

Optimising the SABRE hyperpolarisation of amines using *in-situ* Earth's Field NMR

Aminata Sakho¹, Fraser Hill-Casey², Meghan E. Halse², Simon B. Duckett¹

¹Centre for Hyperpolarisation in Magnetic Resonance, University of York, York, UK

²Department of Chemistry, University of York, York, UK

*Aminata.sakho@york.ac.uk

1. Introduction

Previously, amines have been successfully hyperpolarised by SABRE and detected using high field (HF) instruments.[ref] Amines are of particular interest because they can be used as polarisation carriers in SABRE-relay experiments, allowing for the hyperpolarization of alcohols through proton exchange.[1] In this study, we report the detection of amine hyperpolarisation using an Earth's field NMR (EFNMR) instrument, where the catalytic activation process of SABRE can be followed *in situ*. The hyperpolarization level of these amines is increased by adding a co-ligand, dimethyl sulfoxide (DMSO). The effect of the co-ligand is studied here using *in situ* EFNMR and directly compared to the SABRE polarization detected using a 43 MHz benchtop NMR spectrometer. In parallel, the chemical exchange rate of the ligands (both amines and hydrides) and the corresponding thermodynamic parameters for these complexes have been explored at 11.7 T (500 MHz).

4. Benzylamine (BA) vs Phenoxyethylamine (PEA)

- ❖ For equivalent concentration (25eq) compared to the pre-catalyst, PEA (A-2 complex) and BA (A-1 complexes) show different SABRE polarization levels using EFNMR detection.
- ❖ At 298 K, complex A-2 exhibits a higher PEA loss rate of 7.85 s^{-1} when compared to A-1 whose values is 4.91 s^{-1} .
- ❖ A dissociation rate of 7.85 s^{-1} is therefore slightly too high for optimal transfer on this basis.

