17O-NMR spectroscopy to study the coordination of oxygen-based ligands to lanthanide ions in solution

Zhijin Lin and Matthew J. Allen

Department of Chemistry, Wayne State University, Detroit, MI, USA

ABSTRACT
The number of oxygen-based ligands coordinated to lanthanide ions influences the physical and chemical properties of lanthanide complexes, making this number important to study. We used peak shifts in 17O-NMR spectroscopy to determine the number of individual nonhydroxyl-oxygen-based ligands coordinated to Dy3+. Oxygen-containing organic solvents were used as models to represent oxygen-based ligands to explore the scope of the technique because they contain a range of functional groups that have different electron-donating abilities and steric bulk. The measured coordination numbers of dimethylformamide, dimethyl sulfoxide, acetone, diethyl ether, tetrahydrofuran, di-isopropyl ketone, and hexamethyl acetone were consistent with reasonable values, indicating that 17O-NMR spectroscopy is a useful technique to study the coordination chemistry of nonhydroxyl ligands to lanthanide ions in solution.

1. Introduction
Lanthanide complexes prepared using ligands with oxygen-donors have applications in sensing and imaging [1–8], catalysis [9–11], separations [12], and information storage [13]. The usefulness of lanthanide complexes in these applications often depends on the coordination environments of the complexes in solution, including the number of coordinated ligands. Consequently, the number of oxygen-containing ligands coordinated to lanthanide ions in solution has been studied using a variety of techniques including X-ray diffraction spectroscopy [14], neutron diffraction spectroscopy [15], extended X-ray absorption spectroscopy [16, 17], Fourier transform-IR spectroscopy [18], Raman spectroscopy [19], 17O-NMR spectroscopy [20-24], and luminescence spectroscopy [25–27]. The majority of these techniques are used to study hydroxyl-based donors, but relatively few studies have been reported that focus on the coordination numbers of nonhydroxyl-based ligands [18, 19, 21–23]. Here, we report the use of 17O-NMR
spectroscopy to study the number of nonhydroxyl oxygen donors coordinated to Ln$^{3+}$ ions in solution and a potential application of the technique in the study of a model for lanthanide-based catalysis.

Ln$^{3+}$-induced $^{17}$O-NMR chemical shift is an important aid in studies of oxygen nuclei coordinated to lanthanide ions in solution [20]. The observed changes in chemical shift resulting from the interactions of the nuclei of coordinated oxygen with Ln$^{3+}$ ions occur due to diamagnetic, pseudocontact, and contact interactions. Of the Ln$^{3+}$ ions, the selection of Dy$^{3+}$ simplifies $^{17}$O-NMR studies because contact shifts from Dy$^{3+}$ contribute more than 85% of the total chemical shift allowing the other components to be neglected [20]. One complication associated with using Dy$^{3+}$ is changes in bulk magnetic susceptibility. To account for changes in bulk magnetic susceptibility, the concentration of Dy$^{3+}$ ions can be measured, deuterated versions of the exchanging molecules can be used, or internal standards are used [20, 28]. For example, the use of tert-butanol as an internal standard works for molecules, such as water and methanol, that can outcompete tert-butanol with respect to coordination to Dy$^{3+}$ ions. For the study of molecules that bind to Dy$^{3+}$ ions less effectively than tert-butanol, the use of deuterated versions of exchanging molecules or measurements of the concentration of Dy$^{3+}$ ions to calculate the change of bulk magnetic susceptibility are preferred.

The use of Dy$^{3+}$-induced $^{17}$O-NMR chemical shift, pioneered by Peters and coworkers, has been demonstrated to work with ligands containing hydroxyls, carboxylates, and ethers [22-24]. We explored oxygen-containing functional groups that are found commonly in ligands that coordinate to lanthanide ions, including ketones, esters, ethers, amides, sulfonyls, and aldehydes (figure 1). Here, we report the use of $^{17}$O-NMR measurements to study solvents that contain these functional groups as monodentate ligands and compare our results with other reported methods. In addition, we report the use of $^{17}$O-NMR measurements to measure the coordination numbers of ligands that have the same functional groups but different amounts of steric bulk.

