

Recent Developments in DNP NMR

Dr. Damir Blazina

Applications Chemist

Oxford Instruments Molecular Biotools Ltd.

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Overview

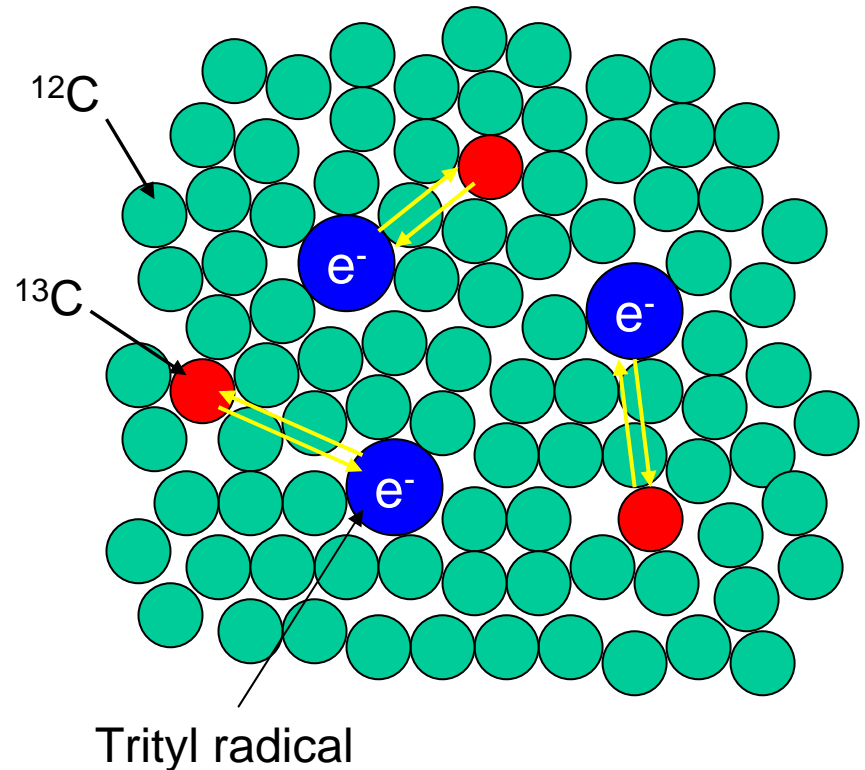
- DNP at Oxford Instruments
- Dissolutions with methanol
- ^{15}N DNP NMR
- Polarisation transfer experiments
- Acquisition of multiple spectra

Dynamic Nuclear Polarisation (DNP)

- NMR hyperpolarisation technique
- Can yield $>10,000$ fold increase in SNR
- Limited to a single scan
- Cool sample in a strong magnetic field
 - Hyperpolarise unpaired electrons
- Irradiate with microwaves
 - Transfer polarisation to atomic nuclei

