Probing the Structure and Dynamics of Hydrogen Bonds and Aromatic Pi-Pi Interactions by Solid-State NMR

Steven P. Brown

Department of Physics
University of Warwick

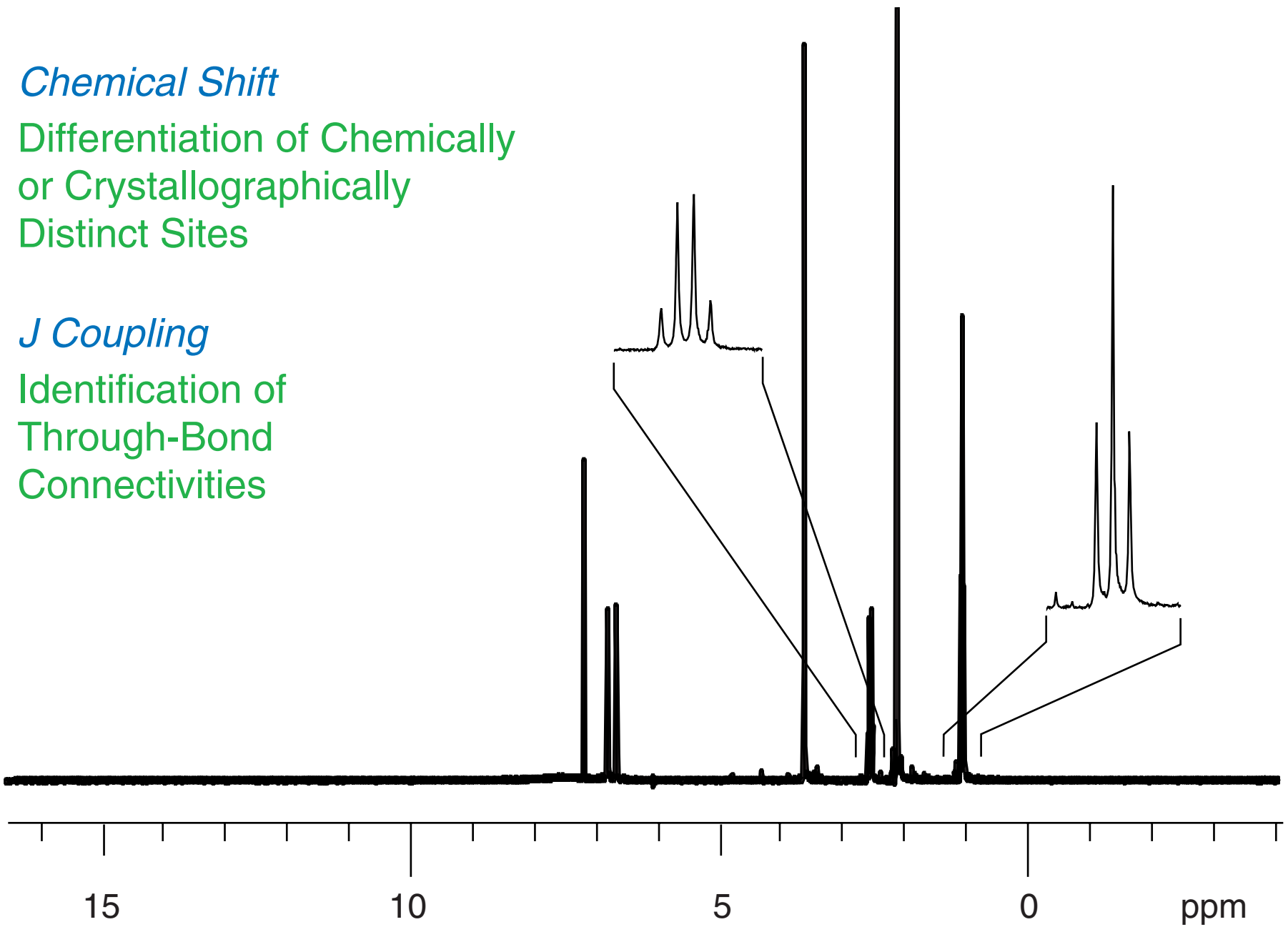
Solution-State NMR

Chemical Shift

Differentiation of Chemically or Crystallographically Distinct Sites

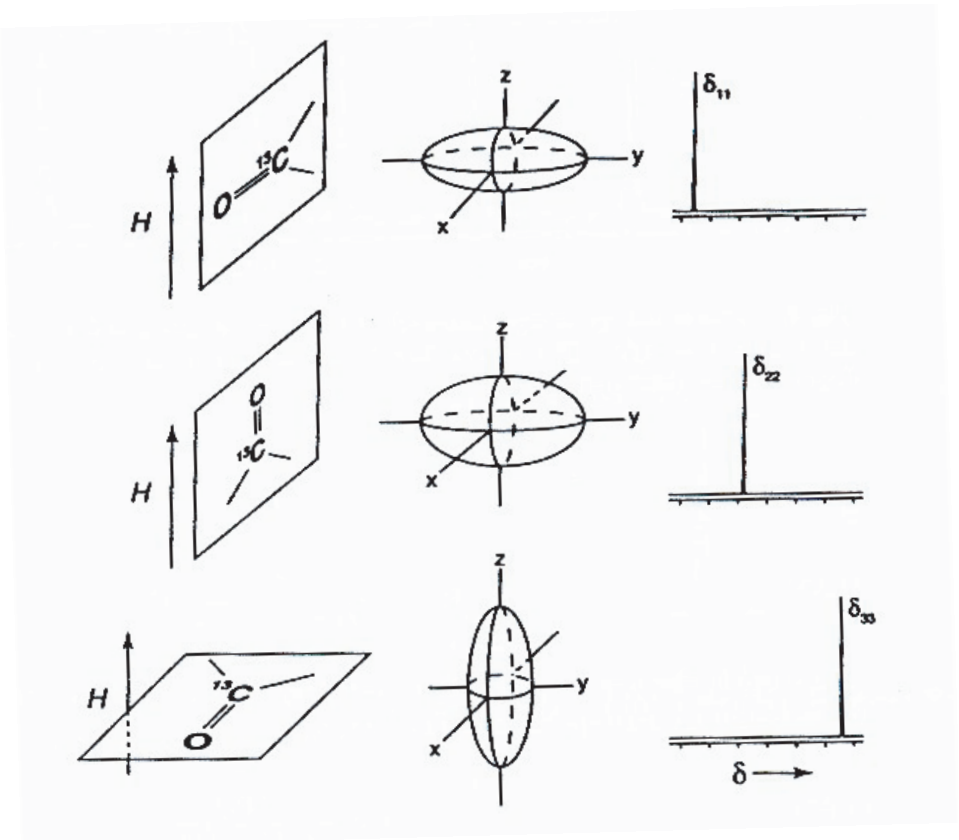
J Coupling

Identification of Through-Bond Connectivities

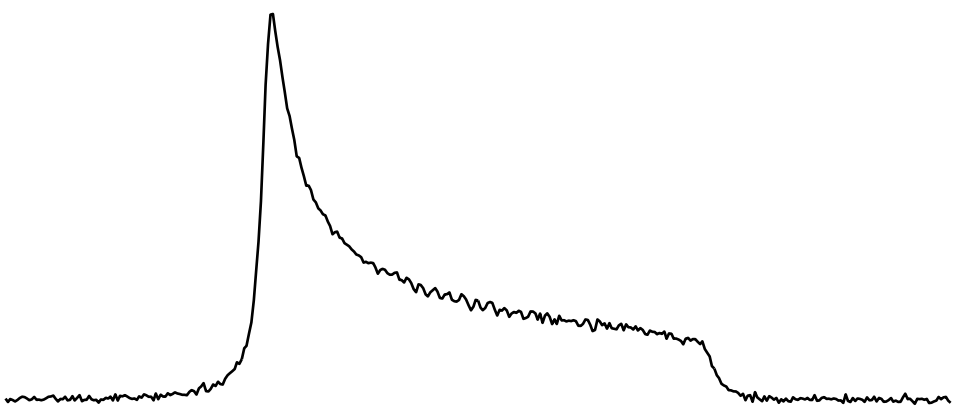


Solid-State NMR: Anisotropic Interactions

The resonance frequency of a
given nucleus within a particular crystallite
depends on the orientation of the crystallite



For a powdered sample, anisotropic
broadening is observed

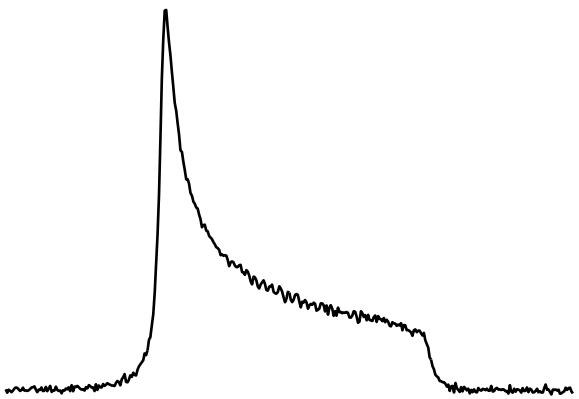


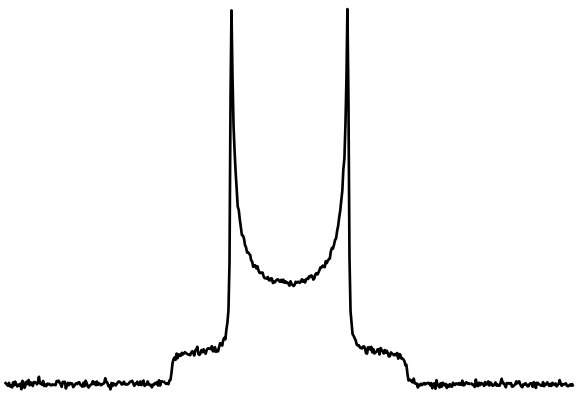
Solid-State NMR: Anisotropic Interactions

Dipolar Coupling

Chemical Shift Anisotropy

Quadrupolar Coupling





Electronic Structure and Bonding

Internuclear Proximities and Distances

Motional Processes

Relative Magnitudes of Solid-State NMR Interactions

Dipolar Couplings

^{13}C-^{1}H = 23 kHz (directly bonded CH pair)

^{1}H-^{1}H = 20 kHz (CH_2 group)

^{13}C-^{13}C = 3 kHz (directly bonded CC pair)

Chemical Shift Anisotropy

^{13}C = 9 kHz (carbonyl group, at 500 MHz)

Isotropic Chemical Shift Range

^{1}H = 20 ppm = 10 kHz (at 500 MHz)

^{13}C = 200 ppm = 25 kHz (at 500 MHz)

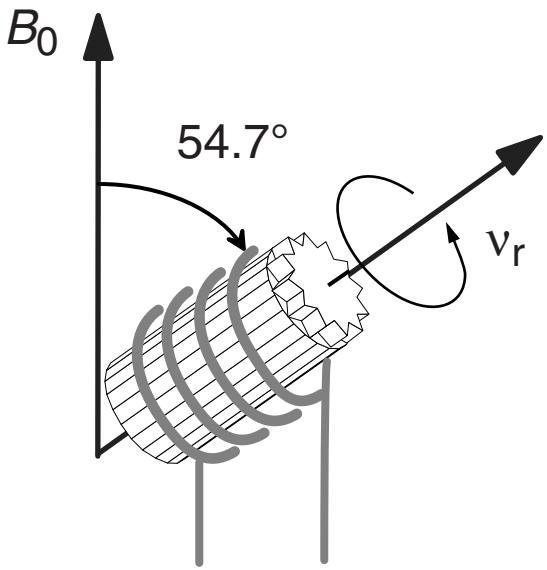
J Couplings

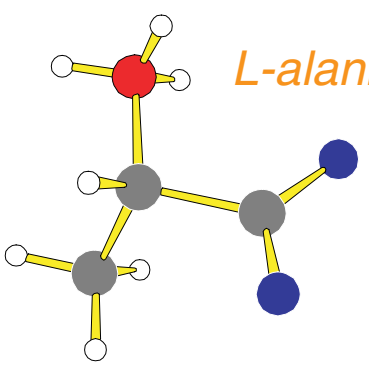
^{15}N-^{1}H = 90 Hz (directly bonded NH pair)

^{13}C-^{13}C = 35 Hz (directly bonded aliphatic CC pair)