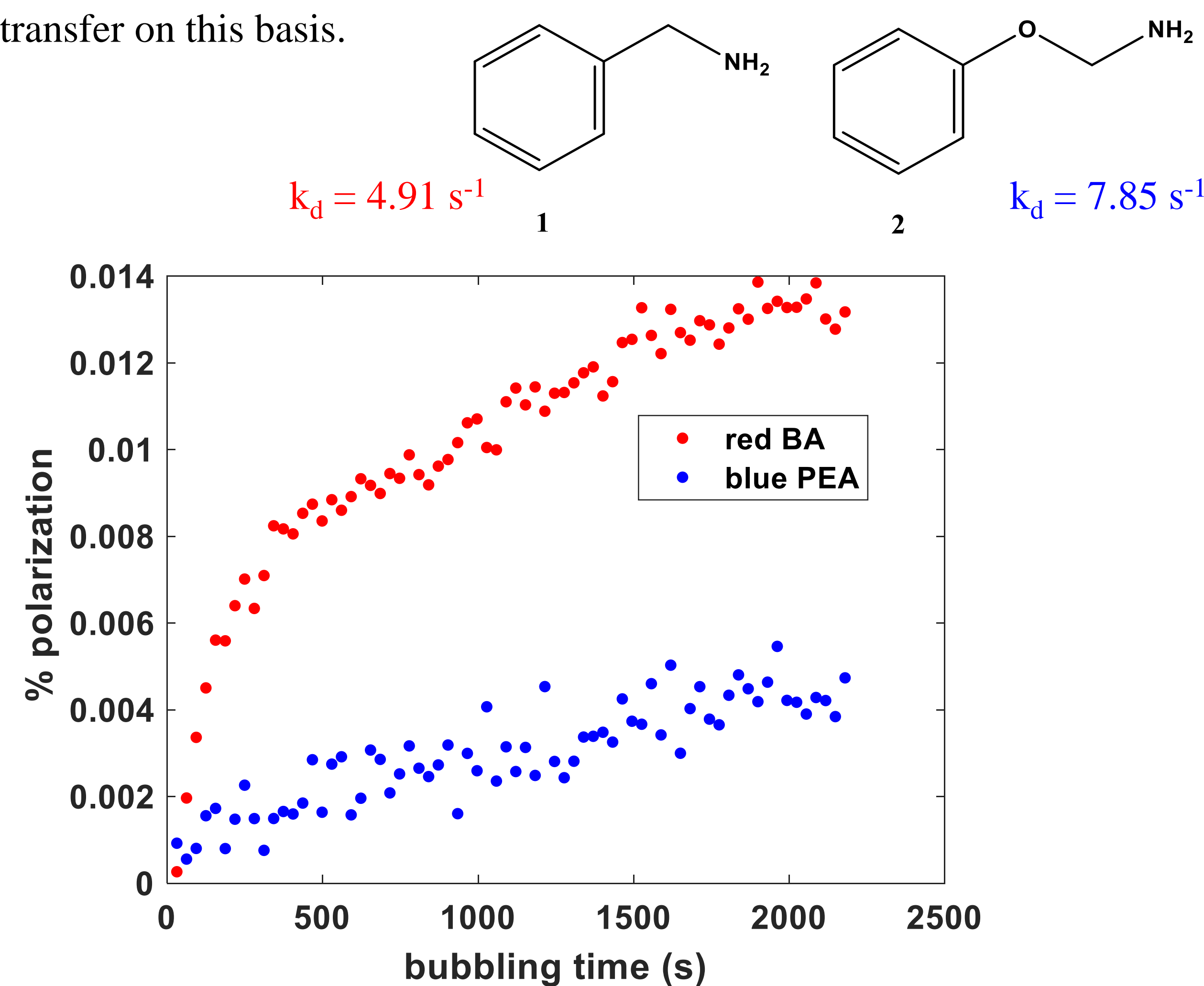


Figure 8. Increase in polarization during activation of same concentration BA (red) and PEA (blue) at EFNMR

- ❖ The free Gibbs activation energies are $67.30 \text{ kJ mol}^{-1}$ for A-1 and $68.08 \text{ kJ mol}^{-1}$ for A-2.
- ❖ These data confirm that lower barriers to ligand loss promote more effective SABRE polarisation transfer.

