Solid-State $^{25}\text{Mg}$ NMR Study of Inner-Sphere Mg$^{2+}$ Binding Complexes

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Magnesium is one of the most abundant metal ions in cellular organisms. Like other alkali and alkaline metal ions (Na$^+$, K$^+$, and Ca$^{2+}$), Mg$^{2+}$ is involved in a wide variety of physiochemical activities necessary to sustain life. For instance, magnesium serves as a cofactor responsible for the biochemical transfer of phosphate-related enzymes. Mg$^{2+}$ also occurs as an integral component in a number of non-phosphate-transferring proteins, including carbohydrate isomerases and DNA-activating topoisomerases. A recent study of ribozymes has suggested that the Mg$^{2+}$ ion may play a key functional role in regulating the catalysis of this class of metalloenzymes. Crystallographic studies of yeast tRNA$^{\text{phe}}$ have suggested that binding of the metal ion may play a role in stabilizing the tertiary conformation of the RNA molecule. Mg$^{2+}$ has also been found to maintain the carbamate formation which activates the catalytic activities of ribulose-1,5-bisphosphate carboxylase/oxygenase ("rubisco") in carboxylation formation which activates the catalytic activities of ribulose-1,5-bisphosphate carboxylase/oxygenase ("rubisco") in carboxylation.

Application of $^{25}\text{Mg}$ NMR has been very limited because of the unfavorable nuclear properties of $^{25}\text{Mg}$ (spin = $\frac{5}{2}$, natural abundance = 10.1%, nuclear quadrupole moment = 0.22 × 10$^{-28}$ m$^2$). In the liquid phase, NMR relaxation of $^{25}\text{Mg}$ nuclei is slowed by an efficient quadrupole mechanism and consequently leads to broad NMR signals. Nevertheless, $^{25}\text{Mg}$ NMR has been demonstrated to be a useful technique in studying kinetic and binding properties of Mg$^{2+}$ in solutions.

To understand the structural and catalytic roles of Mg$^{2+}$ in biological systems requires a full knowledge of the coordination chemistry of Mg$^{2+}$ ions at active sites. In principle, solid-state $^{25}\text{Mg}$ NMR can provide site-specific information about the Mg$^{2+}$ coordination environment. However, very little is known about solid-state $^{25}\text{Mg}$ NMR parameters in various biologically relevant binding sites; the only solid-state $^{25}\text{Mg}$ studies were focused on tRNA$^{\text{phe}}$. It is anticipated that recent advances in solid-state NMR instrumentation, it is possible to extend solid-state NMR to biologically important low-$\gamma$ metal nuclei such as $^{65}\text{Zn}$. We believe that solid-state $^{25}\text{Mg}$ NMR will also be useful for studying magnesium chemistry in a biological context. In this Communication, we report preliminary solid-state $^{25}\text{Mg}$ NMR results for four-inner sphere Mg$^{2+}$ binding complexes.

The Mg compounds studied in this work are Mg(H$_2$O)$_4$L$_2$, L = methylmalonate (1), formate (2), acetate (3), and orotate (4). These compounds can be treated as models for the inner-sphere Mg$^{2+}$ binding sites often found in various biological systems. In compound 1, the Mg$^{2+}$ ion is coordinated with six oxygen atoms in a slightly distorted octahedral geometry. Four of the six oxygen ligands are water molecules, and the other two are from the α-methylmalonate ligand. Such a Mg$^{2+}$ coordination geometry mimics those of inner-sphere binding sites where two of the six water molecules of the [Mg(H$_2$O)$_2$]$^{2+}$ ion are replaced by anionic ligands. The binding of Mg$^{2+}$ to the α-methylmalonate ligand in 1 serves as a good model for the Mg binding to β-carboxylapartatic acid (Asa), which is found in ribosomal proteins.

$^{25}\text{Mg}$ nuclear quadrupole coupling constant


(12) Colorless crystals of magnesium methylmalonate tetrahydrate (1) were formed after slow evaporation of an ethanol solution containing 0.020 g of $^{25}\text{MgO}$ and 0.058 g of Mg$^{2+}$-methylmalonate. Crystals of magnesium formate dehydrate (2) and magnesium diacetate tetrahydrate (3) were formed by slow evaporation of solutions obtained by neutralizing 0.5 M formic acid with 0.023 g of $^{25}\text{MgO}$ and 0.5 M acetic acid with 0.019 g of Mg$^{2+}$-acetate, respectively. Tetraaquaurorotato-NO$_2$ magnesium 2.5 hydrate (4) was prepared by mixing 21 mg of enriched $^{25}\text{MgO}$ and 91 mg of orotic acid, i.e., equimolar, in a total 15 mL of water with gentle warming. Small needle-shaped crystals were formed after the solvent was slowly evaporated. Magnesium oxide ($^{25}\text{Mg}$ 99.1% atom) was purchased from Trace Science International (Toronto, Ontario, Canada).


of the 25 Mg MAS spectrum yields 4 and one nitrogen ligand. The Mg coordination sphere in the Mg octahedral with bond length varying from 2.028 to 2.106 Å for 3 reveals that the Mg 2+ ion is coordinated with the four oxygen atoms of the water molecules and two oxygen atoms of the acetate ions. The following 25 Mg chemical shifts are referenced to 3 M MgSO4 (aqueous) by setting the signal of solid MgO at 26 ppm. The inset illustrates the general structure of the Mg compounds studied in this work.


In summary, we have presented a solid-state 25 Mg NMR study of magnesium complexes as models for inner-sphere Mg coordination. We have also demonstrated the first 25 Mg MQMAS NMR experiment. The present study was carried out at 11.75 T where 25 Mg MAS NMR spectra with a reasonable signal-to-noise ratio can be obtained in an hour or so for 25 Mg-enriched samples. On the basis of our results, it can be concluded that Mg–DNA oligomer complexes should be accessible by solid-state 25 Mg NMR. As high-field NMR instruments (18.8 T or above) are becoming available, the sensitivity of solid-state 25 Mg NMR experiments will be drastically improved. Finally, the present solid-state 25 Mg NMR characterization of Mg sites has yielded benchmark values for the 25 Mg NQCCs in the Mg(H2O)4L2 coordination environment, which will be useful for the interpretation of solution 25 Mg NMR relaxation data. We hope that the preliminary results presented in this work will encourage further solid-state 25 Mg NMR studies.

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