Getting Ahead of the Game:
Complete Analysis of New Psychoactive Substances

PANIC 2019

Anna Codina[1], Eduardo Nascimento[2]

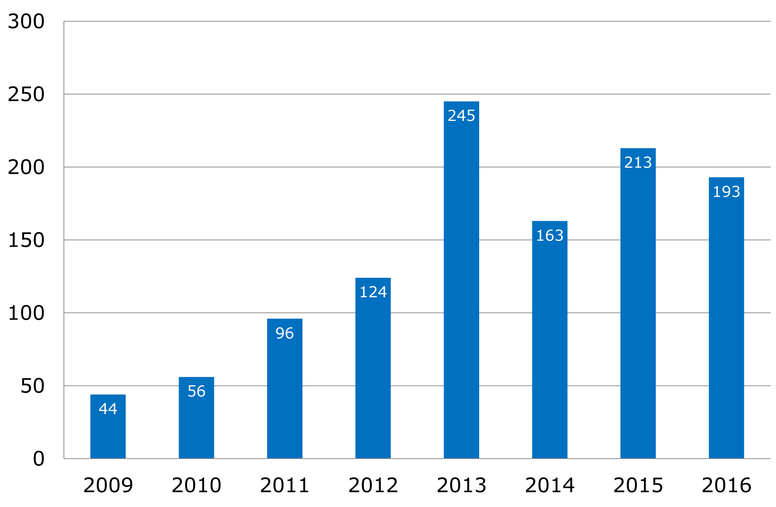
[1]Bruker UK Limited, Banner Lane, Coventry, CV4 9GH, UK
[2]Bruker BioSpin, 15 Fortune Drive, Billerica MA 01821, USA

Introduction

New psychoactive substances (NPS) are emerging every year.[1] There can be a high degree of structural similarity between illegal entities and legal analogues, regioisomers for example, which means that the analytical data used during drug cases should be able to discern between those compounds with certainty.

We propose and demonstrate the utility of NMR to complement IR and MS data for the unequivocal structural identification of illegal drugs and legal highs. We show the use of DOSY experiments together with computer-aided structure elucidation[2] of the different compounds that constitute synthetic drugs such as China White. Also illustrated is how to leverage the acquired structural knowledge in order to streamline the identification and quantification of compounds in recreational drug substances by using library search and matching tools.[3]

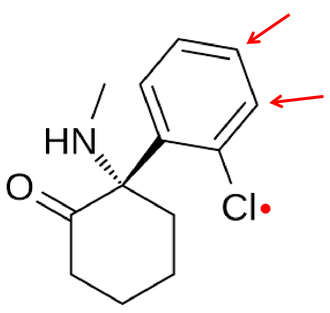
Number of different NPS reported by year in North America and Central America, 2009 to 2016.



Results

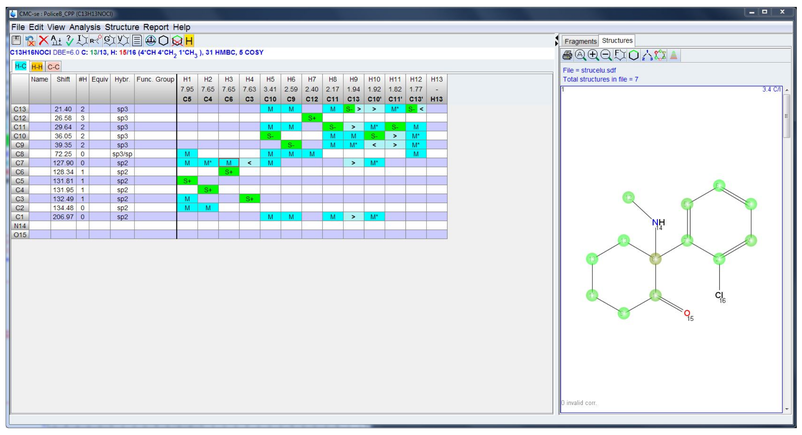
Confirming regioisomerism

Ketamine



A ketamine sample was analysed by NMR with the aim of confirming the structure and rule out regioisomers.

