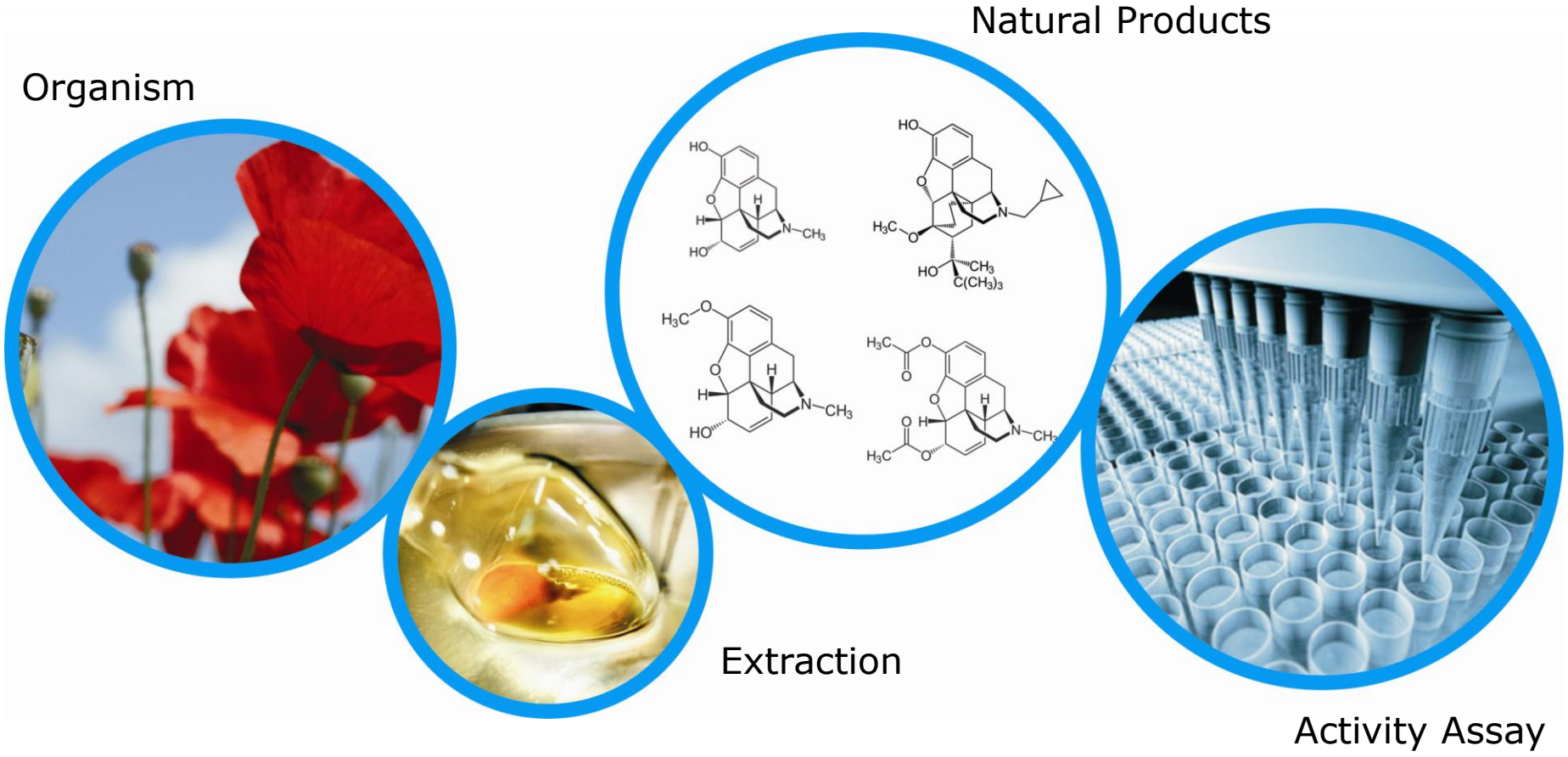
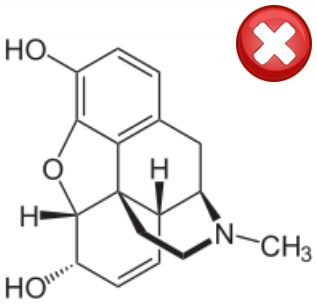
Tools for Structure Elucidation

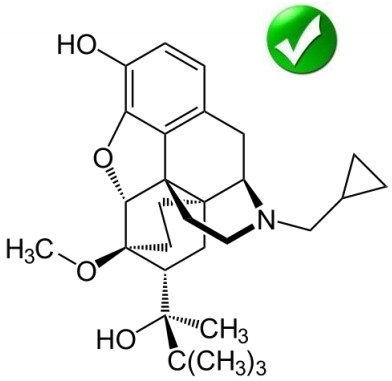
Sandra Groscurth

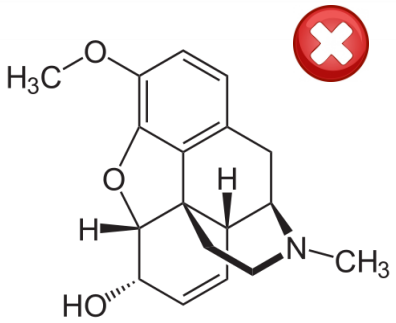
Workflow in Natural Product Research

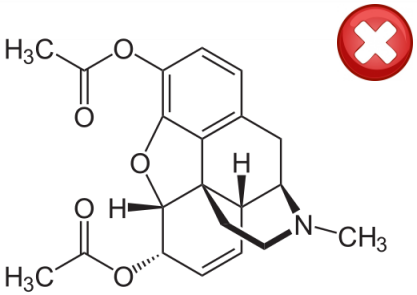


Characterization of Unknown Structures









<u>characterization of extracted compounds that show activity:</u>

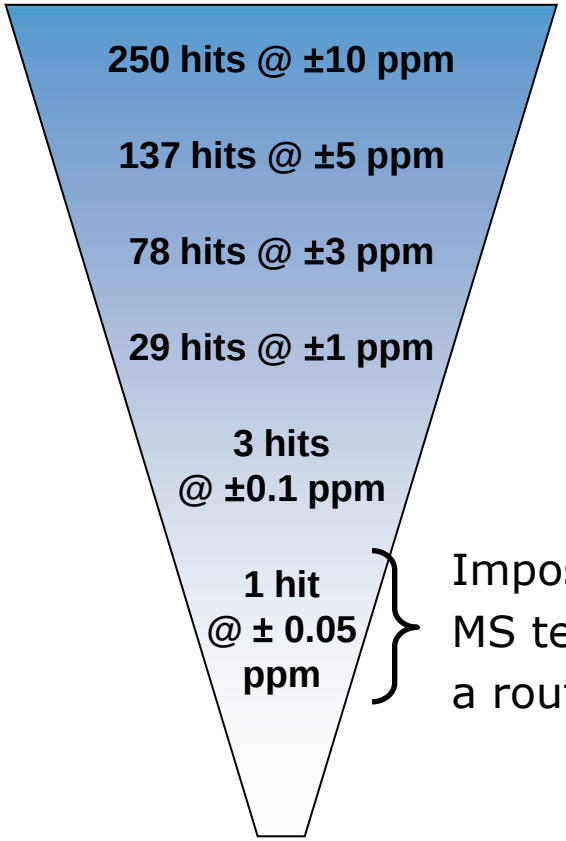
first of all, is it a new compound, is the structure unknown?

⇨ dereplication by MS/MS

⇨ molecular formula determination by mass spectrometry

Structural Characterization by MS

Number of hits depending on mass accuracy



Impossible for any MS technology on a routine basis

m/z = 609.28:

10 ppm ⇨ 0.006 Da

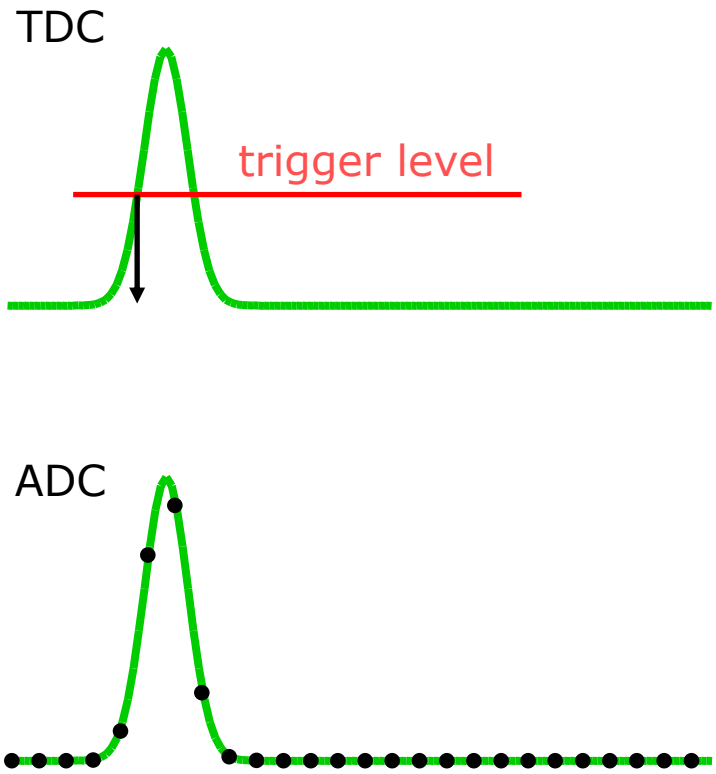
0.05 ppm ⇨ 0.00003 Da

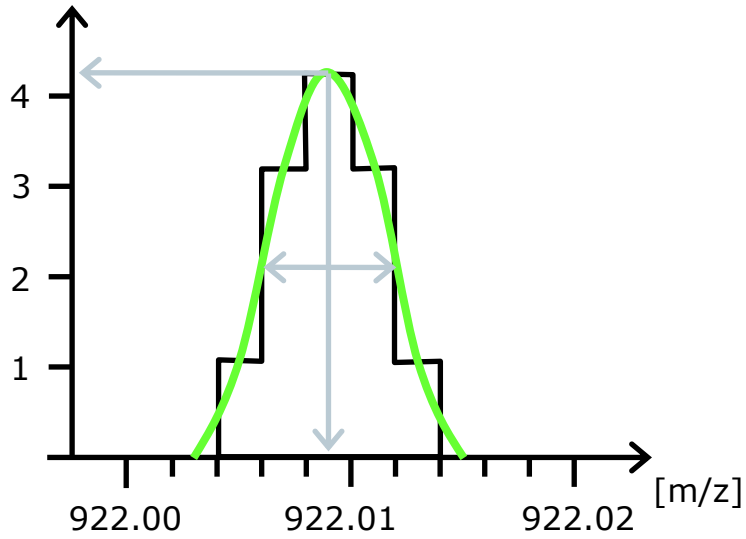
0.03 mDa

- resolution 20000 FWHM
- accuracy 1–2 ppm

Accurate Mass Determination

detection of single ion signal:





2 GHz Digitizer = sampling rate 0.5 ns

Time to Digital Converter

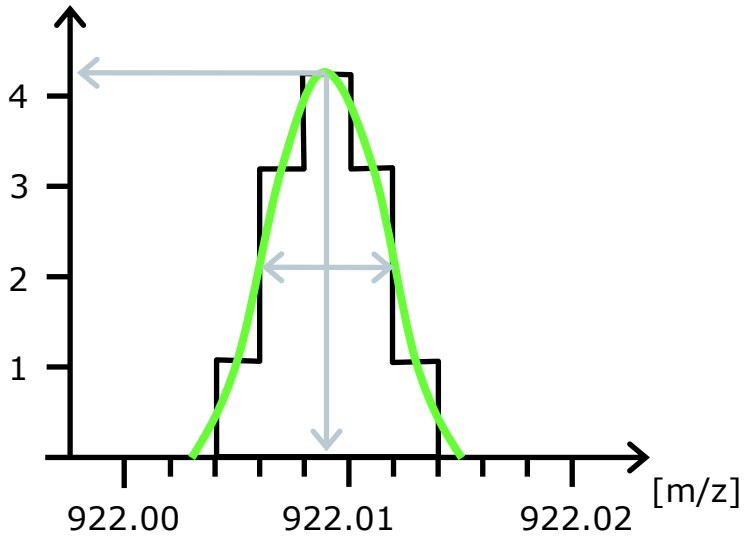
time information of the histogram peak is converted by interpolation and calibration into mass information

mass position = 922.009 m/z

intensity = 4 counts

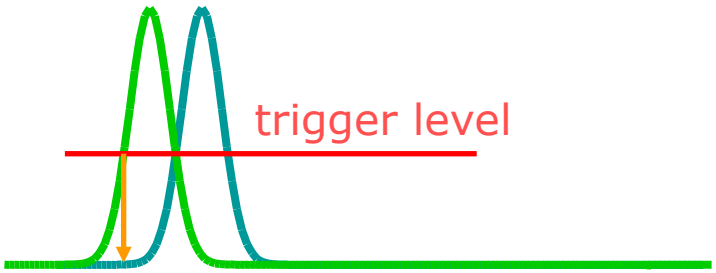
peak width (FWMH) = 0.06 Da

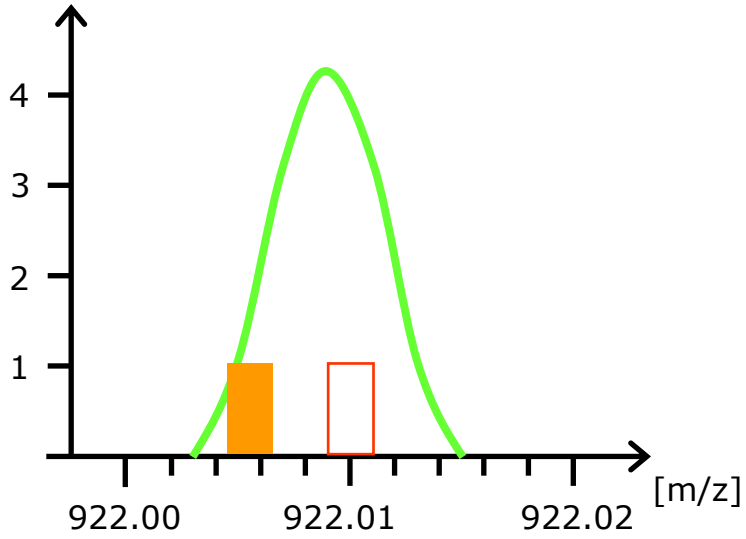
$$\text{resolution} = \frac{\text{mass position}}{\text{peak width}} = 15400$$



Time to Digital Converter

with higher sample concentration two or more ions per acceleration pulse may reach the MCP detector





⇨ only the first ion causes a trigger event

⇨ the second ion is not converted

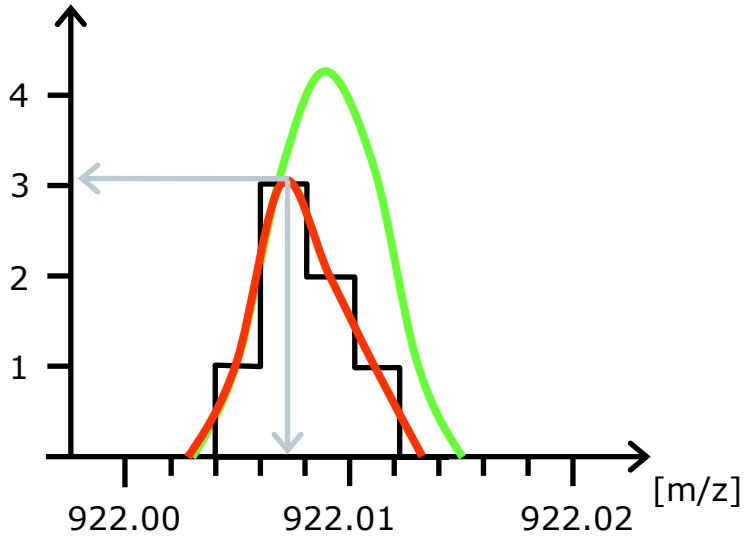
Time to Digital Converter

with higher sample concentration two or more ions per acceleration pulse may reach the MCP detector

in this example with the same number of ions reaching the detector, only 60% of these ions were converted

⇨ wrong intensity

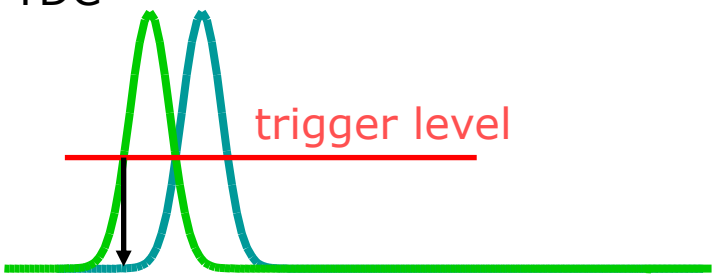
⇨ wrong mass position



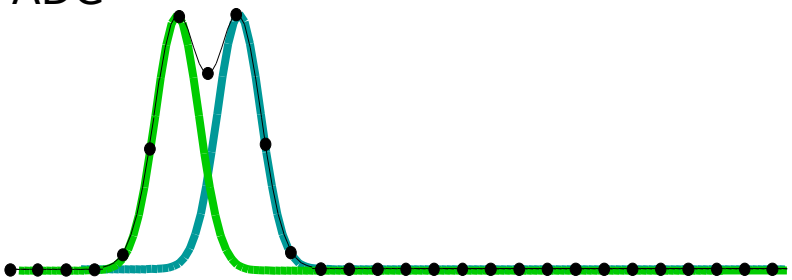
Accurate Mass Determination

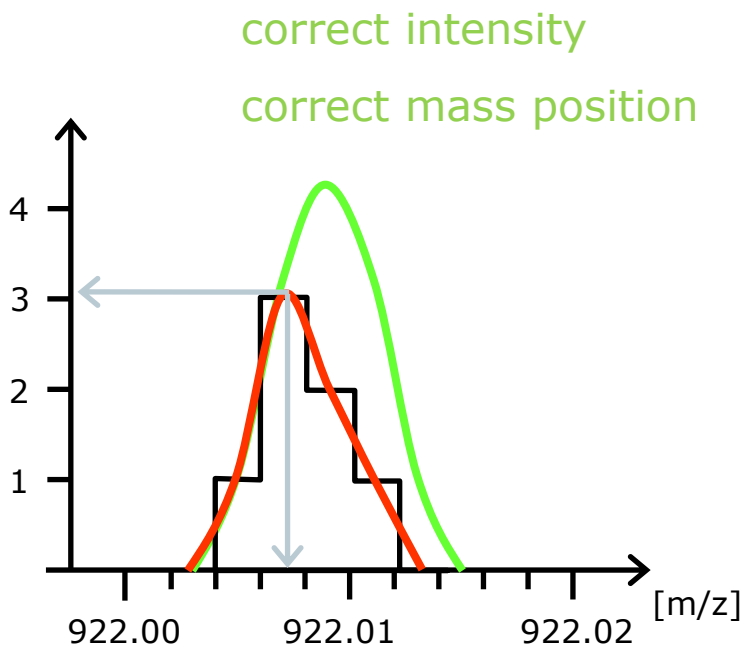
to avoid dead time effects: different digitizer technology

TDC



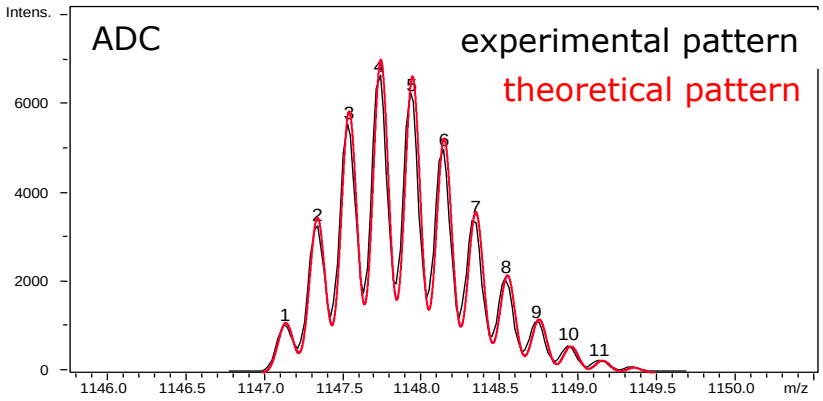
ADC

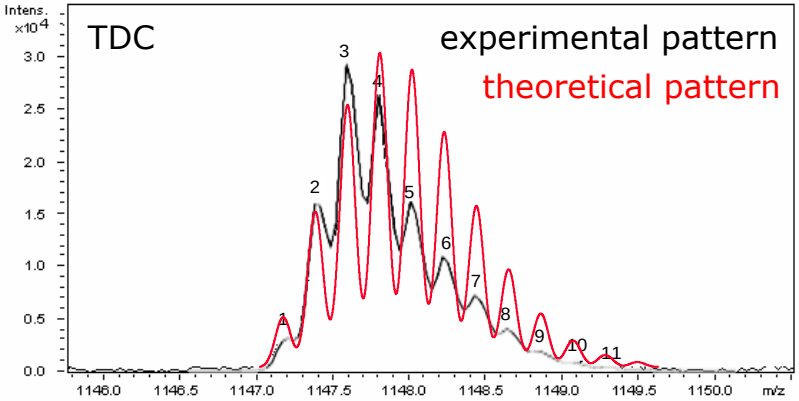




Accurate Mass Determination

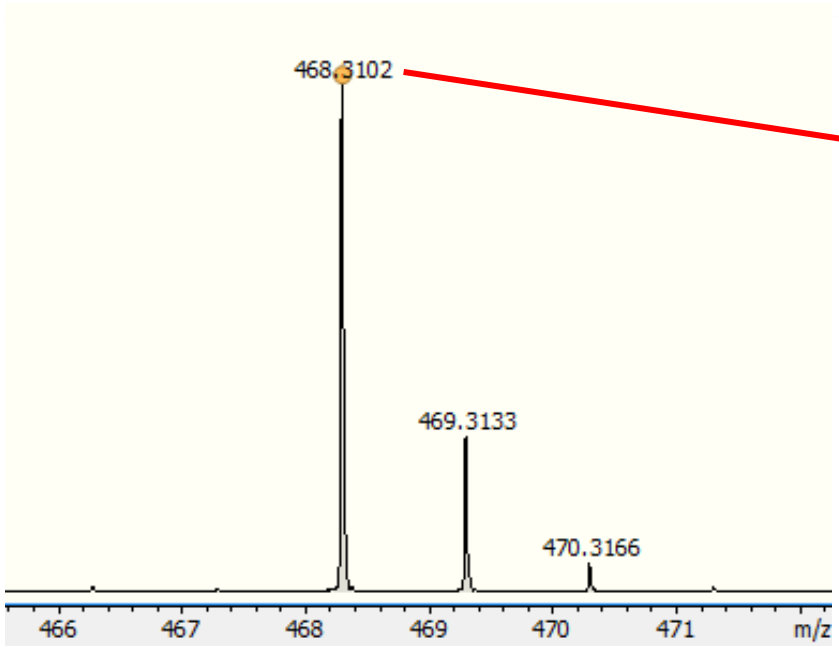
comparing true isotopic pattern of insulin

