
MAGNETIC RESONANCE DAY
23/9/2021
lecture hall
ÚOCHB AV ČR
IOCB PRAGUE
NMR SPECTROSCOPY
RESEARCH–SERVICE GROUP
IOCB PRAGUE

Program,
NMR Spectroscopy Group

PROGRAM

9:30–10:30	Introduction Variable-temperature NMR experiments NMR spectroscopy with in situ irradiation Solid-state NMR spectroscopy
10:30–11:00	Coffee break
11:00–12:05	^{3}H NMR of radioactive samples (300MHz NMR spectrometer) NMR-based structural biology (850MHz NMR spectrometer) EPR Spectroscopy
12:05–14:00	Lunch break
14:00–14:45	User meeting of the NMR self-service facility
14:45–15:00	Coffee break
15:00–16:00	Tips and tricks for structural analysis Tips and tricks for spectral processing with MNova

NMR Spectroscopy Group – Equipment

- Self-service measurements: 2 × 400MHz spectrometer

- NMR spectrometers with cryoprobes: 1 × 600MHz and 1 × 500MHz spectrometer

NMR Spectroscopy Group – Equipment

- Versatile NMR spectrometers: 2 × 500MHz spectrometer (temperature, F decoupling)

- Solid-state NMR: 1 × 600MHz

- EPR spectroscopy

NMR Spectroscopy Group – Cryoprobes

- Low sensitivity of NMR ➡ Fight for signal-to-noise ratio (S/N)
- NMR signal detected as electric current
- Electronic noise: in any conductor (NMR coils, wires)
- Lower temperature – lower electronic noise

– Helium-gas cooled probes

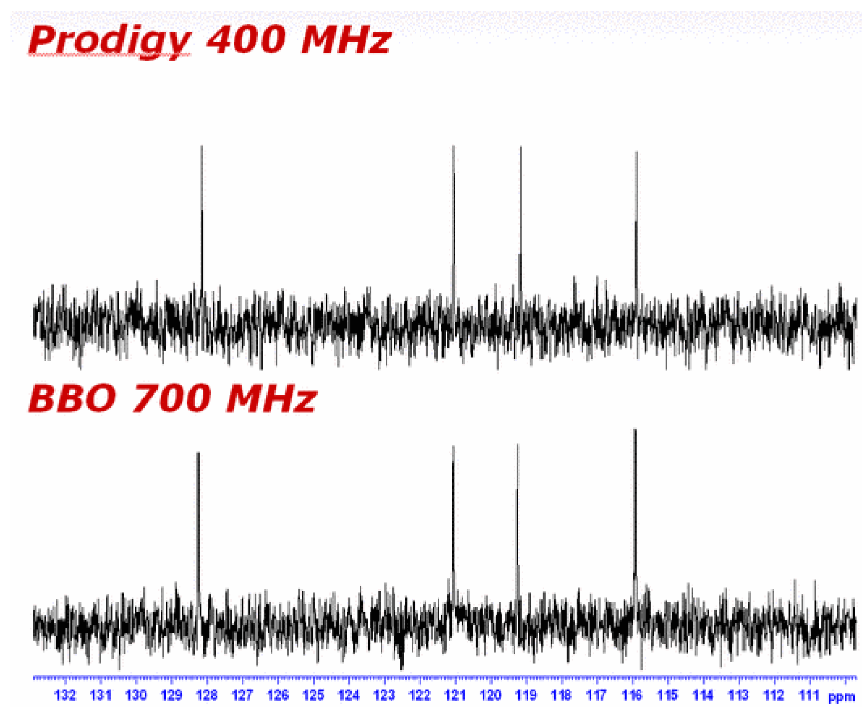
➕ 4–5 × higher sensitivity

➖ Expensive

➖ Regular maintenance necessary

– Nitrogen-liquid cooled probes (PRODIGY)

➕ 2 × higher sensitivity



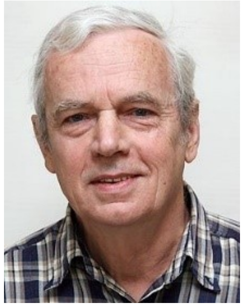
NMR Spectroscopy Group – Contacts

Building A1 – NorthEast wing

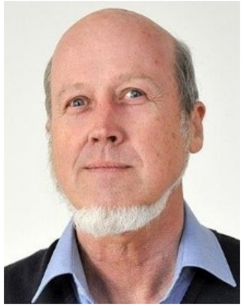
- NMR senior staff

Martin Dračínský

Radek Pohl



Miloš Buděšínský



David Šaman (emeritus)

Lenka Poštová Slavětínská

Eliška Procházková

- EPR senior staff

Ján Tarábek

- 400MHz maintenance

Ondřej Socha

Jakub Štoček

ÚOCHB AV ČR
IOCB PRAGUE

MAGNETIC RESONANCE DAY

Variable Temperature NMR

NMR SPECTROSCOPY
RESEARCH–SERVICE GROUP
IOCB PRAGUE

Why VT NMR?

- solubility issues ⬆
- broad NMR signals -simplifying spectrum for easier analysis ⬆
- monitoring of reaction kinetics at various temperatures – slowing down or speeding up the reaction rate ⬇⬆
- structure determination of metastable compounds ⬇
- study of chemical exchange (conformation, restricted rotation, tautomerism, hydrogen bonding, complexation…) ⬇⬆

Chemical Exchange: any process in which a nucleus exchanges between two or more environments and results in a change in NMR parameters (chemical shift, coupling constant, and/or relaxation rate).

VT NMR instrumentation at IOCB

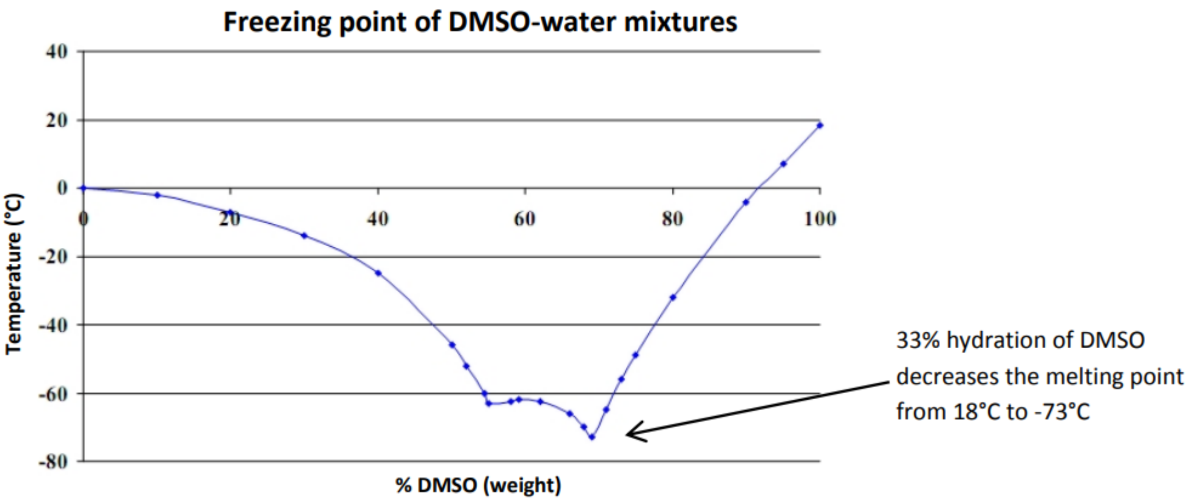
NMR SPECTROSCOPY
RESEARCH–SERVICE GROUP
IOCB PRAGUE

name (location)	**A601** (A.1.58)	**J600** (A.1.63)	**J500** (A.1.63)	**A501** (A.1.60)	**U500** (A.1.62)
magnet (^{1}H freq.)	Bruker (600.1 MHz)	JEOL (600.2 MHz)	JEOL (500.2 MHz)	Bruker (500.0 MHz)	Oxford (499.9 MHz)
console	Bruker Avance III HD	JEOL EZC600R	JEOL EZC500R	Bruker Avance III HD	Bruker Avance II
probehead	5 mm TCI cryo ^{1}H/^{13}C/^{15}N	3.2 mm HX MAS	5 mm ROHFX	5 mm CPBBO cryo	5mm TBO BB/^{1}H/^{19}F
probe temp. limits	-40 to +170 °C	-100 to +200 °C	-100 to +150 °C	0 to +135 °C	-150 to +150 °C
VT range	**+5 to +120 °C**	**-100 to +200 °C**	**-100 to +150 °C**	**+5 to +120 °C**	**-150 to +150 °C**

Initial consideration

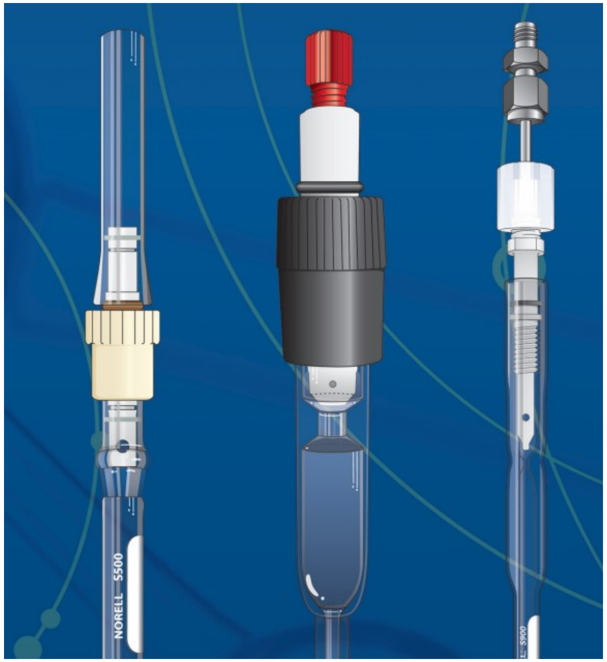
- solubility of your compounds at given temperature
- boiling/melting point of used solvent (or solvent mixture)
- NMR temperature calibration
- magnetic field homogeneity at given temperature

} NMR lab



J. Am. Chem. Soc., **2002**, *124*, 6206.

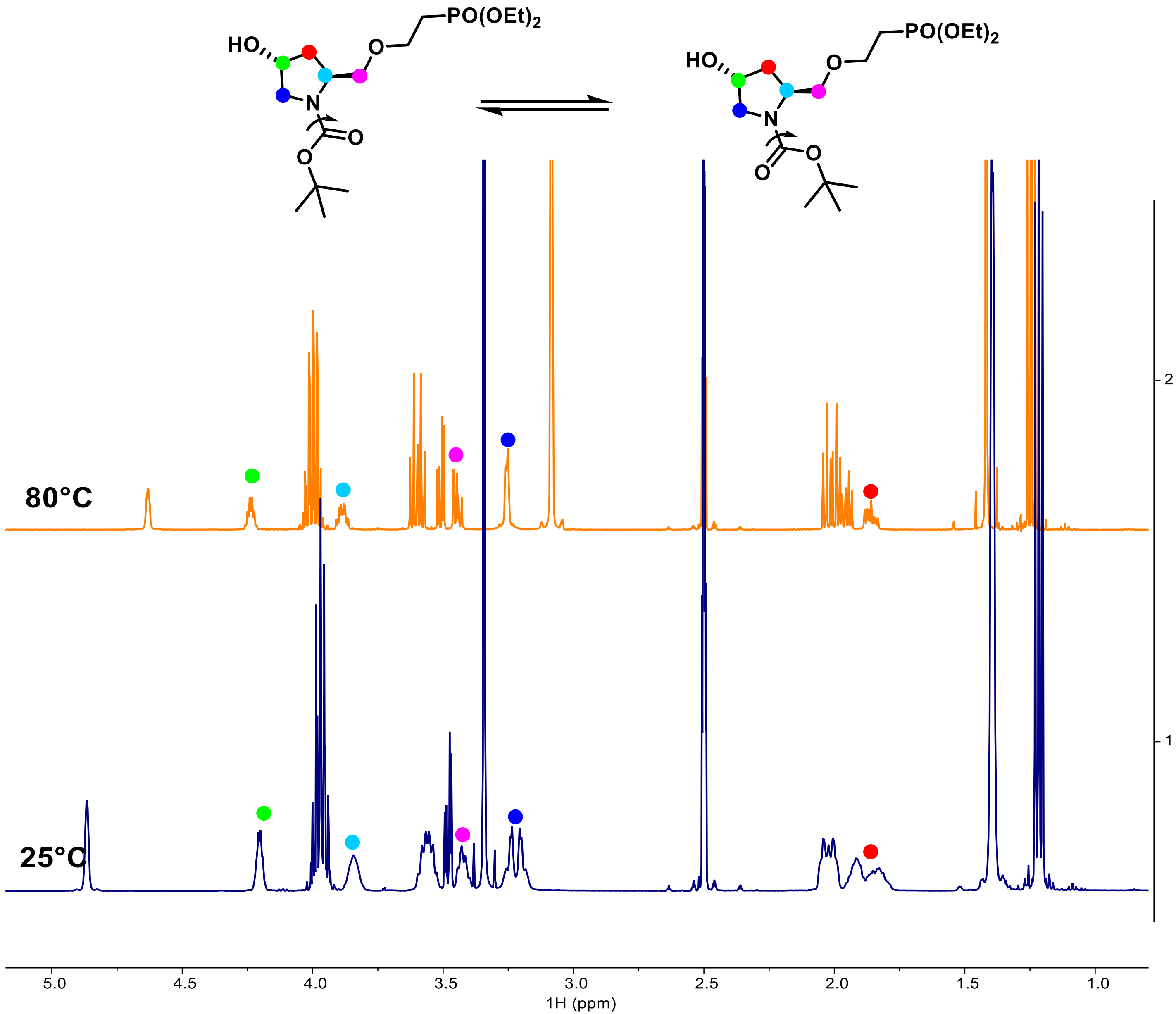
special NMR tubes



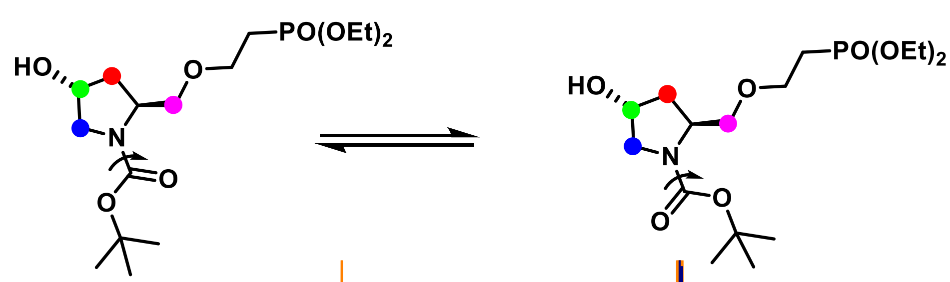
Other mixtures:

