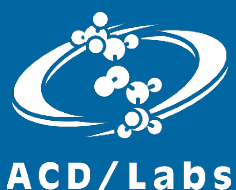


Optimizing Your Analysis: The Many Ways NMR Predictors Can Be Applied




Grace Kennedy
ACD/Labs NMR Software Symposium
March 4th, 2018

Evolution of NMR Spectra Prediction

CNMR PREDICTION & INTERPRETATION

- Demo CD includes:
 - Product Description, What's New & Technical Information
 - Independent reviews: ACD/CNMR vs. Competition
 - Working Demo
 - Printable Tutorial & Demo Movie



"The program CNMR ... gives the best results in our work ... Future developments in this field should be oriented on the results of the CNMR program ..." (J. Chem. Inf. Comput. Sci. 1997, 37, 726)

"Ninety minutes after starting to install the program I had printed CNMR spectra for ten compounds ... I found the program did an excellent job predicting carbon spectra" (Concepts in Magnetic Resonance, July 1997)

*S295 - Academics
S495 - Industry
(includes all products on the left page!)*

2002
1,700,000 ¹³C shifts
1,200,000 ¹H shifts

2008
2,547,046 ¹³C shifts
1,755,262 ¹H shifts

2017
3,295,442 ¹³C shifts
2,401,629 ¹H shifts
369,210 C+H structures
49,081 ¹⁹F shifts
37,911 ³¹P shifts

SpecManager Platform

Spectrus Platform

1994

ACD/CNMR

1995

ACD/HNMR

1998

ACD/XNMR
ACD/2DNMR

2006

Neural Network
Predictions v. 1

2008

Neural Network
Predictions v. 2
Improved HNMR
and CNMR algorithms
New Incremental
prediction schemes

2011

Predictions for mixtures,
Biosequences, Pure Shift spectra.
Full incorporation into
Spectrus Platform

ACD/Spectrus

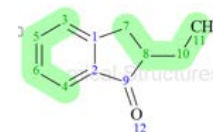


Spectrus Platform introduced

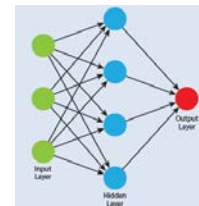
2017

The Ways NMR Predictors Can Be Applied

Enhance structure verification using NMR predictions



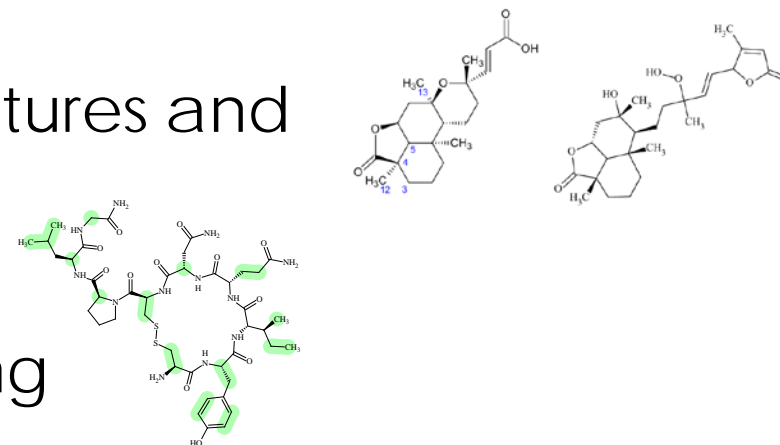
Improve NMR prediction accuracy through training



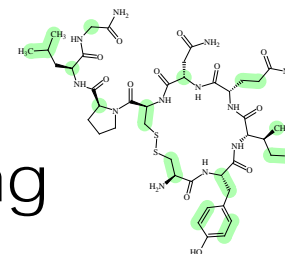
How you can use 2D NMR predictions to optimize instrument time



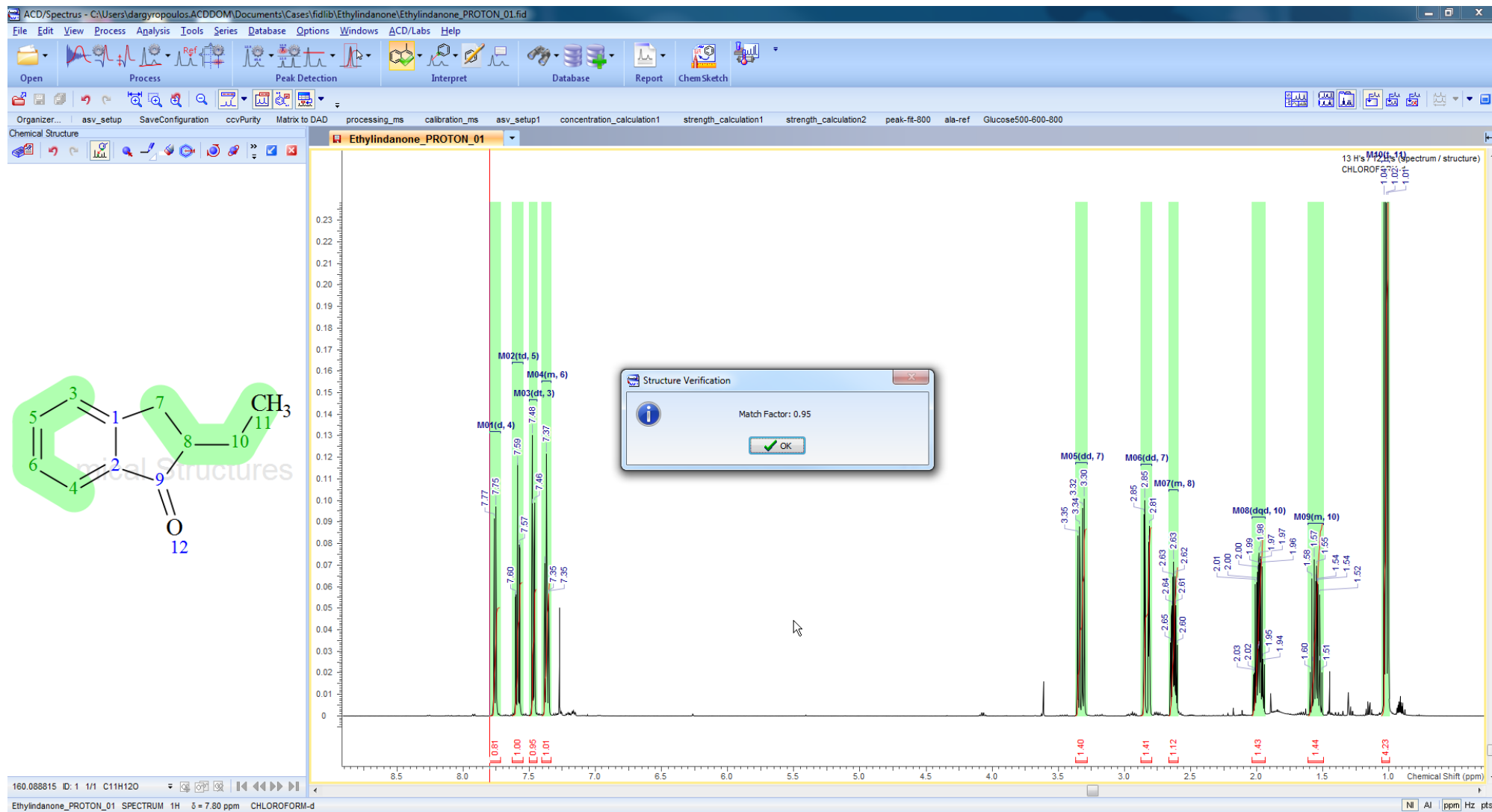
How to use the NMR predictors for analyzing mixtures and complex ¹H NMR spectra



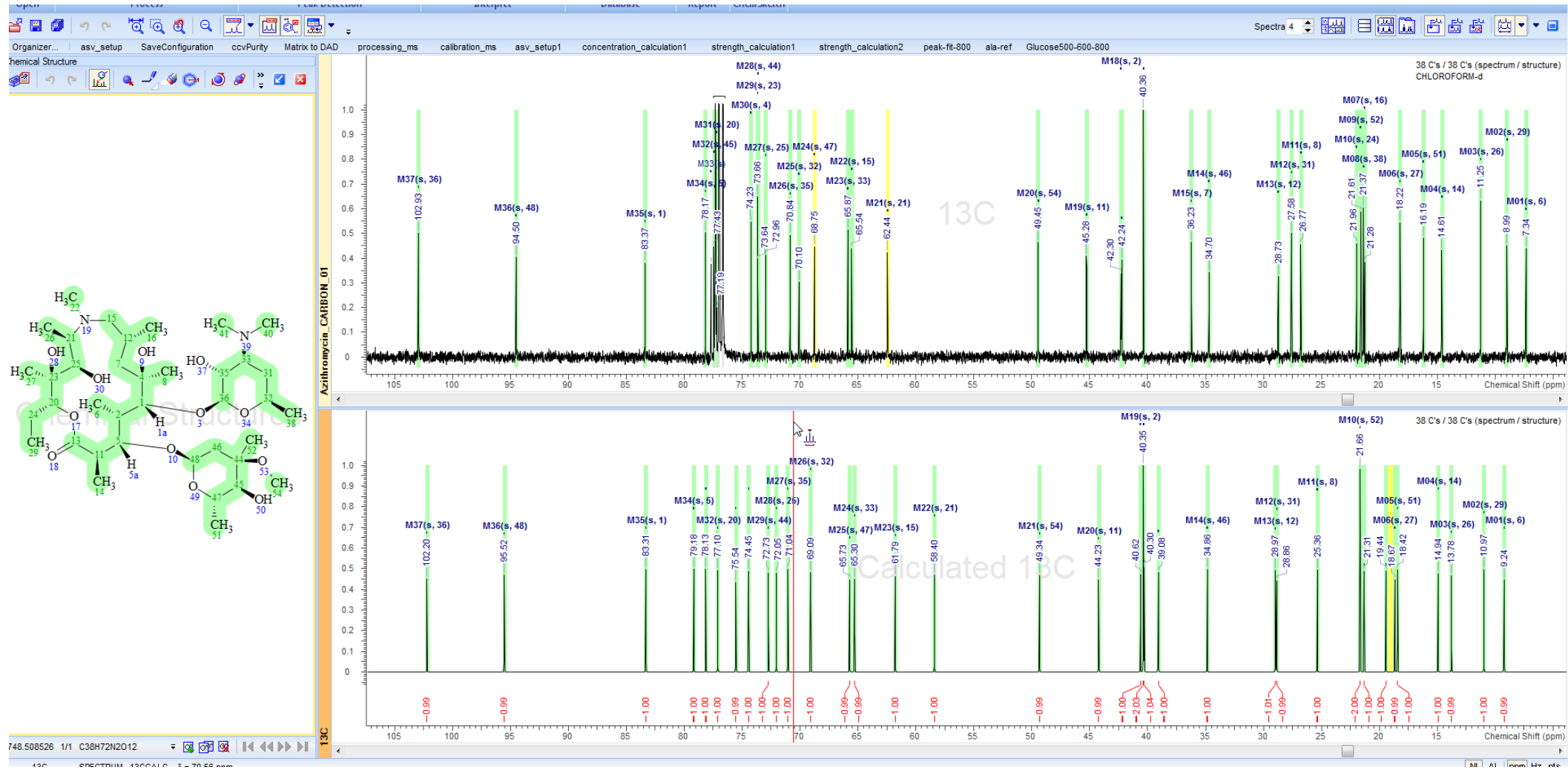
How to use the NMR predictors for biosequencing