2. Earth's field NMR with *in-situ* SABRE

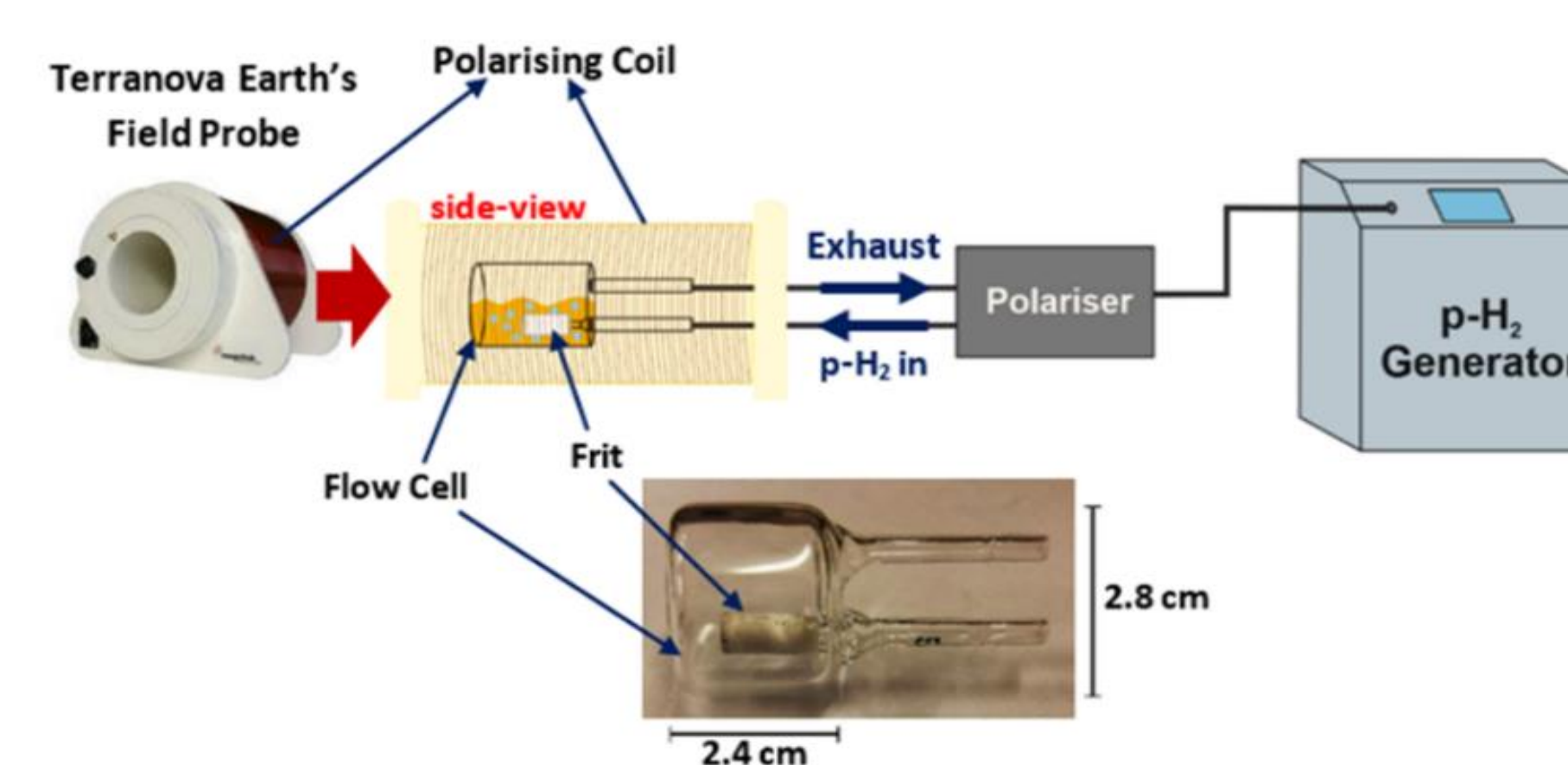


Figure 1. *In situ* SABRE EFNMR instrument set-up.

- ❖ EFNMR spectrometer with integrated *p*-H₂ generator for *in situ* SABRE experiments.[2]
- ❖ The SABRE process takes place inside a glass cell within the EFNMR probe.
- ❖ The pressure and flow of *p*-H₂ through the cell is controlled by the polariser.