DNP at Oxford Instruments

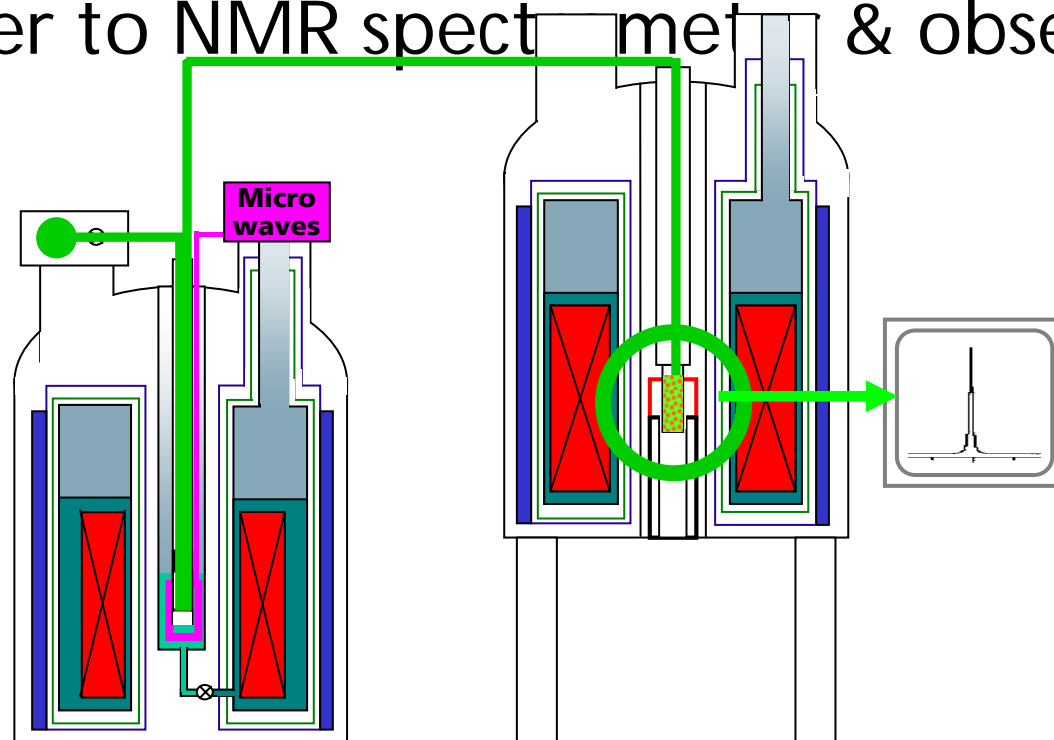
- Method developed by Amersham Health (GE)
- Dope sample with trityl radical
- Dissolve in mixture of solvents to form a glass when frozen
- Cool to <4 K at 3.35 T
- Irradiate with microwaves at 94 GHz (commercial source)



J. H. Ardenkjær-Larsen et al., *PNAS* 2003, 100, 10158

DNP NMR

- Rapidly thaw sample by injecting hot solvent
- Transfer to NMR spectrometer & observe

