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NMR chemical shifts in crystalline compounds

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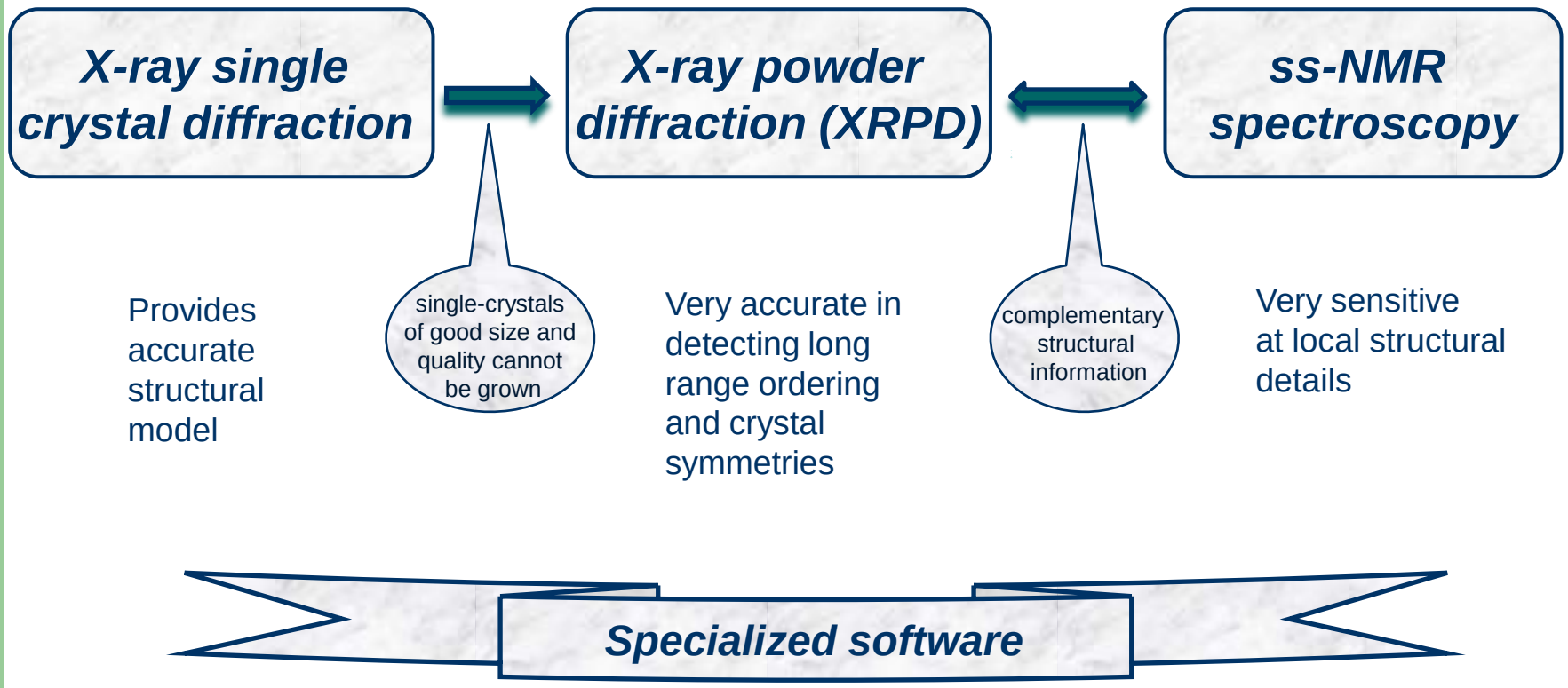
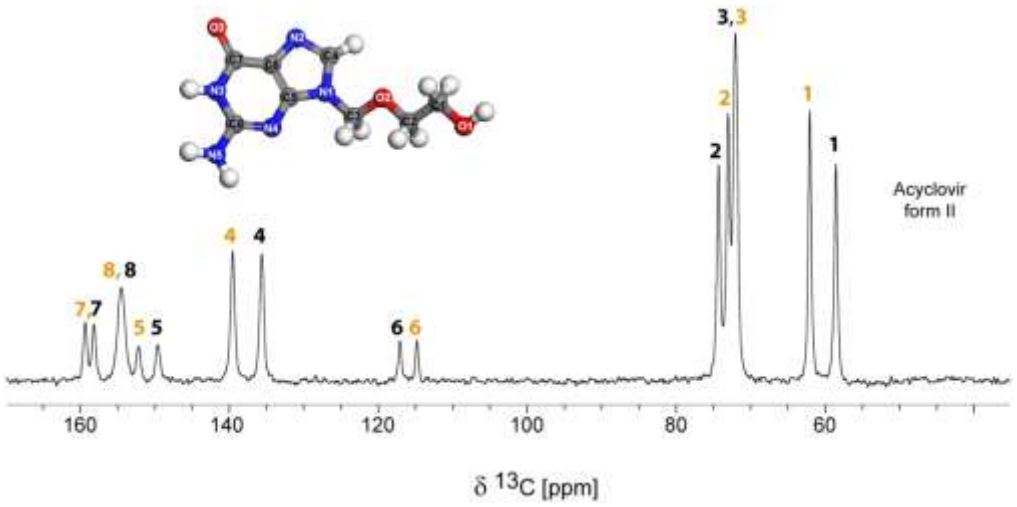
Crystal structure