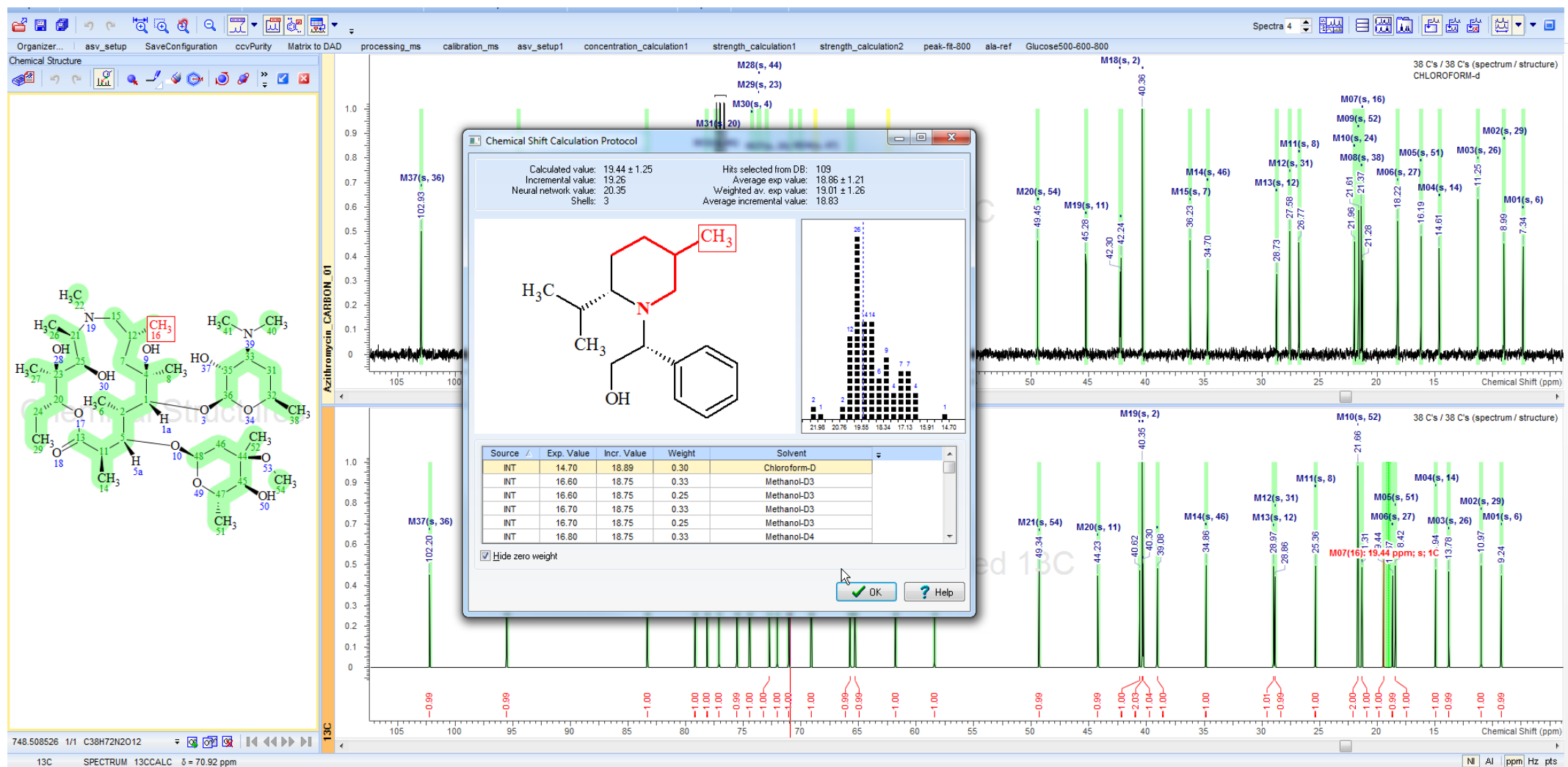
Enhance Verification with NMR Predictions



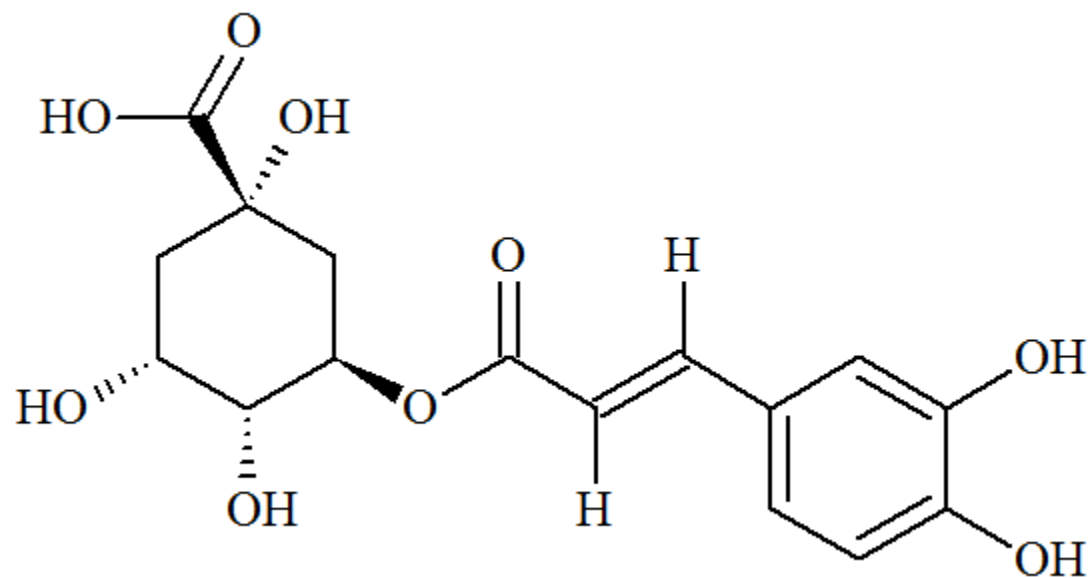
Enhance Verification with NMR Predictions



Enhance Verification with NMR Predictions



NMR Predictor Database Built from Literature



Formula: $C_{16}H_{18}O_9$

FW: 354.3087

Name: 3-(((2E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl)oxy)-1,4,5-trihydroxycyclohexanecarboxylic acid

Trivial Name: chlorogenic acid

Ref1: J. Nat. Prod., 2004, v. 67, p. 1818 (CNMR: Methanol- d_4 : 125 MHz; 25 C; HNMR: Methanol- d_4 : 500 MHz; 25 C)

Ref2: Chem. Pharm. Bull., 1988, v. 36, p. 87 (HNMR: Acetone- d_6 , Water- d_2 : 200 MHz)

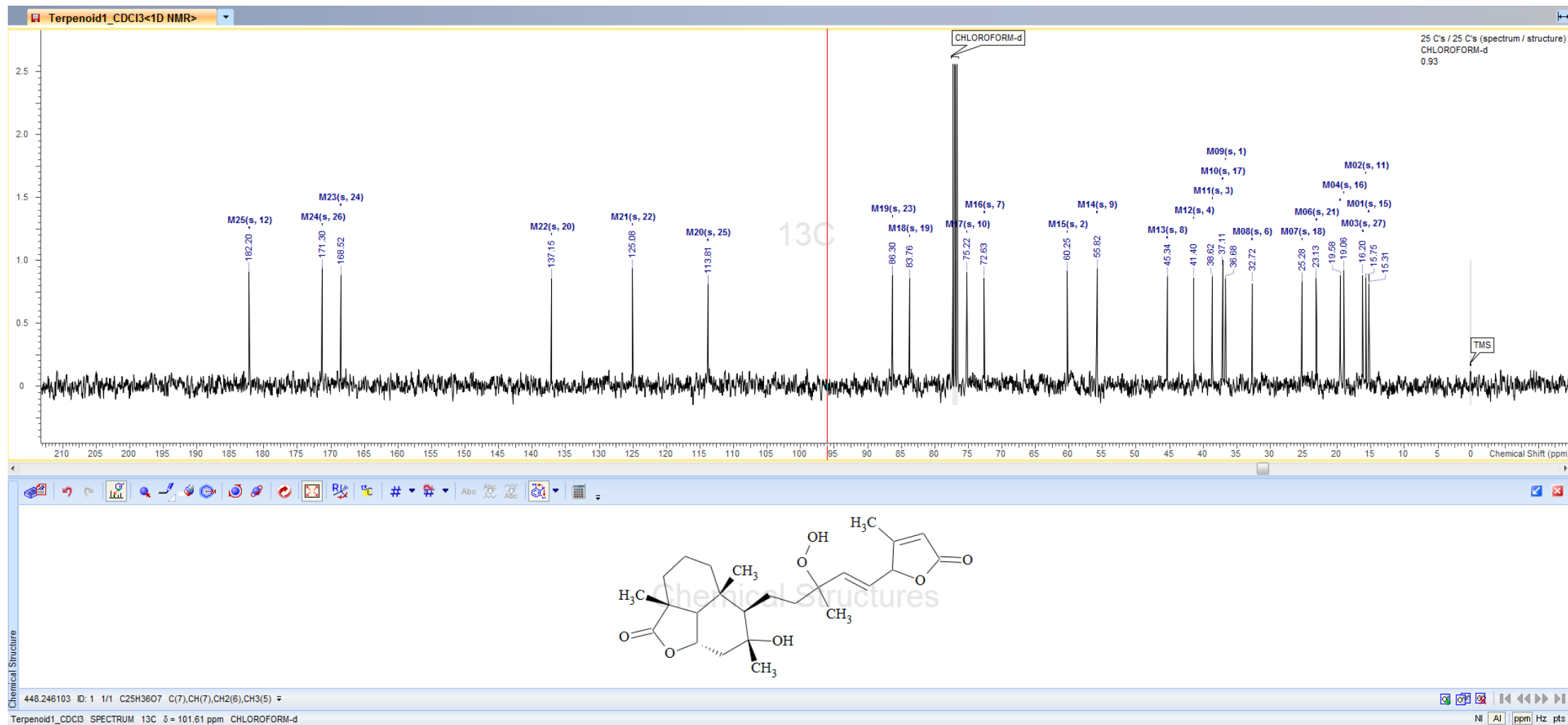
Ref3: J. Nat. Prod., 1999, v. 62, p. 405 (CNMR: Methanol- d_4 , Water- d_2 : HETCOR, COLOC; 75 MHz)