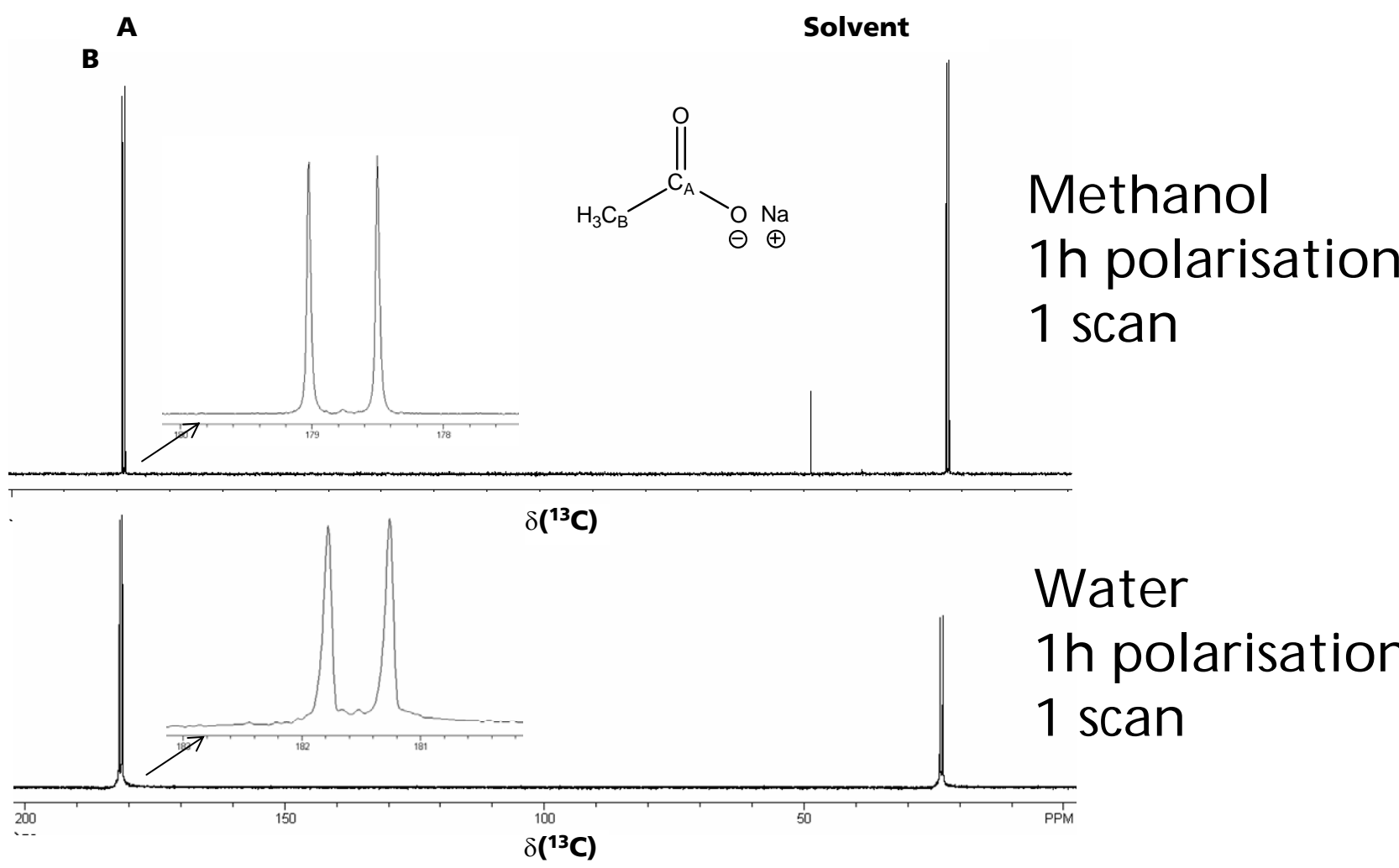


Properties of Methanol

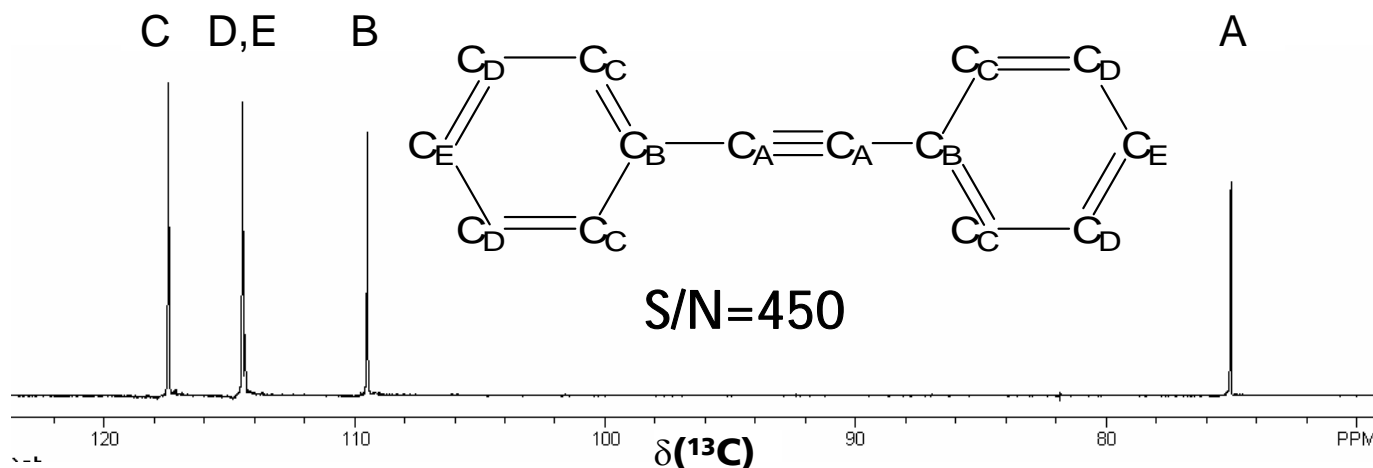
- Can dissolve wide range of hydrophobic and hydrophilic compounds
- Low viscosity and surface tension
- Very low freezing point
- Exhibits annular flow
- Single NMR resonance

→ Desirable DNP solvent!