NMR chemical shifts

Most of NMR crystallography applications relied on ^{13}C (^{15}N) Cross-Polarization Magic Angle Spinning (CP-MAS) spectra recorded on natural abundance samples



C.Tripon, I. Kacso, M. Miclaus, X. Filip, I. Bratu, C. Filip, "*Molecular structure elucidation of a new anhydrous polymorph of Acyclovir: experimental and computational approach*", **Acta Chimica Slovenica**, submitted

Provided information:

- number of molecules in the asymmetric unit
- presence of impurities
- different solid forms
- presence of structural and/or dynamical disorder in the lattice
- can validate the proposed structure solution (RMSD = 1.9 ppm)

NMR chemical shifts computations

Software:

DFT
plane waves
pseudopotentials
GIPAW module

Quantum ESPRESSO: integrated suite of *Open Source* computer codes

CASTEP / NMR CASTEP: modules of Materials Studio environment from Accelrys Company

- a tool for predicting NMR chemical shift for many types of material
- very good parallel efficiency

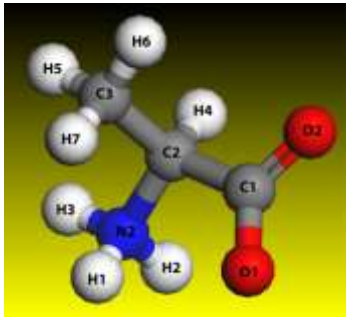
Hardware:

Datacenter INCDTIM Cluj

- **Past**: *2xOpteron dual-core 2224E, 16GB RAM 333 MHz*
- **Present:** *Hewlett Packard Blade C7000 with 16 Proliant BL280c G6 (2 Intel Quad-core Xeon x5570 @ 2.93 GHz, 16 GB RAM, 500 Gb HDD)*

Future: *IBM System x iDataPlex DX360 M4, Two Head Node Server: 6-core, with 2.93 GHz, and 12 MB L3 cache, 28 Nodes: Two Intel XeonSandy Bridge E5-2665 8-Core 2,4 GHz, 20 MB L3 cache, DDR3 64 GB 1600 MHz ECC (448 cores) (2 of this nodes have also NVIDIA Tesla M2090 GPU); Network Connection: FDR Infinte band with 56 GB band width*

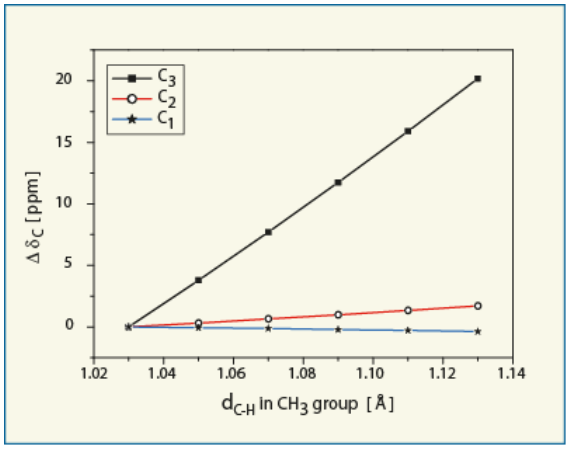
NMR chemical shifts dependencies on C-H and N-H bonds length