2. Experimental

2.1. Materials and reagents

4-Chlorobenzaldehyde was purchased from TCI America and used as received. $^{17}$O-enriched water (35–40%) was from Cambridge Isotope Laboratories, Inc. Dysprosium(III) trifluoromethanesulfonate (triflate) was purchased from Sigma-Aldrich and dried at 0.38 Torr and 200 °C for 12 h before use. Anhydrous solvents – dimethylformamide (DMF), dimethyl sulfoxide (DMSO), acetone, diethyl ether, and tetrahydrofuran (THF) – were obtained from eMD Millipore and stored over 3 Å molecular sieves under Ar prior to use [29]. Di-isopropyl ketone and hexamethyl acetone were purchased from Alfa Aesar, purified by fractional distillation, and stored over 3 Å molecular sieves under Ar prior to use.

2.2. Preparation of samples for $^{17}$O-NMR measurements

All $^{17}$O-NMR measurements were performed using natural $^{17}$O-abundance except for 4-chlorobenzaldehyde. Generally, dysprosium(III) triflate (5–12 mg) was added to a solvent (1 mL), sonicated (5 min, 23 °C) using a sonicator (Fisher Scientific FS60H), and then filtered through a 0.2 μm hydrophobic filter into an NMR tube. Corresponding reference samples were prepared by filtering solvents without dysprosium(III) triflate through 0.2 μm hydrophobic filters into NMR tubes. After NMR data were

Figure 1. Nonhydroxyl oxygen-containing functional groups that coordinate to lanthanide ions.
collected, the concentration of Dy$^{3+}$ in each sample was determined using inductively coupled plasma mass spectrometry (Agilent 7700x series) in the Lumigen Instrument Center at Wayne State University.

Enrichment of $^{17}$O-labeled 4-chlorobenzaldehyde was performed following a procedure for the enrichment of benzaldehyde [30]. Briefly, $^{17}$O-enriched water (35–40%, 75 μL) followed by an aqueous solution of HCl (6 M, 10 μL) was added to a solution of 4-chlorobenzaldehyde (500 mg, 3.6 mmol) in THF (3 mL). The reaction was stirred at ambient temperature until the integrated intensity-ratio of 4-chlorobenzaldehyde to water from $^{17}$O-NMR spectroscopy remained constant (30 min). The reaction mixture was passed over MgSO$_4$ and stored over 3 Å molecular sieves under Ar. For $^{17}$O-NMR measurements of $^{17}$O-labeled 4-chlorobenzaldehyde, dysprosium(III) triflate (12 mg) was added to a solution of $^{17}$O-labeled 4-chlorobenzaldehyde (166 mg) in THF (1 mL). The mixture was sonicated for 5 min and then filtered through a 0.2 μm hydrophobic filter into an NMR tube. The corresponding reference was prepared by filtering the same solution of $^{17}$O-labeled 4-chlorobenzaldehyde in THF without dysprosium(III) triflate through a 0.2 μm hydrophobic filter into an NMR tube. After measurements were performed, the concentration of $^{17}$O-labeled 4-chlorobenzaldehyde was quantified using high-performance liquid chromatography [isocratic elution (water/acetonitrile = 1 : 4, flow rate = 1 mL/min) with a C18 column (ZORBAX) on a high-performance liquid chromatography system (Shimadzu) with a photodiode array detector monitoring at 244 nm]. The concentration of Dy$^{3+}$ solution was determined using inductively coupled plasma mass spectrometry.

2.3. $^{17}$O-NMR measurements

The theory and equations needed to use $^{17}$O-NMR spectroscopy to measure the number of oxygen-based ligands bound to Dy$^{3+}$ in solution have been derived by Peters and co-workers [20, 31]. Key results of their work are summarized by equation (1), where $n$ is the number of oxygen nuclei coordinated to Dy$^{3+}$, $\delta_{\text{obs}}$ is the observed difference in chemical shift of an $^{17}$O-NMR peak between the absence and the presence of Dy$^{3+}$ ions in ppm, $[\text{Dy}]$ is the concentration of Dy$^{3+}$ ions in M, $P_m$ is the molar ratio of Dy$^{3+}$ ions to oxygen nuclei of interest, and $T$ is temperature in K, $A/\hbar$ is the hyperfine coupling constant for the oxygen nucleus that is between $-4.2 \times 10^6$ and $-3.6 \times 10^6 \text{ rad s}^{-1}$ [20, 32, 33]. The coefficients $5.84 \times 10^4$ and $-0.176$ are from constants that did not change in our study, including the shape of the sample and its position in the magnetic field, the effective magnetic moment of Dy$^{3+}$, and the projection of the total electron spin magnetization of the Dy$^{3+}$ ion in the direction of the external magnetic field. We initially used the median value of $A/\hbar$ ($-3.9 \times 10^6 \text{ rad s}^{-1}$) in equation (1) to calculate $n$. The $n$ values calculated using the median value of $A/\hbar$ were <9% different than $n$ values calculated using the lowest ($-4.2 \times 10^6 \text{ rad s}^{-1}$) and highest ($-3.6 \times 10^6 \text{ rad s}^{-1}$) values of $A/\hbar$ (table S1). These differences suggest that the largest error that would arise from variations in $A/\hbar$ would be $\pm 9\%$ of $n$. Based on these calculations, we only report $n$ values calculated using the average value of $A/\hbar$ throughout the remainder of this manuscript.

