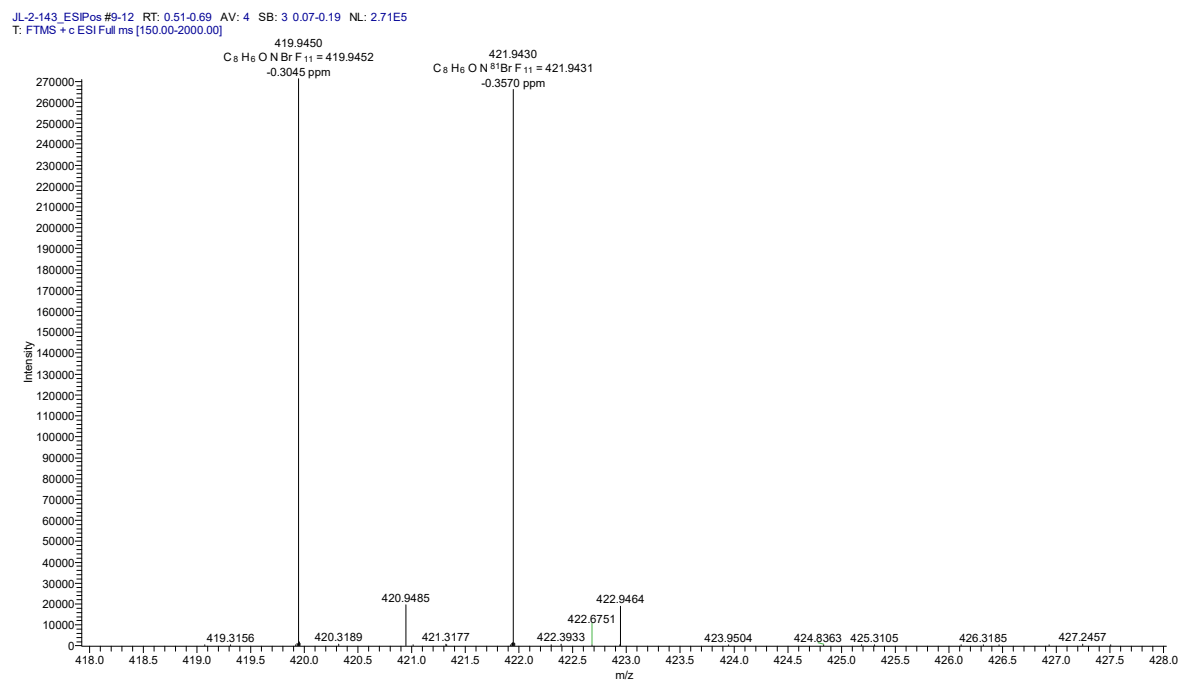


## Supporting Information

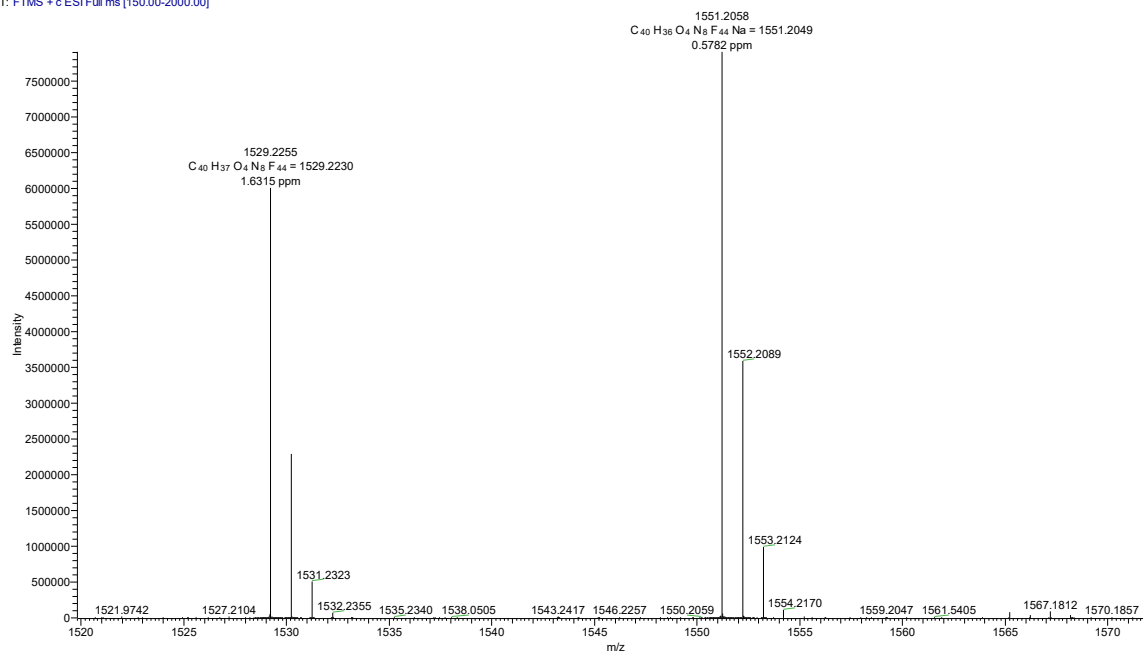
**Outersphere Approach to Increasing the Persistence of Oxygen-Sensitive Europium(II)-Containing Contrast Agents for Magnetic Resonance Imaging with Perfluorocarbon Nanoemulsions toward Imaging of Hypoxia.