Ref4: Chem. Pharm. Bull., 1988, v. 36, p. 807 (CNMR: 100 MHz)

Database Statistics

	Structures	Shifts	Coupling Constants
C+H NMR Database	369,210	4,973,786	998,168
CNMR Database	240,361	3,295,442	132,792
HNMR Database	260,342	2,401,629	908,473
NNMR Database	10,216	24,277	5,077
FNMR Database	26,069	49,081	57,662
PNMR Database	31,102	37,911	42,364

Training the NMR Predictor Database



Training the NMR Predictor Database

The screenshot displays the ChemSketch interface with a chemical structure and its corresponding NMR data table. A red circle highlights a methyl group (CH₃) in the structure, another red circle highlights a methyl group (CH₃) in the table, and a third red circle highlights the 'Include in Calculations' button in the bottom status bar.

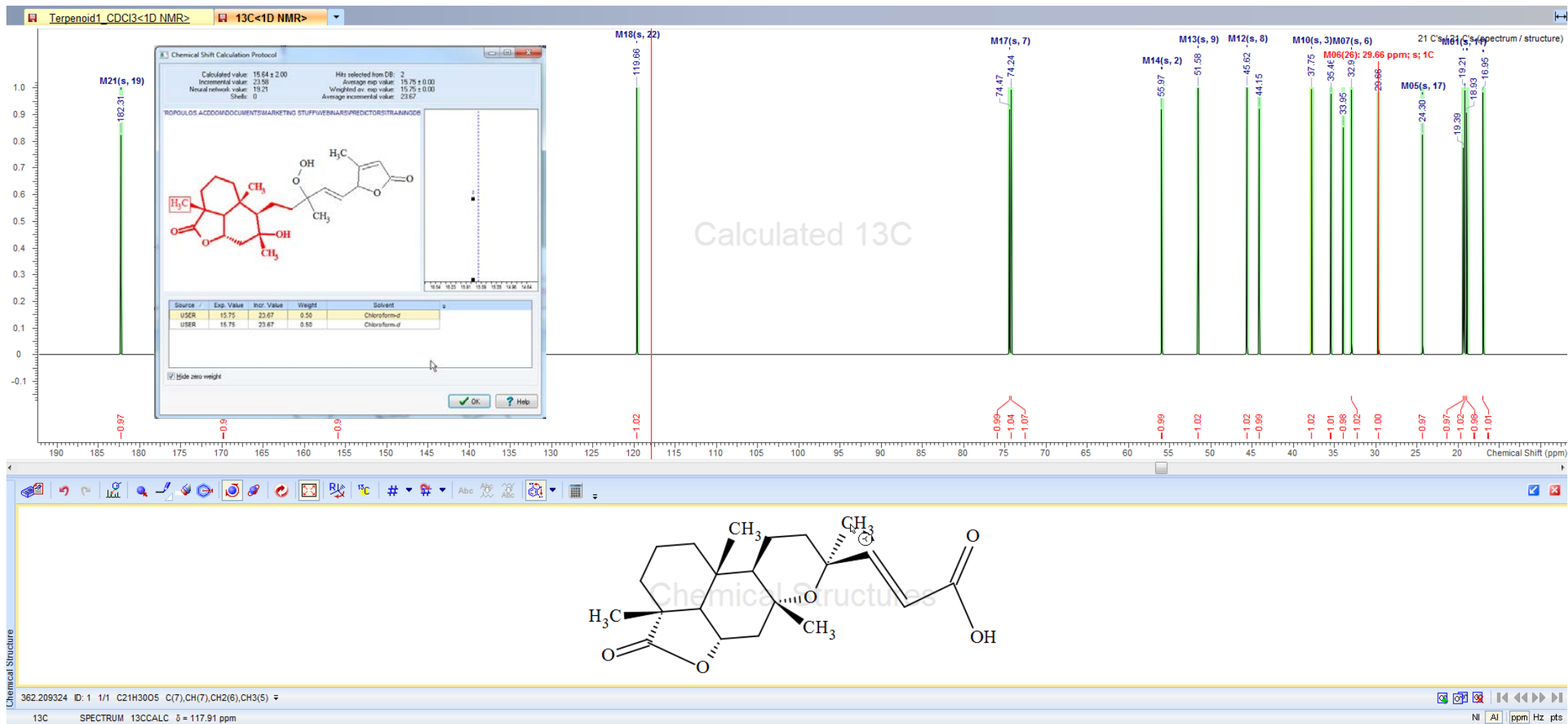
Atom No.	¹³ C Shift	¹ H Shift
1	36.68	
2	60.25	
3	38.62	
4	41.4	
5	19.58	
6	32.72	
7	72.63	
8	45.34	
9	55.82	
10	75.22	
11	15.75	
12	182.2	
13	15.31	
14	19.08	
15	37.11	
16	25.28	
17	83.76	
18	137.15	
19	23.13	
20	125.08	
21	86.3	
22	168.52	
23	113.81	
24	171.3	
25	16.2	

Formula: C₂₅H₃₆O₇
FW: 448.5491
Solvent: Chloroform-d
Frequency (MHz): 100.0000
d_N(¹³C): 0.889
sd_N(¹³C): 1.563
max_d_N(¹³C): 4.809
MF (Multi Spec): 0.93

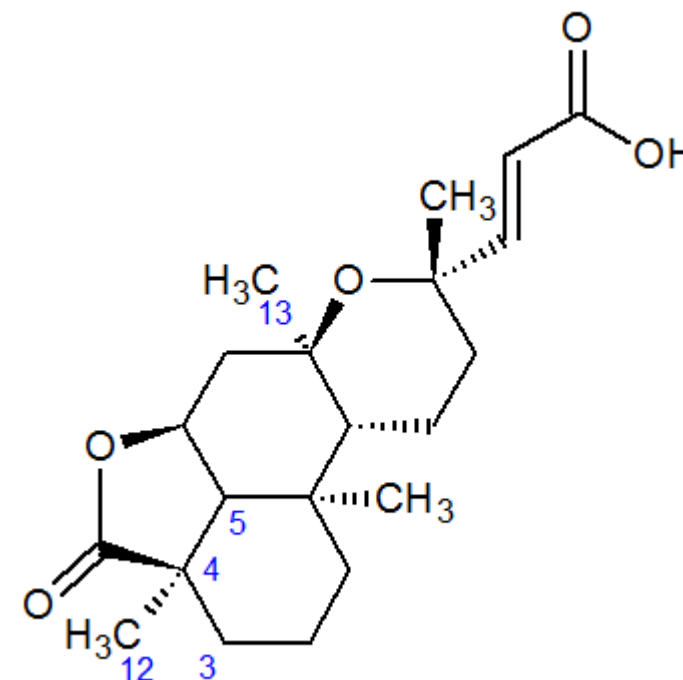
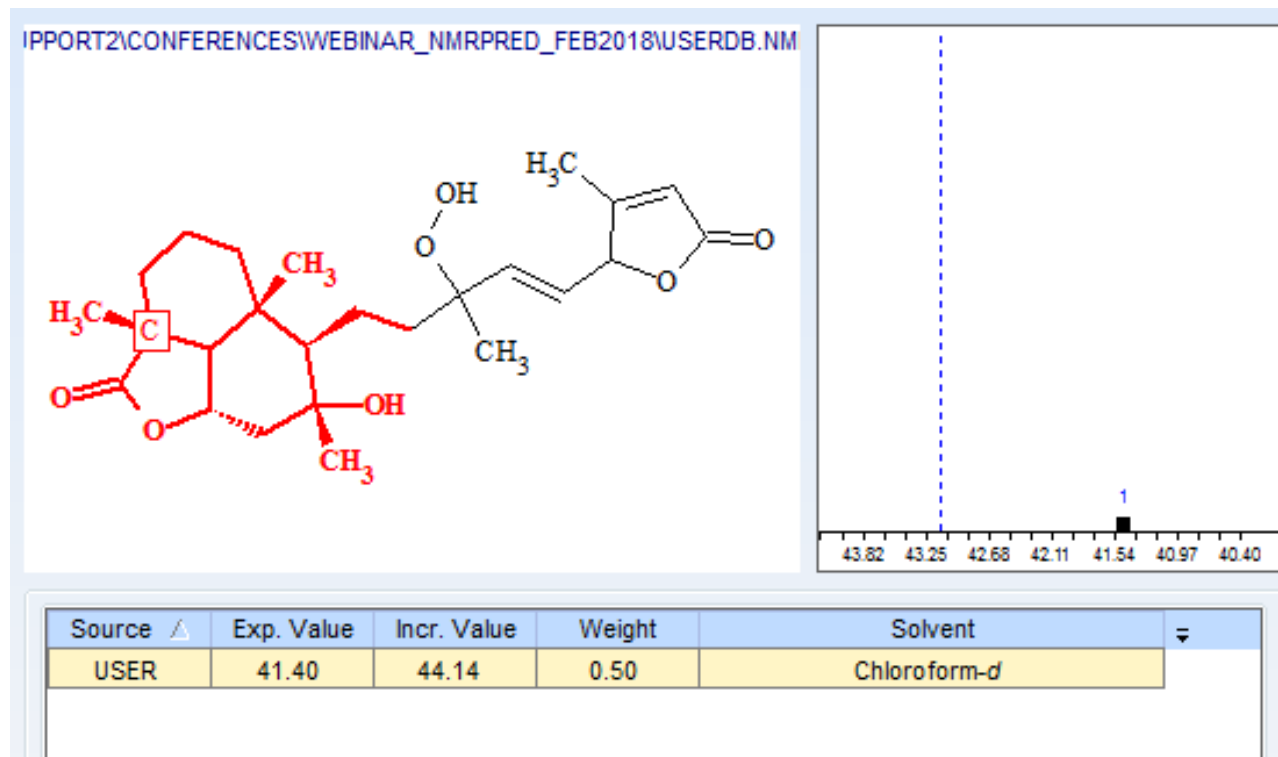
ID: 3 | A: 2/2 | B: 2 | Last Updated: 28/02/20 | 17:10 | **Include in Calculations** | Spine DB

