

Temperature dependency of singlet relaxation times in a switchable iron(II) complex

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Abstract: Herein we report about an iron(II) complex and its temperature dependent relaxation times. An octahedral iron(II) complex has been investigated with regard to the singlet relaxation and its temperature dependency. We could show that the influence of the temperature on this relaxation time could be a useful tool for possible application as a directly observable MRI contrast agent.

Zusammenfassung: An dieser Stelle berichten wir über einen Eisen(II)komplex und seine temperaturabhängigen Relaxationszeiten. Ein oktaedrischer Eisen(II)komplex wurde hinsichtlich seiner Singulettrelaxation und deren Temperaturabhängigkeit untersucht. Es konnte gezeigt werden, dass der Einfluss der Temperatur auf die Relaxationszeiten ein nützliches Werkzeug im Rahmen einer möglichen Anwendung als direkt beobachtbares MRT-Kontrastmittel sein kann.

Motivation

The development of MRI contrast agents for medical diagnostics is a highly interesting topic and the demand for contrast agents which enable higher resolution is very high.

The most common approach is to use lanthanoid complexes (gadolinium) to influence the relaxation properties of water. Alternatives in which such complexes are observed directly have also been explored, though.

The big challenge in that particular field (direct contrast agent observation) in MRI is the high presence of water and fats which makes the development of directly observable contrast agents rather challenging. A possibility to make the direct observation of those agents possible is to make use of the observability of ¹⁹F using NMR spectroscopy.

Recently there have been new developments regarding ¹⁹F agents and their use in the newly developed paraSHIFT experiments. These experiments lower the relaxation times of the observed ¹⁹F nuclei, thusly opening the possibility to pulse rather frequently and accumulating the signal rather

fast (1). A direct observation of dynamic processes with those experiments still remains a challenge.

Herein we now investigate the possibility to make use of compounds that enable the population of nuclear singlet states in protons for high sensitivity. Singlet filtering pulse sequences can be utilized to suppress omnipresent water and proton signals arising from a metabolite background. In using compounds that are, with regard to their relaxation times, temperature and pH dependent we open the door for a diverse use in medical diagnostics.

Materials and methodology

Using special pulse sequences a singlet state can be populated in two spin ½ nuclei coupling with each other. It is an NMR “silent state” which is not influenced by intermolecular dipole interactions giving rise to long singlet relaxation times (T_s). This time typically exceeds observed T_1 or T_2 relaxations. (2)

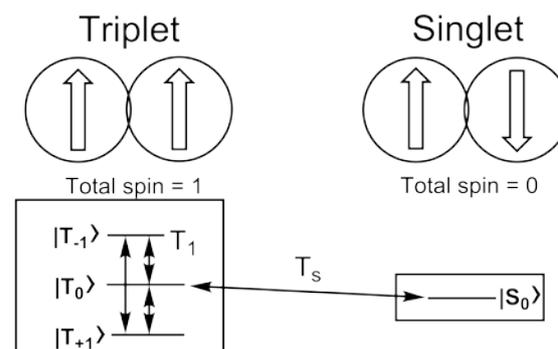


Fig. 1: Sketch of different relaxations. While the T_1 relaxation takes place within a triplet state, the singlet relaxation happens completely independent of that.

In this study a octahedral iron(II) complex has been investigated by classical NMR spectroscopy *in vitro*. The investigated iron complex can be switched from a diamagnetic high-spin complex to a paramagnetic low-spin complex by changing pH values and temperature. The fraction in which the different states occur in a water solution is highly

dependent of the temperature and the pH value of the solution. In an acidic solution the ligands are protonated and ultimately dissociating of the iron partially (Fig. 2)

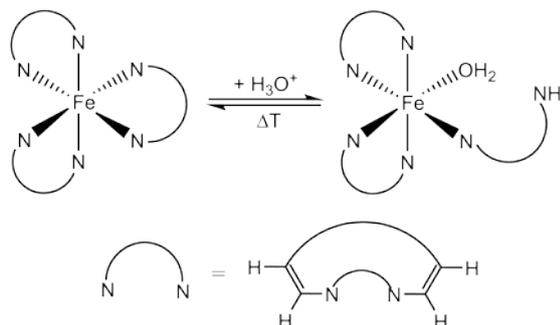


Fig. 2: Temperature and pH dependency of the equilibrium of the complex. The complex with an open ligand (right) is the high-spin complex. A singlet state can be induced in the explicitly shown protons.

It has already been established that the singlet relaxation is not as strongly influenced by paramagnetic surroundings as the T_1 relaxation (3). T_1 and T_s have been investigated at different temperatures and pH values on two different NMR spectrometers ($B_0 = 7$ and 14.1 T). The influence of the NMR field was considered to be a factor in the influence on the relaxation times.

Results and Discussion

A sample of the investigated complex with a concentration of 10 mM in H_2O/D_2O (95/5) has been adjusted to a pH of 1.50 . This sample then has been investigated at different temperatures and magnetic fields. The shown datapoints (Tab. 1) represent the average of three measurements each.

Tab. 1: Relaxation times of the 10 mM in H_2O/D_2O (95/5) at different temperatures and different field strengths.

T [K]	300 MHz		600 MHz	
	T1 [s]	Ts [s]	T1 [s]	Ts [s]
283	0,800	1,197	1,164	0,337
325	1,747	2,348	1,770	0,633
365	0,969	1,059	1,115	0,404

The obtained data show that there is a high dependency of the singlet relaxation time on the magnetic field of the used spectrometer. On the other hand, the T_1 relaxation seems to hardly be influenced by the strength of the magnetic field at all (Abb. 3). An increase in both, T_1 and T_s relaxation time, occurs with rising temperature until, close to the boiling point of water a sudden decrease can be observed.

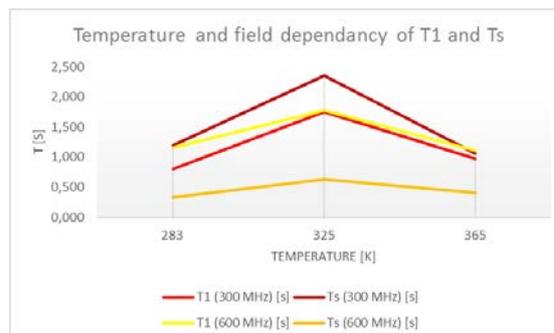


Fig. 3: Temperature and field strength dependency of T_1 and T_s .

The observed increase in T_s relaxation with higher spectrometer frequency could be caused by the high magnetic susceptibility of the investigated complex. The induction of magnetism into the highly susceptible sample cause a strengthening in paramagnetic relaxation which in this case influences the singlet relaxation more than T_1 . The decrease in relaxation times – both T_1 and T_s – can possibly be attributed to the loosening of one of the ligands and additional rotations inside the compound.

Conclusion

In this work, we could show that the relaxation times in an iron complex which can be switched from a paramagnetic high-spin to a diamagnetic low spin complex, are dependent on the temperature and the spectrometer frequency. With these first investigations into that matter a new possible MRI contrast agents that can be observed directly by populating a singlet state have been introduced. The knowledge of relaxations times at different temperatures and pH values could open a new possibility to estimate temperatures and pH *in vivo*.

References

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