Benchtop NMR: What can it do for *you* ?

Sanel Suljić
sanel@magritek.com

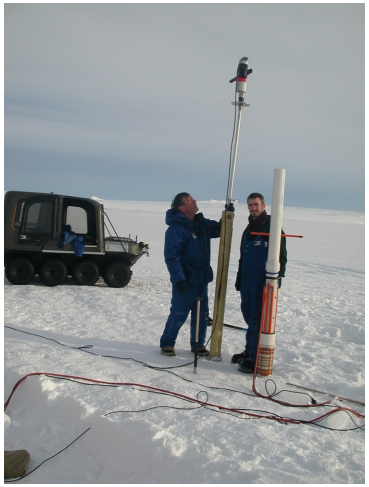
Spinsolve
The fastest compact NMR spectrometer

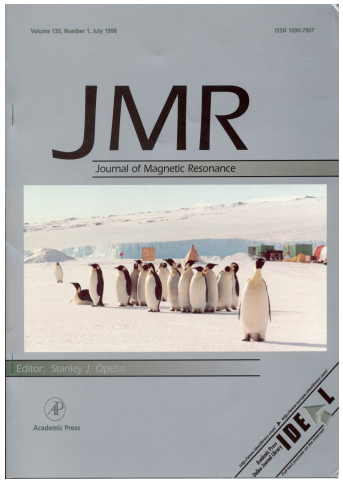
The history of Magritek

Magritek was founded in 2004 to **develop mobile and benchtop NMR and MRI instruments** to enable new applications in Industry, Research and Education.

The original IP was developed during two decades of research by teams at RWTH Aachen in Germany and Massey and Victoria Universities in New Zealand

Prof Bernhard Blümich, Ampere Prize Mobile NMR, Germany





Prof Paul Callaghan, Günther Laukien Prize, NMR in Antarctica, New Zealand

The history of Magritek

2004 Founding of Magritek Ltd

2006 Founding of act GmbH

2010 Move to MTZ, Aachen

2012 Merge of Magritek Ltd and act GmbH

2013 Establishment of US office

2014 Move to Rothe Erde, Aachen

2015 Establishment of UK office

2004 Terranova

2006 profile NMR-MOUSE

2010 Rock Core Analyzer

2011 Tomograph

2012 Spinsolve 43

2014 Spinsolve Carbon

2016 Spinsolve 60

2017 Spinsolve Ultra

2017 Spinsolve 80

Spinsolve family

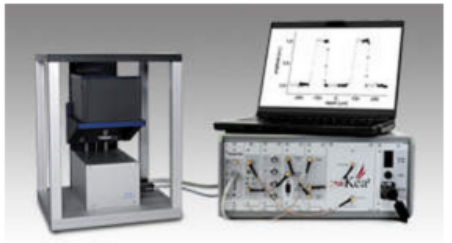
Magritek today

Magritek today has manufacturing and research facilities in Germany and New Zealand, sales and support offices in the USA and UK, and a network of distributors and agents around the world

NMR Spectroscopy

MRI

TD-NMR
T1, T2, Diffusion

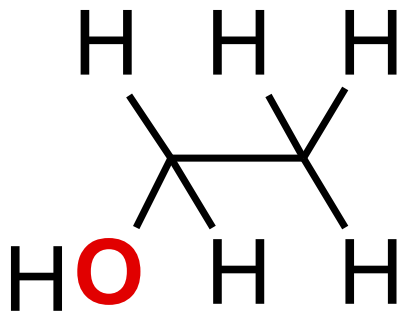


Magritek's facility in Aachen

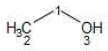
In the Aachen facility

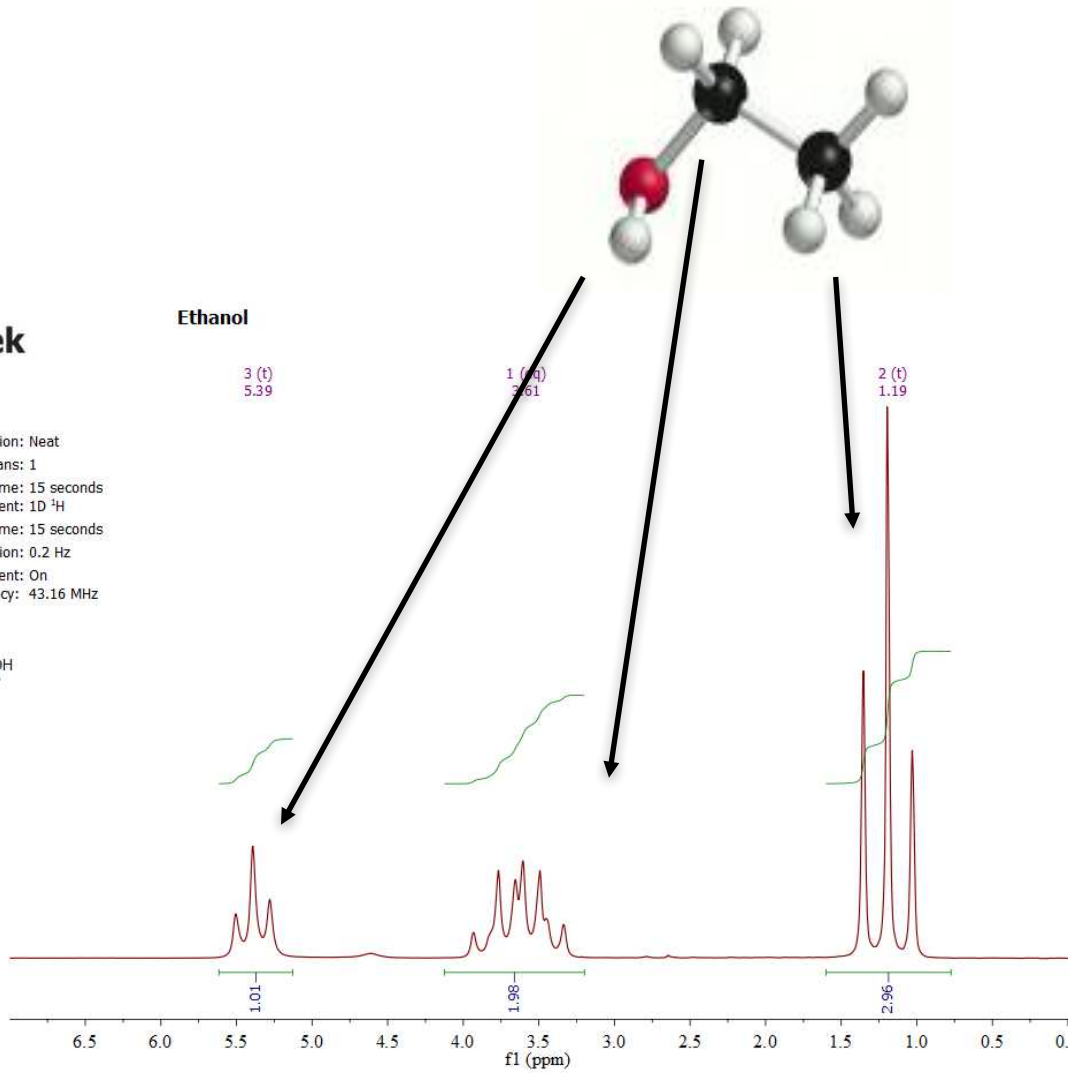
- Production
- R&D
- Application / Application Lab
- ***Sample Analysis***
- Customer Demonstrations
- Marketing
- Administration and Controlling

1D ^{1}H NMR spectrum of ethanol

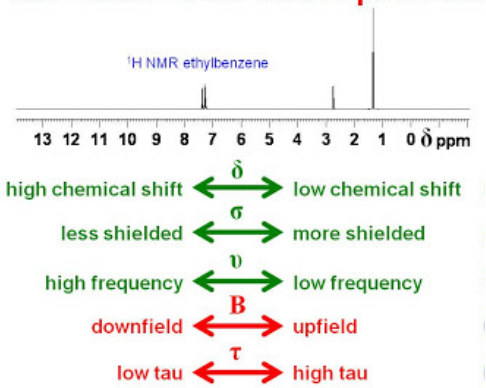


Concentration: Neat
Number of scans: 1
Repetition time: 15 seconds
Experiment: 1D ^{1}H
Total acquisition time: 15 seconds
Apodization: 0.2 Hz
Resolution enhancement: On
Spectrometer frequency: 43.16 MHz





The Scale of an NMR Spectrum



This ethanol sample has very little water in it, which means the hydroxyl proton couples to the CH_2. This results in the OH appearing as a triplet and the CH_2 appears as a doublet of quartets.

Benefits of NMR

- NMR is a powerful, information rich analytical technique, that can **elucidate molecular structures**
- Essential for organic or synthetic chemists

  "Have I made what I thought I made?"
- Quantifiable

  "How much or how pure is my product?"
- Non-destructive

Why Benchtop NMR Spectroscopy ?

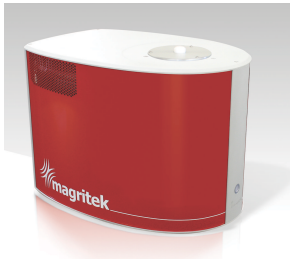
High-field NMR systems

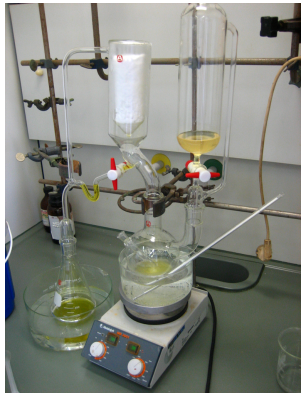
- **Expensive** (capital, cryogen fills, operation, requires special facilities)
- **Complicated** (limited to experts)
- **Fragile** (environment)

Take the sample to the spectrometer

Benchtop NMR Spectroscopy technology

- **Affordable** (cryogen-free, no special requirements, minimum running costs)
- **Easy to use** (more people can access the technology)
- **Robust** (operates in wide range of environments)





Take the spectrometer to the sample

Spinsolve Benchtop NMR

Spinsolve™ 43 Spinsolve™ 60 Spinsolve™ 80 NEW

43, 60 and 80 MHz Permanent Magnets
with ^{1}H, ^{19}F
and
^{13}C, ^{31}P, ^{15}N, ^{29}Si, ^{11}B, ^{2}H Capabilities
(one of those / X nuclei)

[1] Each Spinsolve System features patented magnet technology.

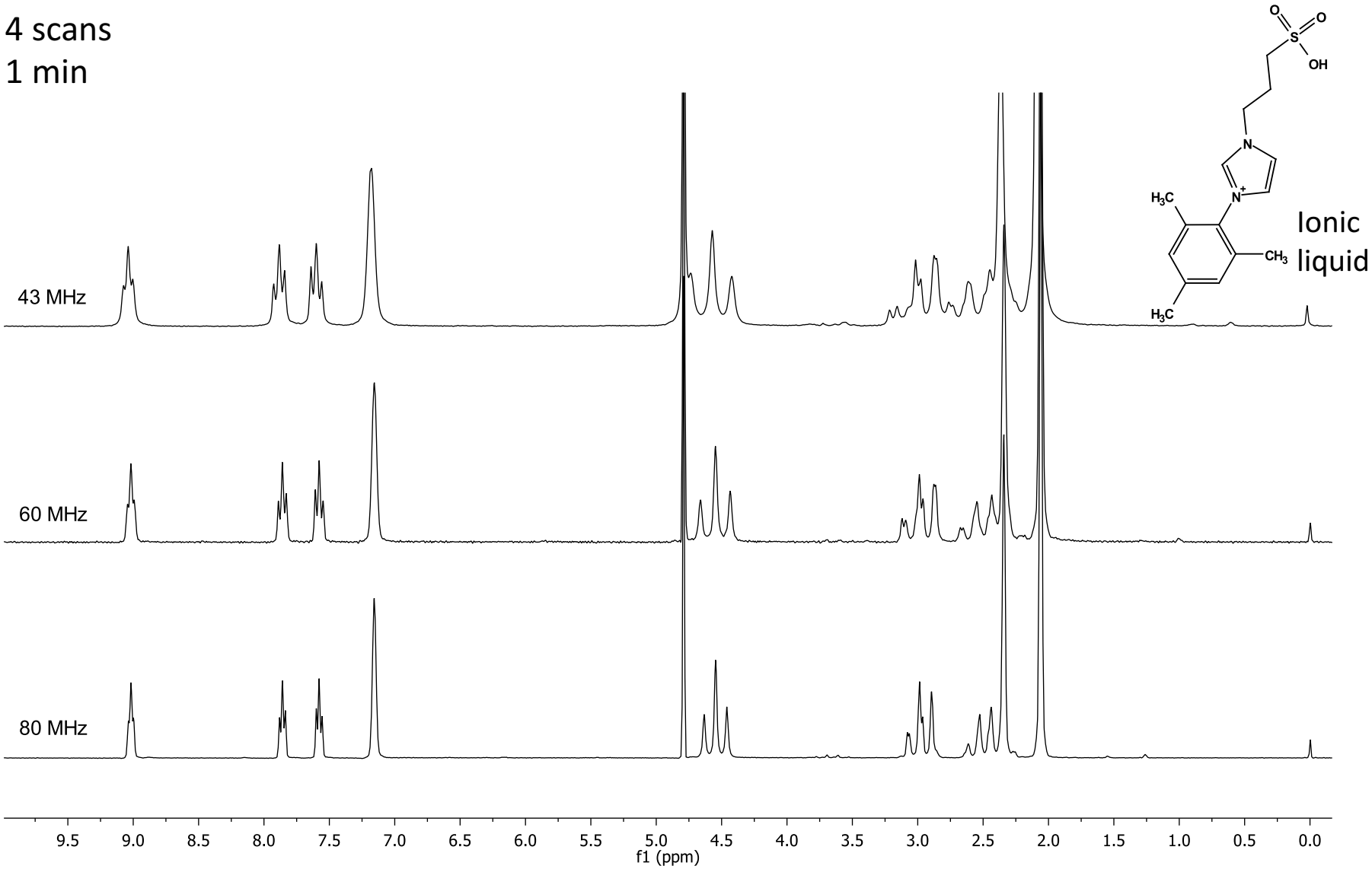
The following patents apply: US20100013473A1, US8148988, EP2144076A1, EP2144076B1