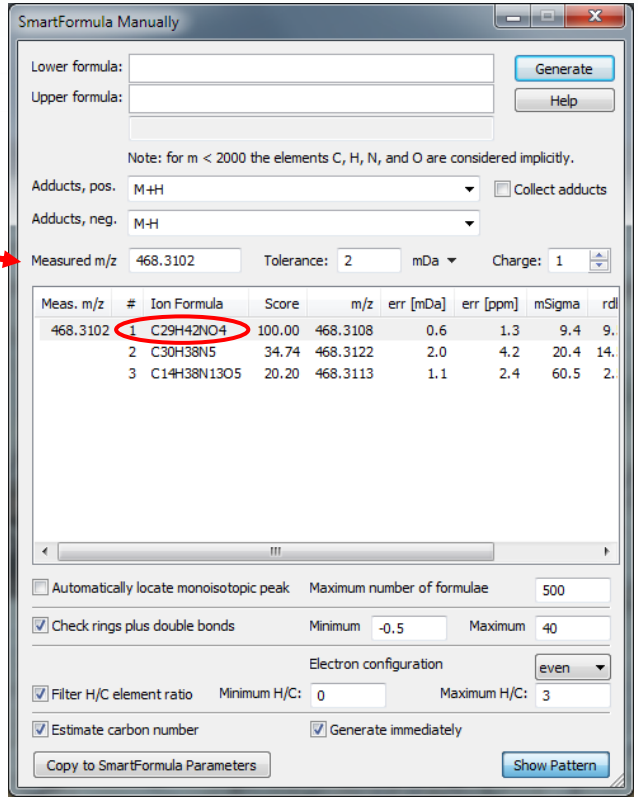




⇨ ADC digitizer technology preferred for any MS instrument

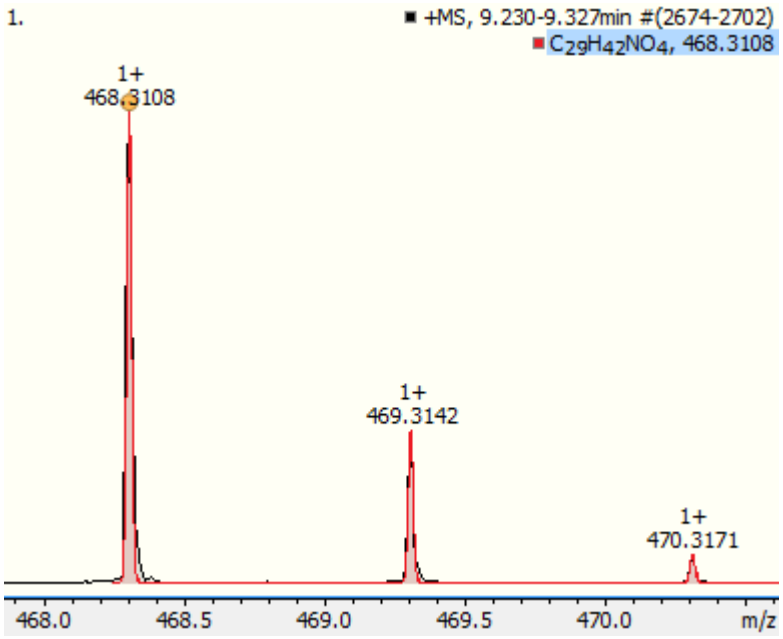
SmartFormula – MS Data Interpretation

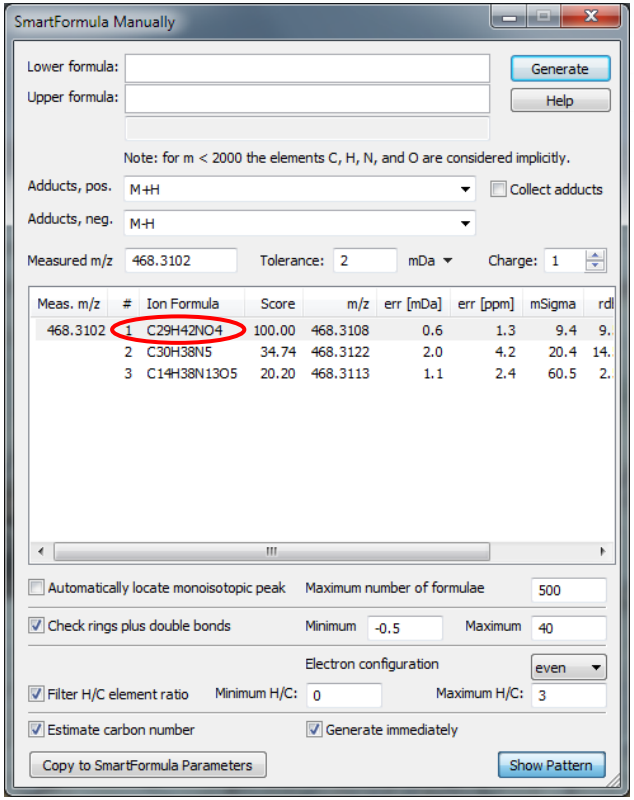




⇨ unambiguous elemental composition determination by combined accurate mass and isotopic pattern information

SmartFormula – MS Data Interpretation



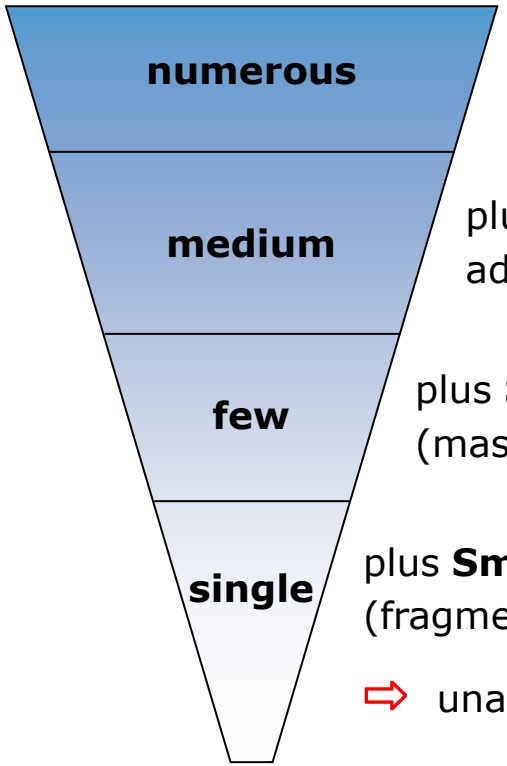


Overlay of **measured** and **simulated** spectrum:

⇨ sum formula $C_{29}H_{42}NO_4$ shows perfect match for the isotopic patterns

Accurate molecular formula from MS/MS

possible formulae



mass accuracy
several ppm accuracy

plus **chemical expertise**
additional confidence

plus **SmartFormula**
(mass accuracy + TIP)

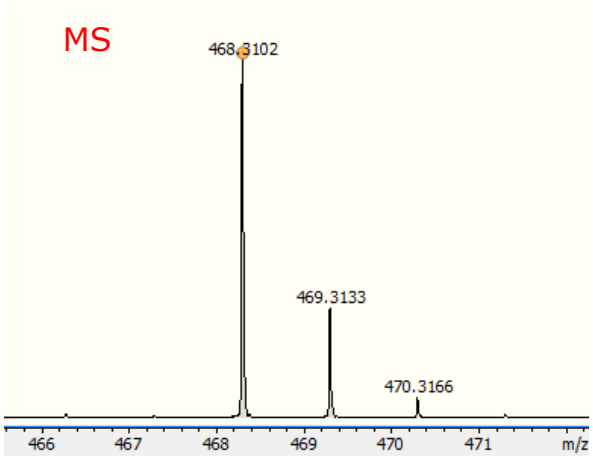
plus **SmartFormula3D**
(fragments-based TIP)

⇨ unambiguous formula ID

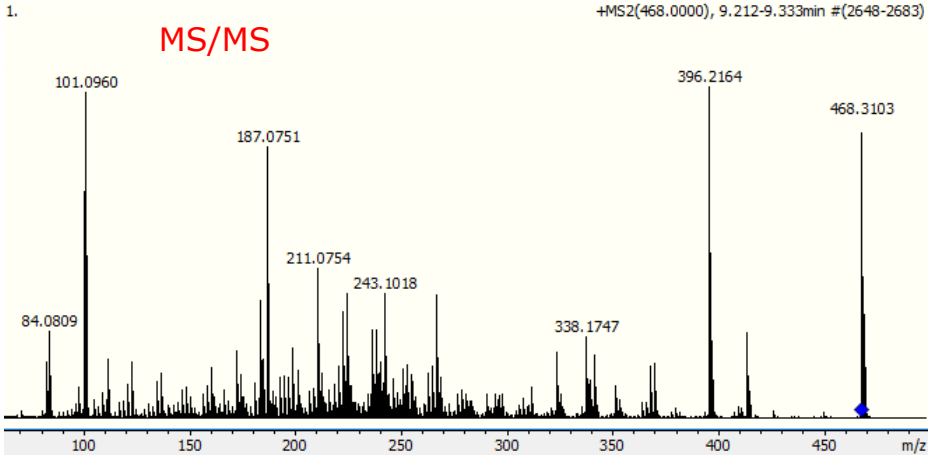
⇨ definitive molecular formulae

- resolution 40-60000 FWHM
- accuracy 1 ppm (MS & MS/MS)
- 20 full spectra/sec

Accurate molecular formula from MS/MS



Parent



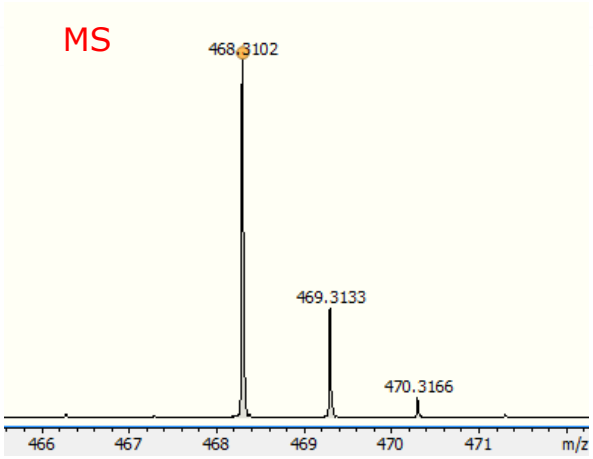
Fragments

- elemental formulae for parent ions by SmartFormula
- elemental formulae for fragment ions by SmartFormula

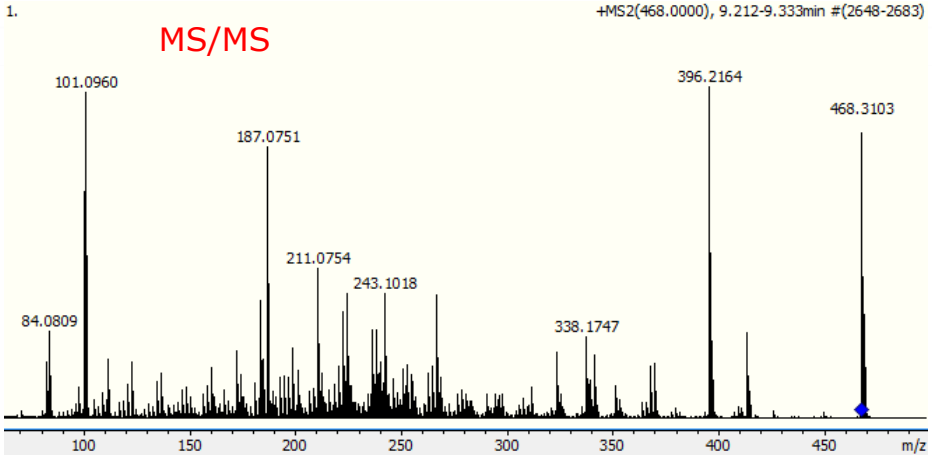
⇨ every ‘true’ fragment formula must be a sub-set of the ‘true’ parent formula

⇨ SmartFormula3D

Accurate molecular formula from MS/MS



Parent



Fragments

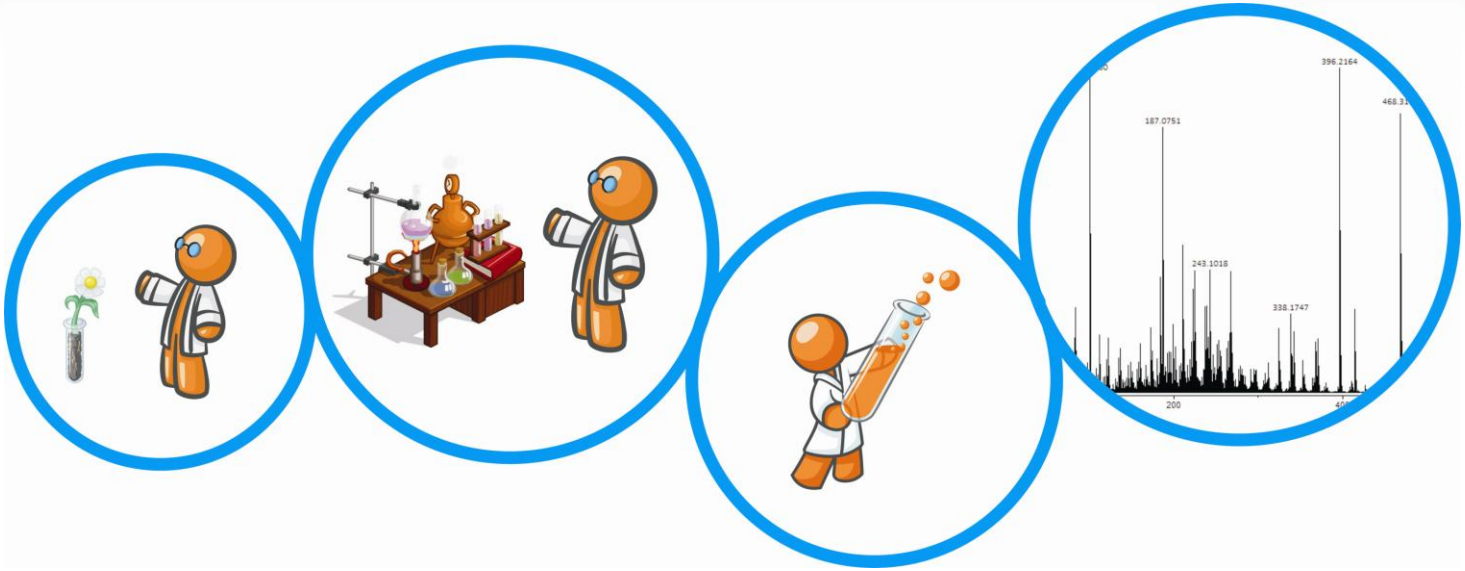
SumFormula	m/z calc	err[mDa]	err[ppm]	mSigma	eConf
$C_{29}H_{42}NO_4$	468.3108	0.6	1.2	21.2	even

proposed molecular formulae of precursor ion after combination of MS and MS/MS information

SumFormula	SumFormula Loss	m/z Loss	err[mDa] Loss
$C_{24}H_{30}NO_4$	C_5H_{12}	72.0938	0.1
$C_{24}H_{30}NO_4$	C_5H_{12}	72.0938	0.1
$C_{22}H_{26}NO_3$	$C_7H_{16}O$	116.1189	1.2
$C_{22}H_{26}NO_3$			1.2
$C_{18}H_{15}O$			0.1
$C_{12}H_{11}O_2$			0.3
$C_6H_{13}O$			0.5

molecular formulae of fragment ions

Accurate molecular formula from MS/MS



<u>characterization of unknown compound by MS/MS:</u>

molecular formula based on TIP of MS and MS/MS spectra

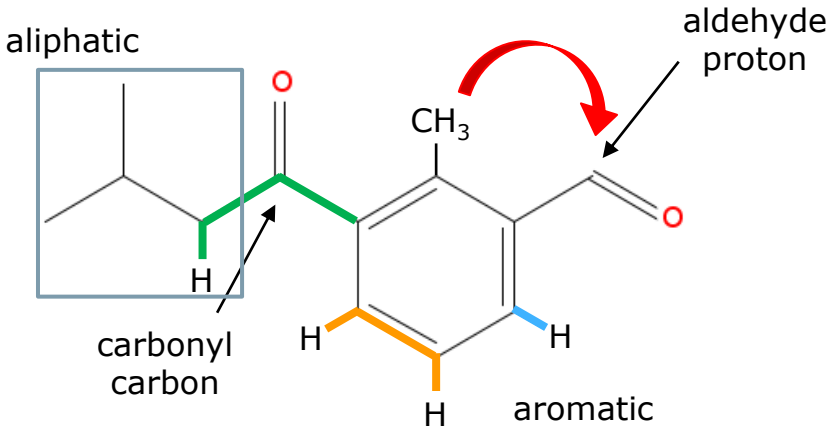
⇨ $C_{29}H_{41}NO_4$

⇨ structure elucidation by NMR

NMR Spectra for Structure Elucidation

- 1D NMR spectra
  - 1D Proton
  - 1D Carbon

  } chemical shifts ⇨ functional groups



- 2D NMR spectra
  - HSQC ⇨ $^{1}J_{CH}$
  - COSY ⇨ $^{3}J_{HH}$
  - HMBC ⇨ $^{2}J_{CH}/^{3}J_{CH}$
  - TOCSY ⇨ spin system
  - ROESY ⇨ through space

  } correlations ⇨ neighboring atoms

NMR Hardware Developments

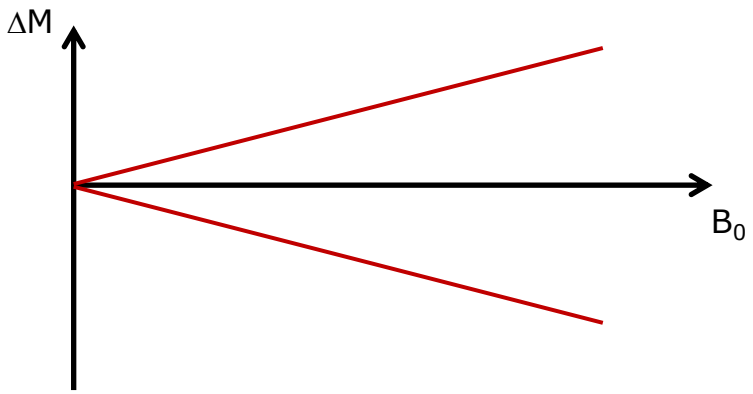
experiment	rel. sensitivity
^{1}H	1.00
^{13}C	0.01
HSQC	0.25
COSY	0.20
HMBC	0.07
TOCSY	0.12
ROESY	0.07

- NMR spectra for structure elucidation are less sensitive
- sample amounts are typically very little

in order to reduce the experimental time ⇨ increase NMR sensitivity

Increase NMR Sensitivity

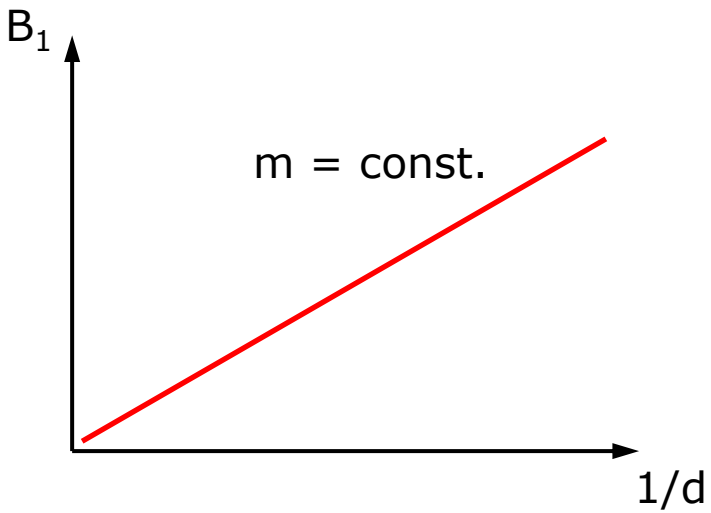
- increase sensitivity by increasing the magnetic field strength



- increase (mass) sensitivity through probe technology
  - small volume probes: increase mass sensitivity
  - CryoProbes: decrease noise and thus increase signal to noise
  - combine both: best signal to noise and highest mass sensitivity