$$n = \frac{5.84 \times 10^4 [\text{Dy}] - \delta_{\text{obs}} T}{-0.176 P_m \left( \frac{A}{\hbar} \right)}$$ (1)

All $^{17}$O-NMR measurements were performed on a Varian-500S (67.78 MHz) spectrometer in the Lumigen Instrument Center at Wayne State University. $^{17}$O-NMR measurements were carried out using non-deuterated solvents without locking the frequency as described by Peters and coworkers [20]. Drifts of $^{17}$O-NMR signals caused by changes of the magnetic field during the measurements were measured by comparing the chemical shift of the $^{17}$O-NMR peak of DMF before and after every measurement. Every drift was smaller than 0.05 ppm, which is 9.8% of the smallest $\delta_{\text{obs}}$ from all of the measurements in this study. This drift indicates that the maximum error in the number of oxygen-based ligands coordinated to Dy$^{3+}$, resulting from the drift of magnetic field, is less than 0.1 molecules. Therefore, it is reasonable to measure $\delta_{\text{obs}}$ without locking the NMR spectrometer in these measurements.

For studies in acetone and THF, $^{17}$O-NMR measurements were performed with 128 scans at 40 or 50 °C to avoid boiling of the solvents. For studies in other solvents, $^{17}$O-NMR measurements were performed
at 70 °C to obtain sharp peaks with either 128 or 256 scans, depending on the intensities of the $^{17}$O-NMR signals. All $^{17}$O-NMR measurements were performed after temperatures were stable for 10 min. In addition, all $^{17}$O-NMR measurements were repeated three times with independently prepared samples, and values are reported as the mean ± standard error of the independent measurements.

### 3. Results and discussion

To use $^{17}$O-NMR measurements to determine the number of oxygen nuclei coordinated to Dy$^{3+}$, bound ligands must exchange with bulk (noncoordinated) ligands faster than the $^{17}$O-NMR timescale to observe average exchanging $^{17}$O-NMR chemical shifts of the ligands. Because exchange of ligands with Dy$^{3+}$ depends on electron-donating ability, we studied a series of solvents with different donor numbers (table 1) [34]. Donor number is a term used to evaluate Lewis basicity that correlate to binding affinity for Lewis acids, such as Dy$^{3+}$. Solvents with larger donor numbers are expected to coordinate to Dy$^{3+}$ in greater number than solvents with smaller donor numbers. We applied $^{17}$O-NMR spectroscopy to study the individual coordination numbers of Dy$^{3+}$ (the number of solvent molecules bound to Dy$^{3+}$ in the first coordination sphere) in acetone, ethyl acetate, THF, DMF, DMSO, di-isopropyl ketone, and hexamethyl acetone. These solvents were chosen because they contain the functional groups in figure 1, vary in steric bulk, and cover a range of donor numbers from 17.0 to 29.8 kcal mol$^{-1}$ [34]. To quantify the coordination number of individual solvents to Dy$^{3+}$, we measured the $^{17}$O-NMR spectra of individual solvents in the presence and absence of Dy$^{3+}$. The observed shifts were used to calculate the average coordination number of solvent to Dy$^{3+}$ using equation (1).