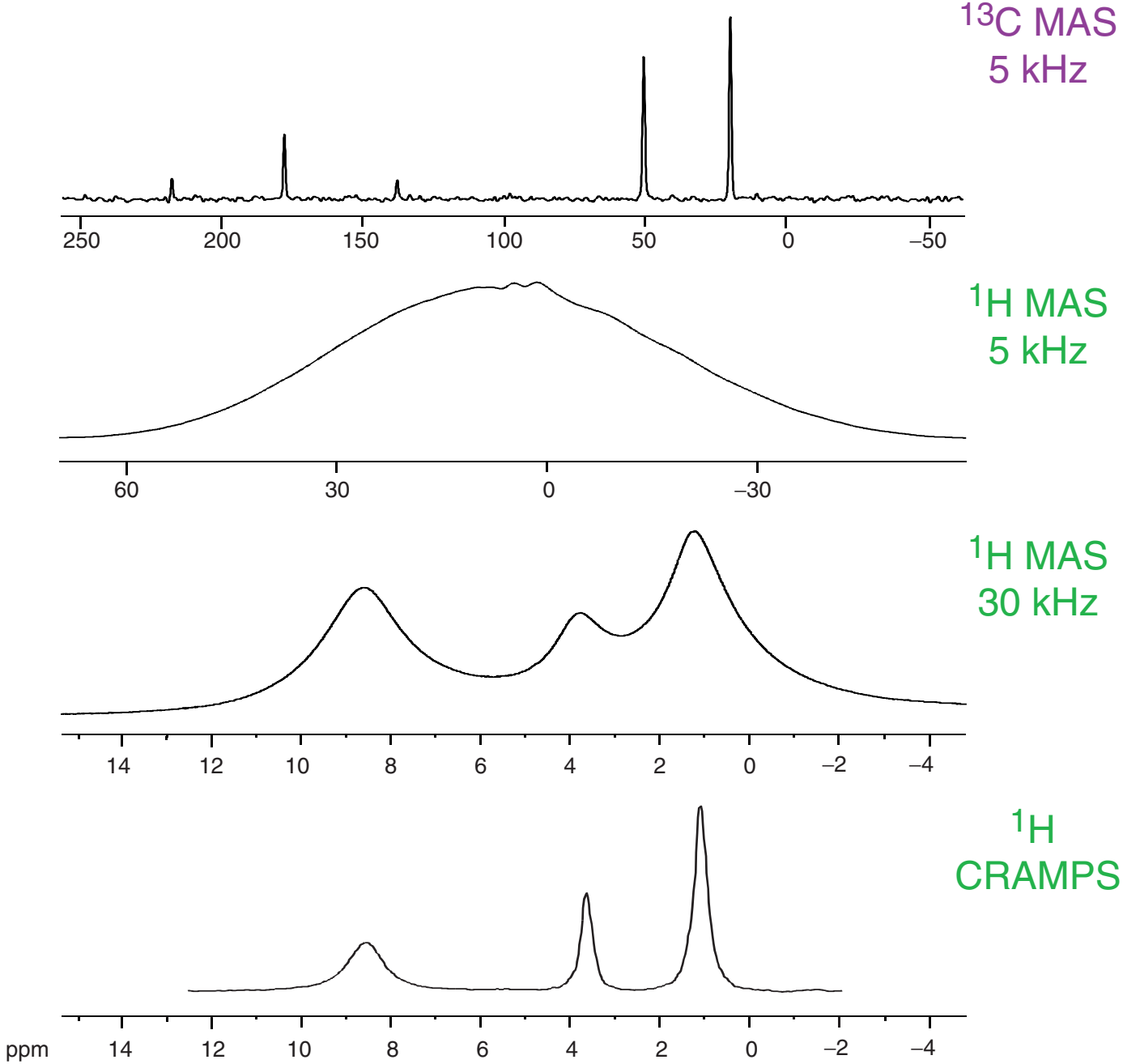
High-Resolution Solid-State NMR

Magic-Angle Spinning



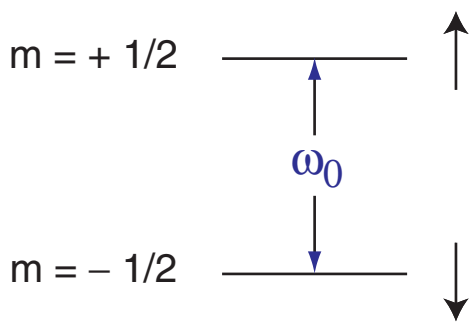


L-alanine

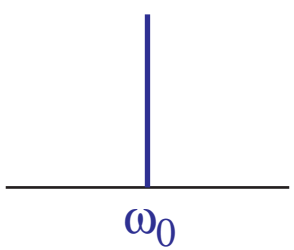


Double-Quantum Coherence

An isolated spin I = 1/2 nucleus

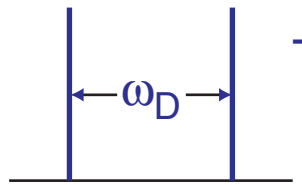


$\Delta m = \pm 1$ Single-Quantum coherence

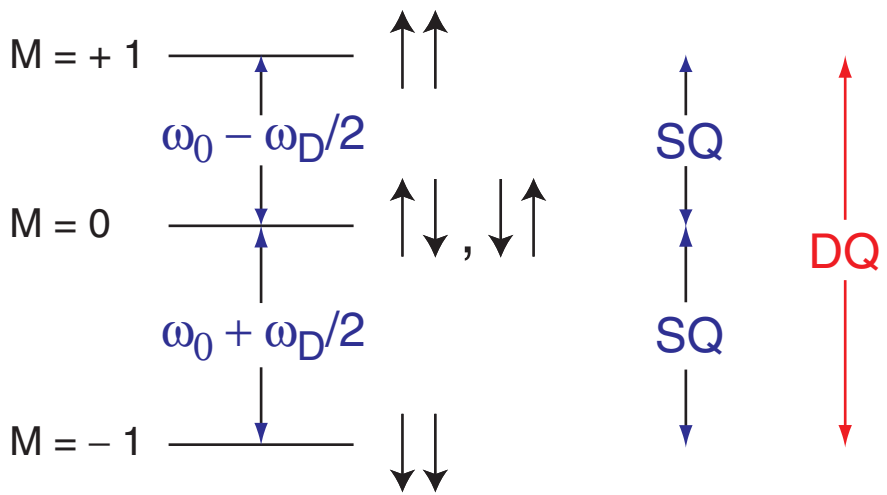


A single resonance at the Larmor frequency

A through-space dipolar-coupled pair of spin I = 1/2 nuclei



The observable (SQ) spectrum



(Also applies to a through-bond *J*-coupled spin pair)

Double-Quantum (DQ) ($\Delta m = \pm 2$) coherences cannot be directly observed in an NMR experiment, but they can be indirectly probed by a 2D experiment

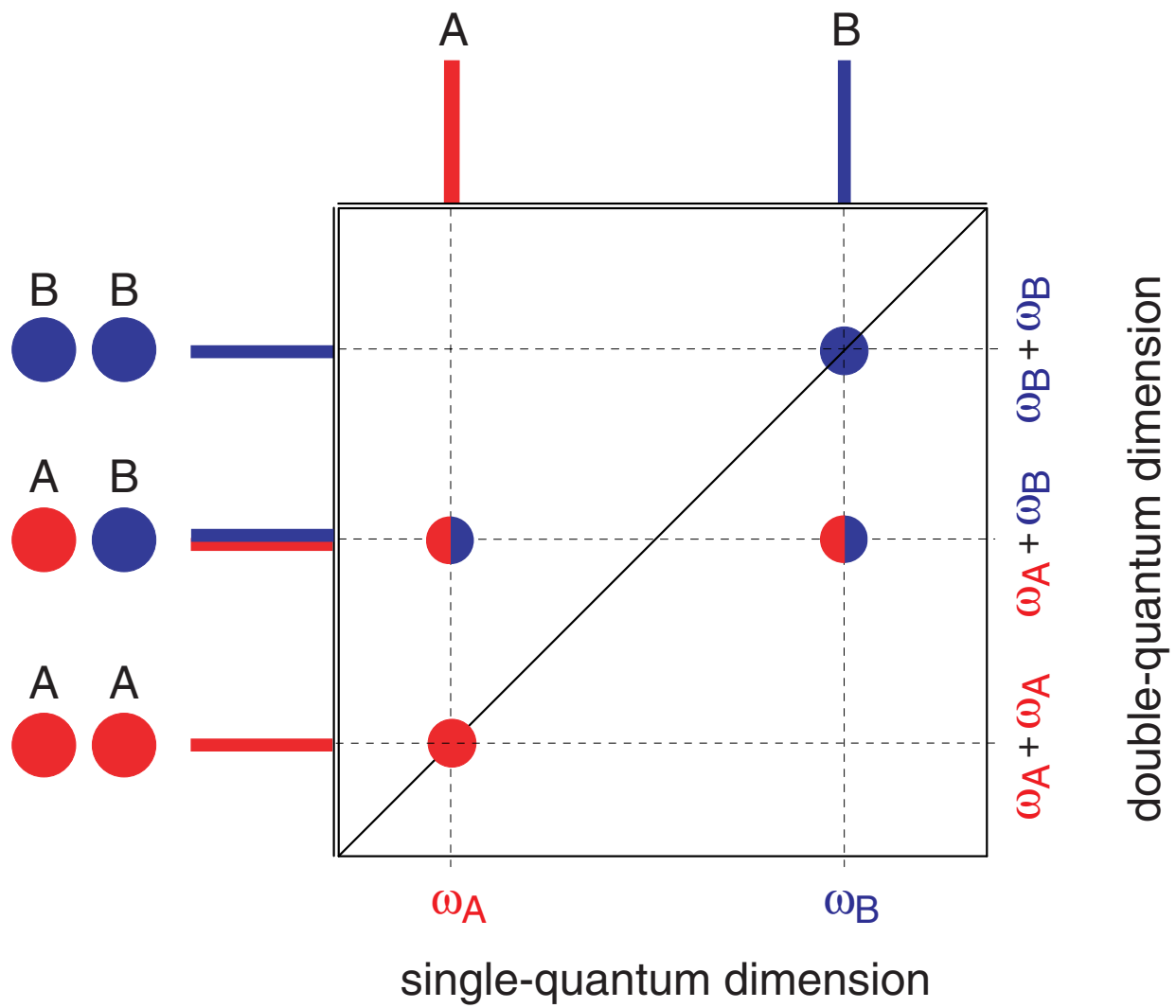
Excitation of DQC	Evolution of DQC (t_1)	Conversion to SQC	Acquisition of FID (t_2)

A Two-Dimensional Double-Quantum Spectrum

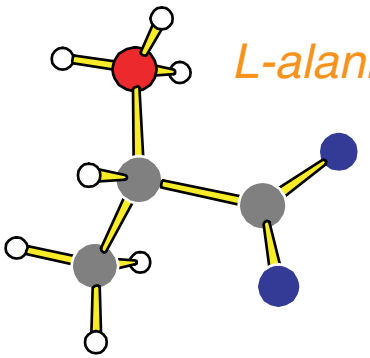
To a first approximation, the signal intensity is proportional to the dipolar coupling squared (double-quantum coherences must be both excited and reconverted),

i.e., the signal intensity is inversely proportional to the internuclear distance to the sixth power.

Therefore, a DQ peak is only observed if there is a close proximity of the involved protons.



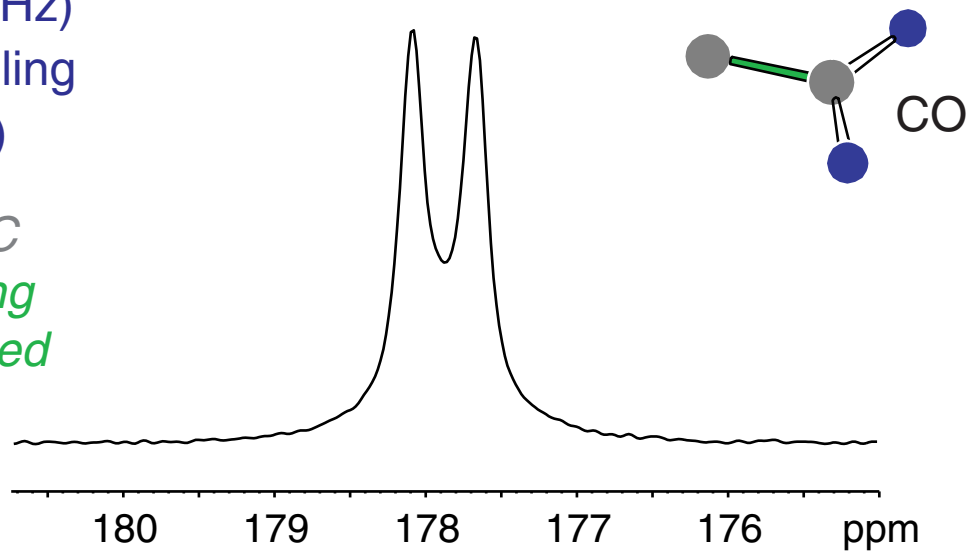
Recovering the ^{13}C-^{13}C *J* Coupling

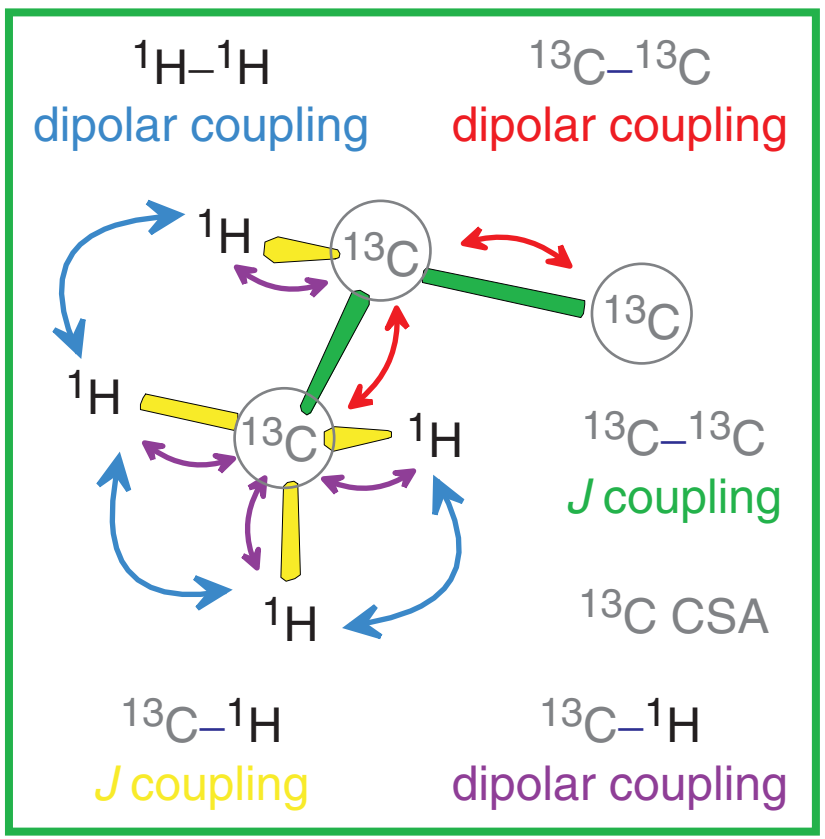


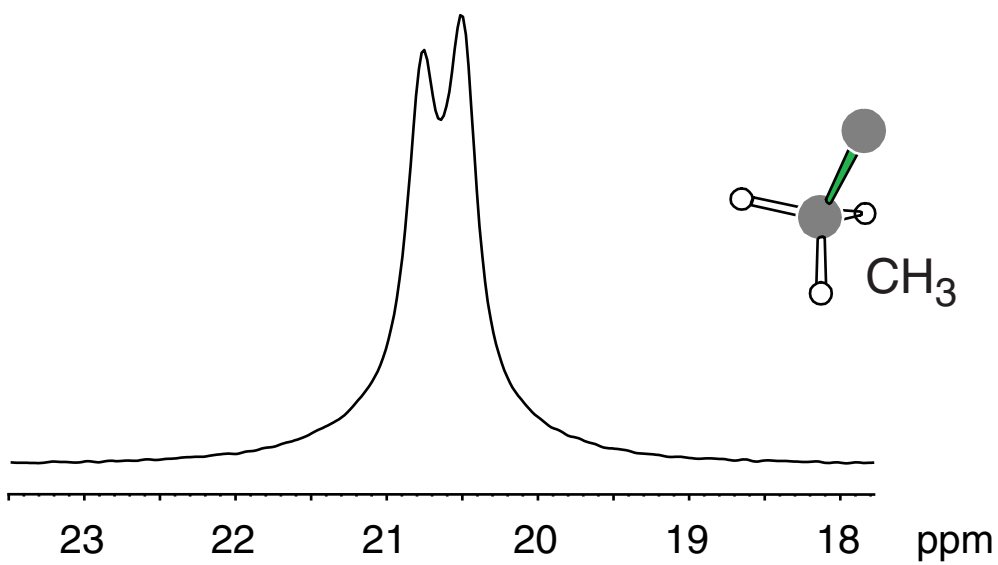
L-alanine

MAS (30 kHz)
^{1}H decoupling
(TPPM)

^{13}C–^{13}C
J coupling
is observed





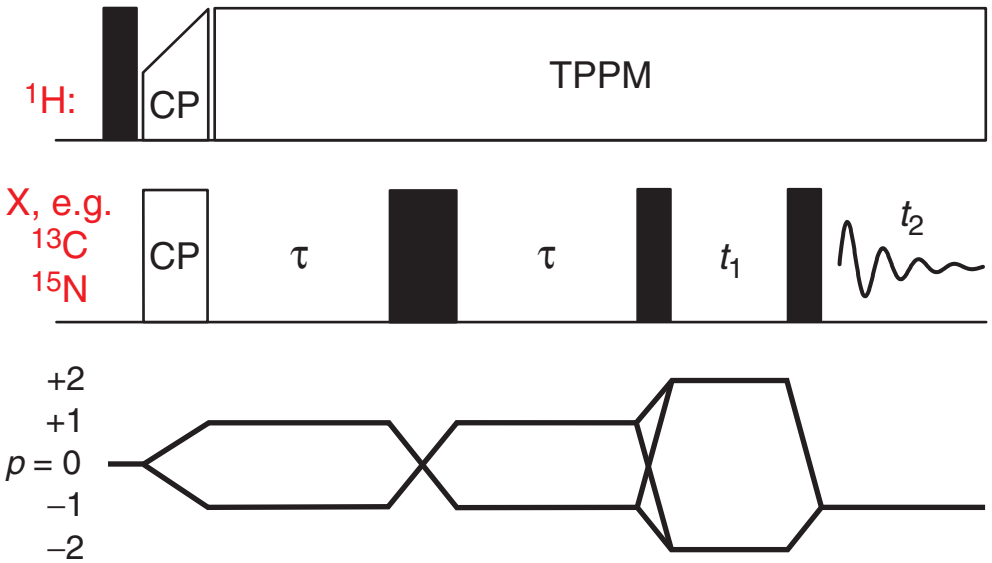


^{13}C Chemical Shift / ppm

The Solid-State INADEQUATE Experiment

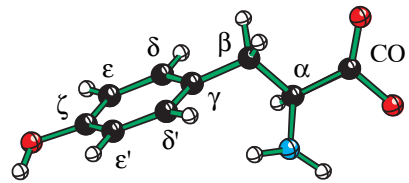
Fyfe *et al*, JACS 112, 3264 (1990)

