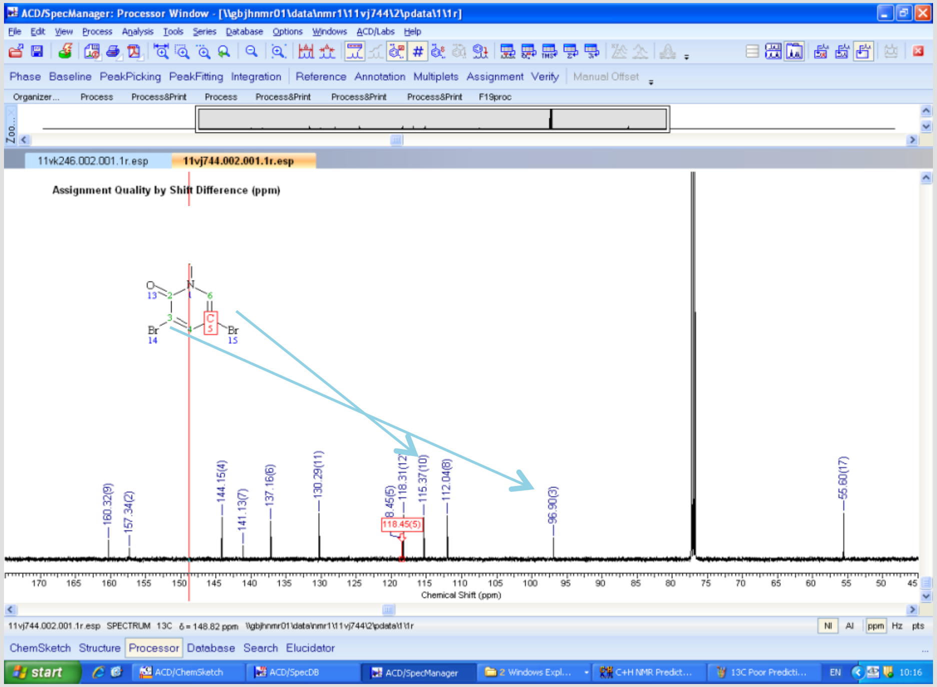

ACD/SpecManager: Processor Window - [\\gbjhnmr01\data\nmr1\11we412\1\pdata\1\1r]
11we412.001.001.1r.esp
O
R
NH
H
3.70(11a)
4.24
Chemical Shift (ppm)
ChemSketch Structure Processor Database Search Elucidator
ChemSketch Calc CNMR Calc HNMR CNMR Spectrum HNMR Spectrum History Database Search Update DB


ACD/SpecManager: Processor Window - [\\gbjhnmr01\data\nmr1\11we352\1\pdata\1\1r]
11we352.001.001.1r.esp
H
NH
O
R
4.26(11a)
4.24
Chemical Shift (ppm)
ChemSketch Structure Processor Database Search Elucidator
ChemSketch Calc CNMR Calc HNMR CNMR Spectrum HNMR Spectrum History Database Search Update DB