Spinsolve 80 Carbon

- 80 MHz permanent magnet
- No cryogens
- ^{1}H, ^{19}F and ^{13}C
- Built in External Lock
- No spinning, no air required
- Benchtop size and weight
- 5mm NMR tubes
- Easy to use software
- Robust and Low Maintenance

Benefit of higher frequency – 1D ^{1}H

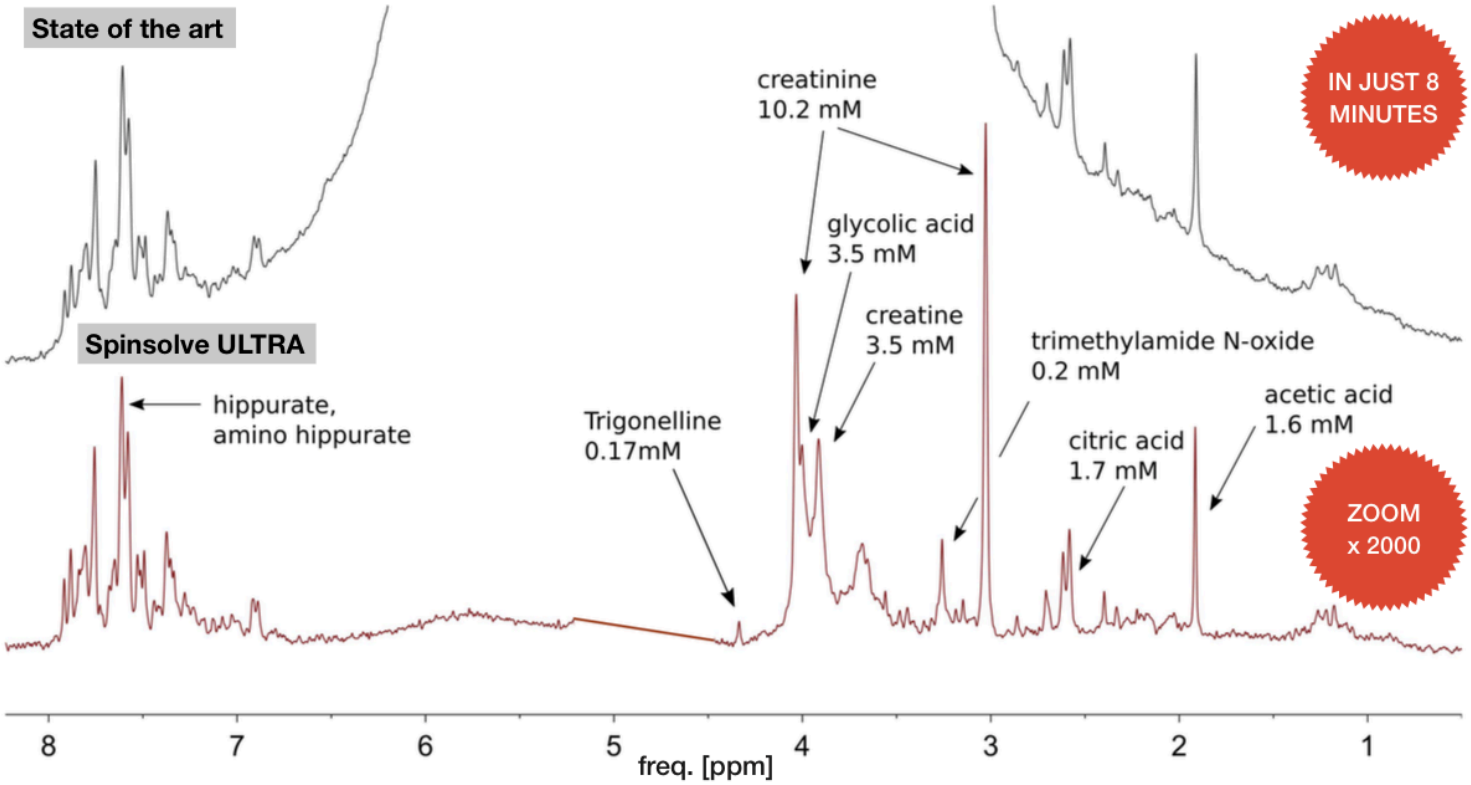
4 scans
1 min



Spinsolve ULTRA (43 / 60 MHz)

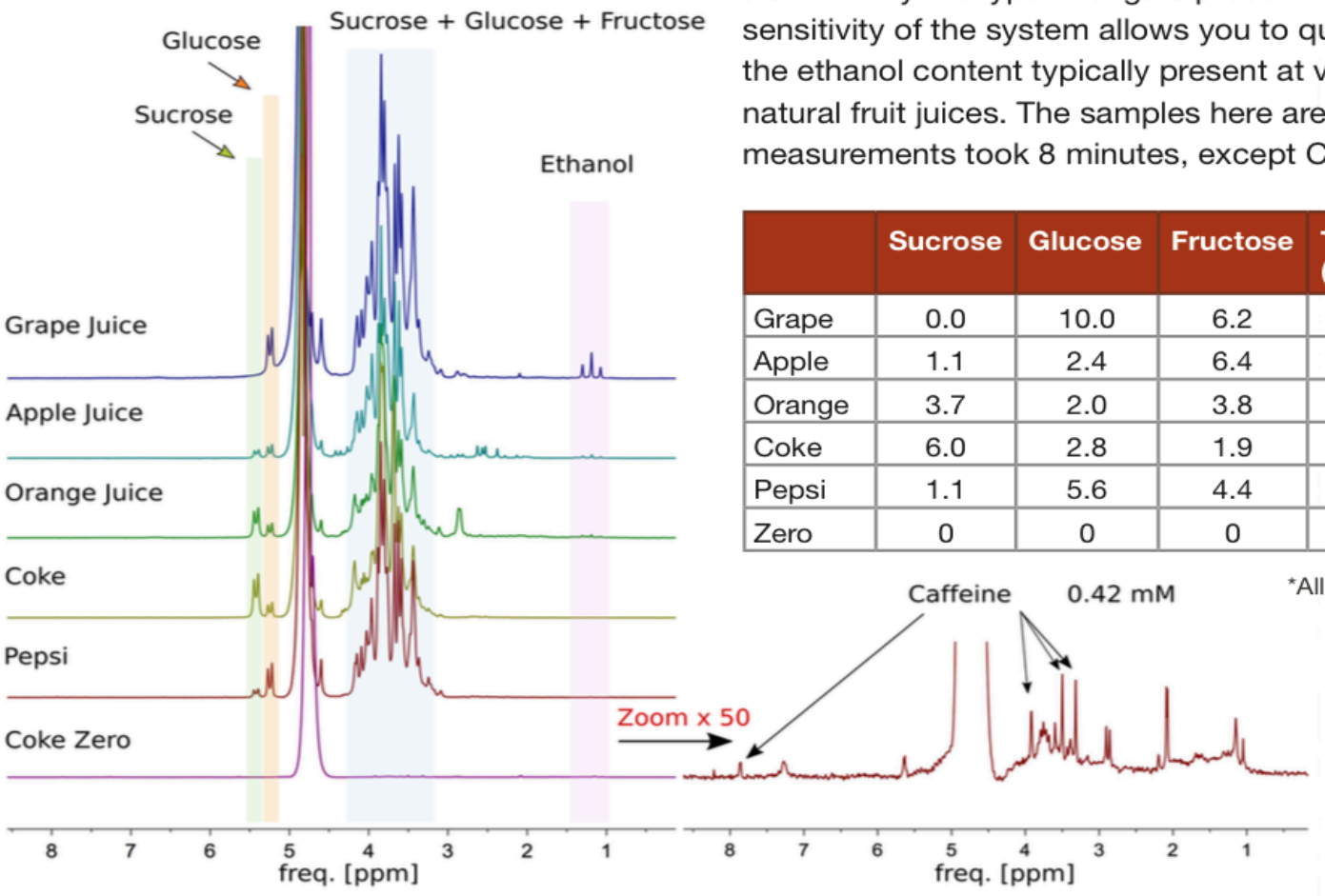
Ultra-high field homogeneity combined with solvent suppression allows you to resolve compounds dissolved at sub-millimolar concentrations in protonated solvents, such as water.

Resolving metabolites in urine at milli-molar concentrations



ULTRA Applications

Measuring sugar content in soft drinks



Spinsolve ULTRA measures not only the sugar content but can also identify the type of sugars present in the sample. The high sensitivity of the system allows you to quantify with high accuracy the ethanol content typically present at very low concentrations in natural fruit juices. The samples here are all neat. All measurements took 8 minutes, except Coke Zero was 1 hour.

	Sucrose	Glucose	Fructose	Total (NMR)	Total (Label)	Ethanol
Grape	0.0	10.0	6.2	16.2	16.0	0.16
Apple	1.1	2.4	6.4	9.8	9.8	0.03
Orange	3.7	2.0	3.8	9.5	9.0	0.02
Coke	6.0	2.8	1.9	10.7	10.7	0
Pepsi	1.1	5.6	4.4	11.2	10.7	0
Zero	0	0	0	0	0	0

*All units g/100ml. Ethanol is % vol.

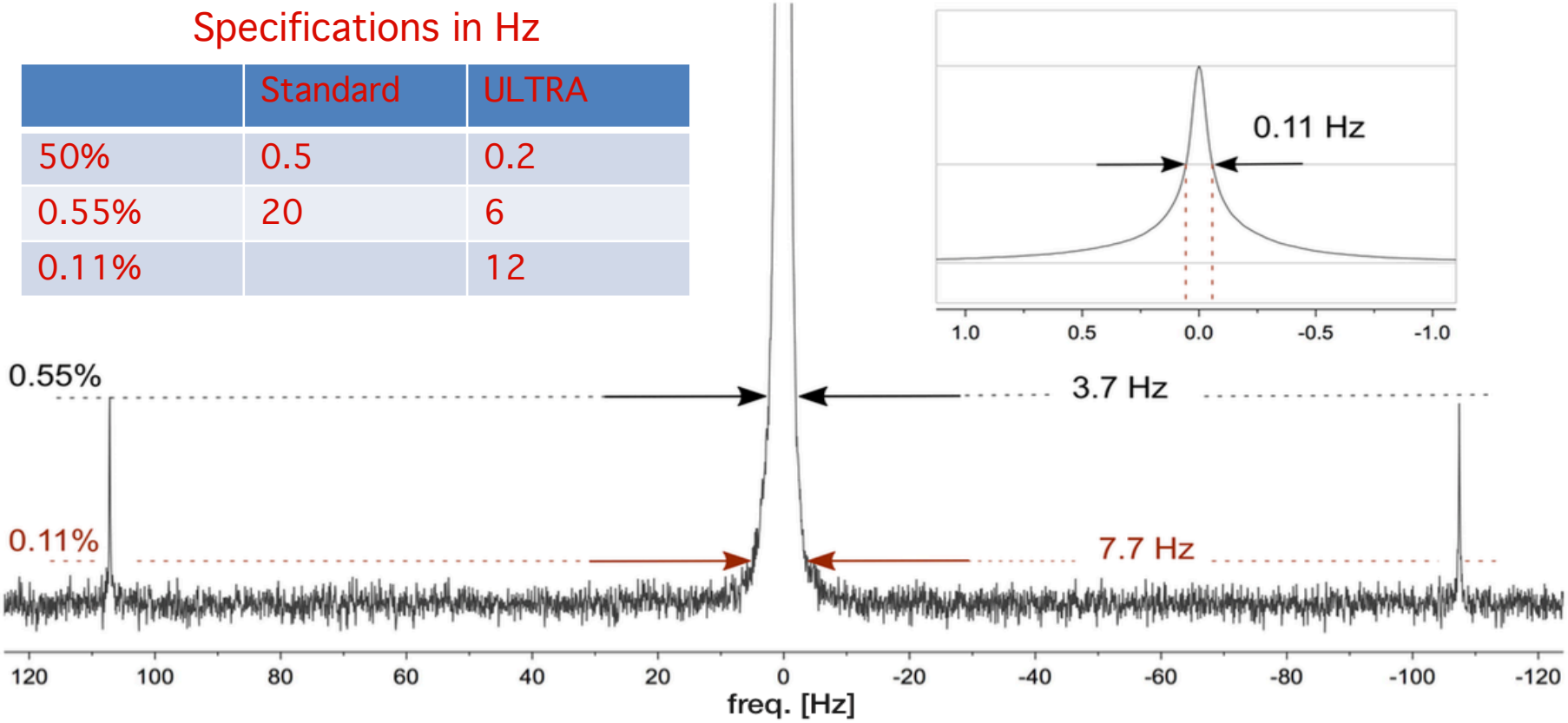
Resolution (Standard and ULTRA) / Line Shape