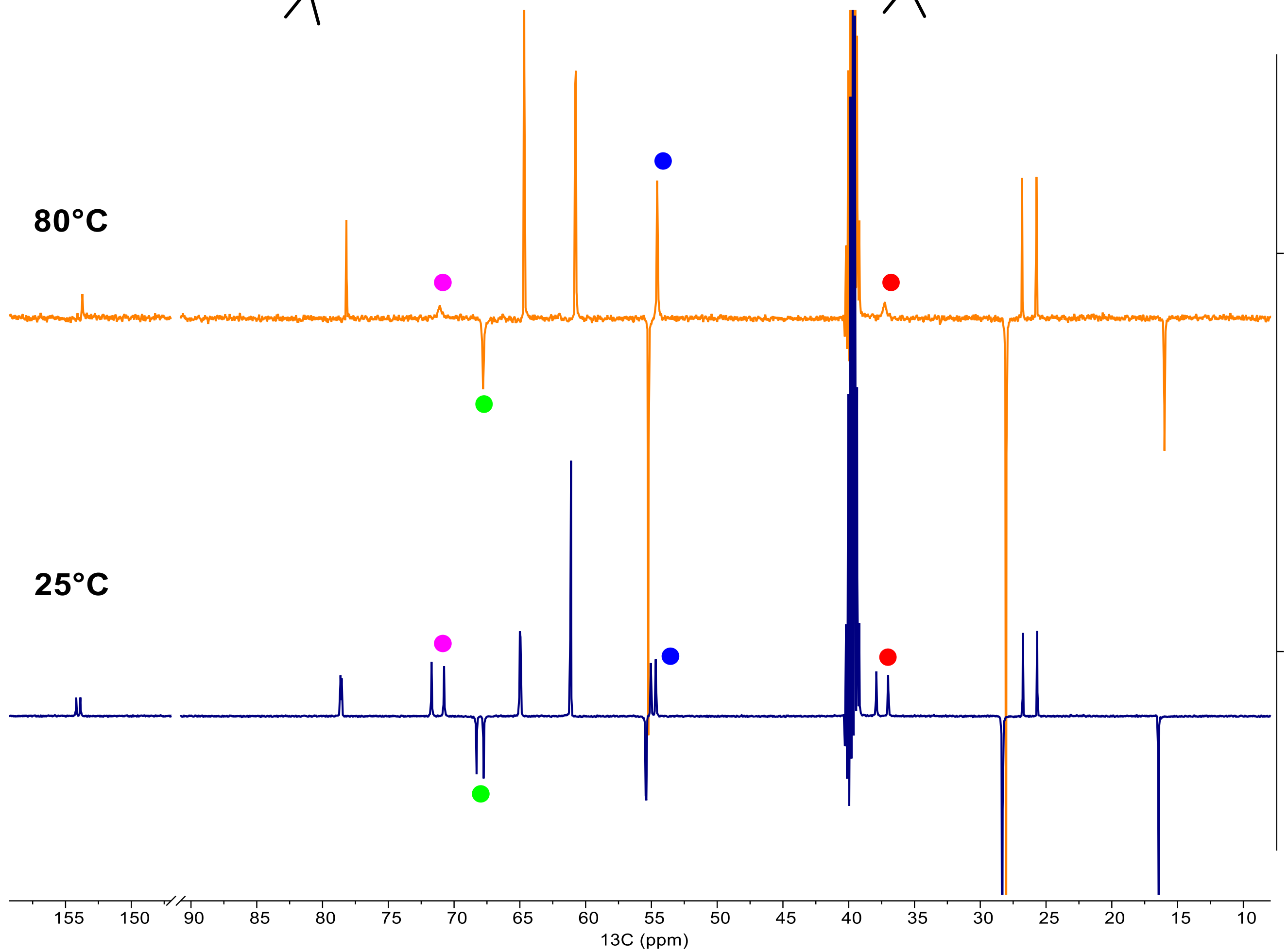
$CD_2Cl_2/CHFCl_2/CHF_2Cl$	-165 °C	*Organomatallics*, **2013**, *32*, 6996.
CD_2Cl_2/Me_2O	-153 °C	*J. Org. Chem.*, **2007**, *72*, 2003.
$DMF\text{-}d_7/CD_2Cl_2$	-125 °C	*Chem. Eur. J.*, **2018**, *24*, 492.

Example – broad signals

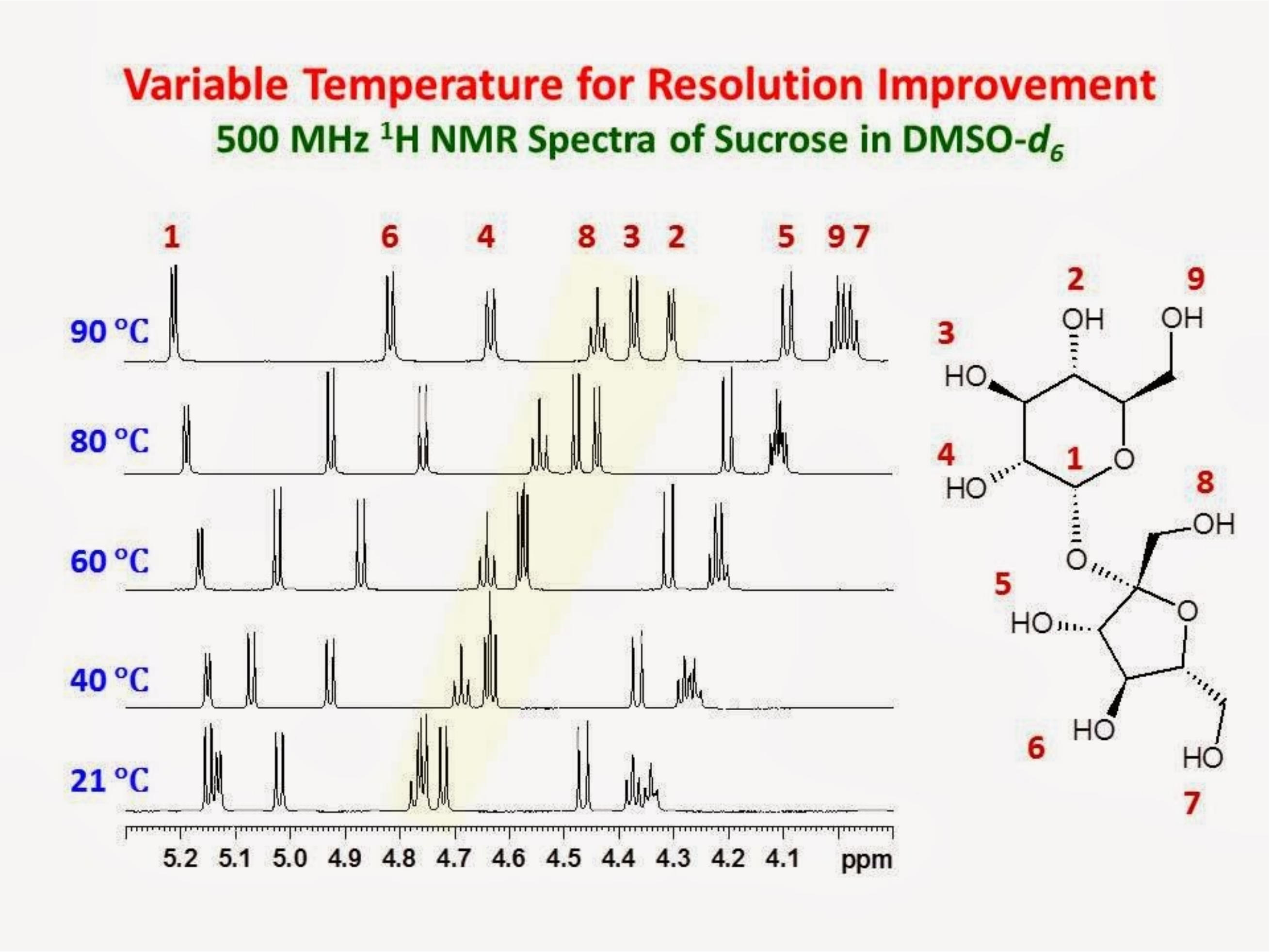


Example – two sets of signals



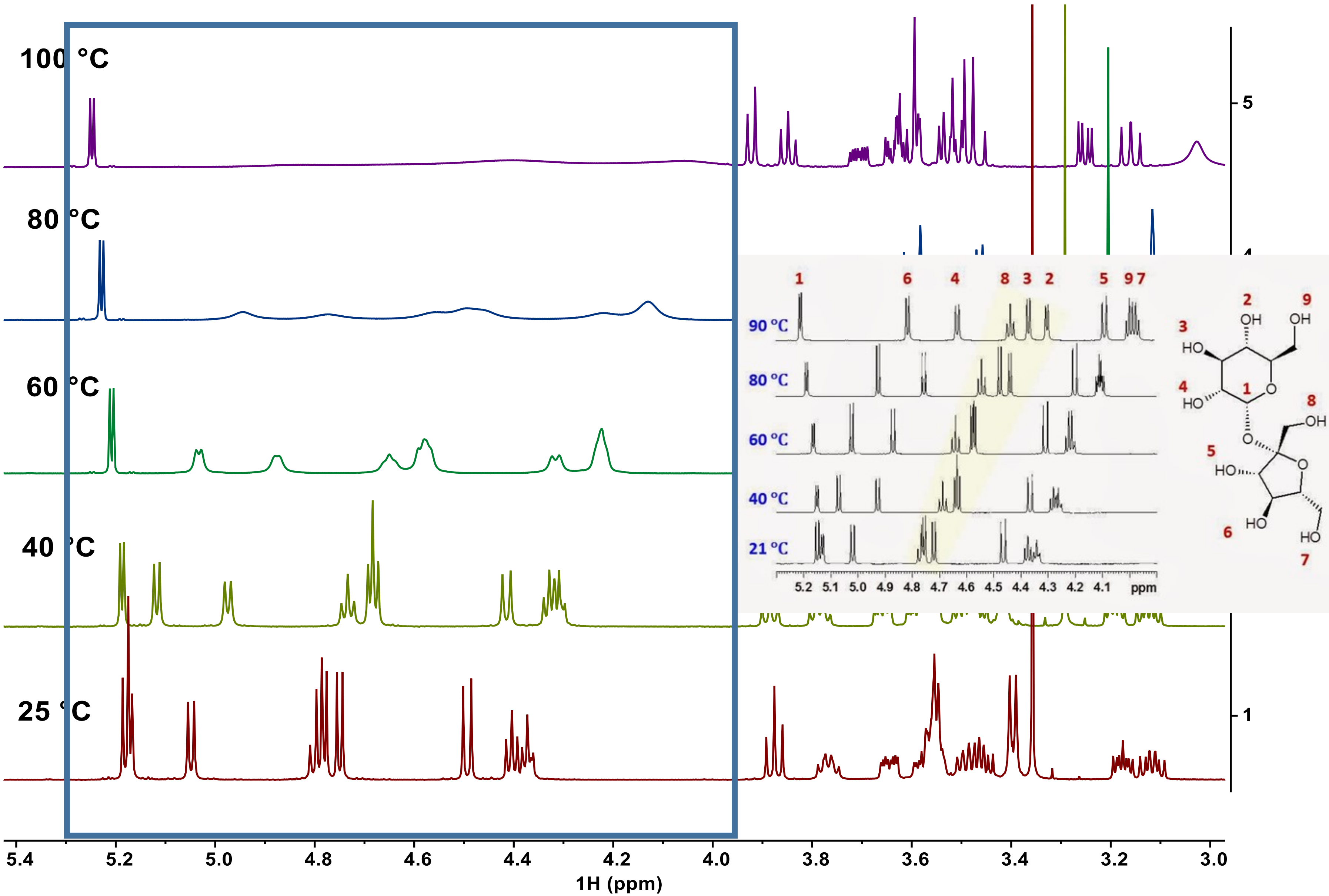


Example – sucrose exchangeable protons

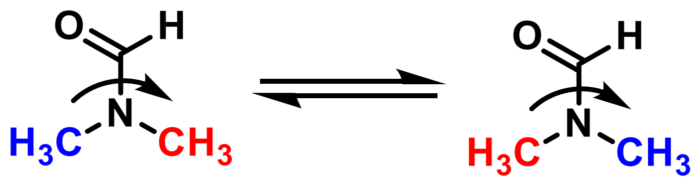


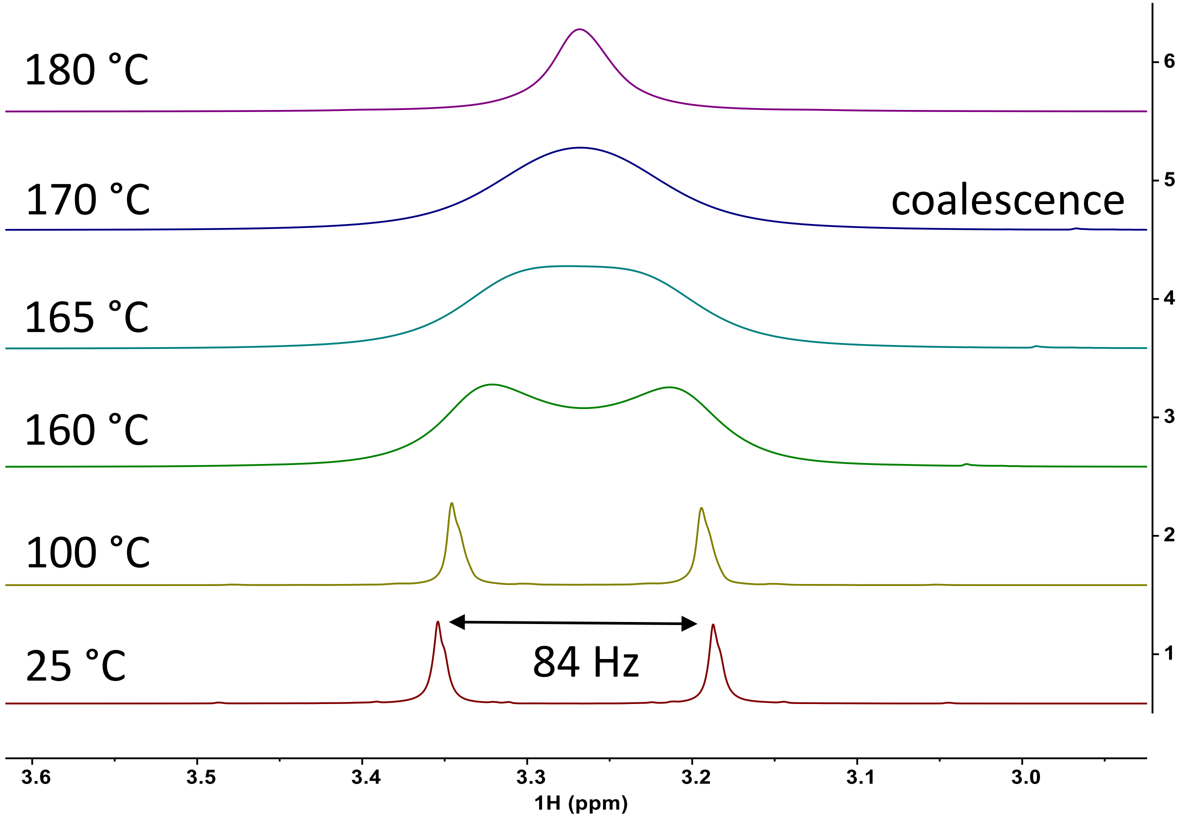
http://u-of-o-nmr-facility.blogspot.com/2014/03/variable-temperature-to-improve-nmr.html