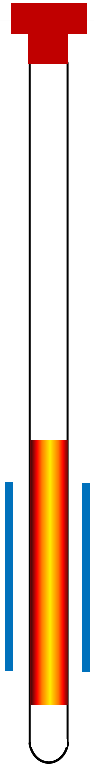
Small Volume NMR Probes

benefit of small volume NMR probes: increase mass sensitivity



relevant parameters:

- distance ^{1}H coil to NMR tube
- diameter of NMR tube



⇨ same number of spins increases sensitivity for small volume probes

Small Volume NMR Probes

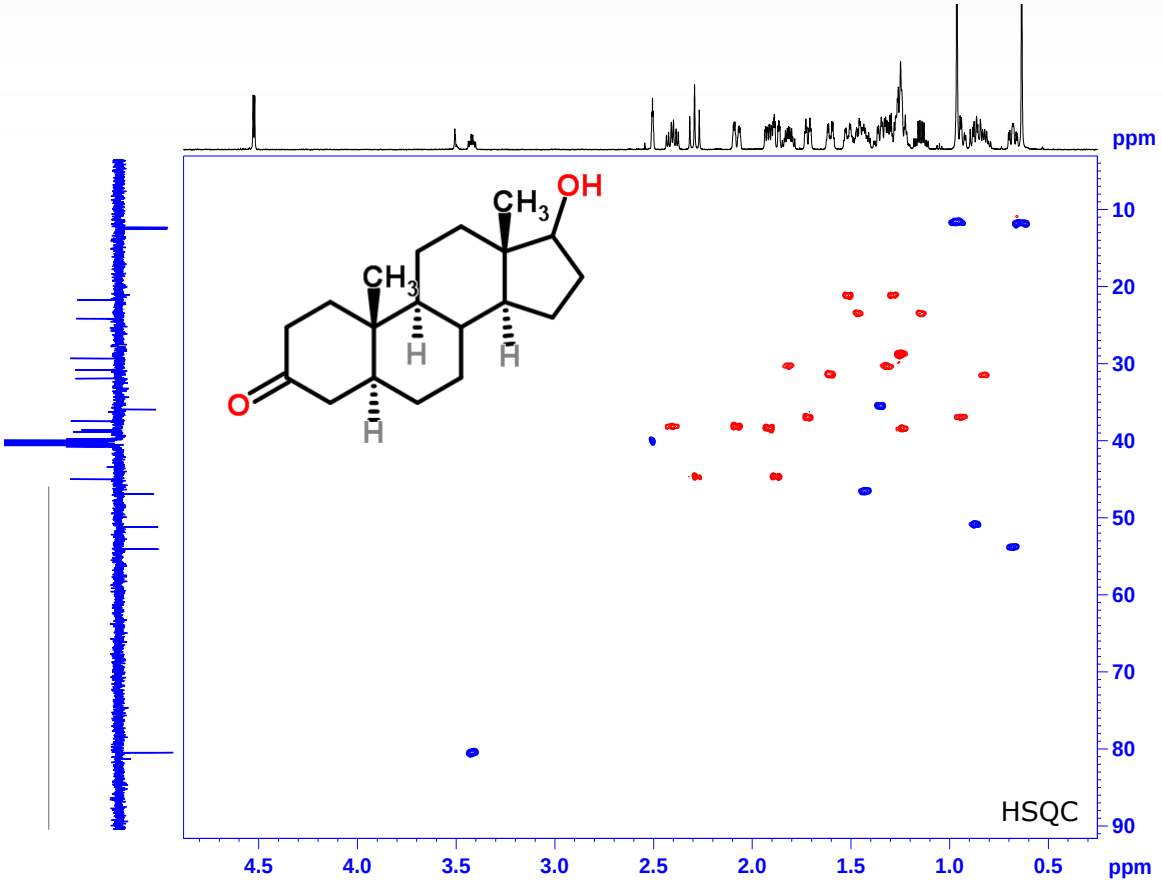
- no problems with solvent impurities (high analyte concentration even with very small sample amounts)
- no problems with solvent suppression (no radiation damping, etc.)
- advantage of working with small sample amounts
  - often easier to get clean samples in small amounts
  - no danger to overload HPLC columns
  - possibility to use analytical HPLC columns and fraction collect (better separation with small sample amounts)

Small Volume NMR Probes

Probehead Diameter [mm]	1	1.7	3	5
Sample Volume [µl]	5	30	180	500
Recommended Concentration [mM]	30	10	2.2	1
Sample Amount [µmol]	0.15	0.30	0.40	0.50
Mass Sensitivity	~ 4	~ 2.8	~ 1.4	1
Experiment Time	1	2	8	16

⇨ **0.6 mg** of compound is enough to acquire all required 1D and 2D NMR spectra on a 1.7mm RT @ 400 MHz over the weekend

Small Volume NMR Probes: 1.7mm RT

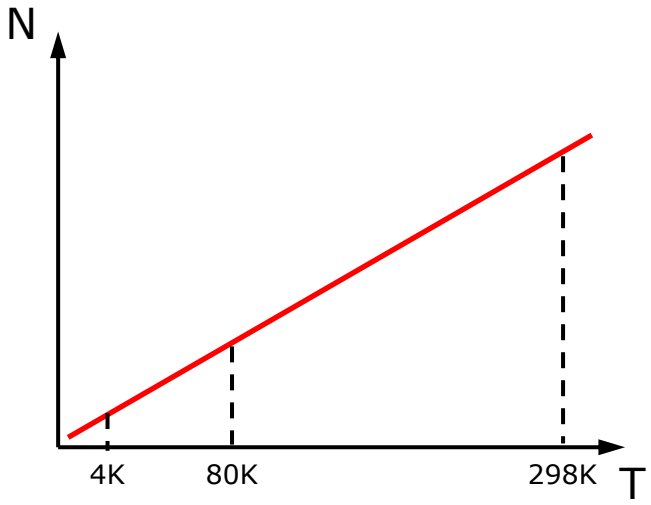


1D ^{1}H	1 scan
COSY	20 min
TOCSY	45 min
NOESY	4 h
HSQC	10 min
HMBC	3.5 h
H2BC	4 h
1D ^{13}C	8 h

120µg of a Steroid (≈ 350g/mol) in 30µl (≈ 11mM) < 24 h on 600MHz

Cryogenic NMR Probes

<u>benefit of cryogenic NMR probes: decrease noise</u>



$$S/N \sim \frac{M \cdot B_0}{\sqrt{R_c(T_c + TPA) + R_s(T_s + TPA)}}$$

M:	magnetization
B_0:	static field
R_c:	'resistance in coil'
R_s:	'resistance in sample'
T_c:	coil temperature
T_s:	sample temperature
TPA:	preamplifiers equivalente noise temperature

cooling NMR coil reduces electronic noise ⇨ increases signal/noise

Cryogenic NMR Probes: huge selection

He cooled

CryoProbes	400	500	600	700	800	850	900	950	1000
DCH C-H-D	✓	✓	✓	✓					
TCI H-C/N-D	✓	✓	✓	✓	✓	✓	✓	✓	✓
TCI H-C/N-D 1.7mm		✓	✓	✓	✓	✓			
QCI H/P-C/N/D		✓	✓	✓	✓	✓			
QCI H/F-C/N/D		✓	✓	✓					
TXO C/H-N-D		✓	✓	✓	✓				
DUX 2H		✓	✓	✓	✓	✓			
DUL-C-H-D 10mm	✓	✓	✓						
BBFO		✓							
BBO H&F	✓	✓	✓	✓					

N_2 cooled

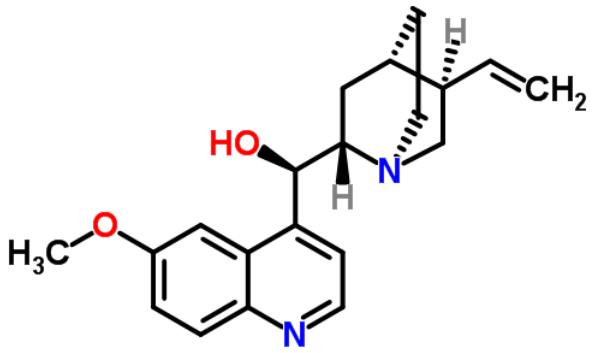
CryoProbe Prodigy	400	500	600	700
Prodigy BBO	✓	✓	✓	
Prodigy TCI		✓	✓	✓

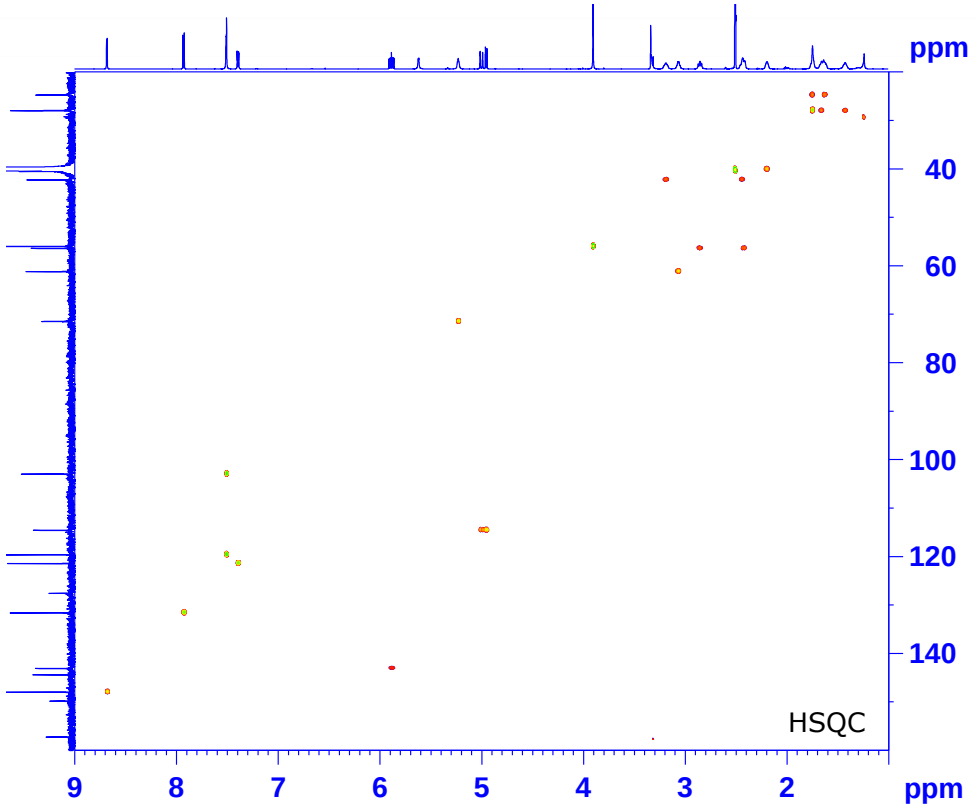
Highest Versatility: BBO CryoProbe

- ^{13}C sensitivity 4 * BBO RT
- ^{15}N sensitivity 4 * BBO RT
- ^{1}H sensitivity 3 * BBO RT
- observe and inverse detection
- cold preamplifiers for BB/^{1}H/^{2}H
- z-gradient
- ATM compatible
- 0 ° – 80 °C (standard sample temperature range)
- available for 400 – 700 MHz

Maximum Carbon Sensitivity: DCH

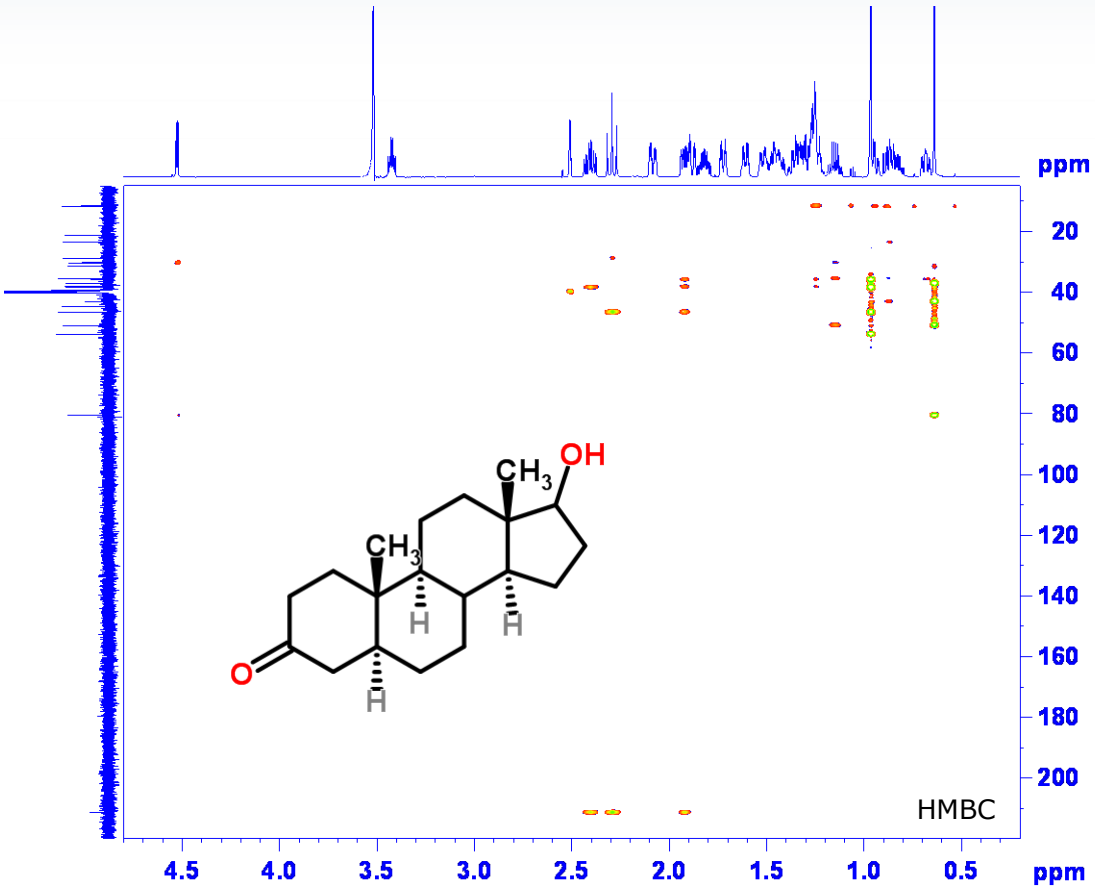
1D ^{1}H	1 min
HSQC	10 min
1D ^{13}C	30 min





0.5mg of Quinine (≈ 225mol/l) in 600µl (≈ 2.4mM) on 700MHz

Maximum Mass Sensitivity: 1.7 CryoProbe

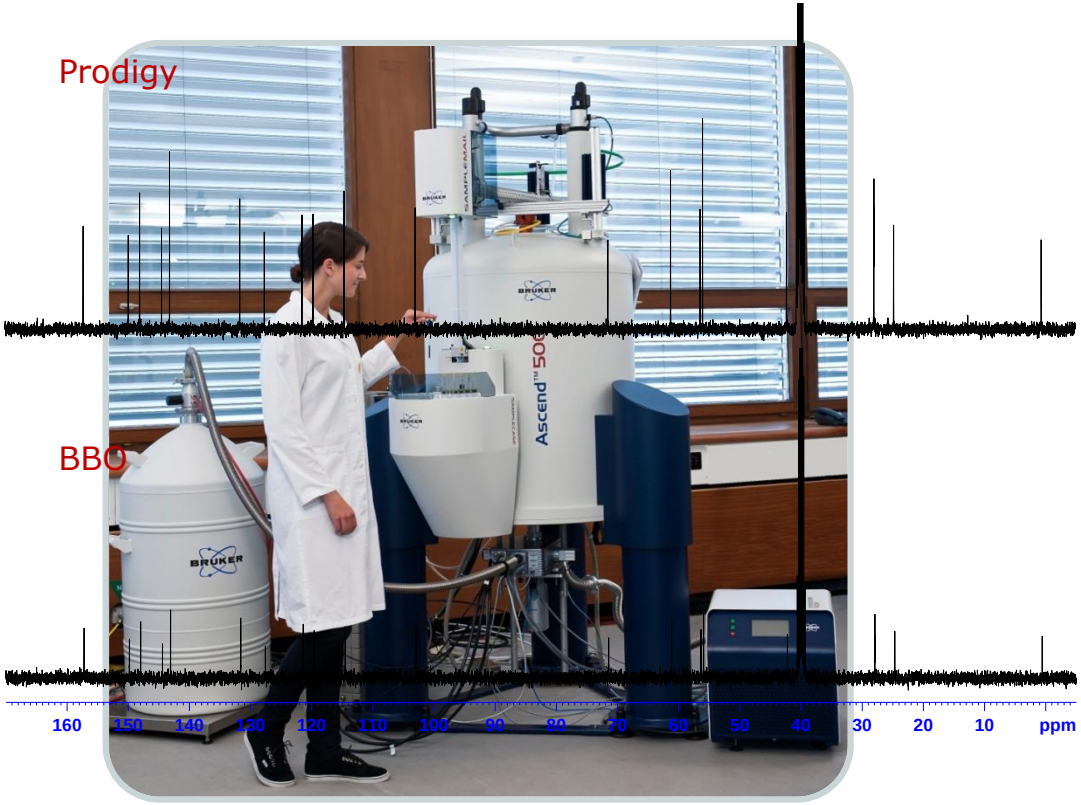


1D ^{1}H	1 scan
HSQC	5 min
HMBC	10 min
1D ^{13}C	40 min

120µg of a Steroid (≈ 350g/mol) in 30µl (≈ 11mM) < 2 h on 600MHz

CryoProbe Prodigy

CryoProbe Prodigy: alternative at medium field



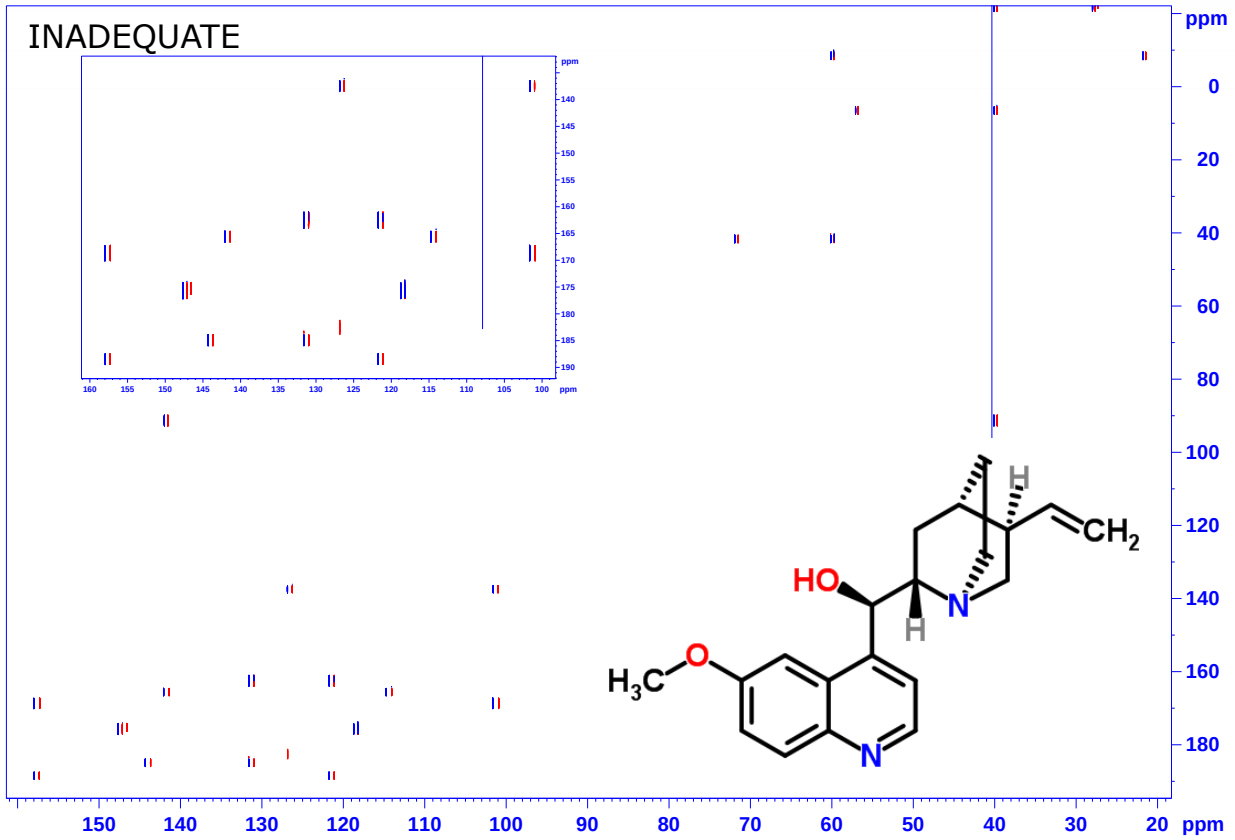
50mM Quinine, 32 scans

- liquid nitrogen for cryo-cooling
- small footprint

- Prodigy BBO
- Prodigy TCI

⇨ ^{13}C sensitivity 2-3 * BBO

CryoProbe Prodigy: ^{13}C sensitivity



17.5mg of Quinine (≈ 225g/mol) in 600µl (≈ 100mM): expt. time 16 h

Summary NMR Probes

small volume probes

⇨ increasing mass sensitivity

- 1.7mm RT
- 1mm RT

cryogenic probes

⇨ decrease noise and increase signal/noise

<u>N_2 cooled</u>

- Prodigy ⇨ sensitivity boost at affordable price

<u>He cooled</u>

- BBO ⇨ highest versatility
- DCH ⇨ highest carbon sensitivity
- 1.7mm ⇨ highest mass sensitivity

