From FID to Structure in 30 minutes?

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INTRODUCTION

Speed
Increase Productivity

[Image of a person in water with text: OH, NO!]

Maintaining Quality
Computer Assisted Structure Elucidation (CASE)
High sensitivity, accuracy, isotopic fidelity and resolution
Elucidator
Elucidator Workflow

NMR: pp 2D

Check data/add information

Generate MCD

Check MCD

Generate Structures From MCD/s

Find the Best Structure!

MS: MF

Data base
Before NMR Workbook

CASE limiting Step
After NMR Workbook
ANTIPYRIN

Proof of concept
1. Create new project and data folder

2. Short cut mode: H peak picking and multiplet analysis

3. Finish the peak picking in the HSQC

4. Save the project
• Molecular formula added
• HSQC parameters: multiplicity edited CH₂ positives
• HMBC calibration: mainly 3 bond correlations
• Number of Carbons – Symmetry / number of protons
MCD check and Elucidation

• Allow bonds between heteroatoms
• No fuzzy generation
• Filter by carbon assignment
Generate Structure From MCD

The Best Structure

Generated Molecules
Current Structure

Database: Generated Molecules
- $d_{N}(^{13}C)$ (ListA) (8 pts)
- $d_{N}(^{1}H)$ (ListA) (8 pts)

Properties

# in ListA
2
4
6
8

# in ListA

Database: Generated Molecules
- $d_{N}(^{13}C)$ (ListA) (8 pts)
- $d_{N}(^{1}H)$ (ListA) (8 pts)
• Processing: 1-2 min
• Data grooming: 12 min ➔ limiting step!
• Structure Calculation: 8/27636 in 8m 36s
• Total time: 22 min

• Added additional data: $^{13}$C, CN_HMBC and COSY ~ 3 h
  (Calculation time: 2 s)
INTRODUCTION

FLUCONAZOLE

Increasing Difficulty
Fluconazole

$^{13}$C acquired and used to count carbons, taking into account F-C coupling.
The Clock is Ticking

12/2550 8h and still calculating structures!
Calculation Stopped!
Data Grooming: 3 h
Structure calculation > 8h

11 h!
Structure search based on chemical shifts before starting the elucidation is the first step to success!
Fluconazole

<< 30 min

No need for data grooming
SILDENAFIL

Increasing Difficulty
Decreasing Amount of Material (100 µg)
Elucidator Workflow

NMR: pp 2D

Check data/add information

Generate MCD

Check MCD

Generate Structures From MCD/s

Find the Best Structure!

Data base

MS: MF
Training

NMR: pp 2D → Check data/ add information → MCD from fragments → Check MCD → Generate Structures From MCD/s → Find the Best Structure!

MS: MF → Data base

Data base
Dunn, P.J et al; Green Chem., 2004, 6, 43-48

1. Create Fragments
2. Create MCD from Fragment
3. Calculate Structures
The Best Structure

Incorrect structure – substitution pattern wrong

standard 1H (auto)

1H(exp)
AV600, 1.7 mm ICI CryoProbe

100 ug Sildenafil in 33 ul DMSO-d6
edited HSQC
NS=2
Conclusions

What has changed?

» Synchronisation of spectra
» Good automatic peak picking
» Easier and faster structure elucidator module
» Enhanced NMR and MS instruments

Fast CASE with small amounts of material is now reality
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Structure 2010

Advances in Structure Elucidation
24th-25th February 2010
Hinckley Island Barceló Hotel, Leicestershire, U.K.

www.nmrds.org.uk/structure2010.htm

Registrations are invited for this 2-day meeting showcasing new and evolving techniques, workflows and applications in the broad framework of molecular structure elucidation of "small" molecules, mainly but not exclusively in the context of NMR Spectroscopy and Mass Spectrometry.

Format of Meeting
The meeting will combine plenary and invited presentations, a poster session, vendor exhibitions, conference dinner and will include the award of the Duncan Bryant Memorial Prize.

Day 1
10.00-12.00 Registration and Vendor Exhibitions
12.00-13.00 Lunch
13.00-15.00 Lectures
15.00-15.30 Breakout/Refreshment
15.30-17.00 Lectures
17.00-19.30 Reception, Posters and Vendor Exhibitions, Parallel Software Workshop
20.00-22.00 Conference Dinner and After Dinner Speaker
22.00-24.00 Vendor Exhibitions/Bar

Day 2
09.00-10.00 Lectures
10.00-10.30 Breakout/Refreshments
10.30-12.00 Lectures
12.00-13.30 Lunch
13.30-15.00 Lectures
15.00-15.30 Refreshments and Close of Meeting

Confirmed Speakers
Lucio Frydman (Weizmann Institute, Israel) ● Herb Hill (Washington State University, USA) ● Mark O'Neil-Johnson (Sequola Sciences, USA) ● David Watkin (University of Oxford, UK) ● Christina Thiele (Technische Universität Darmstadt, Germany) ● Ian Wilson (AstraZeneca, UK) ● Jean-Claude Wolfe (GlaxoSmithKline, UK) ● Colin Creaser (University of Loughborough, UK) ● Don Richards (Pfizer, UK) ● Roy Goodacre (University of Manchester, UK)

Registration Costs
The all inclusive¹ cost for the meeting prior to the early bird deadline of December 31st 2009 is £250 for RSC members and £300 for non-members rising to £300 and £350 respectively after the early bird deadline. Students presenting posters are encouraged to apply for a meeting bursary before December 1st 2009.

¹Includes meeting registration, overnight hotel accommodation, refreshments and all meals. Inclusive of conference dinner and reception drinks together with complimentary access to the hotel Health/Lounge Club.

A meeting organized jointly by the RSC Molecular Spectroscopy and NMR Discussion Groups and the British Mass Spectrometry Society.