

Bruker Fusion-SV



Wenxin Xu, Ph.D.

Application

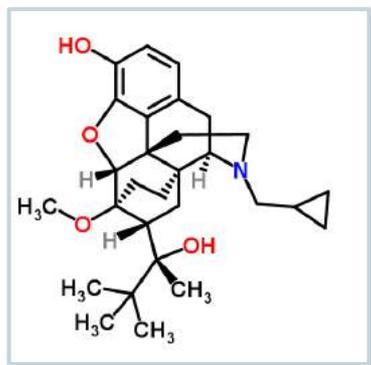
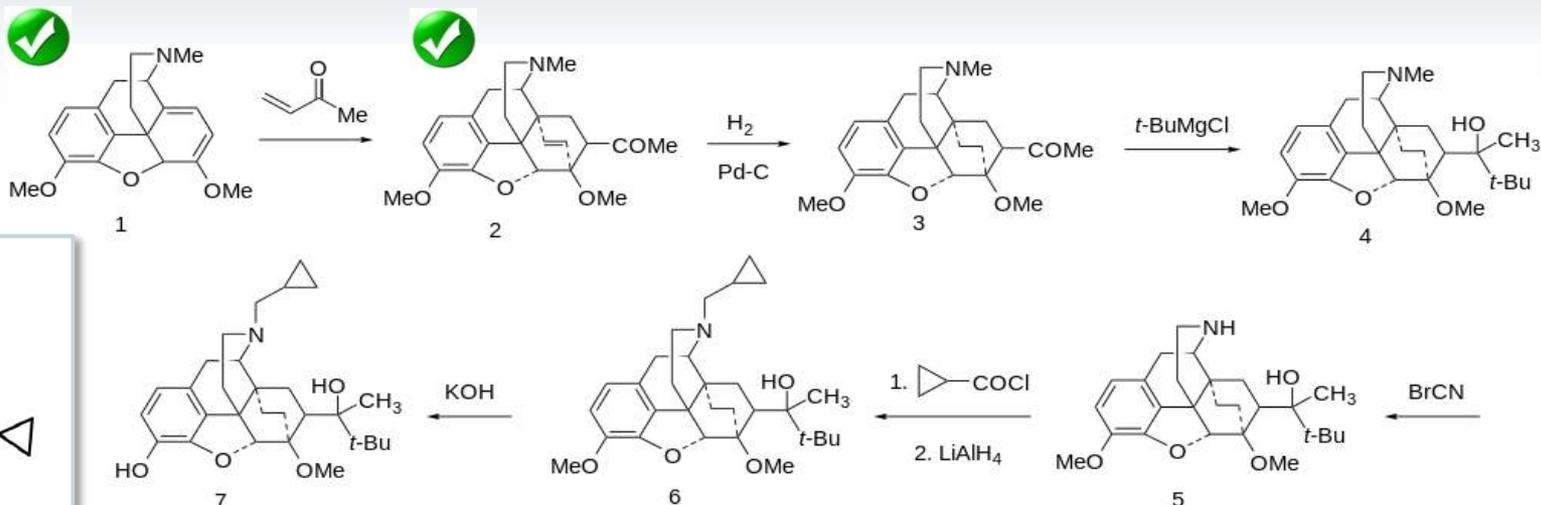
Sep, 2016

Would you like to learn more? Contact a customer service representative.

Bruker
FUSION-SV

N
HRAM-MS
R

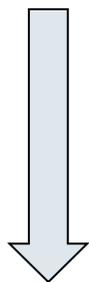
Chemical Synthesis Control



Anything from:

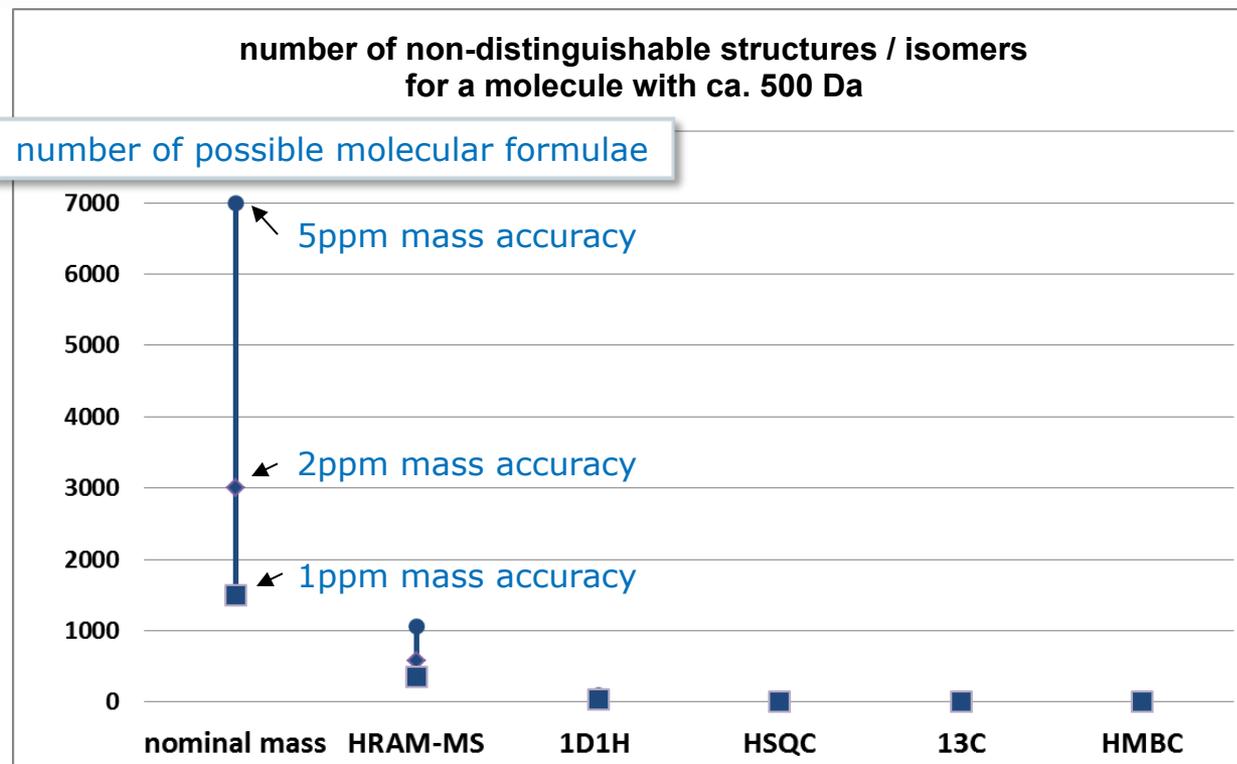
- ⇒ quick and dirty check of intermediates of synthetic process
- ⇒ Verification of final product
- ⇒ Several analytical technique used
- ⇒ depends on chemical question and required certainty

- They want to be sure, **not to file the wrong structure** as a drug candidate
- **Orthogonal data** is needed to minimize the chance for false positives
- MS can do things NMR can not (Cl/Br, S/O ...)
 - Nominal mass → leaves 1'000s of potential false positives
 - **HRAM-MS** → verifies the **molecular formula**
- **NMR** can do things MS can not
 - 100's of possible structures per molecular formula → potential false positives
 - 1D¹H
 - HSQC
 - HMBC
 - ¹³C