Linewidth measured in a chloroform spectrum

- No sample spinning, no spinning side bands, no requirement for compressed air
- No reference deconvolution, only standard NMR data processing is used

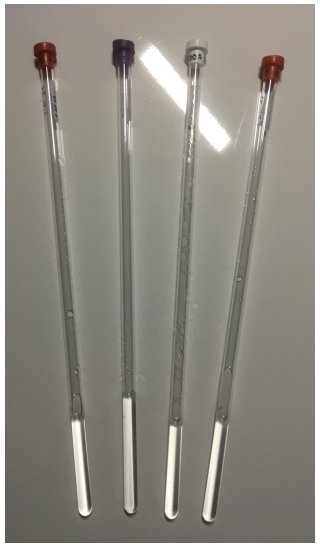
Specifications in Hz

	Standard	ULTRA
50%	0.5	0.2
0.55%	20	6
0.11%		12

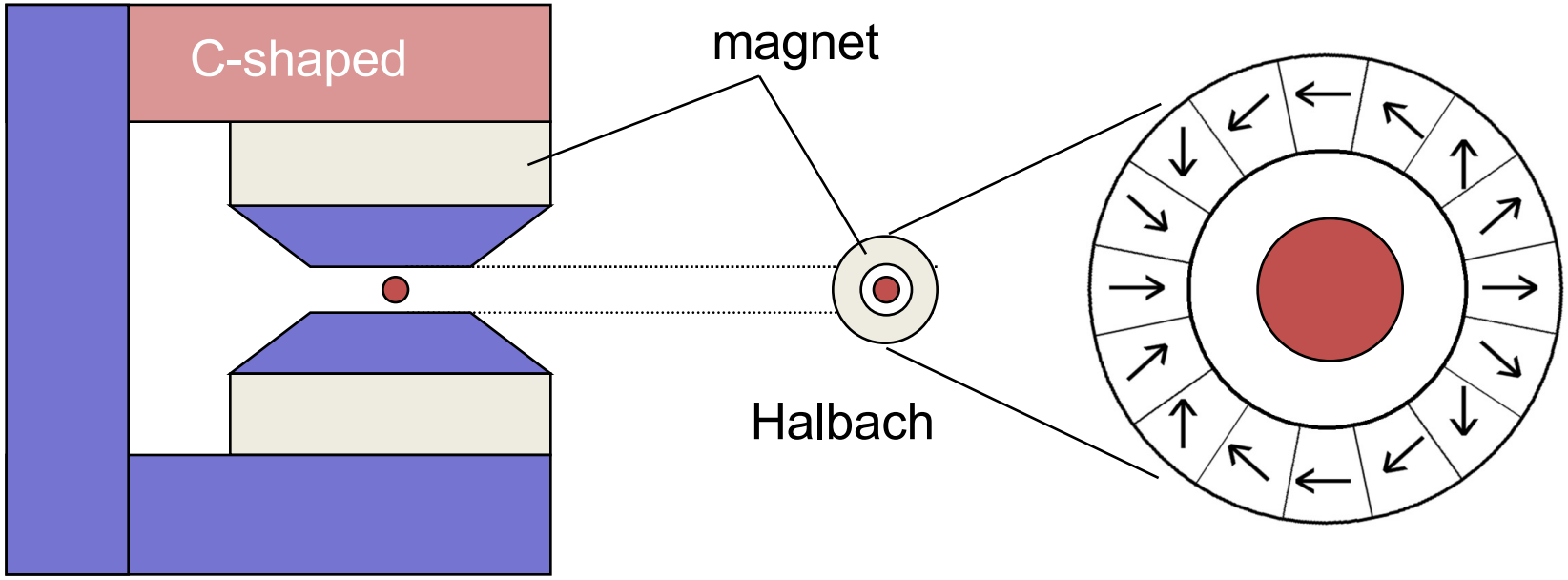


Benefits of the Spinsovle

- Compact, fits on normal lab bench
- No cryogens needed
- Robust and easy to use software
- Fast results
- Standard size economy style 5 mm NMR tubes can be used
- Alternative: Reaction Monitoring Setup
- No sample spinning/compressed gas
- Deuterated solvents are not necessary
- Superior sensitivity, resolution, and stability compared to other benchtop NMR

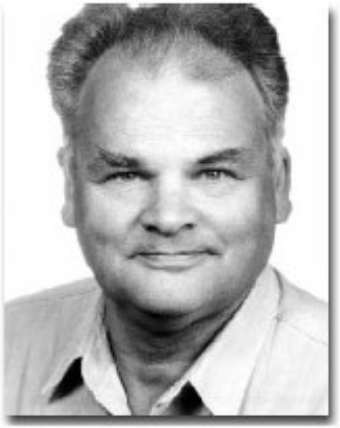


Halbach Magnet vs. C-Shaped Magnet



$$B_0(\vec{r}) = K \ln(r_{out} / r_{in})$$

K. Halbach, Nucl. Instr. Meth. 169 (**1980**)



[1] Each Spinsolve System features patented magnet technology.

The following patents apply: US20100013473A1, US8148988, EP2144076A1, EP2144076B1

Spinsolve 80 Carbon Hardware (73 kg)

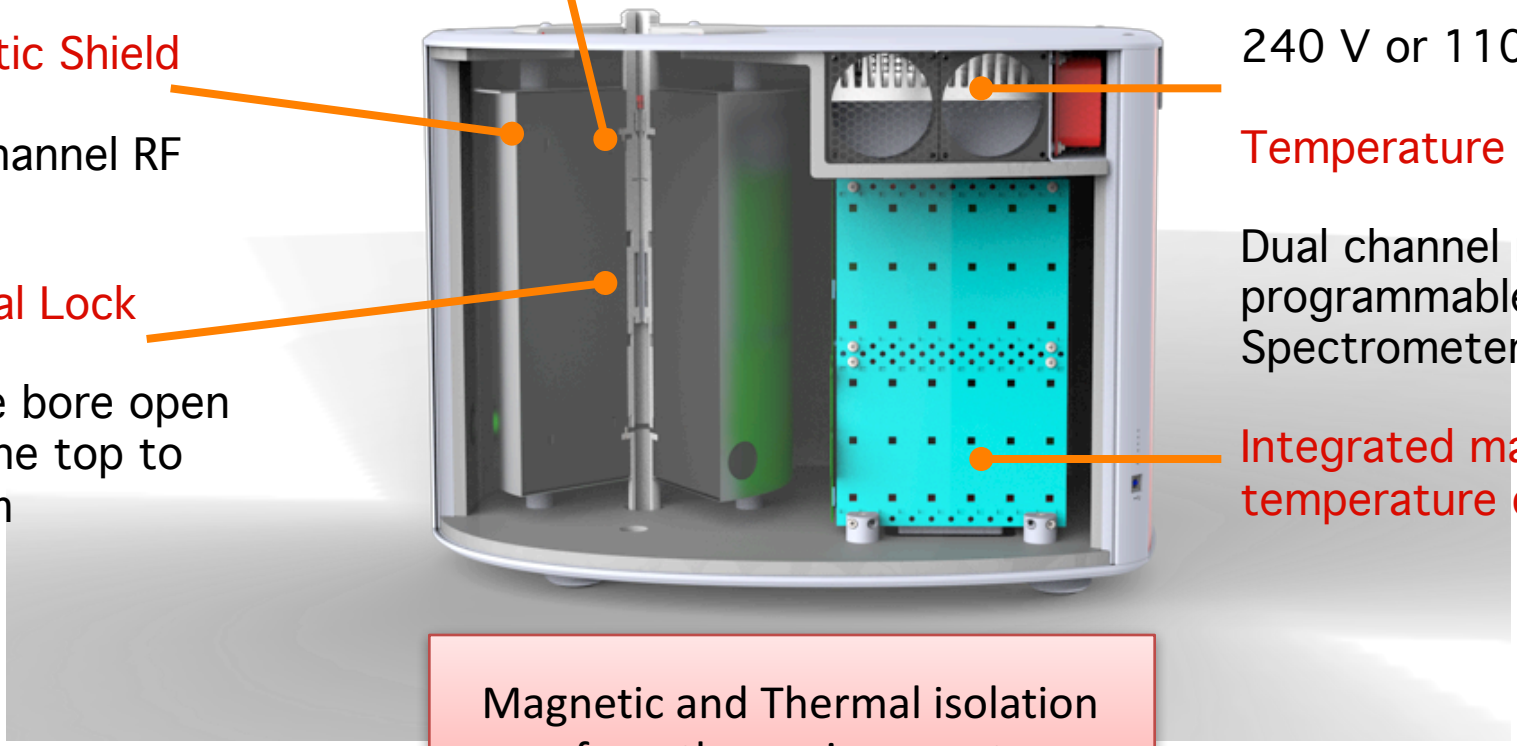
1.9 Tesla high homogeneity
Halbach permanent magnet

Magnetic Shield

Dual channel RF probe

External Lock

Sample bore open from the top to bottom



240 V or 110 V power

Temperature Regulation

Dual channel modern programmable Spectrometer

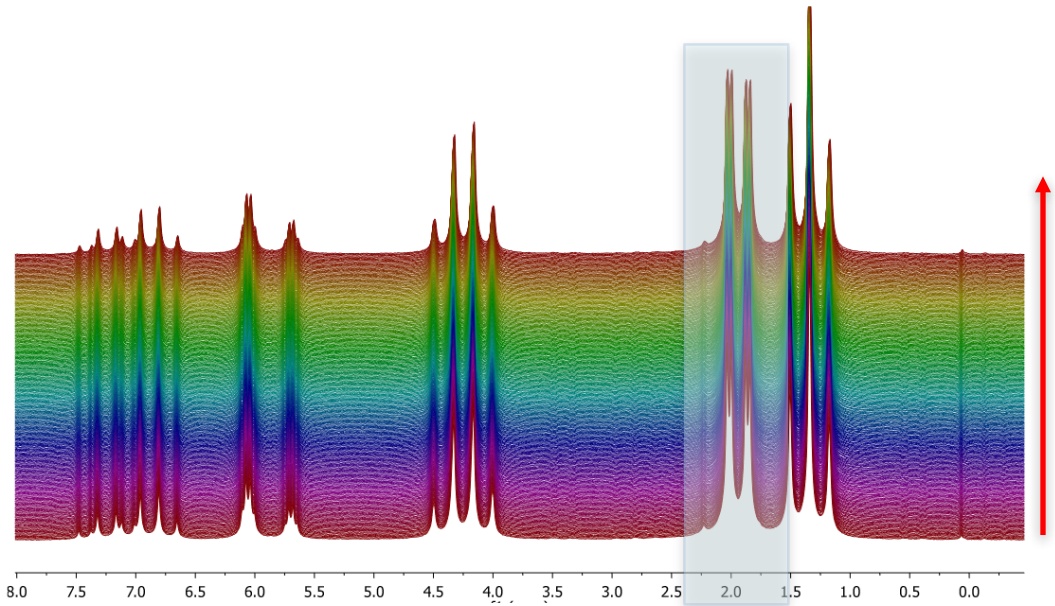
Integrated magnet temperature control

Magnetic and Thermal isolation from the environment

Footprint 58 cm x 43 cm

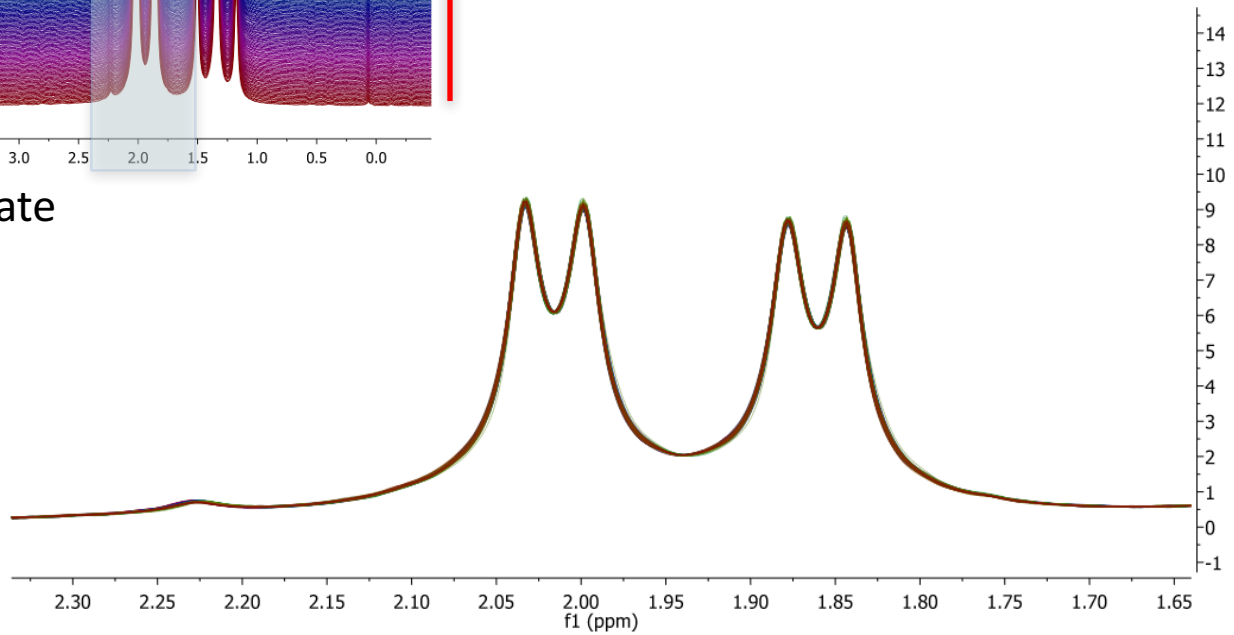
Very similar situation for the 43/60 MHz Spinsolve Systems (55/60 kg)