**

Jacob C. Lutter,<sup>‡</sup> Andrea L. Batchev,<sup>‡</sup> Caitlyn J. Ortiz, Alexander G. Sertage, Jonathan Romero, S. A. Amali S. Subasinghe, Steen E. Pedersen, Md Abul Hassan Samee, Robia G. Pautler,\* and Matthew J. Allen\*

**ESI-HRMS Spectra**

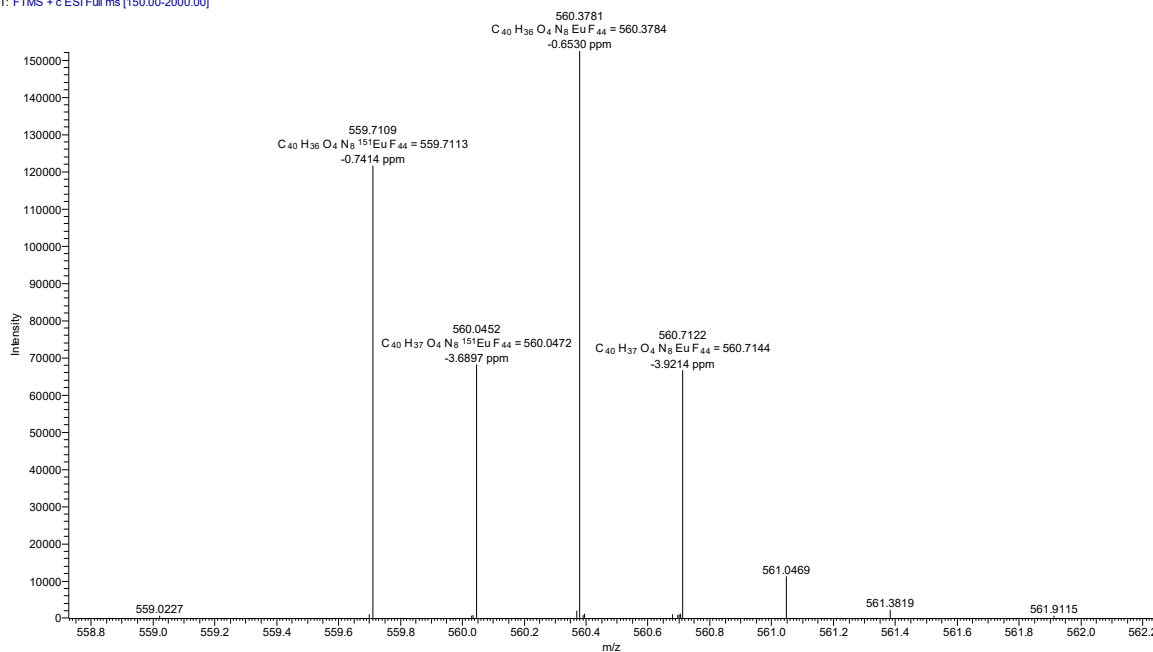
**Figure S1.** ESI-HRMS of N-(1H,1H-undecafluorohexyl)bromoacetamide in methanol using positive ion mode.