Example – sucrose exchangeable protons



Example – DMF



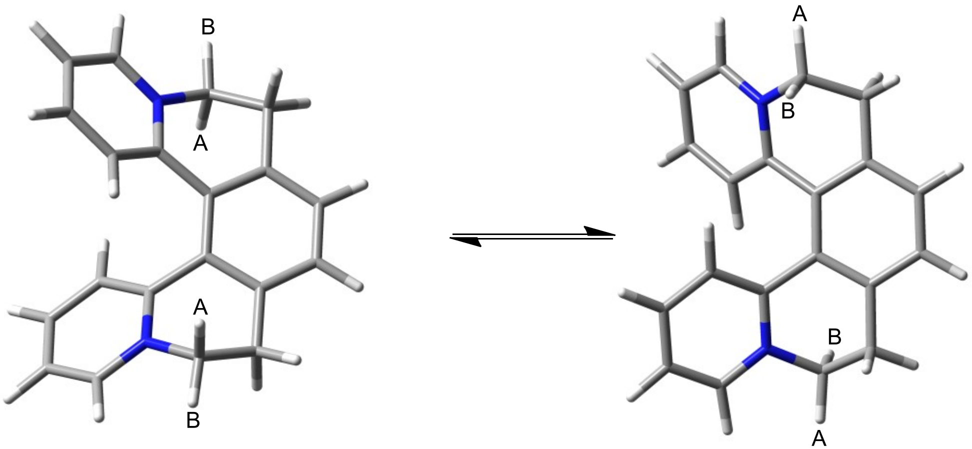


$k_c = 2.22 * \Delta\nu$

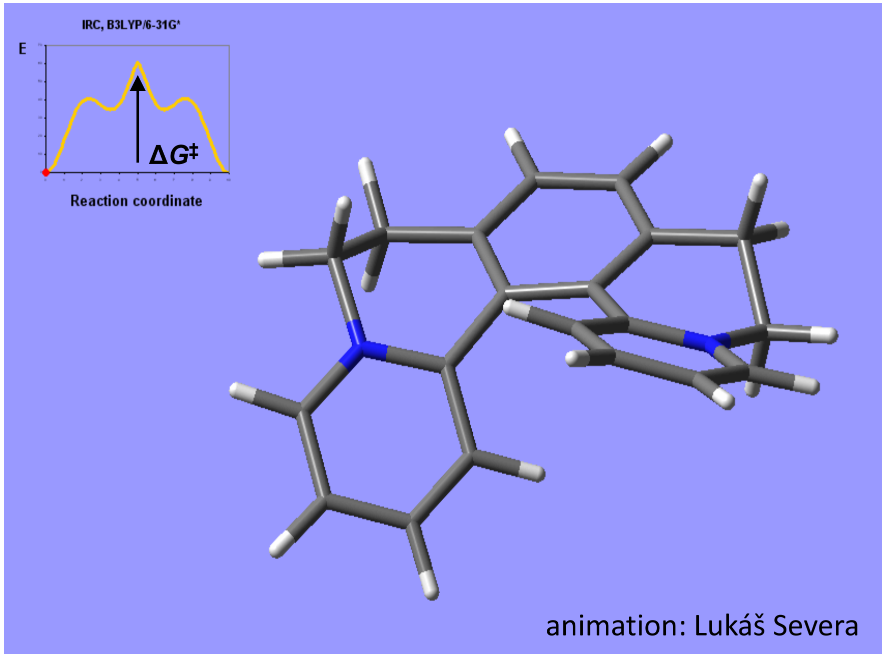
$k_c = 186.5\ s^{-1}$

$\Delta G^{\ddagger}_{170°C} = 21.6$ kcal/mol

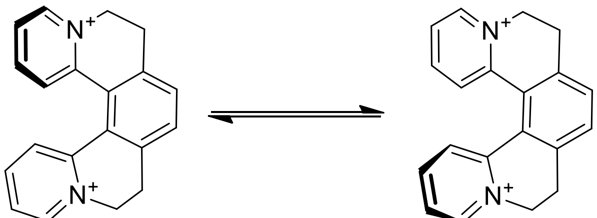
Example – helquat racemization



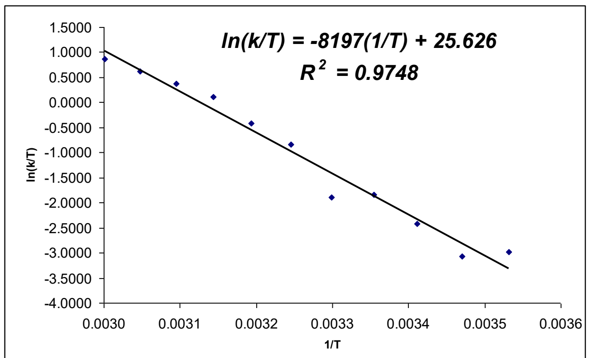
***P*-[5]helquat** **M-[5]helquat**

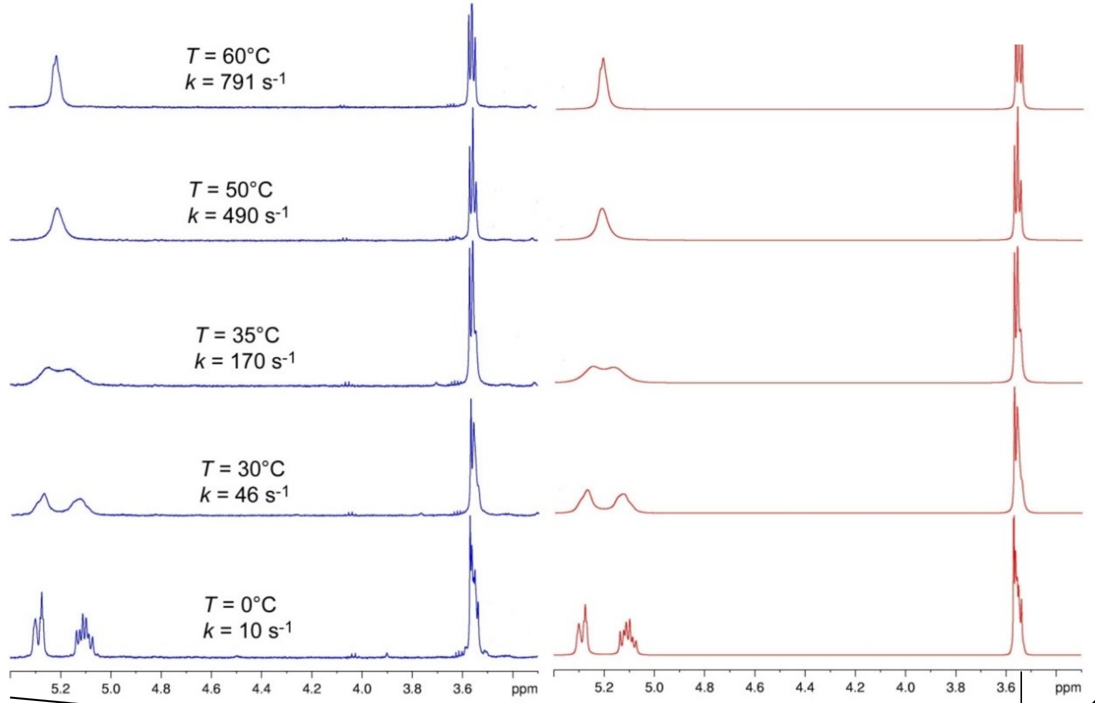


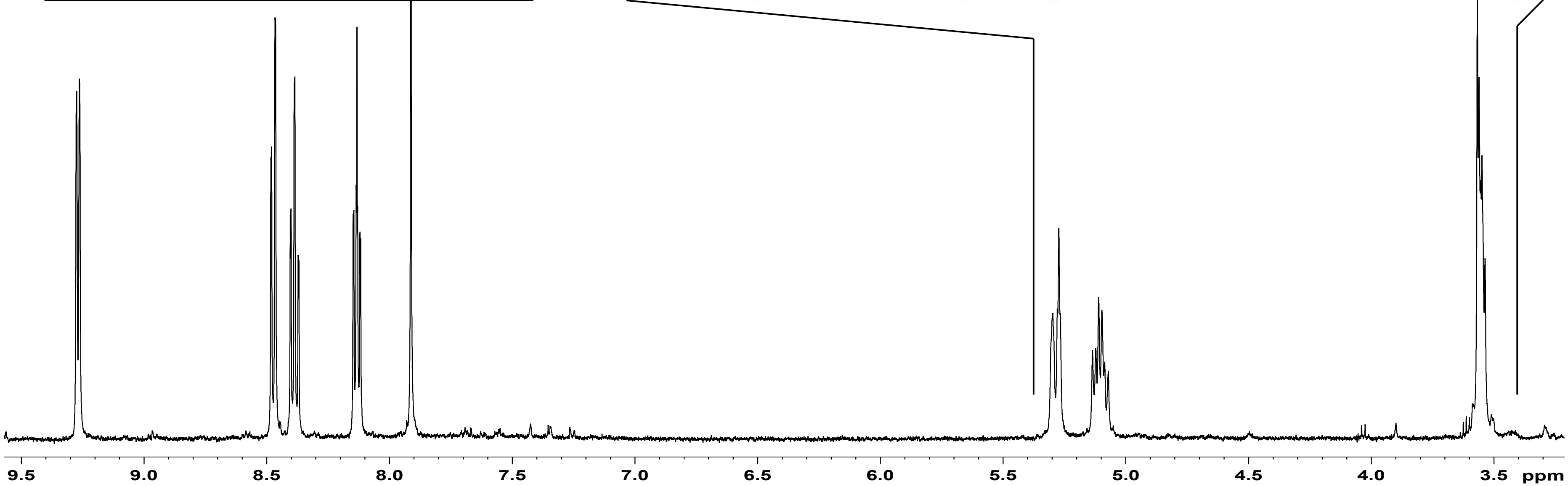
Example – helquat racemization



$\Delta G^{\ddagger}_{25°C}$ = 64 kJ/mol







ÚOCHB AV ČR
IOCB PRAGUE

MAGNETIC RESONANCE DAY

NMR spectroscopy with *in situ* irradiation

NMR SPECTROSCOPY
RESEARCH–SERVICE GROUP
IOCB PRAGUE

NMR spectroscopy with *in situ* irradiation

- Useful tool for photochemical processes
- Samples are irradiated by LED lamp directly inside the NMR tube
- Detection and characterization of metastable forms using advanced NMR methods (^{13}C, ^{15}N, 2D experiments with longer measurement time)
- Variable temperature NMR measurements

LED setup

- ✚ No special NMR probe is essential
- ✚ No special safety rules
- ✚ Variety of LED lamps (λ) available
- ✚ Comfortable LED changing (for λ_1/λ_2 photoswitching)
- ✚ Universal usage for all spectrometers (including EPR spectrometer)

Experimental setup

- Implemented at IOCB in 2017
- Device from Thorlabs, Germany

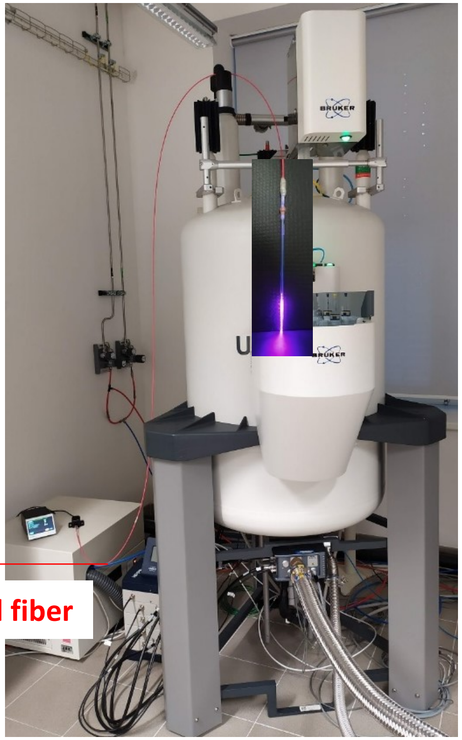
LED driver

- Suitable for LED with 280–1050 nm
- Level of brightness
- Pulse modulation
- TTL modulation – triggering directly in the pulse sequence

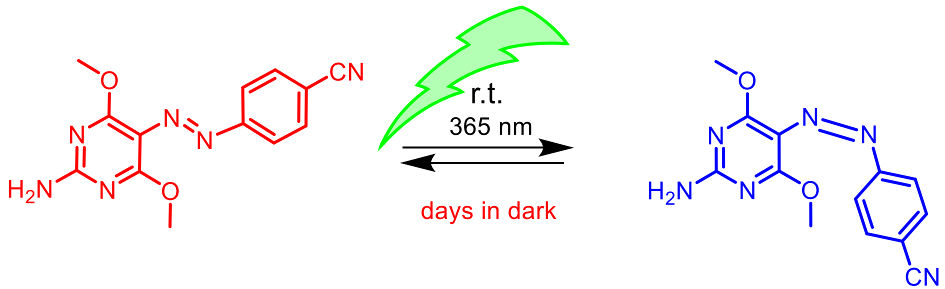
LED lamp

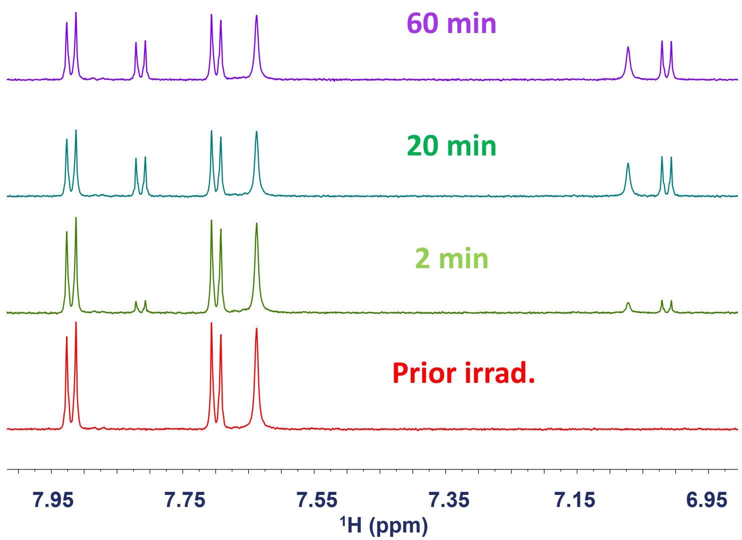
- Different λ available
- At IOCB we have so far:

