

DYNAMIC NUCLEAR POLARISATION and NATURAL ABUNDANCE ^{15}N NMR

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Introduction

The recent installation of the Oxford Instruments *HYPERSENSE* equipment for dynamic nuclear polarization experiments has prompted a number of projects at Queen Mary.

The first of these projects explores the applicability of DNP to generate solution state natural abundance (0.37%) ^{15}N NMR spectra of low molecular mass compounds.

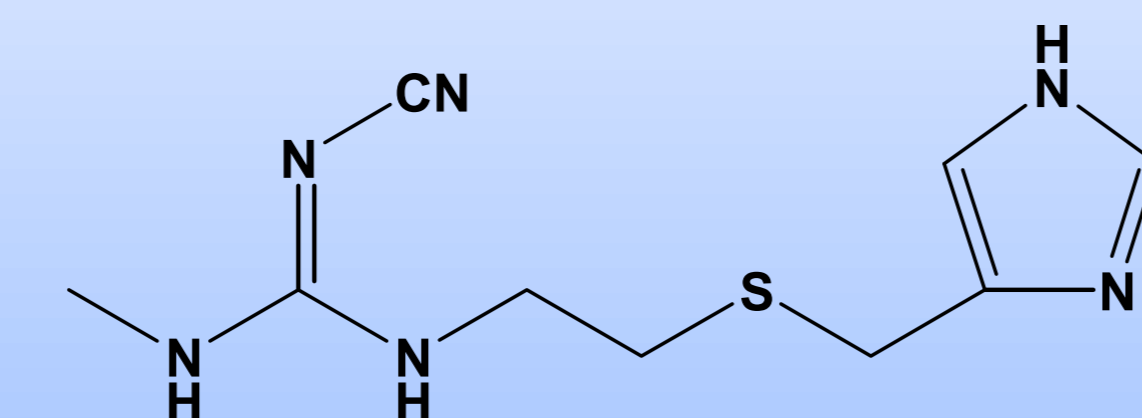
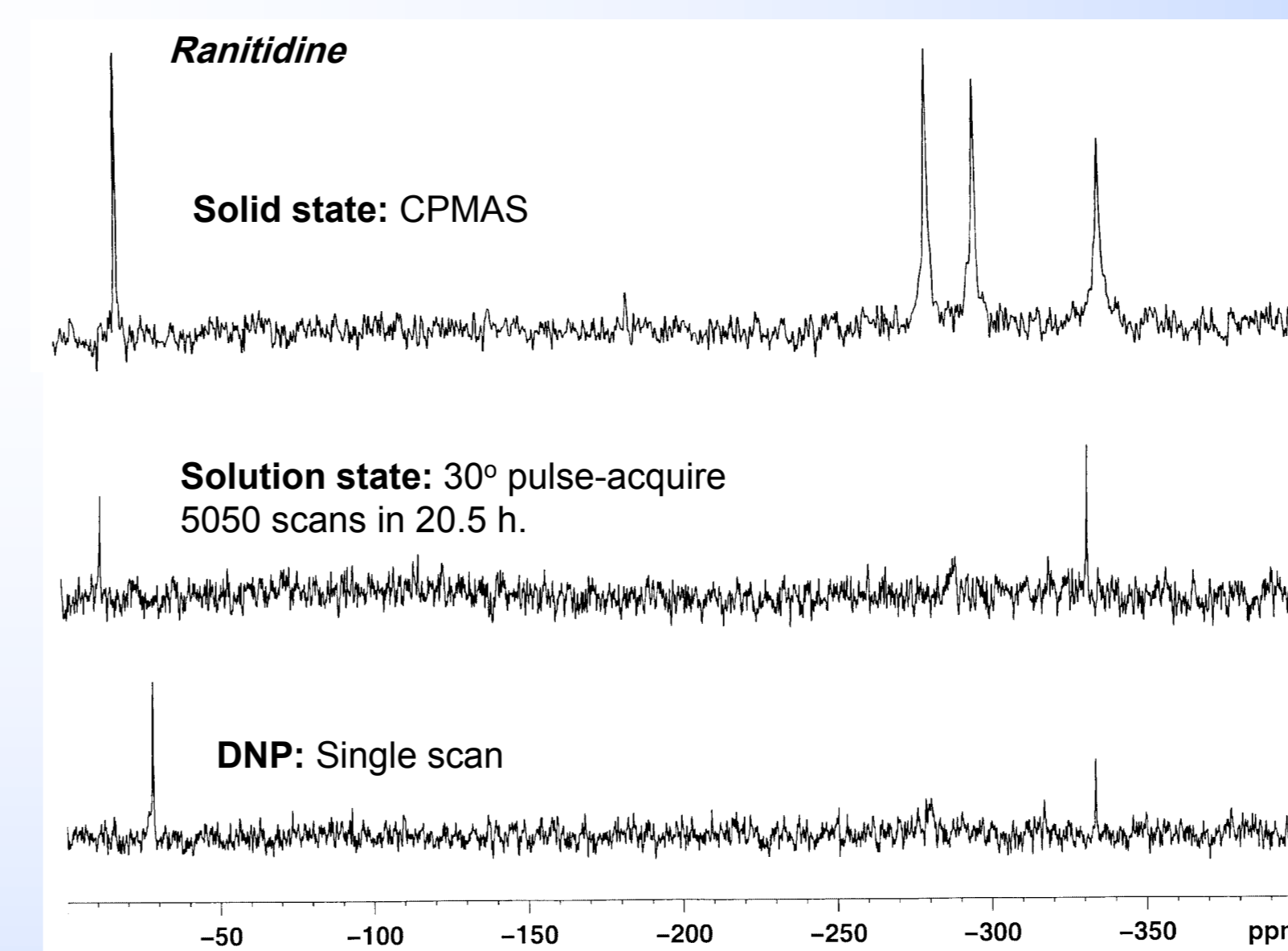
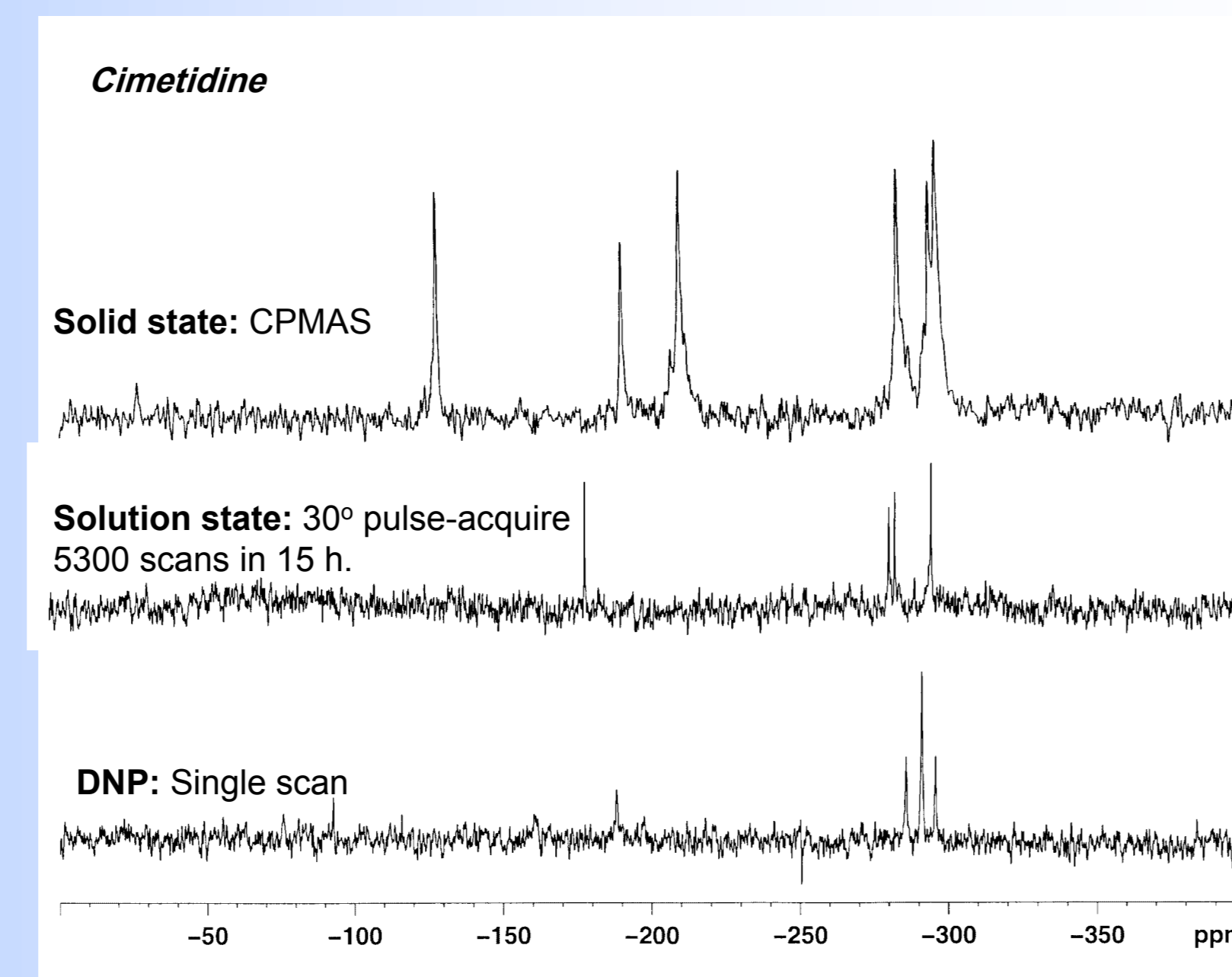