JL-1-97\_ESIPos#5-14 RT: 0.26-0.76 AV: 10 NL: 7.90E6  
T: FTMS + c ESI Full ms [150.00-2000.00]



**Figure S2.** ESI-HRMS of *N,N',N'',N'''*-tetra(*N*-(1*H*,1*H*-undecafluorohexyl)acetamidyl)-1,4,7,10-tetraazacyclododecane in methanol using positive ion mode.

JL-1-155\_ESIPos#14 RT: 0.83 AV: 1 SB: 252 3.01-18.88 NL: 1.52E5  
T: FTMS + c ESI Full ms [150.00-2000.00]



**Figure S3.** ESI-HRMS of **Eu1** in methanol using positive ion mode.

## NMR Spectra

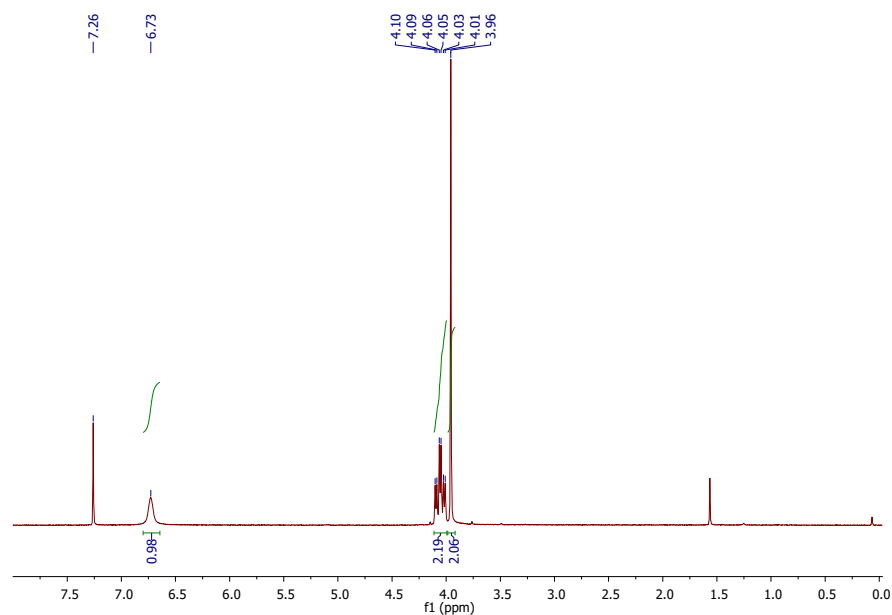


Figure S4.  $^1\text{H}$ -NMR of *N*-(1H,1H-undecafluorohexyl)bromoacetamide in  $\text{CDCl}_3$ .