Spinsolve Stability



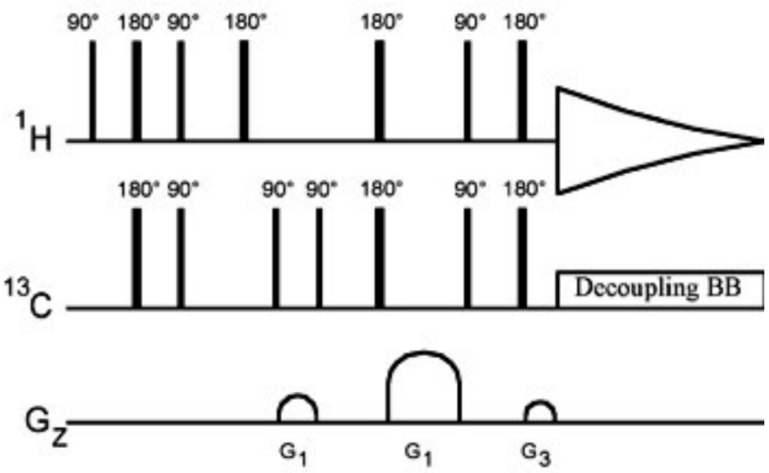
Ethyl Crotonate

- 1 scan every 30 minutes
- 250 scans
- No shimming between scans
- **5 day experiment !!**



5 days of scans superimposed

Modern NMR Pulse Sequences



2D HETCOR
2D HMBC
2D HMQC
2D HSQC
2D HSQC-ME …

Modern NMR Pulse sequences

- Multipulse electronics capability
- 2D NMR sequences
- Inverse detection
- Coherence selection
- Decoupling

- Artifacts : T_1 noise, phase, …

Stability

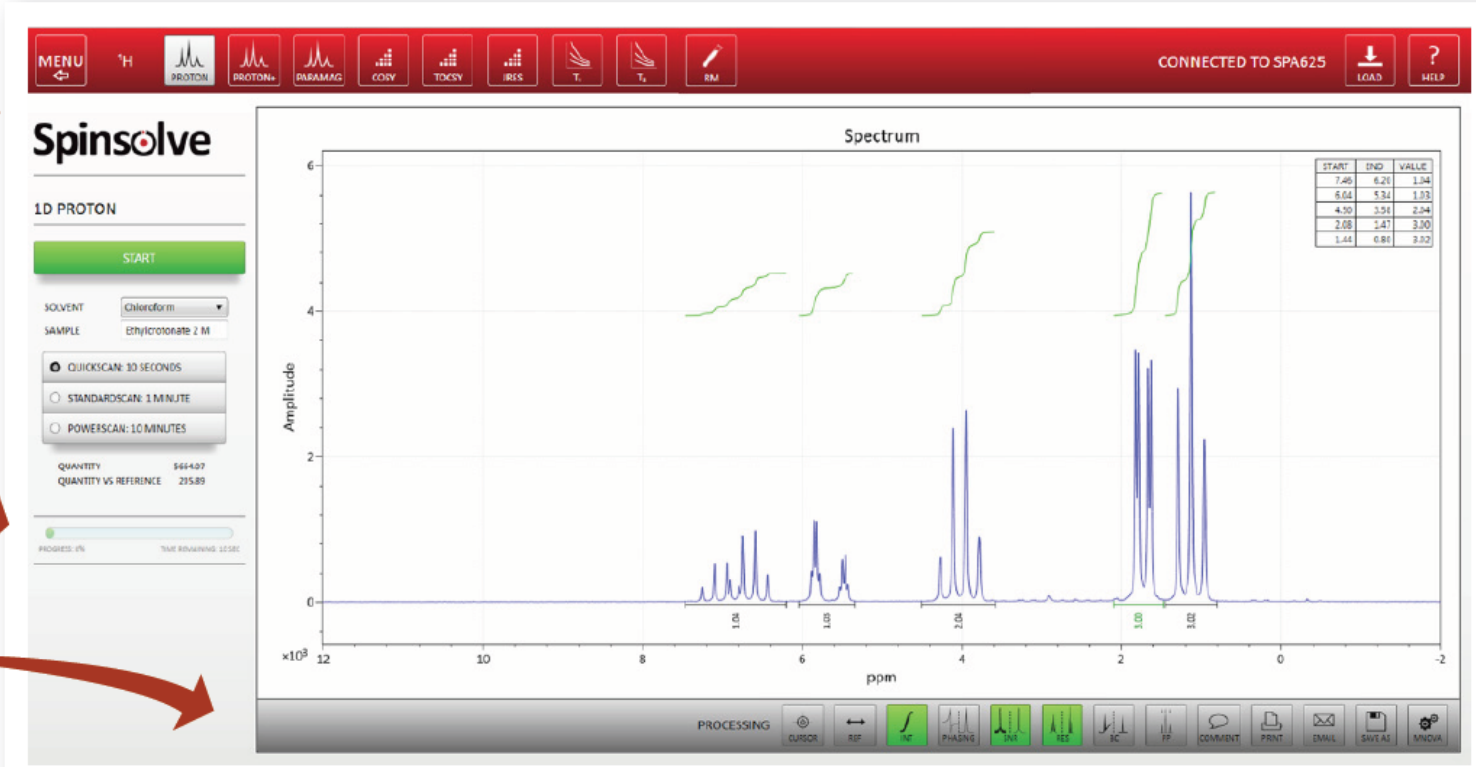
Easy to Use Standard Software

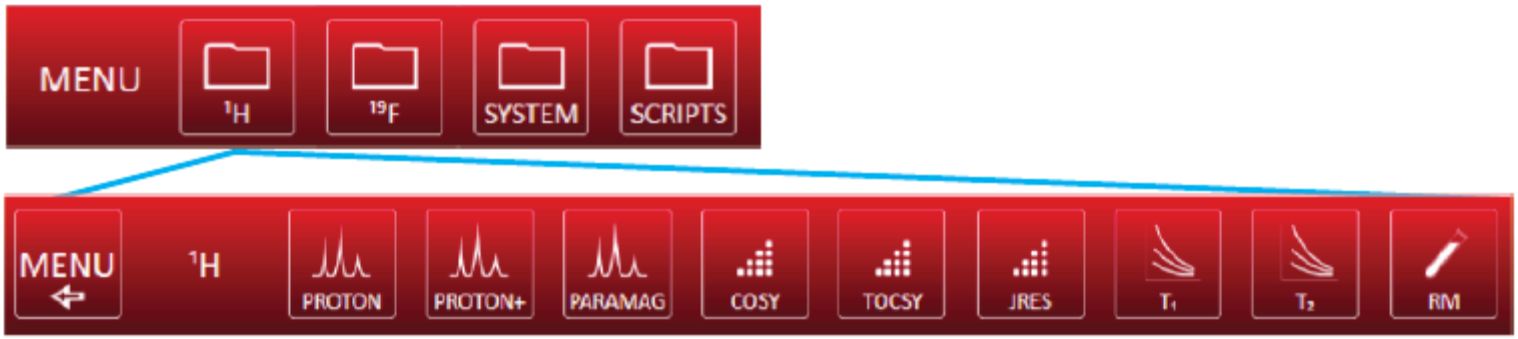
Easy experiment selection in the upper menu