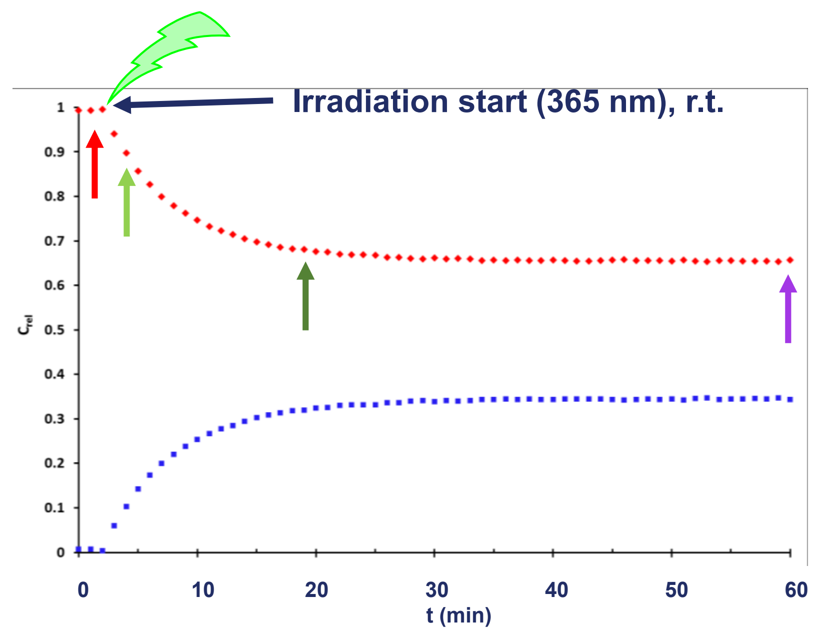
365 nm
405 nm
470 nm
505 nm
660 nm



Structural and kinetic information extracted



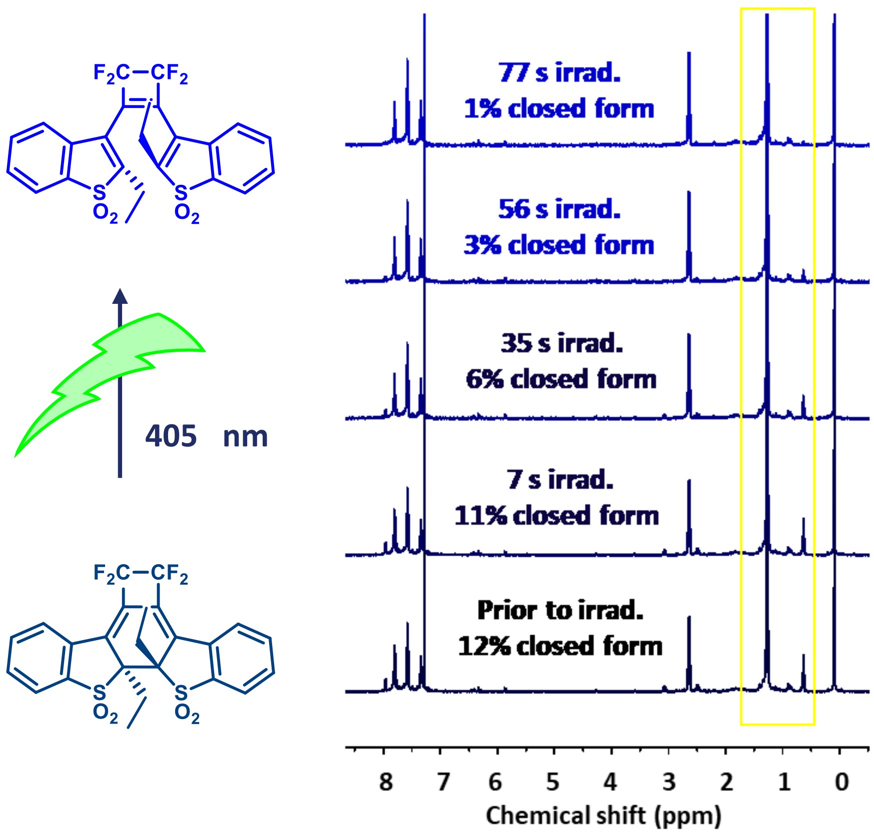


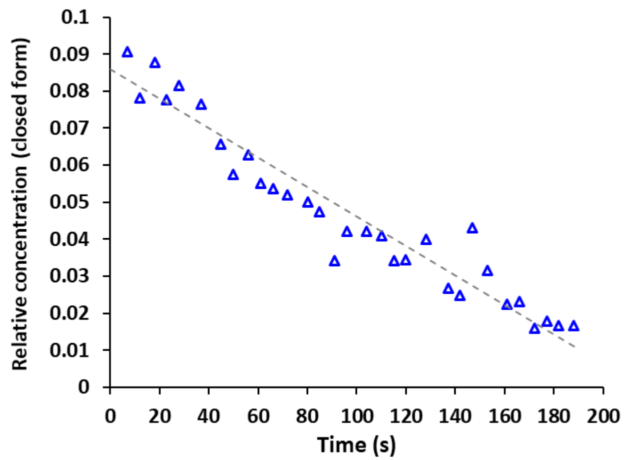


Čechová L., Kind J., Dračínský M., Filo J., Janeba Z., Thiele C., Cigáň M., Procházková E.: *J. Org. Chem.* **2018**, 83, 5986-5998.

Suitable for fast photoreactions

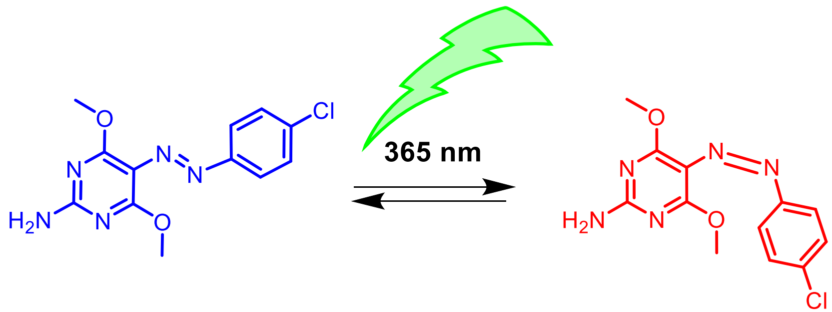
- A second time-scale reactions

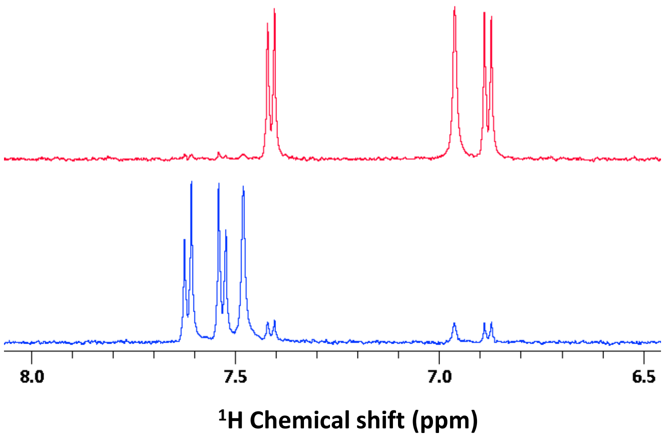


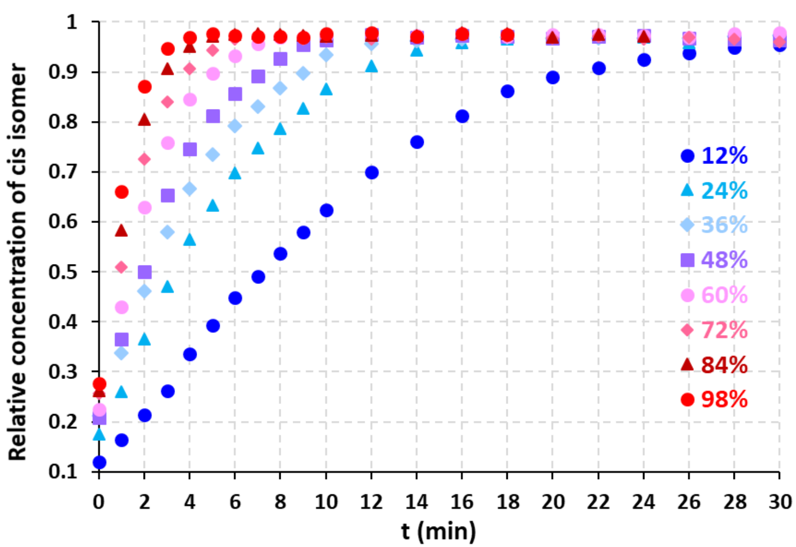


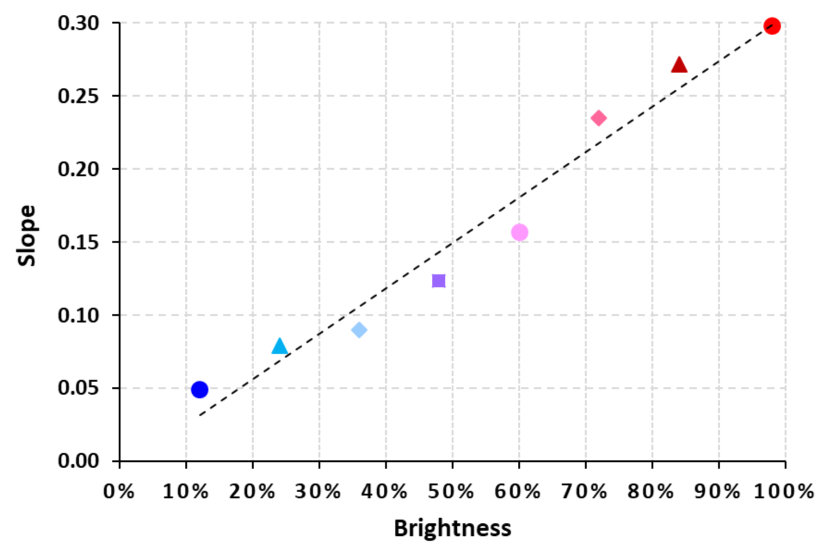
Sysoiev D., Procházková E., Semenenko A., Pohl R., Shishkina S., Klepetářová B., Shvadchak V., Yushchenko D. A.: *ChemPlusChem* **2020**, 85, 2084–2092.

Light intensity modulation



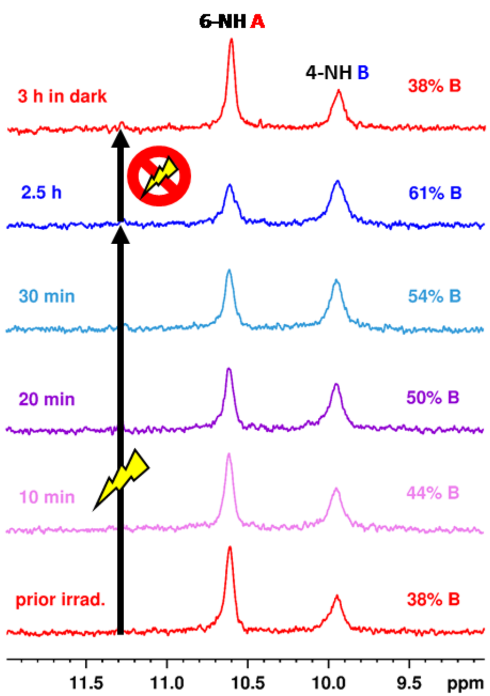




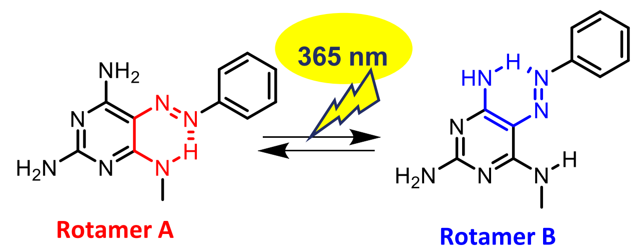


Low-temperature measurements

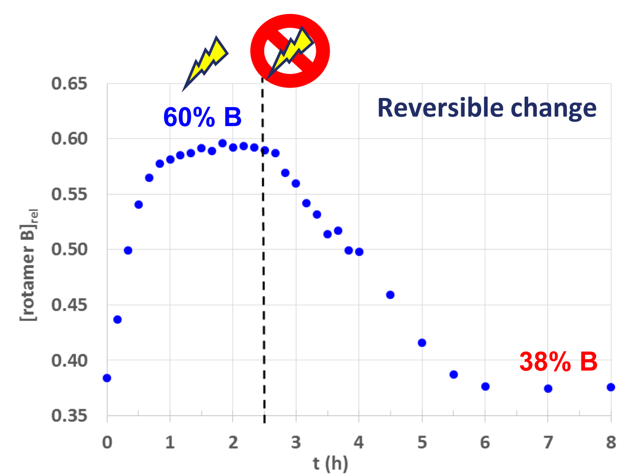
- At 25 °C, no spectral changes were found
- At –105 °C, significant changes in NH region: **Rotamer ratio changes significantly upon irradiation**, no *cis* isomer detected
- Photoswitchable intramolecular hydrogen bonds revealed



365 nm, –105 °C, 50% DMF/CD_2Cl_2

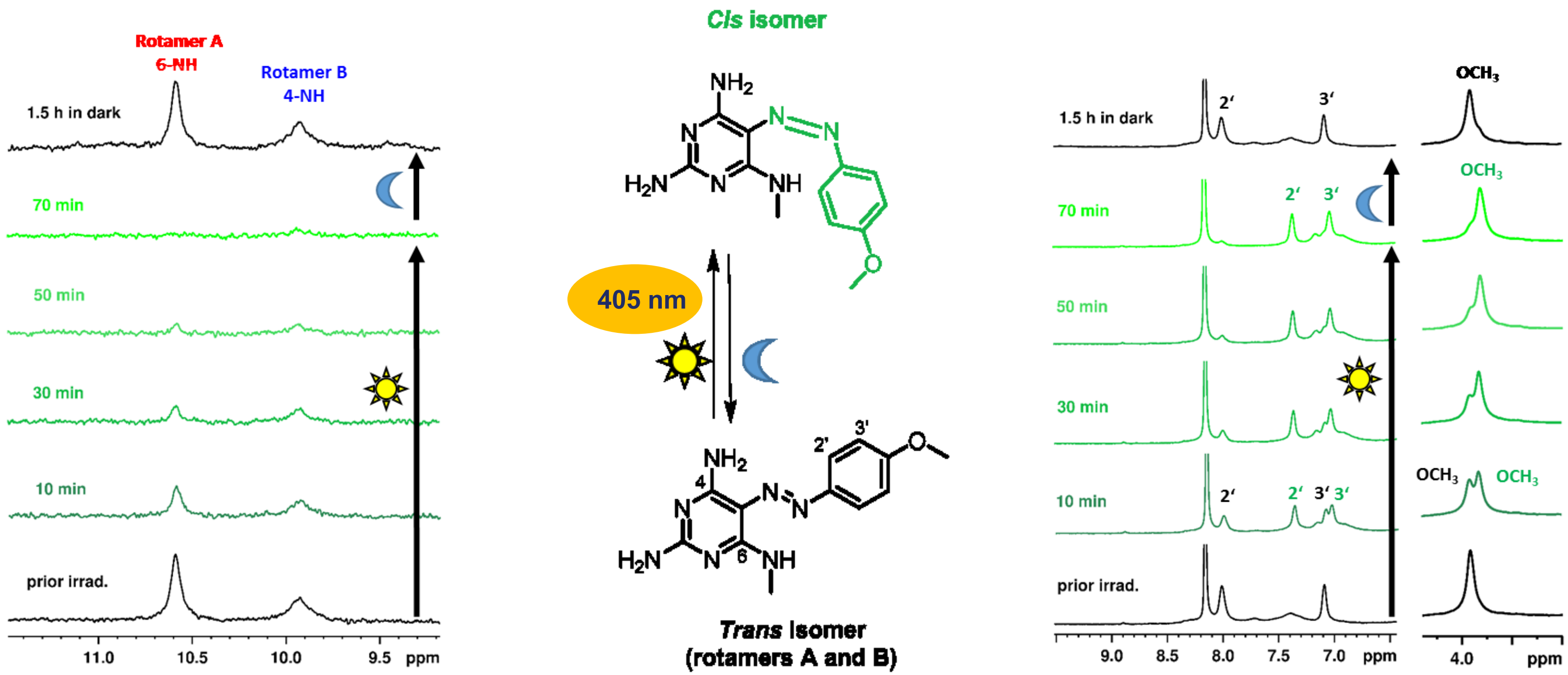


Rotamer B concentration profile



Procházková E., Čechová L., Kind J., Janeba Z., Thiele C., Dračínský M.: *Chem. Eur. J.* **2018**, 24, 492.