For acetone, the difference in $^{17}$O chemical shift between the absence and the presence of Dy$^{3+}$ (17.6 mM) was –13.6 ppm, corresponding to an average number of acetone molecules of 5.7 ± 0.1. We attempted to compare this value to a reported value determined by another technique; however, we were unable to find a reported value for the number of acetone molecules coordinated to Ln$^{3+}$ in acetone. Therefore, we compared our result to the number of acetone molecules coordinated to Eu(OTf)$_3$ in water/acetone (1% water by volume) measured using luminescence-decay rates [27], which was the most similar system that we could find. The comparison of Dy$^{3+}$ to Eu$^{3+}$ is valid because many ligands form similar complexes with multiple Ln$^{3+}$ ions [35]. Therefore, we would expect the coordination number of Dy$^{3+}$ to be similar to that of Eu$^{3+}$, and if anything, a little smaller because of the slightly smaller ionic radius of Dy$^{3+}$ relative to Eu$^{3+}$. The average number of water molecules coordinated to Eu$^{3+}$ was 5.3 in water/acetone (1% water by volume) calculated from luminescence-decay measurements. If the total number of coordination sites of Eu$^{3+}$ is assumed to be nine, then the average number of acetone molecules coordinated to Eu$^{3+}$ is ≤3.7. This number is smaller than the number in our study (5.7 ± 0.1) because water (donor number = 18.0 kcal mol$^{-1}$) [34] competes with acetone. Given that our value is greater than the value for Eu$^{3+}$ in water/acetone and less than nine, this comparison suggests that the technique of $^{17}$O-shifts is reasonable for studying the coordination of acetone. To increase the validity of the comparison with luminescence-decay data, we repeated the $^{17}$O-NMR experiment in acetone with the addition of 1% water. The shifts from this experiment resulted in calculations of 4.7 coordinated water molecules and 2.3 coordinated molecules of acetone, numbers that are consistent with the luminescence-decay data.

### Table 1. Number of solvent molecules ($n$) coordinated to Dy$^{3+}$.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Donor number (kcal mol$^{-1}$) [34]</th>
<th>$n$</th>
<th>$T$ (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td>29.8</td>
<td>7.5 ± 0.2</td>
<td>70</td>
</tr>
<tr>
<td>DMF</td>
<td>26.6</td>
<td>8.3 ± 0.1</td>
<td>70</td>
</tr>
<tr>
<td>THF</td>
<td>20.0</td>
<td>3.3 ± 0.1</td>
<td>50</td>
</tr>
<tr>
<td>Ethyl acetate</td>
<td>17.1</td>
<td>5.4 ± 0.1</td>
<td>70</td>
</tr>
<tr>
<td>Acetone</td>
<td>17.0</td>
<td>5.7 ± 0.1</td>
<td>40</td>
</tr>
<tr>
<td>Di-isopropyl ketone</td>
<td>Not reported</td>
<td>1.3 ± 0.1</td>
<td>70</td>
</tr>
<tr>
<td>Hexamethyl acetone</td>
<td>Not reported</td>
<td>1.6 ± 0.4</td>
<td>70</td>
</tr>
</tbody>
</table>
For ethyl acetate, there were two $^{17}$O-peaks that corresponded to the carbonyl oxygen and the ethoxy group (figure 2). The differences in $^{17}$O chemical shifts in the absence and presence of Dy$^{3+}$ (18.9 mM) were –16.6 ppm for the carbonyl oxygen and 3.1 ppm the ethoxy oxygen. The observed shift of the carbonyl oxygen led to an average number of ethyl acetate molecules coordinated to Dy$^{3+}$ of 5.4 ± 0.1. When the ethoxy oxygen shift was used, the coordination number was 0.02 ± 0.01. To the best of our knowledge, there is no reported value for the number of ethyl acetate molecules coordinated to Ln$^{3+}$ ions; therefore, we compared our value to the value of acetone based on the similar donor numbers and steric effects of the two solvents. The steric effects of ligands can be estimated by their cone angles [36]. We calculated the cone angles of ethyl acetate and acetone coordinated to La$^{3+}$ to be 95 and 92°, respectively, from published crystal structures [37, 38] as described in the Supplementary Material [39]. Because ethyl acetate and acetone have similar donor numbers (17.1 and 17.0 kcal mol$^{-1}$) and cone angles, it is reasonable for them to have similar coordination numbers to Dy$^{3+}$. Unlike the carbonyl oxygen, the ethoxy oxygen did not coordinate to Dy$^{3+}$ likely due to the more nucleophilic nature of the carbonyl oxygen relative to the ethoxy oxygen. This result shows that $^{17}$O-NMR spectroscopy can be used to study the coordination of oxygen-based ligands that contain multiple oxygen atoms.