**Further reduction of
potential wrong passes**

MW 467.298



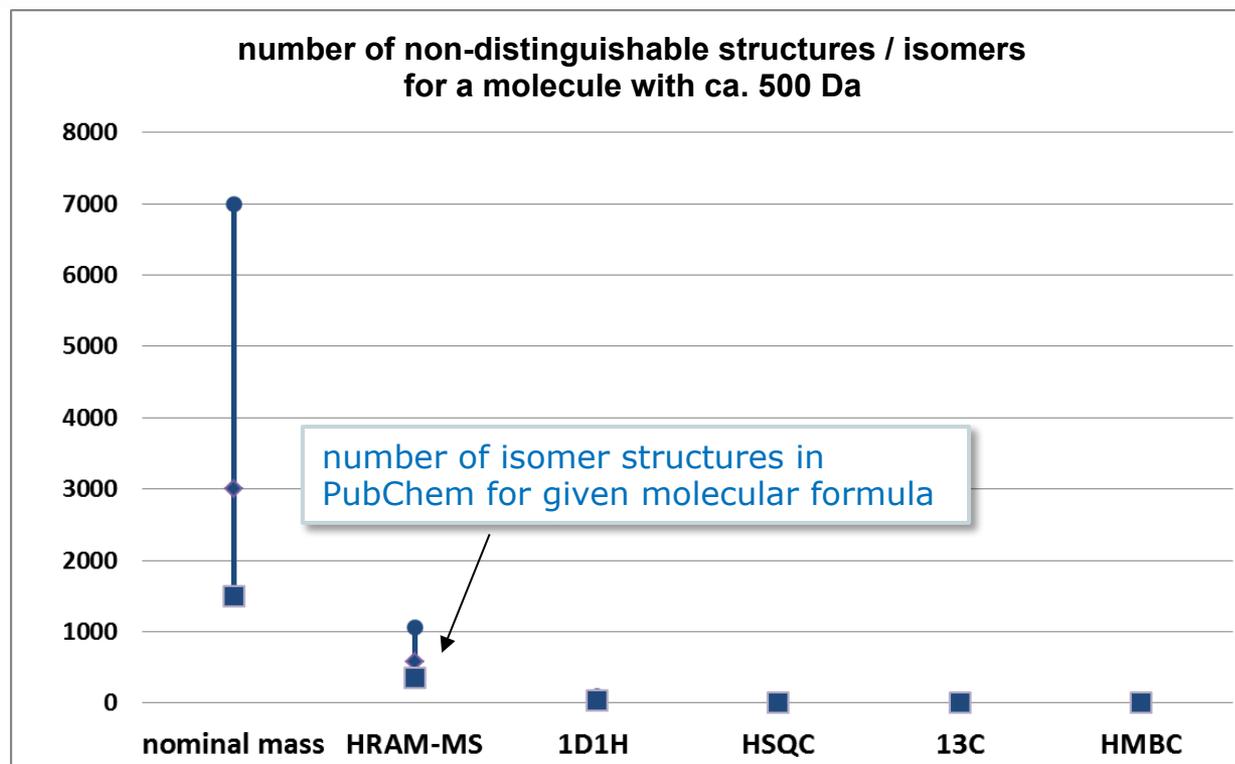
⇒ nominal mass only is not able to rule out 1000s of potentially false positives

Structure Verification



MW 467.298

$C_{20}H_{22}NO_4$



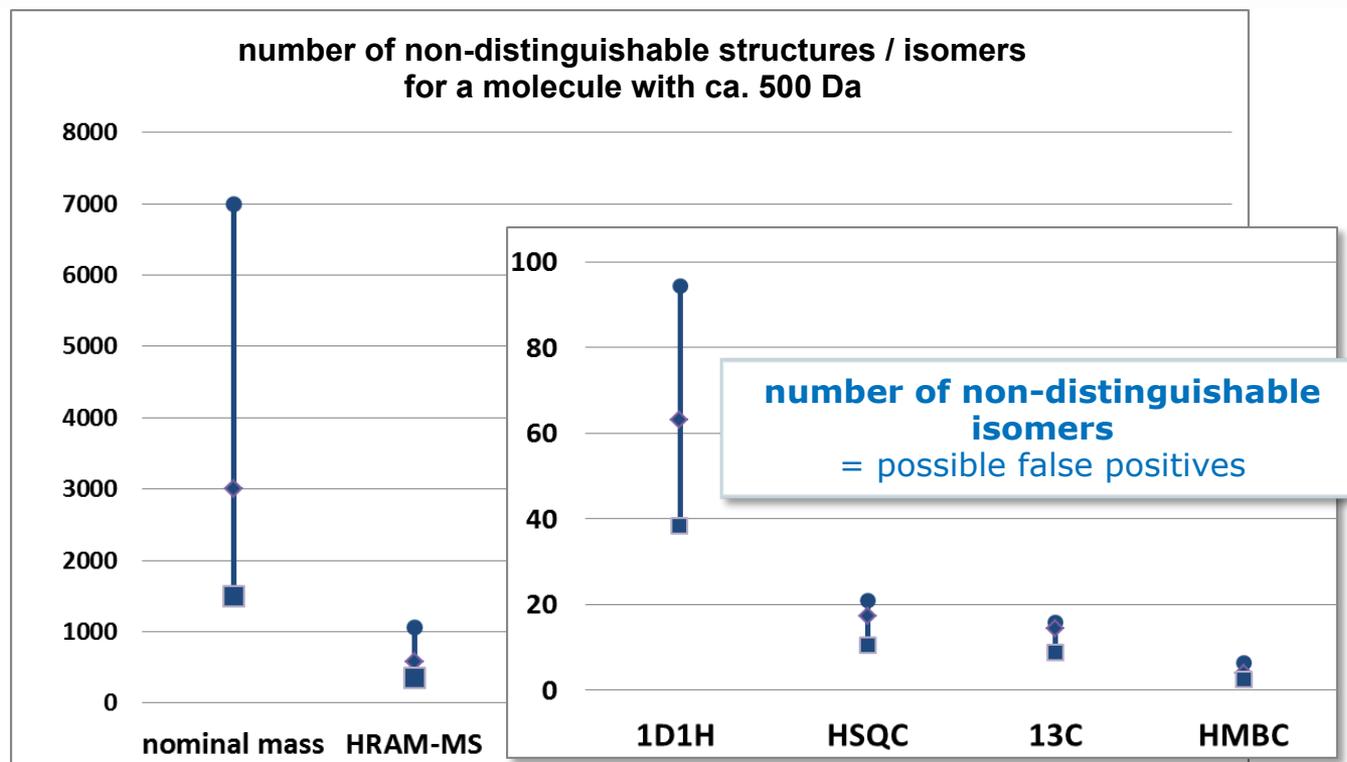
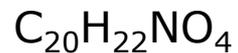
⇒ HRAM-MS verifies the molecular formula

⇒ still several 100 isomers that cannot be ruled out (potential false positives)

Structure Verification

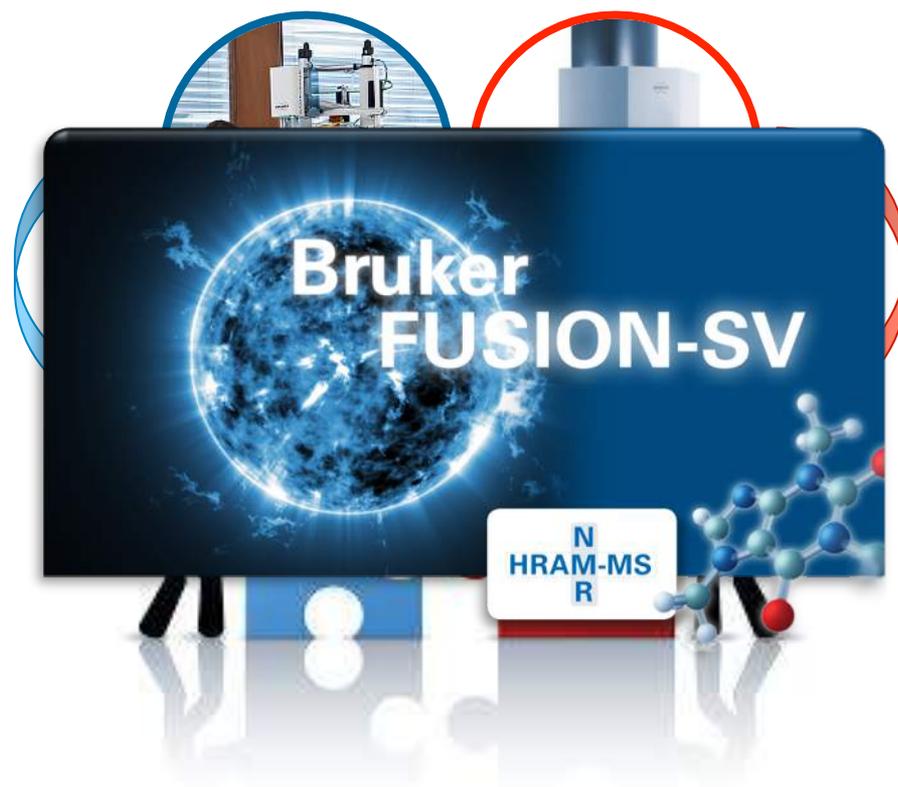


MW 467.298

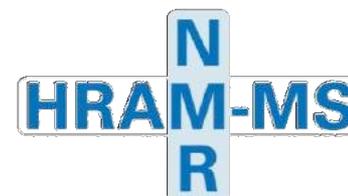


⇒ 1H NMR still leaves many potential isomers that cannot be distinguished

⇒ clever combination of orthogonal information adds confidence



new, fully automatic analysis solution using HRAM-MS and NMR structure verification (SV)



Designed for Chemists

- structure centered
- workflow oriented
- Network embedded

New: Bruker Fusion-SV 1.1



The screenshot displays the Bruker Fusion-SV 1.1 software interface. The main window shows a project navigator with a tree view of projects and compounds. A table lists data for various compounds, including MS, NMR_1H, and NMR_HSQC data. A 'Detailed Information' window is open, showing analysis results for AM-879-4201094. A 1H NMR spectrum is displayed in the bottom right corner. A 'Report' window is also visible at the bottom left.