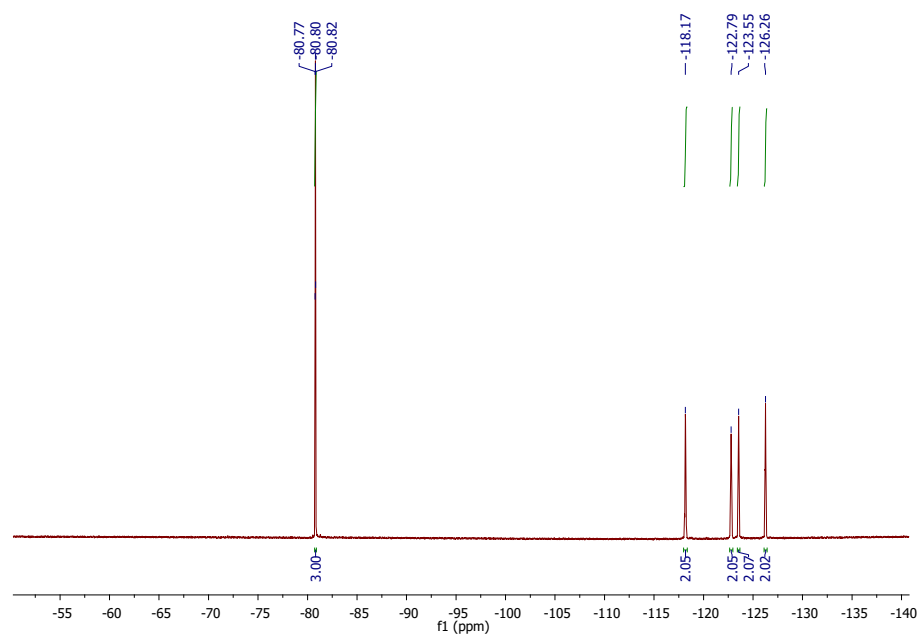
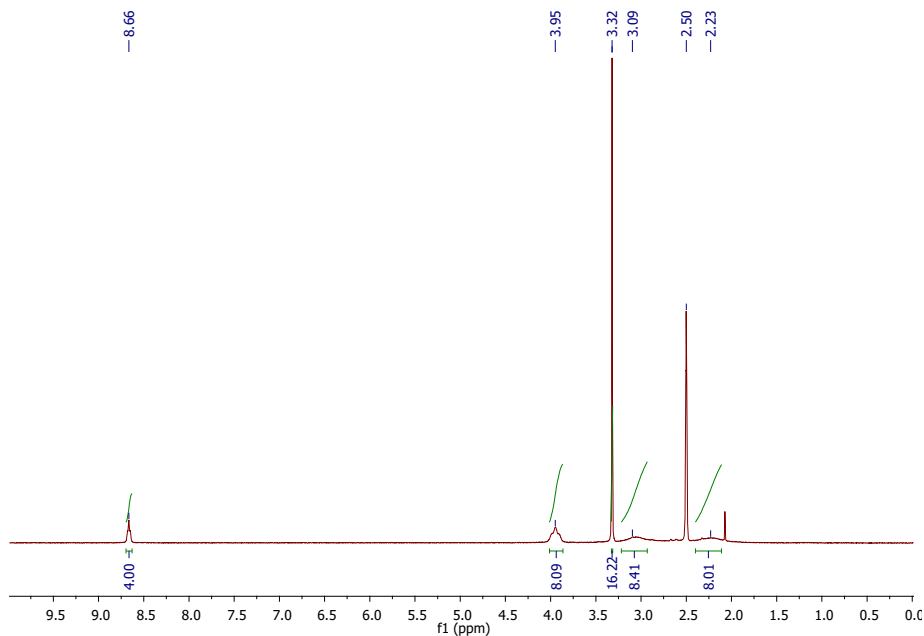
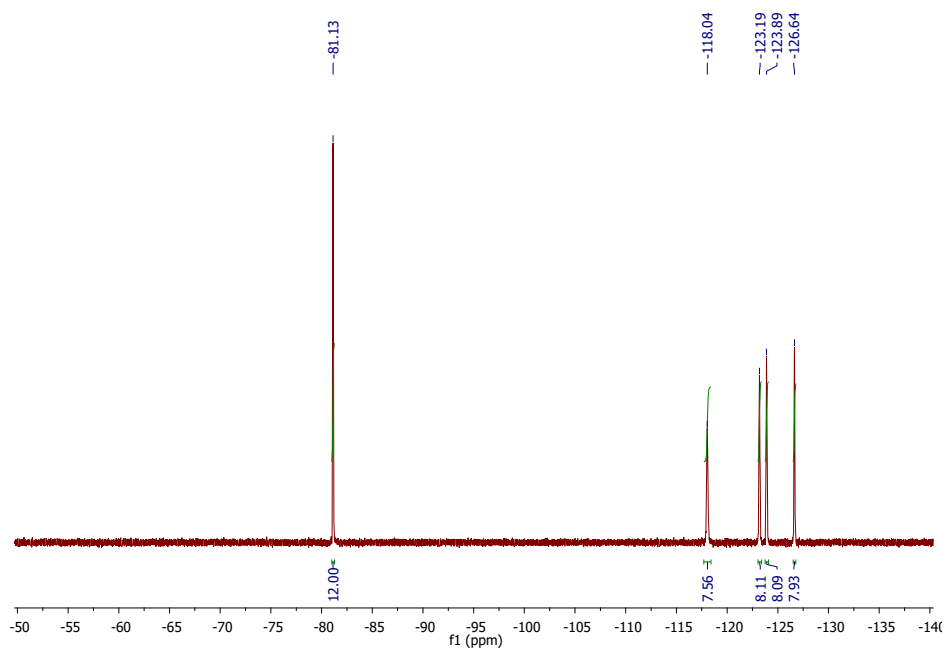