Single button start

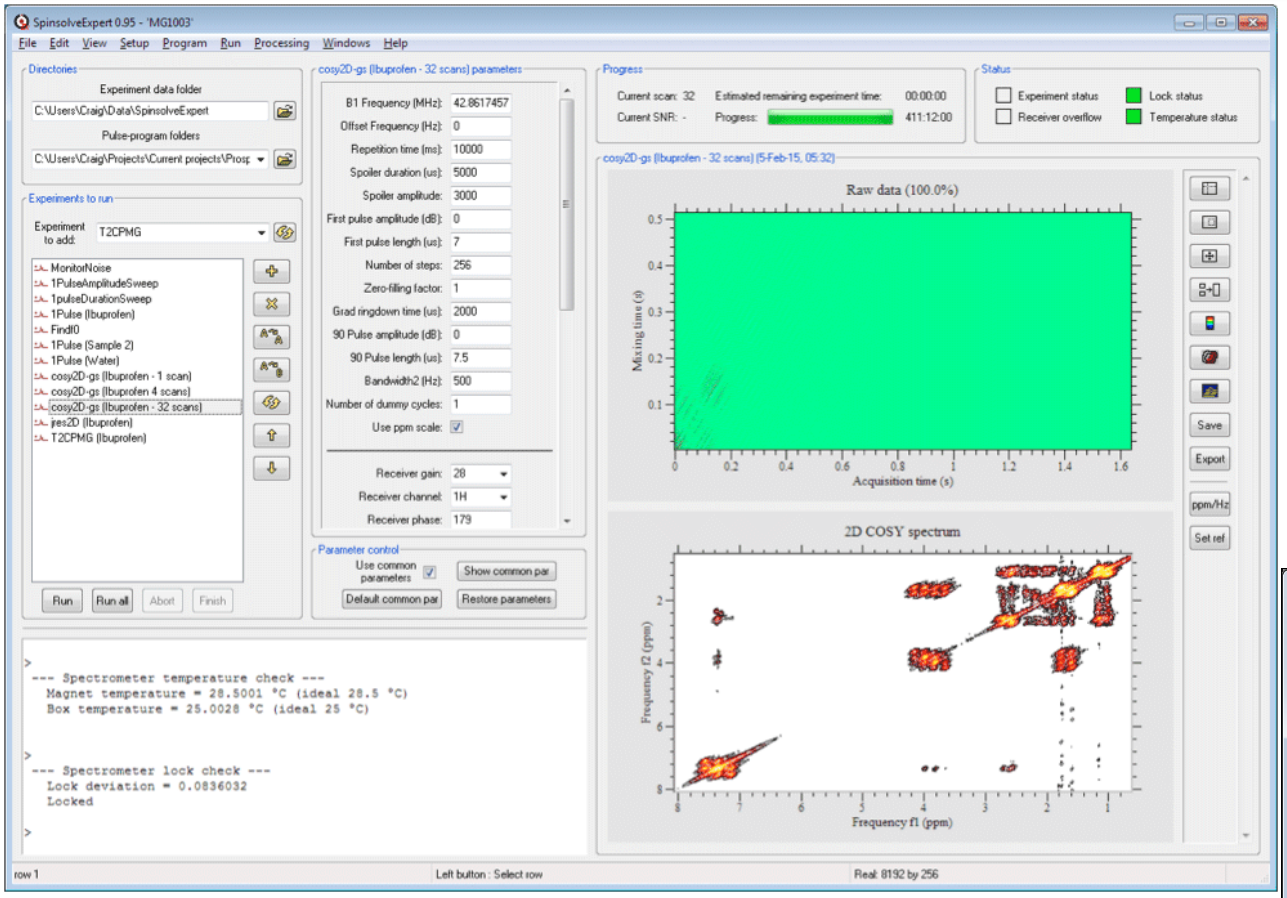
Progress bar

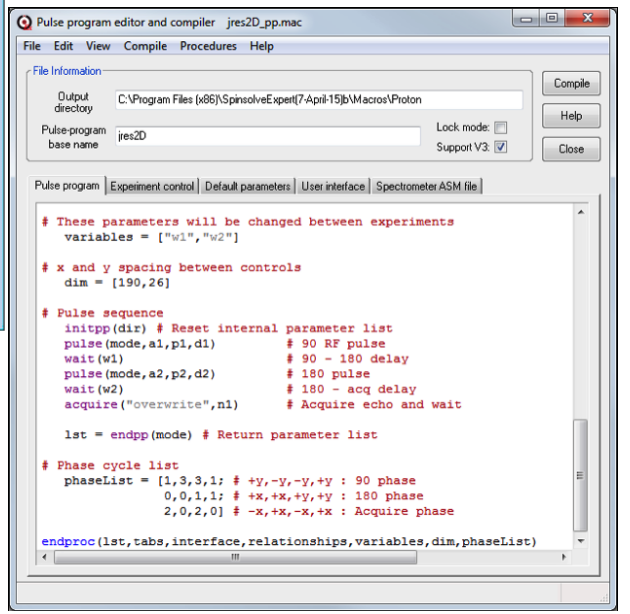
One-click processing buttons





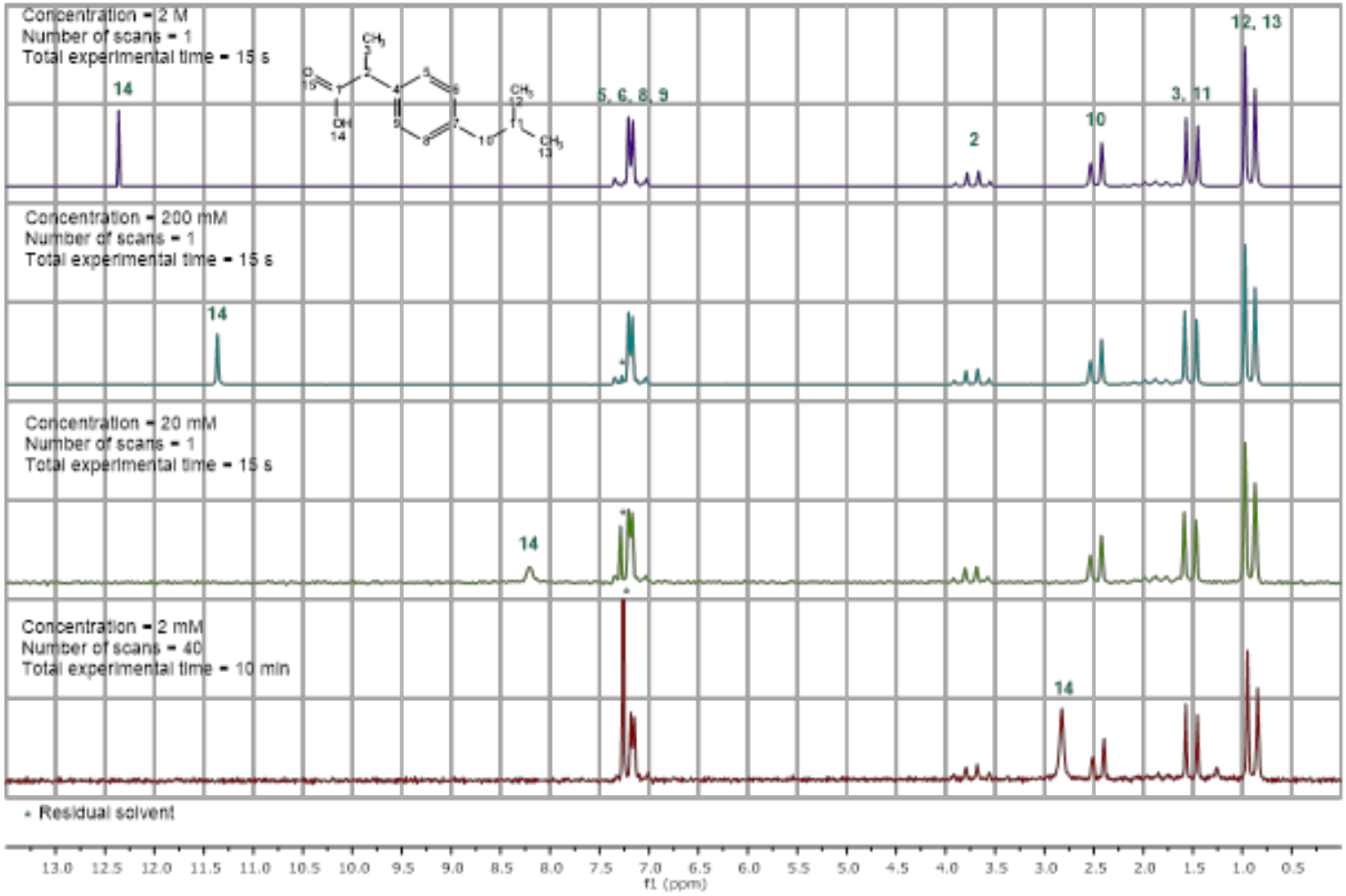
Advanced Expert Software



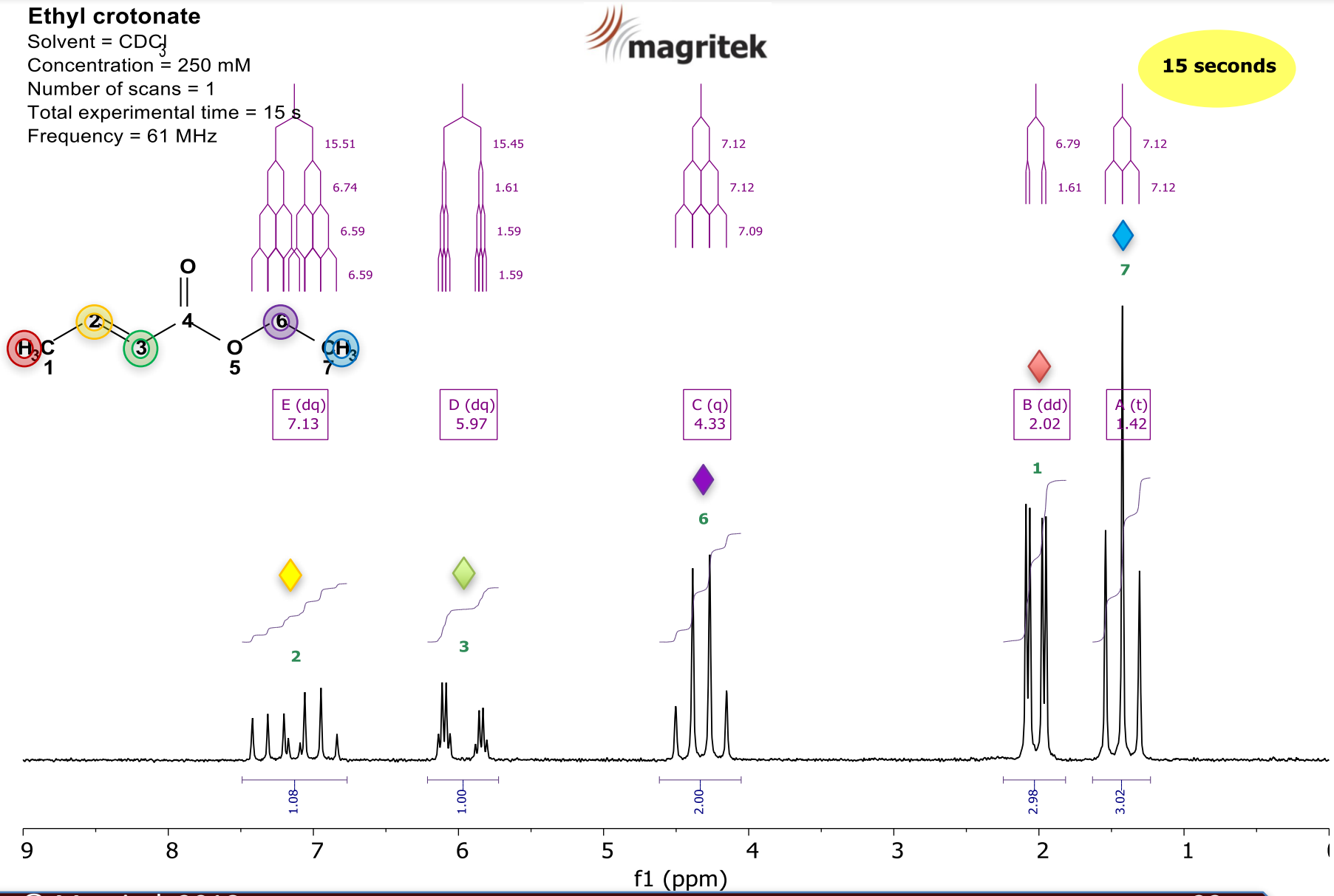


Proton Sensitivity

NMR Spectra (60 MHz) of Ibuprofen
2 M, 200 mM, 20 mM and 2 mM in Chloroform



1D ^{1}H Ethyl crotonate



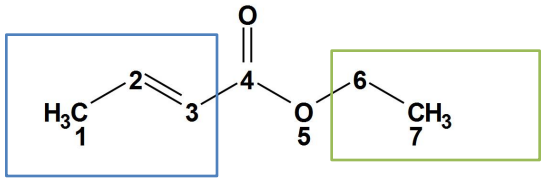
2D Homonuclear COSY

magritek
www.magritek.com

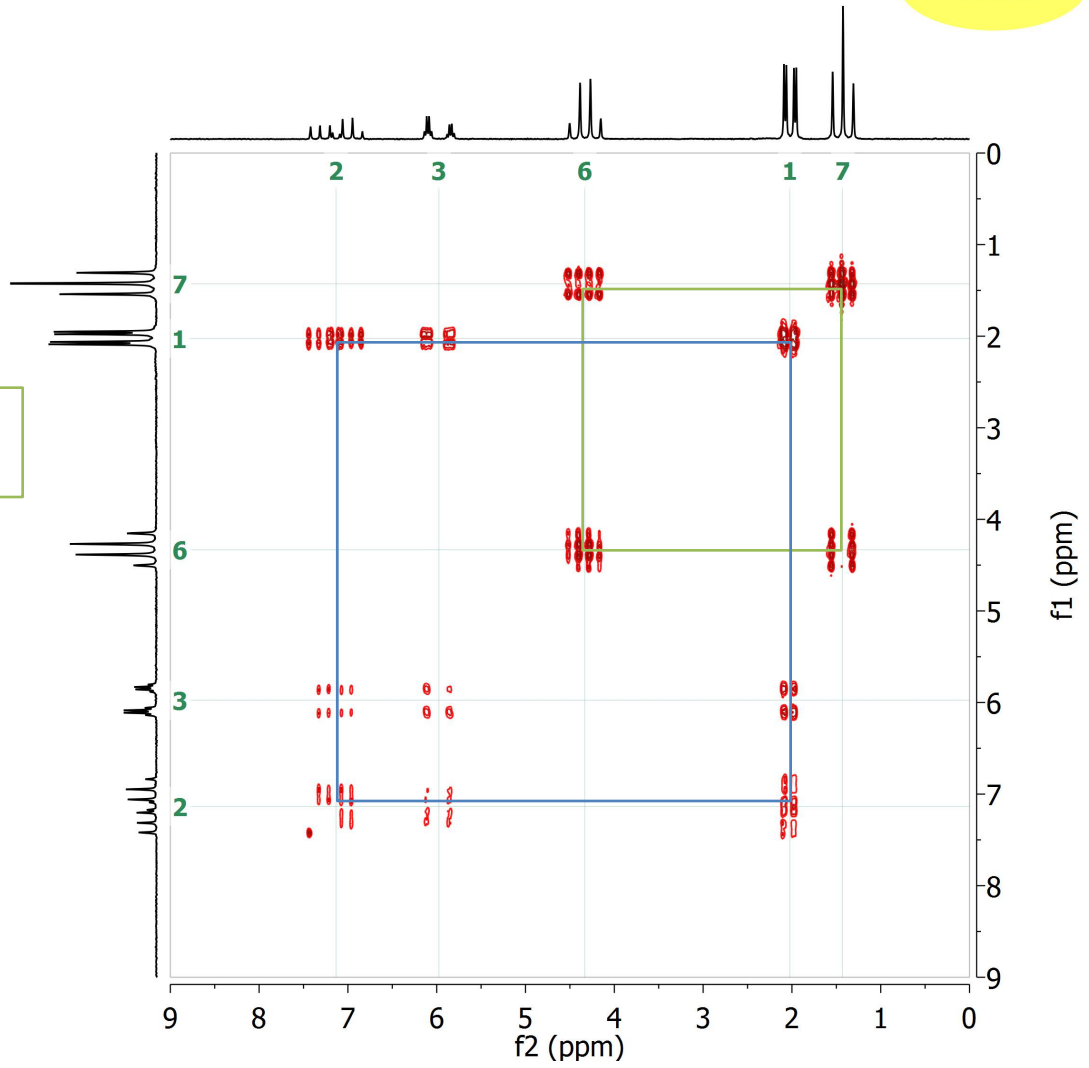
magritek

10 min

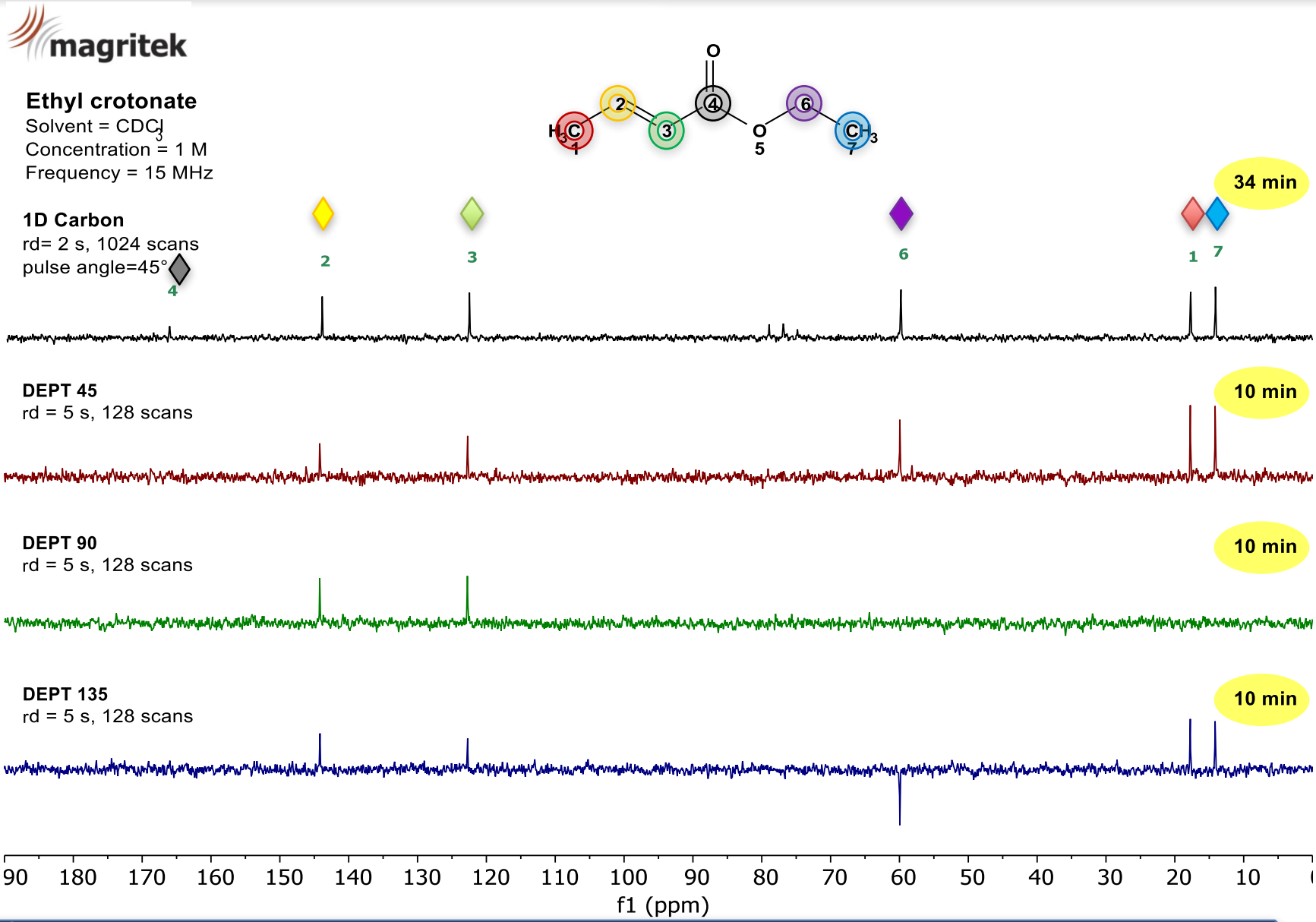
Ethyl crotonate
Solvent = $CDCl_3$
Concentration = 250 mM
Number of scans = 1
Total experimental time = 10 min
Frequency = 61 MHz