Project Navigator Table:

Structure ID	Sample ID	MS	NMR	Report
Project_13				
Compound 2	Synthesis_2_A	✓	✓	Short 2015-11-02 10:42:13
MS	AN-329-42613559			
NMR_1H	AN-329-42613559			
NMR_HSQC	AN-329-42613559			
Compound 1	Synthesis_1_A	✓	✗	
Project_42				
Compound 4		-	✓	
Compound 3		-	-	
MS	AK-778-15446017			
NMR_1H	AK-778-15446017			
NMR_HSQC	AK-778-15446017			
Project_77				
Compound 99	Synthesis_Step_Final	✓	✓	Long 2015-11-02 10:42:47 Open
MS	AK-918-12349040			
NMR_13C	AK-918-12349040			
NMR_1H	AK-918-12349040			
NMR_HSQC	AK-918-12349040			

Detailed Information Window:

AM-879-4201094

Include in Report	Status	✓	Evaluation	
<input checked="" type="checkbox"/> MS	Confirmed	✓	automatic	
<input checked="" type="checkbox"/> NMR_13C	Confirmed	✓	automatic	
<input checked="" type="checkbox"/> NMR_1H	Confirmed	✓	automatic	
<input checked="" type="checkbox"/> NMR_HMBC	Confirmed	✓	automatic	Only available for a
<input checked="" type="checkbox"/> NMR_HSQC	Confirmed	✓	automatic	

1H NMR Spectrum:

Report Window:

Comment: Final compound successfully synthesized. Purity > 97%

Bruker Fusion-SV 1.1: Workbench



Bruker FUSION-SV - Admin - localhost

Projects | Verification Demo 2 Compound 4 | Verification Demo 2 Compound 3 | Project_77 Compound 4

Project Navigator | Last Imported | Recently Reviewed

+ New | Import | Report | More

Structure ID	Sample ID	MS	NMR	Rep
Project_77				
Compound 4	Drug_2222_10_04_15	✓	✓	Generati
MS	AM-879_42010943_GC8_01_2029.d			
NMR_1H				
NMR_HSQC				
Project_78				
Compound 3				
MS				
NMR_1H				
NMR_HSQC	AK-778-15446017			
Structure Verification Demo 1				
Structure Verification Demo 2				
Verification Demo 1				

Create New Project

Project name: Project_79

Project description: DrugDevelopment No_123

Share project with other users

OK Cancel

Bruker Fusion-SV 1.1: Workbench

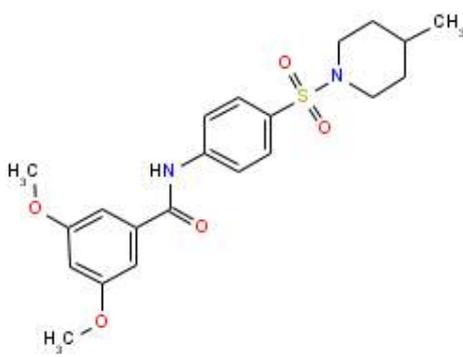


New Verification

Project Name: Sample ID:

Structure ID:

- ▲ AJ-292-4169549 [6]
 - AJ-292-4169549
 - AJ-292-4169549_001
 - AJ-292-4169549_002
 - AJ-292-4169549_003
 - AJ-292-4169549_004
 - AJ-292-4169549_005
- ▶ AK-778-1544601 [2]
- ▶ AM-879-4201094 [1]
- ▶ AN-329-4261355 [1]
- ▶ Structure verification demo data [4]



The chemical structure shown is a sulfonamide derivative. It features a central benzene ring with a methoxy group (-OCH₃) at the 3-position and a methyl group (-OCH₃) at the 5-position. An amide group (-NH-) is attached to the 1-position of this ring. The nitrogen of the amide group is connected to a para-substituted benzene ring. This second benzene ring is further substituted with a sulfonamide group (-SO₂-N(CH₂)₄CH₃), where the nitrogen is part of a piperidine ring with a methyl group (-CH₃) attached to the 4-position.

.mol or .sdf

Structure Editor



Structure Editor

Chemical structure displayed:

CC1=CC=C(C=C1)C(=O)CC2(O)C3=CC=CC=C3N(C2)CC4=CC=C(Cl)C=C4

Structure Editor interface details:

- Toolbar: Selection, Zoom, Pan, Rotate, Copy, Paste, Delete, Undo, Redo, Save, Print, Settings, Help.
- Left Sidebar: Ring templates (Square, Pentagon, Hexagon, Heptagon, Octagon, Nonagon, Decagon).
- Right Sidebar: 3D visualization tools (Ball-and-stick, Wireframe, Surface, etc.).
- Status Bar: Select or move atoms | new structure | C₂₄ H₂₀ N O₃ Cl | MW: 405.874
- Bottom Panel: C H N O S F P I Cl Br X A R | Au

Import MS & NMR data

Structure ID	Sample ID	MS	NMR	Report
Structure Verification Demo 1				
Structure Verification Demo 2				
project01				
▶ AJ-292-4169549_001	AJ-292-4169549	✓	✓	Long 2016-08-23 16:18:20
project02				
▶ AK-778-1544601	AK-778-1544601	✓	✗	Long 2016-08-23 16:17:06
project03				
▶ AM-879-4201094	AM-879-4201094	✓	✓	Long 2016-08-23 16:37:54
project04				
▶ AN-329-4261355	AN-329-4261355	✓	✓	Long 2016-08-23 16:57:48
project05				
AJ-292-4169549_003	AJ-292-4169549_003			<input type="button" value="Import"/>

Verify



Structure ID	Sample ID	MS	NMR	Report
Structure Verification Demo 1				
Structure Verification Demo 2				
project01				
project02				
project03				
project04				
project05				
AJ-292-4169549_005	AJ-292-4169549_005			
MS	AJ-292_41695498_RA8_01_2120.d			
NMR_13C	AJ-292-41695498 6 1			
NMR_1H	AJ-292-41695498 1 1			
NMR_HMBC	AJ-292-41695498 5 1			
NMR_HSQC	AJ-292-41695498 3 1			

Verification review



The screenshot displays the Bruker EUSION SV software interface. The top navigation bar includes 'Projects' and 'Compound' sections. The main window is divided into several panels:

- Chromatograms / Detailed Information / MS Calibration Info:** Shows 'Base Calibration' and 'Calibration graph' tabs. The 'Calibration graph' tab displays a table of calibration data.
- Mass Spectrum:** Shows a mass spectrum with peaks labeled at m/z 430.9174, 412.9172, 400.9174, 382.9172, and 370.9174.
- Structure:** Shows the chemical structure of a brominated compound with the formula $C_{18}H_{13}Br_2N_2O_3$ and a monoisotopic mass of 467.0684 Da.
- 1H NMR Spectrum:** Shows a 1H NMR spectrum with peaks at 10.0 ppm (1H) and 7.1 ppm (1H, 3H).
- 13C NMR Spectrum:** Shows a 13C NMR spectrum with peaks at 100.0 ppm (1H) and 7.1 ppm (1H, 3H).
- HSQC NMR Spectrum:** Shows an HSQC NMR spectrum with peaks at 100.0 ppm (1H) and 7.1 ppm (1H, 3H).

Annotations and callouts:

- A red box highlights the 'Projects' and 'Compound' sections in the top navigation bar.
- A blue box highlights the 'MS Calibration Info' panel, with a callout stating 'accurate mass and isotopic pattern information'.
- A blue box highlights the '1H NMR Spectrum' panel, with a callout stating 'assignment of NMR data'.
- A 'Manual Spectra Alignment' dialog box is open, showing 'Currently marked positions in spectra are:' with '1D: 2.200 ppm' and 'HSQC: 2.148 ppm'. The 'Align to:' field is set to '2.200 ppm'.

