INTRODUCTION

Lanthanide aquo ions have frequently been used as shift reagents for the determination of the structure of water soluble molecules; more recently, lanthanide EDTA complexes have been used for the same purpose (1,2). The applicability and utility of aqueous shift reagents could be further increased if problems such as limited pH range, presence of higher than 1:1 complexes, contact shifts, and non-axial symmetry could be overcome. With these considerations in mind, we have investigated the shift reagent properties of the lanthanide complexes of two ligands, DOTA and NOTA, and we have compared them to the LnEDTA shift reagents.

The complexes with DOTA and NOTA are axially symmetric. Moreover, the LnDOTA complexes are eight-coordinate, and are unlikely to form higher than 1:1 adducts with substrate molecules because of steric crowding (7). Potentiometric titrations show that LnDOTA complexes do not coordinate OH\textsuperscript{−} even at pH 12. These features suggest that LnNOTA and LnDOTA complexes could be superior to LnEDTA as aqueous shift reagents. To determine the relative utility of the three types of complexes as aqueous shift reagents with respect to positively charged, neutral, and negatively charged substrates, we...
measured the $^{23}$Na shifts of Na$^+$, the $^2$H and $^{17}$O shifts of deuterated water, and the $^{35}$Cl shifts of Cl$^-$ in 0.1M solutions.

**EXPERIMENTAL**

The ligand DOTA was prepared as described in (7), and the ligand NOTA was prepared as the trisodium salt according to (8). All spectra were obtained on a Varian XL-100/12 NMR spectrometer modified for multinuclear observation as described in (9).

**DISCUSSION**

The paramagnetic shift is a combination of a contact (through-bonds) shift and a dipolar (through-space) shift, expressed by the equation $\delta = F<S_z> + GC^D$ where the measured shift in ppm is $\delta$, the first term on the right hand side represents the contact shift as the product of a ligand dependent parameter $F$ and a lanthanide ion dependent parameter $<S_z>$, and the second term on the right hand side represents the dipolar shift as the product of a ligand dependent parameter $G$ and a lanthanide ion dependent parameter $C^D$ (3). The lanthanide dependent parameters $<S_z>$ and $C^D$ have been calculated for all the lanthanides (4-6) and the separation between the contact and the dipolar contributions was performed as described elsewhere (3,9). When the shift reagent is axially symmetric (at least a C$_3$ axis), $G$ is proportional to the crystal field coefficient $\langle r^2 \rangle A_0^0$, and a geometric term $(3\cos^2 \theta - 1)r^3$, where $r$ and $\theta$ are the coordinates of the observed nucleus. It is the dipolar shift that is of interest for the determination of the structures of substrate molecules.

The NMR shifts induced by the DOTA, EDTA and NOTA complexes and by the aquo lanthanides (4,10) are presented in Figs. 1 and 2. The solid line in each plot represents the dependence of the pseudo-contact parameter $C^D$ or the contact parameter $<S_z>$ scaled to the observed shifts.

The most outstanding aspect of the results in Figs. 1 and 2 is that all of the shifts in DOTA solutions follow the theoretical dipolar shifts. In solutions of the other three complexes, the water $^{17}$O shifts follow the theoretical contact shifts. It is likely that the very different shifting patterns of the complexes originate from their structures in solution. NMR studies (7) have indicated that the DOTA complexes are sterically very crowded, the encapsulated metal ions being completely surrounded by the tetra-azacycle and by the four acetate groups. Furthermore, it can be assumed that these substrates are located near to the carboxylate groups of DOTA in the vicinity of the C$_4$ axis since the dipolar shifts of all the nuclei investigated exhibit the same sign. In contrast, the NOTA, EDTA, and aquo complexes have more open, less