Verification was done using CMC-se, including long range HC correlations. The figure below presents the ^{1}H-^{13}C correlation table and structure generated automatically.

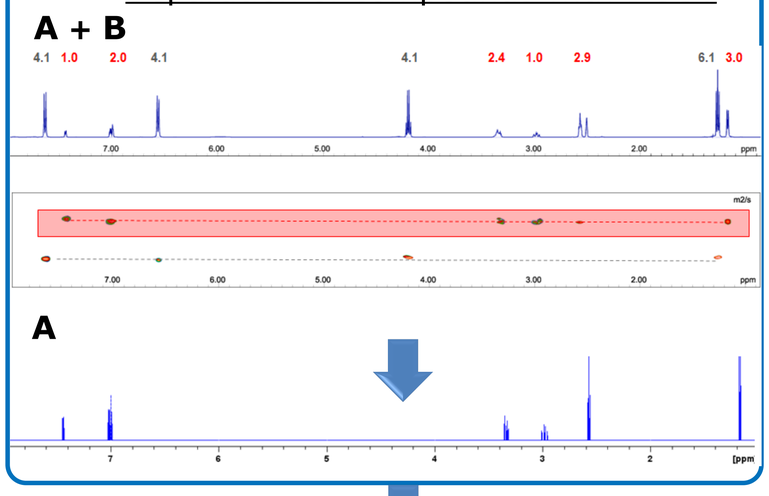


Mixture Analysis Workflow

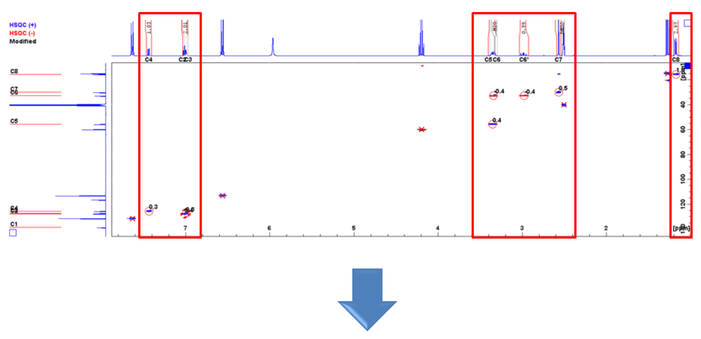
China White

The same process was repeated for compound **B**, which was identified as benzocaine.