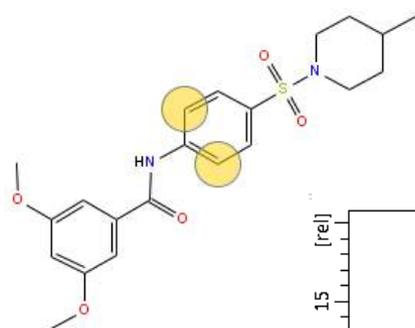
New: Bruker Fusion-SV 1.1



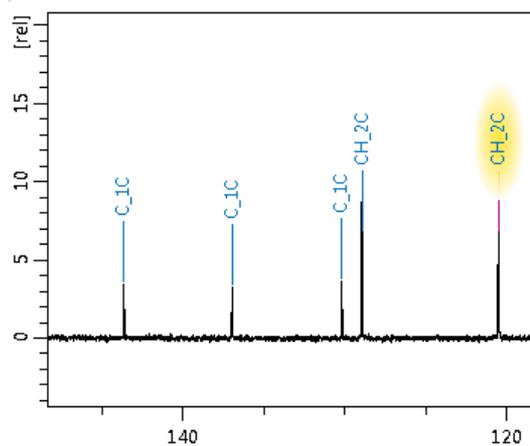
Automatic analysis of combined **1D¹H**, **HSQC**, **HMBC** and **1D¹³C** data for

⇒ Automatic processing of NUS data (HSQC, HMBC)

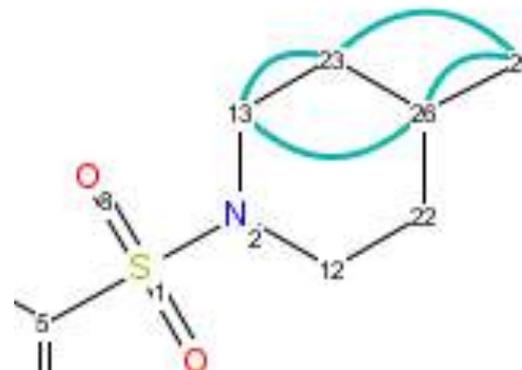
⇒ Spectra interpretation easily understandable



¹³C assignment



HMBC correlations



Generate Report

101: Conf

Posi
176.0
166.0
135.0
132.0
130.0
128.0
126.0
125.0
53.4
50.6
47.7
41.1
39.9
37.7
18.2

19

20

The 4
Journ
1H NN
2.27 (

Journ
1H NN
2H), 2
18.2

Journ
1H NN
2.0, 3
41.2,

Ange
1H-NN
2H), 2
18.2

Chem
1H-NN
2H), 2
37.8,

Helve
1H-NN
J=10.

Tetra
1H-NN
3.4 Hz
37.8,

Assignments as Patent String

Journal Type: Journal of the American Chemical Society (JACS)

Detail Level: High Ascending Descending

¹H NMR (400 MHz, DMSO): d, ppm 12.72 (1H, s), 11.58 (1H, s), 7.90 (2H, d, J = 8.7 Hz), 7.80 - 7.71 (3H, m), 7.27 (2H, dd, J = 7.2, 7.2 Hz), 7.22 - 7.14 (3H, m), 3.02 - 2.95 (2H, m), 2.88 - 2.76 (1H, m), 2.69 (2H, t, J = 7.4 Hz), 1.11 (6H, d, J = 6.7 Hz).

¹³C NMR (101 MHz, DMSO): d, ppm 179.8, 179.8, 141.7, 139.1, 137.9, 129.1, 128.8, 127.6, 126.7, 124.7, 44.6, 40.0, 35.7, 34.9, 19.3.

Copy OK

3.4 Hz,
7.8, 18.2;

3.4 Hz,
40.0, 37.8,

H, dd, J =
50.6, 47.7,

3.4 Hz,
40.0, 37.8,

3.4 Hz,
40.0,

(d,

J = 2.0,
41.2, 40.0,

Br Bru Bru Bru Bru

Printed: November 2, 2015 10:42:42 AM GMT+01:00

15

MS & NMR Analysis Settings



MS Analysis Settings

Method:

instrument01

Calibration

Mass lists:

Mass tolerance [Da]:

Chromatogram

BPC num peaks:

EIC num peaks:

Chromatogram Peak Finder

Sensitivity [%]:

Intensity threshold mode:

Intensity threshold:

Area threshold mode:

Area threshold:

Verification

Adducts:

Mass tolerance [Da]:

Isotopic fidelity:

Saturation intensity:

Low abundance warning[%]:

NMR Analysis Settings

project01

Expert Settings

Suppression frequency:

Eretic signal: @ ppm

13C decoupling

NMR Analysis Settings



NMR Analysis Settings - Define Impurities

Known Impurities

TMS TSP H2O MeOH
 DMSO_D5 DMSO_H6 Dimethylsulfon EtOH
 iPrOH C6H6 Acetone CH3CN
 CHD2CN Ethylacetate DMF NH4
 CYCLOHEXANE ACETIC_ACID

Custom Impurities

Active	Identifier	Shift [ppm]	Multiplicity	Coupling	Protons	Carbons	
							New
							Edit
							Delete
							Cancel

NMR Analysis Settings - Edit Impurity

Identifier default

Protons

Enable

Shift [ppm] from to

Multiplicity DOUPLET

Coupling [Hz]

Number of Protons ?

Carbons

Enable

Shift[ppm] from to

Number of Carbons 1

OK Cancel

NMR Analysis Settings



NMR Analysis Settings

project01 New Delete

project01

Expert Settings

Quantification reference directory Browse

Known impurities Edit

Suppression frequency Edit

Eretic signal @ ppm

13C decoupling

Apply

OK Cancel

NMR Analysis Settings - Edit Suppression Frequencies

Suppression Frequencies Location

- Unsuppressed
- Suppression Frequency File
- NMR Parameter O1P
- Custom

Edit Suppression Frequencies

Filename for suppression frequencies

Number of suppression frequencies

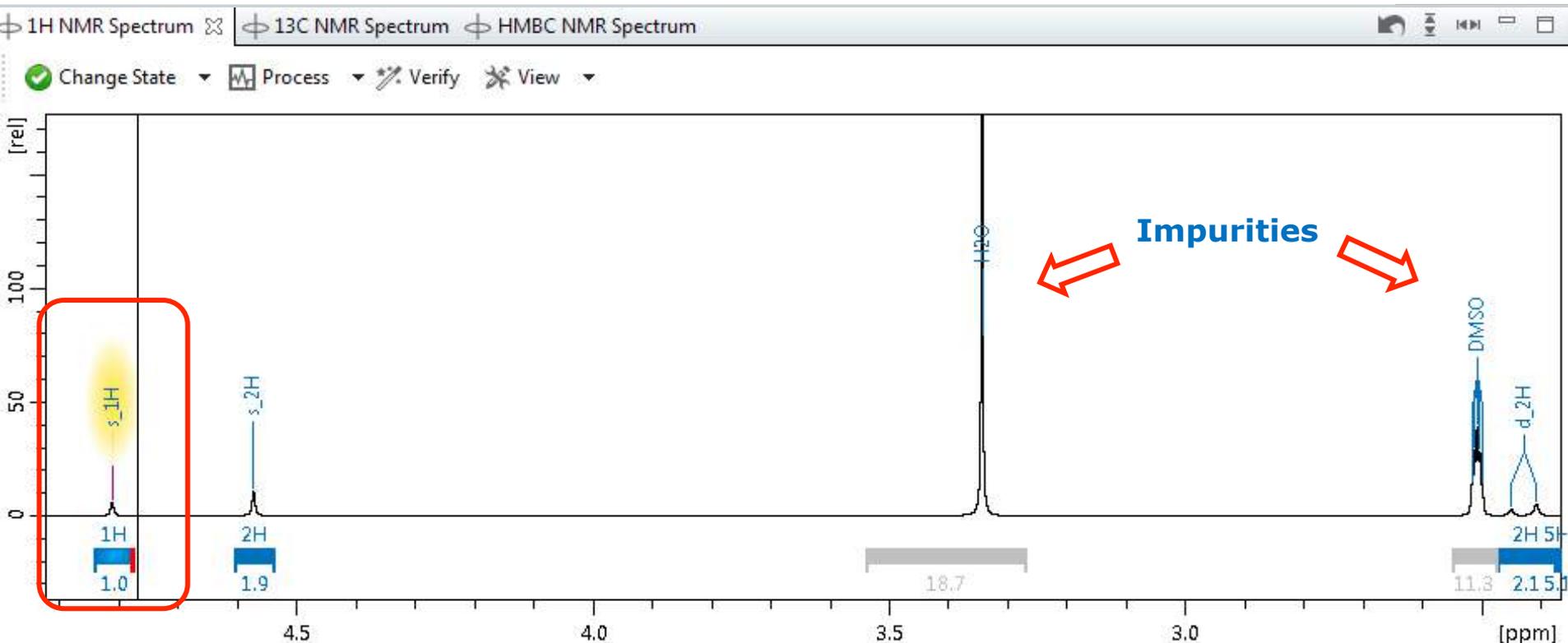
Suppression frequency [ppm]

Remove region around solvent [Hz]

Outer region around solvent [Hz]

