Reaction monitoring using SABRE-hyperpolarised benchtop (1 T) NMR spectroscopy

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Abstract

This thesis develops novel methods for reaction monitoring using a low field (1 T, 43 MHz) benchtop NMR spectrometer combined with hyperpolarisation using the signal amplification by reversible exchange (SABRE) technique. Industry-friendly benchtop NMR spectrometers suffer from insensitivity, which is overcome here by hyperpolarisation. This work is focused on N-heterocyclic primary amines and amides as the target SABRE substrates. The optimisation of substrate concentration and polarisation transfer field was performed for individual compounds and their mixtures. Reaction monitoring studies were completed on an amide formation reaction, specifically conversion of 4-aminopyridine (4-AP) with benzoic anhydride to form N-(4-aminopyridyl)benzamide (4-PBA), and the reactivity of the SABRE catalyst itself. The transformation of the pre-catalyst [Ir(Cl)(COD)(IMes)] with the substrates 4-AP and 4-MP under hydrogen to form [Ir(H)₂(IMes)(substrate)₃]Cl was investigated. In addition, hydrogen isotope exchange (HIE) on the substrate in the presence of the SABRE complexes was explored in methanol-d₄, where the source of the deuterium was the solvent. A new method was developed to monitor this reactivity using the lifetime of the SABRE-hyperpolarised ¹H NMR response. For this purpose, a single-shot hyperpolarisation lifetime (hyperT₁) measurement based on variable flip angles was developed that takes just five times the T₁ time constant, typically tens of seconds, to complete with high SNR. This method was implemented with both high-field (9.4 T, 400 MHz) and low-field (1 T, 43 MHz) ¹H NMR detection and comparable results were obtained using both instruments. In addition, the low sensitivity of the benchtop (1 T) NMR enabled the use of a protio solvent, which allowed for the differentiation between the effects of the catalyst formation and substrate deuteration. Calibration SABRE lifetime measurements fitted well to an analytical model of the kinetics of the SABRE process proposed in the literature. However, the quantification of the reaction monitoring data using this calibration revealed limitations of this simplified kinetic model.