Comparison of Dissolution Solvents

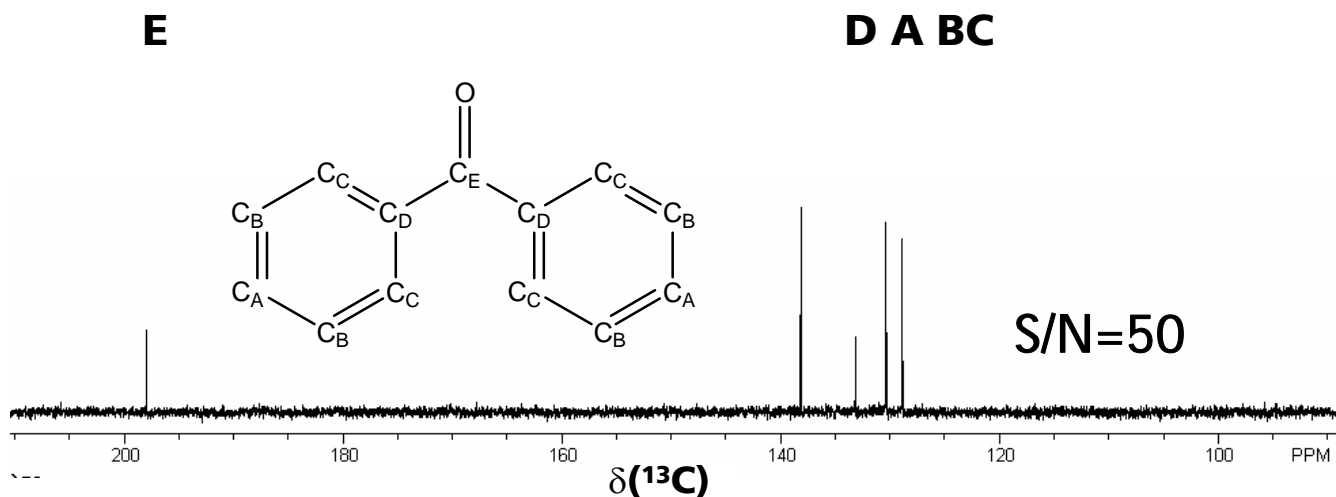


Organic Compounds



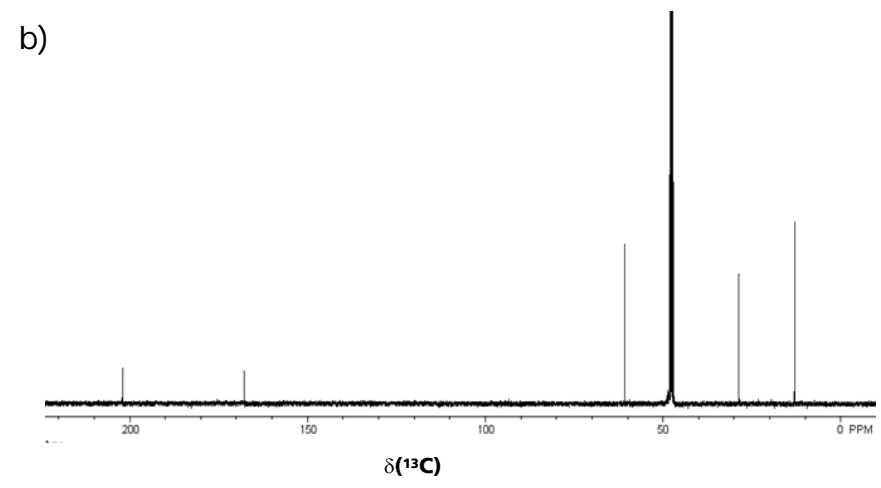
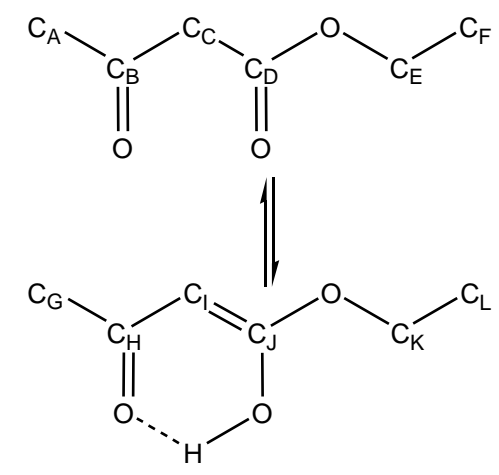
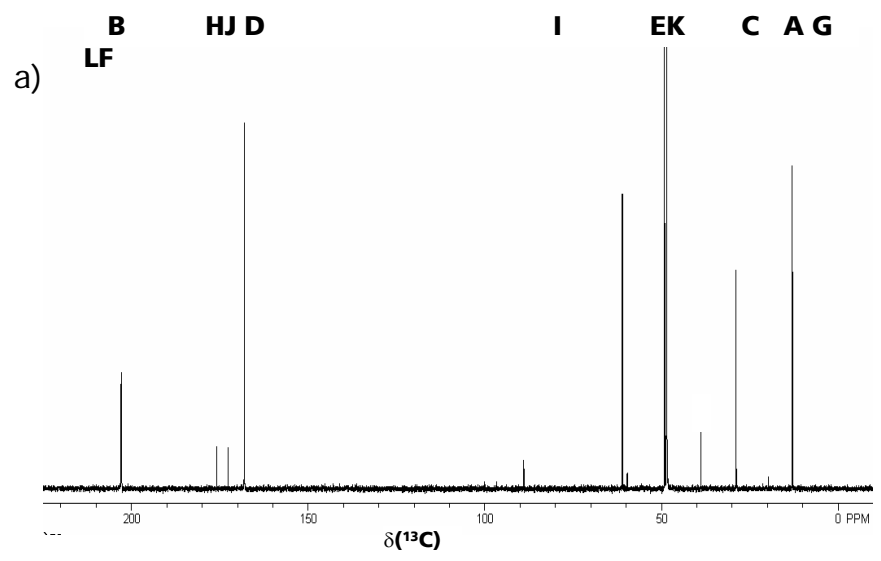
- One scan ^{13}C DNP NMR spectrum of 20 μmol of natural abundance diphenylacetylene
- Sample poorly soluble in water
- Methanol/DMSO mixture in sample cup
- Dissolution with methanol