OK Cancel

Modifying results from an automated analysis



- Calibrate Current Integral
- Cut Current Integral
- Properties...
- Delete
- Protons
- Signal Type
- New Multiplet
- New Integral

- Substance
- Mixed
- Impurity

Edit Cluster Properties

Status: Substance

Proton Content: 1.0

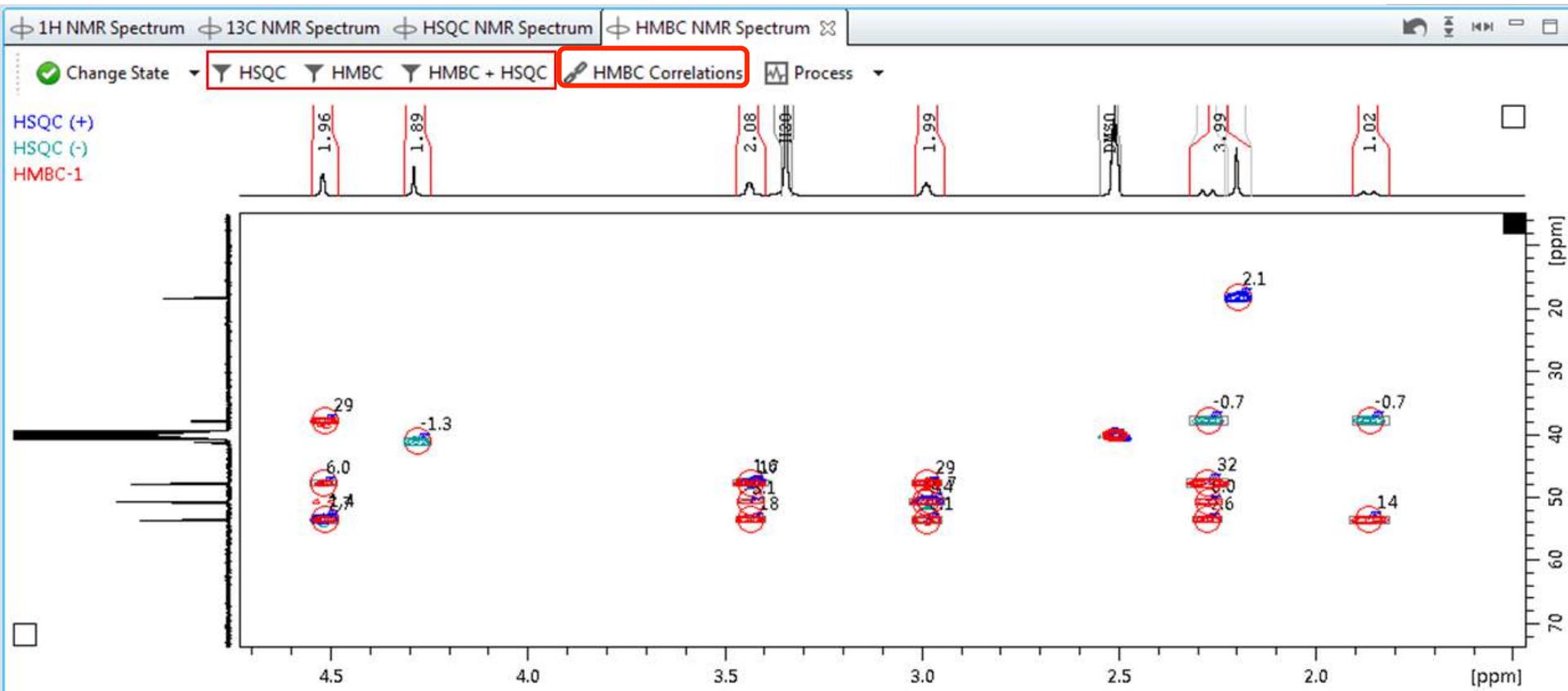
Integral (4.84... 4.78 ppm): 0.991

Annotation:

Calculate concentration by this integral

OK Cancel

HMBC spectrum



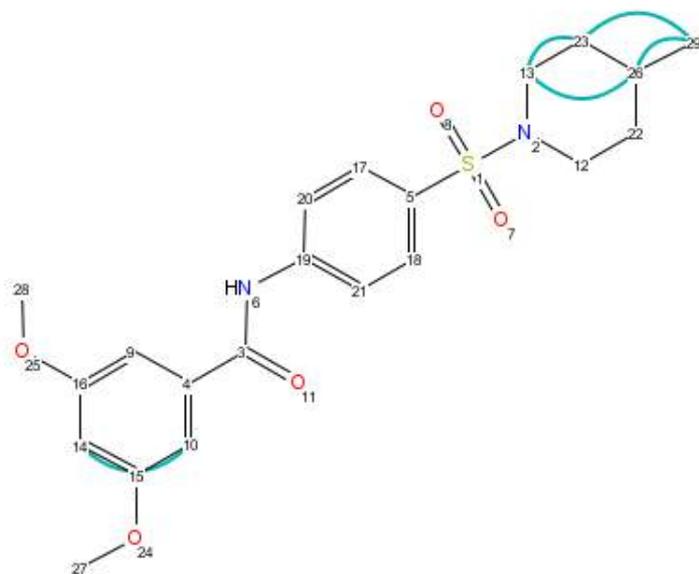
HMBC Correlation



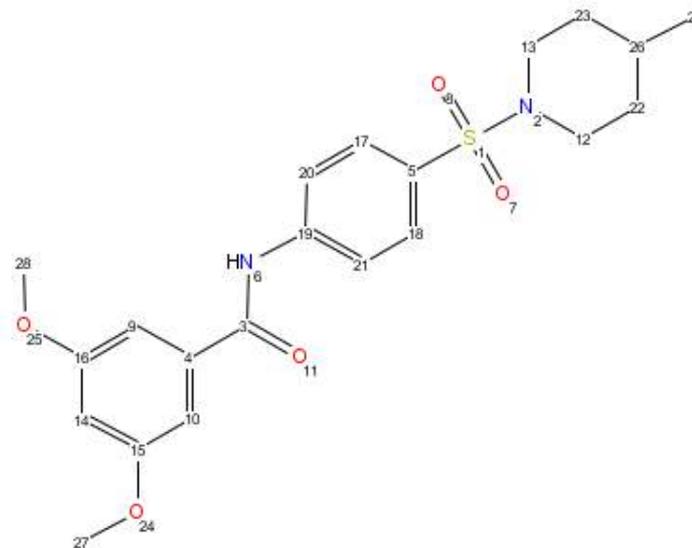
HMBC Correlations



Confirmed correlations:



Violated correlations:



OK

Substructure search



Bruker FUSION-SV - Admin hbqsswtest-0

Projects Structure...on Demo 2 Compound 4

Analyte Group Navigator View Analyte Editor View Analyte SubStructure Search

Clear filter

PO4500270762 [79]
Structure verification demo data [4]
Compound 1
Compound 2
Compound 3
Compound 4

Compound: Modified Structure
Formula: C7H7NO
Monoisotopic Mass: 121.05276
Process: Start

Results Overview Found 14 Hits

Nr.	Name	Formula	Mass
1	Compound 3	C24H20ClNO3	405.1130
2	Compound 1	C21H26N2O5S	418.1560
3	PO4500270762_006	C22H30N2O3	370.2256
4	PO4500270762_029	C16H14N2O2	266.1055
5	PO4500270762_004	C25H29NO4	407.2097
6	PO4500270762_021	C21H19NO2	317.1416
7	PO4500270762_065	C14H11N3O3	269.0800
8	PO4500270762_078	C13H11NO4	245.0688
9	PO4500270762_074	C15H16N2O3	272.1161
10	Compound 4	C32H35ClN2O4	546.2290
11	PO4500270762_036	C23H26N2O4	394.1893
12	PO4500270762_014	C26H18N2O3	406.1317
13	PO4500270762_057	C15H14N2O2S	286.0776
14	PO4500270762_069	C15H15NO4	273.1001

Edit Structure Import Structure Clear All

Substructure search



Brucker Fusion-SV - Admin - hbqsswtest-0

Projects Structure...on Demo 2 Compound 4

Analyte Group Navigator View Analyte Editor View Analyte SubStructure Search

Clear filter

- PO4500270762 [79]
- Structure verification demo data [4]
 - Compound 1
 - Compound 2
 - Compound 3
 - Compound 4