NMR – Workflow for Structure Elucidation

1D Proton, 1D Carbon
functional groups

⇩

2D HSQC
$^{1}J_{CH}$ correlation (CH, CH_2, CH_3)

⇩

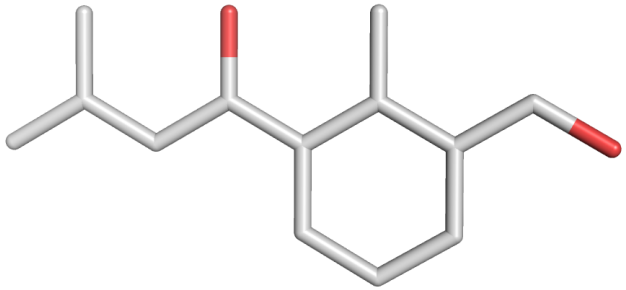
2D COSY
$^{3}J_{HH}$ correlation

⇩

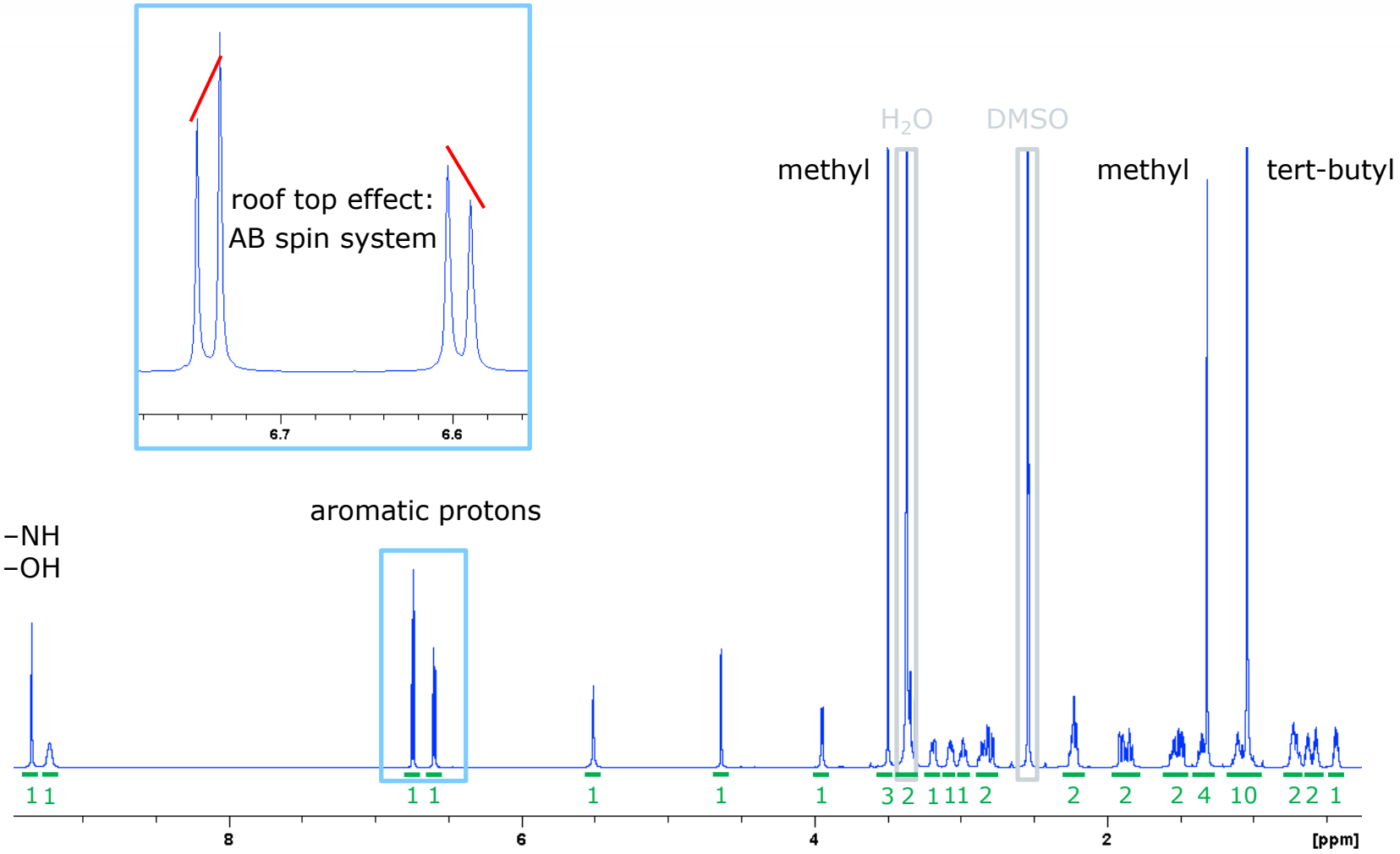
2D HMBC, 2D TOCSY
$^{2}J_{CH}$/$^{3}J_{CH}$ correlation, spin system

⇩

2D ROESY, 2D NOESY
through space correlation



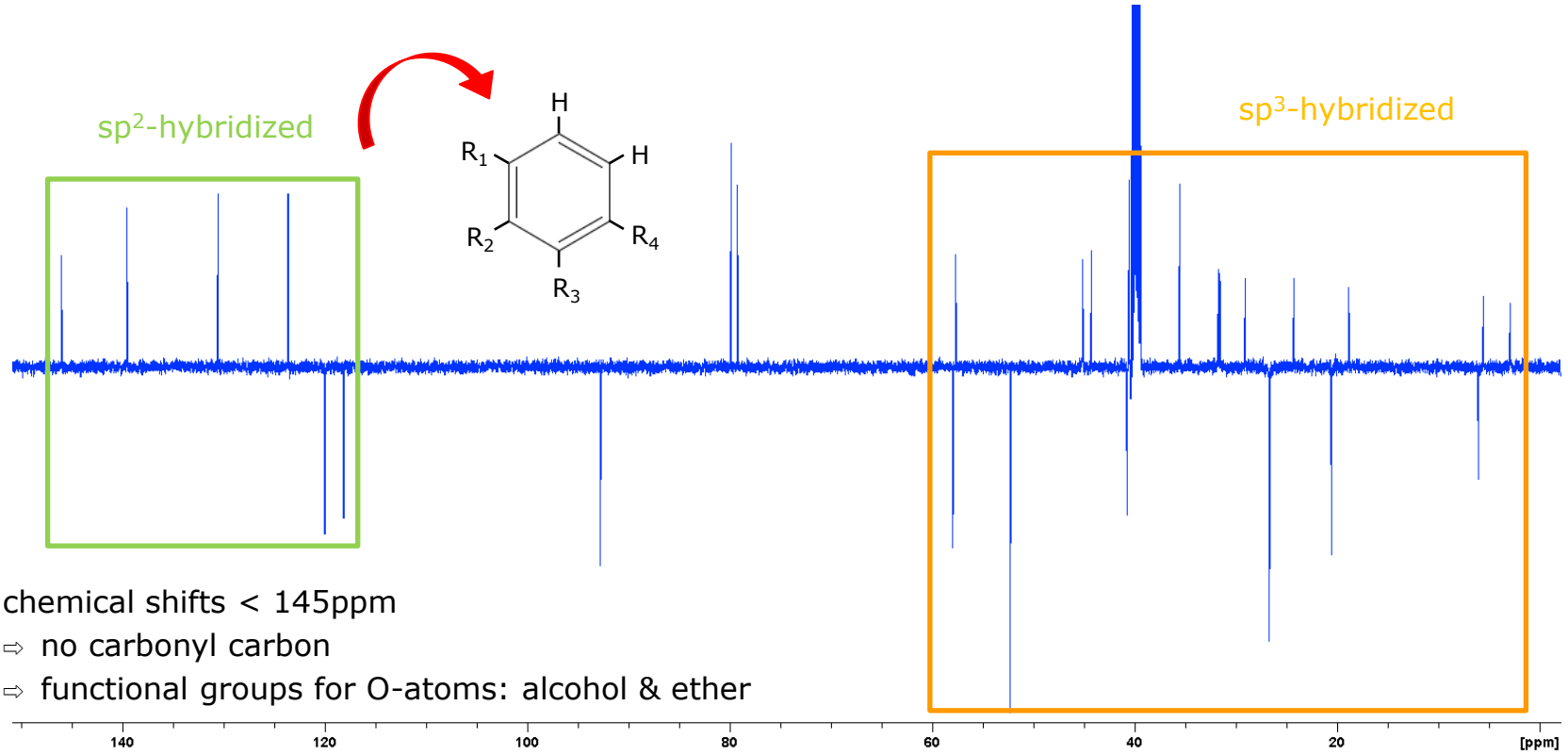
NMR Spectroscopy – 1D Proton



NMR Spectroscopy – 1D Carbon

APT (**A**ttached **P**roton **T**est) spectrum for assigning multiplicities in ^{13}C spectra

- ⇨ positive signals: CH_2-groups & quaternary C
- ⇨ negative signals: CH-groups & CH_3-groups



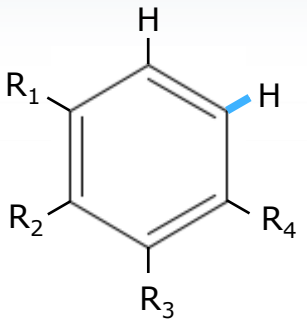
chemical shifts < 145ppm

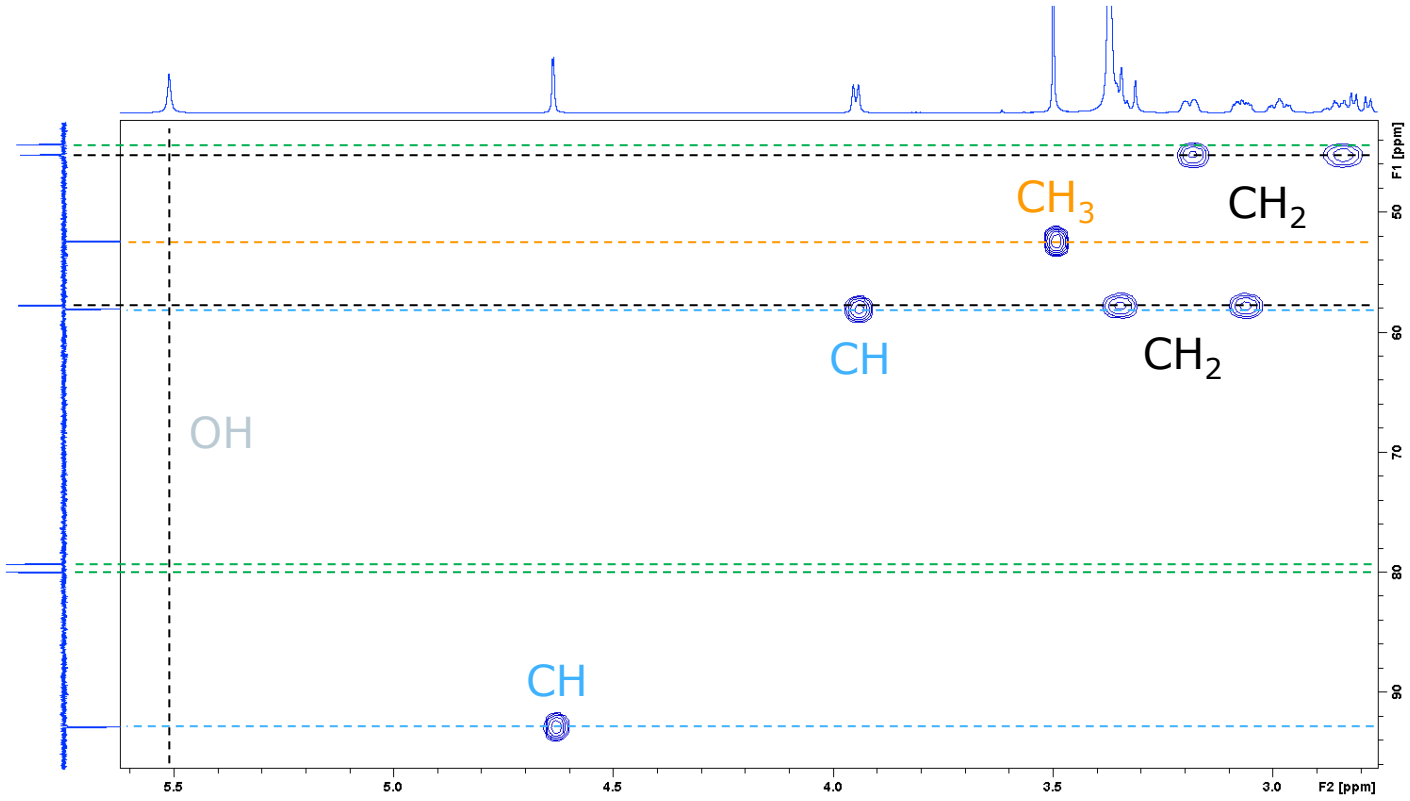
- ⇨ no carbonyl carbon
- ⇨ functional groups for O-atoms: alcohol & ether

NMR Spectroscopy – 2D HSQC

HSQC spectrum ⇨ $^{1}J_{CH}$ correlation

(identifying protons & carbons that are bound to each other)





⇨ 5x CH_3

9x CH_2

4x CH sp^3

2x CH sp^2

5x C sp^3

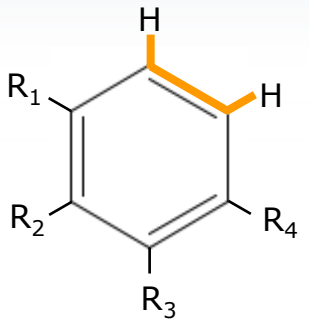
4x C sp^2

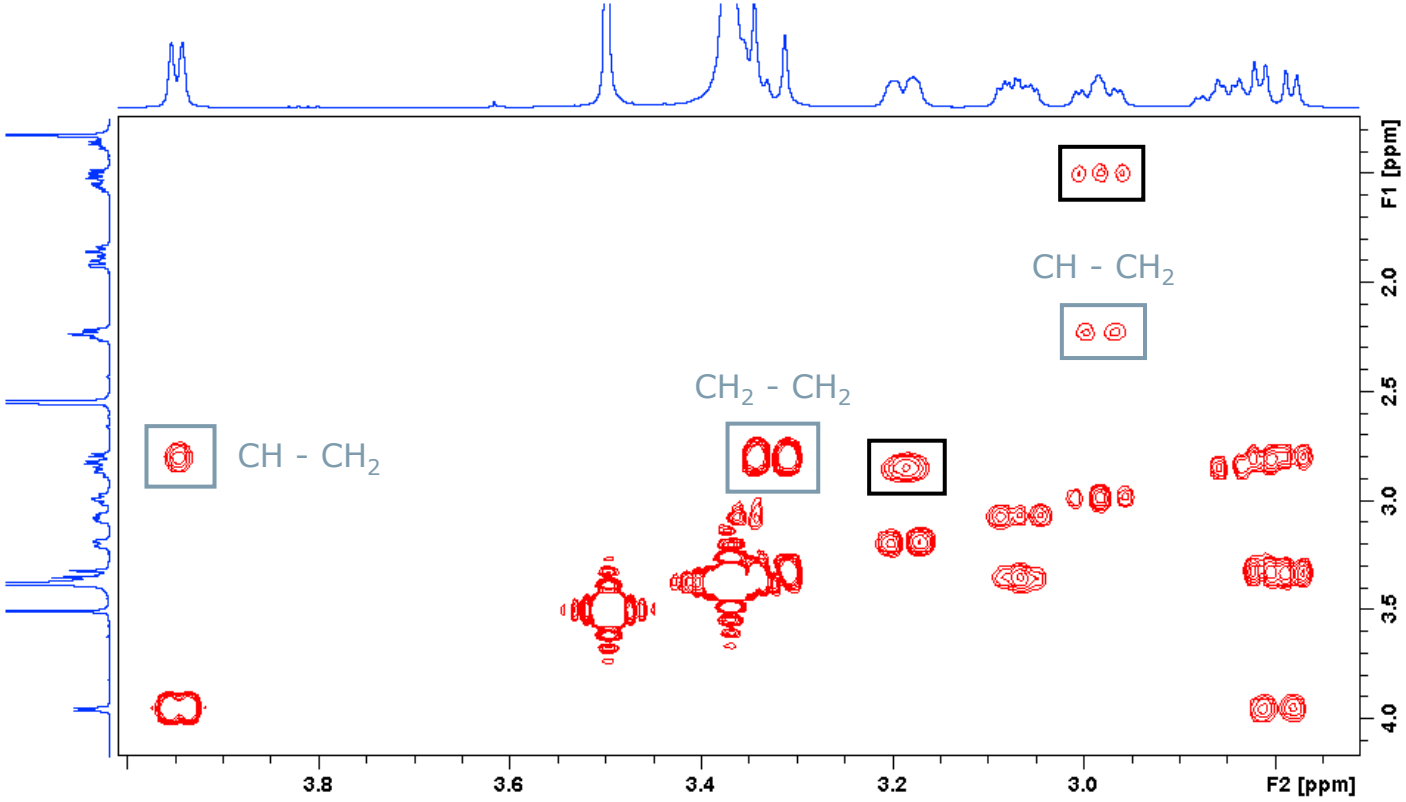
2x OH/NH

NMR Spectroscopy – 2D COSY

COSY spectrum ⇨ $^{3}J_{HH}$ correlation

(identifying CH_x-fragments that are covalently bound)





geminal correlations

⇨ no additional information

vicinal correlations

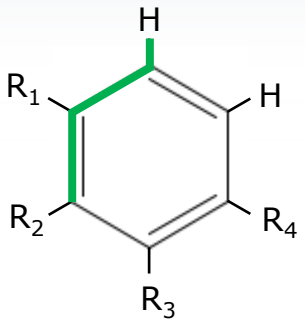
⇨ covalently bound CH_x-fragments

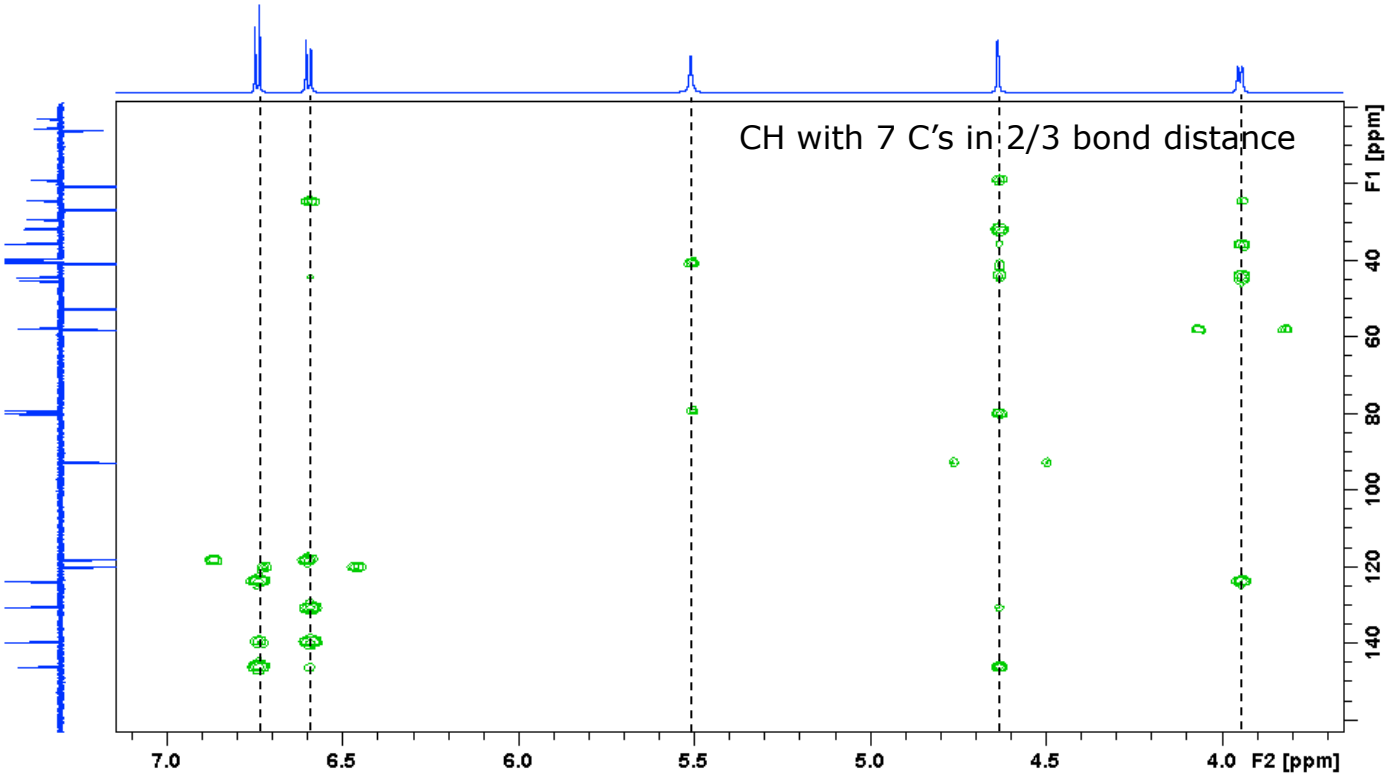
NMR spectra by courtesy of Wim Vermeulen, Johnson & Johnson

NMR Spectroscopy – 2D HMBC

HMBC spectrum ⇨ $^{2}J_{CH}/^{3}J_{CH}$ correlation

(connecting CH_x- fragments with neighbored carbons)





⇨ information about quaternary carbons

Putting together the fragments

1D Proton, 1D Carbon
functional groups

⇩

2D HSQC
$^{1}J_{CH}$ correlation (distinguish CH, CH_2, CH_3)