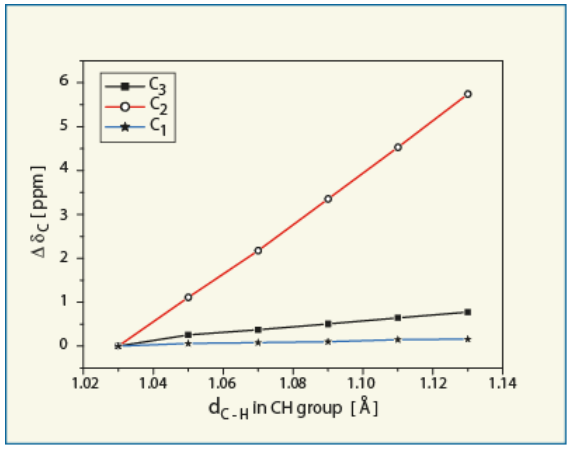


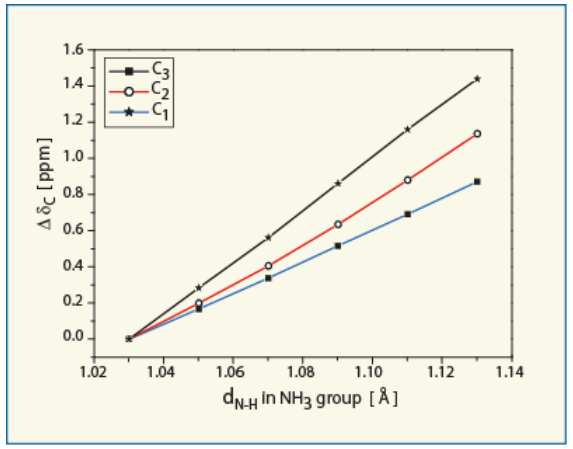
L-alanine

✓ The isotropic chemical shifts for each carbon and proton site were computed on a set of molecular structures obtained by varying the C-H and N-H bond length in the range 1.03 – 1.13 Å

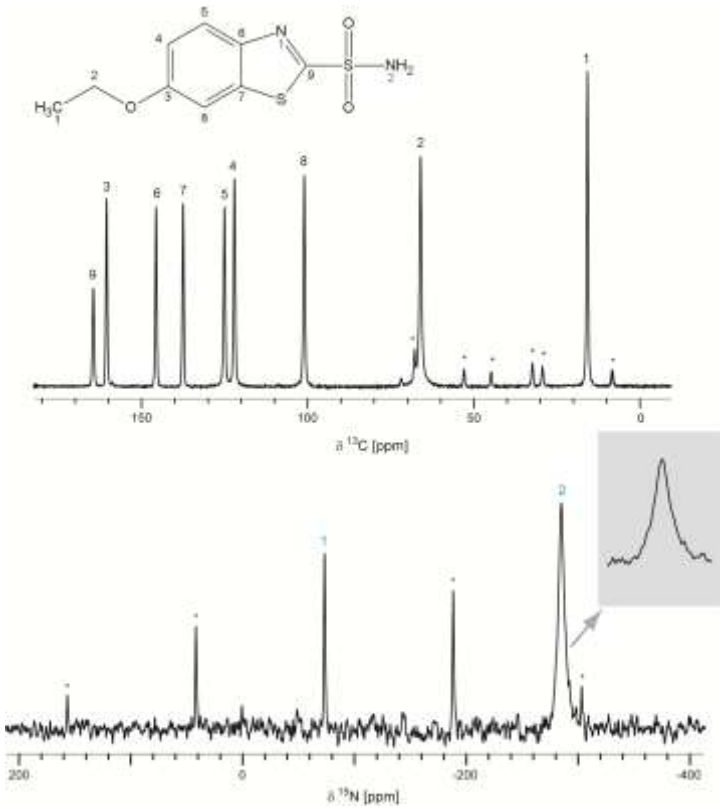
✓ The maximum variations were obtained for nuclear spins belonging to directly bonded C-H and N-H, namely 6-6.5 ppm per each C-H bond within a CHn moiety in the case of 13C, and 2-3.5 ppm for 1H, respectively