Compound: Modified Structure

Formula: C7H7NO

Monoisotopic Mass: 121.05276

Process: Start

Results Overview Found 14 Hits

Nr.	Name	Formula	Mass
1	Compound 3	C24H20ClNO3	405.1130
2	Compound 1	C21H26N2O5S	418.1560
3	PO4500270762_006	C22H30N2O3	370.2256
4	PO4500270762_029	C16H14N2O2	266.1055
5	PO4500270762_004	C25H29NO4	407.2097
6	PO4500270762_021	C21H19NO2	317.1416
7	PO4500270762_065	C14H11N3O3	269.0800
8	PO4500270762_078	C13H11NO4	245.0688
9	PO4500270762_074	C15H16N2O3	272.1161
10	Compound 4	C32H35ClN2O4	546.2290
11	PO4500270762_036	C23H26N2O4	394.1893
12	PO4500270762_014	C26H18N2O3	406.1317
13	PO4500270762_057	C15H14N2O2S	286.0776
14	PO4500270762_069	C15H15NO4	273.1001

Edit Structure Import Structure Clear All

Mapping sub structure is high lighted

Admin Structure verification (sv-admin) hbqsswtest-0

Substructure search



Analyte Editor View | Analyte SubStructure Search

Compound: Modified Structure

Formula: C6H6

Monoisotopic Mass: 78.04695

Process:

Results Overview Found 176 Hits

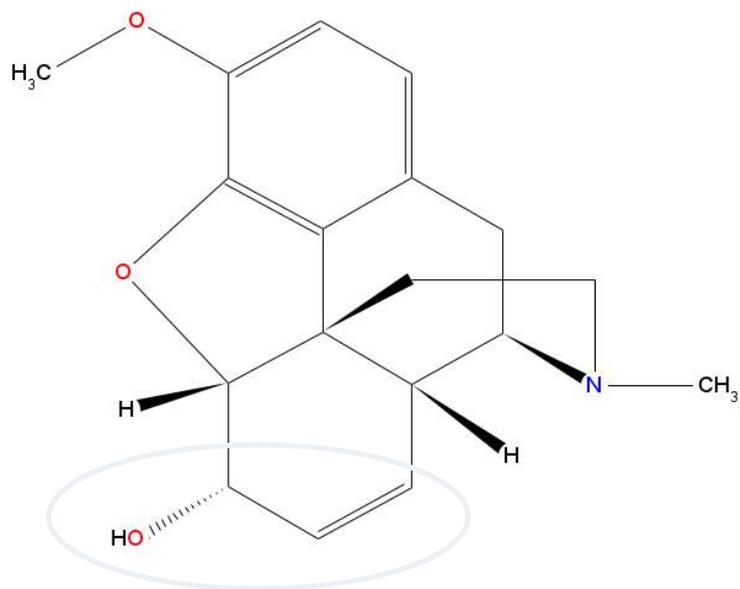
Name	Formula	Mass
New Structure 2 jhgjhg	C17H15N...	281.1052
New Structure	C17H14Cl...	315.0662
Compound 4	C32H35Cl...	546.2285
Compound 3	C24H20Cl...	405.1132
Compound 2	C19H23N...	405.1181
Compound 1	C21H26N...	418.1562
AO-476-40672079_001	C26H24Cl...	477.1278
AO-476-40672079_001	C26H24Cl...	477.1278
AO-299-15047109_001	C29H31N...	513.2198
AO-299-15047109	C29H31N...	513.2198
AO-081-41887499_001	C26H26Br...	527.0943
AO-081-41887499	C26H26Br...	527.0943
AO-081-40770617_001	C21H19Cl...	415.0854
AO-081-40770617	C21H19Cl...	415.0854
AN-919-15231075_001	C25H26Cl...	435.1714
AN-919-15231075	C25H26Cl...	435.1714
AN-919-15231074_001	C25H26Cl...	435.1714
AN-919-15231074	C25H26Cl...	435.1714
AN-919-15231054_001	C26H24Cl...	477.1278
AN-919-15231054	C26H24Cl...	477.1278
AN-329-42613590_001	C19H21N...	403.1024

Edit Structure | Import Structure | Clear All

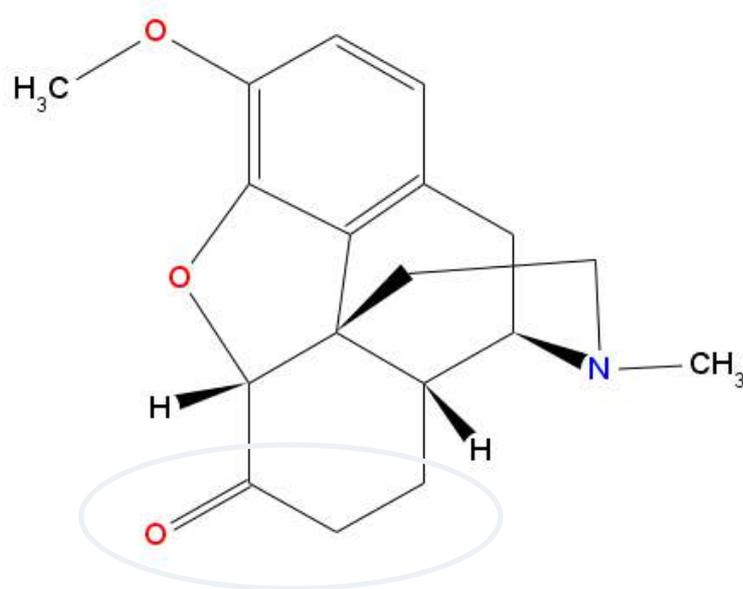
The chemical structure shows a complex heterocyclic system. It features a central benzene ring highlighted in yellow, which is part of a larger fused ring system. The structure includes a thiophene ring, a pyridine ring, and a piperidine ring. A chlorine atom is attached to the thiophene ring, and a methyl group is attached to the piperidine ring. The overall structure is a complex polycyclic molecule.

Example

Codeine and Hydrocodone



Codeine
 $C_{18}H_{21}NO_3$
 299.365



Hydrocodone
 $C_{18}H_{21}NO_3$
 299.365

Example

Codeine and Hydrocodone

Bruker FUSION-SV

Projects

Codeine codeine  Codeine codeine 

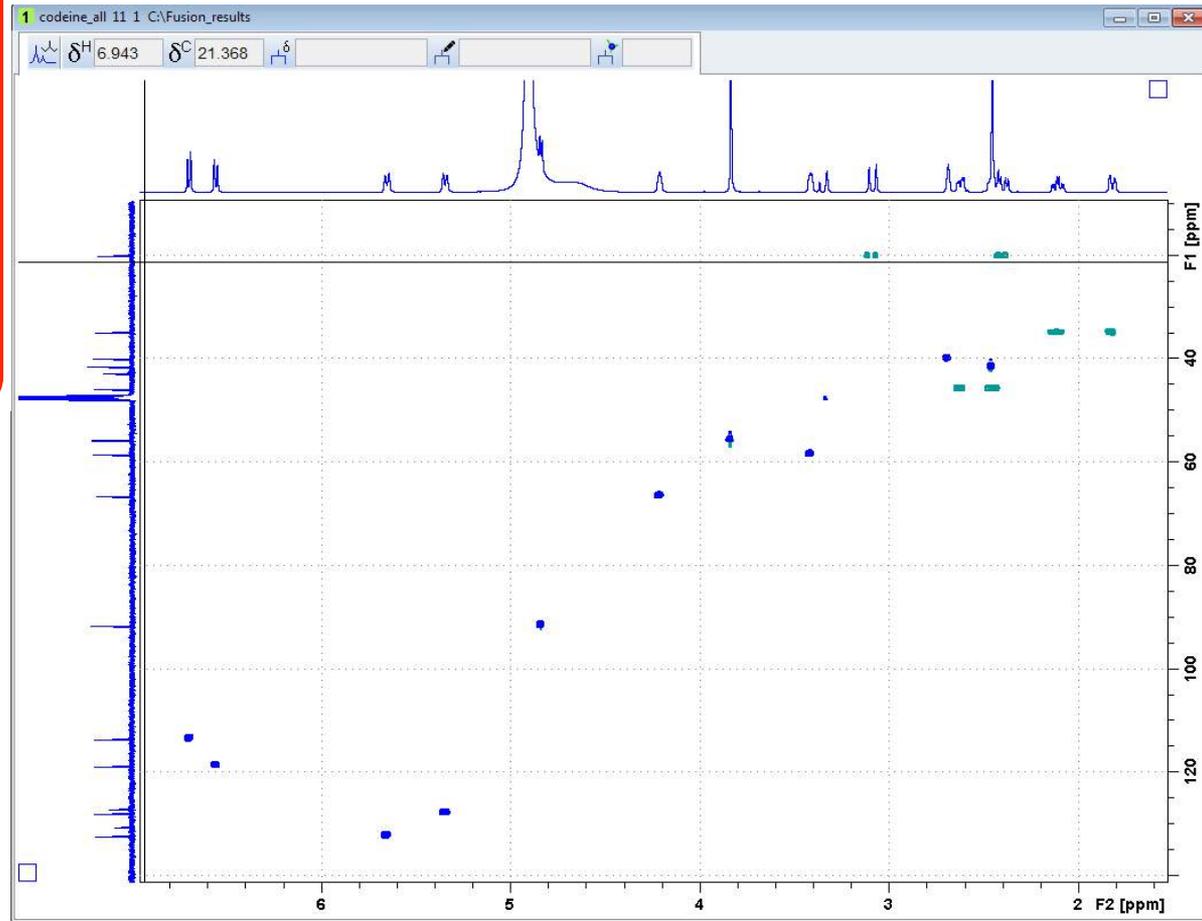
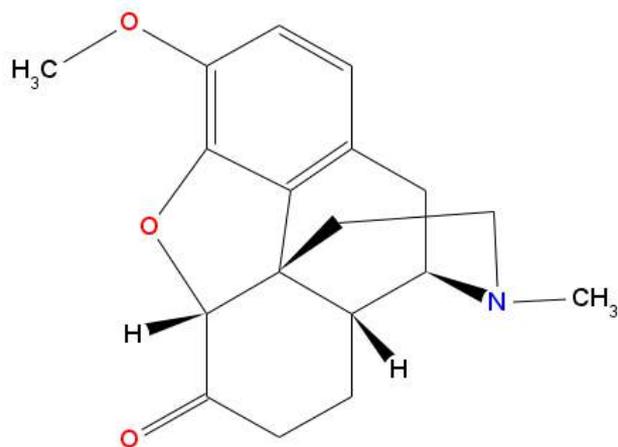
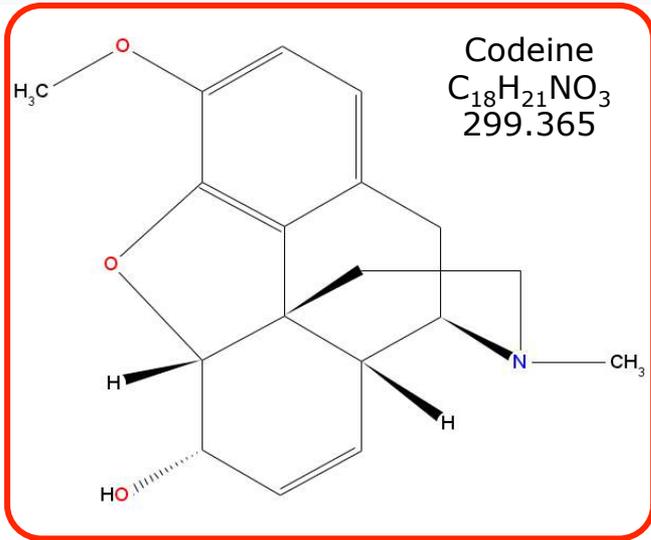
Project Navigator  Last Imported  Recently Reviewed

