I) Utilization of dipolar couplings for structure refinement

II) Polymorphism and segmental dynamics

NMR Crystallography

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Joint Laboratory of Solid-State NMR
Solid-state NMR spectroscopy

NMR

XRD

(visualization of H dipolar couplings)

NMR crystallography

Dynamic disorder and crystal stability

New crystal form of metergoline – structural fragments and segmental
Dipolar coupling constant depends on $1/J_{CH}$.

$J_{CH} = \frac{\gamma_1 \gamma_2 h}{2\pi} \frac{4\pi \mu_0}{3} \frac{\cos^2 \theta}{r^6}$

where $\gamma_1$ and $\gamma_2$ are the gyromagnetic ratios of $H_1$ and $C$, respectively, and $r$ is the distance between the nuclei.
NMRCrystallography

Basic Experimental Approach
Dipolar couplings and internuclear distances

Standard 2D experiment
H-13C FSLG-LC6P-HEtCOR

Long-range (through-space)

One bond

13C-LR pairs
Basic Experimental Approach

Dipolar couplings and interatomic distances

NMR Crystallography
Basic Experimental Approach
Dipolar Couplings and Interatomic Distances

NMR Crystallography
New low-temperature polymorphs of Simvastatin
Resulting conformational changes of the ester tail

Simvastatin (Zocor®)

Low-temperature polymorphs of simvastatin
Form II - Two stable positions of the ester tail in the conformation 231 229.
Form II - Dynamic disorder of the ester tail in the conformation 231 229.
Form I - Dynamic disorder of the ester tail in the conformation 239 229.

Structure Refinement of PXRD data

Conformational polymorphism of simvastatin
Polymerisation of metrogoline
Hydrogen bonding

Polymorphism of metagoline
Polymerization of metrogoline
Polyorphism of metrogolme

Form I

Form II

Form III

Comparison with PXRD Results

Structural Fragments

PXRD and single crystal X-ray
Diamond is the best friend of woman.

Diamonds are forever.

$T_1$ (10°C) relaxation time – up to 2 days

Fully immobilized carbon atoms

NMR cryo spectroscopy
Differences in segmental dynamics

Polymorphism of metrogoline
Macrosopic behavior of APL S?
Properties determined by ssNMR and
Is there any connection between molecular
V) And what about practical results

IV) Segemntal dynamics and motional amplitudes

III) Input data for Refinement of PXRD Results

II) Fragments of molecular arrangement

I) Conformation of single molecule

Summary

Dipolar spectroscopy & ssNMR crystallography
The crystal unit irreversibly converts to the Form I less stable form containing two symmetry independent molecules in Form II forms (always broad an narrow signals detected in NMR spectra from aprotic solvents or by moderate short-term heating of other in modern amicably most stable form - prepared by slow crystallization).

Dynamic disorder and crystal stability

Dipolar spectra & ssNMR crysfallography
\[ \Delta G = -6.7 \text{kJ/mol} \]

Temperature stabilization energy (i.e., increase in conformation entropy at given transition: Form I \( \leftrightarrow \) Form II)

\[ \left( \frac{S_{\text{II}}}{S_{\text{I}}} - 1 \right) \ln \frac{S_{\text{II}}}{S_{\text{I}}} = \Delta G \]

Upper bound of Gibbs energy

\[ \theta = 30 - 40^\circ \]

Average fluctuation angle of disordered fractions:

\[ \langle \theta \rangle \frac{2}{3} = 1 - S \]

Rotational diffusion motion model:

\[ S = 0.36 \]

Order parameter: (determined from dipolar spectra)

\[ S = 0.95 \]

The observed disorder is dynamic (high amplitude, ca. 30% of molecules have undefined conformation, Form I)

**Dynamic disorder and crystal stability**

**Dipolar spectra & ssNMR crysIallography**
Acknowledgement