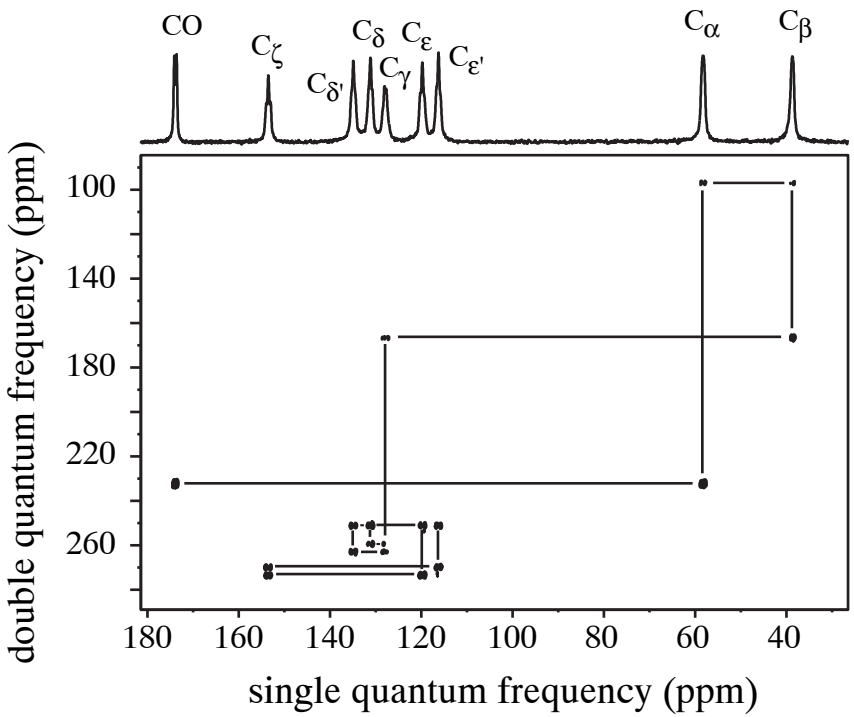
Lesage *et al*, JACS 119, 7867 (1997)



Only homonuclear *J* couplings are active during 2τ

Double-Quantum Coherence is created for *J*-coupled nuclei

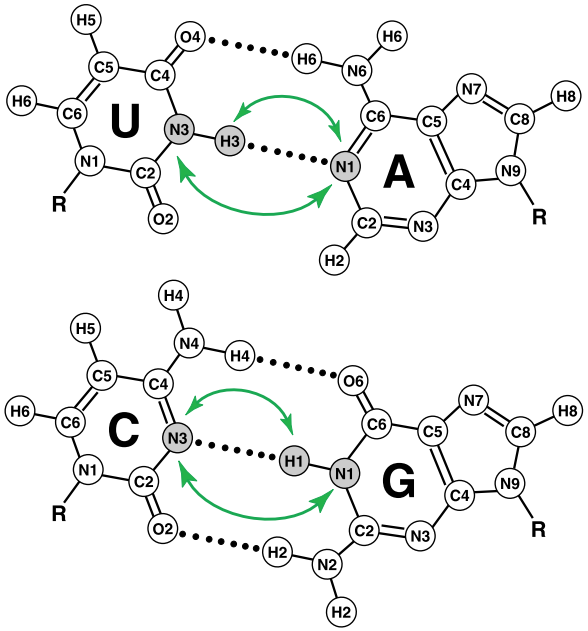




through-bond connectivites are traced out

Hydrogen-Bond Mediated *J*-Couplings: Solution-State NMR of Biomacromolecules

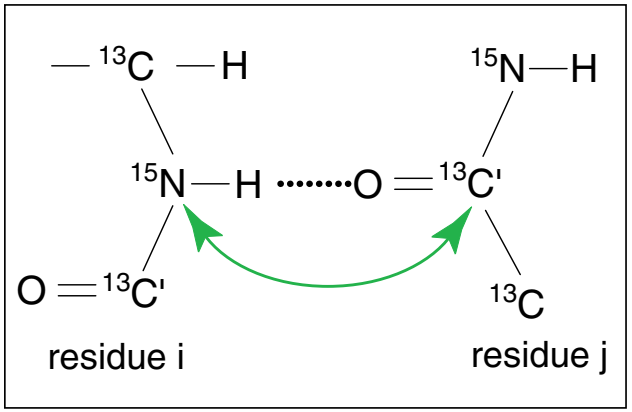
Watson-Crick Base Pairs



$^{2h}J_{NN}$ = 7-10 Hz $^{1h}J_{HN}$ = 2-4 Hz

Dingley & Grzesiek
JACS 120, 8293 (1998)

The Secondary Structure of Proteins

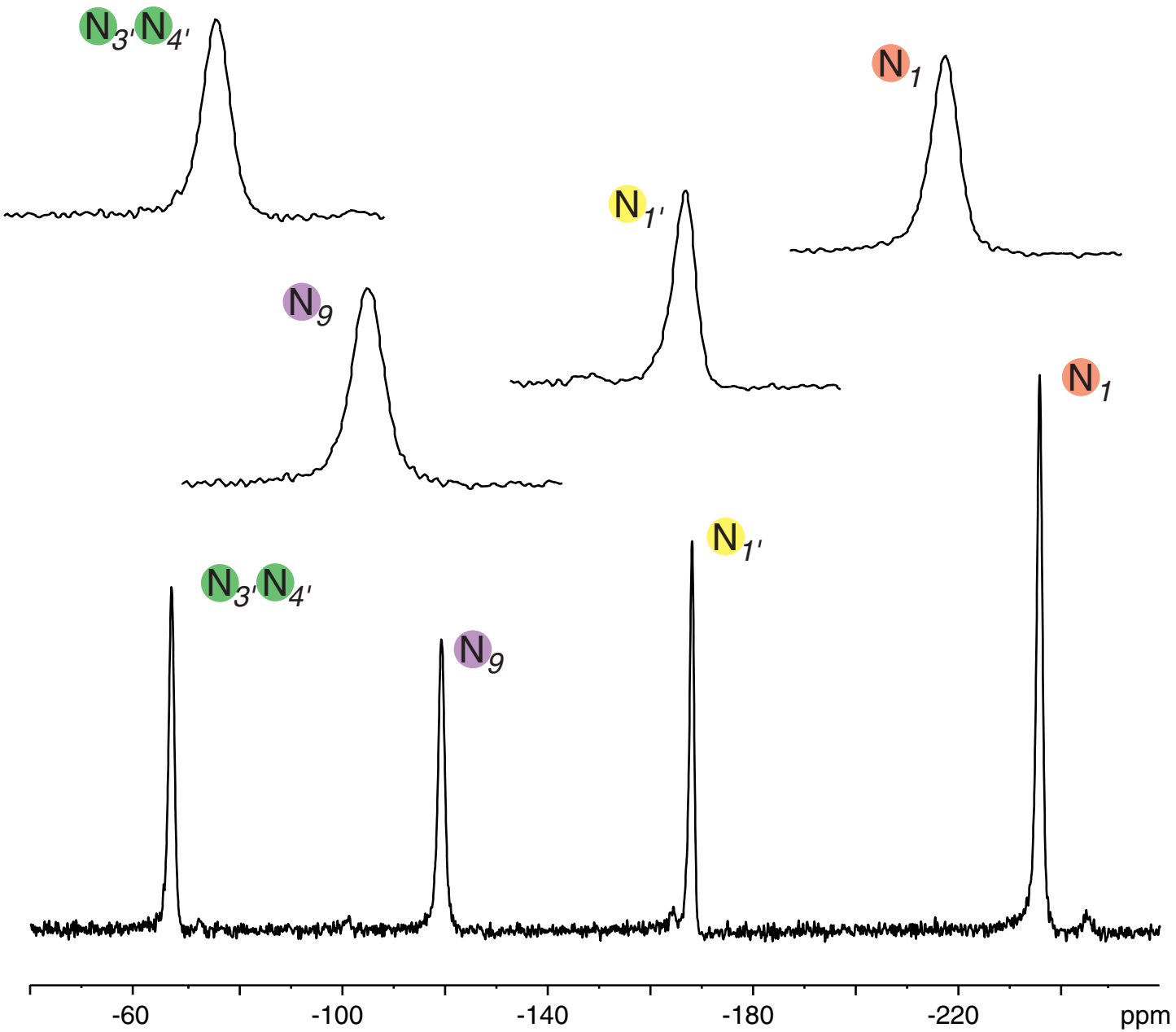


$^{3h}J_{NC'}$ = 0-1 Hz

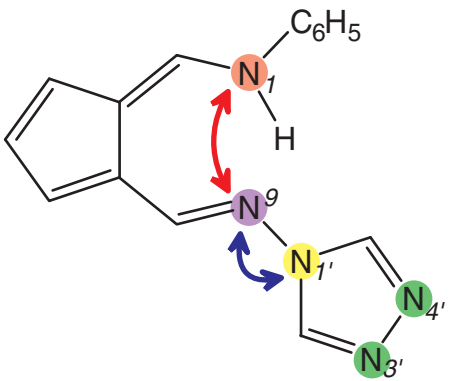
Cordier and Grzesiek,
JACS 121, 1601 (1999)
Cornilescu et al,
JACS 121, 2949 (1999)

The hydrogen-bond mediated *J* couplings depend on the hydrogen-bonding distances and geometries, and are also correlated with the ^{1}H chemical shifts.

Is it Possible to Observe Hydrogen-Bond Mediated *J*-Couplings in the Solid State?



^{15}N Chemical Shift / ppm (relative to nitromethane)



solution ($CDCl_3$)
(Claramunt *et al*
Angew. Chem. 40, 420):

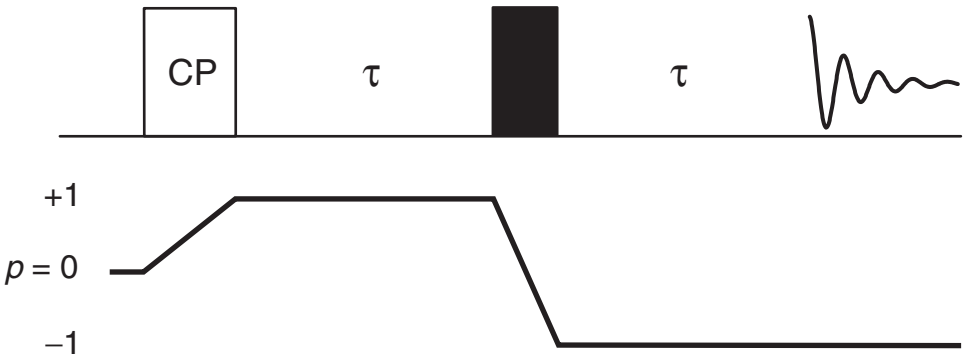
$^{1}J_{NN}$ = 11.8 Hz

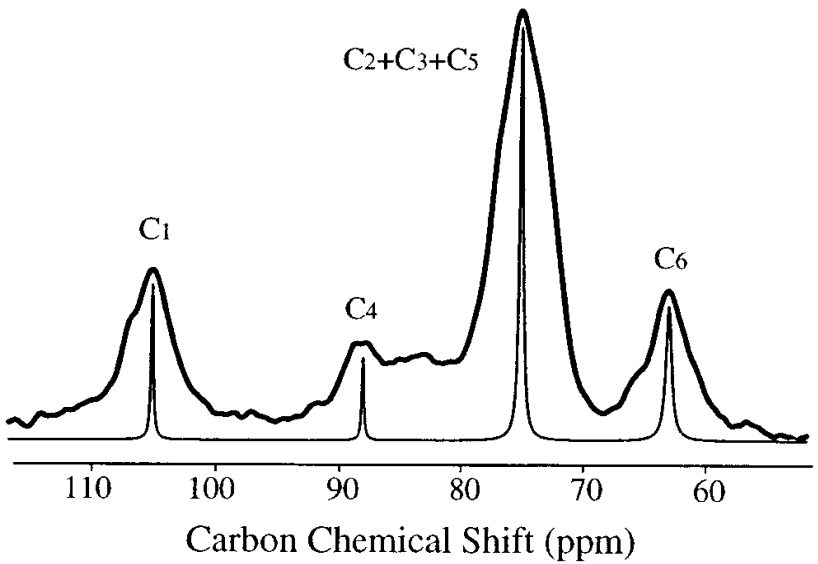
$^{2h}J_{NN}$ = 8.6 Hz

The homonuclear *J* couplings are not resolved in the ^{15}N CP-MAS spectrum

The Spin-Echo Experiment and Refocused Linewidths

The spin-echo experiment





All terms that appear as offsets (due to e.g. a chemical shift distribution or imperfect decoupling) are refocused (i.e., removed)

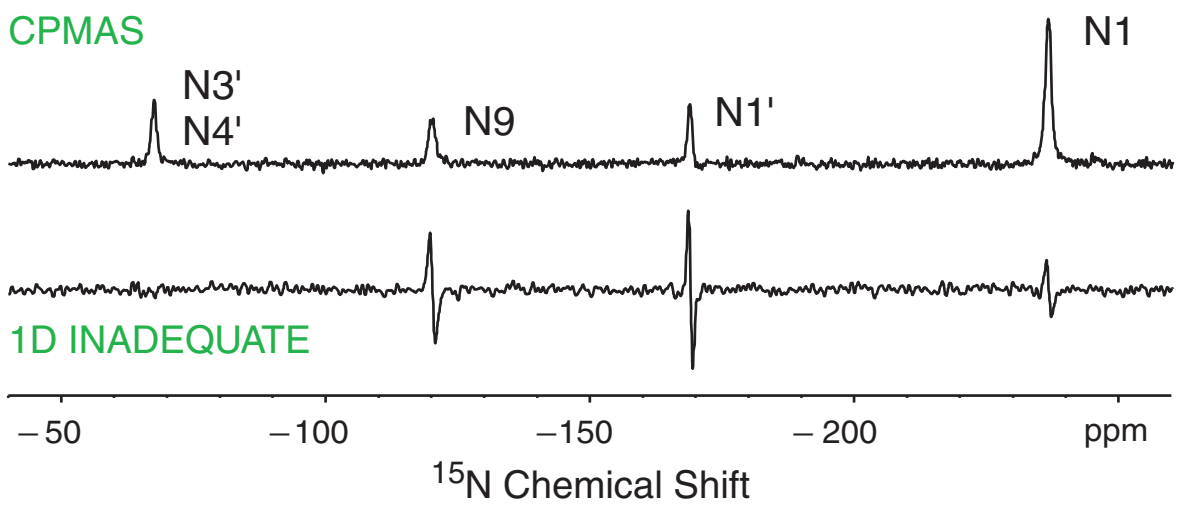
Earl & VanderHart
JACS 102, 3251 (1980)