⇩

2D COSY
$^{3}J_{HH}$ correlation

⇩

2D HMBC, 2D TOCSY
$^{2}J_{CH}$/$^{3}J_{CH}$ correlation, spin system

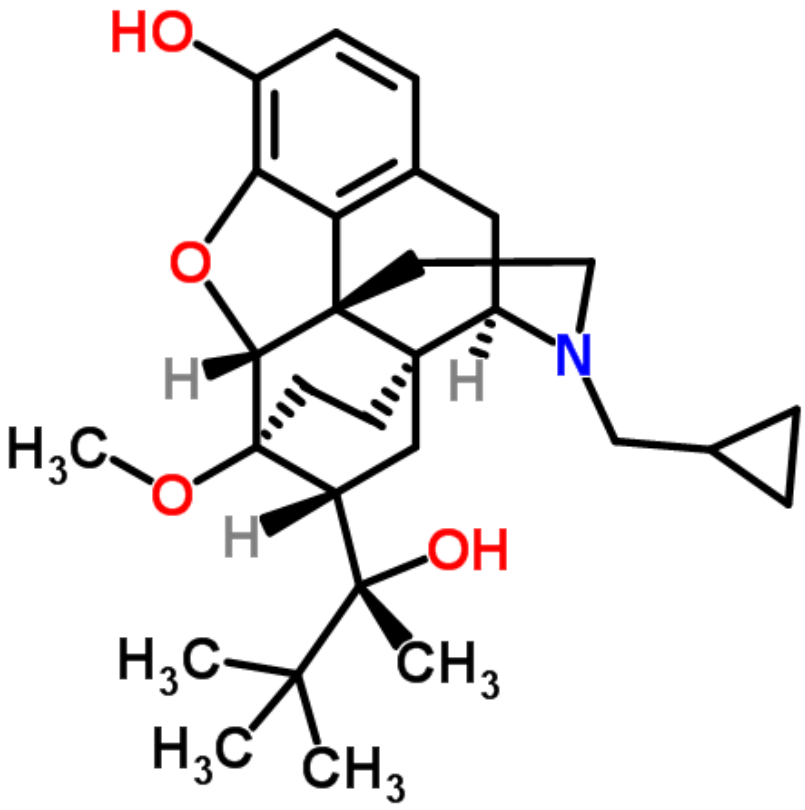
application of the rule of double-bond equivalents (DBE):

- 10 DBE for $C_{29}H_{41}NO_4$
- 3 DBEs C=C

⇨ 7 ring closure left for $C_{29}H_{41}NO_4$

NMR Spectroscopy – 2D Structure

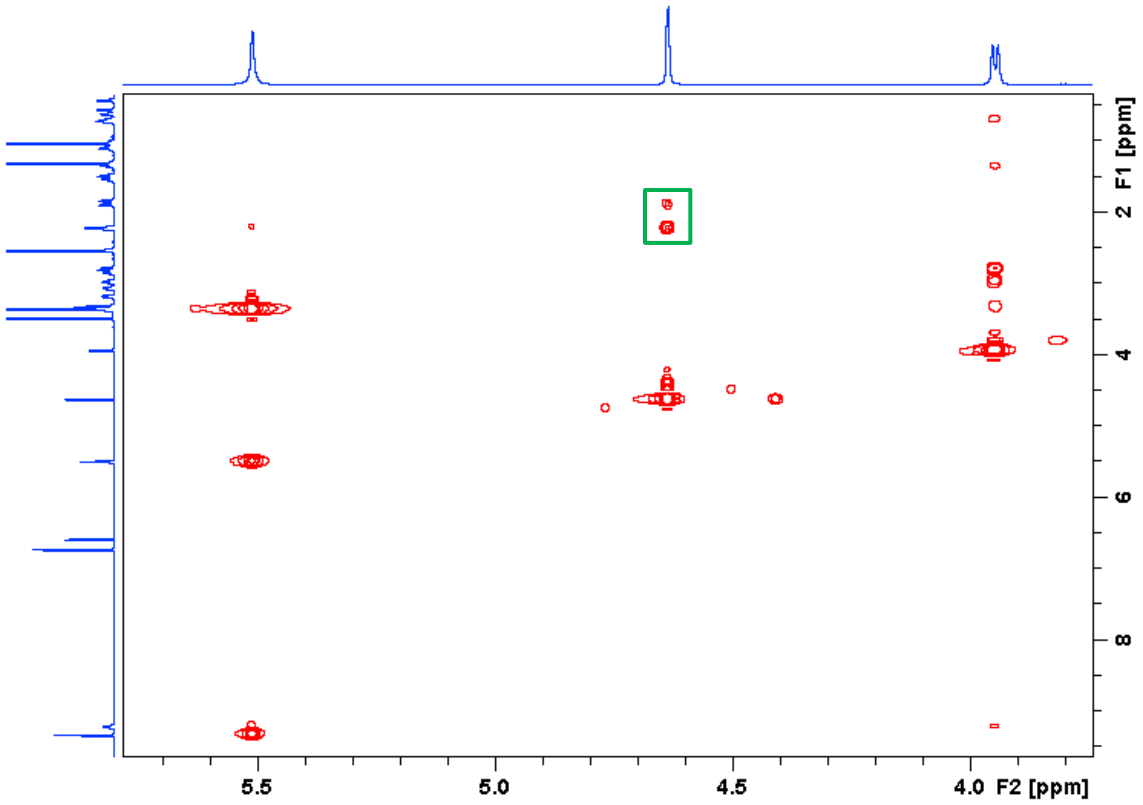
… after quite some detective work …

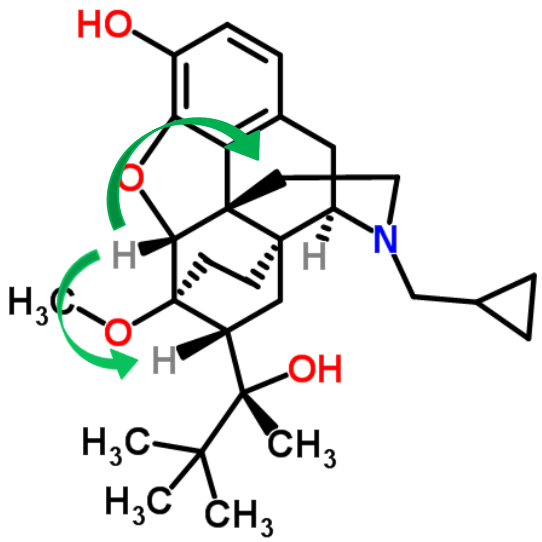


NMR Spectroscopy – 2D NOESY

ROESY / NOESY spectrum ⇨ through space correlation

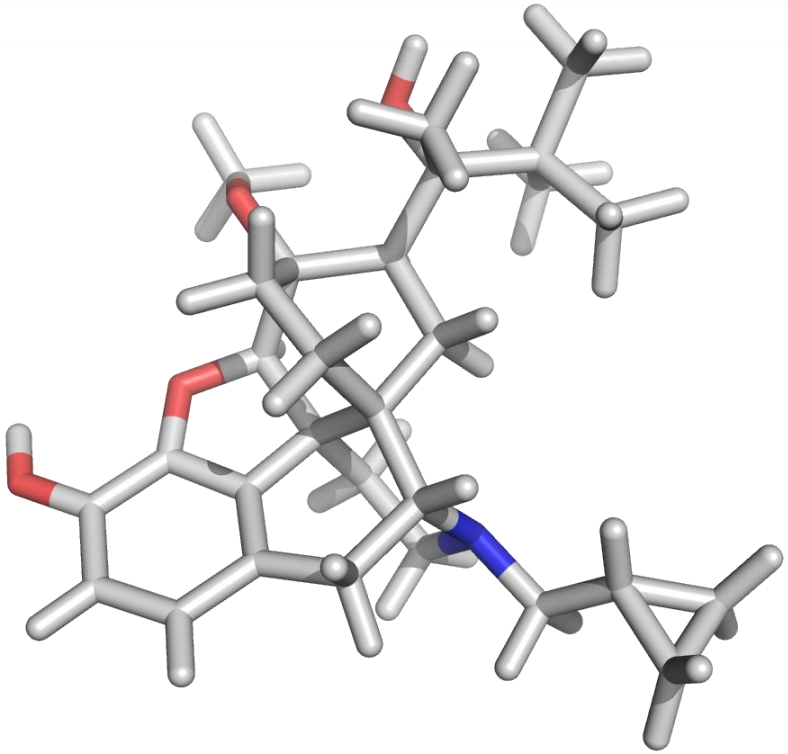
(stereochemistry and 3D structure)





NMR Spectroscopy – 3D Structure

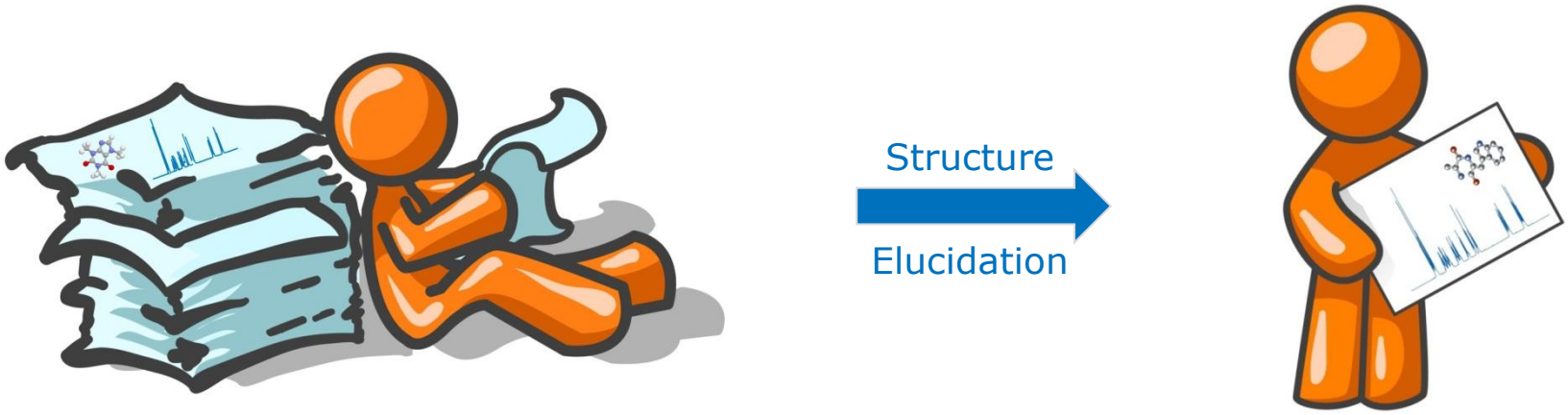
3D structure of Buprenorphine



⇨ small volume NMR probes allow acquisition of all 1D & 2D spectra required for structure elucidation on only **0.6** mg of compound within one weekend

Computer Assisted Structure Elucidation

structure elucidation is a time-consuming and challenging task



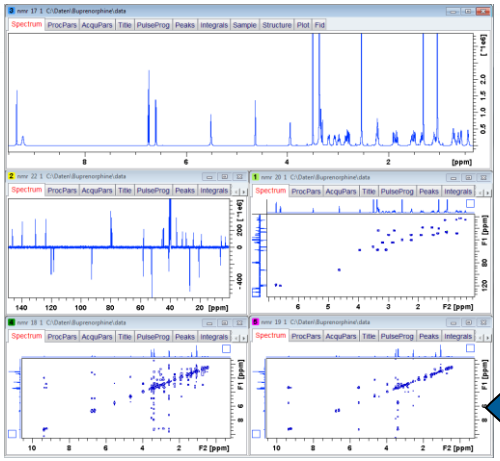
a lot of analytical data have to be analyzed in order to find the right structure

⇨ computer assisted data interpretation

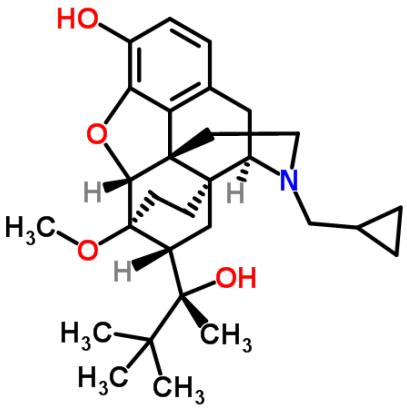
for small organic molecule NMR: ***CMC-se***

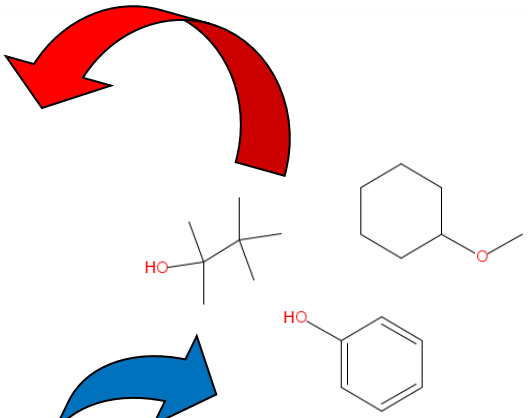
Manual Structure Elucidation

Acquired Data



Generate Structure





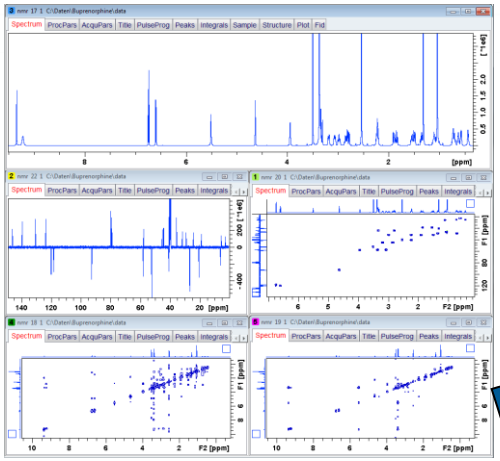
Identify Fragments

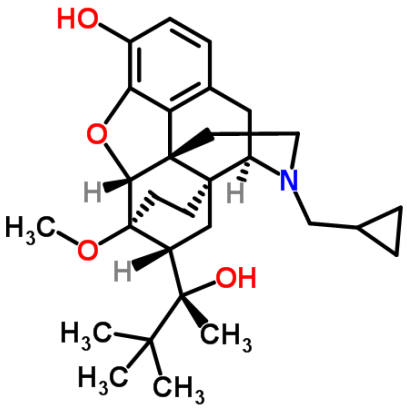
Extract Information

#	^{13}C chem. shift	^{1}H chem. shift	Equivalent	Hybridization	Func. group	HMBC	COSY
21	26.69	1.04	3	sp^3	tert-butyl	16, 9	
12	52.31	3.49		sp^3	methoxy	8	
5	120.01	6.59		sp^2	aromatic	2, 3, 22	
6	118.15	6.74		sp^2	aromatic	1, 2, 4	
18	31.73	2.23		sp^2		3, 7, 14	13
18’	31.73	1.90		sp^2		3, 7, 14	13
15	40.78	2.22		sp^3		7, 8, 9, 23, 24	19

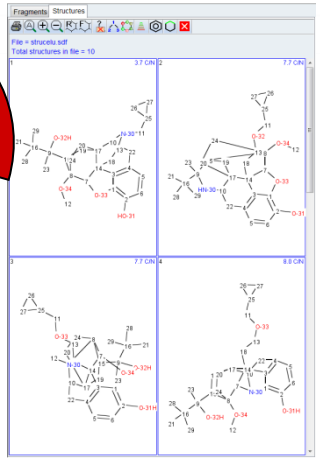
CMC-se – Assisted Structure Elucidation

Acquired Data





Structure Evaluation



Structure Generation

Populates Table

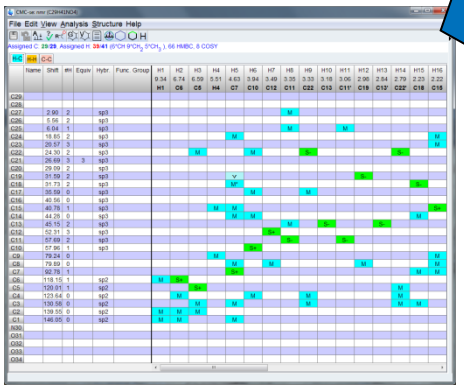
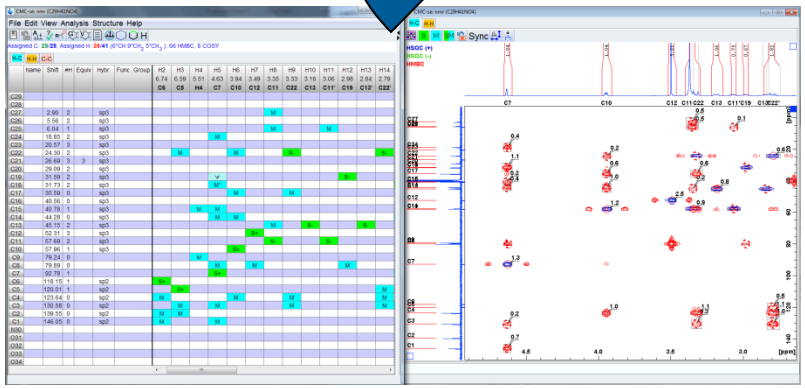
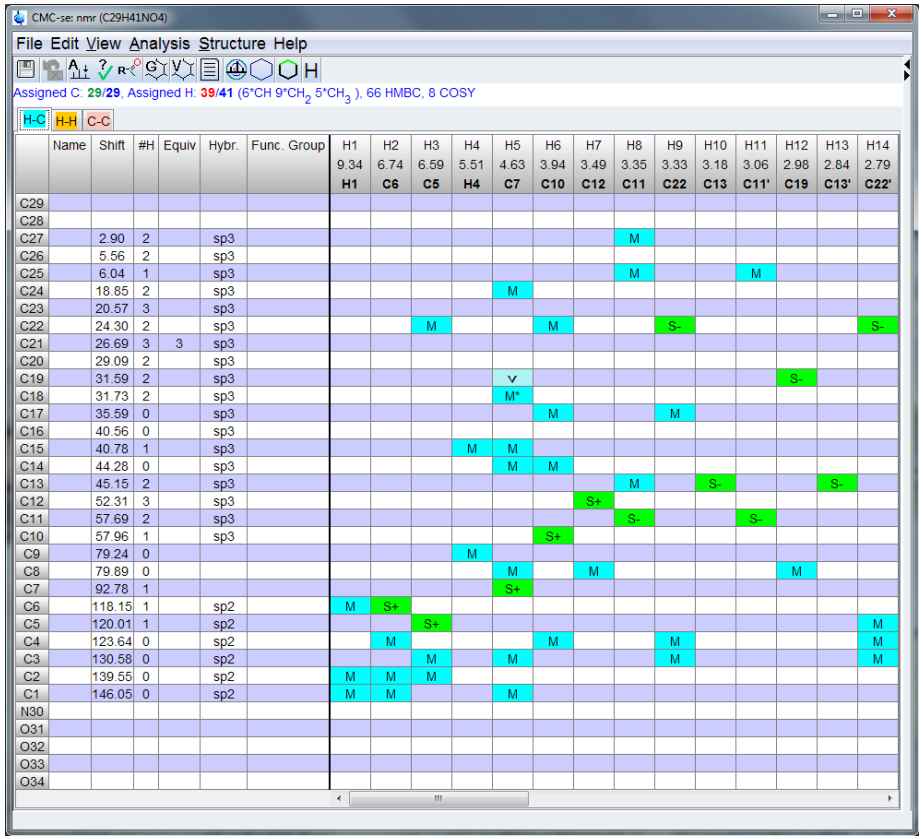


Table Refinement



CMC-se – Assisted Structure Elucidation

The Correlation Table



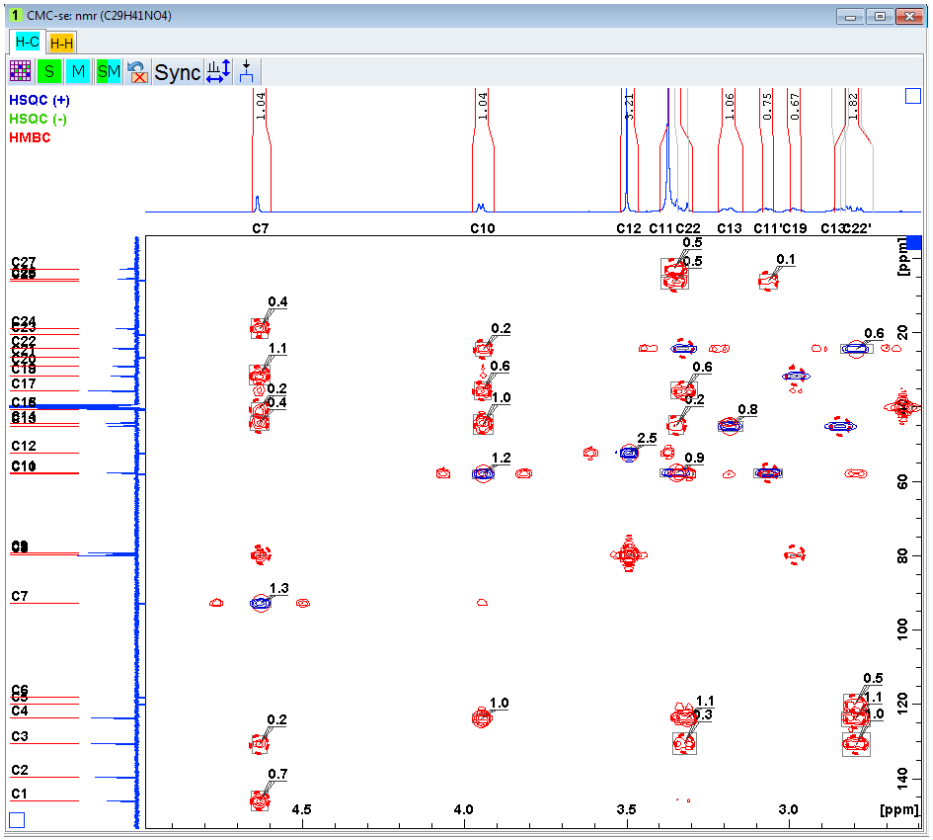
	Name	Shift	#H	Equiv	Hybr.	Func. Group	H1 9.34 H1	H2 6.74 C6	H3 6.59 C5	H4 5.51 H4	H5 4.63 C7	H6 3.94 C10	H7 3.49 C12	H8 3.35 C11	H9 3.33 C22	H10 3.18 C13	H11 3.06 C11'	H12 2.98 C19	H13 2.84 C13'	H14 2.79 C22'
C29																				
C28																				
C27		2.90	2		sp3									M						
C26		5.56	2		sp3															
C25		6.04	1		sp3									M			M			
C24		18.85	2		sp3						M									
C23		20.57	3		sp3															
C22		24.30	2		sp3				M			M			S-					S-
C21		26.69	3	3	sp3															
C20		29.09	2		sp3															
C19		31.59	2		sp3						v							S-		
C18		31.73	2		sp3						M*									
C17		35.59	0		sp3							M			M					
C16		40.56	0		sp3															
C15		40.78	1		sp3					M	M									
C14		44.28	0		sp3						M	M								
C13		45.15	2		sp3									M		S-			S-	
C12		52.31	3		sp3								S+							
C11		57.69	2		sp3									S-			S-			
C10		57.96	1		sp3							S+								
C9		79.24	0							M										
C8		79.89	0								M		M					M		
C7		92.78	1								S+									
C6		118.15	1		sp2		M	S+												
C5		120.01	1		sp2				S+											M
C4		123.64	0		sp2			M				M			M					M
C3		130.58	0		sp2				M		M				M					M
C2		139.55	0		sp2		M	M	M											
C1		146.05	0		sp2		M	M			M									
N30																				
O31																				
O32																				
O33																				
O34																				