ChemSketch 2-Back to Processor 3-Calc CNMR 4-Calc HNMR 5-CNMR Spectra 6-HNMR Spectrum 7-History 8-Database 9-Search Update DB

Training the NMR Predictor Database



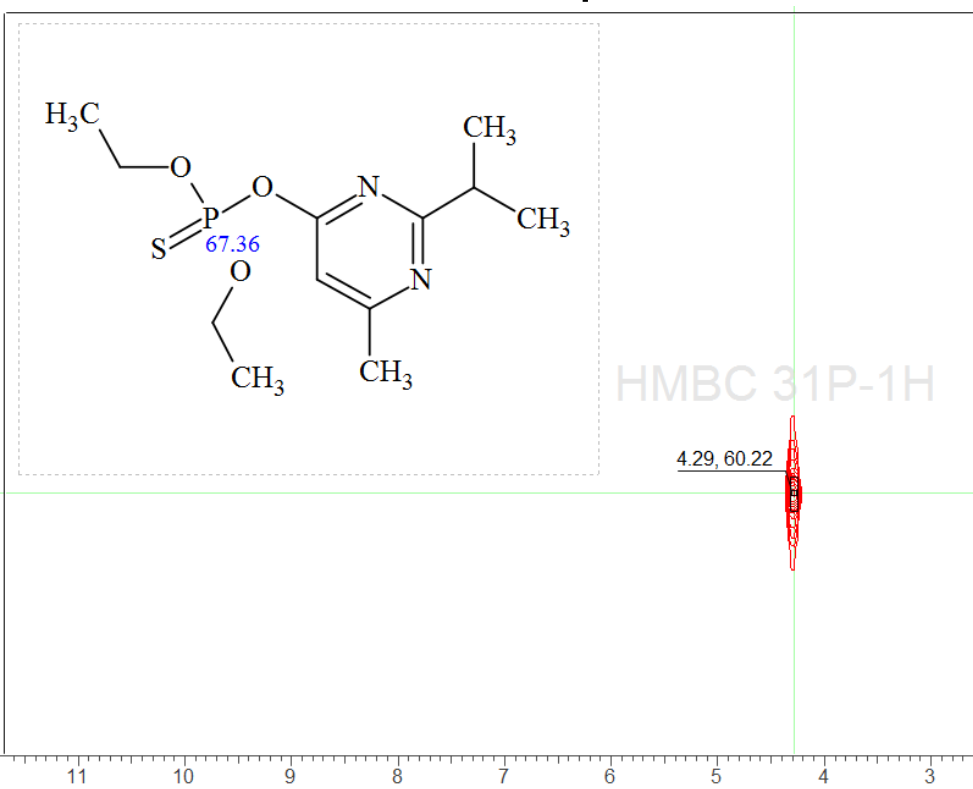
Accurately Predict Novel Compounds



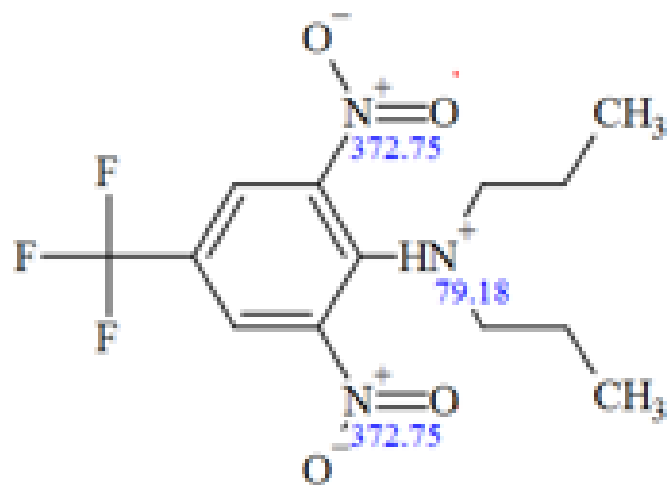
J. Nat. Prod., 2010, v. 73, 10, 1601–1605

^{15}N , ^{19}F , ^{31}P NMR Prediction

- Determine spectral widths based on expected chemical shifts



Optimize Instrument Time with 2D NMR Predictions



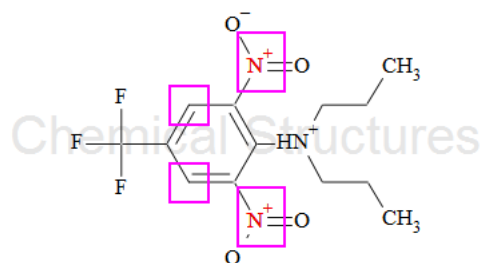
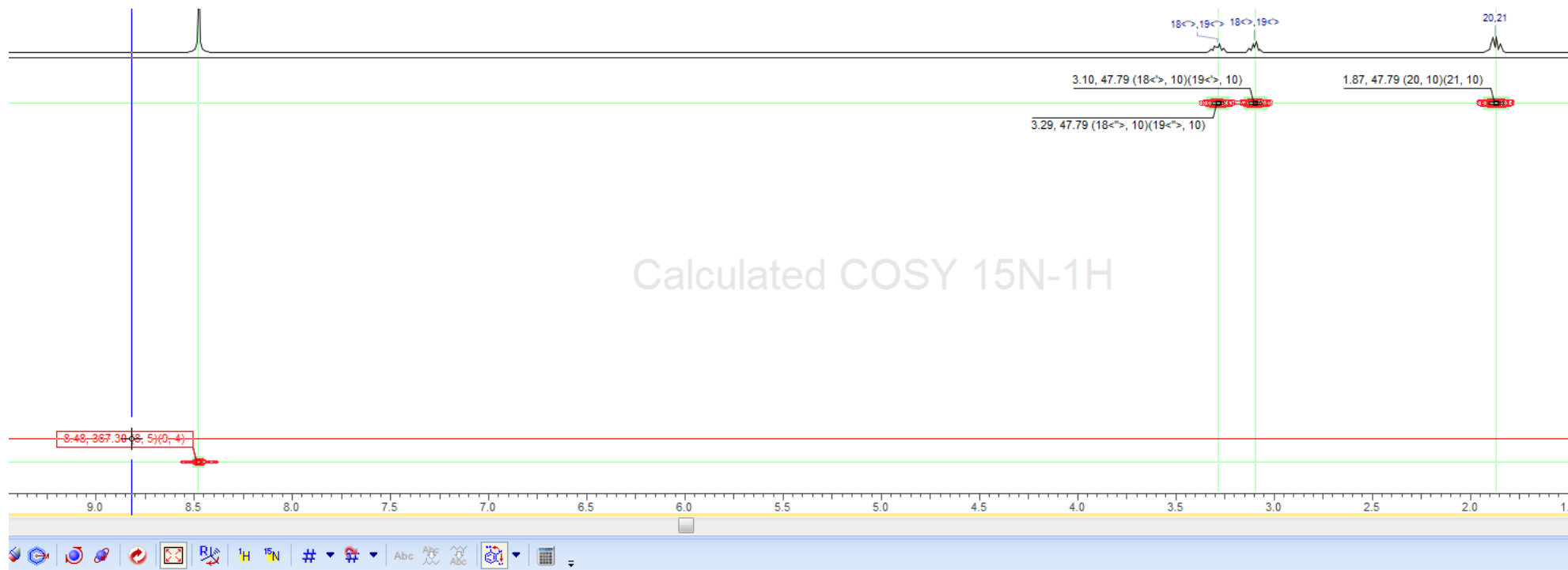
Calculate Spectrum X

Correlation
H,H COSY

Experiment
H,H COSY, 2J-3J

Comment:

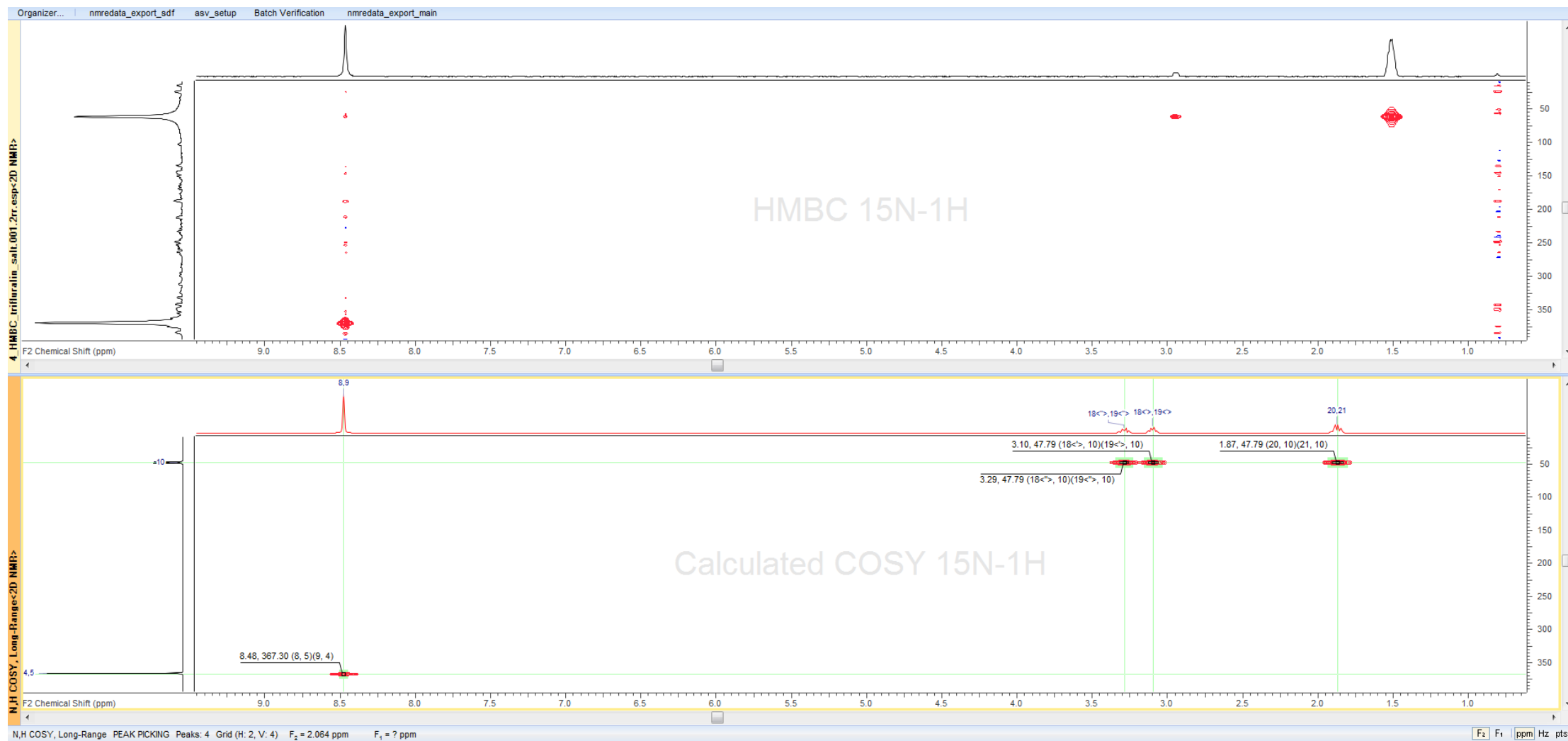
Optimize Instrument Time with 2D NMR Predictions



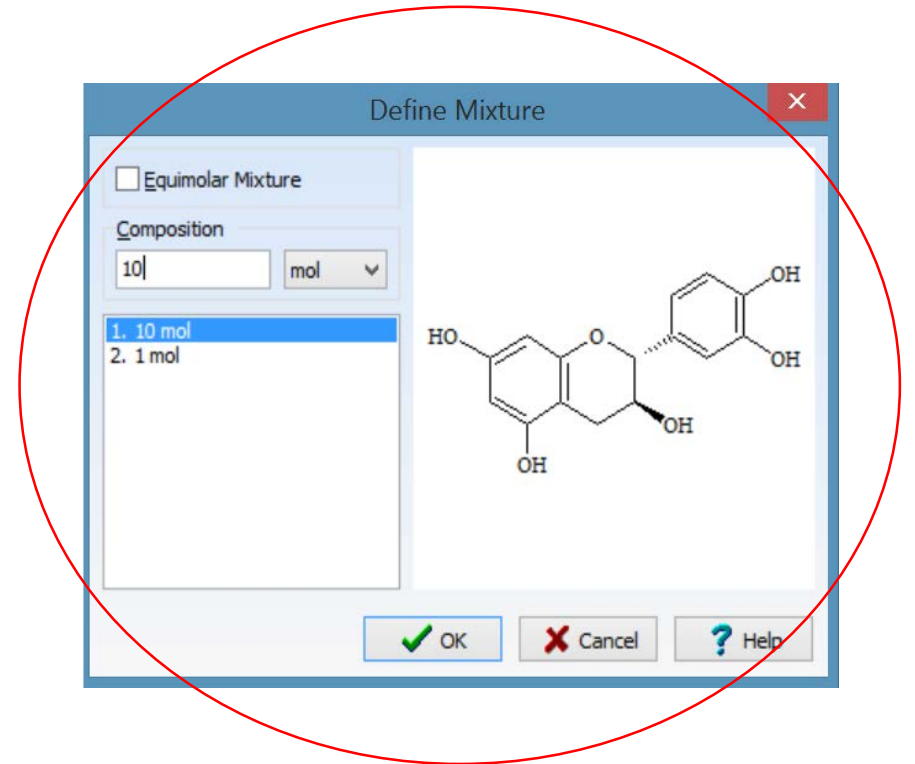
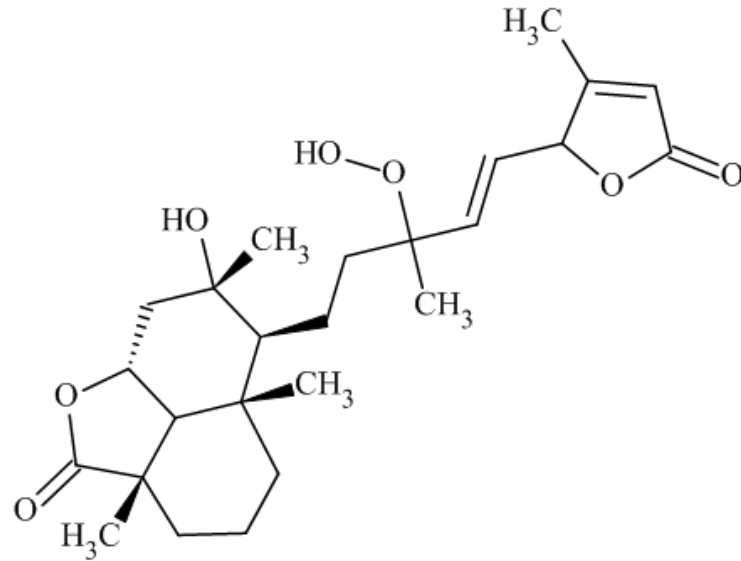
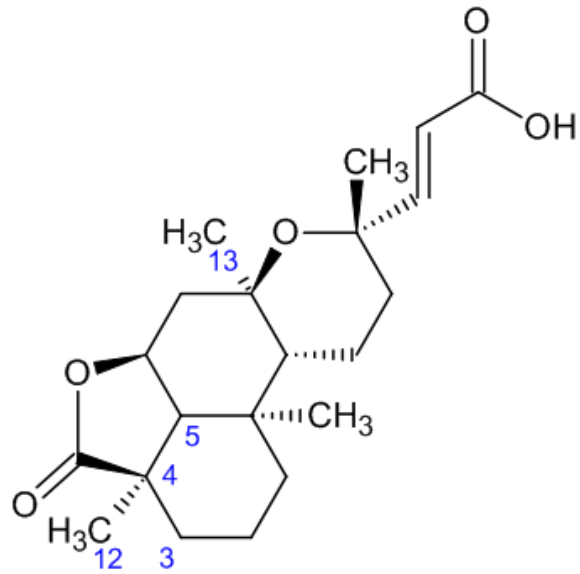
+) C(5),CH(2),CH2(4),CH3(2) ▾

aks: 4 Grid (H: 2, V: 4) $F_2 = 8.818$ ppm $F_1 = 346.724$ ppm

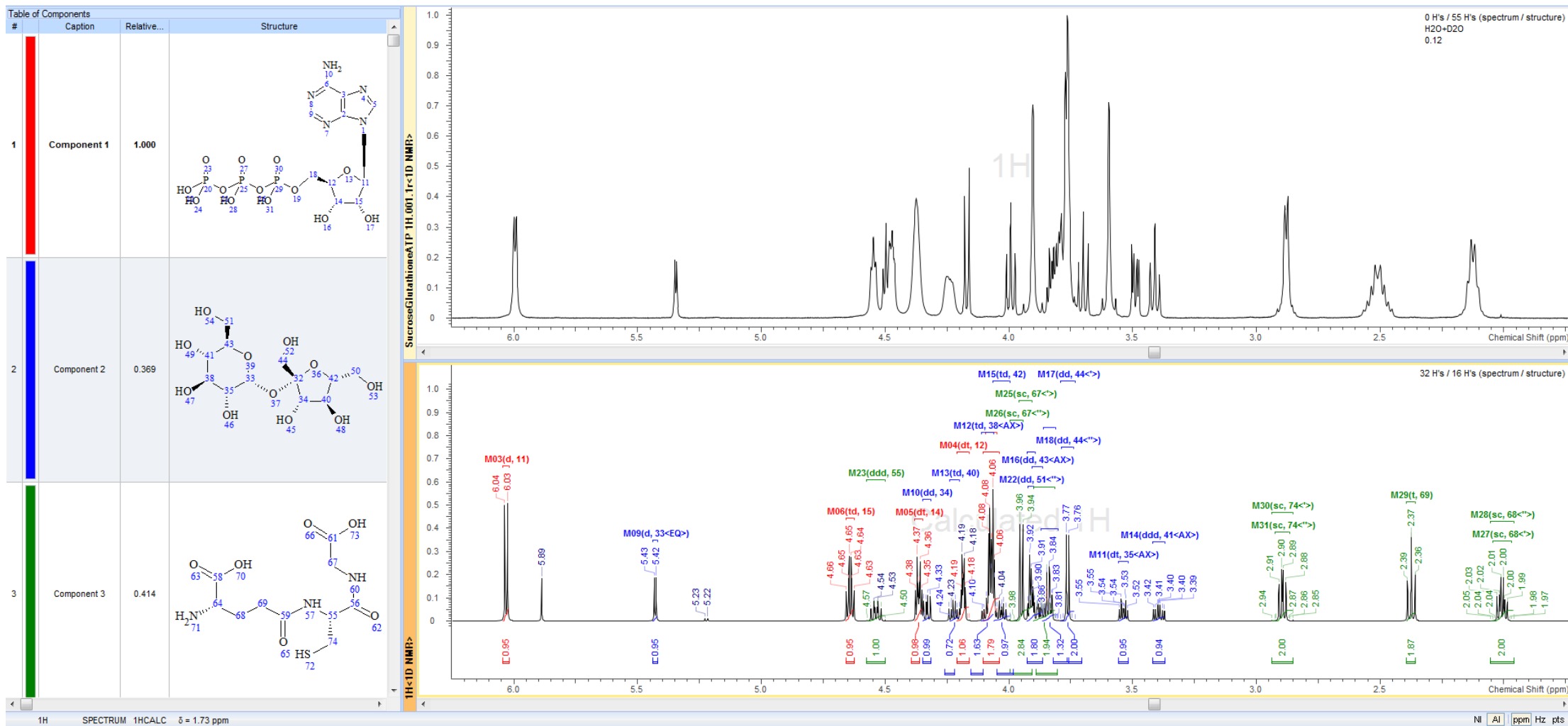
Optimize Instrument Time with 2D NMR Predictions