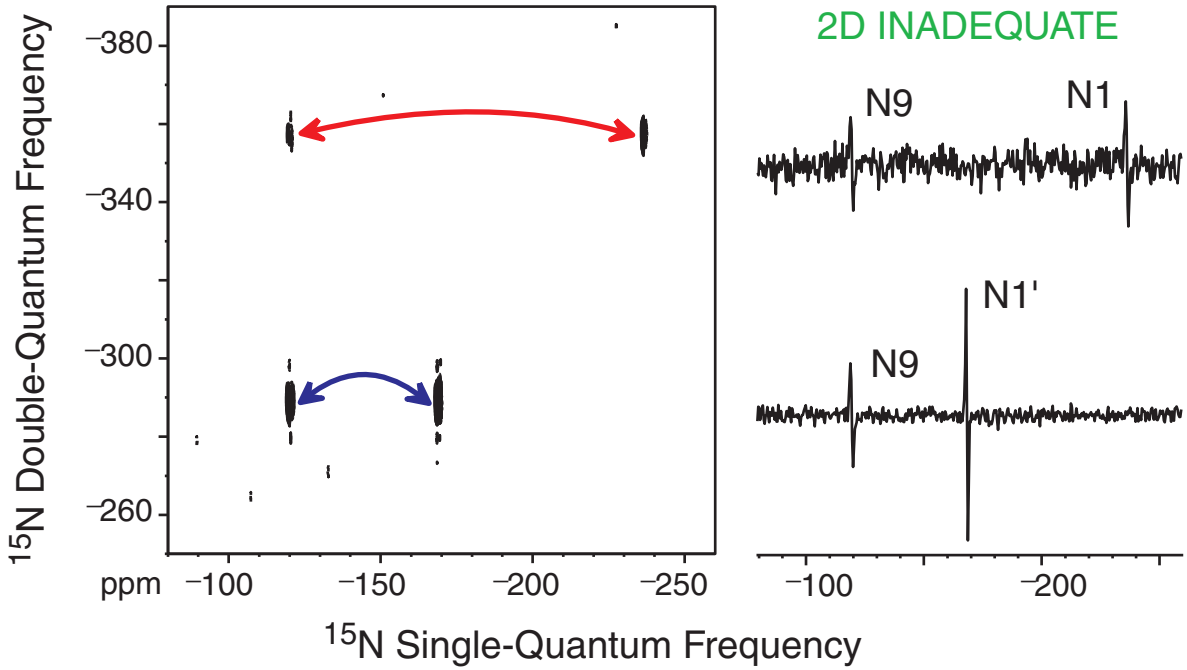
Cowans & Grutzner
JMR A105, 10 (1993)

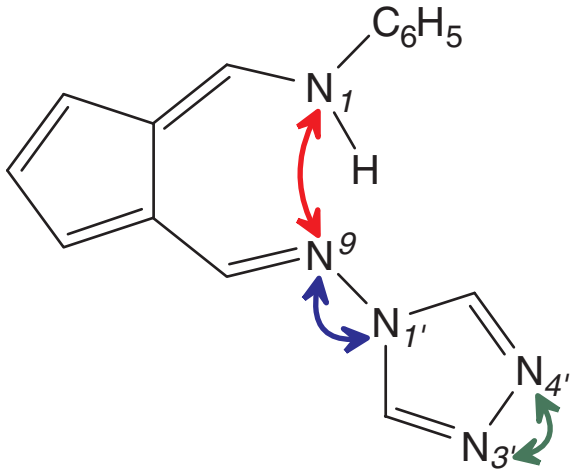
Refocused linewidths as small as a few Hz are observed.

Lesage, Bardet, & Emsley,
JACS 121, 10987 (1999)

^{15}N INADEQUATE Spectra





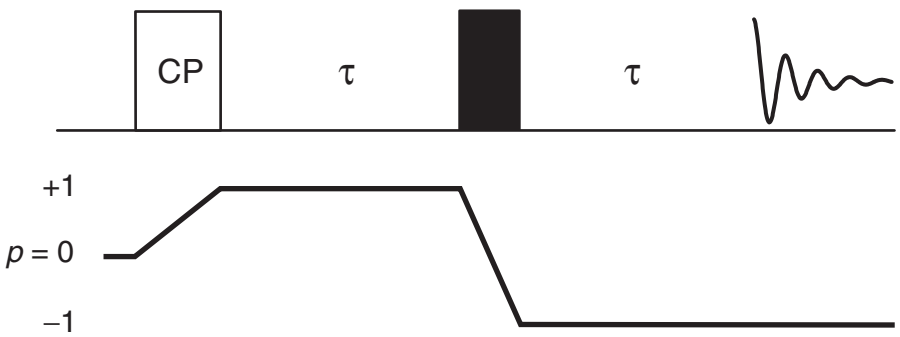


Direct Detection of a Solid-State Hydrogen Bond

Brown *et al*, JACS 124, 1152

Homonuclear *J* Spectroscopy

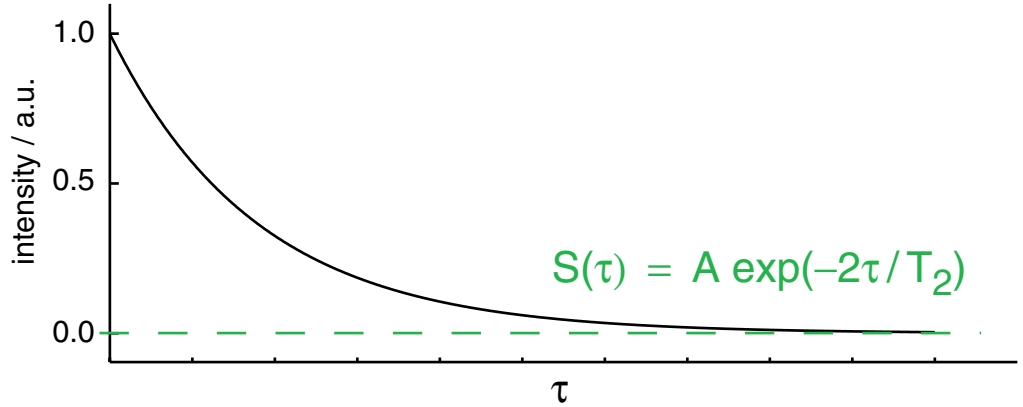
The spin-echo experiment

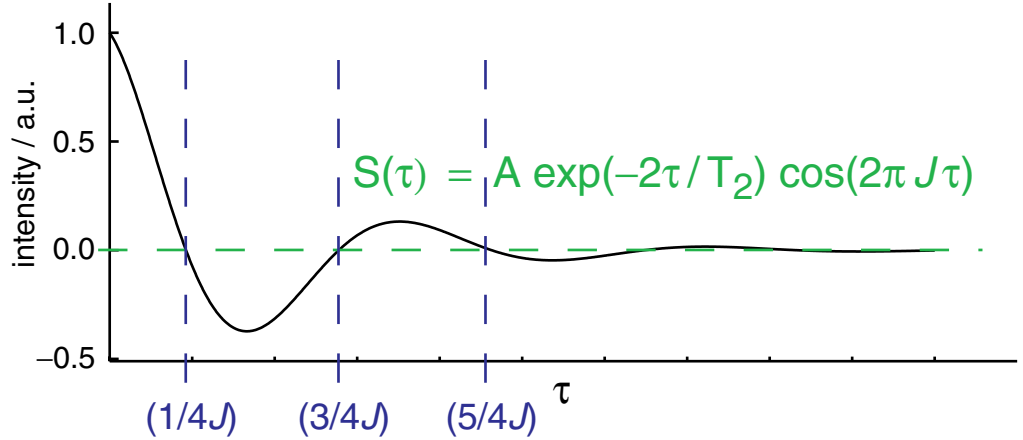


Kubo & McDowell
JCP 92, 7156 (1990)

Wu & Wasylichen
Organometallics 11, 3242 (1992)

For a series of rotor-synchronised τ values, measure the integrated intensity (after Fourier transformation) for a given resonance



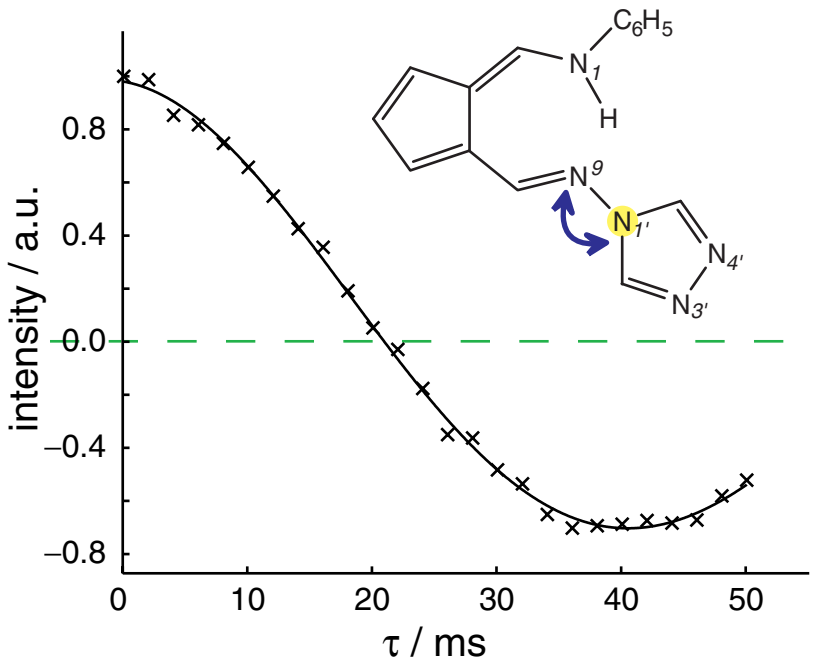


Zero crossings at: $2\pi J\tau = (2n-1)(\pi/2)$

Homonuclear *J* Spectroscopy: Measuring Homonuclear *J* Couplings

one *J*-coupled neighbour

fit to $A \exp(-2\tau / T_2) \cos(2\pi J \tau)$



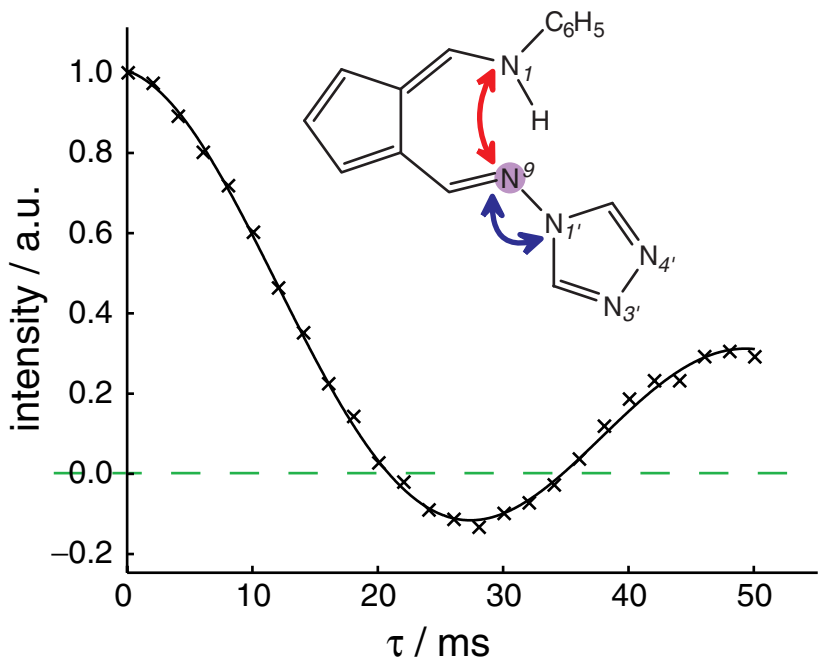
$T_2 = 248 \pm 15$ ms

FWHMH = 1.3 Hz

^1J(N9,N1') = 11.9 ± 0.1 Hz

two *J*-coupled neighbours: fit to

$A \exp(-2\tau / T_2) \cos(2\pi J_1 \tau) \cos(2\pi J_2 \tau)$



$T_2 = 194 \pm 15$ ms

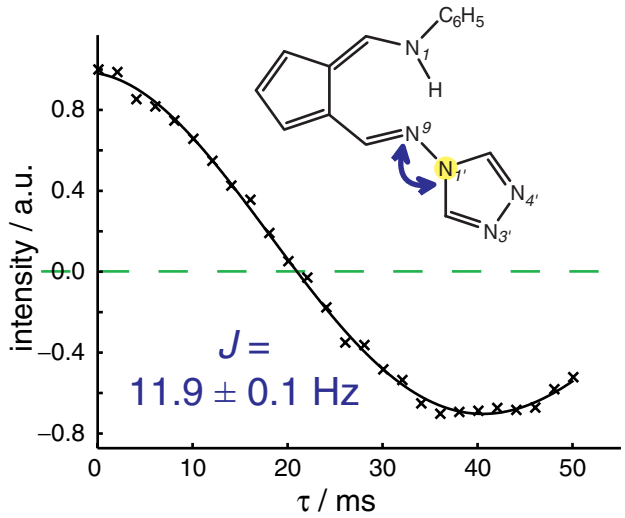
FWHMH = 1.6 Hz

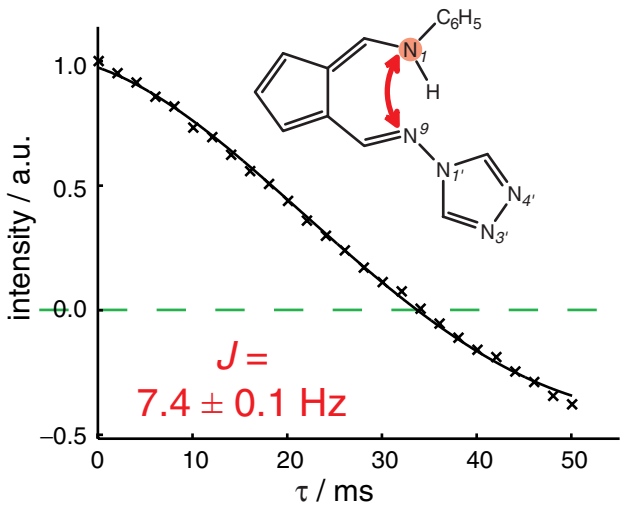
^1J(N9,N1') = 12.0 ± 0.1 Hz

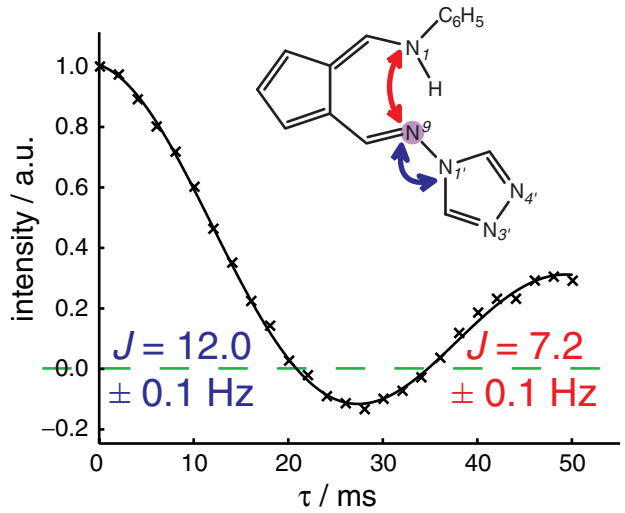
^{2h}J(N1···H···N9) = 7.2 ± 0.1 Hz

The Determination of ^{15}N-^{15}N *J* Couplings

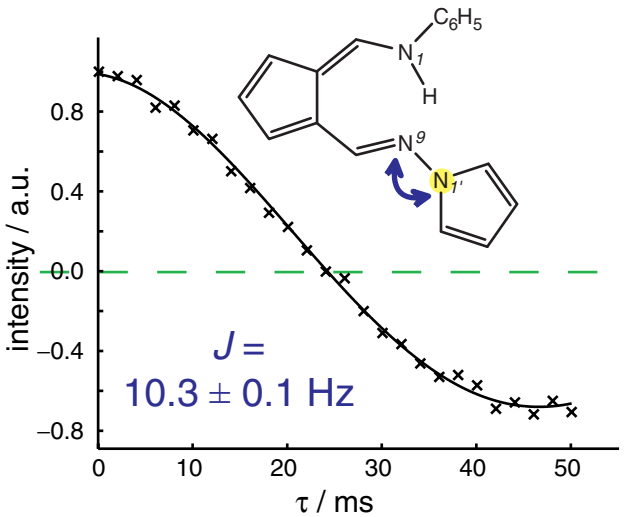
Triazole derivative in solution ($CDCl_3$): *J* = 11.8 Hz *J* = 8.6 Hz