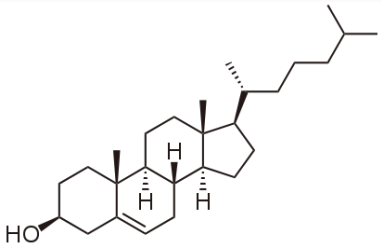
No Symmetrization



1D ^{13}Carbon DEPT Cycle



Structure elucidation – ^{13}C Spectra are similar



Cholesterol

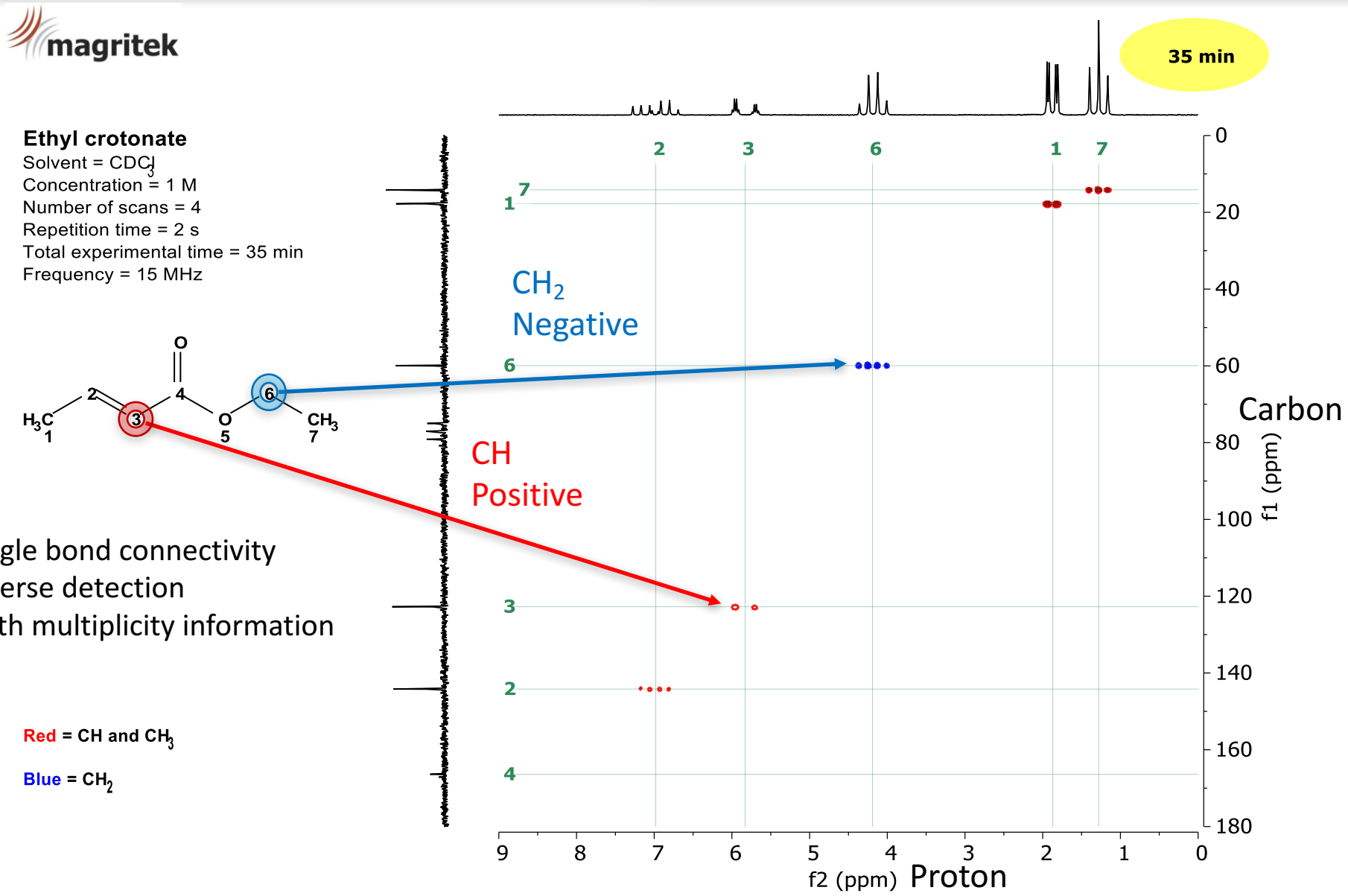
(75 MHz – $CDCl_3$)

300 MHz ^1H

(15 MHz – $CDCl_3$)

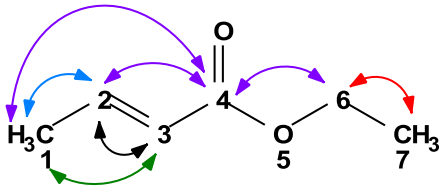
60 MHz ^1H

2D HSQC – Multiplicity Edited (ME)

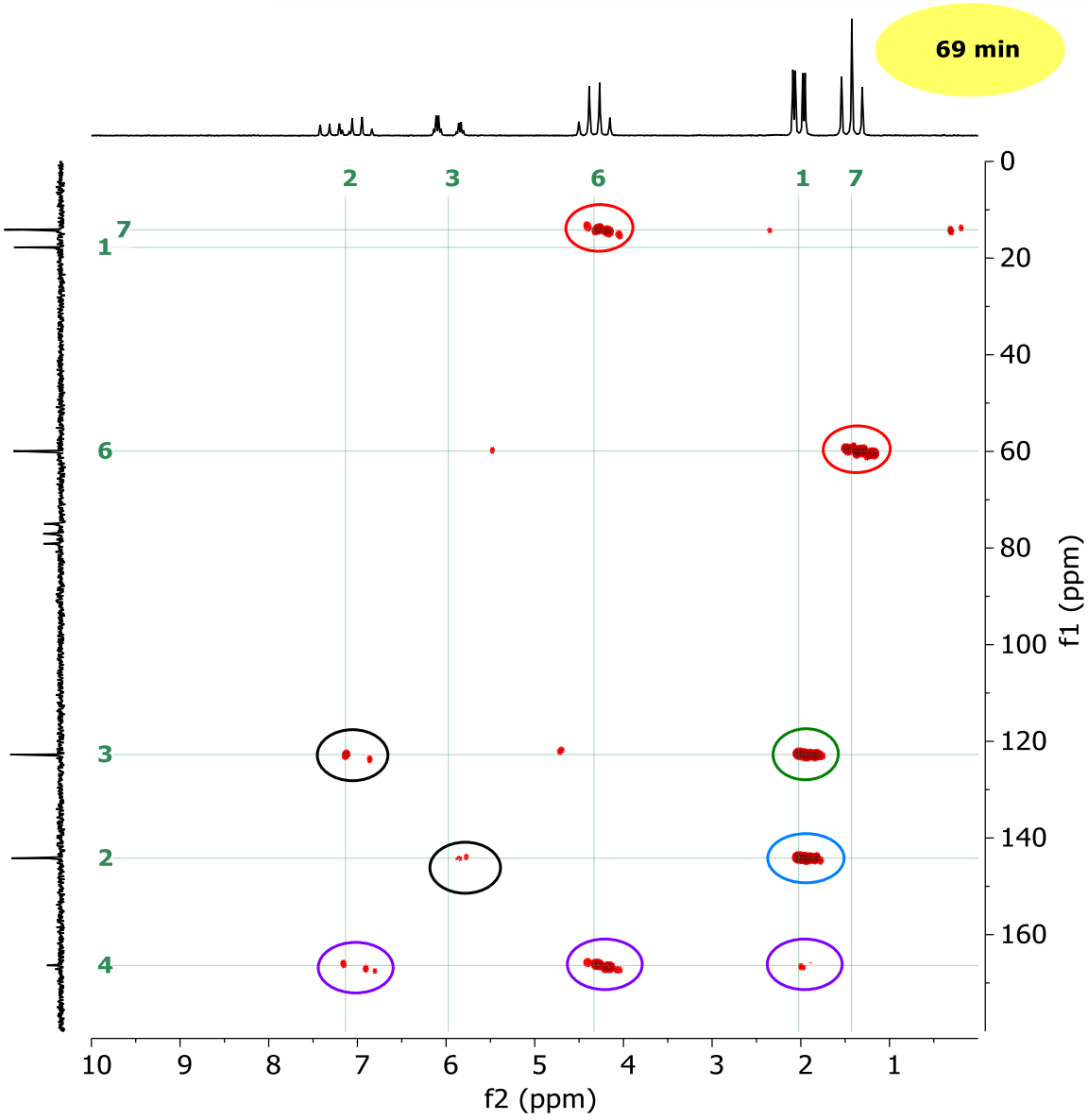


2D HMBC Ethyl crotonate

Ethyl crotonate
Solvent = $CDCl_3$
Concentration = 1 M
Number of scans = 16
Repetition time = 2 s
Total experimental time = 69 min
Frequency = 15 MHz



Multiple bond connectivity
Inverse detection

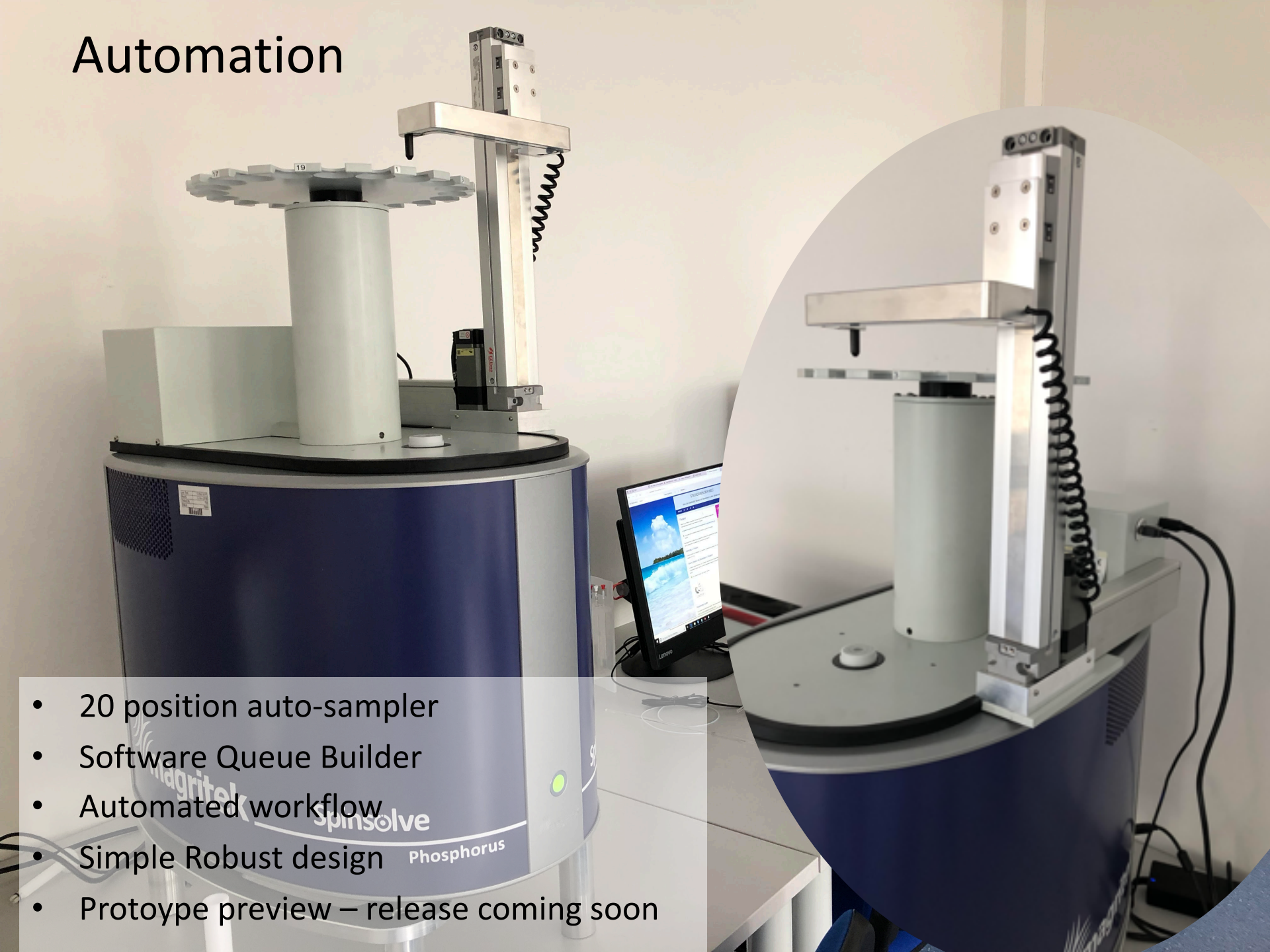


Spinsolve Pulse Sequences

1H Proton	19F Fluorine	^{13}C Carbon (^{31}P, X)	Expert

• 1D PROTON
• Paramagnetic Wideband
• 13C-decoupled 1D Proton
• 19F-decoupled 1D proton
• 2D COSY
• 2D TOCSY
• 2D ROESY
• 2D JRES
• T1, T2
• Reaction Monitoring
	• 1D Fluorine
	• Paramagnetic Wideband
	• 1H-decoupled 1D Fluorine
	• 2D F COSY
	• 2D F JRES
	• 2D FH COSY
	• Reaction Monitoring
		• 1D spectra
		• DEPT
		• 2D HETCOR
		• 2D HMBC
		• 2D HMQC
		• 2D HSQC
		• 2D HSQC-ME
		• PLUS
		  • Scripting
		  • Automation
		  • qNMR
		  • Autoshim
			• 2D NOESY
			• DQF-COSY
			• Non Uniform Sampling (NUS)
			• PGSE (Diffusion)
			• PSYCHE
			• Pure Shift HSQC