3. *In-situ* EFNMR SABRE

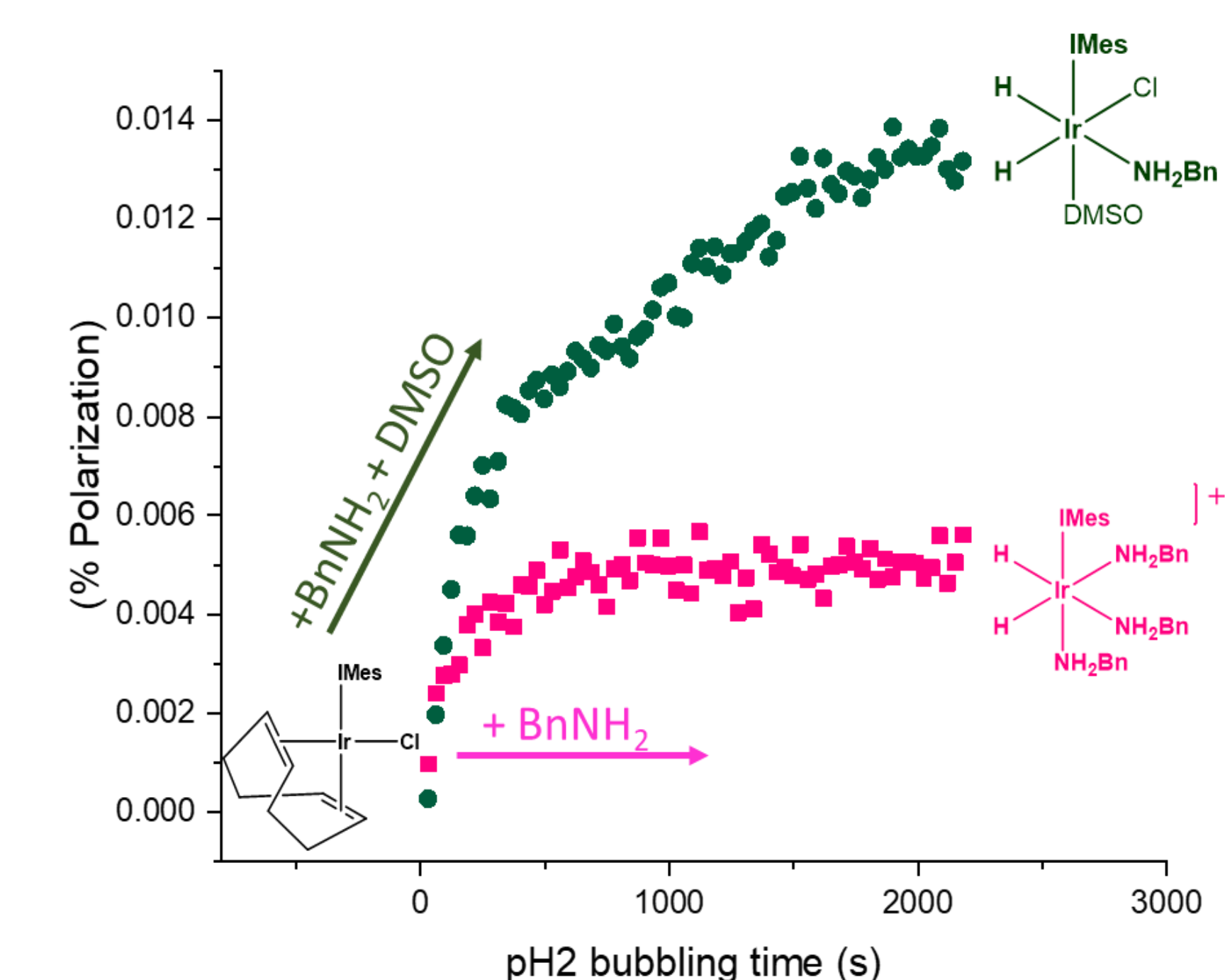


Figure 2. Increase in SABRE polarisation level during catalyst activation for benzylamine (pink) and benzylamine with DMSO (green).

Active SABRE complexes

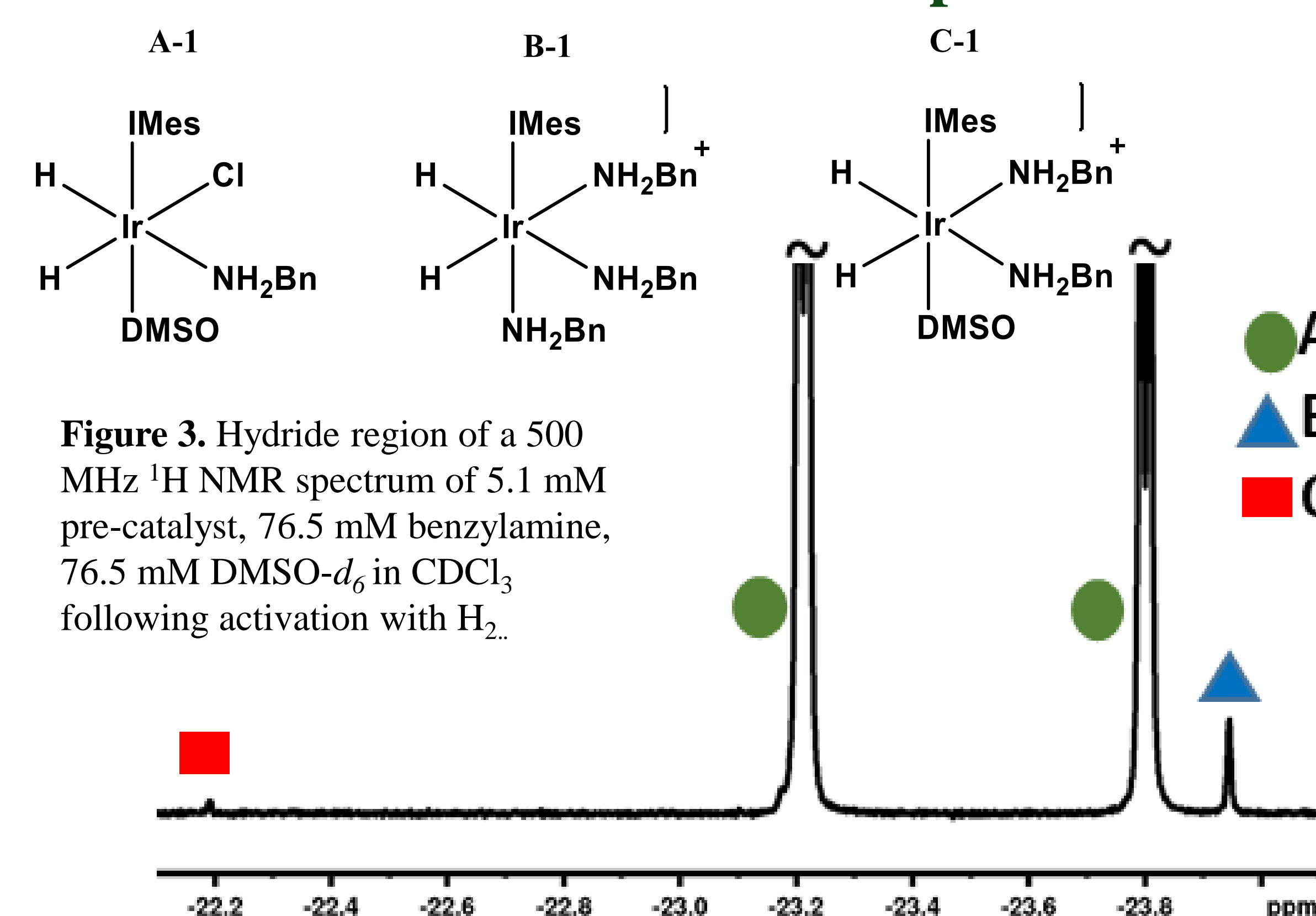


Figure 3. Hydride region of a 500 MHz ¹H NMR spectrum of 5.1 mM pre-catalyst, 76.5 mM benzylamine, 76.5 mM DMSO-*d*₆ in CDCl₃ following activation with H₂.