Figure S5.  $^{19}\text{F}$ -NMR spectrum of *N*-(1H,1H-undecafluorohexyl)bromoacetamide in  $\text{CDCl}_3$ .



**Figure S6.** <sup>1</sup>H-NMR spectrum of *N,N,N',N''*-tetra(*N*-(1H,1H-undecafluorohexyl)acetamidyl)-1,4,7,10-tetraazacyclododecane in DMSO-*d*<sub>6</sub>.



**Figure S7.** <sup>19</sup>F-NMR spectrum of *N,N,N',N''*-tetra(*N*-(1H,1H-undecafluorohexyl)acetamidyl)-1,4,7,10-tetraazacyclododecane in DMSO-*d*<sub>6</sub>.

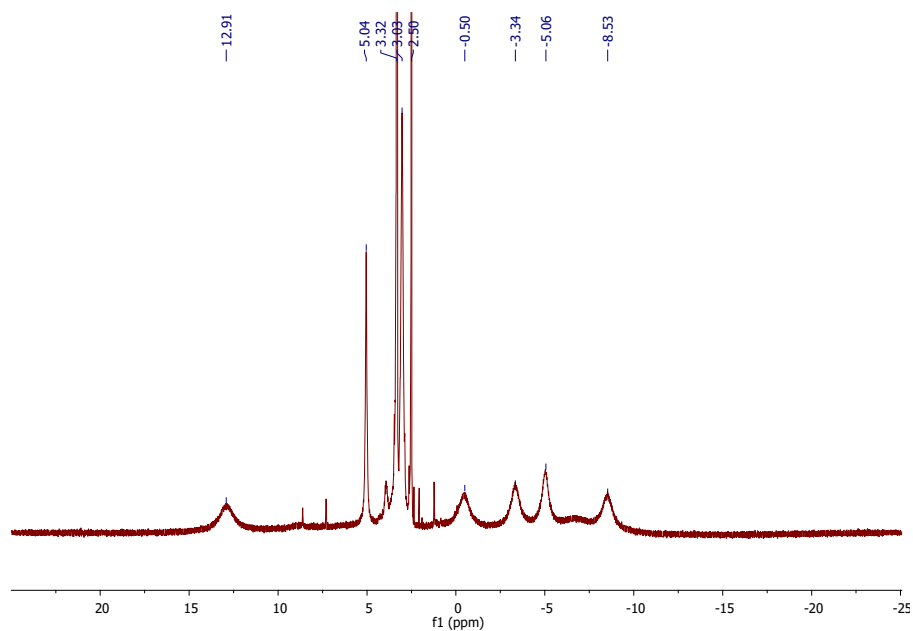


Figure S8.  $^1\text{H-NMR}$  spectrum of Eu1 in  $\text{DMSO-}d_6$ .