+ New Import Report More

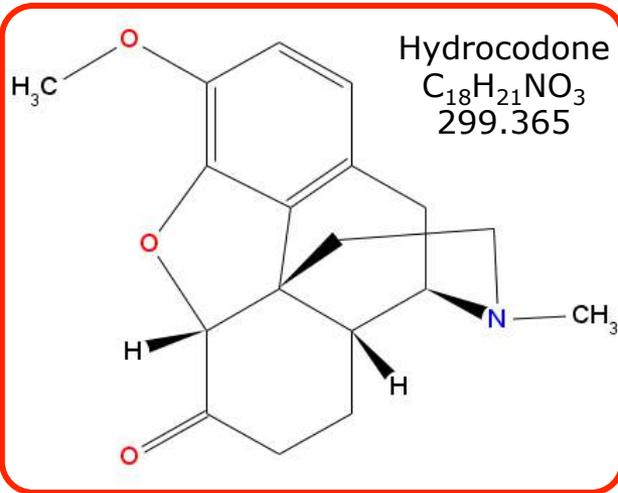
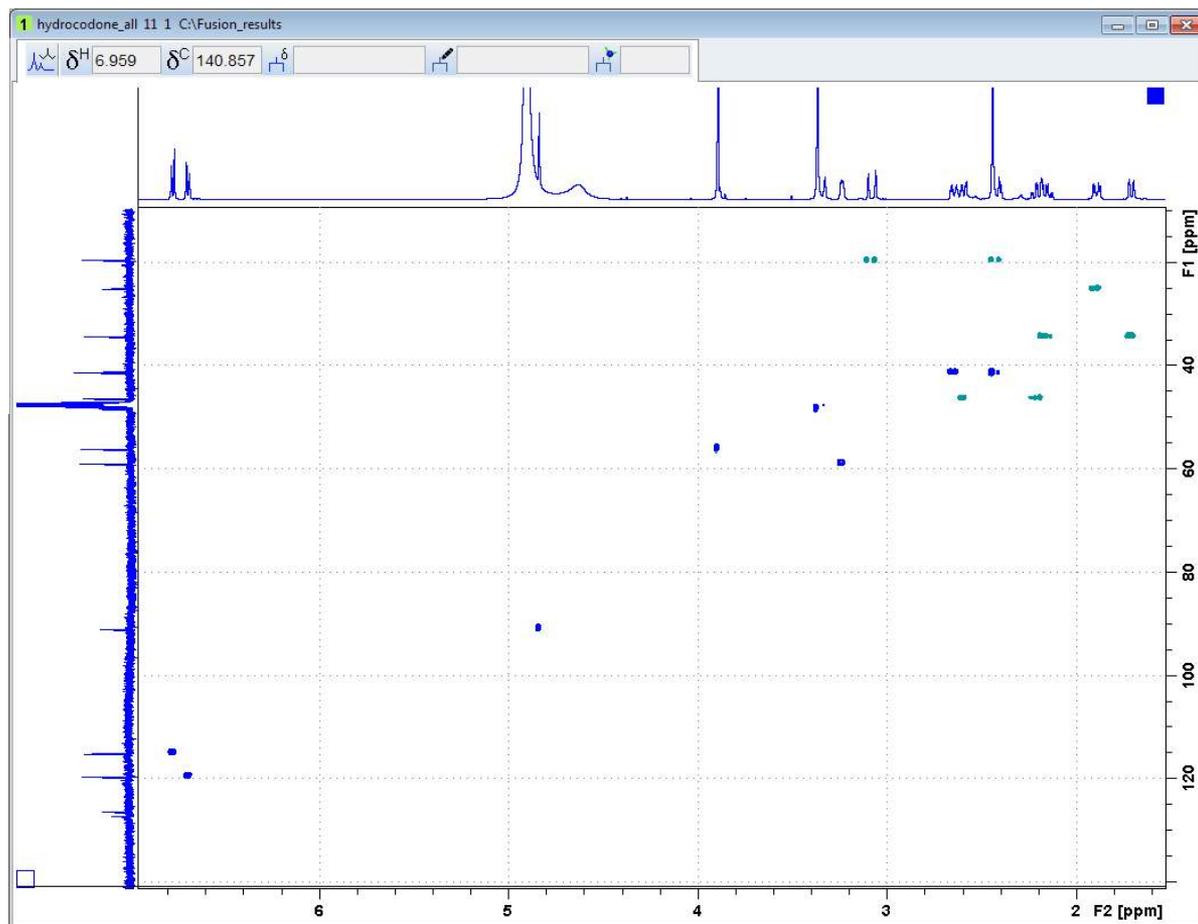
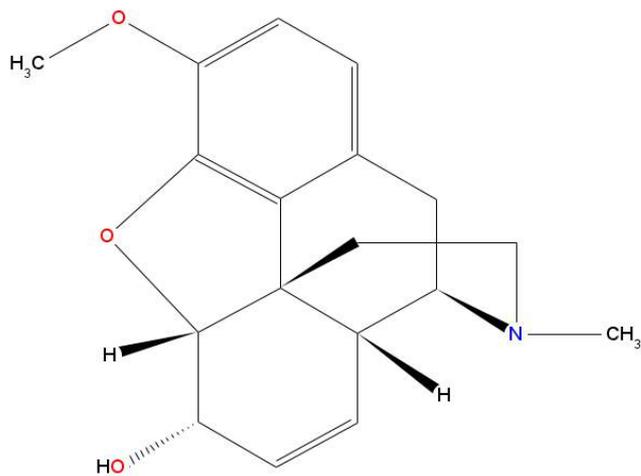
Structure ID	Sample ID	MS	NMR	Report
codeine	codeine			
MS	Codeine_1ppm_GE4_01_675.d			
NMR_13C	codeine_1H_13C 13 1			
NMR_1H	codeine_1H_13C 10 1			
Codeine_TN				
hydrocodone	hydrocodone			
hydrocodone	hydrocodone			
MS	Codeine_1ppm_GE4_01_675.d			
NMR_13C	codeine_1H_13C 13 1			
NMR_1H	codeine_1H_13C 10 1			

- with the wrong structure FUSION reports NOT OK from NMR

...But from the data we can tell!