- automatically populated
- all atoms from the molecule included as rows or columns
- filled in cells indicated the presence of correlations
- fully editable by the user
- convenient way for organizing the data for structure elucidation

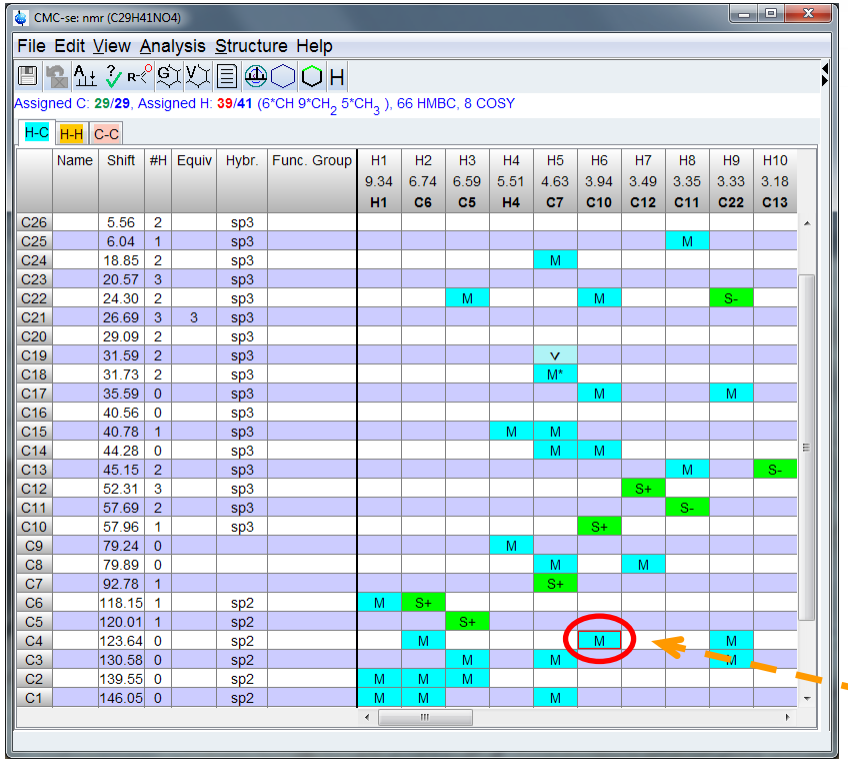
CMC-se – Assisted Structure Elucidation

The Combined Spectra Display

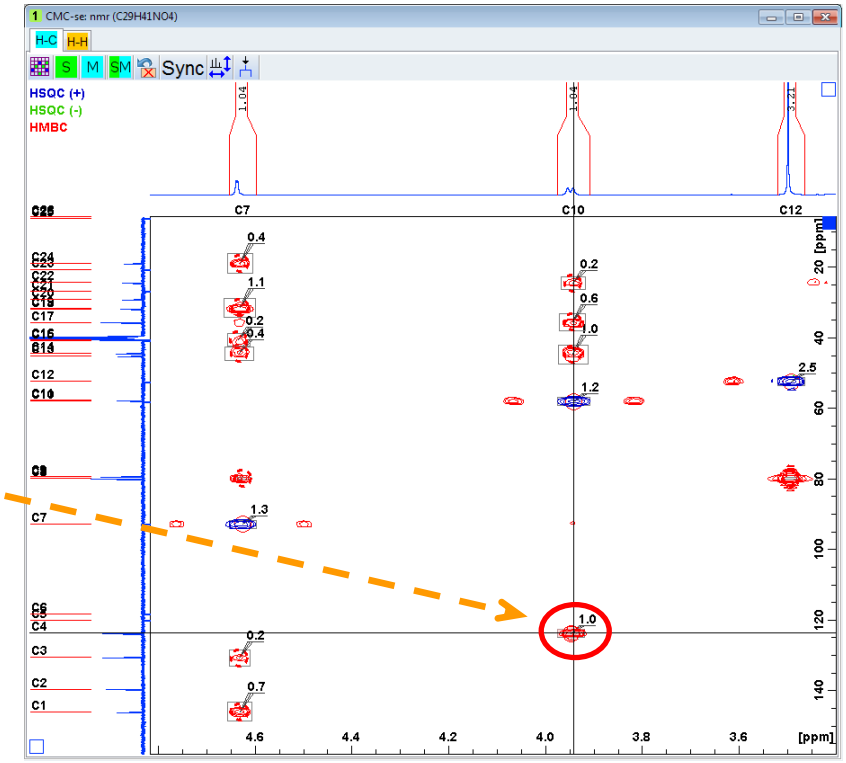
- all data from the project included in a single screen
- all automatically picked peaks are displayed
- manual corrections to the automatic data analysis are possible through this window
- correlated cursor between all windows for data evaluation



CMC-se – Assisted Structure Elucidation



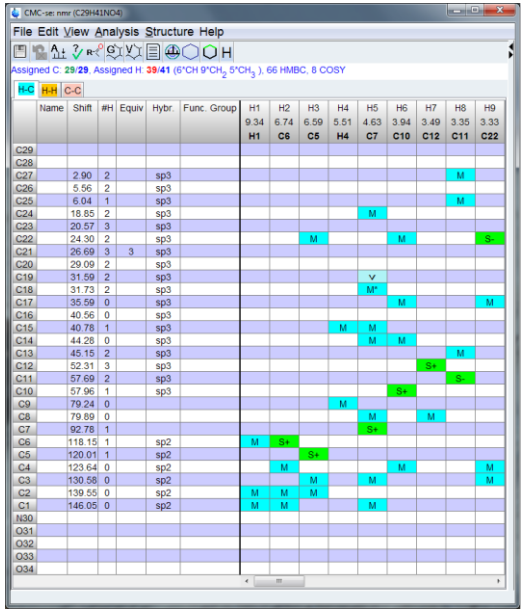
- clicking on a peak in the data results in that cell being highlighted in the table and vice versa



- modifications in the spectra display and correlation table are synchronized

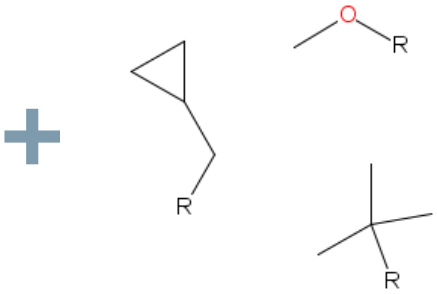
CMC-se – Assisted Structure Elucidation

NMR information



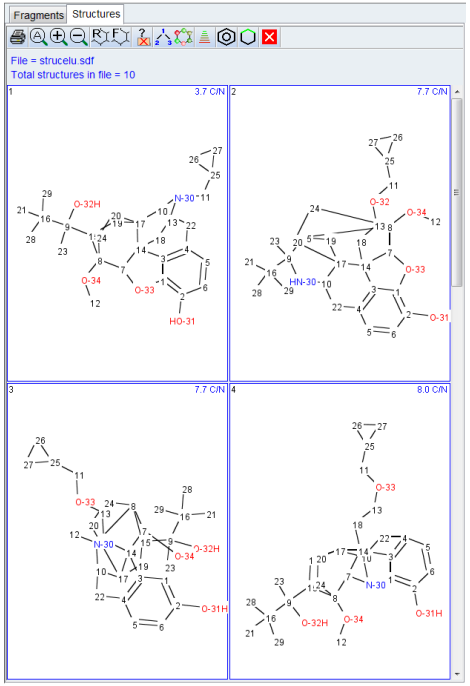
correlation table

MS information

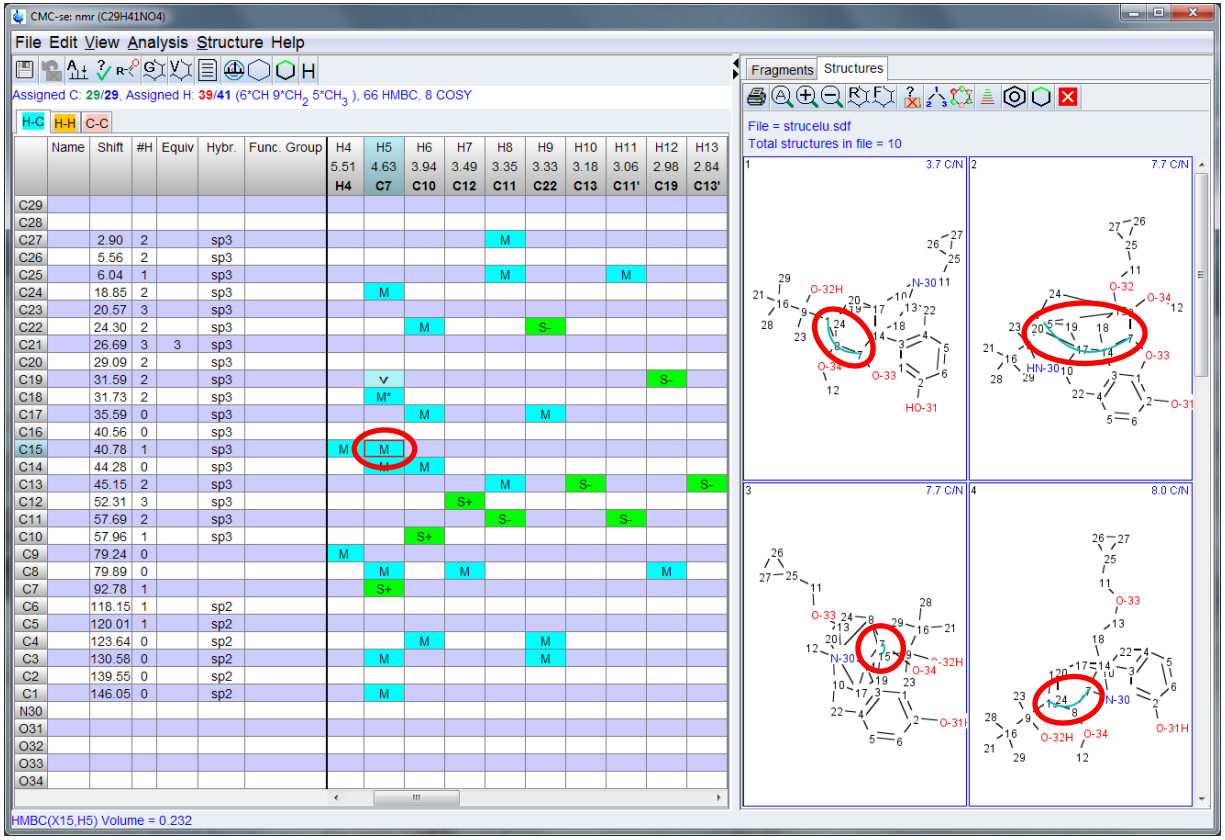


fragments (optional)

structure proposals



CMC-se – Assisted Structure Elucidation



- generated structures are linked to the correlation table
- individual or multiple correlations can be viewed on all structure proposals

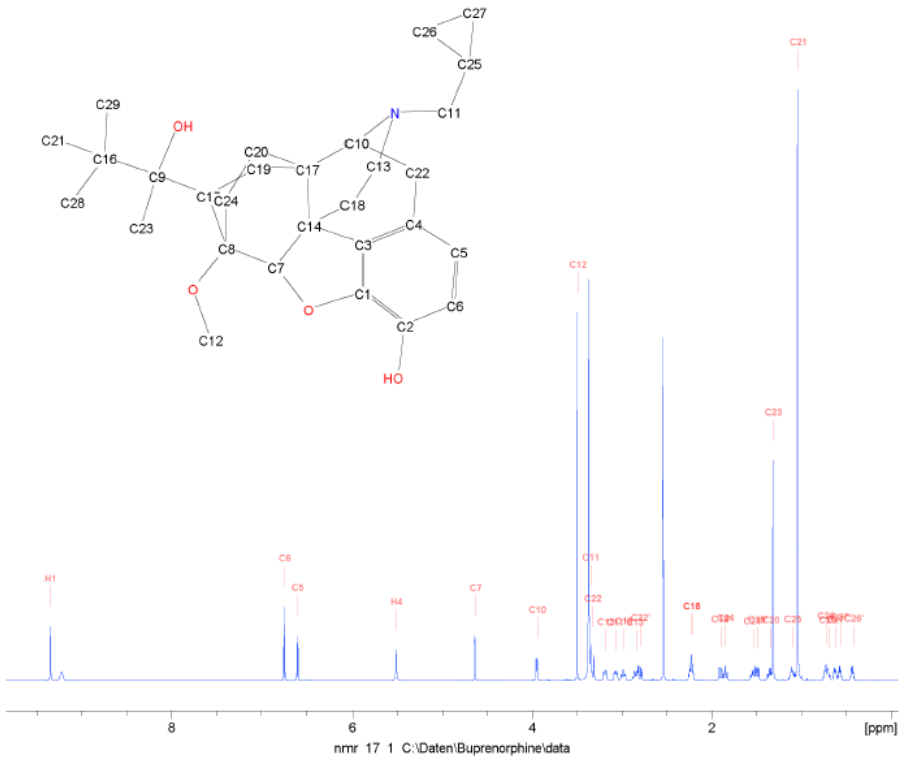
CMC-se – Assisted Structure Elucidation

Bruker Structure Elucidation Report

nmr (C:\Daten\Buprenorphine\data\nmr\strucelu)

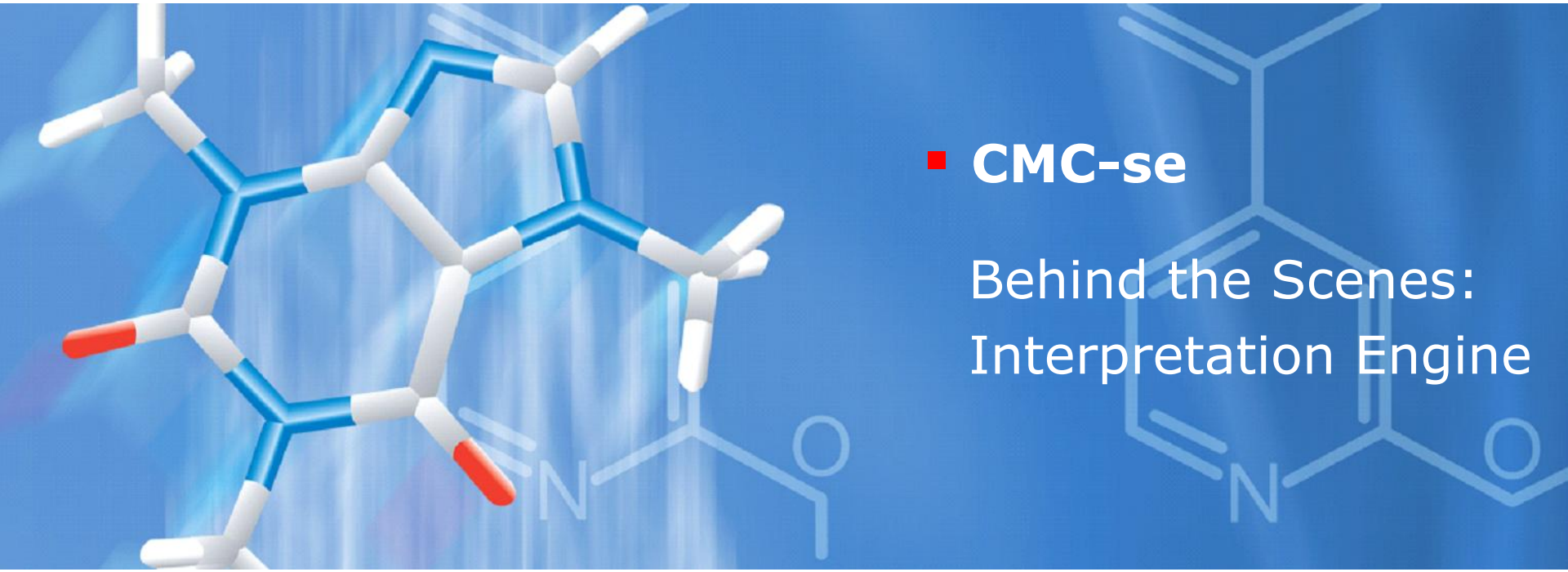
^{1}H table of assignments

Atom	Shift [ppm]	Multiplicty	Bound to	Correlation table
C26'	0.42		(C26)	H29
C27'	0.56		(C27)	H28
C27	0.62		(C27)	H27
C20'	0.70		(C20)	H26
C26	0.73		(C26)	H25
C21	1.04	s	(C21)	H24
C25	1.10		(C25)	H23
C23	1.31	s	(C23)	H22
C20	1.34		(C20)	H21
C19'	1.49		(C19)	H20
C24'	1.54		(C24)	H19
C24	1.85		(C24)	H18
C18'	1.90		(C18)	H17
C15	2.22		(C15)	H16
C18	2.23		(C18)	H15
C22'	2.79		(C22)	H14
C13'	2.84		(C13)	H13
C19	2.98		(C19)	H12
C11'	3.06		(C11)	H11
C13	3.18		(C13)	H10
C22	3.33		(C22)	H9
C11	3.35		(C11)	H8
C12	3.49	s	(C12)	H7
C10	3.94		(C10)	H6
C7	4.63		(C7)	H5
H4	5.51	s		H4
C5	6.59	d	(C5)	H3
C6	6.74	d	(C6)	H2
H1	9.34	s		H1



Aug 20, 2012 (9:07:30 AM)

Page 2 of 4

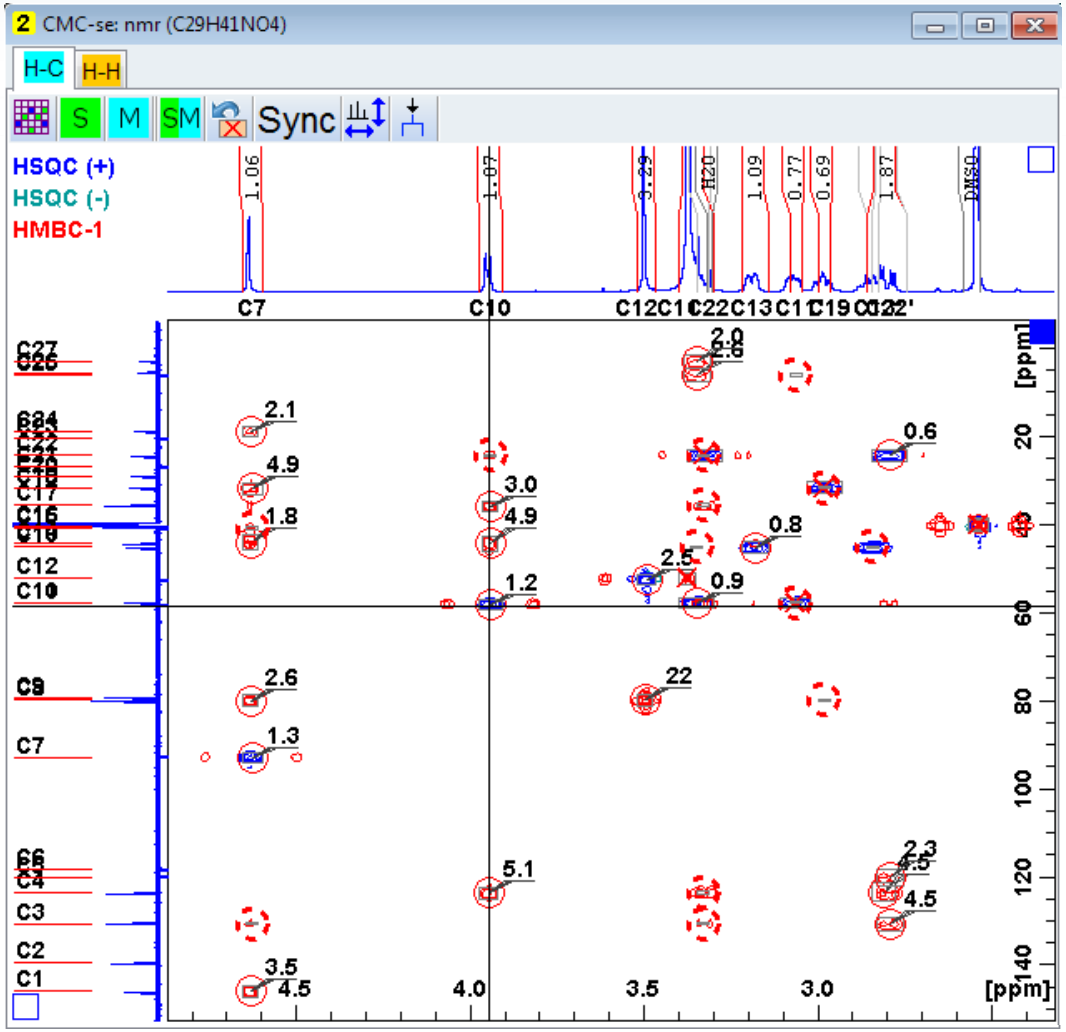


- **CMC-se**

Behind the Scenes:
Interpretation Engine

Automated Data Analysis

- S/N estimation
- peak picking
- artifact removal
- solvent signal search
- build correlation lists
- **find common frequencies**