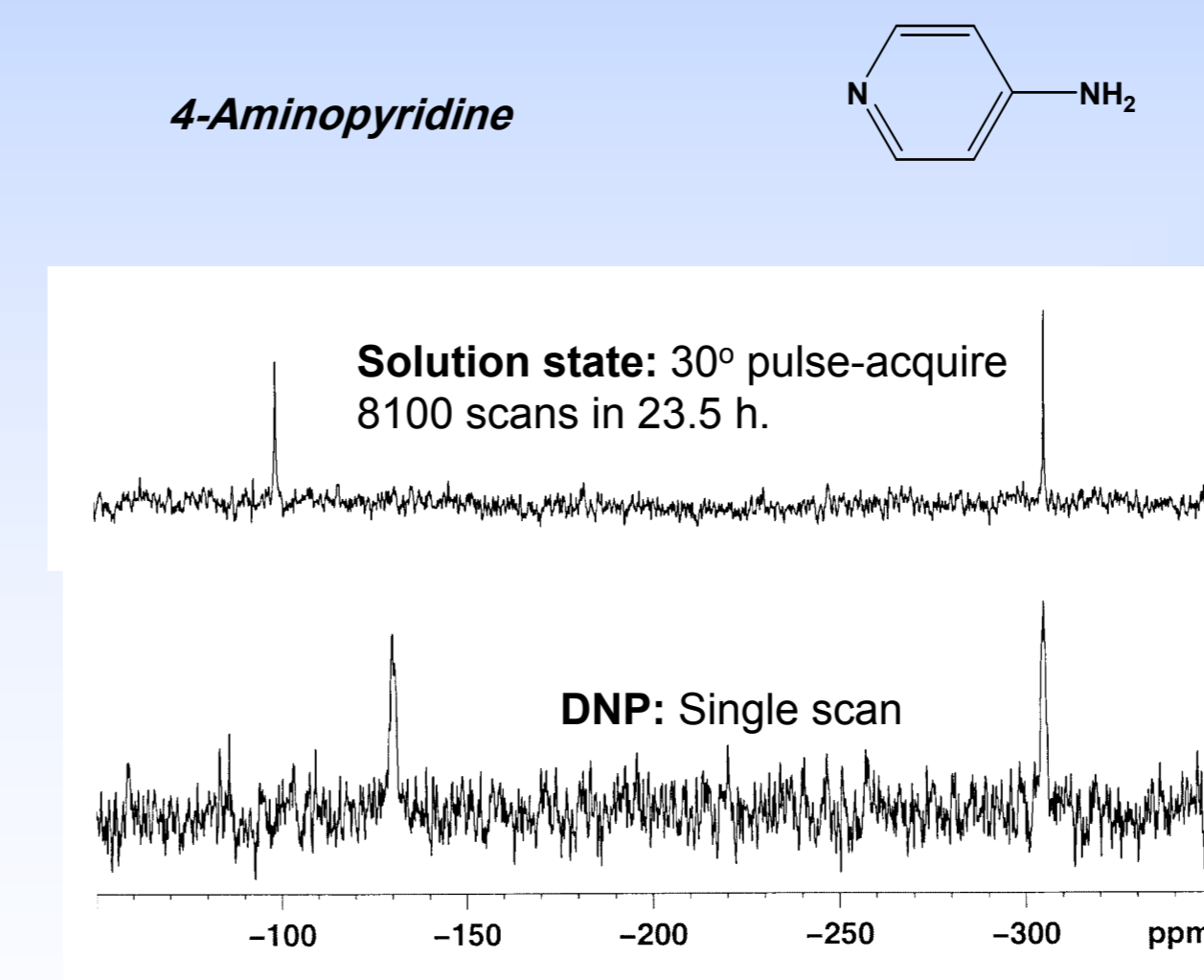
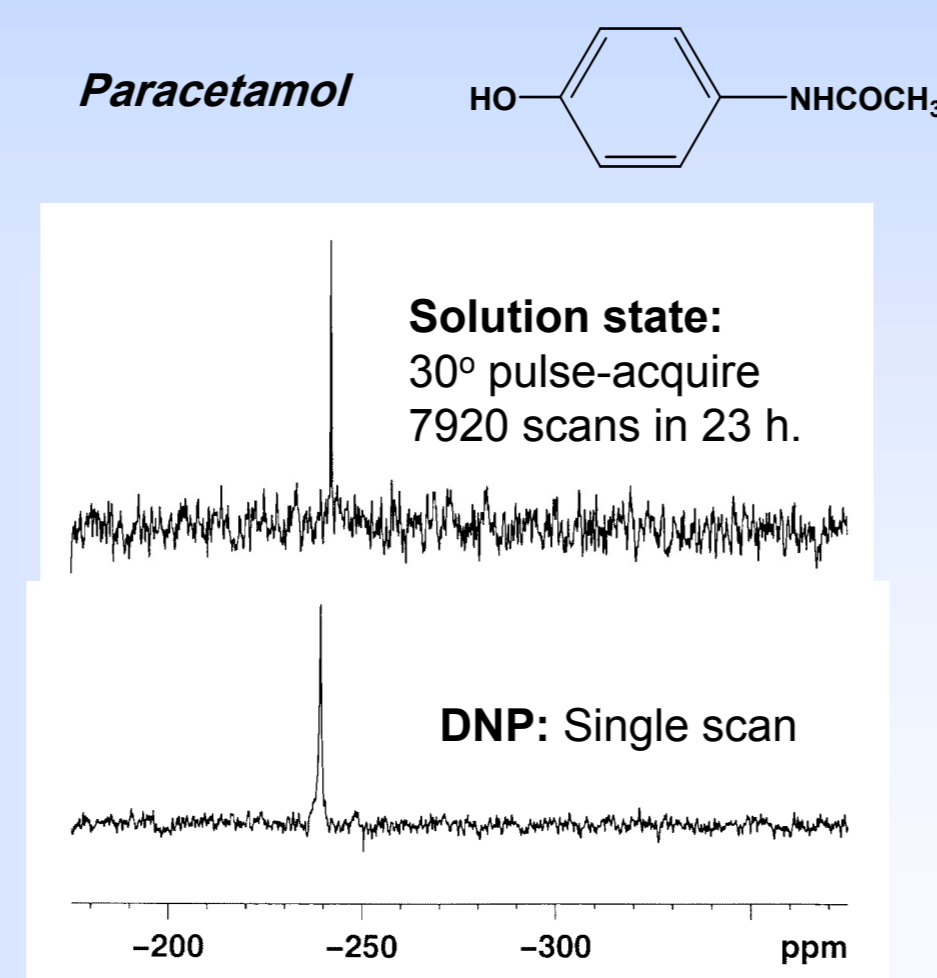
Our results are illustrated in application to paracetamol, 4-aminopyridine, and the anti-ulcer agents cimetidine and ranitidine.