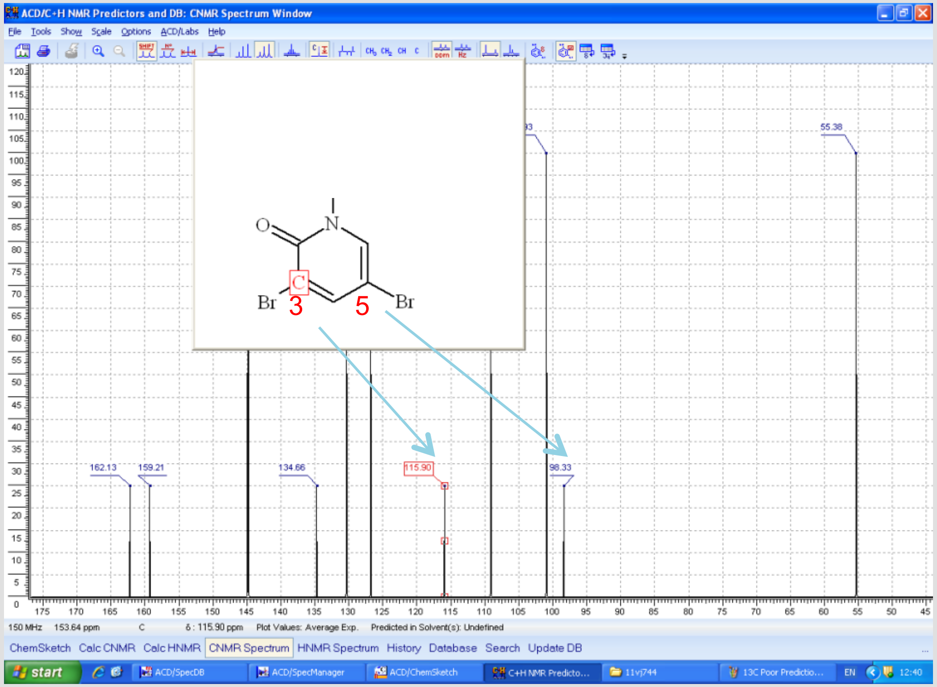
NMR Prediction

The result…

Same principal for any nuclei – in this case ^{13}C. Atoms 3 and 5 are predicted completely the wrong way around. In reality atom 3 is at much lower ppm than atom 5:-



ACD/SpecManager: Processor Window - [\\gbjhnmr01\data\nmr1\11vj744\2\pdata\1\1r]
11vk246.002.001.1r.esp
11vj744.002.001.1r.esp
Assignment Quality by Shift Difference (ppm)
O
N
Br
Br
C
13
14
15
160.32(9)
157.34(2)
144.15(4)
141.13(7)
137.16(6)
130.29(11)
118.45(5)
118.31(12)
115.37(10)
112.04(8)
96.90(3)
55.60(17)
Chemical Shift (ppm)
11vj744.002.001.1r.esp SPECTRUM 13C δ = 148.82 ppm \\gbjhnmr01\data\nmr1\11vj744\2\pdata\1\1r
ChemSketch Structure Processor Database Search Elucidator

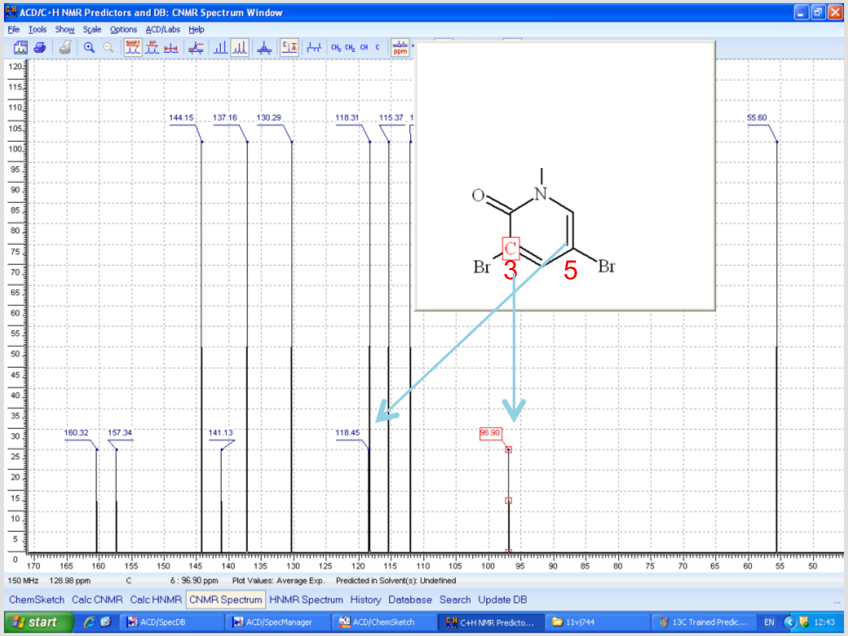


ACD/C+H NMR Predictors and DB: CNMR Spectrum Window
O
N
Br
Br
C
3
5
162.13
159.21
134.66
115.90
98.33
55.38
150 MHz 153.64 ppm C δ : 115.90 ppm Plot Values: Average Exp. Predicted in Solvent(s): Undefined
ChemSketch Calc CNMR Calc HNMR CNMR Spectrum HNMR Spectrum History Database Search Update DB