Interpretation of NMR Constraints

^{1}H-^{13}C HSQC spectrum

- multiplicity edited
  - negative signals ⇨ CH_2-group
  - positive signals ⇨ CH- or CH_3-group
- quantitative
  - integration of peaks ⇨ distinguish CH- from CH_3-groups
  - integral check with 1D ^{1}H spectrum
- ^{13}C chemical shift
  - chemical shift < 60 ppm sp^3 hybridized
  - chemical shift > 100 ppm sp^2 hybridized

Interpretation of NMR Constraints

HSQC

1D Proton

1D Carbon

} proton distribution

carbon hybridization

molecular formula

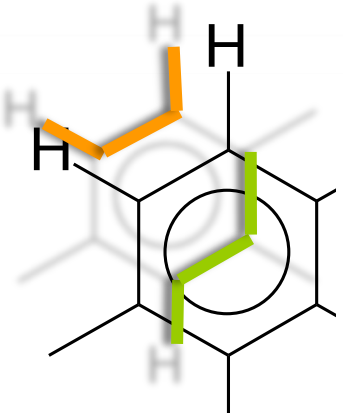
$C_{29}H_{41}NO_4$

⇨

- 5* CH_3 ⇨ sp^3 hybridized
- 9* CH_2 ⇨ 9* sp^3 / 0* sp^2 hybridized
- 6* CH ⇨ 4* sp^3 / 2* sp^2 hybridized
- 9* C ⇨ 5* sp^3 / 4* sp^2 hybridized

Interpretation of NMR Constraints

HMBC and COSY cross peaks for connection of heavy atoms



HMBC (required) ^{2}J – ^{3}J

COSY (optional) ^{3}J

- CH_3 ⇨ one neighboring carbon atom ⇨ 0-1 COSY, 0-2 HMBC correlations
- CH_2 ⇨ two neighboring carbon atoms ⇨ 0-2 COSY, 0-4 HMBC correlations
- …
- sp^2 hybridized carbon has to have a sp/sp^2 hybridized neighbor

Interpretation of NMR Constraints

- first bond correlation:

$H_3C - CH_2 - \Rightarrow$ COSY: $H_3C - CH_2 - CH =$

$\Rightarrow$ ^2J HMBC: $H_3C - CH_2 - CH -$

$\Rightarrow$ ^3J HMBC: $H_3C - X - CH_2 - X - CH -$

$H_3C - CH_2 - \Rightarrow$ COSY: $H_3C - CH_2 - CH =$

$\Rightarrow$ ^2J HMBC: $H_3C - CH_2 - CH -$

$\Rightarrow$ ^3J HMBC: $H_3C - CH_2 - X - CH -$

$H_3C - X - CH_2 - \Rightarrow$ COSY: $H_3C - X - CH_2 - CH =$

$\Rightarrow$ ^2J HMBC: $H_3C - X - CH_2 - CH -$

$\Rightarrow$ ^3J HMBC: $H_3C - X - CH_2 - X - CH -$

too few correlations:

only fragments build up

too many correlations:

even more possibilities

Interpretation of NMR Constraints

HSQC

1D Proton

1D Carbon

} proton distribution, carbon hybridization

HMBC

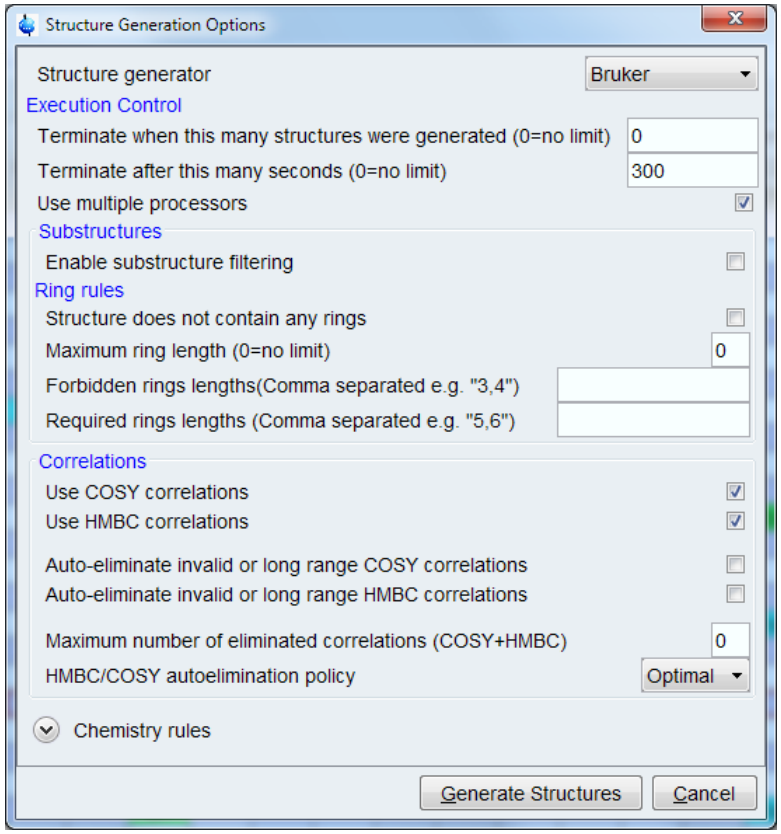
COSY

} atom connection

⇨

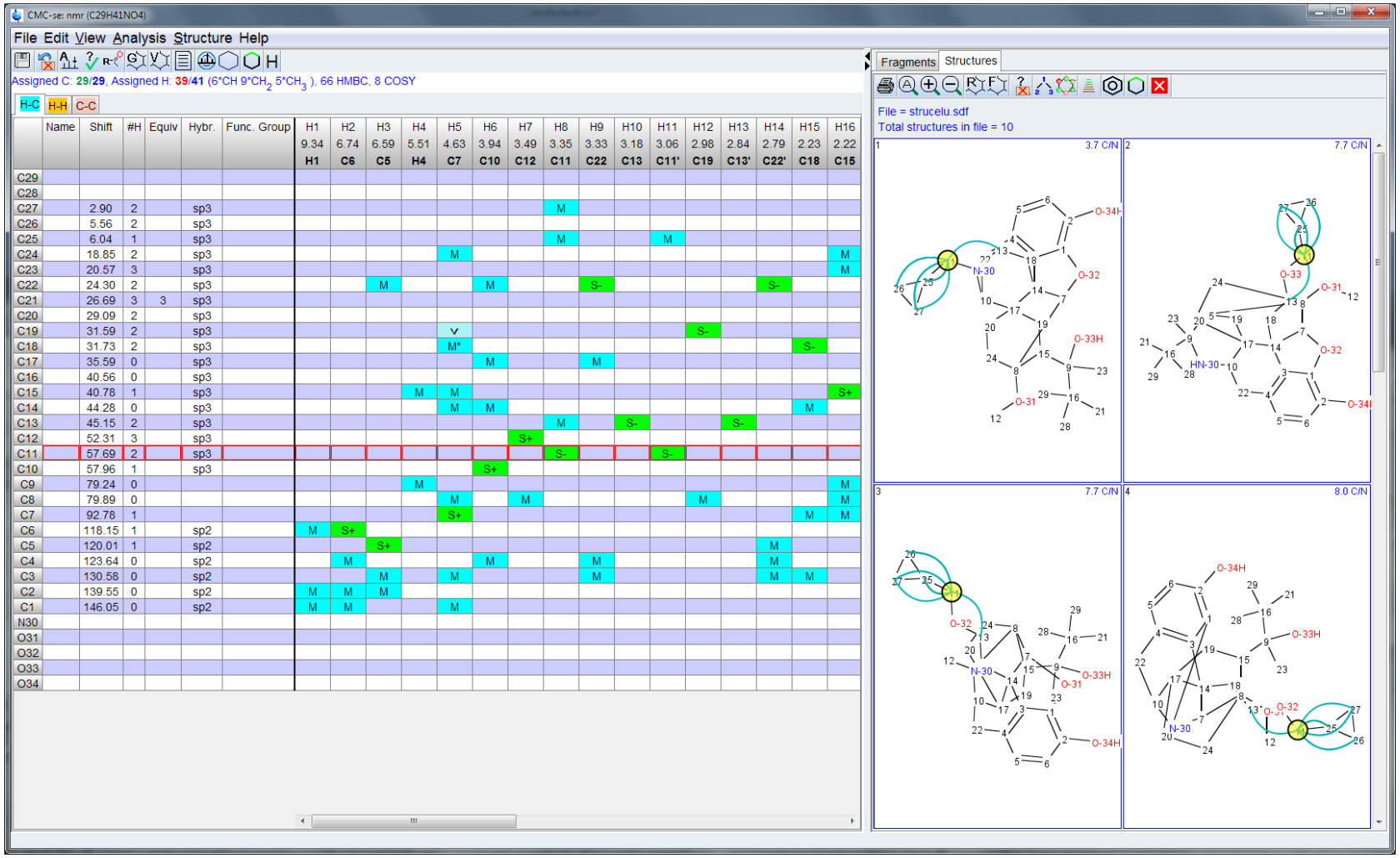
- HMBC correlations are essential to assemble a molecular structure from individual atoms
- number of structure proposals depends on the number of (ambiguous/unambiguous) correlations

Adjustments for Structure Generation



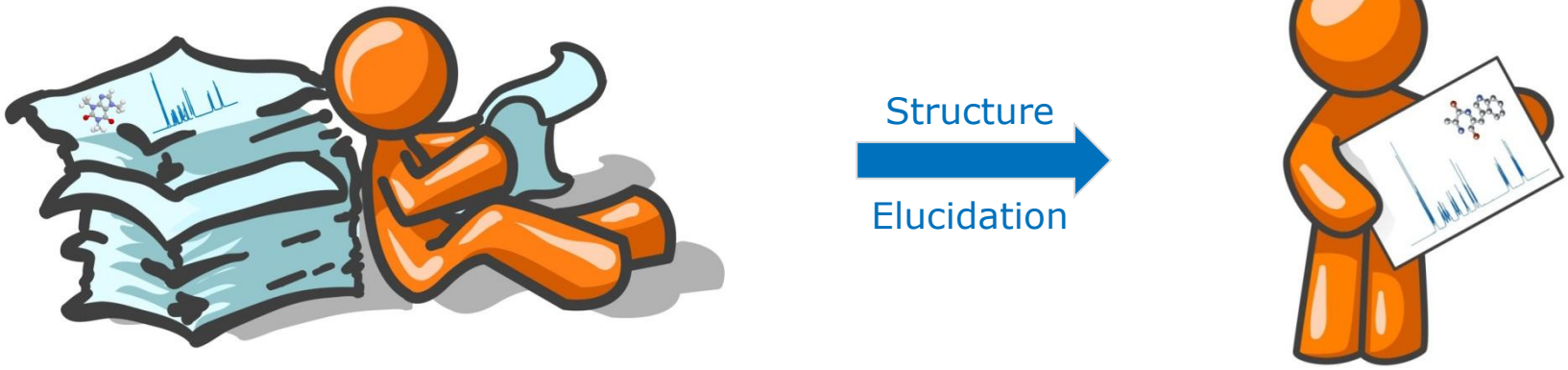
- long range correlations have to be taken into account
  - increasing number of correlations that are auto-eliminated by the software step by step
- information about rings length
- information about substructures (MS fragments)

Evaluating Structure Proposals



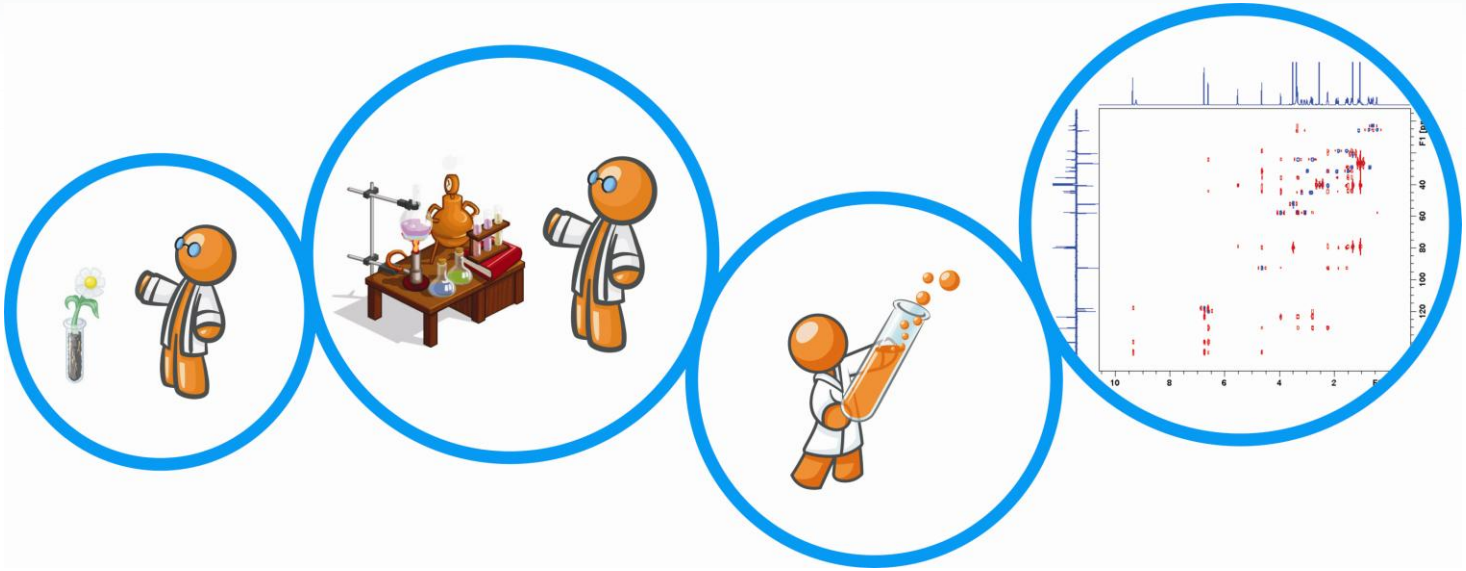
CMC-se – Assisted Structure Elucidation

as structure elucidation is a time-consuming and challenging task …



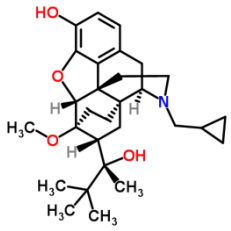
- CMC-se significantly speeds up the process of data analysis
- CMC-se organizes the workflow
- CMC-se generates structure proposals that all fit the experimental data

Structure Elucidation of Natural Products



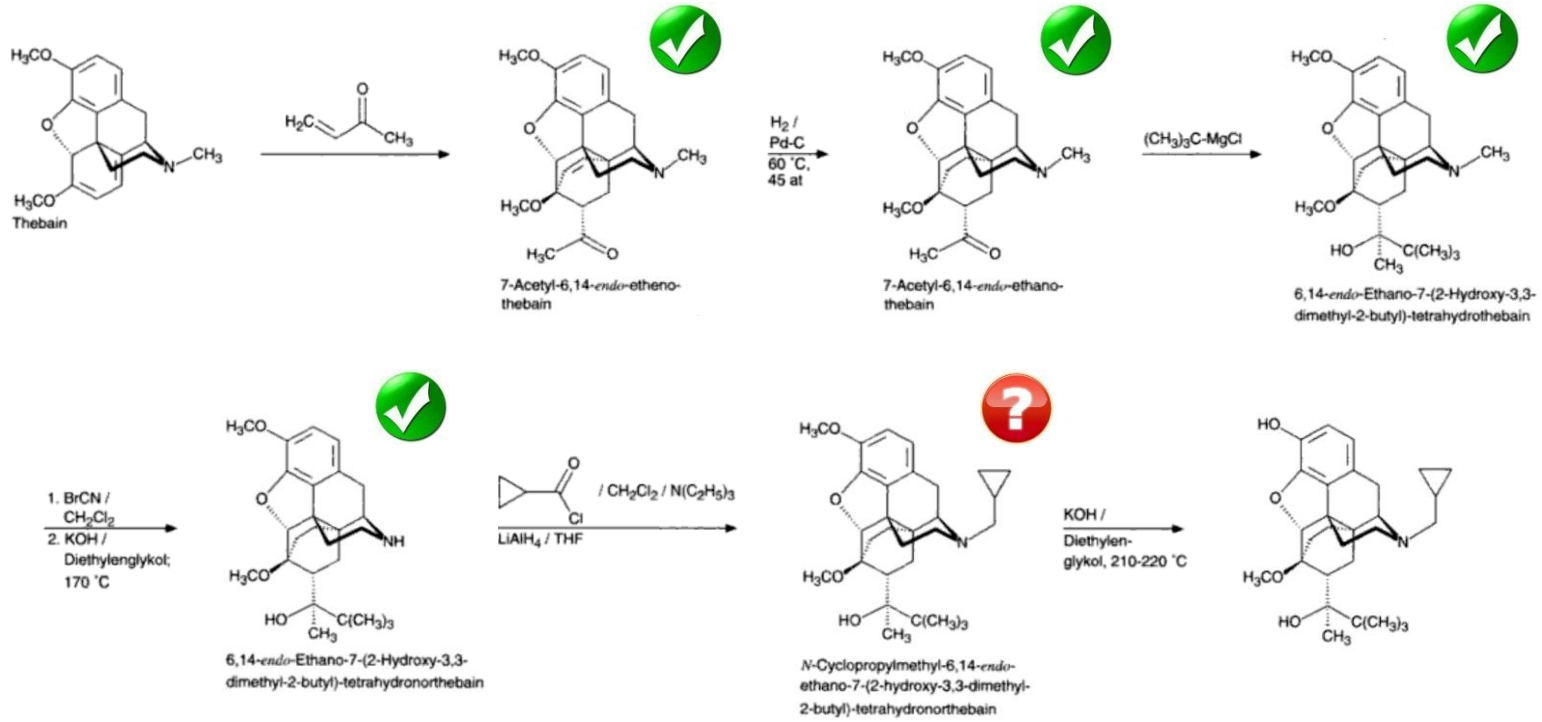
<u>characterization of unknown compound by NMR:</u>

structure elucidation based on 1D and 2D NMR spectra

⇨ 

⇨ synthesizing natural product

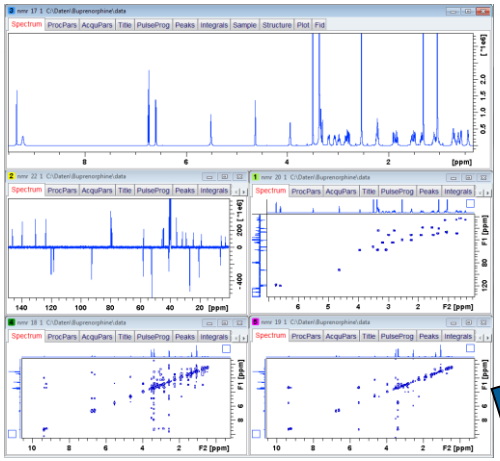
Synthesis of Buprenorphine



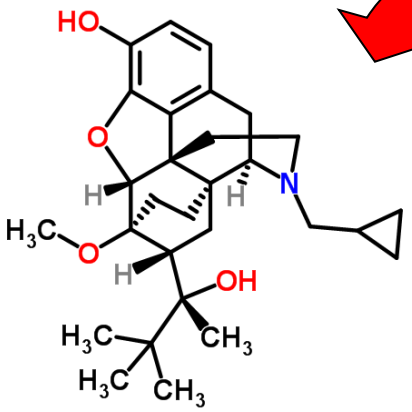
⇨ verifying synthesis steps by NMR

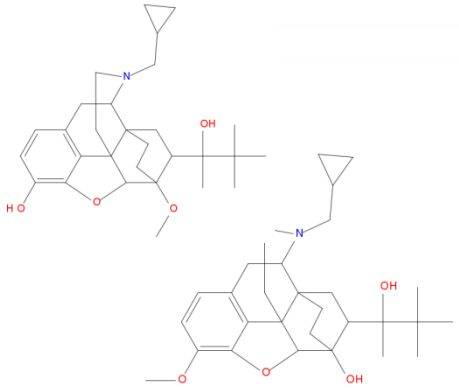
CMC-se – Assisted Structure Verification