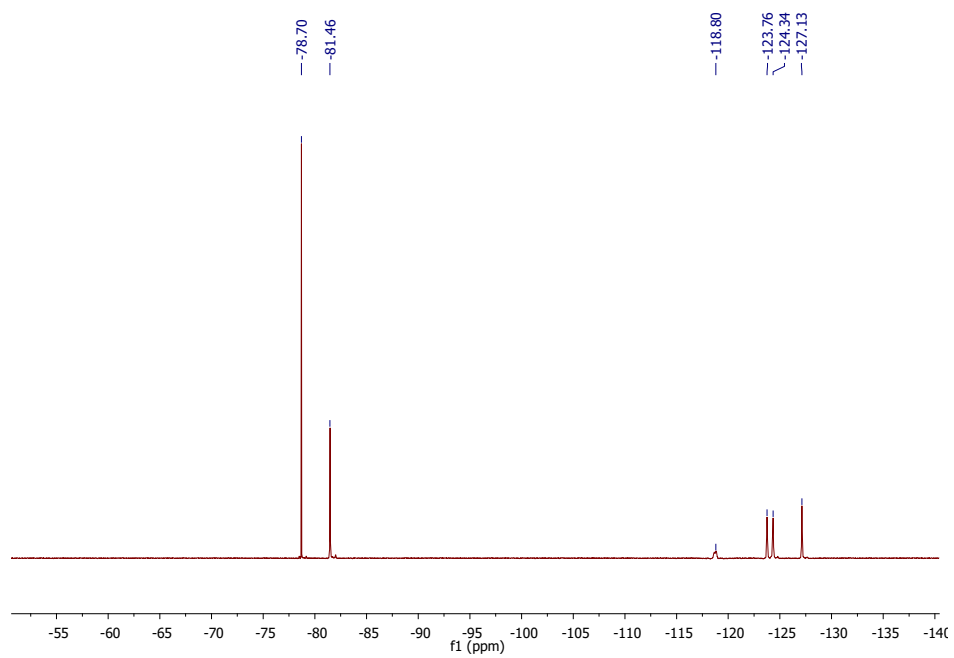


Figure S9.  $^{19}\text{F-NMR}$  spectrum of Eu1 in  $\text{DMSO-}d_6$ .

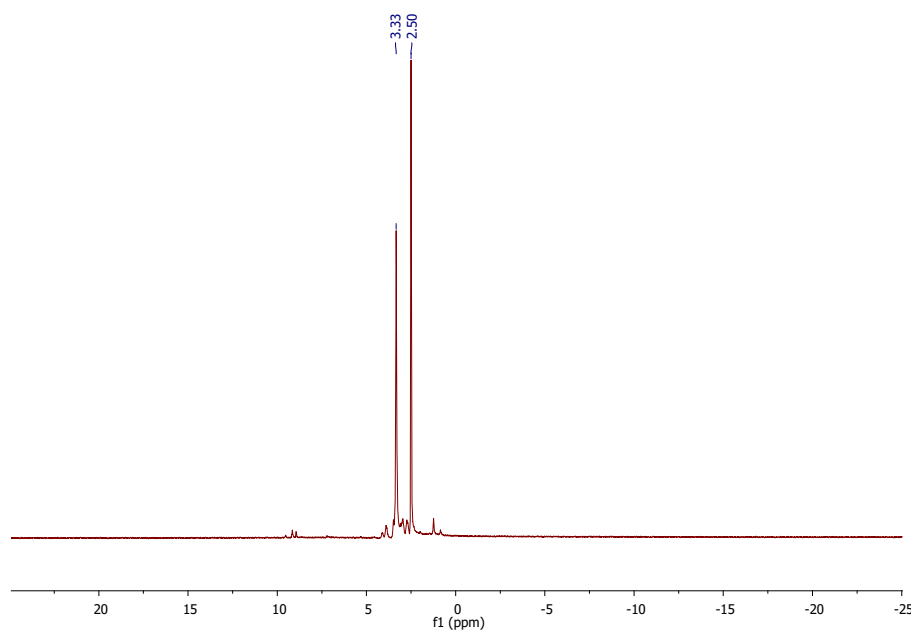


Figure S10.  $^1\text{H-NMR}$  spectrum of Eu2 in  $\text{DMSO-}d_6$ .