Predicting NMR for Mixtures



Predicting Spectra of Mixtures



Pure Shift ^1H Prediction Capabilities

HNMR

HNMR Pure Shift

CNMR

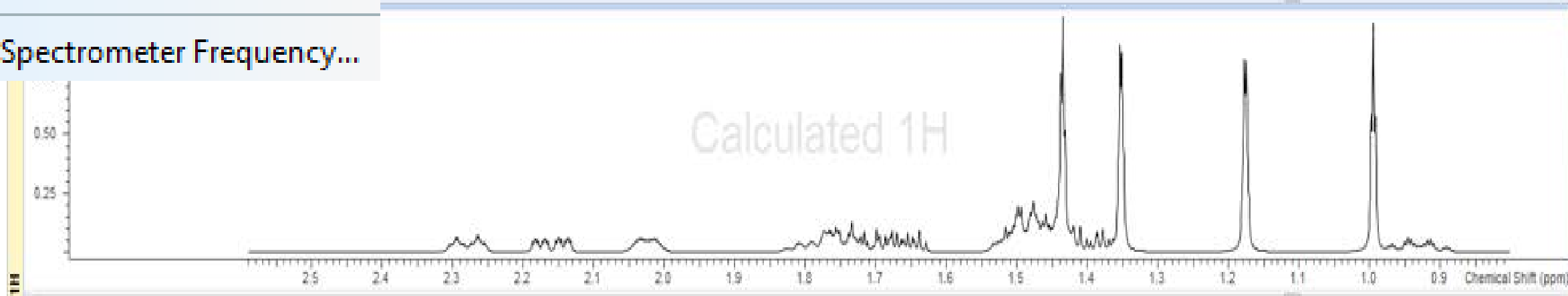
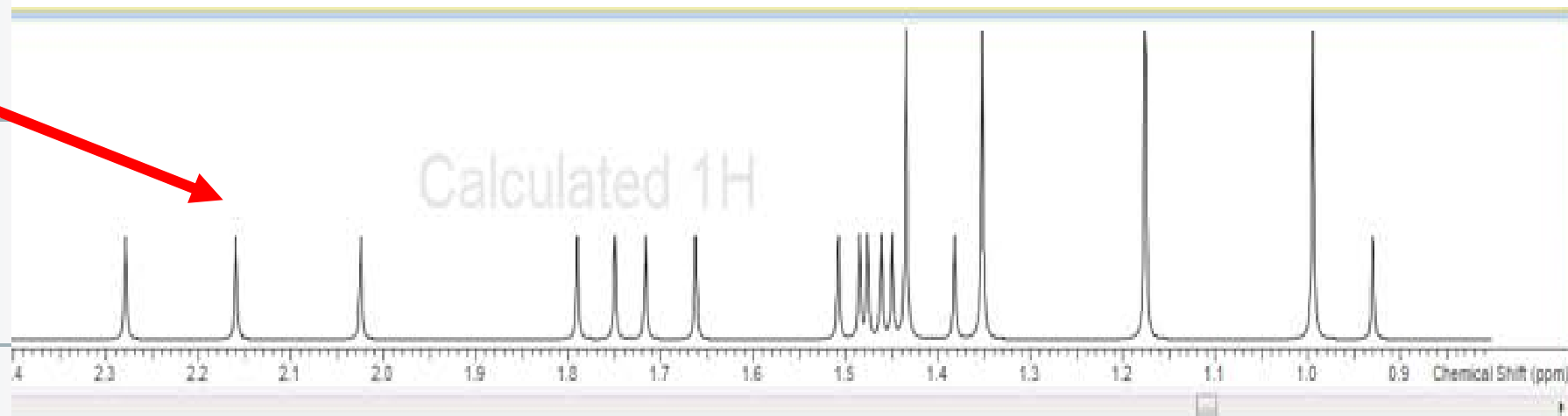
COSY

HSQC

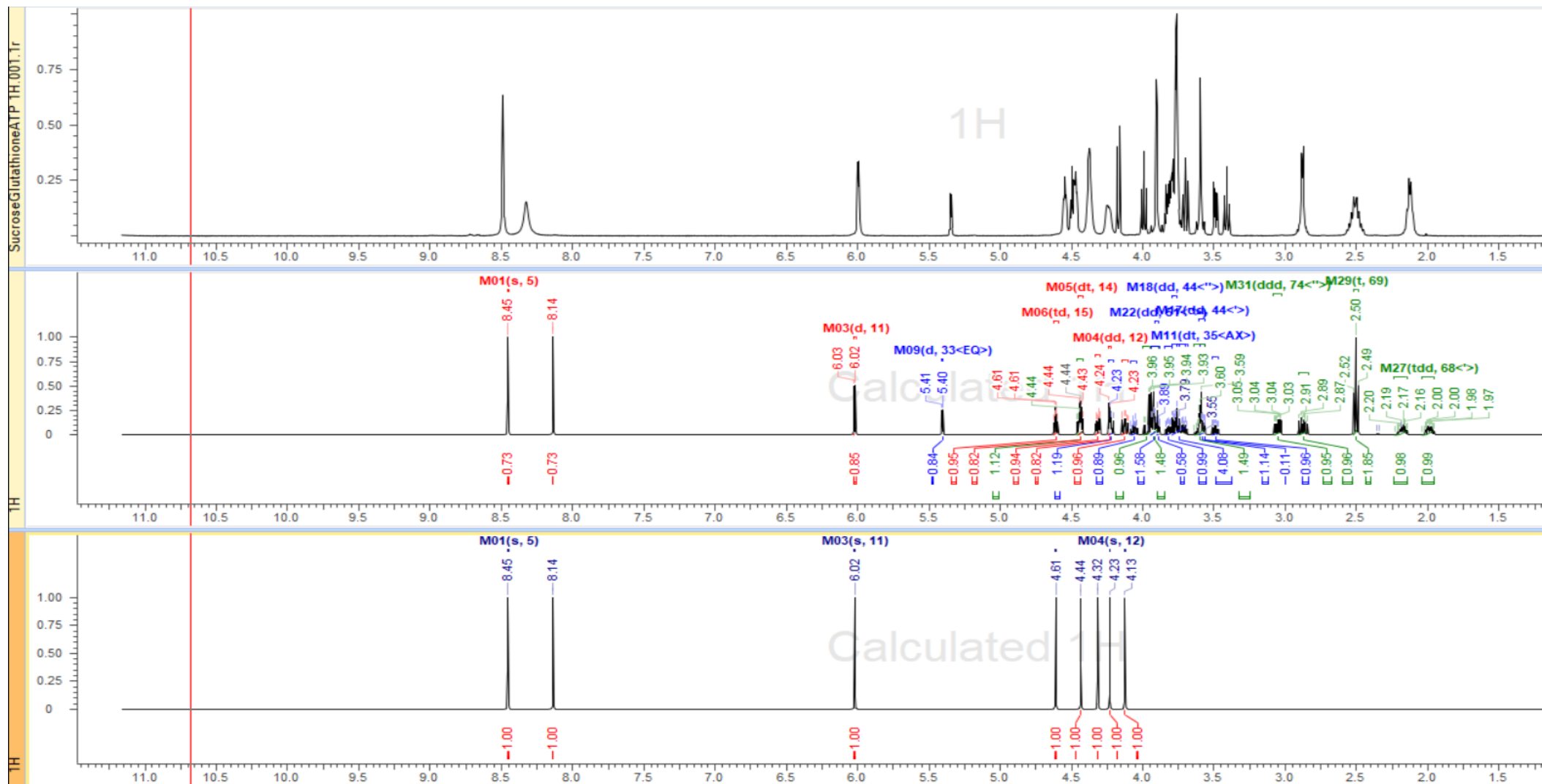
HMBC

More 2D NMR Spectra...