Acquired Data



Structure Verification





Structure Proposals

Populates Table

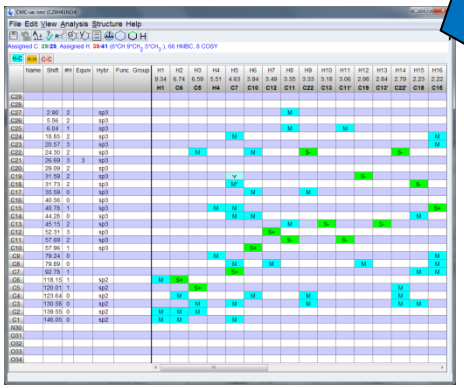
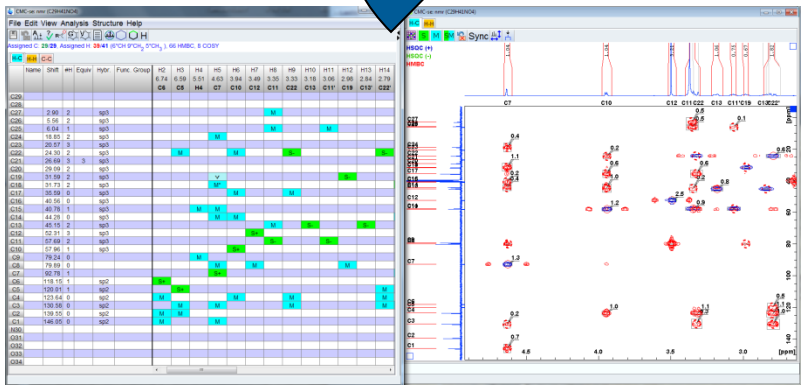
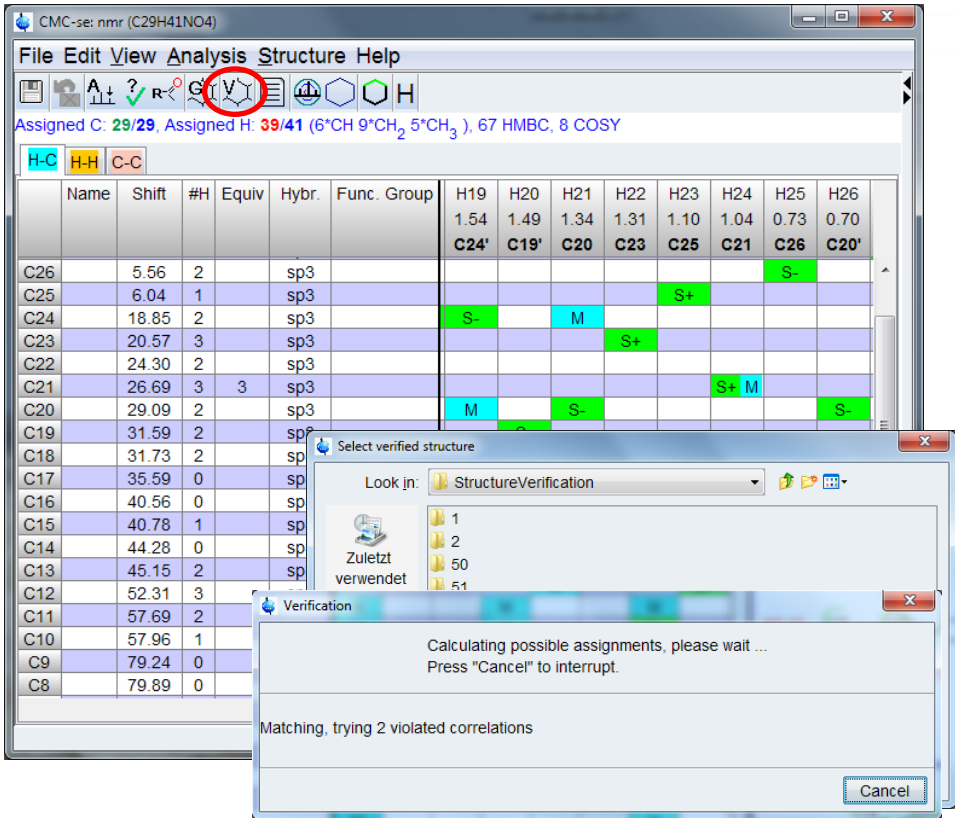


Table Refinement



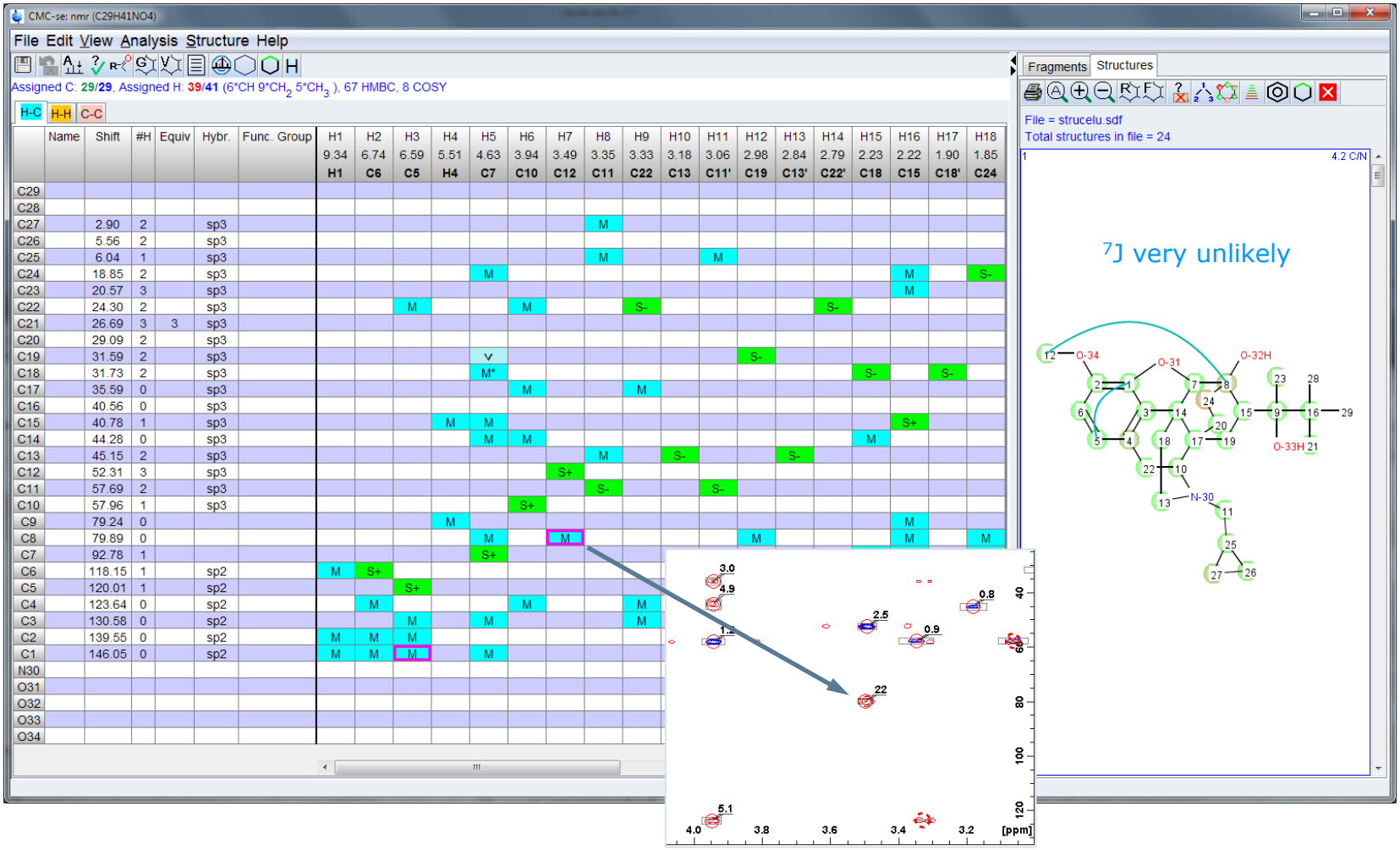
CMC-se – Assisted Structure Verification



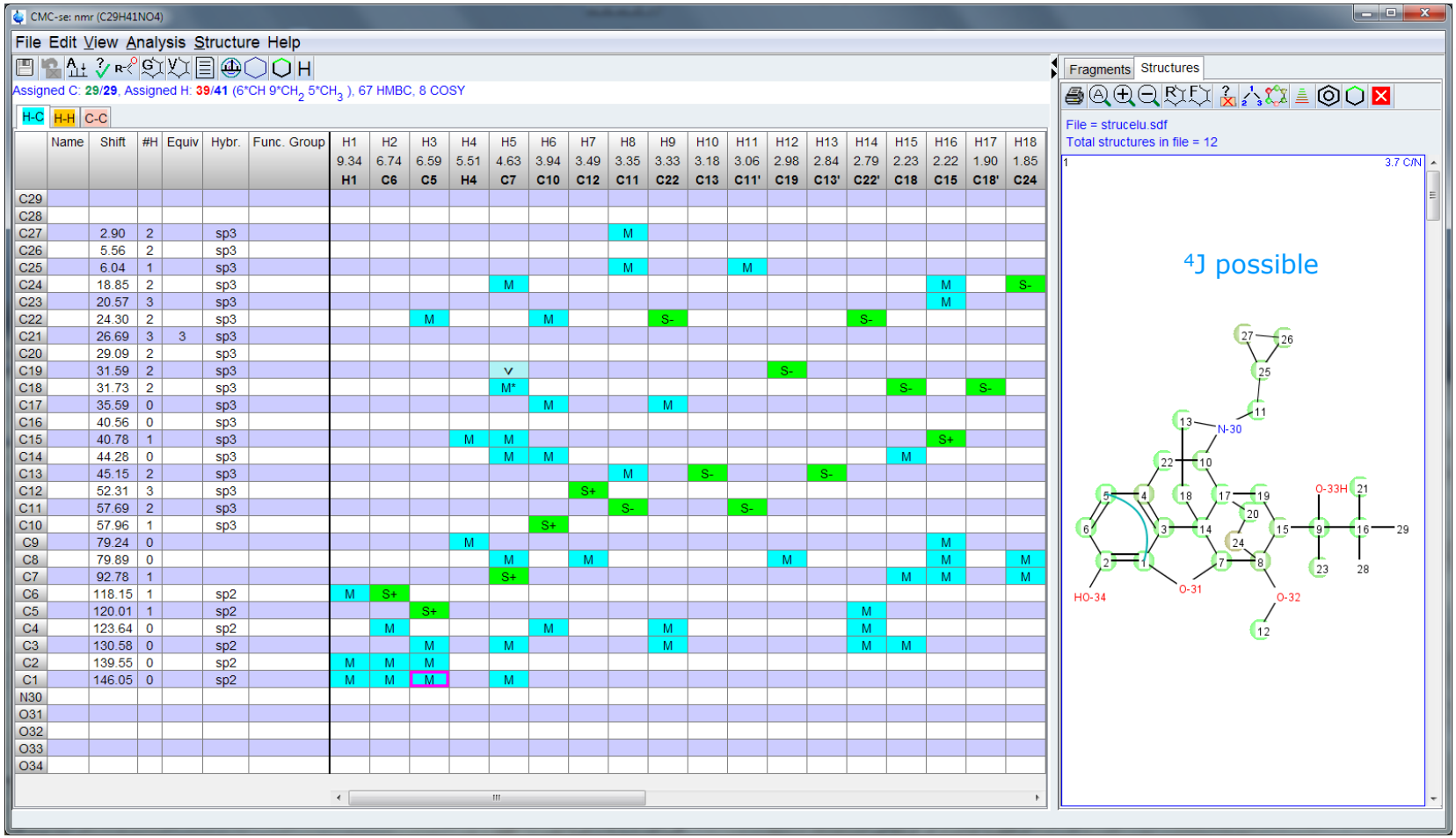
- provide project .sdf file
- perform automated verification
- manually inspect and refine correlation table
- perform automated spectra analysis
- manually inspect and refine correlation table

Verify structure proposals based on the correlation table

CMC-se – Assisted Structure Verification



CMC-se – Assisted Structure Verification

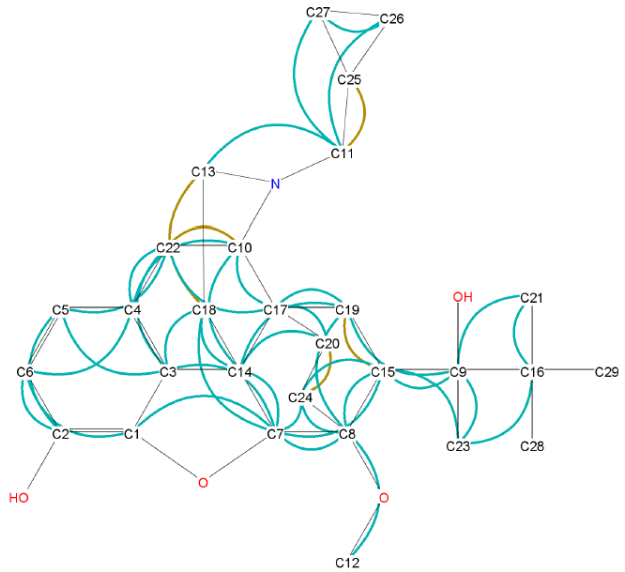


CMC-se – Assisted Structure Verification

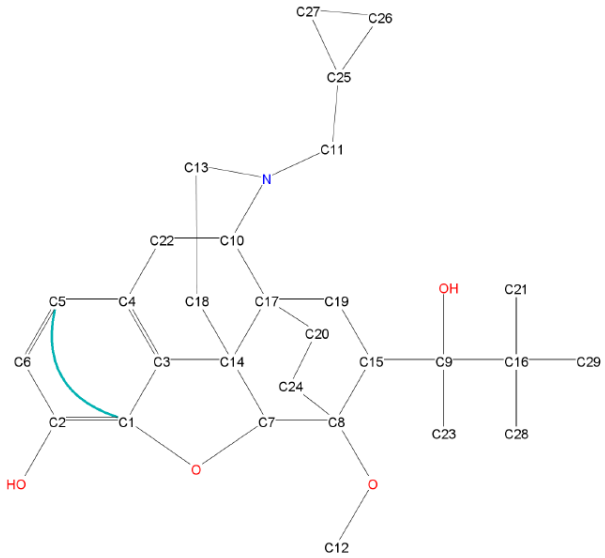
CMC-se Report

nmr (C:\Daten\Buprenorphine\data\nmr\strucelu)

Explained Correlations



Incorrect Correlations



Jul 9, 2013 (8:43:16 AM)

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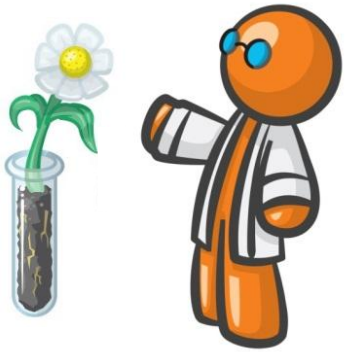
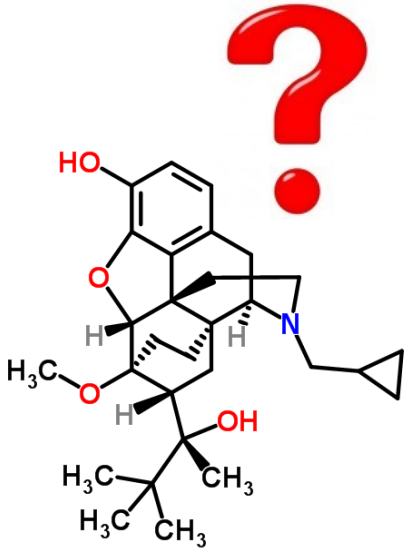
CMC-se – Assisted Structure Verification



Synthesized Compound



Structure Verification

Input:

- full set of NMR spectra
- molecular structures

Output:

- possible assignment

Summary Tools for Structure Elucidation

mass spectrometry:

- ADC digitizer technology for accurate mass determination
- software package SmartFormula:
  - analysis of accurate mass and TIP for MS and MS/MS

NMR spectroscopy:

- small volume probes: increase mass sensitivity
- cryoProbes: decrease noise and thus increase signal to noise
- software package CMCse:
  - assisted structure verification and elucidation
  - automated analysis of 1D and 2D NMR spectra

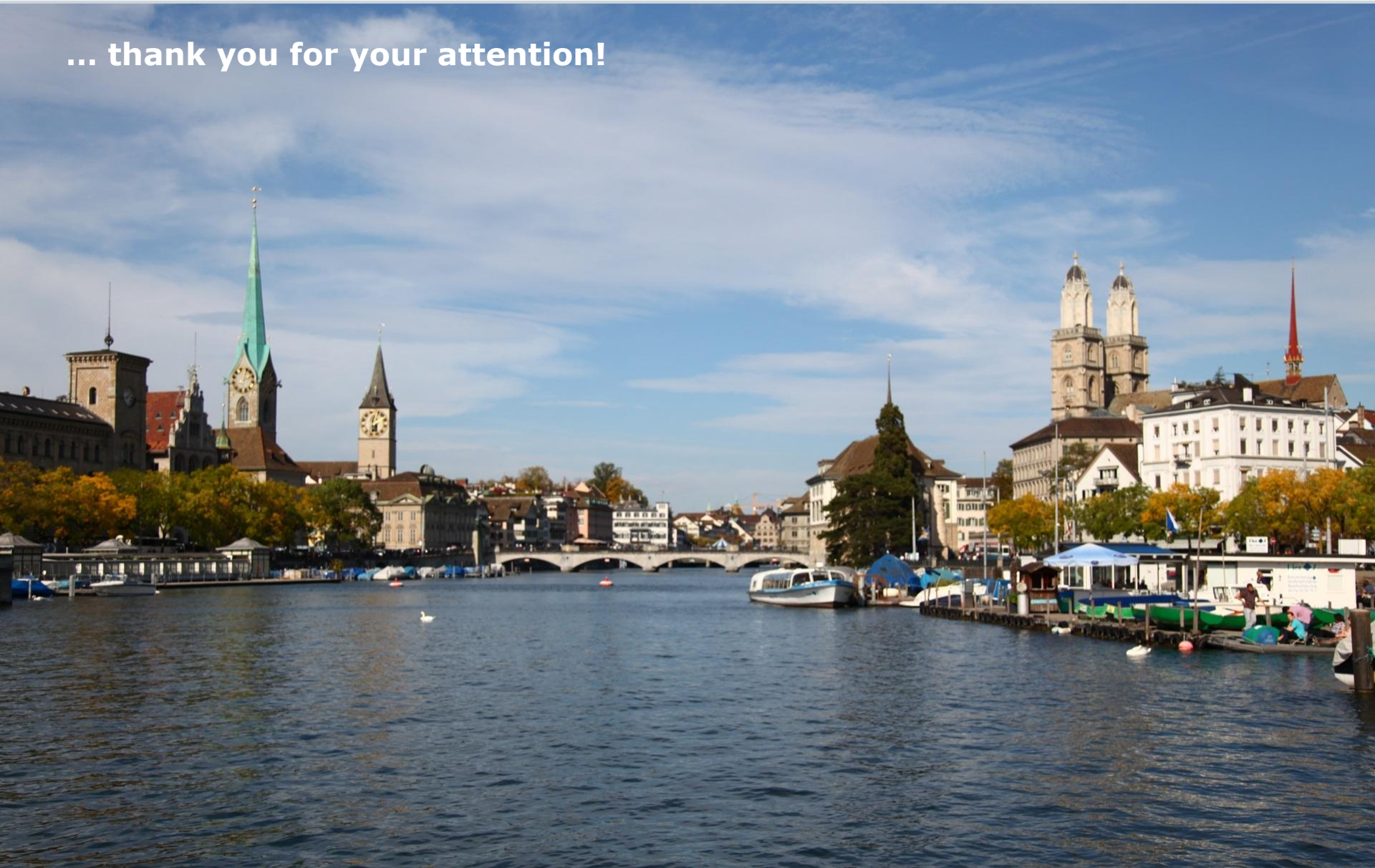
Acknowledgment

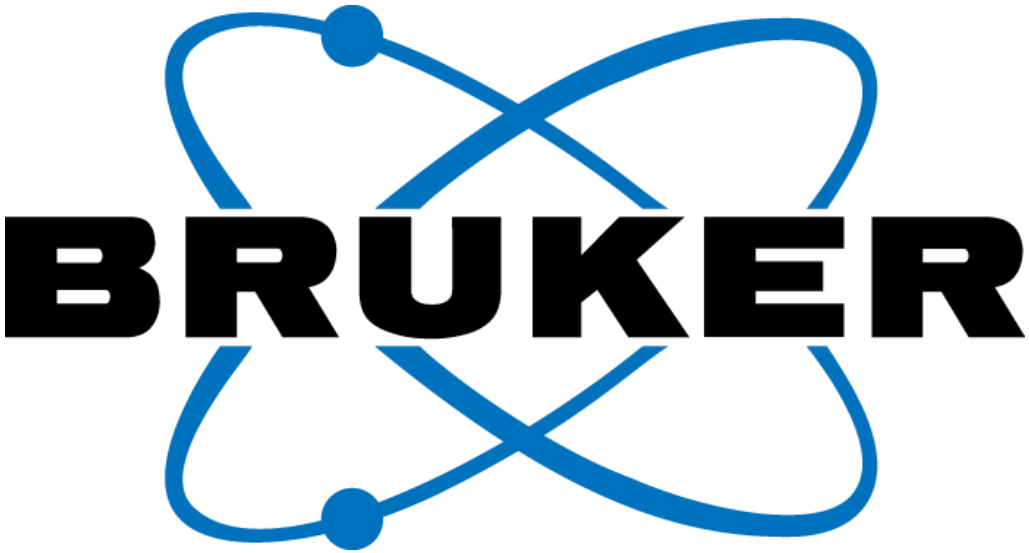
Wim Vermeulen

Lukas Oberer

Application & Development Team

Acknowledgment





Innovation with Integrity