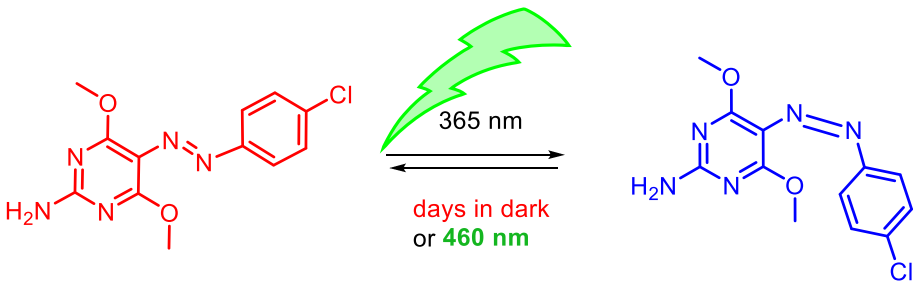
Low-temperature measurements



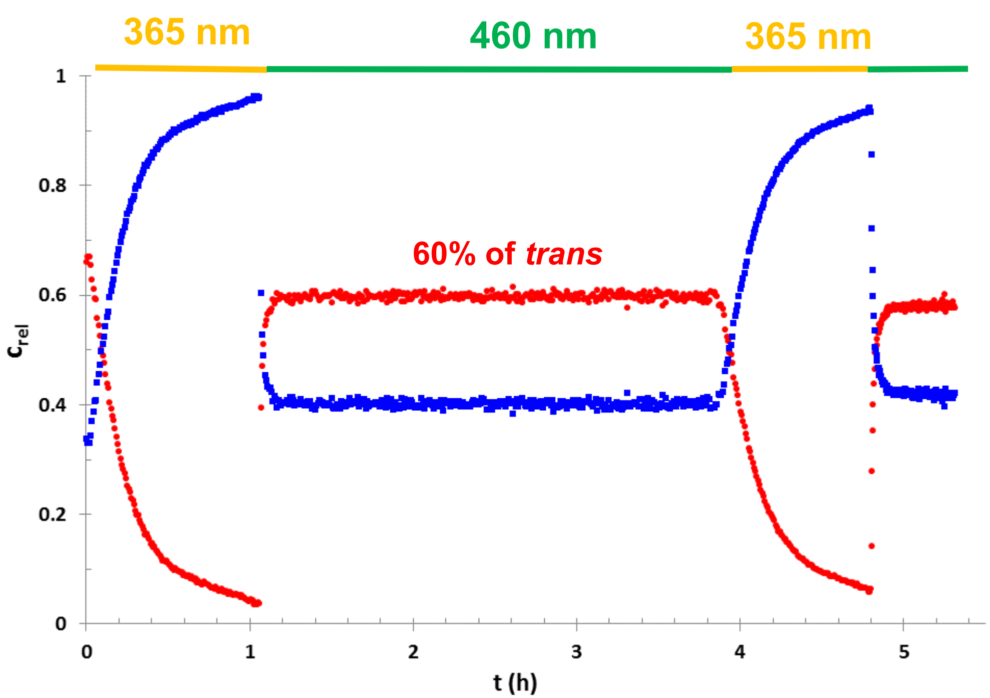
- Upon irradiation at 405 nm (–105 °C), only OCH_3 derivative provided *cis* isomer
- *Cis* isomer of OCH_3 derivative is the most stable
- **H-bonds definitely do not lock the *cis* isomer formation**

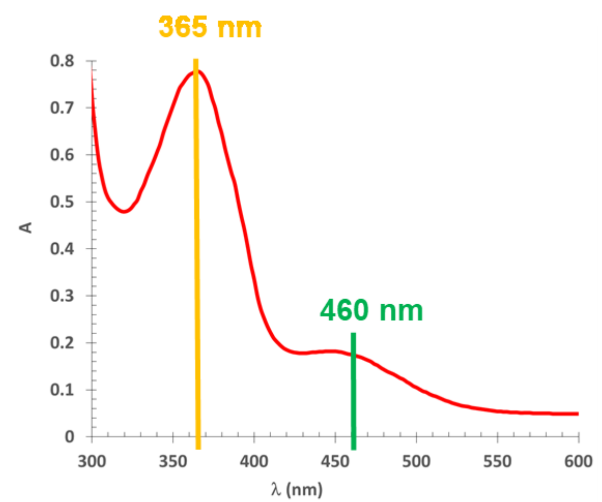
Procházková E., Čechová L., Kind J., Janeba Z., Thiele C., Dračínský M.: *Chem. Eur. J.* **2018**, 24, 492.

Photoswitching by two wavelengths



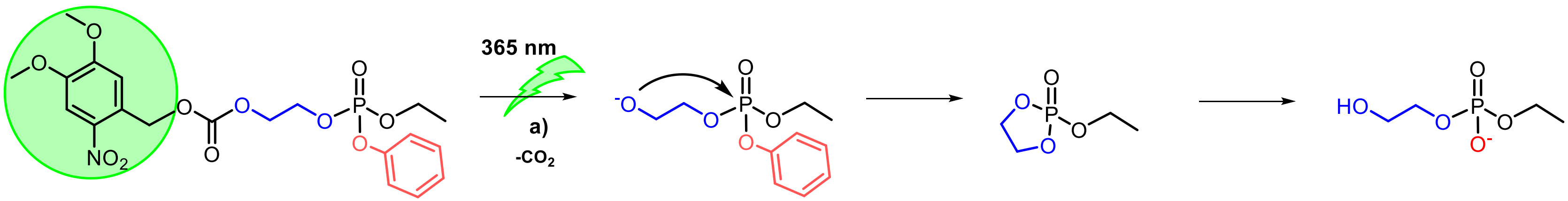
- Upon visible light irradiation (460 nm), only **60% of *trans*** isomer is obtained.
- **Both isomers absorb at 460 nm**

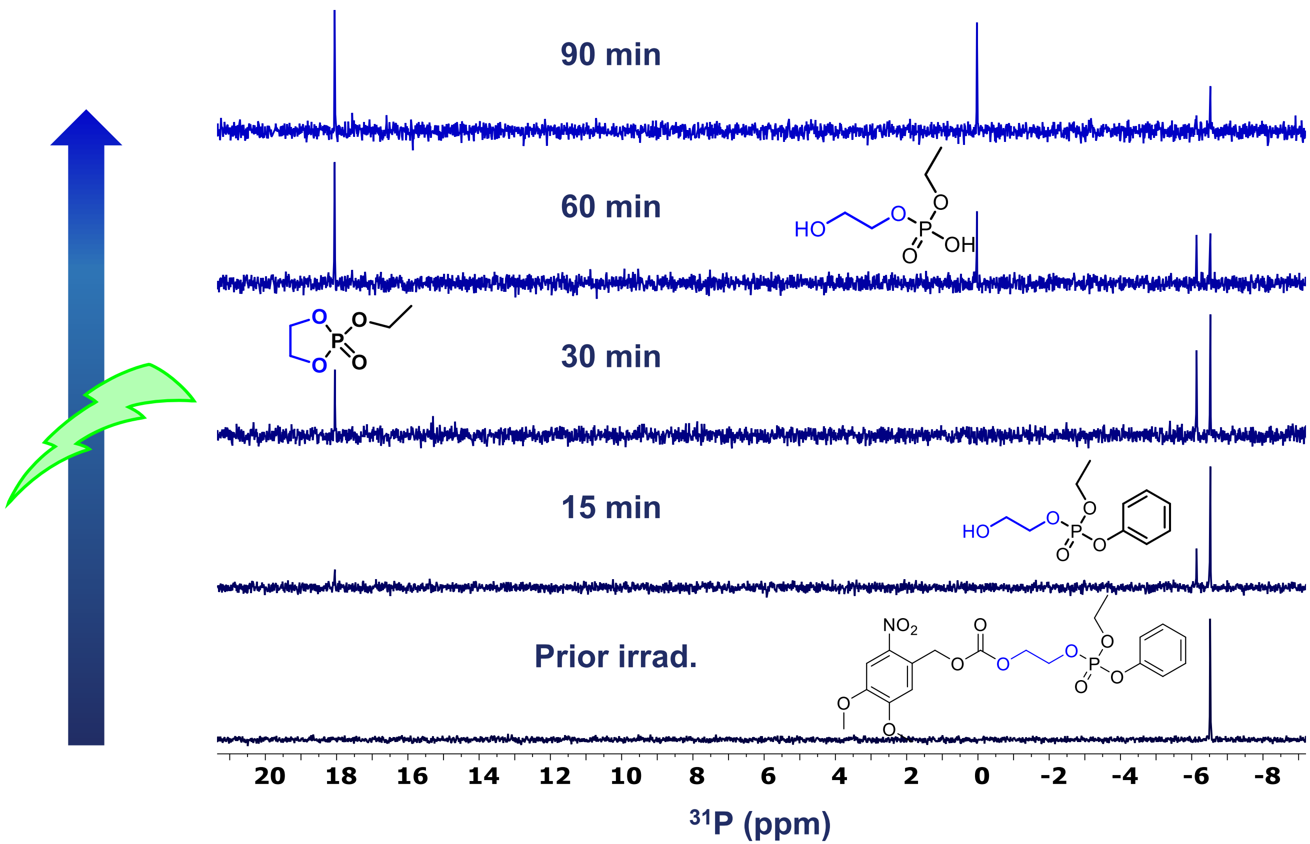




Čechová L., Kind J., Dračínský M., Filo J., Janeba Z., Thiele C., Cigáň M., Procházková E.: *J. Org. Chem.* **2018**, 83, 5986-5998.

Phototriggered bond cleavage





Procházková E., Šimon P., Straka M., Filo J., Májek M., Cigáň M., Baszczyňski O.: *Chem. Commun.* **2021**, 57, 211–214.

ÚOCHB AV ČR
IOCB PRAGUE

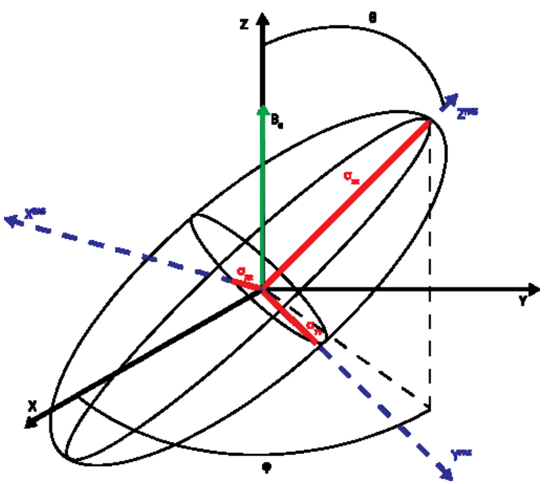
MAGNETIC RESONANCE DAY

Solid-state
NMR spectroscopy

NMR SPECTROSCOPY
RESEARCH-SERVICE GROUP
IOCB PRAGUE

NMR interactions

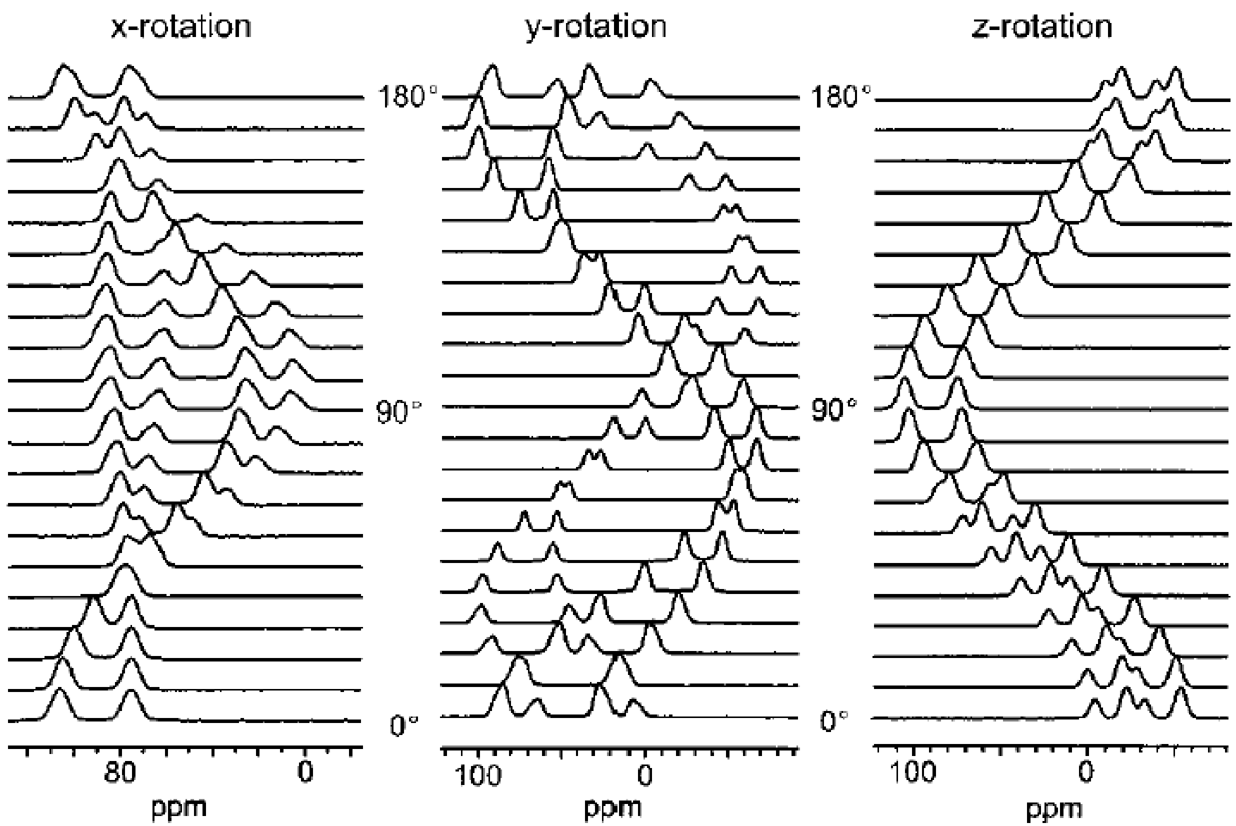
SOLIDS	SOLUTIONS
- Chemical shift anisotropy	δ
- *J*-coupling (indirect coupling)	J
- Direct spin-spin interaction (dipolar coupling)	-
- Quadrupolar interaction	-

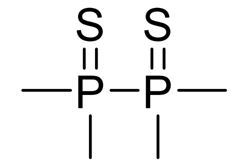


$$(3\cos^2\theta - 1)$$

Chemical shift anisotropy – single crystal

Static ^{31}P NMR

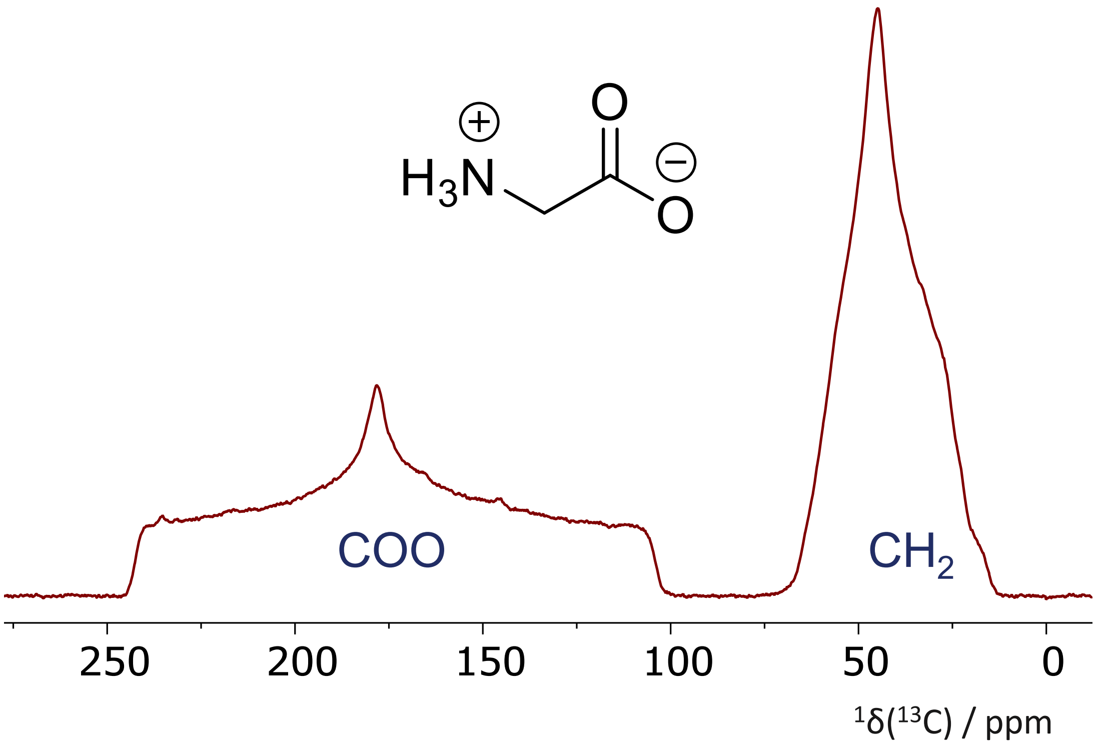




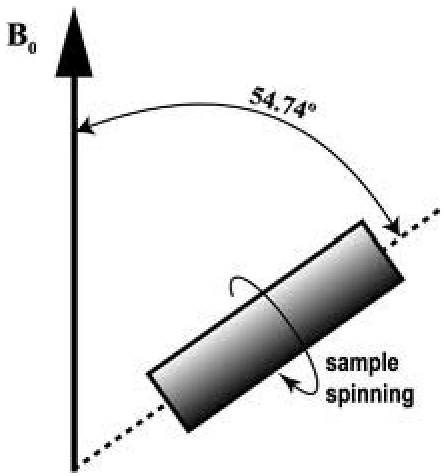
Gee et al. *J. Phys. Chem. A* **2000**, *104*, 4598.