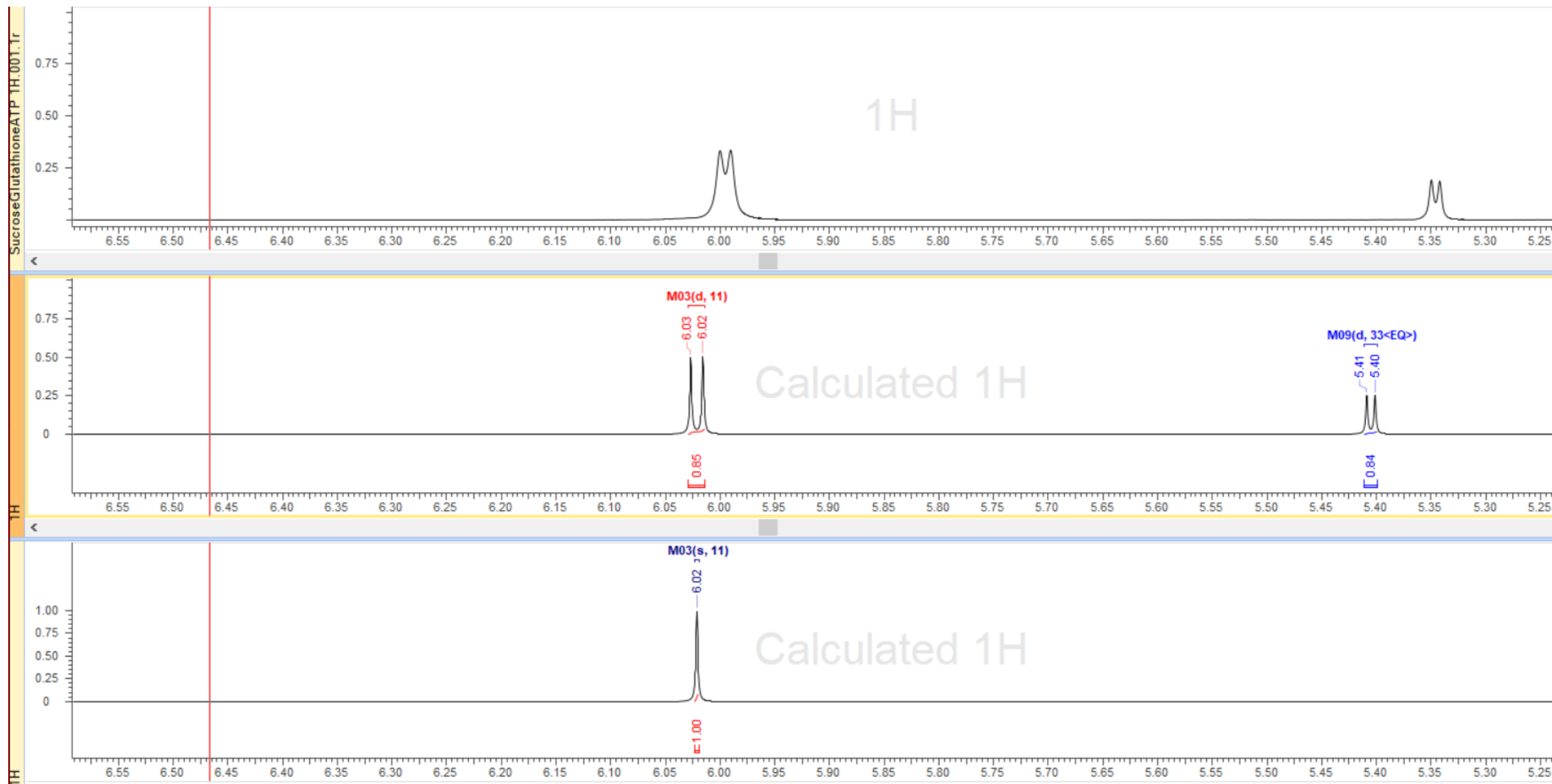
NMR Spectrometer Frequency...



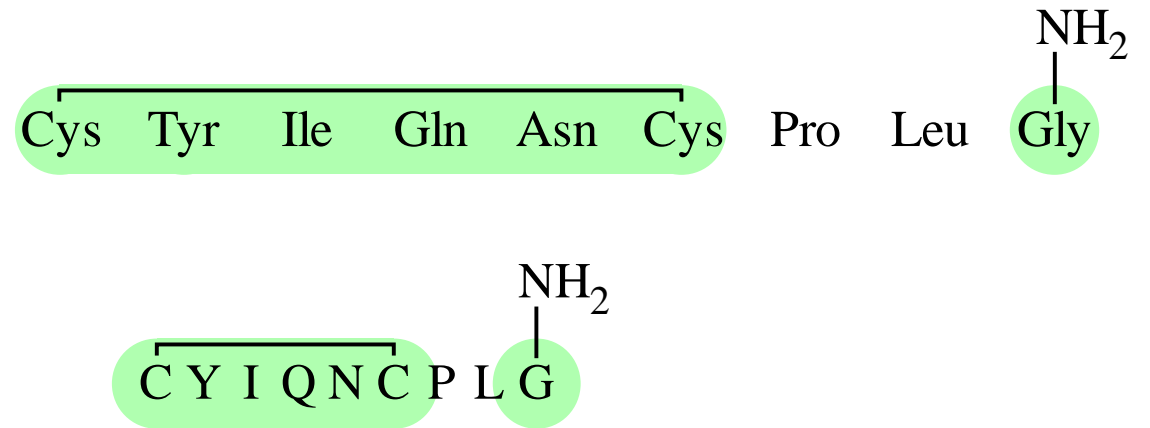
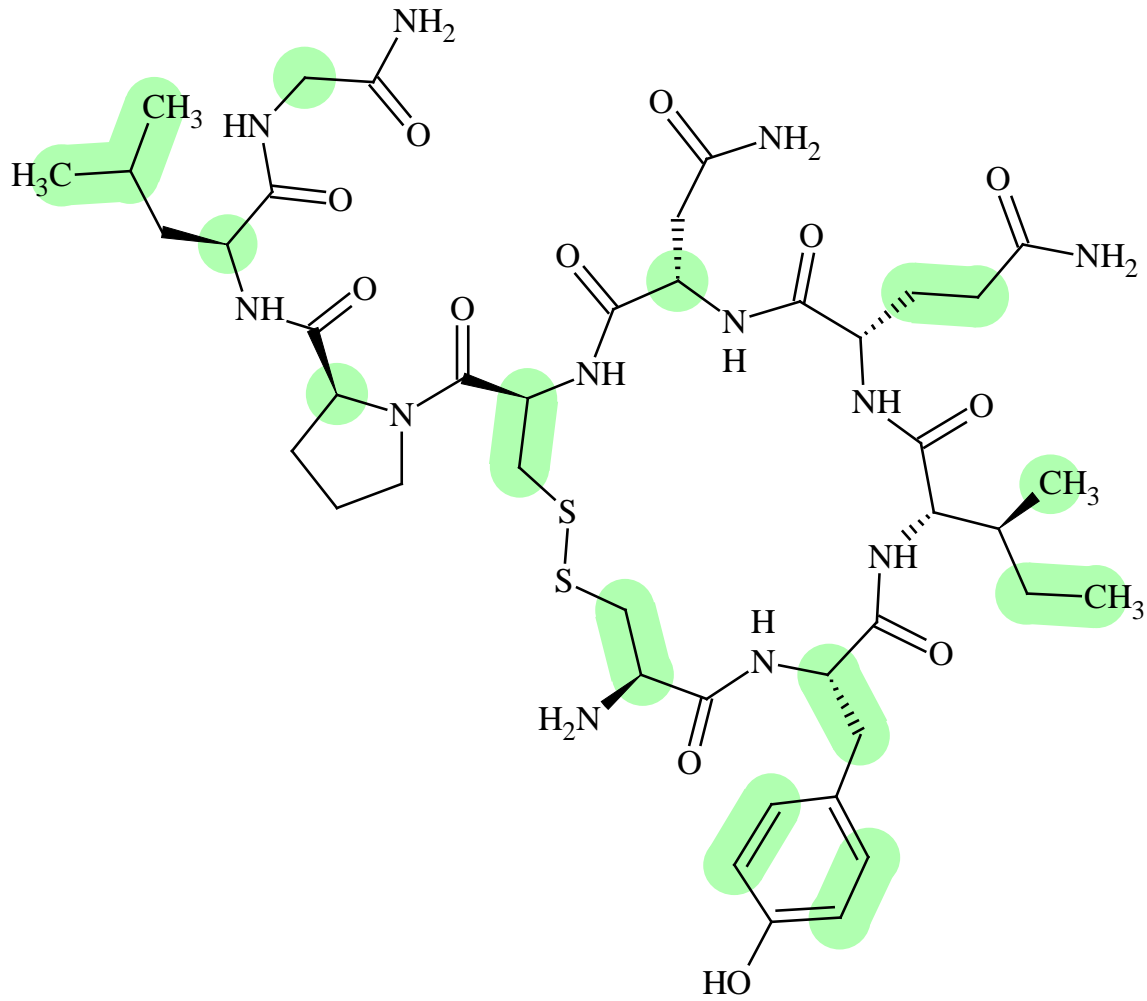
Pure Component Spectrum Simulation from any Mixture Spectrum