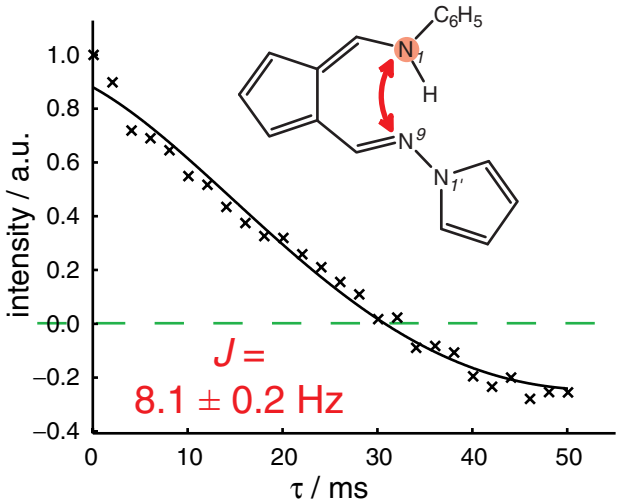


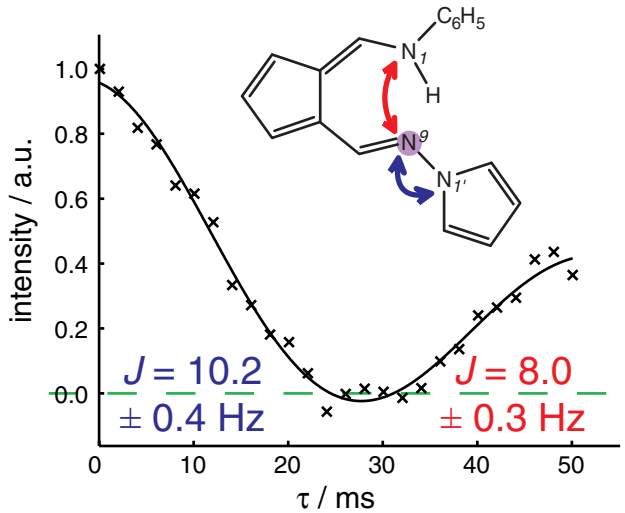




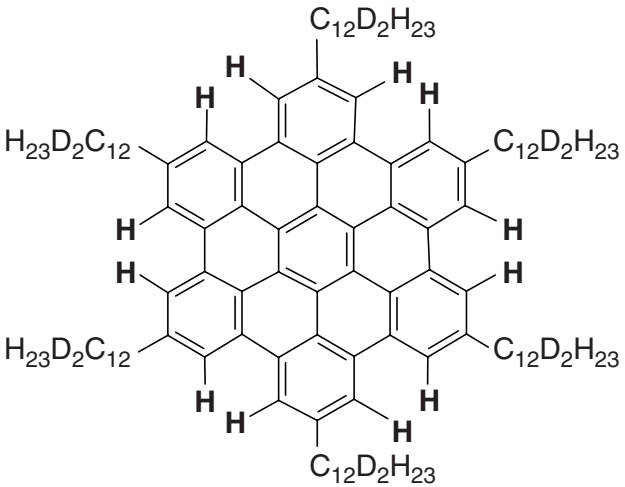
Pyrrole derivative in solution ($CDCl_3$): *J* = 10.3 Hz *J* = 9.0 Hz







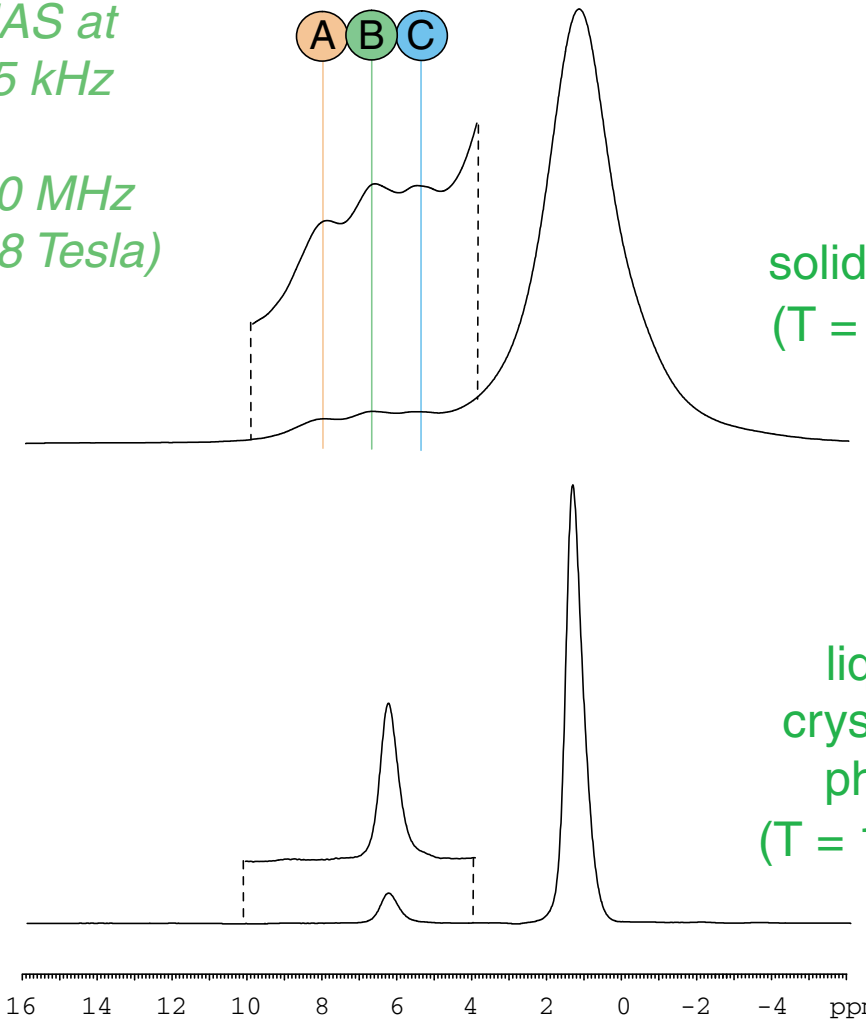
^{1}H MAS NMR of an Alkyl-Substituted Hexabenzocoronene Derivative



Hexabenzocoronene (HBC) derivatives possess very high 1D charge carrier mobilities because of the overlap of the π orbitals due to the polyaromatic cores

MAS at 35 kHz

500 MHz (11.8 Tesla)

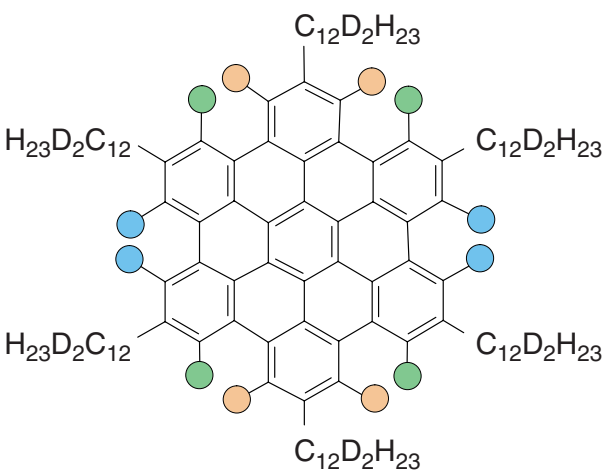


In solution ($CDCl_3$), there is a single aromatic ^{1}H resonance with a concentration-dependent chemical shift between 8.0 and 8.9 ppm

^{1}H DQ MAS NMR of an Alkyl-Substituted Hexabenzocoronene Derivative

MAS at 35 kHz
500 MHz (11.8 Tesla)

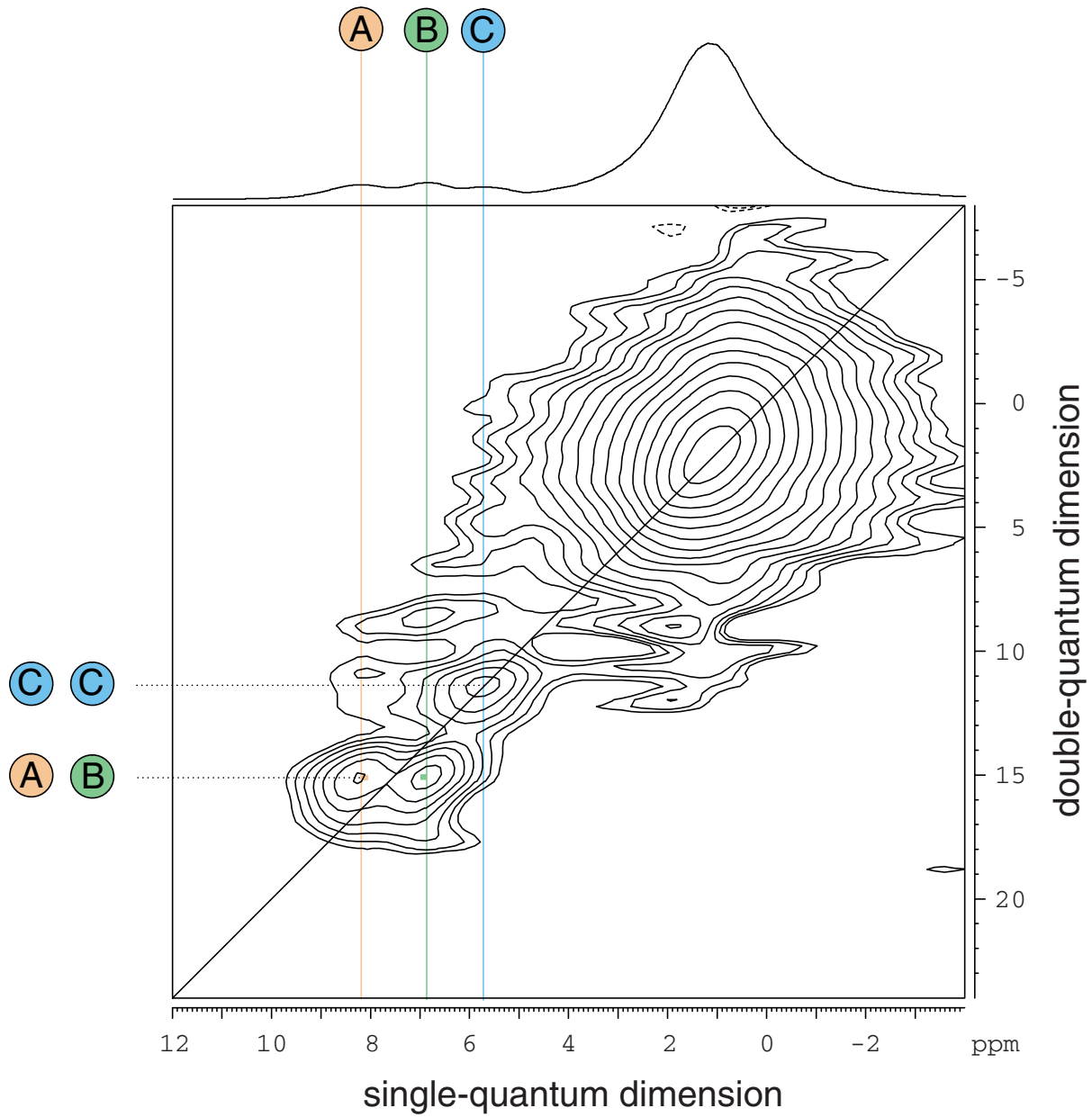
solid phase (T = 60 °C)



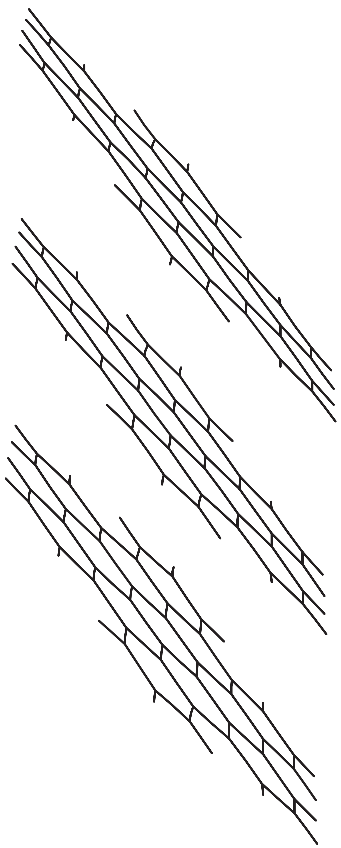
two types of pairs:

A B and C C

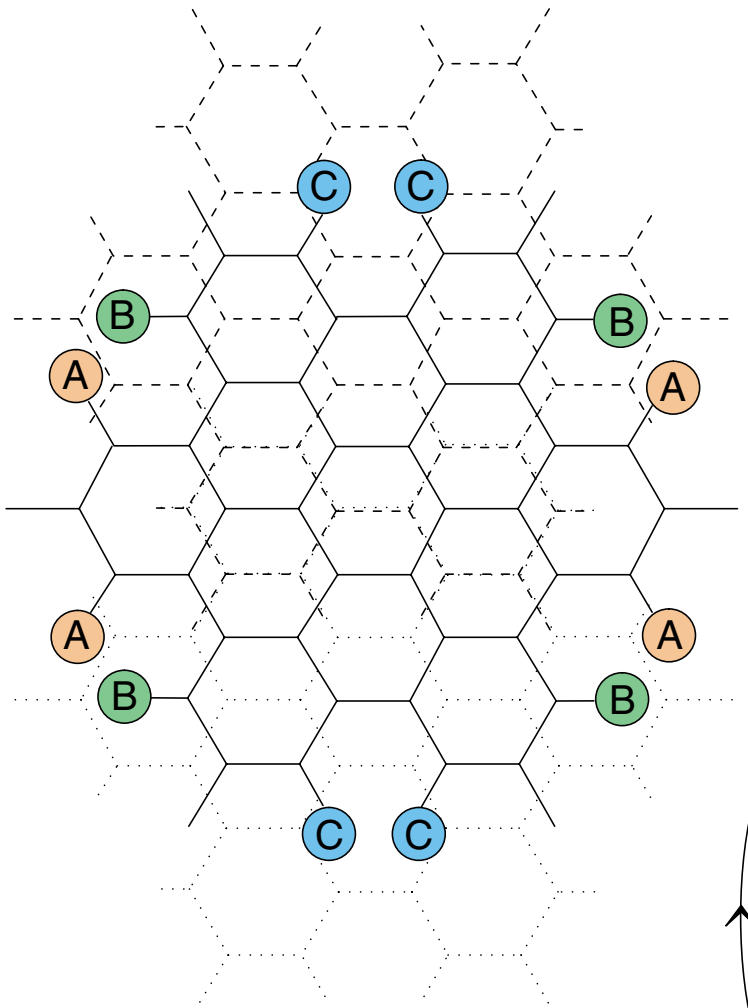
in a ratio 2:1



The Packing of the Aromatic Cores in Hexabenzocoronene

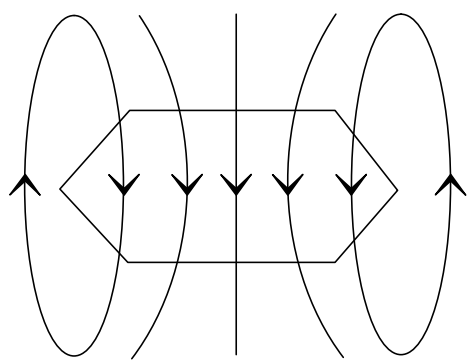


Herring-bone arrangement optimises pi-pi packing



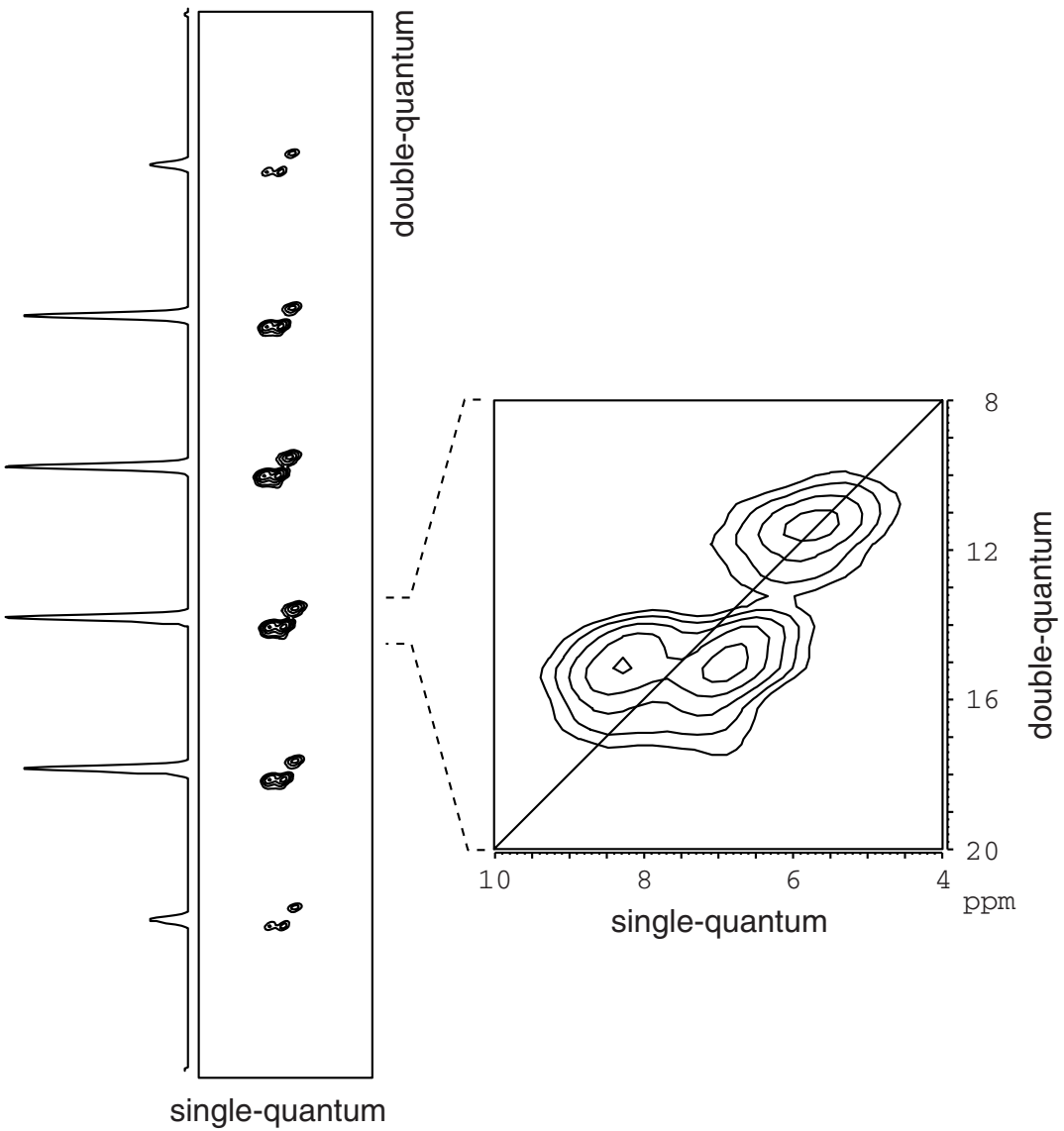
The staggered arrangement of the aromatic cores leads to three different chemical shifts, because of the different ring current effects

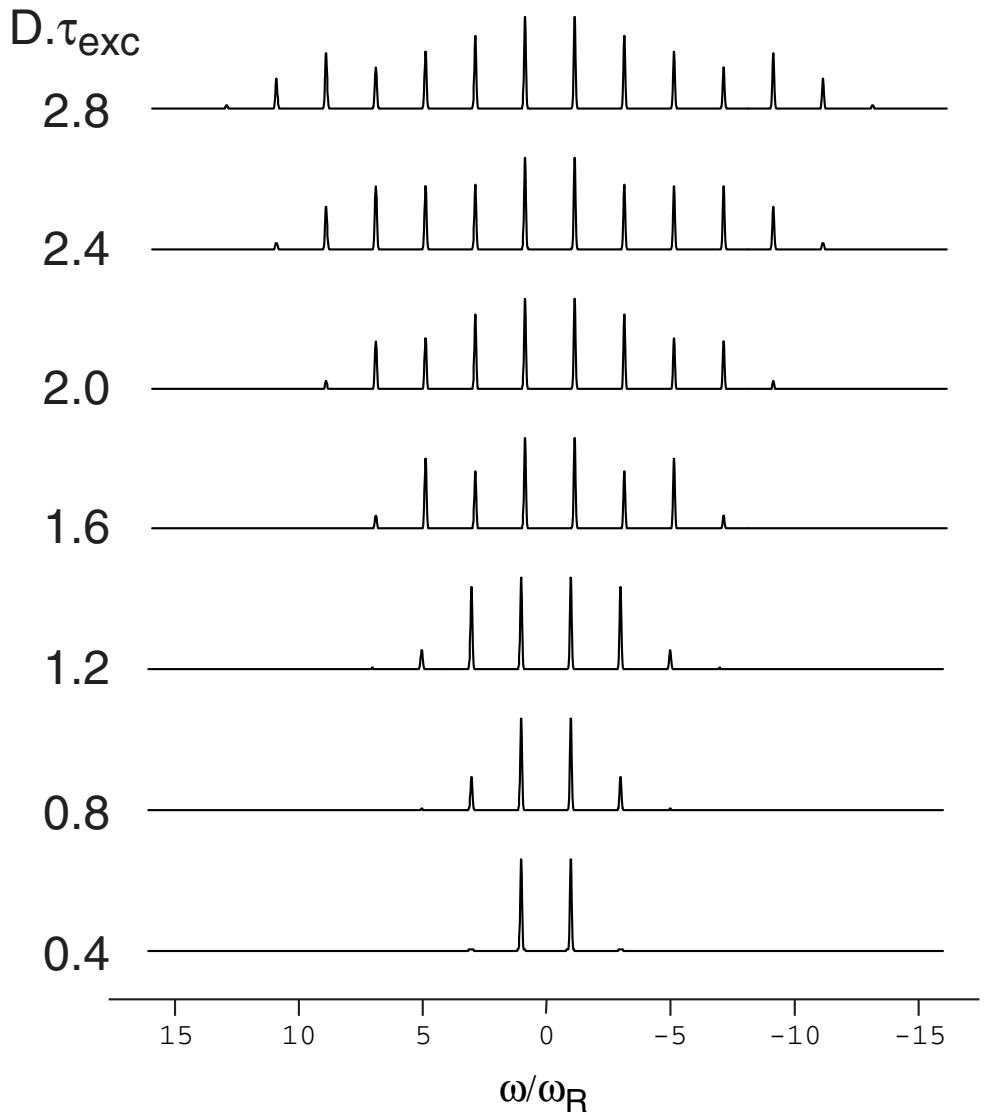
shielded (low ppm)



deshielded (high ppm)

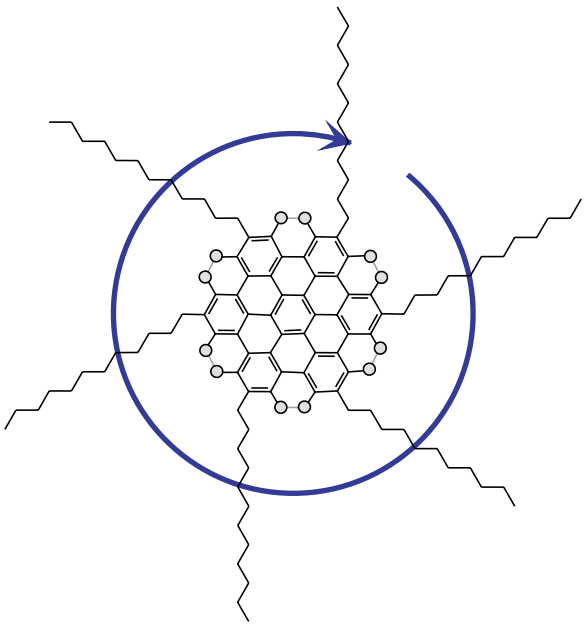
DQ MAS Spinning-Sideband Patterns

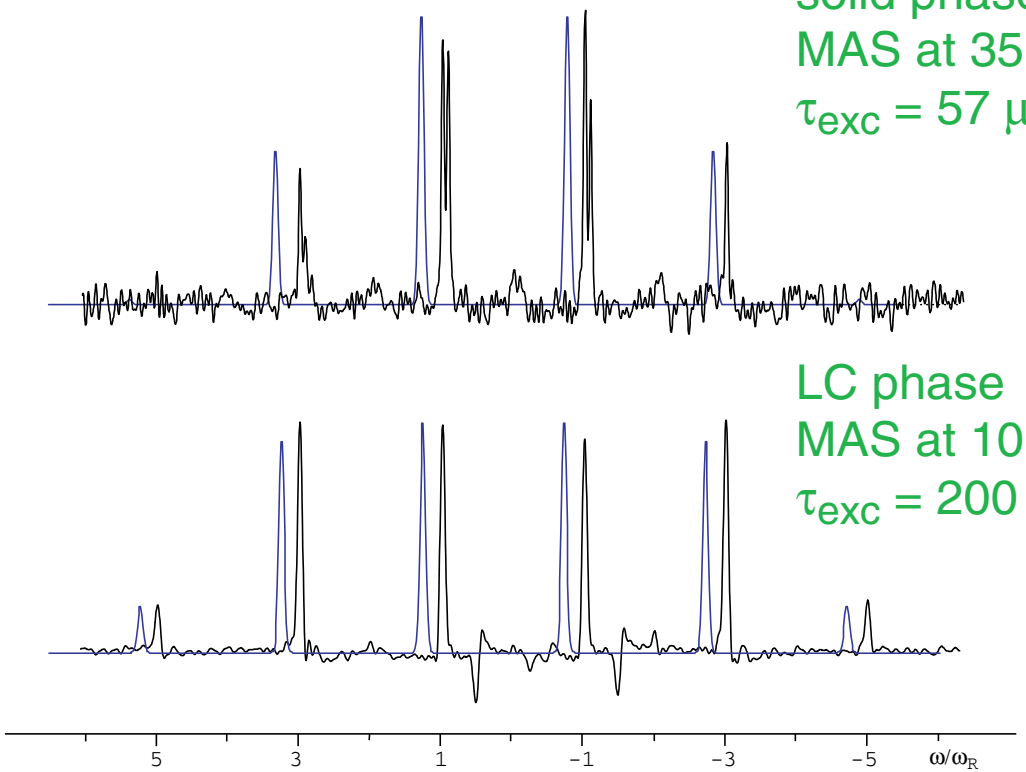




DQ MAS Spinning-Sideband Patterns

^{1}H DQ MAS spinning-sideband patterns are very sensitive to the dipolar coupling





fast rotation about columnar axis:
reduction of dipolar coupling by 0.5

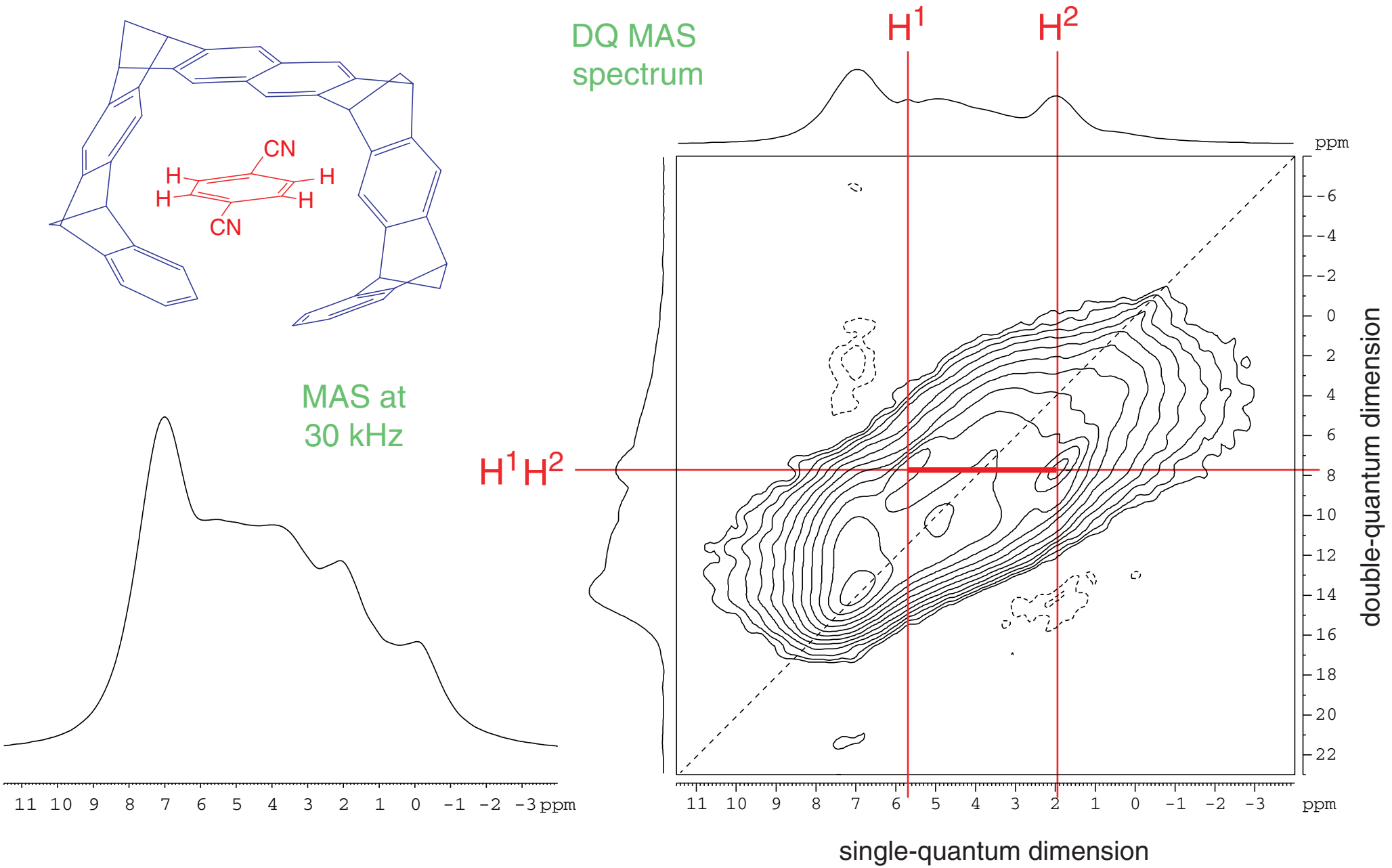
best-fit simulations:

Solid phase: D = 15.0 ± 0.9 kHz

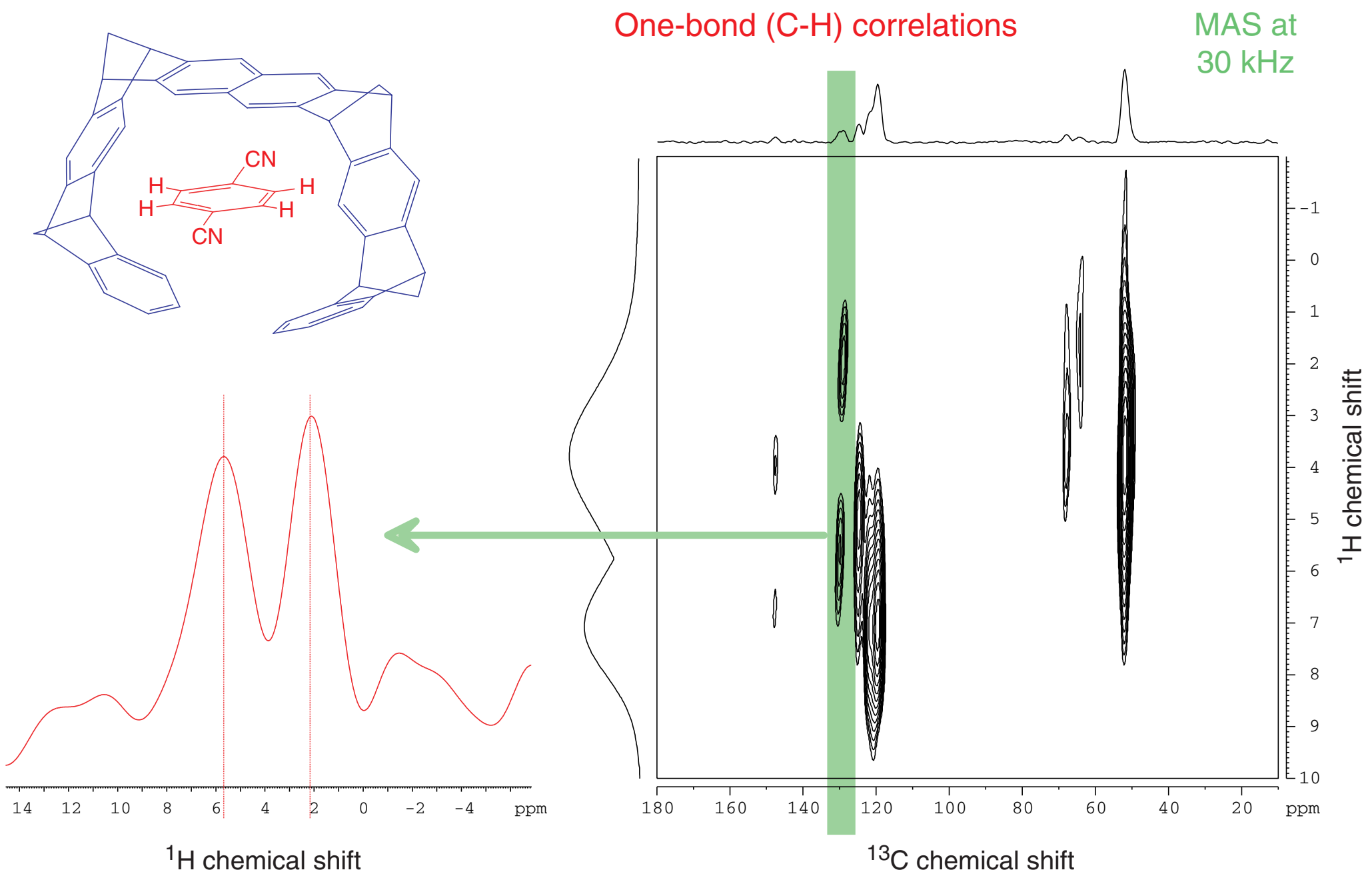
LC phase: D = 6.0 ± 0.5 kHz

LC order parameter S = 0.80 ± 0.08

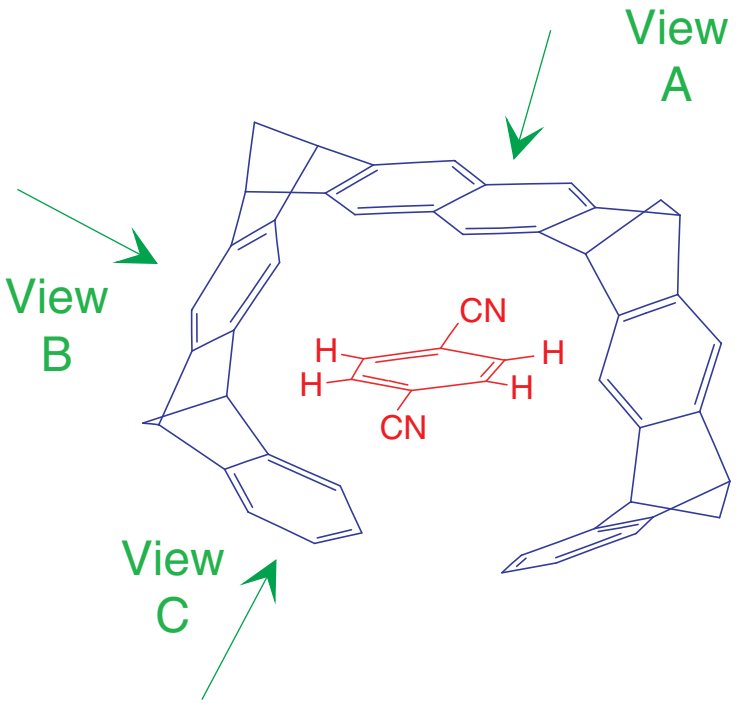
^{1}H (700 MHz) NMR of a Molecular Tweezer



^{1}H-^{13}C (700 MHz) Correlation Spectrum of a Molecular Tweezer



Ring Current Effects on the Guest

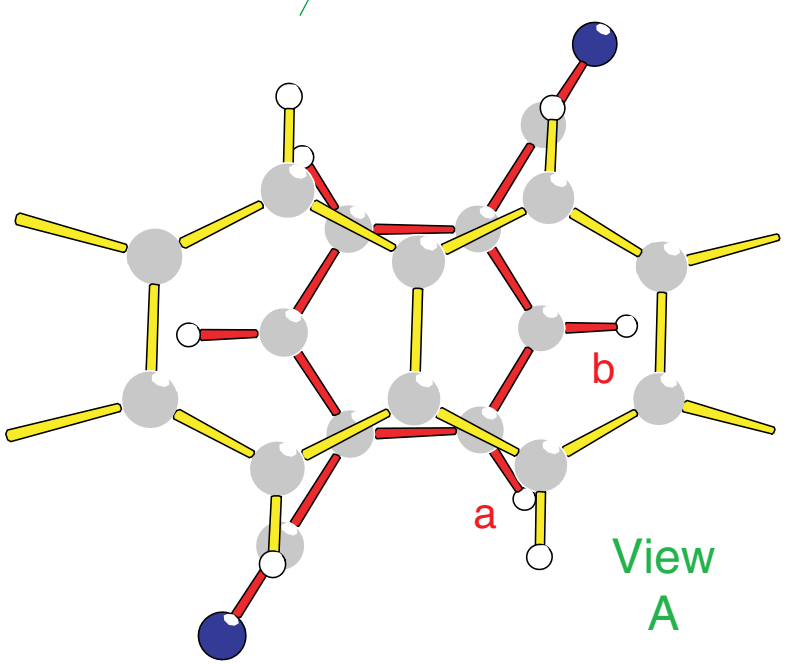


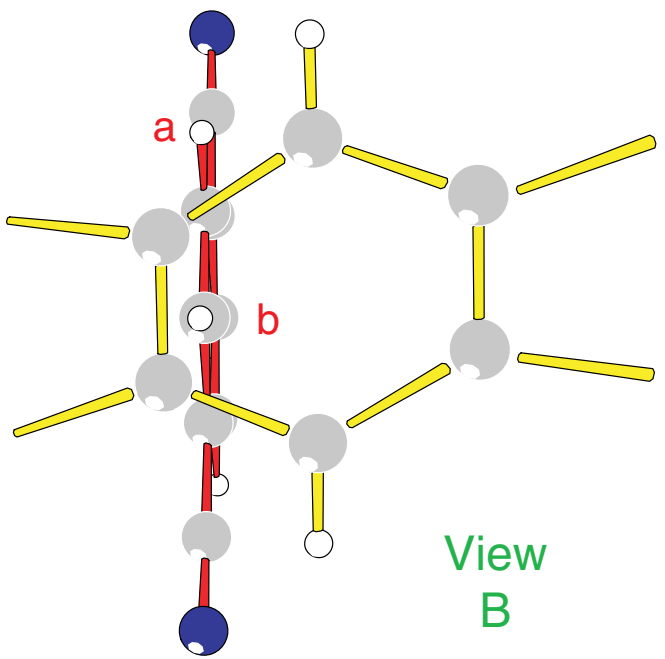
Ab initio ^{1}H chemical shift calculations

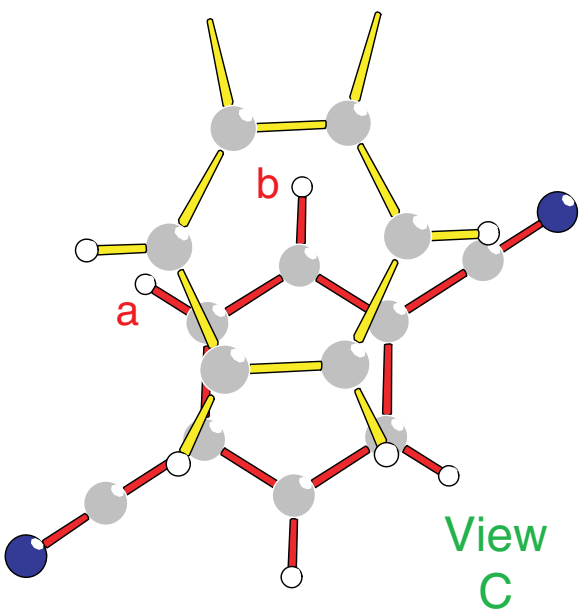
GIAO-HF/TZP//HF/6-31G*

	vac-uum	View A	View B	View C	vacuum –sum	full calc.
Ha	8.0	–0.9	–0.9	–1.0	5.2	5.3
Hb	7.9	–1.2	–3.6	–1.7	1.4	1.7

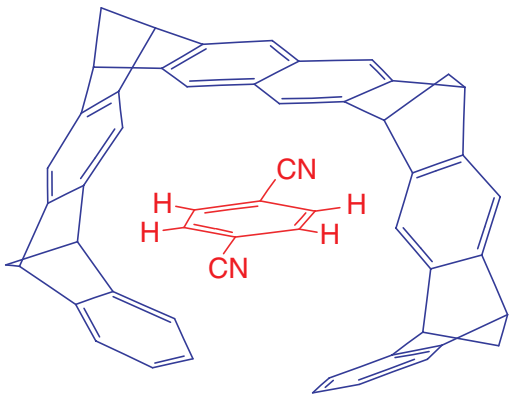
(Ochsenfeld et al, Solid State NMR 22, 128, 2002)