For THF, the difference in $^{17}$O chemical shift upon addition of Dy(OTf)$_3$ (10.2 mM) was –4.0 ppm. This observed shift was used to determine the average number of THF molecules coordinated to Dy$^{3+}$ to be 3.3 ± 0.1 (the remaining coordination sites of Dy$^{3+}$ are likely occupied by triflate anions). We compared this value with the reported values for DyCl$_3$, DyBr$_3$, and DyI$_3$ which are all 3.5 in THF studied with X-ray diffraction spectroscopy [40–42]. The value that we measured is in agreement with these reported values. We also compared our value of the coordination number in THF to the values for ethyl acetate and acetone from our study. Despite THF having a larger donor number than acetone or ethyl acetate, the number of THF molecules coordinated to Dy$^{3+}$ is smaller than that of acetone or ethyl acetate. This observation is likely due to the increased steric bulk of THF relative to ethyl acetate or acetone. We calculated the cone angle of THF bound to La$^{3+}$ to be 103° based on a reported crystal structure [43]. This cone angle is larger than ethyl acetate (95°) and acetone (92°) and likely accounts for the differences in coordination number between these solvents.

For DMF, the difference in $^{17}$O chemical shift upon addition of Dy(OTf)$_3$ (19.2 mM) was –21.9 ppm, predicting an average number of DMF molecules coordinated to Dy$^{3+}$ of 8.5 ± 0.1. To evaluate the accuracy of this value, we compared our value to the coordination number of the most similar reported system that used a different technique: the coordination number of DMF to Gd(ClO$_4$)$_3$ (8.1 ± 0.2) studied by Raman spectroscopy [19]. This comparison is reasonable given the similar ionic radii and coordination angles.

![Figure 2](https://example.com/fig2.png)

**Figure 2.** $^{17}$O-NMR spectra of ethyl acetate in the presence (upper spectrum) and absence (lower spectrum) of Dy(OTf)$_3$ at 70 °C. In both spectra, the peak corresponding to the carbonyl oxygen is on the left.
The chemistries of Gd\(^{3+}\) and Dy\(^{3+}\). Additionally, the triflate anion in our study and the perchlorate anion used in the Raman study are both weakly coordinating and unlikely to interfere with the comparison. The coordination number of DMF to Dy\(^{3+}\) (8.3 ± 0.1) found in our study is not different (Student t test, 95% confidence interval) from the coordination number of DMF to Gd\(^{3+}\) (8.1 ± 0.2) studied by Raman spectroscopy. Moreover, the coordination number for DMF is larger than the values for ethyl acetate, acetone, and THF. Of these solvents, DMF has the largest coordination number likely because it has the largest donor number among these solvents.

The difference in \(^{17}\)O chemical shift of DMSO between the absence and presence of Dy(OTf)\(_3\) (27.7 mM) was −24.0 ppm, indicating that the average coordination number of DMSO was 7.5 ± 0.2. This value is close to the value of eight studied by X-ray diffraction spectroscopy [44]. We also compared our value to the other solvents in our study. The number of DMSO molecules coordinated to Dy\(^{3+}\) is larger than the value for THF, ethyl acetate, or acetone. This trend is reasonable because DMSO has the highest donor number among these solvents. However, DMF has a solvation number that is 0.8 larger than DMSO, despite the donor number of DMF being slightly lower than that of DMSO. Although these values are the inverse of what might be expected, they are close and consistent with the reported binding strength of DMF and DMSO with boron trifluoride in dichloromethane [45].

The number of bound solvent molecules (acetone, ethyl acetate, THF, DMF, and DMSO) that we measured are in agreement with values acquired using other methods. These agreements suggest that \(^{17}\)O-NMR spectroscopy is accurate. It is worth noting that contact shifts from Dy\(^{3+}\) have been reported to contribute only 66% to the total paramagnetic chemical shift in the presence of carboxylate [46]; however, the agreement between our results and those reported by other methods suggests that the assumption that contact shifts from Dy\(^{3+}\) contribute >85% of the total chemical shift is reasonable for the solvents in our studies.