Chemical shift anisotropy – powder

$^{13}C\{^{1}H\}$ NMR spectrum of solid glycine (powder)

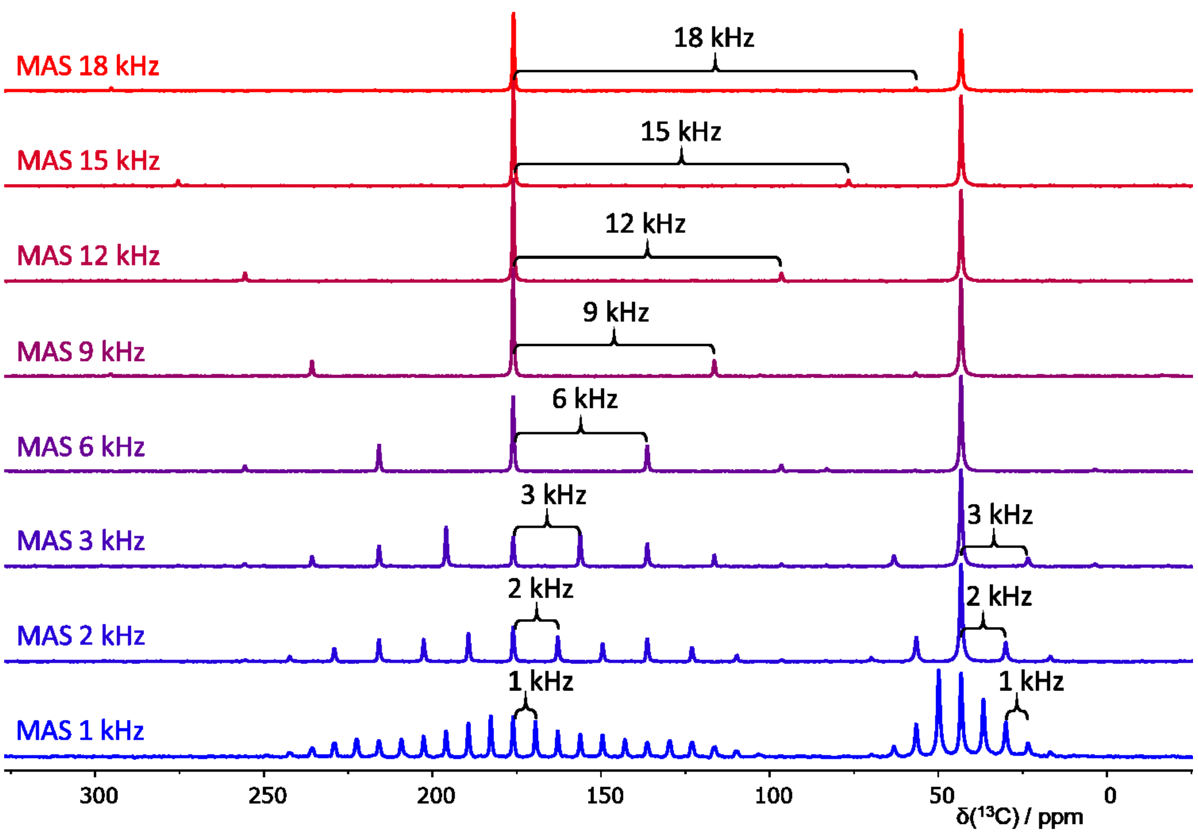


Magic-angle spinning (MAS)



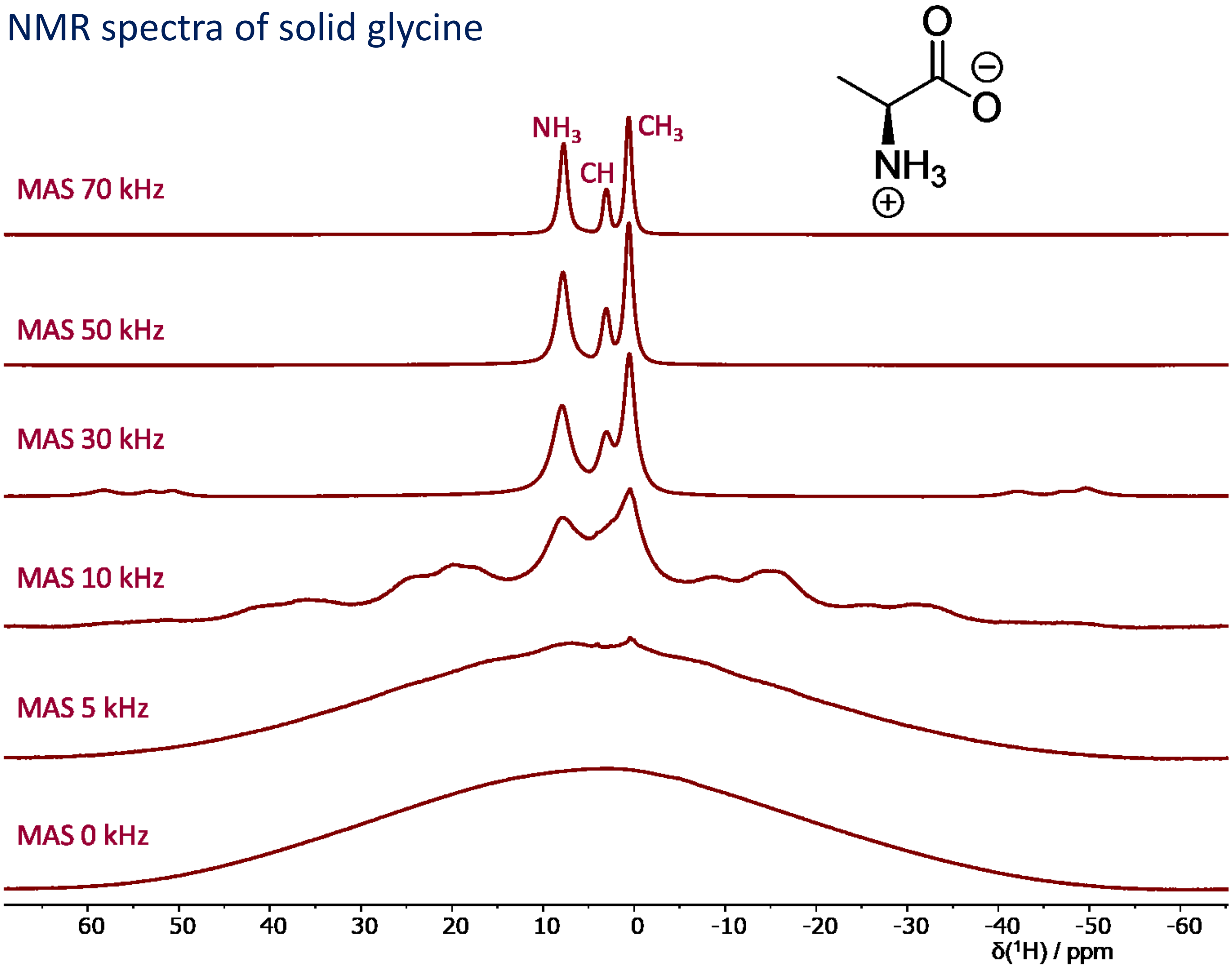
$$(3\cos^2\theta - 1)$$

$^{13}C\{^{1}H\}$ MAS NMR spectrum of solid glycine



Magic-angle spinning (MAS)

^{1}H MAS NMR spectra of solid glycine



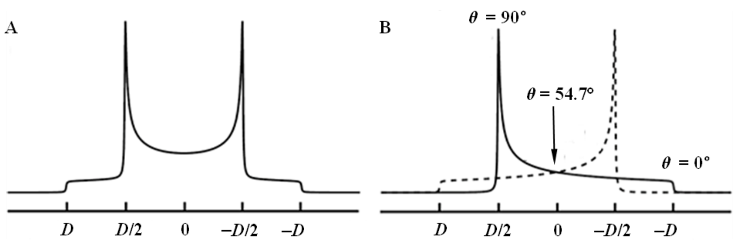
Magic-angle spinning (MAS)

SS-NMR tubes (rotors) for MAS

Dipolar and quadrupolar coupling

Direct spin-spin interaction (dipolar coupling)

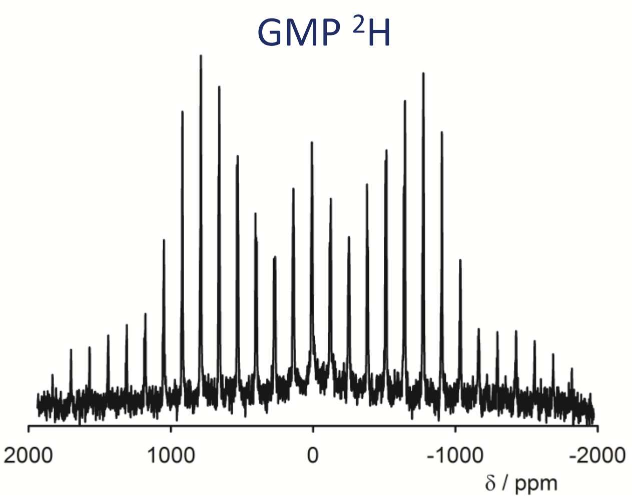
- Depends on gyromagnetic ratio γ and internuclear distance
- C-H ≈ 25 kHz
- High power decoupling



Quadrupolar coupling

- Nuclei with *I* > ½ (e.g. ^{2}H, ^{14}N, ^{17}O, ^{23}Na, ^{35}Cl)
- ≈ MHz

Quadrupolar coupling C_Q ~ 200 kHz
(typical value for O-D groups)



SS-NMR at IOCB

NMR SPECTROSCOPY
RESEARCH–SERVICE GROUP
IOCB PRAGUE

Bruker Avance II

500 MHz spectrometer

3.2 mm MAS probe

BRUKER

JEOL ECZ600R

JEOL Solutions for Innovation

600 MHz spectrometer

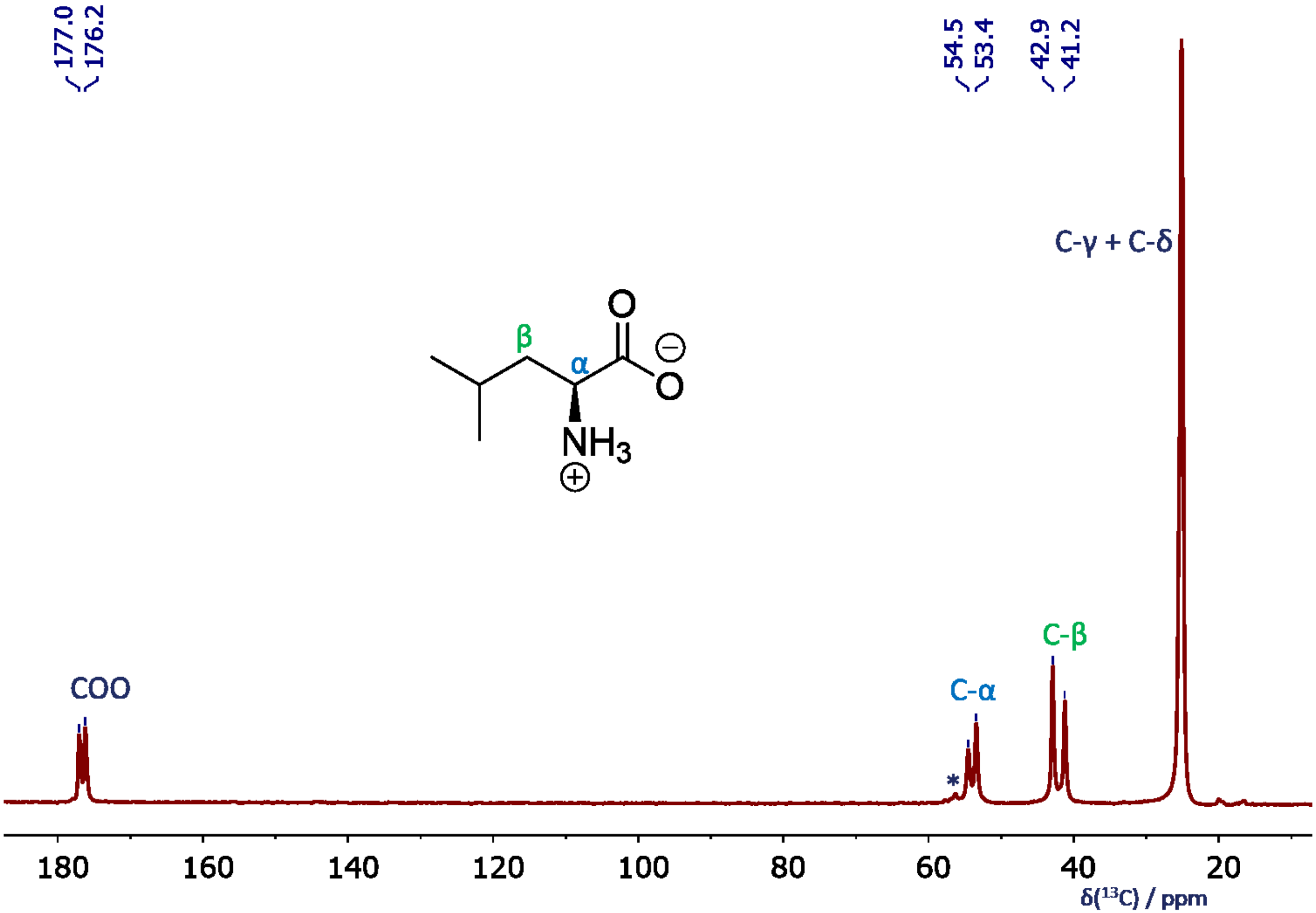
3.2 mm and 1 mm MAS probes

Installed in 2018

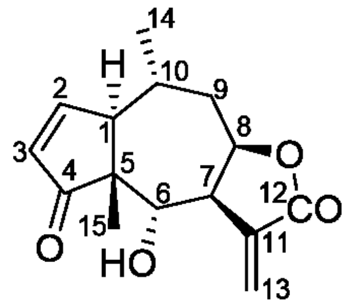
Non-equivalent molecules in asymmetric unit