Automation



- 20 position auto-sampler
- Software Queue Builder
- Automated workflow
- Simple Robust design
- Protoype preview – release coming soon

Applications of Benchtop NMR

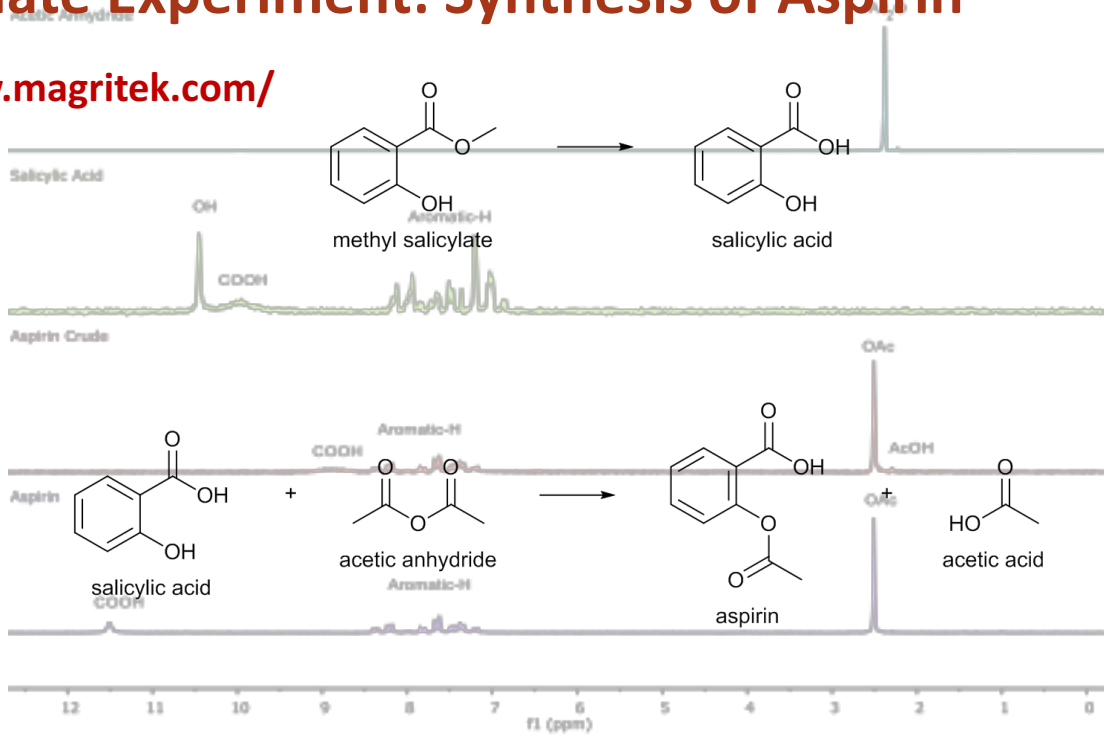
Industrial Applications:

- Education
- Organic Synthesis
- Process Control
- QA/QC
- Chemical Analysis
- Quantification (qNMR)
- Reaction Monitoring
- Fumehood Reactions

Traditional Undergraduate Experiment: Synthesis of Aspirin

Contents of lab manuals (see http://www.magritek.com/applications/chemistry-education/)

- Objectives
- Introduction
- Synthesis of salicylic acid from oil of wintergreen
- Procedure
- Risk Assessment
- ^{1}H-NMR Spectra
- Synthesis of aspirin from salicylic acid
- ^{1}H-NMR Spectra
- Tasks and Questions

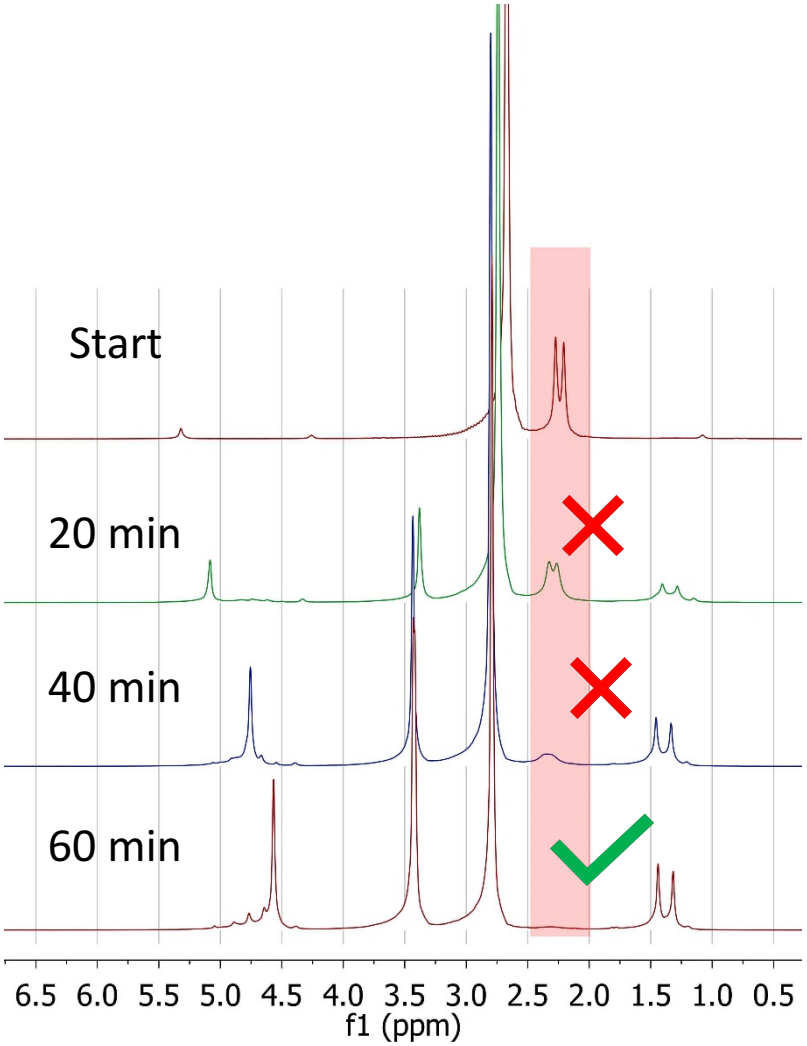


Tasks and Questions

1. Calculate % yield for each step of the synthesis.
2. Assign the peaks in the ^{1}H-NMR spectra of all starting materials and products, and identify functional groups that are unique in each sample.
3. Identify the impurities in the crude products. Did recrystallization remove these impurities?

Reaction completion-^{1}H

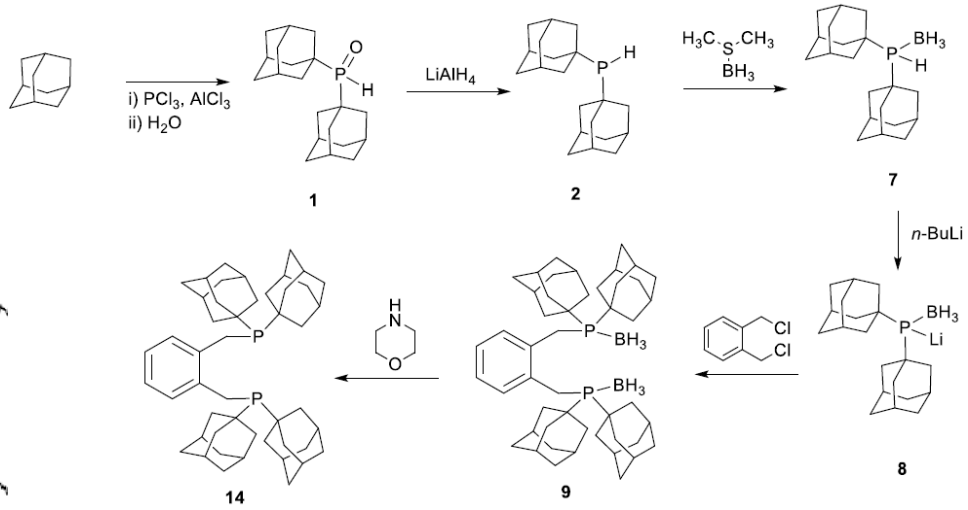
- Reaction complete? Product expected one?
- Check is done by either **high field NMR** (**expensive/takes longer**) or less specific methods like thin layer chromatography (TLC)
- **Spinsolve** offers the chance to **directly do this in the lab** without delays !
- No waiting at high field machine and way more information than TLC

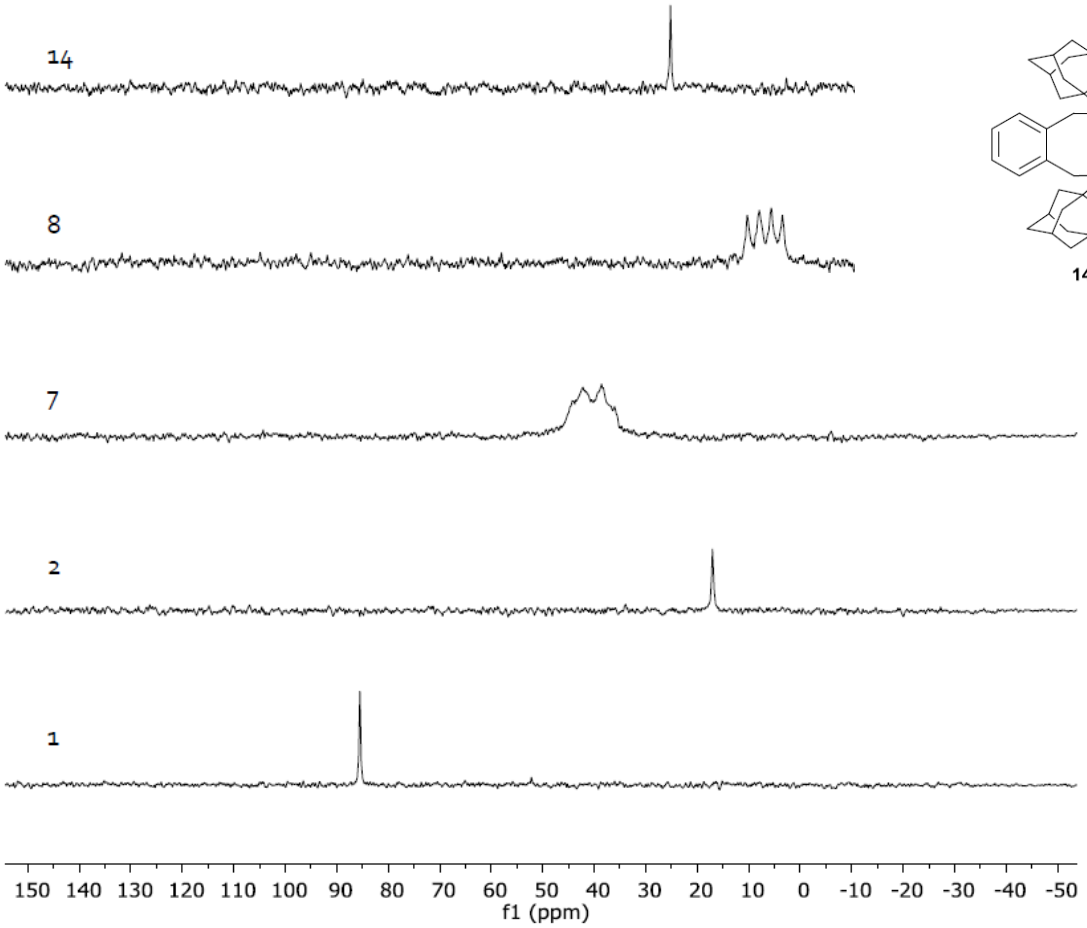


Organometallic chemistry

Preparation of Phosphine ligand

Bis(diadamantylphosphinomethyl)benzene

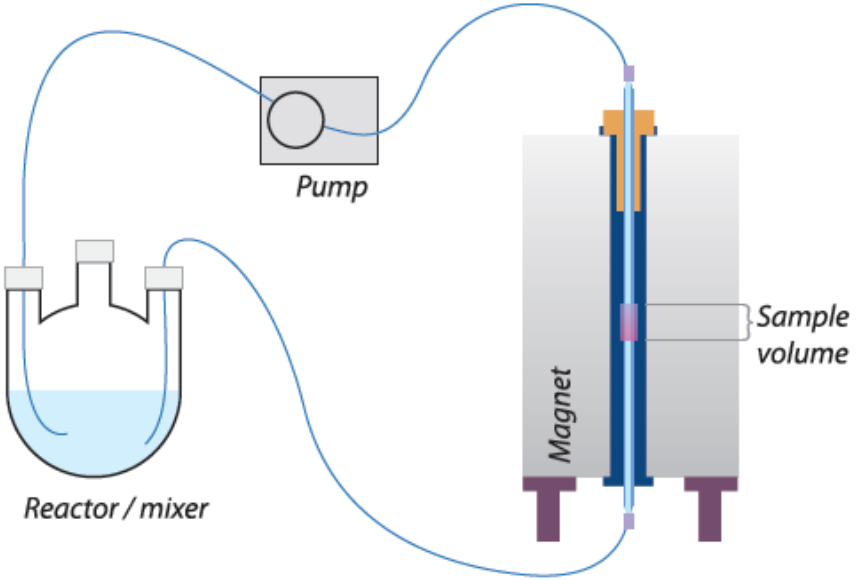




- ^{31}P NMR can be used to follow Phosphorus involving organometallic reactions
- Spinsolve allows the use of Young‘s tubes