Organic Compounds (2)



- One scan ^{13}C DNP NMR spectrum of 15 μmol of natural abundance benzophenone
- 2h polarisation
- Methanol/DMSO mixture in sample cup, dissolution with methanol

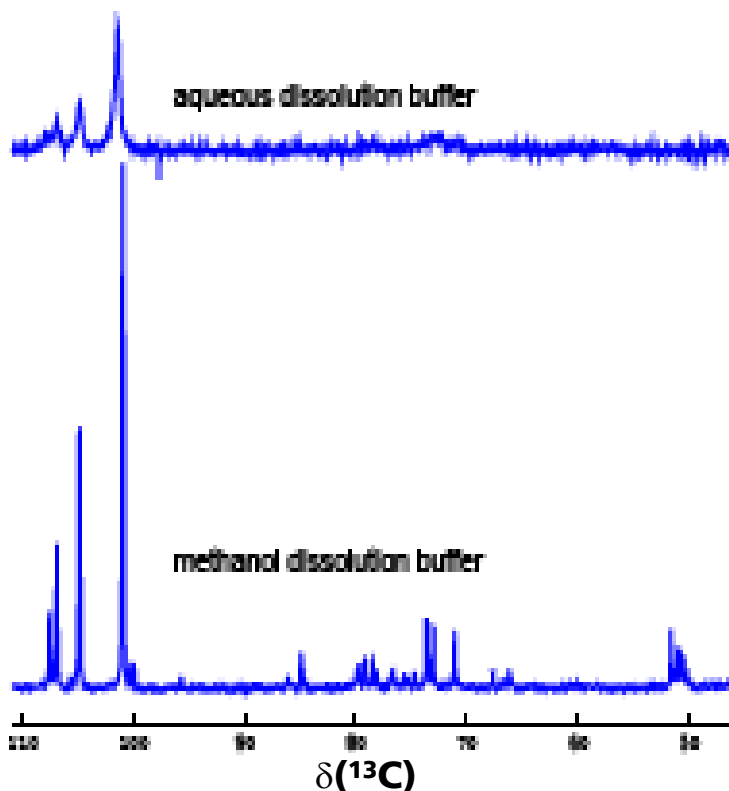
Keto-Enol Tautomerism



^{13}C NMR spectra of ethyl acetoacetate (60 μmol):

- (A) One-scan DNP NMR after 3 hours polarisation.
- (B) Conventional NMR spectrum recorded over 3 hours.