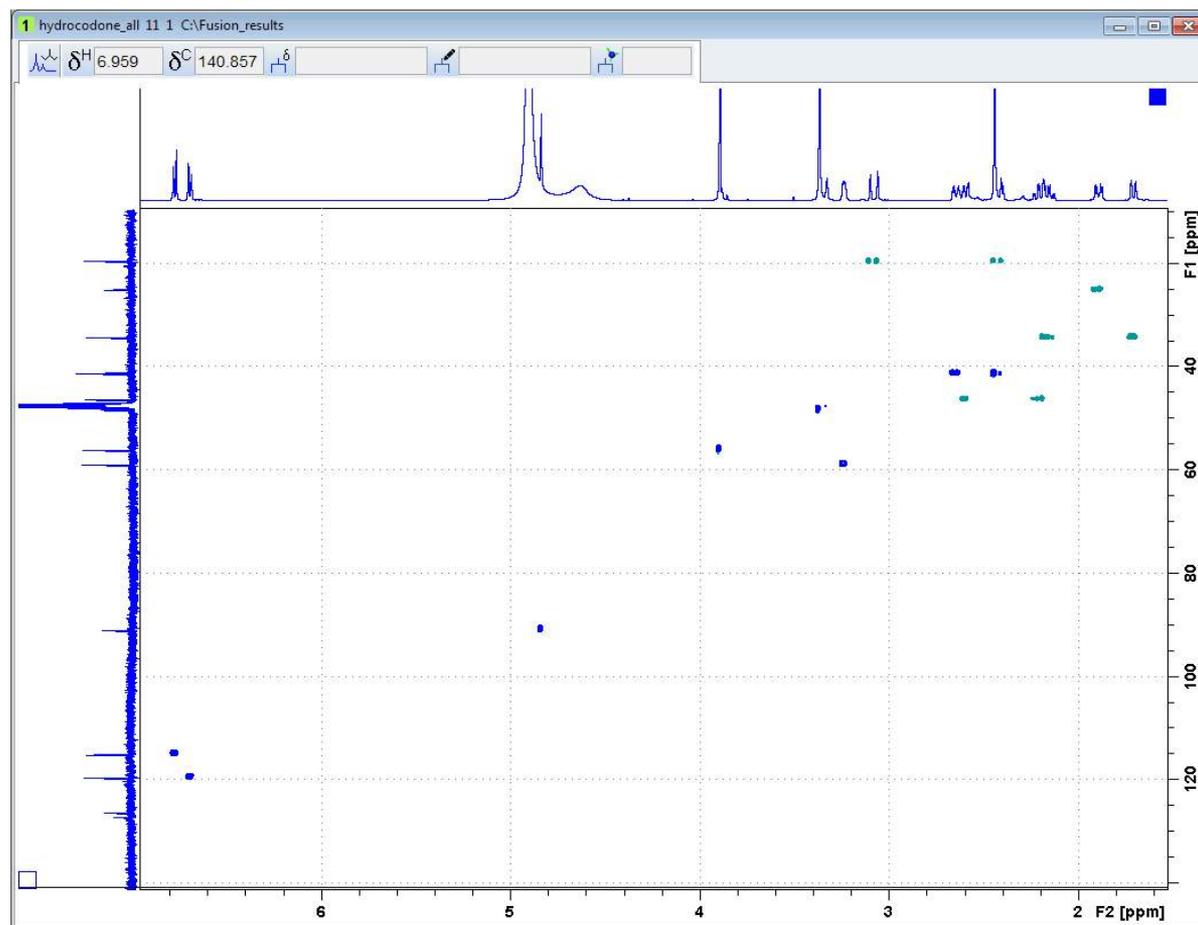
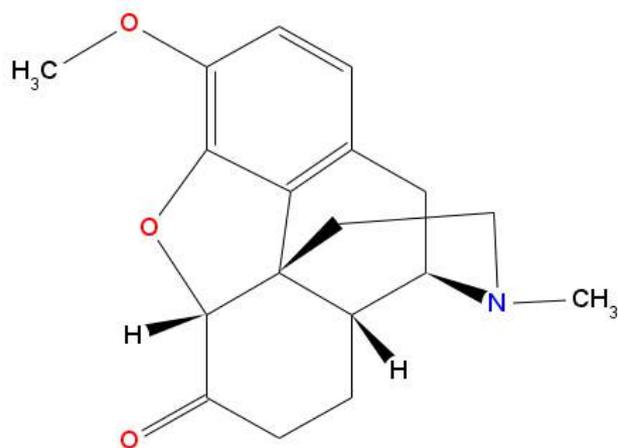


...But from the data we can tell!



...But from the data we can tell!

- HSQC of hydrocodone tells us something has happened, and this isn't hydrocodone anymore!



Let's Demo Fusion!

- CMC-assist and FUSION are a black box yes or no
- Be prepared when going through the data to see some incorrect assignments

Bruker Fusion-SV License Request

Last Name*	<input type="text"/>	Comments, questions, send license to (if different from above), etc.:	<input type="text"/>
First Name*	<input type="text"/>	Type of license request*	
Title	<input type="text"/>	<input checked="" type="radio"/> New License	
Company/Institute*	<input type="text"/>	<input type="radio"/> Demo License	
Street	<input type="text"/>	Please don't forget the order number if you want to upgrade or transfer a license	
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State (USA only)	<input type="text"/>	Add. order numbers	<input type="text"/>
ZIP/Postal Code	<input type="text"/>		
Country	China <input type="button" value="v"/>		
Email*	<input type="text"/>		<input type="button" value="Submit"/>

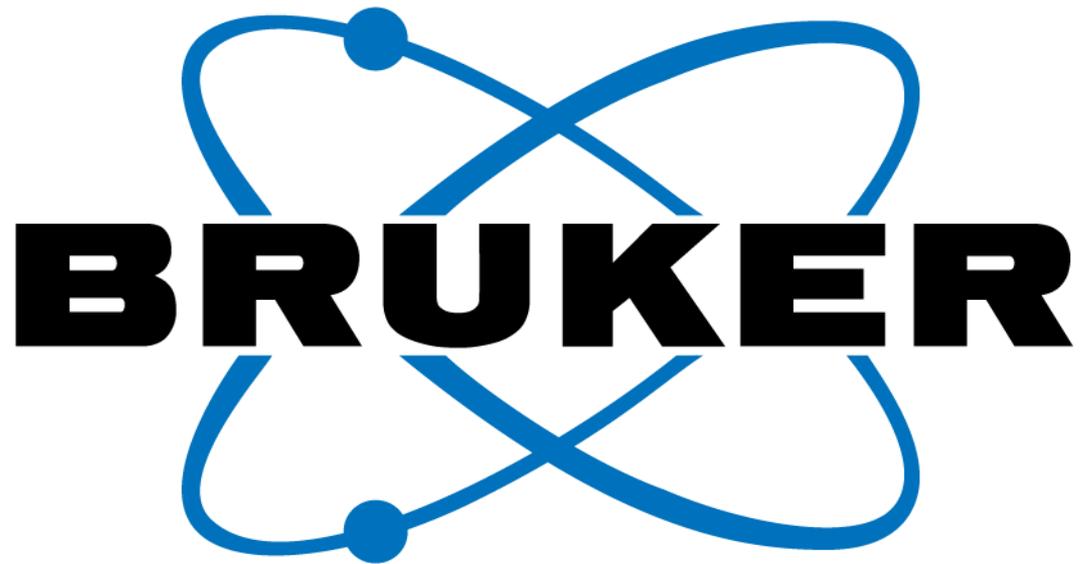
https://www.bruker.com/nmr_license_requests.html

Bruker Fusion-SV: Unique Solution for SV Synthesis Control



full integration HRAM-MS and NMR data (orthogonal techniques)

- significantly increased accuracy and throughput of Structure Verification
 - easily useable – also for non-experts
 - fully automated data analysis
 - proprietary NMR auto-analysis algorithms based on human logic emulation
 - unique *Smart Formula*[™] for mass accuracy and True Isotopic Pattern (TIP)
- ⇒ Bruker FUSION-SV coalesces NMR data with HRAM-MS data and yields a combined result



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Q & A

是否有问题?

请您在 **Q&A 面板中**提交您的问题

我们做的如何?

当您退出webinar的时候, 请填写您对本次webinar的**评价**, 我们非常感谢您的反馈。

Thank you!



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