Paramagnetic relaxation enhancement for the fast acquisition of multidimensional NMR experiments in small and medium size molecules (fast-PRE-NMR)

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Paramagnetic metal ions added to the sample enhance relaxation in the solute under study and therefore allow reducing the inter-scan delay in NMR experiments. This phenomenon, termed intermolecular paramagnetic relaxation enhancement (PRE) has been used widely in studies of the structure and dynamic properties of molecules[1] and also historically to speed up the acquisition 1D ^{13}C spectra.

Recently the PRE strategy has been successfully applied in NMR of macromolecules to speed-up the acquisition of multidimensional experiments in which the proton nucleus is involved[2]. Aimed with these results we have explored here the application of this methodology to small and medium size molecules.

Theoretical calculations predict that for macromolecules, the long correlation time introduces a larger PRE in proton T_1's over T_2's relaxation times[2] that is favorable to the experiment. The situation is different in small molecules since both PRE in T_1's and T_2's are more similar indicating that the successful application of this fast-PRE-NMR strategy requires a careful choice of the experimental conditions.

We have conducted a titration study with a paramagnetic (Mn^{2+}) to evaluate the correlation between PRE in proton T_1's and T_2's and the performance of fast-PRE-NMR with the experiments 2D COSY, 2D TOCSY, 2D HMQC and 2D HMBC. Based on these results a simple protocol for rapid set-up of the optimum concentration of the paramagnetic for fast-PRE-NMR under the particular sample experimental conditions is proposed.

The method was tested with a number of organic samples using very available paramagnetics (Mn^{2+} and Fe^{3+}). It afforded a reduction of the NMR experimental time by a factor of three with comparable line-widths and complete absence of artifacts. We believe this strategy could have applications to speed up NMR based quality control protocols.

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[2] Cai S; Seu C; Kovacs Z; Sherry AD; Chen Y., *J. Am. Chem. Soc.*, **2006**, 128, 13474-13478.