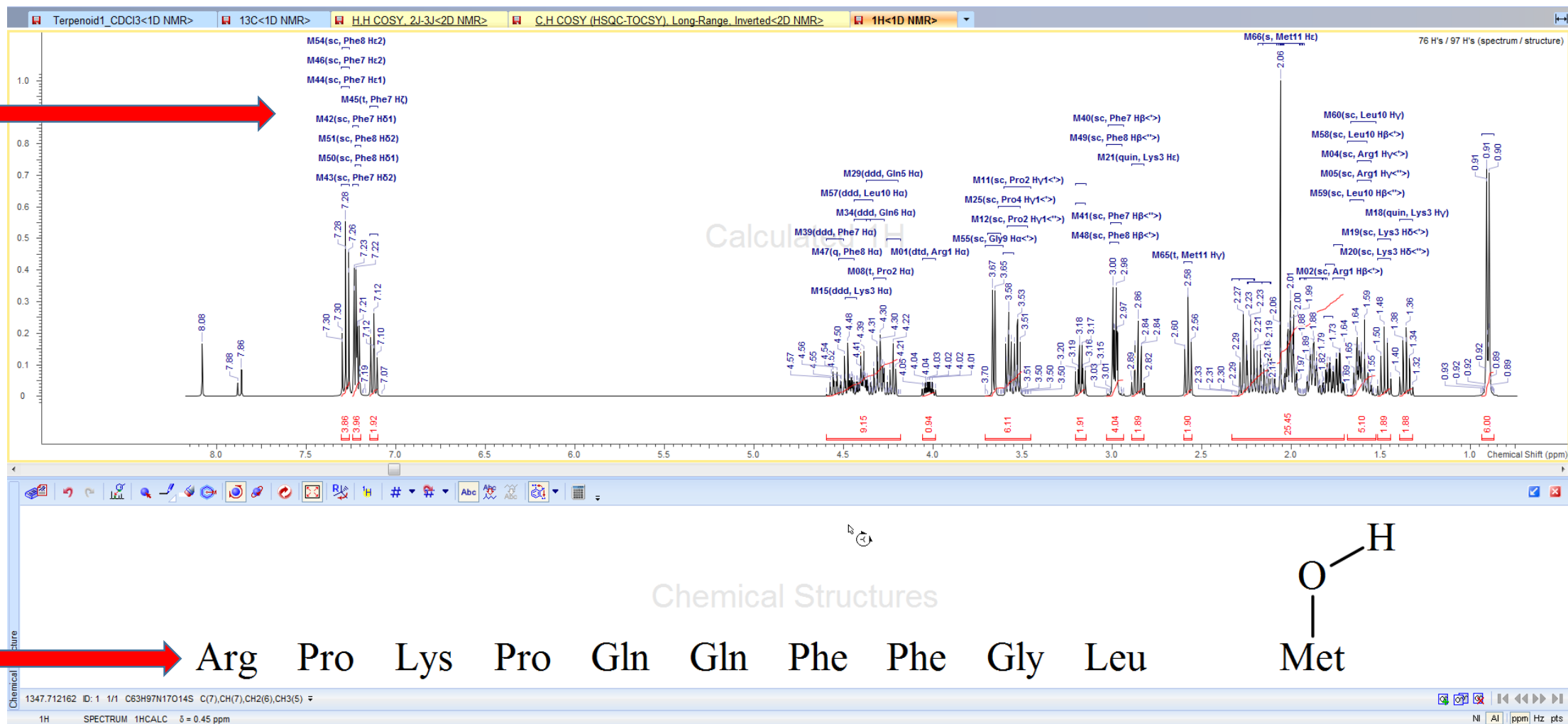
Pure Component Spectrum Simulation from any Mixture Spectrum



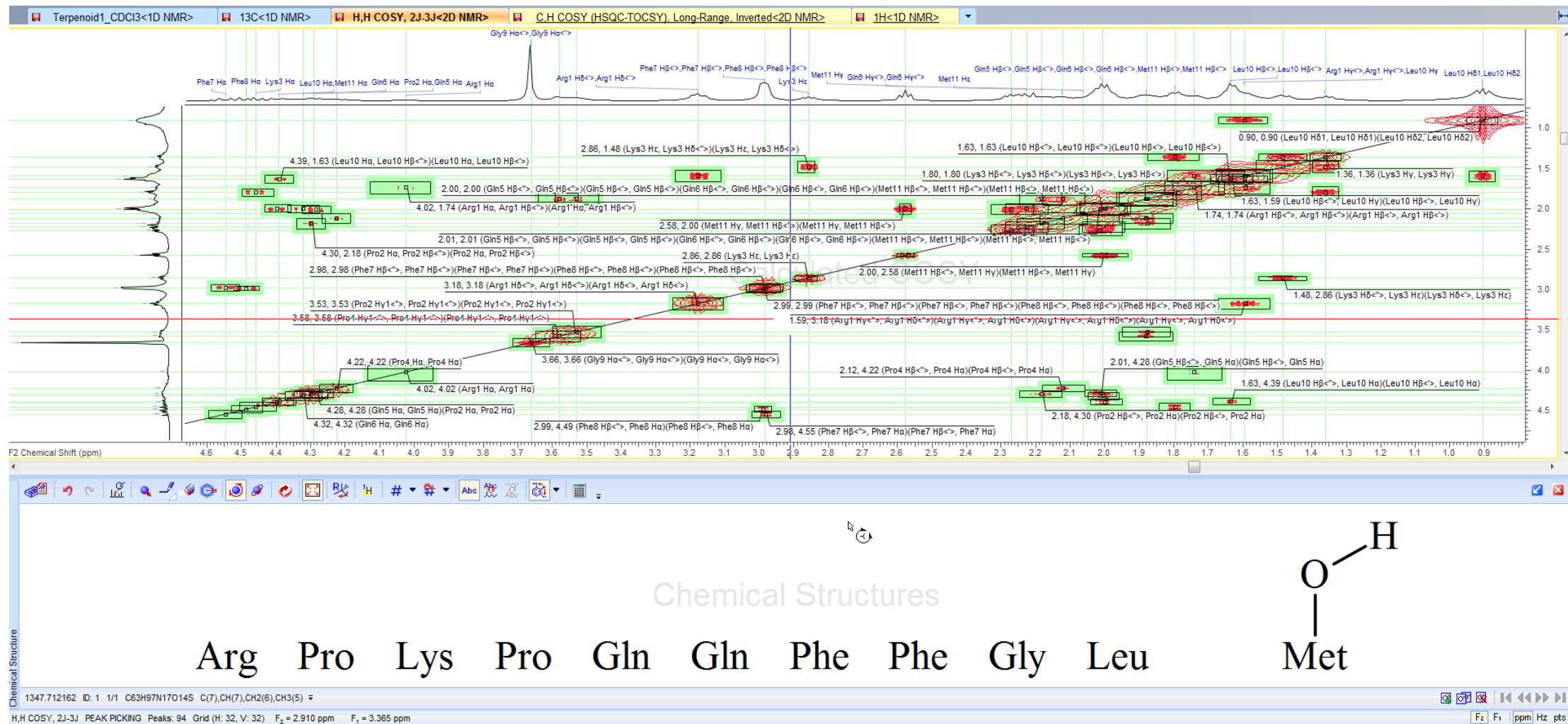
Easily Predict NMR Spectra for Peptides



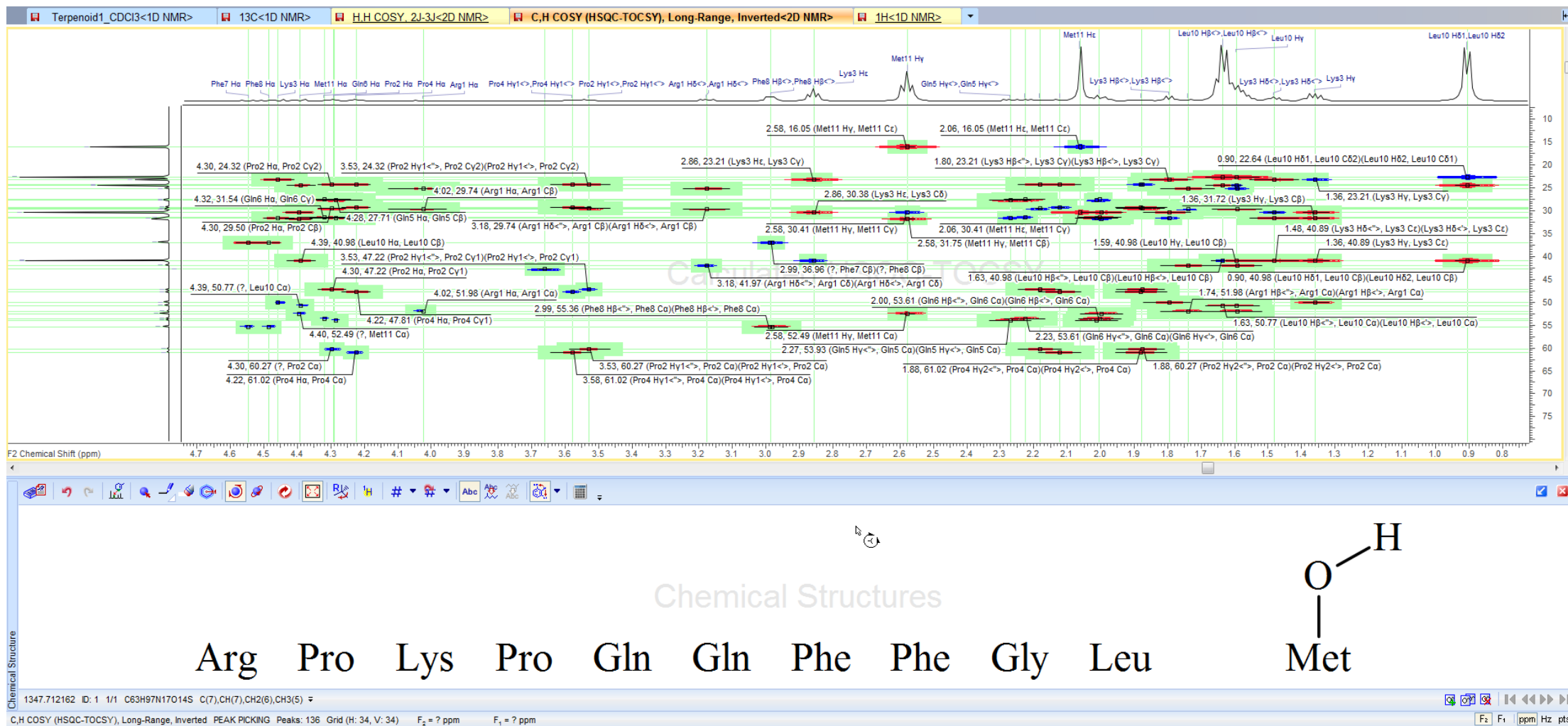
Predicting ^1H spectrum of Substance-P



Predicting the ^1H - ^1H COSY spectrum of Substance-P



Predicting the ^1H - $\{^{13}\text{C}\}$ HSQC-TOCSY spectrum of Substance P



Concluding Remarks

- Today we discussed the following ways of applying NMR predictions:
 - Using 1D Predictors (^1H , ^{13}C , ^{15}N , ^{19}F , and ^{31}P), and 2D Predictors (^1H , ^{13}C , and ^{15}N) to facilitate structure verification and increase confidence in results
 - Training the NMR Predictors to increase confidence and accurately predict for novel compounds
 - Using 2D NMR predictions for complex mixture analysis and for planning experiments
 - Streamlining the NMR analysis for peptides and complex ^1H NMR spectra

Questions?

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