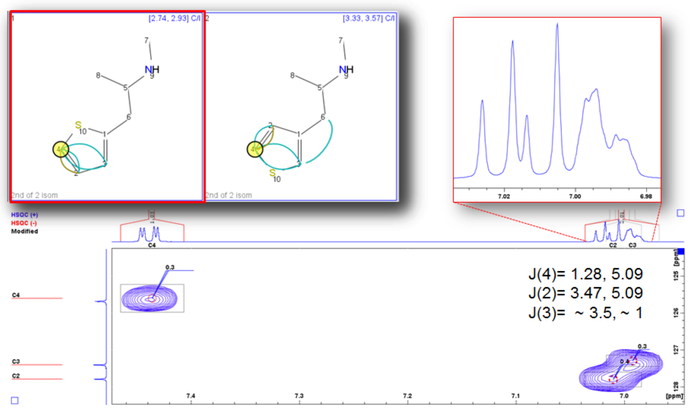
Separation of compounds with DOSY



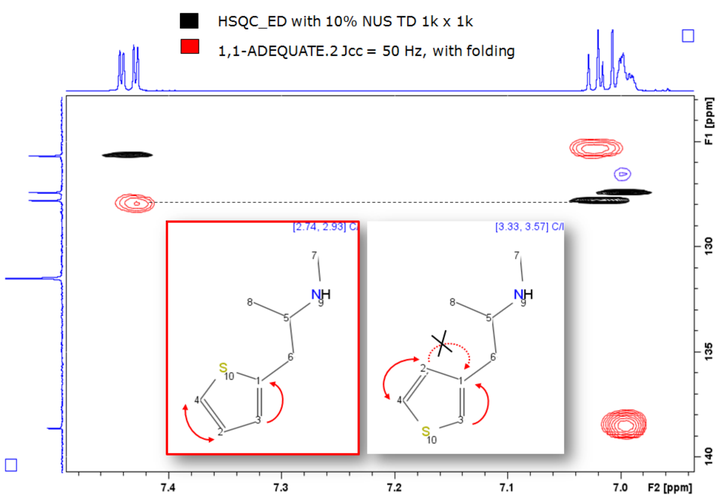
Elucidation of **A** using CMC-se



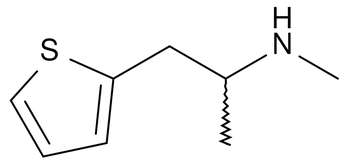
Discriminating regioisomers based on $^{1}J_{HH}$ and HMBC correlations



Discriminating regioisomers based on correlations from 1,1-ADEQUATE



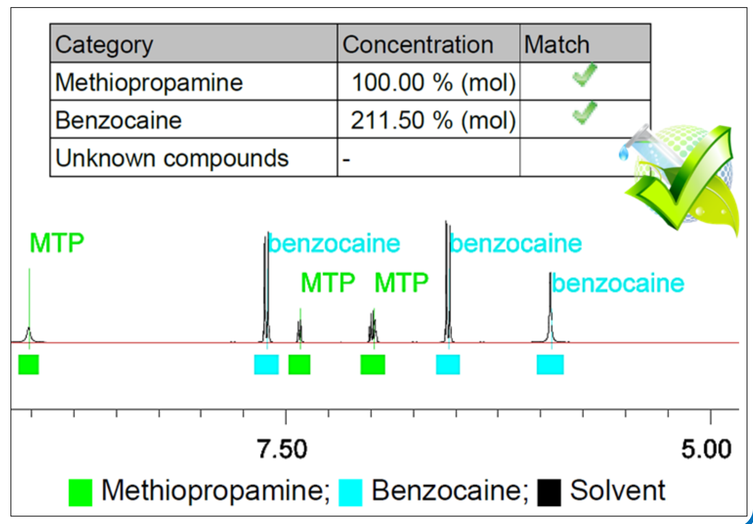
The best structure



A= Methiopropamine

Identification and quantification with Assure RMS

Category	Concentration	Match
Methiopropamine	100.00 % (mol)	✓
Benzocaine	211.50 % (mol)	✓
Unknown compounds	-	



The structure and NMR data for methiopropamine and benzocaine were imported into a spectra base. A method was created for identification and quantification of these compounds in mixtures using Assure Raw Material Screening (Assure RMS). This method can be run in full automation from acquisition to report generation.

Future analysis of other batches of China White will be done by automatically running the Assure RMS method, dramatically reducing the analysis time.

Conclusions

- **NMR** is critical for the full analysis of NPS
- **NPS** analysis with **CMC-se**:
  - ✓ Elucidation of NPS from scratch
  - ✓ Verification of structure
  - ✓ Differentiation of regioisomers
  - ✓ No bias, no tunnel effect
  - ✓ Explore the whole chemical space
- **NPS mixture analysis workflow:**
  1. **DOSY** for compound separation
  2. **CMC-se** of 1 compound at a time
  3. **Assure RMS** for DB, ID and quantification

References

[1] 'Global Synthetic Drugs Assessment' report, UNODC, 22Feb19, https://www.unodc.org/documents/scientific/Global_Drugs_Assessment_2017.pdf

[2] https://www.bruker.com/products/mr/nmr/nmr-software/nmr-software/complete-molecular-confidence/cmc-se/overview.html, accessed 22Feb19

[3] https://www.bruker.com/products/mr/nmr/nmr-software/nmr-software/assurenmr/overview.html, accessed 22Feb19

Acknowledgements

John Ramsey

Forensics