SABRE hyperpolarisation of Benzylamine

- ❖ Activation of the SABRE catalyst can be followed with the *in-situ* SABRE-enhanced EFNMR by monitoring the enhanced NMR signal as a function of *p*H₂ bubbling time. (Figure 2)
- ❖ The maximum observed polarisation level of benzylamine (BA) is significantly increased in the presences of the co-ligand, DMSO.
- ❖ Characterization at 500 MHz (Figure 3) shows the formation of three complexes A, B and C in the ratio 94%, 5% and ~1% respectively, in the presence of the co-ligand. The major complex A is likely to be the main driver of the SABRE hyperpolarization.
- ❖ Ligand exchange rates (for both hydrides and substrates) measured at 500 MHz, show that the benzylamine exchange rate is increased from 3.33 s^{-1} to 4.91 s^{-1} by the presence of DMSO, which is close to the 4.5 s^{-1} optimal regime for pyridine.

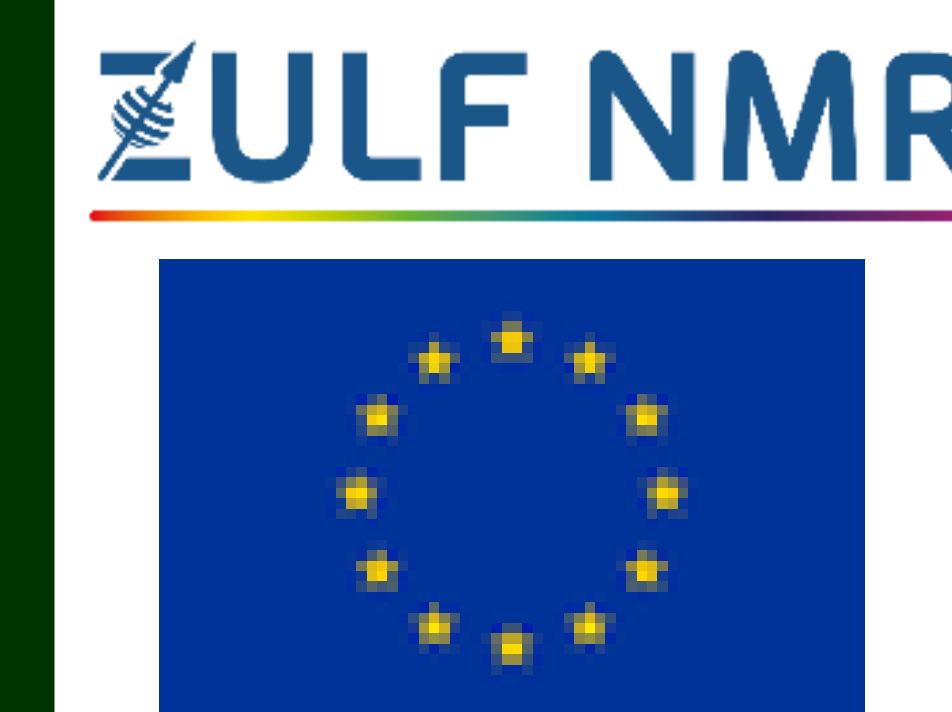
5. Conclusions

- ❖ SABRE hyperpolarization of two amines has been probed using *in-situ* EFNMR. The polarization level gained is considerably increased when a co-ligand, dimethyl sulfoxide, is added into the solution.
- ❖ In parallel, high field NMR studies have allowed us to determine the active SABRE in these solutions.
- ❖ The addition of the co-ligand DMSO is shown to increase the benzylamine exchange rate leading to improved polarization transfer.
- ❖ For, phenoxyethylamine, the exchange rate is increased through the use of the co-ligand in a way that polarization transfer is not optimal.

6. References

1. W. Iali, P. J. Rayner, A. Alshehri, A. J. Holmes, A. J. Ruddlesden and S. B. Duckett, *Chemical Science*, 2018, **9**, 3677-3684.
2. R. W. Adams, S. B. Duckett, R. A. Green, D. C. Williamson and G. G. R. Green, *The Journal of Chemical Physics*, 2009, **131**, 194505.
3. Hill-Casey, Sakho, Mohammed, Rossetto, Ahwal, Duckett, John, Richardson, Virgo and Halse, *Molecules*, 2019, **24**, 4126.

7. Acknowledgements



This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No. 766402.