Methanol with Natural Products

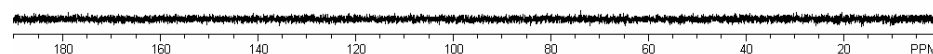
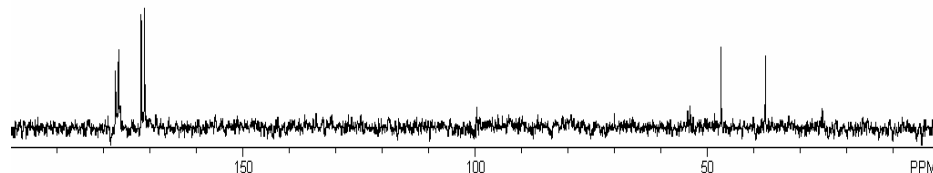
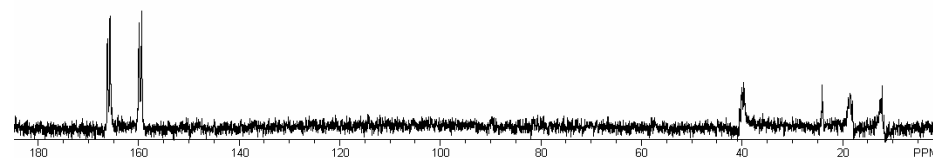
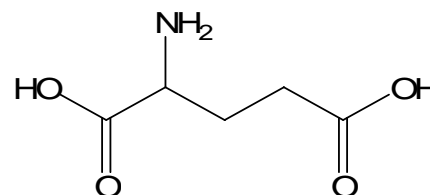


- ^{13}C DNP NMR of apple juice extracts
- 4h polarisation, one scan
- Upper trace: water
- Lower trace: methanol