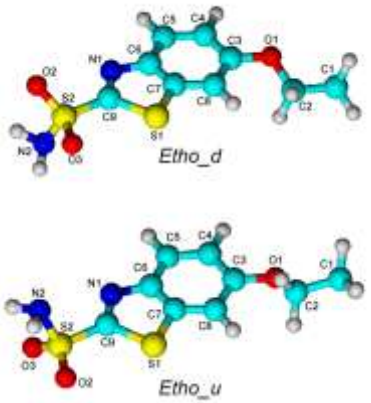


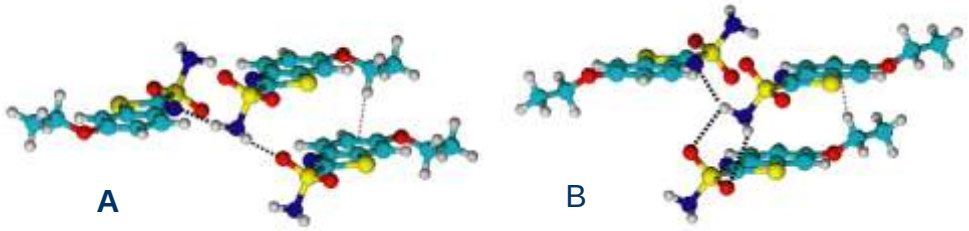




Application: ethoxzolamide structure



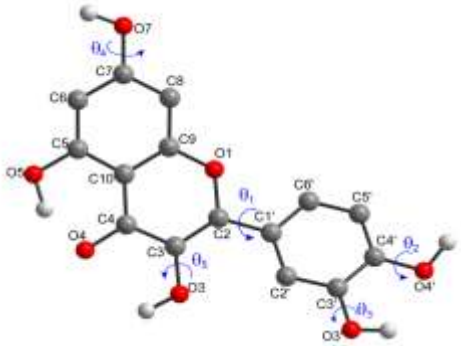


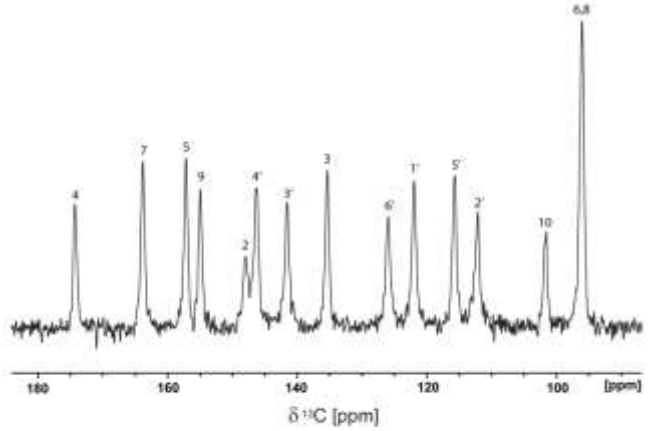


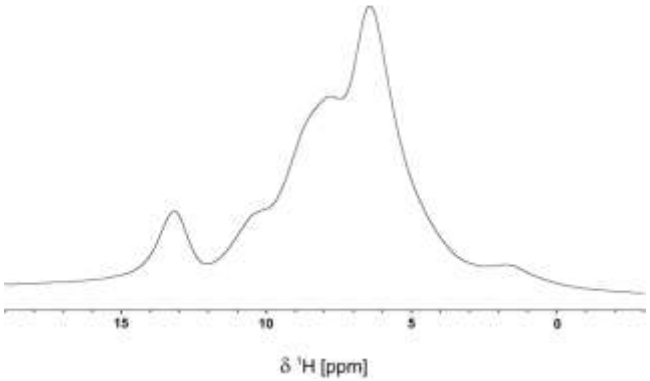
X. Filip, G. Borodi, C. Filip, "*Testing the limits of sensitivity in a solid-state structural investigation by combining X-ray powder diffraction, solid-state NMR and molecular modeling*", **Phys.Chem.Chem.Phys. 13**,17978 (2011)

Application: quercetin structure

anhydrous quercetin







X. Filip, I.G. Grosu, M. Miclaus, C. Filip, "*Structural investigation of anhydrous quercetin on microcrystalline powder by NMR crystallography methods*", **Phys.Chem.Chem.Phys.** (submitted)

Conclusions

NMR assisted crystallography protocol is successfully used to determine the molecular architecture in powders. This protocol, which combines X-ray powder diffraction (XRPD) with complementary techniques such as solid-state NMR (SS-NMR) and molecular modeling (MM), is able to facilitate the validation and selection of the accurate structure solution.

Acknowledgements

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Modern high-throughput methodologies for obtaining and characterizing new solid forms of pharmaceutical compounds / HT-PHARMA (Dr. Mihaela Pop)

-Sectorial Operational Programme "Increase of economic competitiveness"
-Priority Axis 2 – Research, Technological Development and Innovation for Competitiveness

Modern approaches for solid form screening of active pharmaceutical ingredients and structural characterization on powders(Dr. Carmen Tripon)

- PNII – Human Resources - Postdoctoral research project

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Cluster configuration: **Calin Floare**