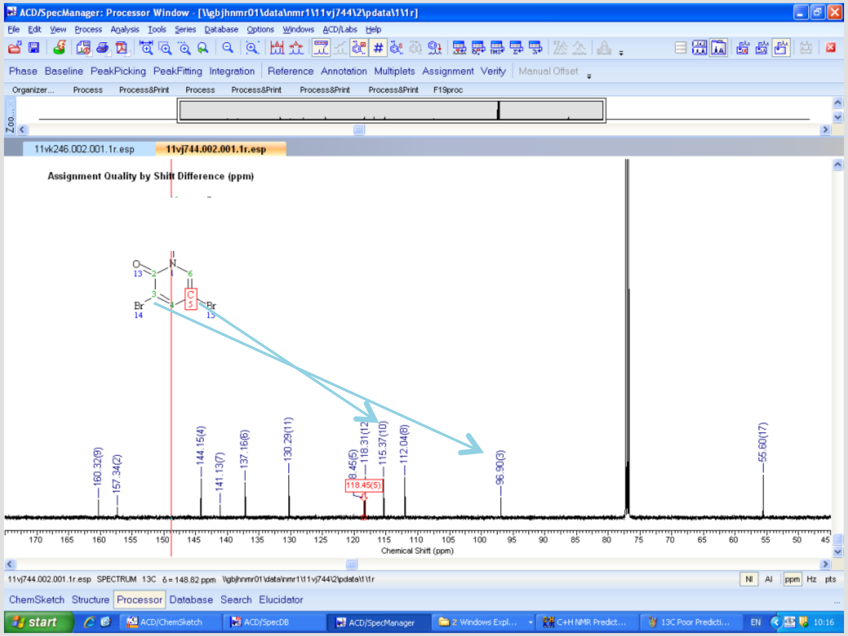
NMR Prediction

The result...

With training, the predicted shifts are corrected and for subsequent compounds that contain the dibromopyridinone fragment the predictions will be a great deal better.


ACD/C+H NMR Predictors and DB: CNMR Spectrum Window
File Tools Show Scale Options ACD/Labs Help
144.15
137.16
130.29
118.31
115.37
55.60
160.32
157.34
141.13
118.45
96.90
O
N
C
Br
3
5
Br
170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50
ChemSketch Calc CNMR Calc HNMR CNMR Spectrum HNMR Spectrum History Database Search Update DB
start ACD/SpecDB ACD/SpecManager ACD/ChemSketch C+H NMR Predicto... 11vj744 13C Trained Predic... EN 12:43

150 MHz 128.98 ppm C δ : 96.90 ppm Plot Values: Average Exp. Predicted in Solvent(s): Undefined


ACD/SpecManager: Processor Window - [\\gbjhnmr01\data\nmr1\11vj744\2\pdata\1\1r]
File Edit View Process Analysis Tools Series Database Options Windows ACD/Labs Help
Phase Baseline PeakPicking PeakFitting Integration Reference Annotation Multiplets Assignment Verify Manual Offset
Organizer... Process Process&Print Process Process&Print Process&Print Process&Print F19proc
11vk246.002.001.1r.esp
11vj744.002.001.1r.esp
Assignment Quality by Shift Difference (ppm)
O
13
2
N
1
6
3
4
C
5
Br
14
Br
15
160.32(9)
157.34(2)
144.15(4)
141.13(7)
137.16(6)
130.29(11)
8.45(5)
118.31(12
115.37(10)
112.04(8)
118.45(5)
96.90(3)
55.60(17)
170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45
Chemical Shift (ppm)
NI AI ppm Hz pts
ChemSketch Structure Processor Database Search Elucidator
start ACD/ChemSketch ACD/SpecDB ACD/SpecManager 2 Windows Expl... C+H NMR Predict... 13C Poor Predicti... EN 10:16

11vj744.002.001.1r.esp SPECTRUM 13C δ = 148.82 ppm \\gbjhnmr01\data\nmr1\11vj744\2\pdata\1\1r

NMR Prediction

Our Internal Databases:-

We have multiple user prediction databases available, all created in house.

- Natural Products database contains ~140 compounds with ^{1}H and ^{13}C data
- Chemistry database contains over 160 compounds
- Natural product ^{13}C database with over 6100 compounds
- Coupling constant database with over 120 ^{1}H-^{13}C coupling constants

These databases are updated regularly. The desire is to start populating ^{19}F and ^{31}P databases

NMR Prediction

Conclusions

Using HOSE code based ACD predictors has numerous advantages over other prediction programs:-

- **Not computationally expensive**
- **They can incorporate neural network algorithms to compliment each other**
- **Multiple nuclei can be predicted quickly and easily**
- **The internal database contains a huge amount of chemical shift and coupling information**
- **The databases can be trained – this ability makes database based predictions very effective**

NMR Prediction

Conclusions

However, the disadvantages:

- **Its very time consuming to get the data into databases. Full and accurate assignment of the experimental data must be performed**
- **The predictions without training are only as good as the data in the ACD internal databases.**
  - How do we know where this data came from?
  - Is it accurate – who recorded it, did they mis-assign the spectrum, etc?