Data courtesy of Ulrich Günther,
University of Birmingham, UK

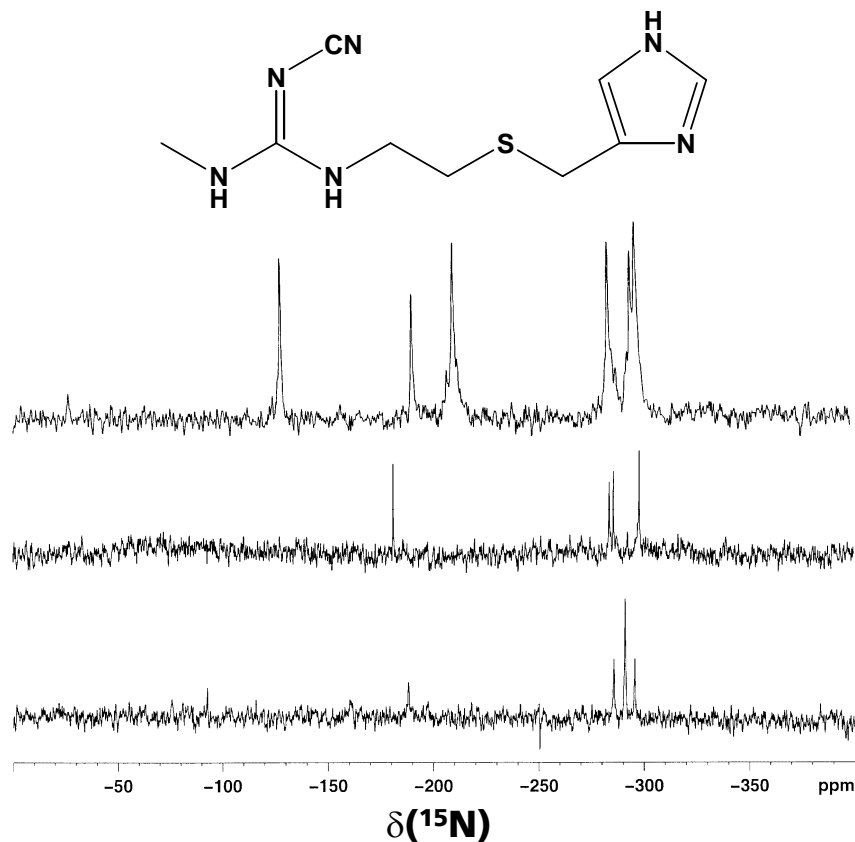
Solubility considerations

- $^{13}\text{C}_5$ glutamic acid, 5 μmol
- Top: 6h polarisation, water, 1 scan
- Middle: 6h polarisation, methanol, 1 scan
- Bottom: conventional NMR, 48h
- Methanol not always optimal choice

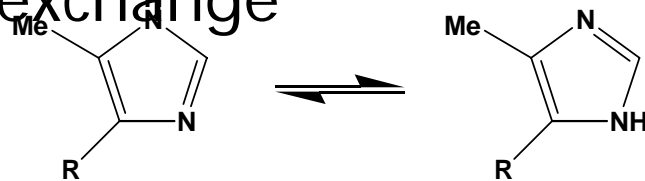


$\delta(^{13}\text{C})$

^{15}N DNP NMR: Cimetidine

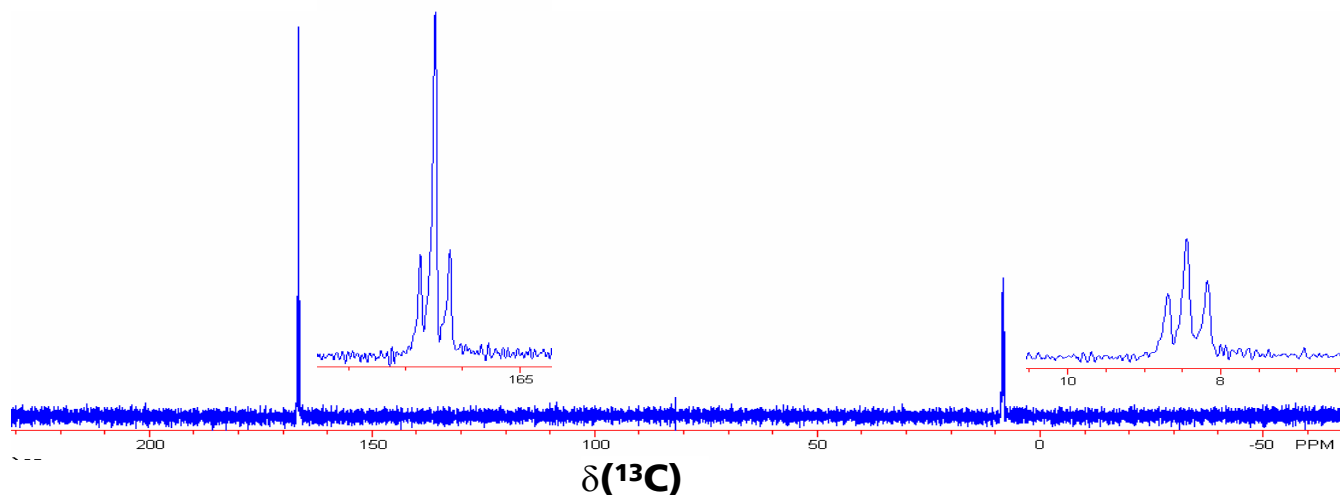


- 25 mg, water dissolution
- Top: solid state CPMAS
- Middle: Conventional NMR, 6000 scans, 18h
- Bottom: DNP NMR, 1 scan, 16h polarisation
- Evidence for tautomeric exchange