Experiment

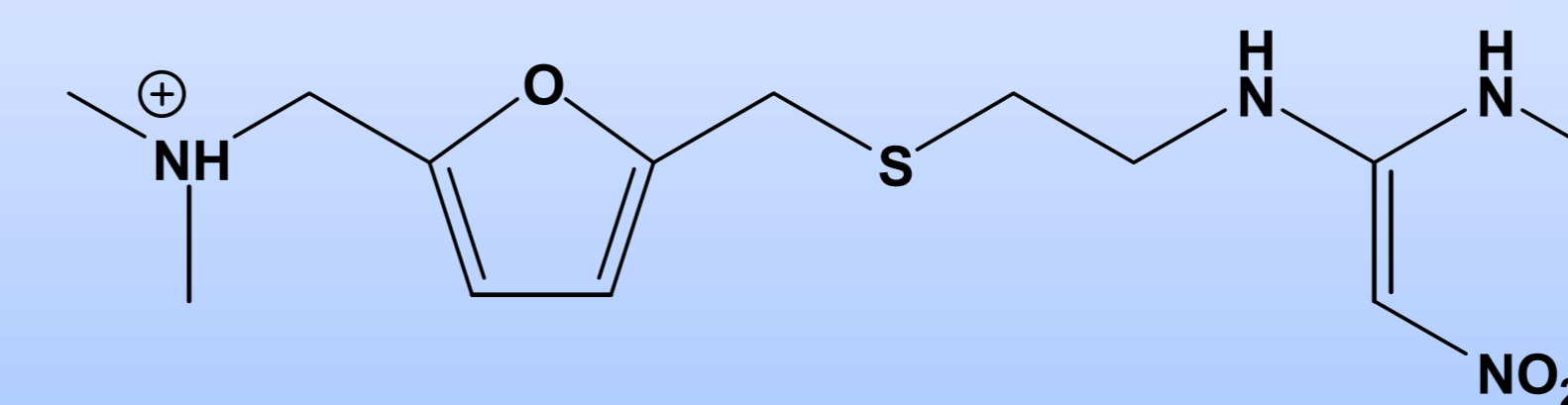
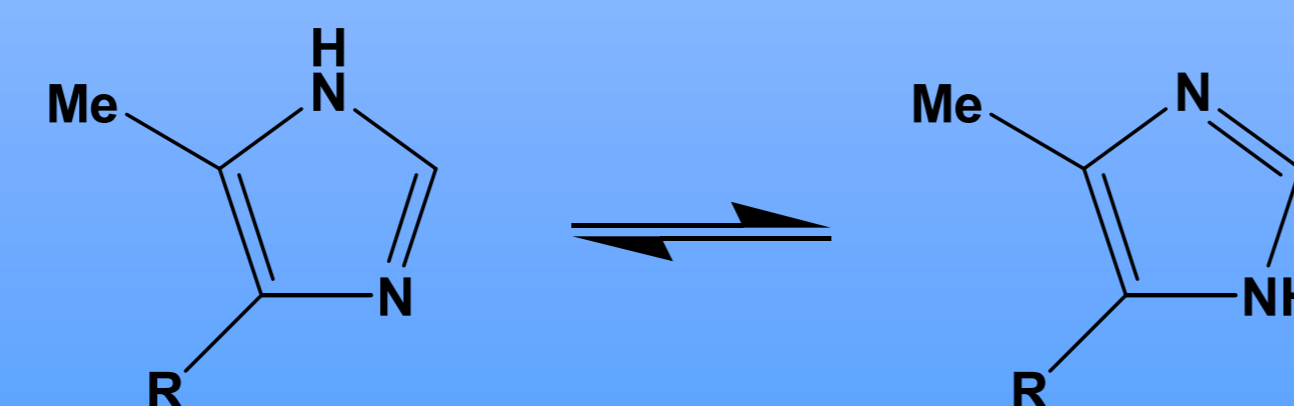
A typical ^{15}N polarization run 25-75 mg of the compound is dissolved in 100-200 μl of a 15mM solution of the stable radical *OX63*. The solvent is a mixture of water and DMSO or methanol and DMSO. Polarization was achieved at 1.4 K, in a 3.5 T field, over 12-24 hours. Subsequent dissolution used 4 ml water, then transfer into a 5 mm tube prepositioned in the NMR magnet (9.4 T). The 40.6 MHz ^{15}N FID was measured after a single 90° pulse. Further 1-pulse FIDs were then acquired at 1 s intervals.

^{13}C spectra were acquired using similar conditions to above, typically using *ca.* 4 mg compound and polarization times around 3 hours.