Reaction Monitoring

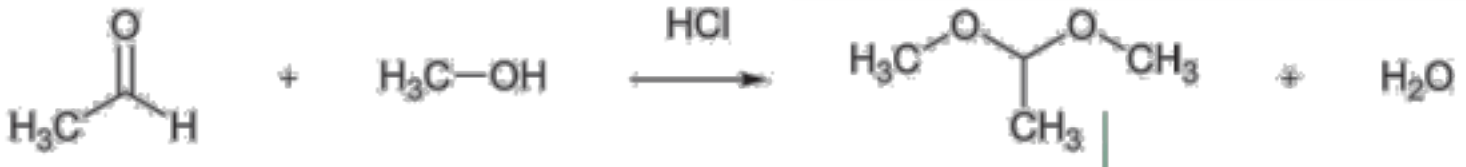
Following the progress of a reaction from starting material to end-point



Flow reaction monitoring setup

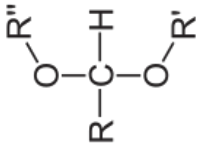
- Every Spinsolve system has an opening all the way from top to bottom
- So a flow cell can be positioned into the NMR spectrometer
- Take an NMR spectrum all 30 … 60 seconds
- Run the setup either in continuous or stop-flow mode

Acetalization of Acetaldehyde

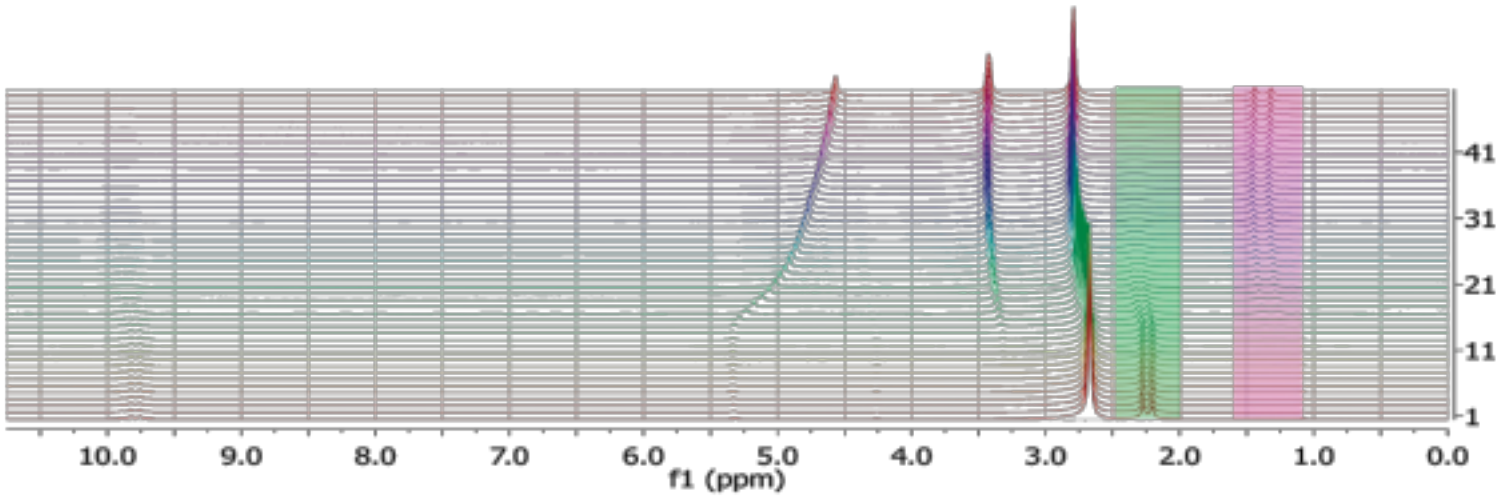


Products (purple)

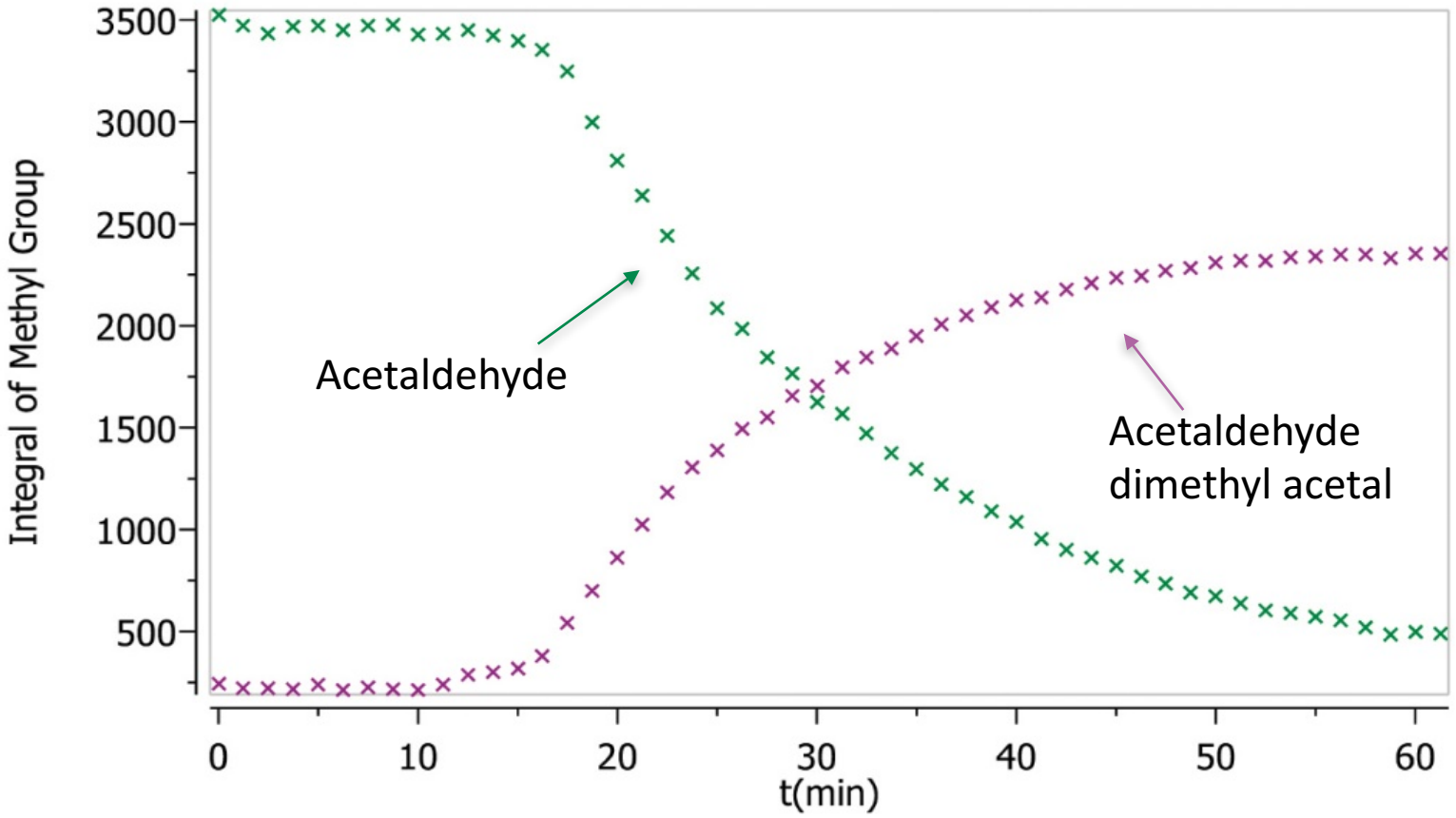
Starting material spectrum (green)



Acetal

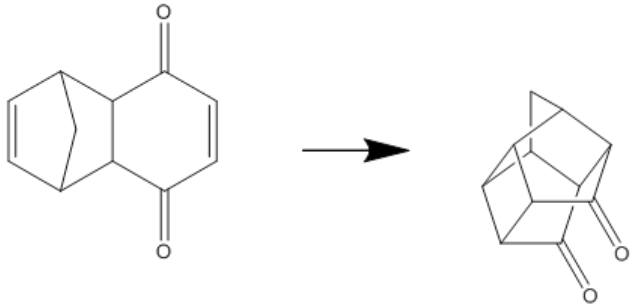


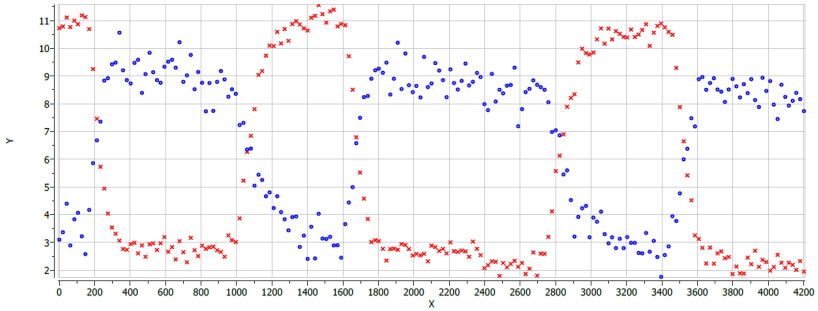
Acetalization of Acetaldehyde

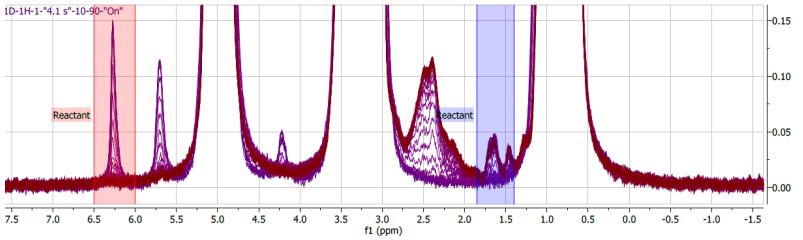


- **Green**: methyl group of the acetaldehyde at 2.25ppm
- **Purple**: methyl group of the product acetaldehyde dimethyl acetal at 1.4ppm
- Can easily and accurately monitor the progress of the reaction as it occurs

Reaction monitoring of UV-induced 1,4-Cycloaddition in Ethanol





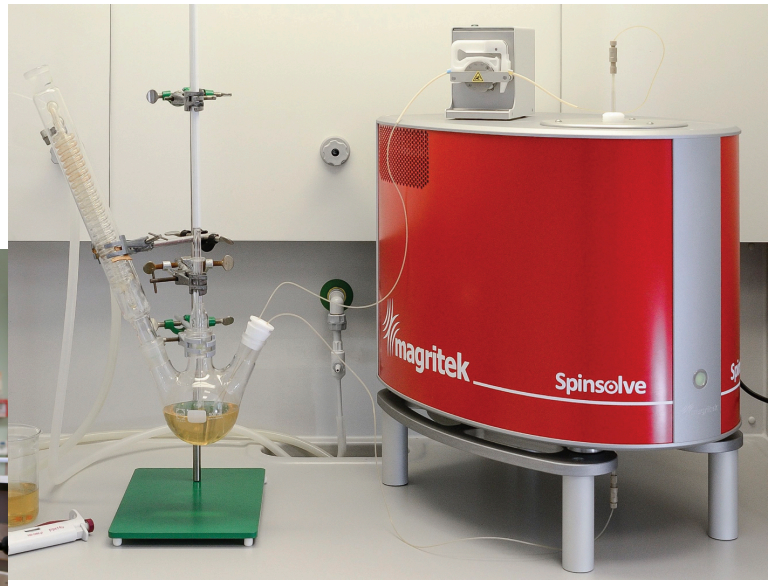


Real-time monitoring of changes within the flow reaction setup

Closure / Thank you

- For further Information, please contact sales@magritek.com
- Further information is also located on the Web page www.magritek.com
- Typical Spinsolve Example Spectra can be found via http://www.magritek.com/products/spinsolve/nmr-spectra-examples/

Standard Laboratory Setup



Reaction Monitoring Setup