Usage of paramagnetic contrast agents to enhance ^{13}C signal detection *in vitro*

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Introduction

Contrast agents are widely used in ^{1}H magnetic resonance imaging (MRI) to increase the detectability of pathology[1,2] by shortening the longitudinal (T_1) or transverse (T_2) relaxation time of the protons. The effect of widely available contrast agents on the relaxation rates of rare spins, such as ^{13}C, is less well studied. In principle, the presence of paramagnetic relaxation agents during the acquisition of ^{13}C spectra can permit shorter repetition times, thus further enhancing sensitivity. The aim of the present study was to evaluate the feasibility of predetermined shortening of the T_1 of formic acid (HCOOH), frequently used in multinuclear *in vivo* experiments for RF power calibration.

Methods

Natural abundance formic acid (analytical grade, >99% pure) was studied with 0, 0.05, 0.1, 0.2 and 0.5 mM concentrations of Omniscan (Gd(DTPA-BMA)(H_2O)), which was chosen because it is neutrally charged and is less prone to complexation with formic acid. All measurements were performed in a 31cm bore actively-shielded 9.4T Varian/Magnex imaging spectrometer with high-performance gradients (400 mT/m in 130 μs). A surface coil with 2 ^{1}H coils (quadrature, 14 mm diameter) and a ^{13}C coil was used for both excitation and detection[2]. Shimming was performed using the ^{1}H formic acid signal. The ^{13}C signal was measured as peak integrals obtained with an inversion recovery sequence (15s - 180_x- τ - 90_x) with adiabatic pulses for inversion and excitation. The inversion time τ was varied logarithmically from 0.01 to 30 s, and the resulting curve was fitted with $I=I_0(1-\alpha e^{-\tau/T1})$ to determine T_1 and to allow for some inversion pulse imperfection. The relaxivity r_1 was calculated from the slope of a linear regression of R_1 ($=1/T_1$) vs. concentration.

Results and Discussion

The relaxation rate of formic acid at 0.1 mM Omniscan was 0.438 s^{-1}, directly evidenced by the inversion-null at τ=1.5 s (Fig. 1). The ^{13}C relaxivity of Omniscan in formic acid was 2.76±0.10 $mM^{-1}s^{-1}$ at 9.4T (Fig. 2). This is about half of the proton relaxivity, which has been reported to be on the order of 4.5 $mM^{-1}s^{-1}$ for a range of field strengths. A possible explanation for this is that the relaxation mechanism involved is almost purely outer sphere relaxation[2], as the inner sphere of the Gd in Omniscan has only one coordination site, which does not provide enough space for a formic acid molecule. The relaxation rate of formic acid was increased by almost an order of magnitude at 0.5 mM of Omniscan. No discernible effect on line width was observed, implying that effects on T_2 were minor.

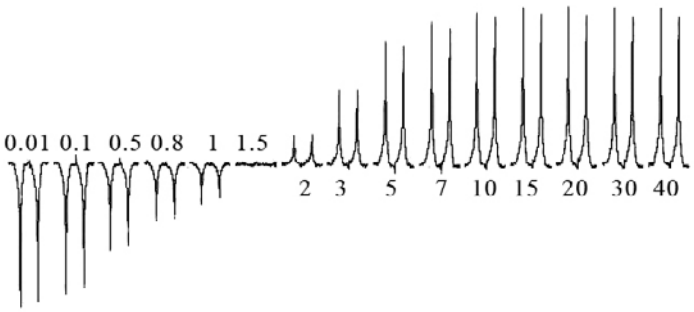

Figure 1. Series of ^{13}C spectra of formic acid with 0.1 mM Omniscan. Inversion times τ (s) are indicated for each trace.

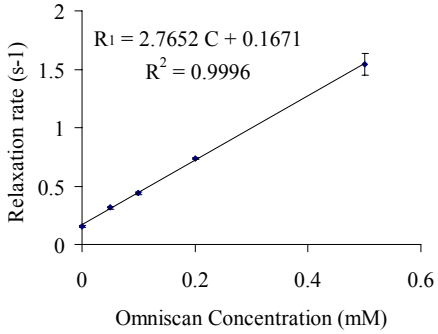

Figure 2. Fit of relaxation rate vs. concentration to obtain relaxivity.

Conclusions

We conclude that the determined relaxivity is strong and accurate enough to allow the preparation of solutions with a predetermined relaxation enhancement, which can be used in carbon spectroscopy with substantial time and sensitivity gains. Since formic acid is frequently used in an external sphere for RF power calibrations, the reduction in T_1 by an order of magnitude greatly reduces spectrometer setup time and performance testing. Similar strategies may be applied to enhance the relaxation rate of slowly relaxing ^{13}C resonances in extract studies, such as the carboxyl resonances of amino acids.

Acknowledgements
Supported by Centre d'Imagerie BioMédicale (CIBM) of the UNIL, UNIGE, HUG, CHUV, EPFL and the Leenaards and Jeantet Foundations; NIH grant R01NS42005.

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