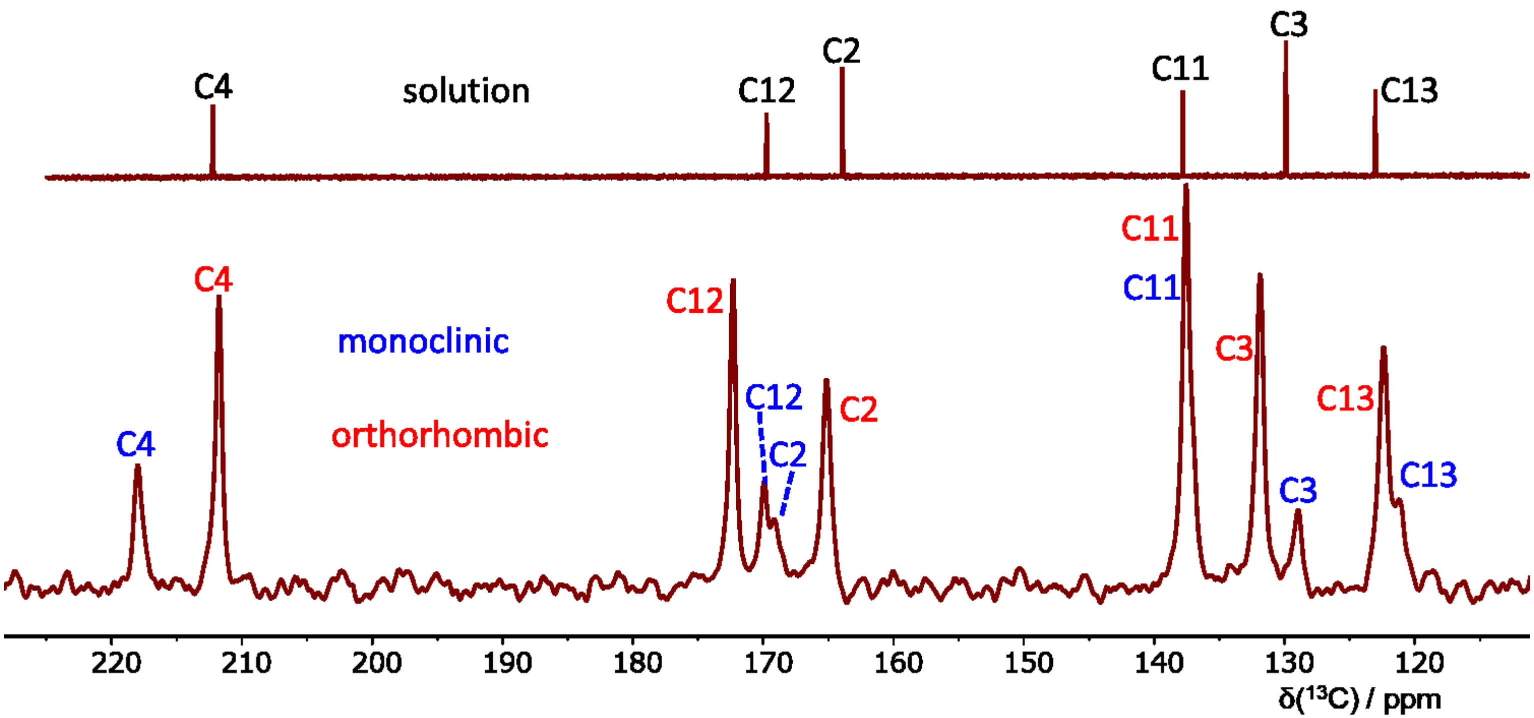
$^{13}C\{^{1}H\}$ MAS NMR spectrum of solid leucine

with two non-equivalent molecules ($Z' = 2$)

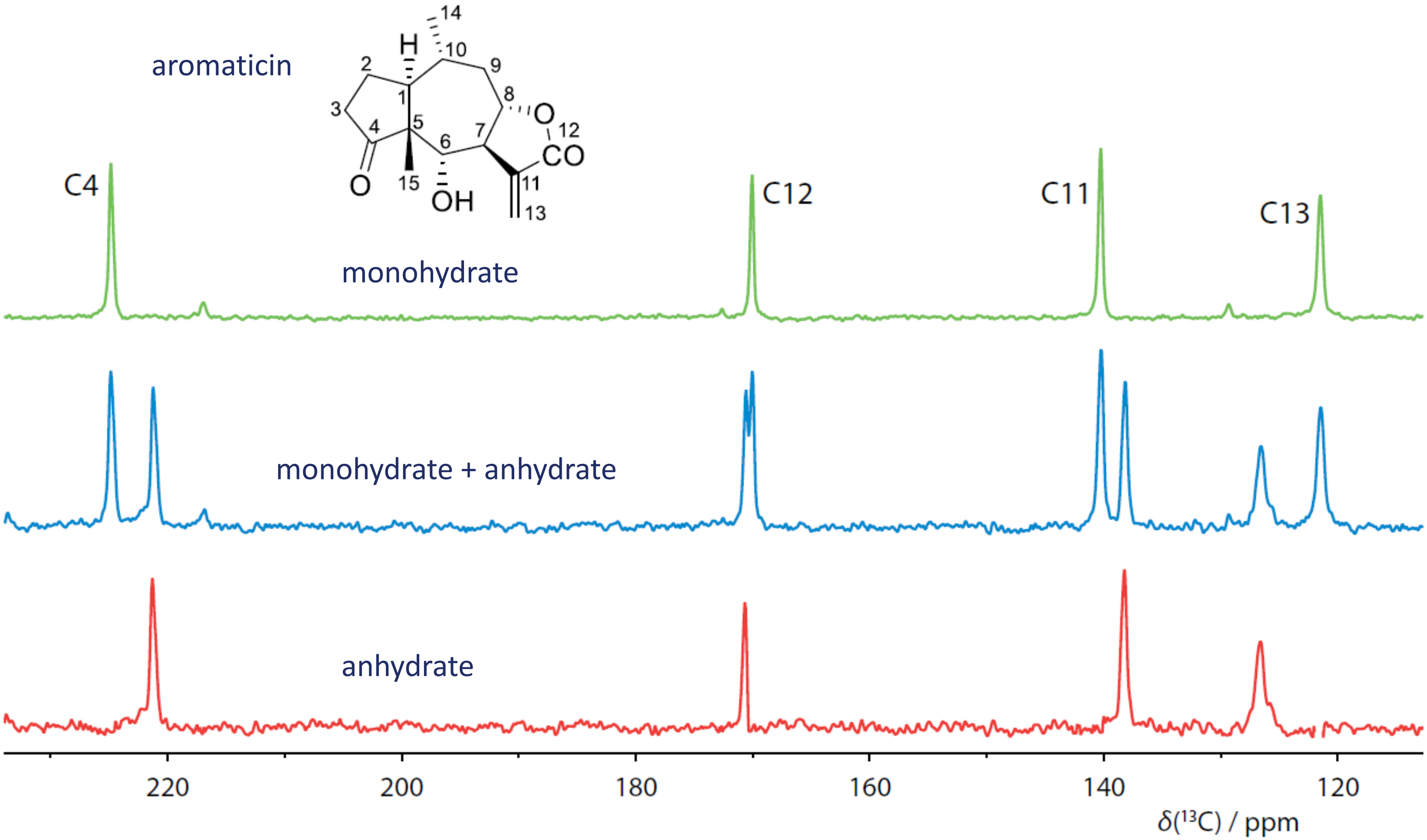


Polymorphism



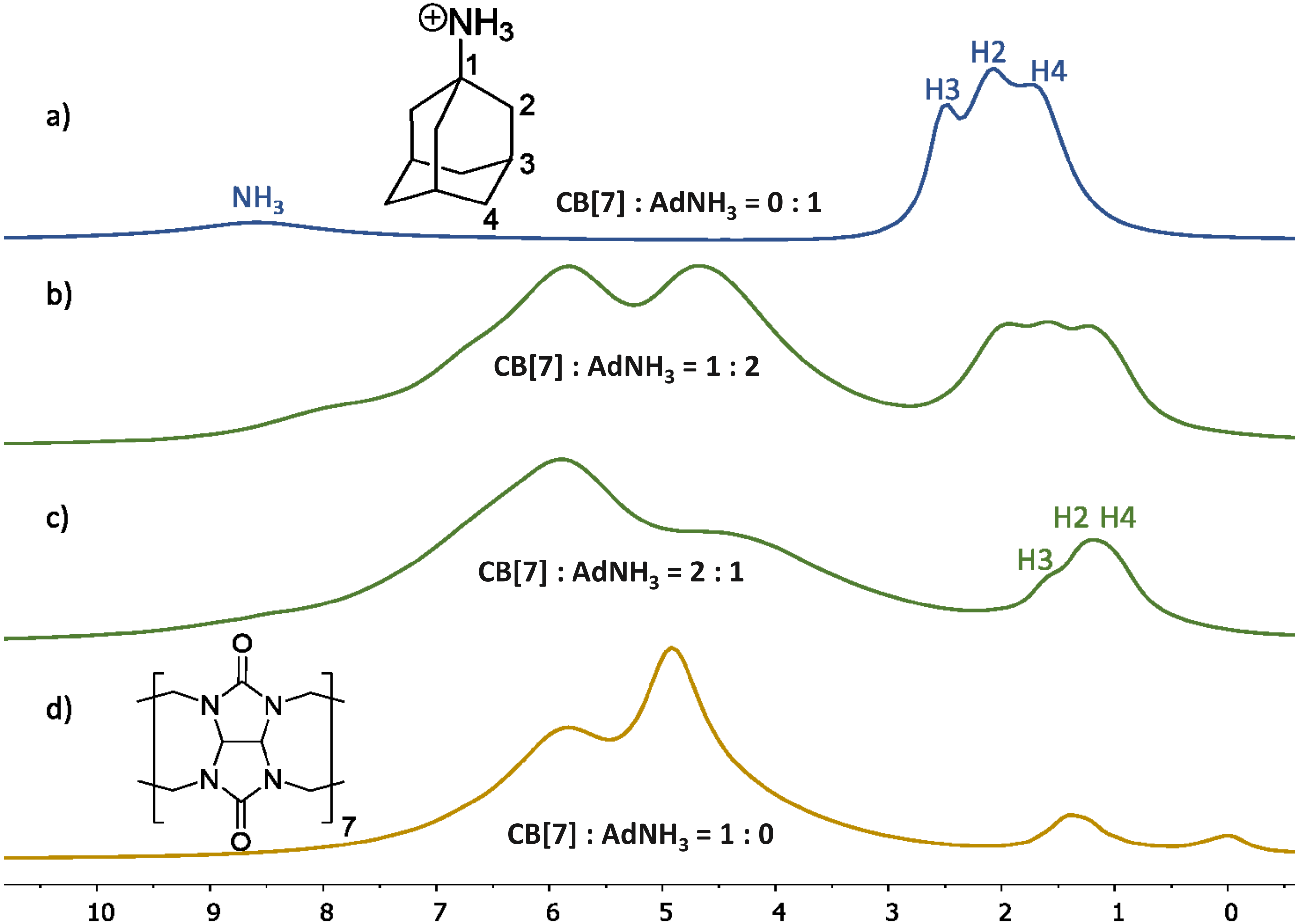


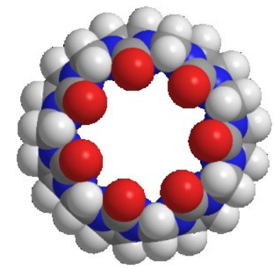
Pseudopolymorphism



Host-Guest Complexes with Cucurbit[7]uril

^{1}H MAS (70 kHz) NMR spectra



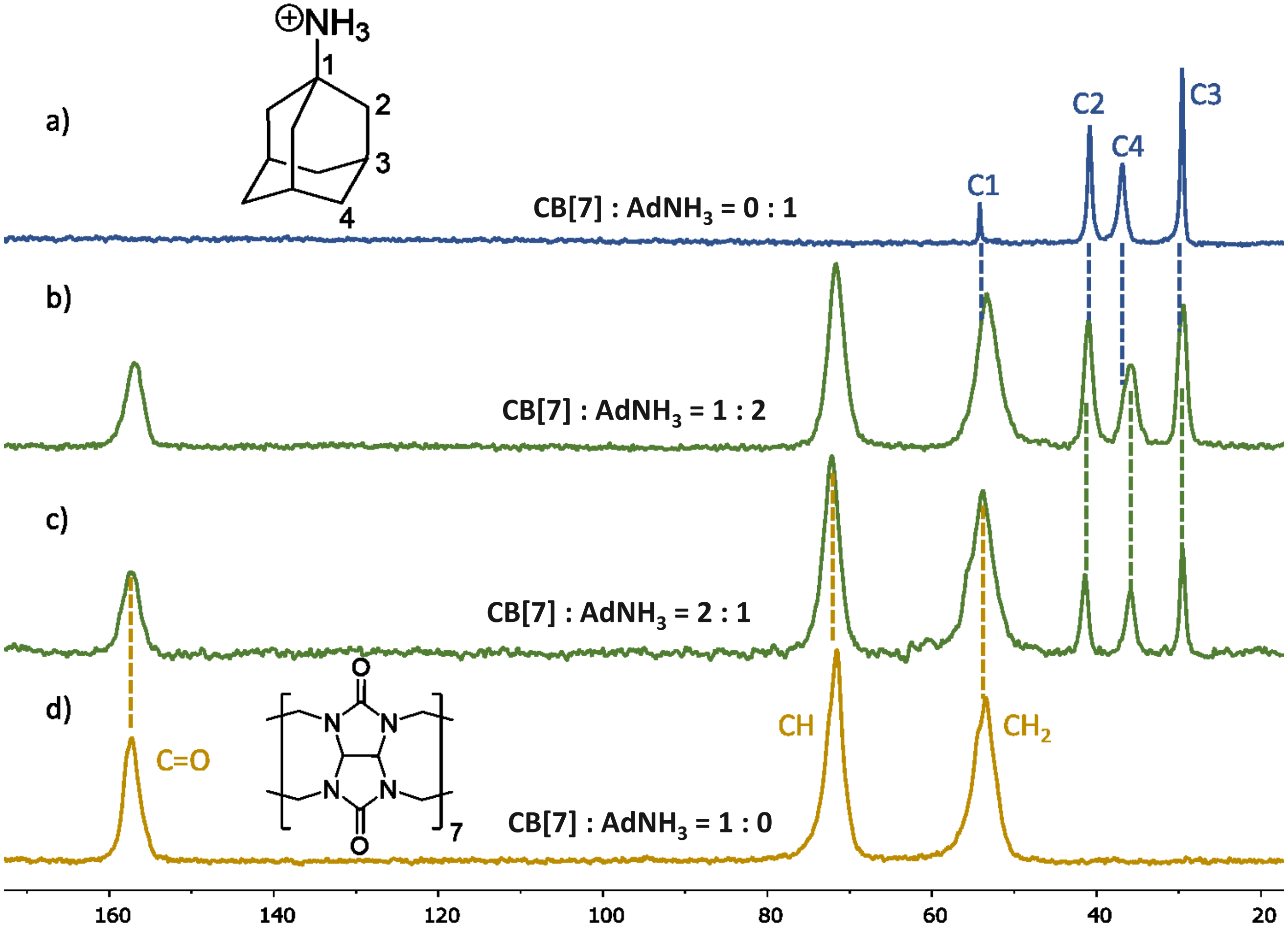


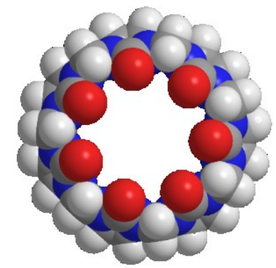
Jiří Kaleta

Host-Guest Complexes with Cucurbit[7]uril

NMR SPECTROSCOPY
RESEARCH-SERVICE GROUP
IOCB PRAGUE

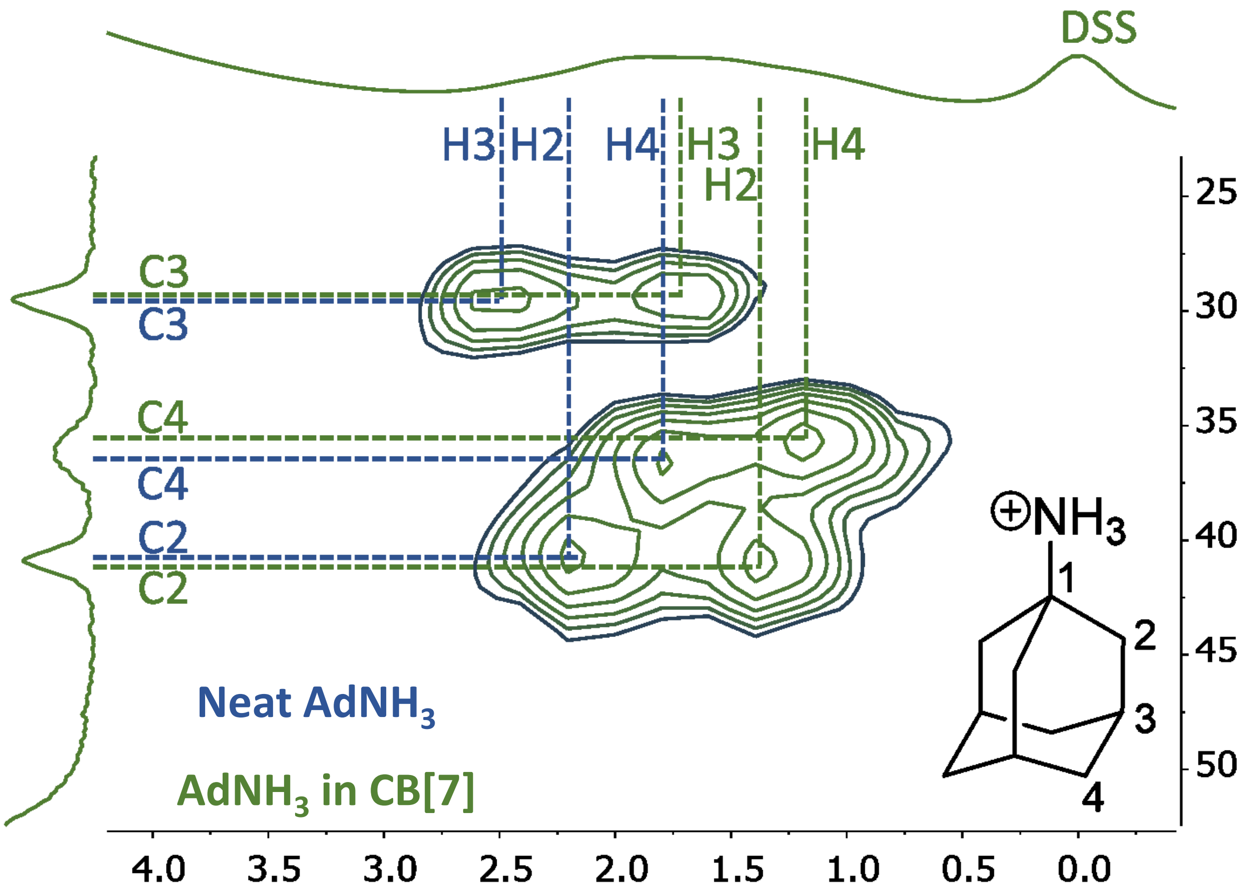
$^{13}C\{^1H\}$ MAS (18 kHz) NMR spectra