Data courtesy of Geoff Hawkes, QMUL,

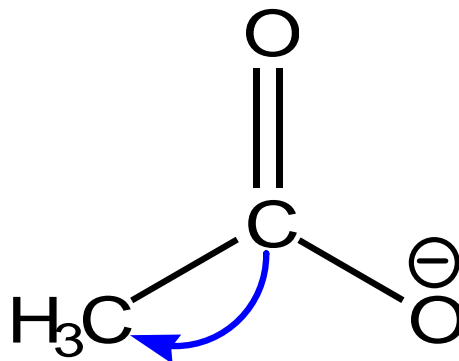
Polarisation transfer experiments



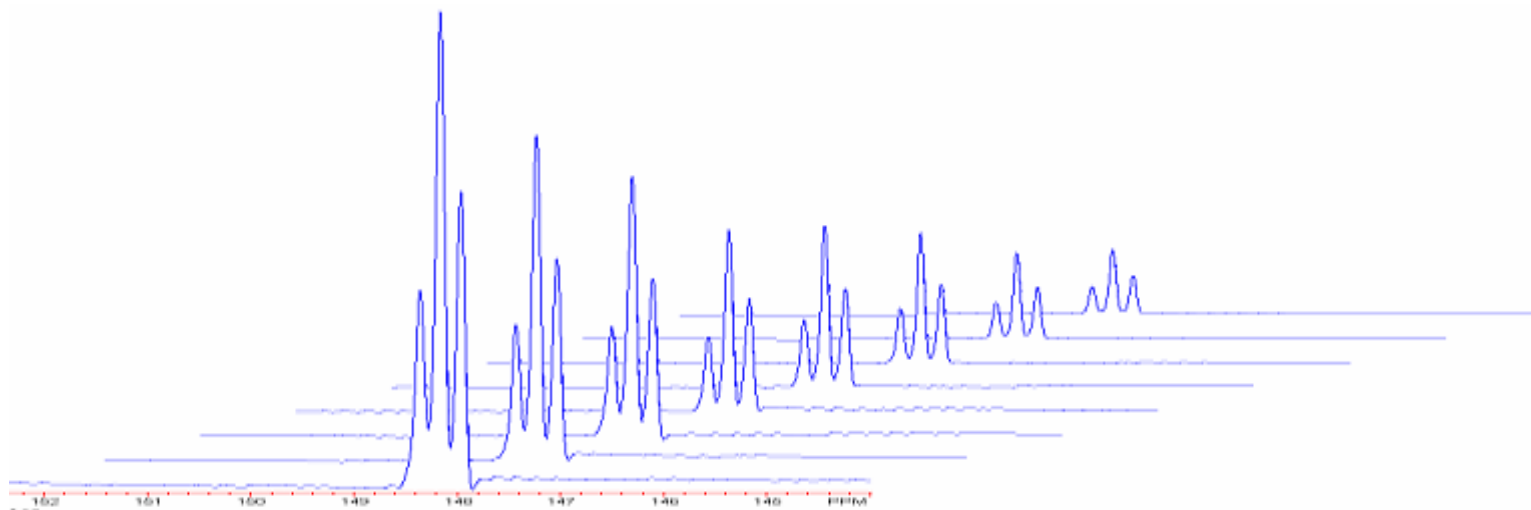
- 1:1:1 mix of 1- ^{13}C , 2- ^{13}C & 1,2- $^{13}\text{C}_2$ sodium acetate
- 1 scan ^{13}C DNP NMR spectrum, water dissolution
- Ratio at each site does not match expectations
 - Carbonyl 1- ^{13}C : 1,2- $^{13}\text{C}_2$ = 1.6 : 1
 - Methyl 2- ^{13}C : 1,2- $^{13}\text{C}_2$ = 0.8 : 1

Polarisation transfer experiments (2)

- Isomers polarise to same extent, have nearly identical relaxation properties
- **Polarisation transfer** from slow-relaxing carbonyl to fast-relaxing methyl in $1,2\text{-}^{13}\text{C}_2$
- Not possible in singly-labelled isomers



Acquisition of multiple spectra



- Eight spectra from one DNP sample with 90° pulses
- >150 spectra possible with 30° pulses
- Reaction kinetics, dynamic processes, 2D DNP NMR

Conclusions

- Methanol as dissolution solvent in DNP NMR
 - Generally superior performance to water
 - Solubility consideration important
- ^{15}N DNP NMR
 - Evidence for tautomeric exchange
- Polarisation transfer
 - Alters observed isomer ratios
 - May be causing observation of multiple spectra

Acknowledgements

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 - Geoff Hawkes (QMUL)
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