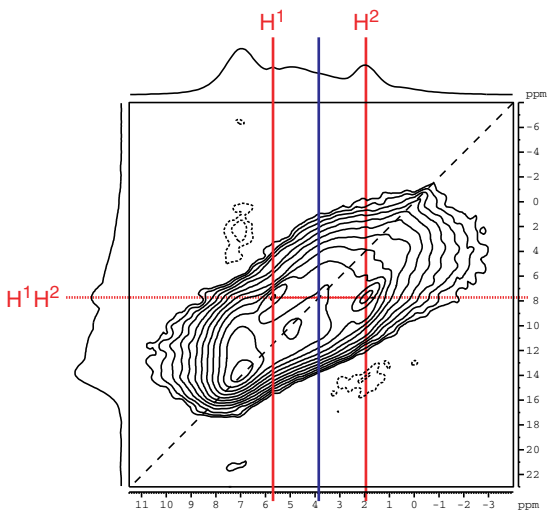


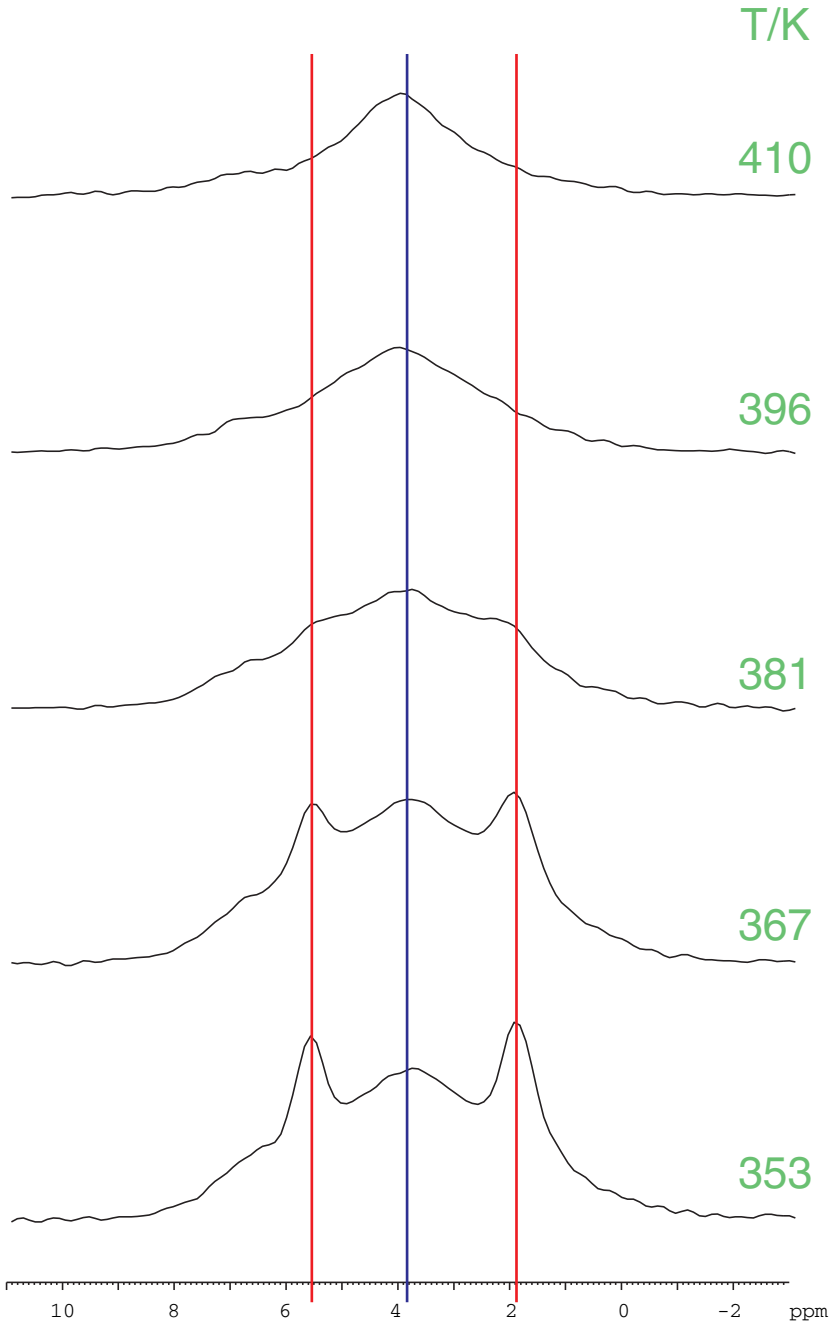


Probing the Guest Dynamics

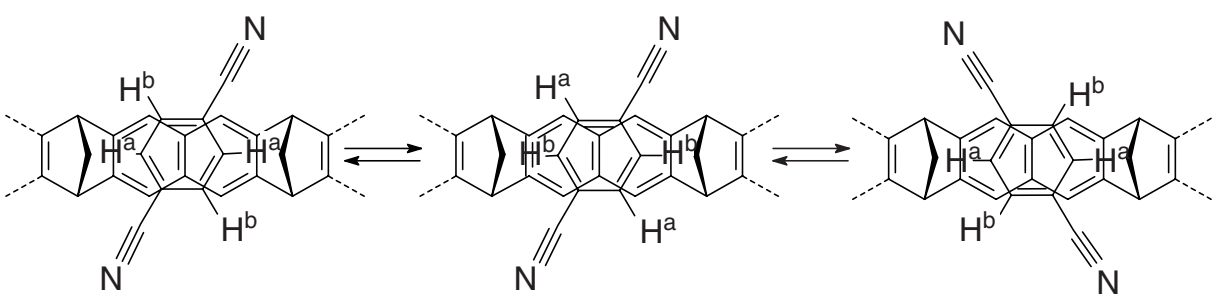


Temperature-dependent changes in slices from ^{1}H DQ MAS spectra



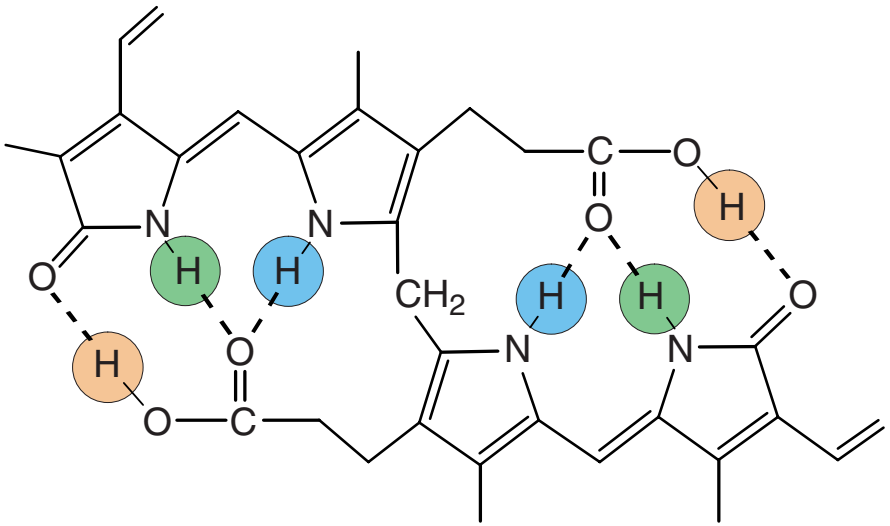


Upon heating, the two ^{1}H guest aromatic resonances coalesce because of guest dynamics

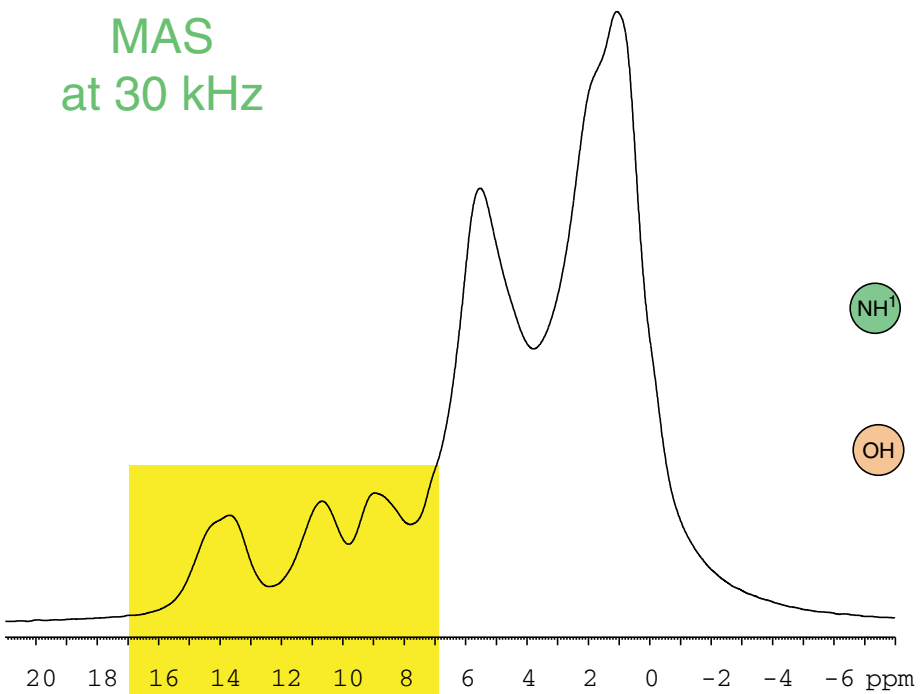


^{1}H (700 MHz) NMR of Bilirubin

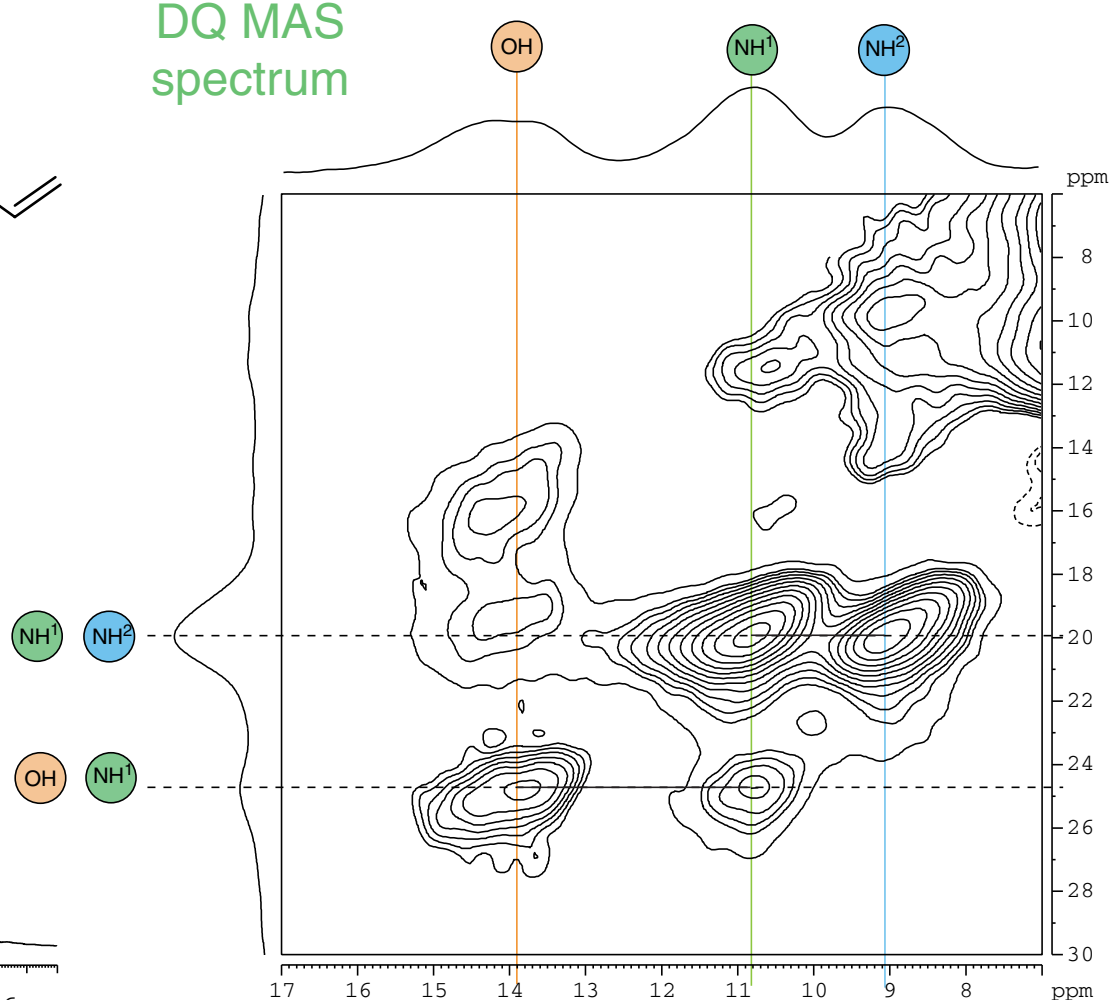
responsible for jaundice in new-born babies
insoluble in aqueous solution, because of
strong intramolecular hydrogen bonding



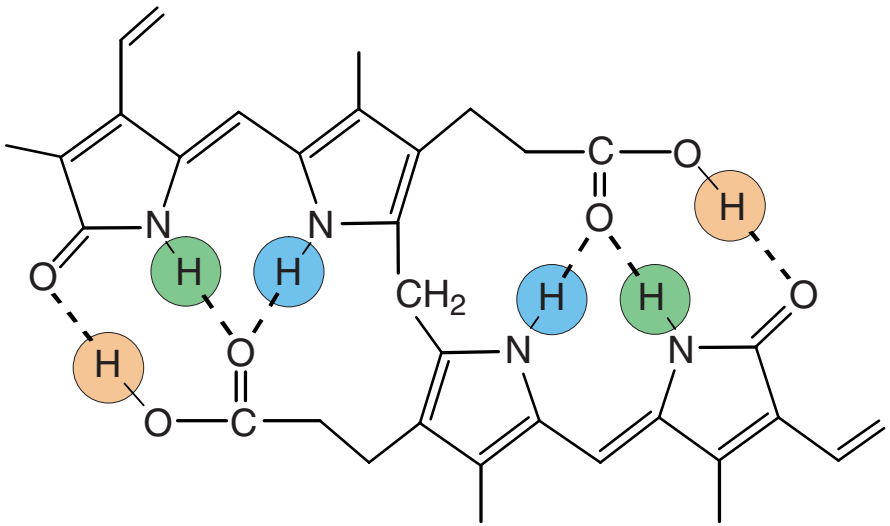
MAS
at 30 kHz

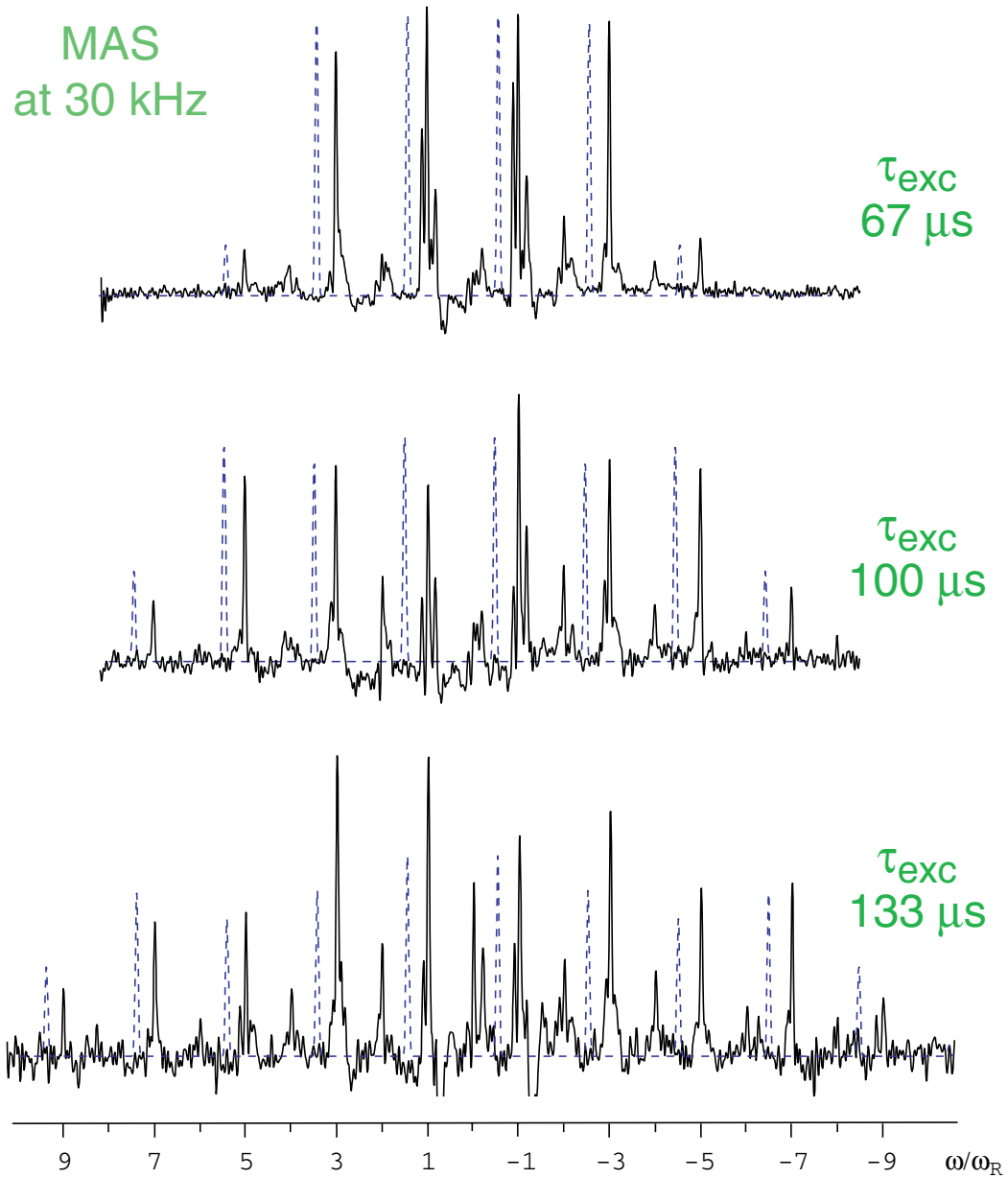


DQ MAS
spectrum

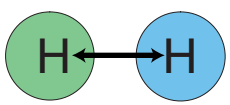


^{1}H (700 MHz) DQ MAS Spinning-Sideband Patterns for Bilirubin





Fitting to the experimental DQ MAS spinning-sideband patterns allows the accurate determination of



186 ± 2 pm

Acknowledgements

Hans W. Spiess,

Max-Planck-Institute for Polymer Research, Mainz, Germany (1998-2000)

Lyndon Emsley,

Ecole Normale Superieure de Lyon, France (2001-2002)

Hydrogen-Bond Mediated *J* couplings:

Rosa Claramunt, Marta Perez-Torralba, Dionisia Sanz (UNED, Madrid, Spain)

Hexabenzocoronenes:

Klaus Muellen, Johann Diedrich Brand, Ingo Schnell (MPI-P, Mainz, Germany)

Molecular Tweezers:

Frank-Gerrit Klaerner, Torsten Schaller, Uta P. Seelbach (Essen, Germany)

Christian Ochsenfeld, Felix Koziol (Tuebingen, Germany)

Bilirubin:

Xiao Xia Zhu (Montreal, Canada)

Alexander von Humboldt-Stiftung (January 1998 - December 1999)

Marie Curie Fellowship (HPMFCT-2000-00525) (January 2001 - September 2002)

EPSRC Advanced Research Fellowship (October 2002-)

Papers

Hydrogen-Bond Mediated *J* couplings:

Brown *et al*, *J. Am. Chem. Soc.* **124**, 1152 (2002)

Brown *et al*, *Chem. Comm.* 1852 (2002)

Hexabenzocoronenes:

Brown *et al*, *J. Am. Chem. Soc.* **121**, 6712 (1999)

Molecular Tweezers:

Brown *et al*, *Angew. Chem. Int. Ed.* **40**, 717 (2001)

Ochsenfeld *et al*, *Solid State NMR* **22**, 128 (2002)

Bilirubin:

Brown *et al*, *J. Am. Chem. Soc.* **123**, 4275 (2001)

Review:

Brown *et al*, *Chem. Rev.* **101**, 4125 (2001)