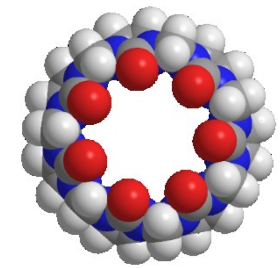




Host–Guest Complexes with Cucurbit[7]uril

^{1}H-^{13}C correlation (HSQC-like), MAS (70 kHz)

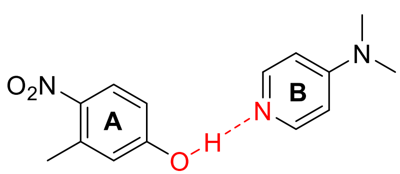




The salt/co-crystal problem

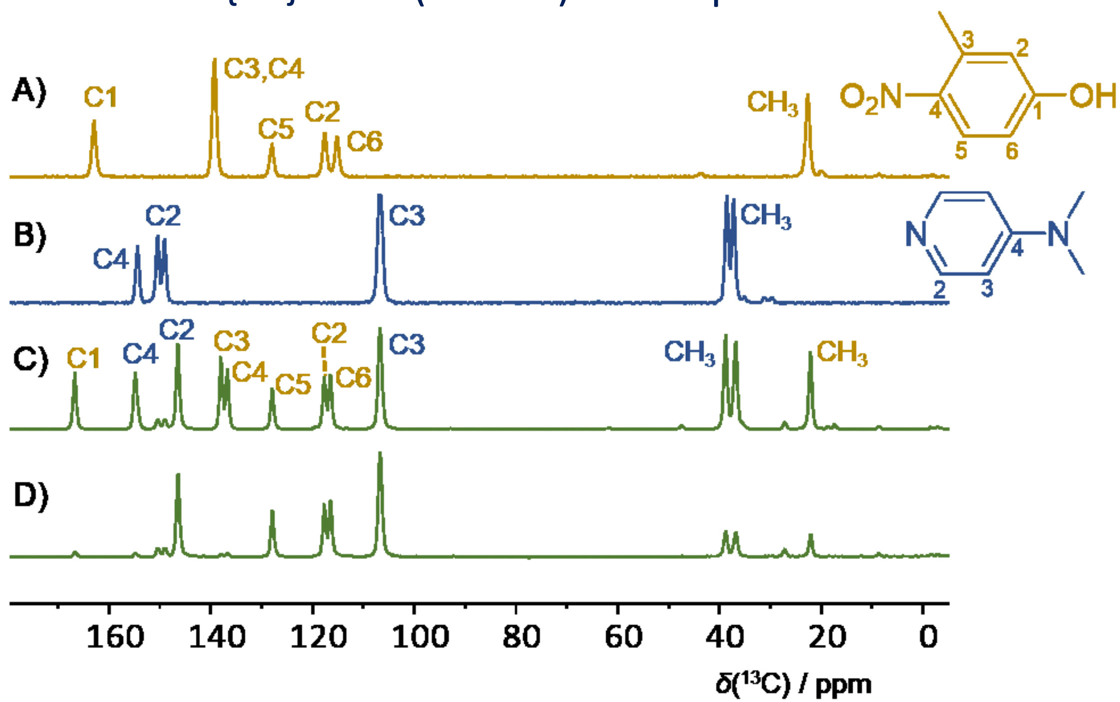
Multicomponent pharmaceutical solids

- Improved solubility, stability, bioavailability, pharmaceutical compatibility
- To determine the salt/co-crystal structure is challenging for X-ray
- Legal and regulatory issues (intellectual property)



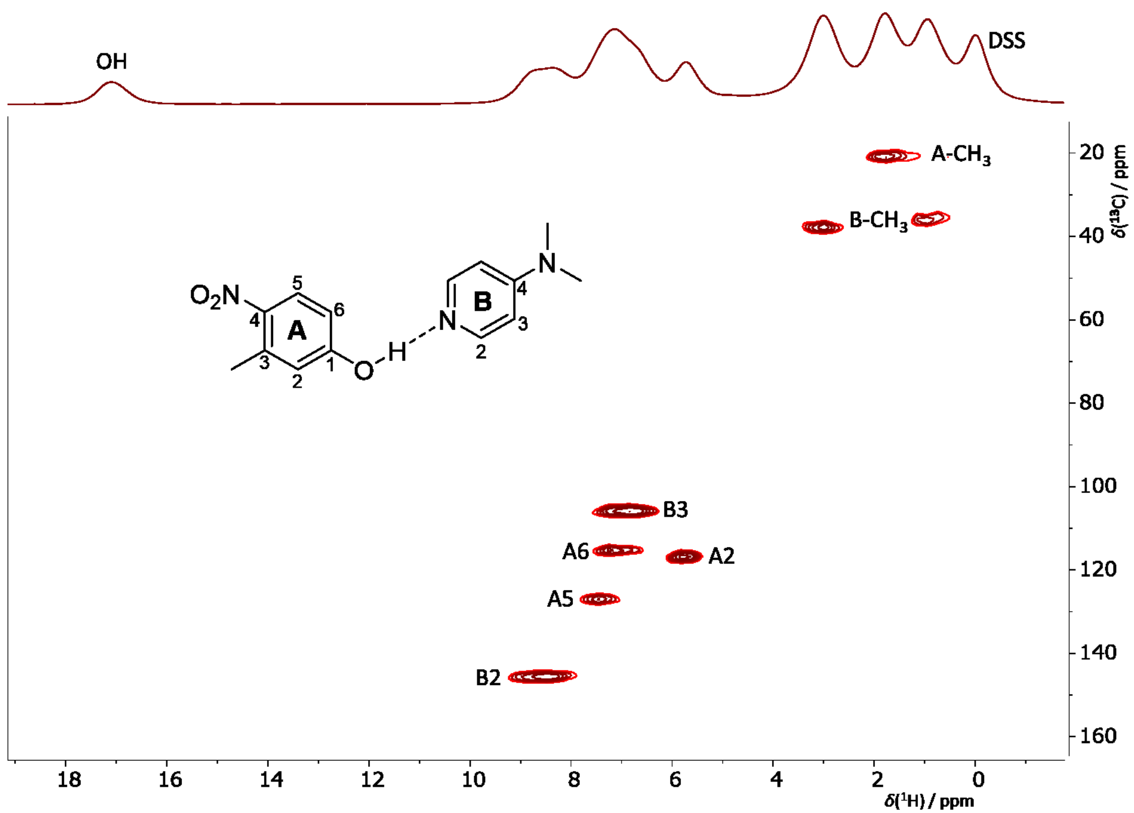
SEDJUI

$^{13}C\{^1H\}$ MAS (18 kHz) NMR spectra



Salt/co-crystal problem

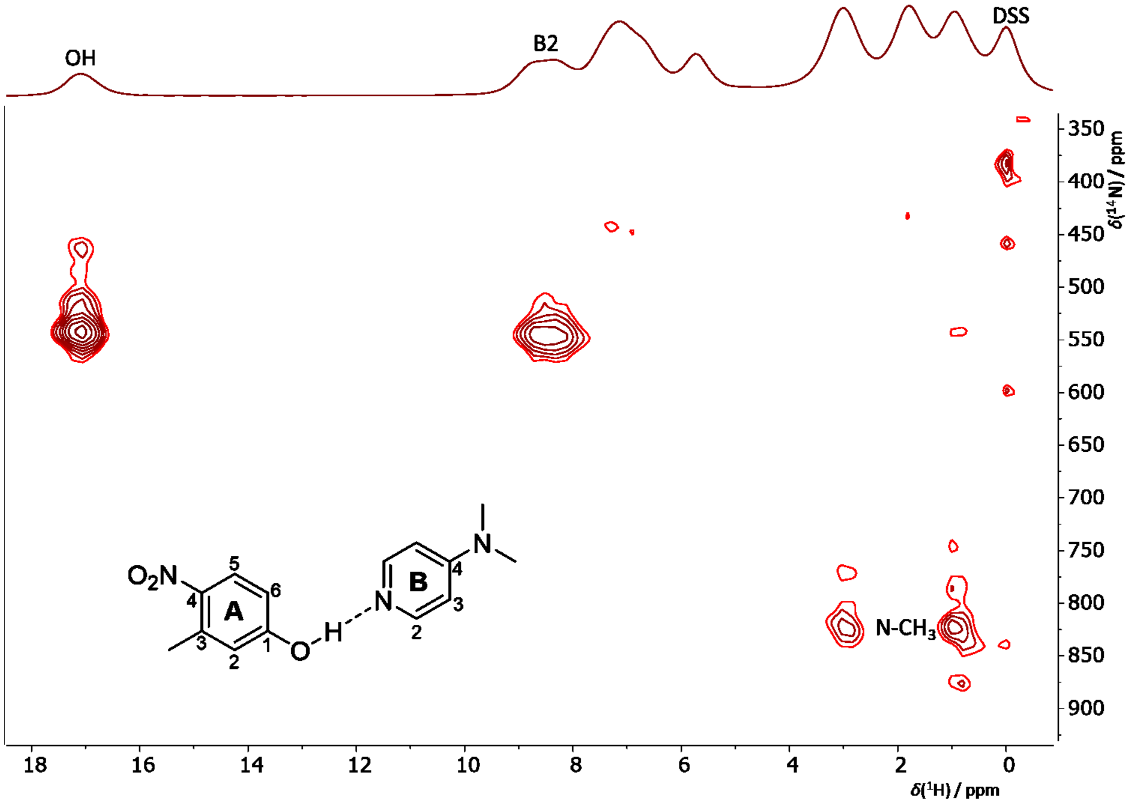
^1H-^{13}C correlation (HSQC-like), MAS (70 kHz)



Salt/co-crystal problem

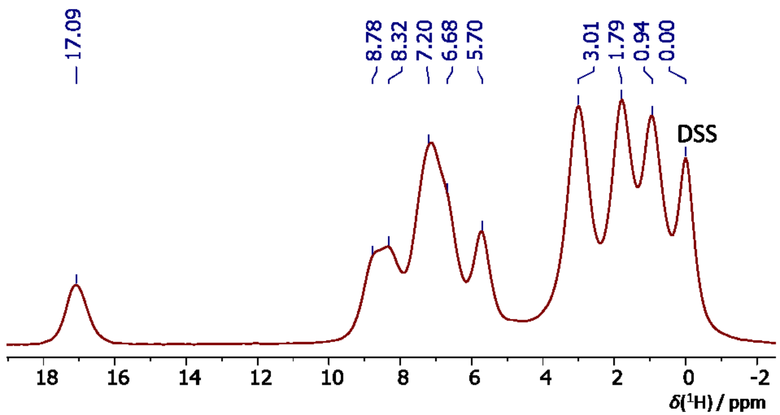
NMR SPECTROSCOPY
RESEARCH–SERVICE GROUP
IOCB PRAGUE

^{1}H-^{14}N correlation (through-space), MAS (70 kHz)

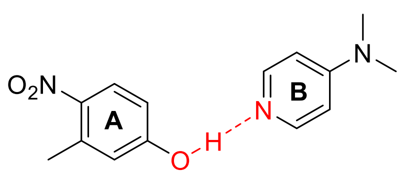


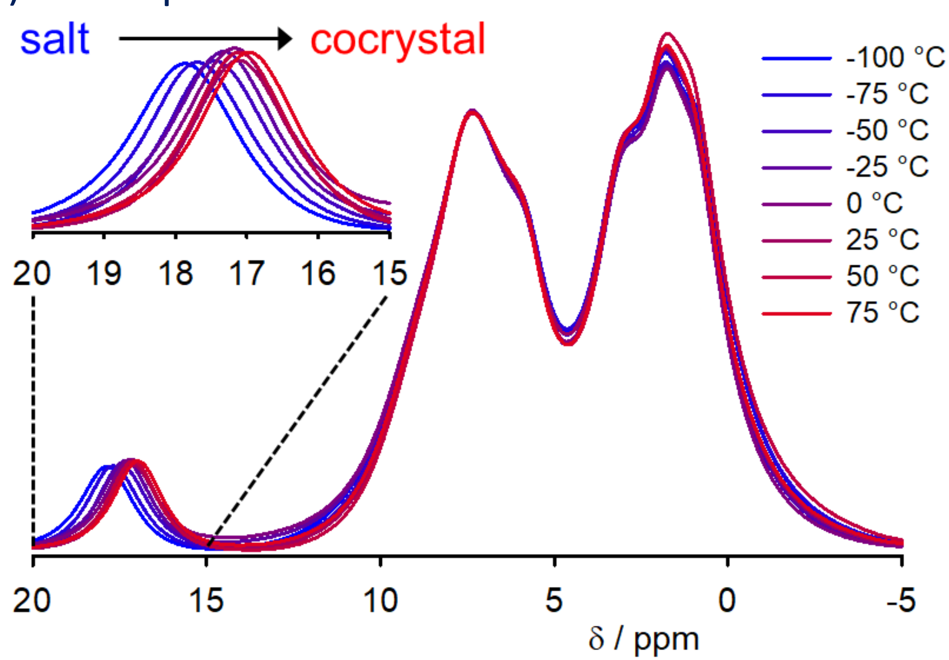
Salt/co-crystal problem

^{1}H MAS (70 kHz) NMR spectrum



Variable-temperature ^{1}H MAS (18 kHz) NMR spectra





Conclusions and Discussion

NMR SPECTROSCOPY
RESEARCH–SERVICE GROUP
IOCB PRAGUE

- Variable-temperature NMR spectroscopy
- NMR spectroscopy with *in situ* irradiation
- Solid-state NMR spectroscopy

State-of-the-art instrumentation available at IOCB

New internal collaborations are welcome