In addition to electron-pair donating ability of ligands, steric effects also impact the coordination environment of Dy\(^{3+}\). This impact was initially observed by comparing the average coordination numbers of THF, ethyl acetate, and acetone. The influence of steric bulk on \(^{17}\)O measurements was further probed by comparing the coordination number of three ketones that differ in bulk: acetone, di-isopropyl ketone, and hexamethyl acetone. For acetone, di-isopropyl ketone, and hexamethyl acetone, the difference in \(^{17}\)O chemical shifts led to average coordination numbers of 5.7 ± 0.1, 1.3 ± 0.1, and 1.6 ± 0.4, respectively (the remaining coordination sites of Dy\(^{3+}\) are likely occupied by triflate anions). The number of solvent molecules coordinated to Dy\(^{3+}\) with these ketones was significantly smaller when the side arms of the ketone changed from methyl to isopropyl or tert-butyl. For di-isopropyl ketone and hexamethyl acetone, the solvation number was not different (Student’s t-test, 95% confidence interval), and this observation is likely due to fast rotation of the isopropyl and tert-butyl groups leading to similar steric size in solution.

In addition to the single-solvent systems described above, we explored the use of \(^{17}\)O-NMR spectroscopy to study the coordination numbers of oxygen nuclei in multiple species simultaneously. Such mixed systems are relevant to lanthanide-catalyzed carbon–carbon bond formation, where coordination numbers are relevant to mechanistic studies [47, 48]. We chose 4-chlorobenzaldehyde as a model substrate and THF as the solvent to simultaneously study the coordination of 4-chlorobenzaldehyde and THF to Dy\(^{3+}\) using \(^{17}\)O-NMR spectroscopy. The selection of aldehyde is relevant because Ln\(^{3+}\) ions can catalyze the conversion of 4-chlorobenzaldehyde to 3,4-dihydropyrimidin-2(1H)-ones, which are important compounds in the synthesis of pharmaceuticals [49]. Because the amount of 4-chlorobenzaldehyde (0.32 mmol) used in the measurement was insufficient to observe via \(^{17}\)O-NMR spectroscopy, the aldehyde was enriched using \(^{17}\)O-enriched water (35–40%) to enhance the \(^{17}\)O-NMR signal. For \(^{17}\)O-labeled 4-chlorobenzaldehyde in THF, the \(^{17}\)O chemical shift of THF was referenced to a reported value (14.0 ppm) [50]. The differences between \(^{17}\)O chemical shifts in the absence and presence of Dy\(^{3+}\) (20.3 mM) were −24.9 ppm for \(^{17}\)O-labeled 4-chlorobenzaldehyde and −7.0 ppm for THF (figure 3). Based on these chemical shifts, the average coordination number of THF was calculated to be 3.1 and the average coordination number of 4-chlorobenzaldehyde was calculated to be 0.3. This result is consistent with the THF to 4-chlorobenzaldehyde (33 : 1) mole ratio. The number of THF molecules coordinated to
Dy$^{3+}$ changed from 3.3 in pure THF to 3.1 with the addition of a small amount of 4-chlorobenzaldehyde. This observation indicates that the method is useful for studying multiple ligands simultaneously.

4. Conclusion
We demonstrated the application of $^{17}$O-NMR spectroscopy to study the average coordination number of non-hydroxyl oxygen-containing ligands to Dy$^{3+}$ in solution using solvents of natural $^{17}$O-abundance. $^{17}$O-NMR spectroscopy was used to study solvation numbers of Dy$^{3+}$ in solvents that vary in electron-pair donating ability and steric bulk. In addition, $^{17}$O-NMR spectroscopy can be used to distinguish bound from nonbound oxygen nuclei in ligands that have multiple oxygen-donors. Finally, $^{17}$O-NMR spectroscopy was applied to study the coordination chemistry of 4-chlorobenzaldehyde in THF that is relevant to lanthanide-based catalysis. Our study suggests that $^{17}$O-NMR spectroscopy can be used to study the coordination environment of lanthanide ions in nonprotic solvents and has wide potential applications in the study of lanthanide ions in solution.

Supplementary material
Supplementary material includes calculated $n$ values, determination of cone angles, $^{17}$O-NMR chemical shifts, and $^{17}$O-NMR spectra.

Acknowledgement
Cambridge Isotope Laboratories, Inc. M.J.A. gratefully acknowledges a Schaap Faculty Scholar Award.

Disclosure statement
No potential conflict of interest was reported by the authors.

Funding
This research was supported by the National Science Foundation [grant number CHE-0955000].

Figure 3. $^{17}$O-NMR spectra of $^{17}$O-labeled 4-chlorobenzaldehyde in THF in the presence (upper spectrum) and absence (lower spectrum) of Dy(OTf)$_3$, at 70 °C. The chemical shift of THF was referenced to a reported value [49].
References