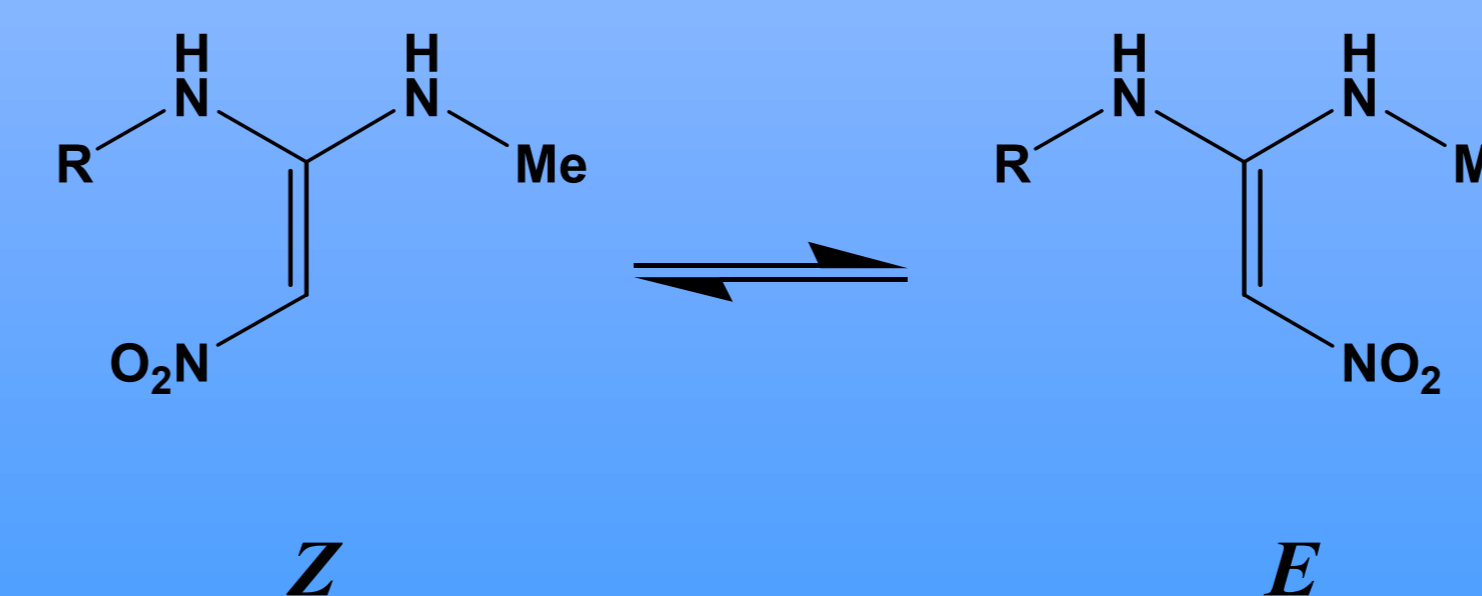
'Normal' solution state (DMSO) ^{15}N spectra were accumulated using the ^1H inverse-gated technique, with 30° pulses repeated at 10 s intervals. 50-150 mg sample dissolved in 0.5 ml.



In solution there are fewer ^{15}N signals than in the solid state because the Tautomeric exchange process is probably occurring at an intermediate rate in solution at ambient temperature



In solution there are fewer ^{15}N signals than in the solid state because the *EZ* interconversion is probably occurring at an intermediate rate in solution at ambient temperature. The C-C link has reduced double bond character due to the electron withdrawing nitro group, and the existence of other Tautomers having a C-C single bond.



Discussion

Three factors can be considered:

- DNP signal enhancement
- Resolution
- Persistence of ambient temperature polarisation

DNP signal enhancement in the 5 mm NMR sample tube, assume active volume is 0.3 ml. Comparison of paracetamol ^{15}N spectra gives enhancement in S/N (**NOT** integrated signal) per ^{15}N *ca.* 5×10^3

Resolution – for these *aqueous* samples ^{15}N linewidths ($\Delta\nu_{1/2}$) in the DNP spectra are in the region 10 – 20 Hz; more comparable to high resolution solid state spectra than to solution state spectra

Persistence of polarization – for ^{13}C observation single scan FIDs contain significant signal for up to 5 – 10 s after transfer of polarized sample to NMR magnet. For natural abundance ^{15}N observation the signal decay appears qualitatively *much more rapid*. This is contrary to prediction, based on relative $^{13}\text{C}/^{15}\text{N}$ T_1 s

Variables to be explored

• Mechanism of polarization – solid state effect; thermal mixing; electron-nucleus n.O.e.

• Optimisation of polarization time and transfer of sample to NMR magnet

• Influence of T_1 on persistence of polarization – mol. wt. and solvent important; effect of ^{15}N - ^1H cross relaxation; proton intermolecular exchange

• Diffusion of polarized sample into coil region following 90° pulse

Acknowledgements

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