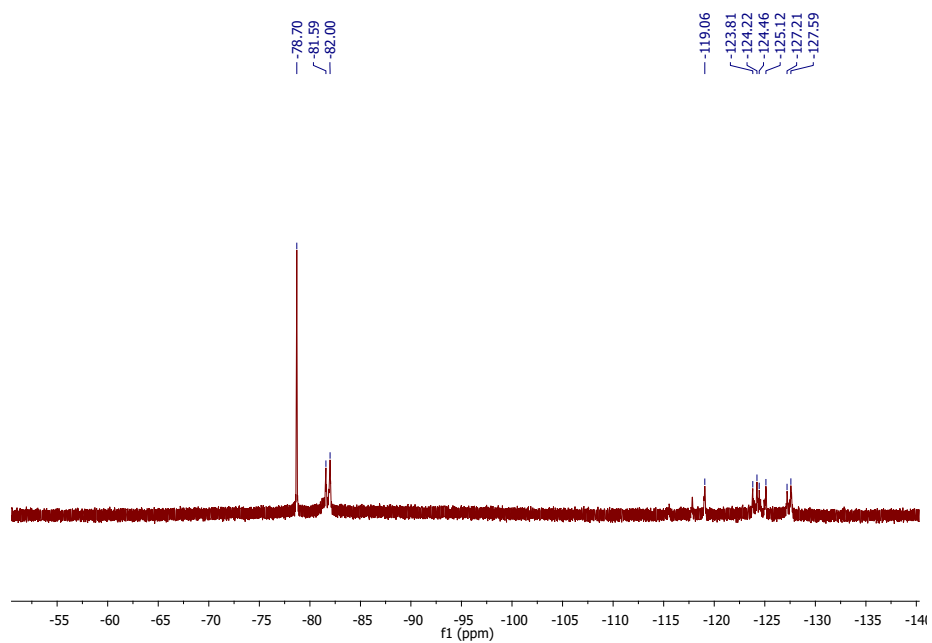
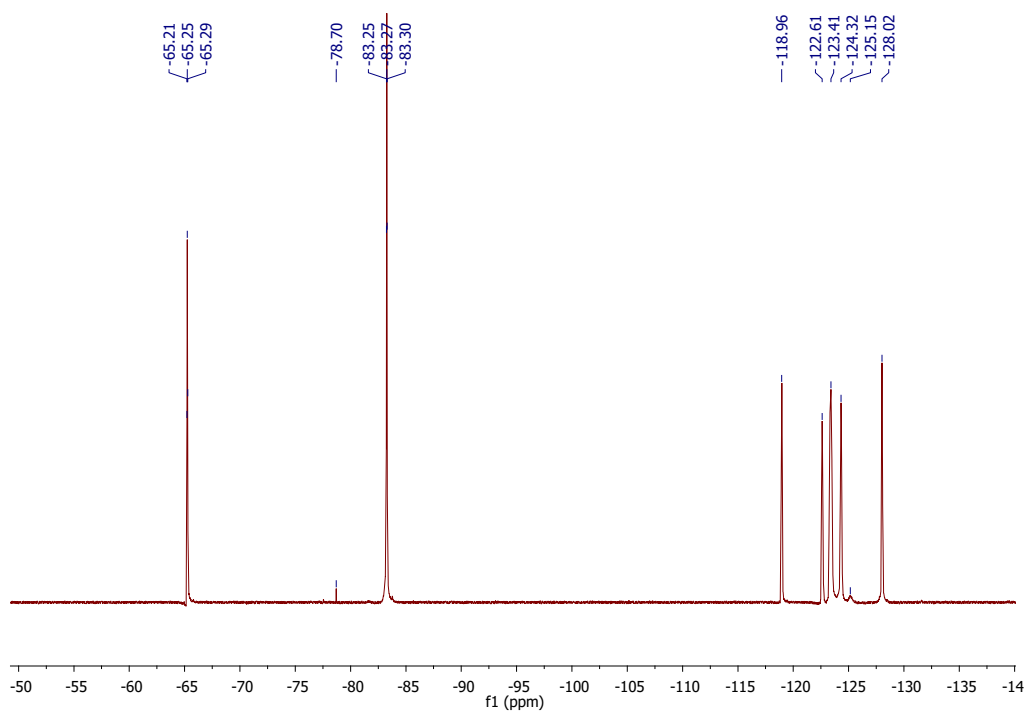
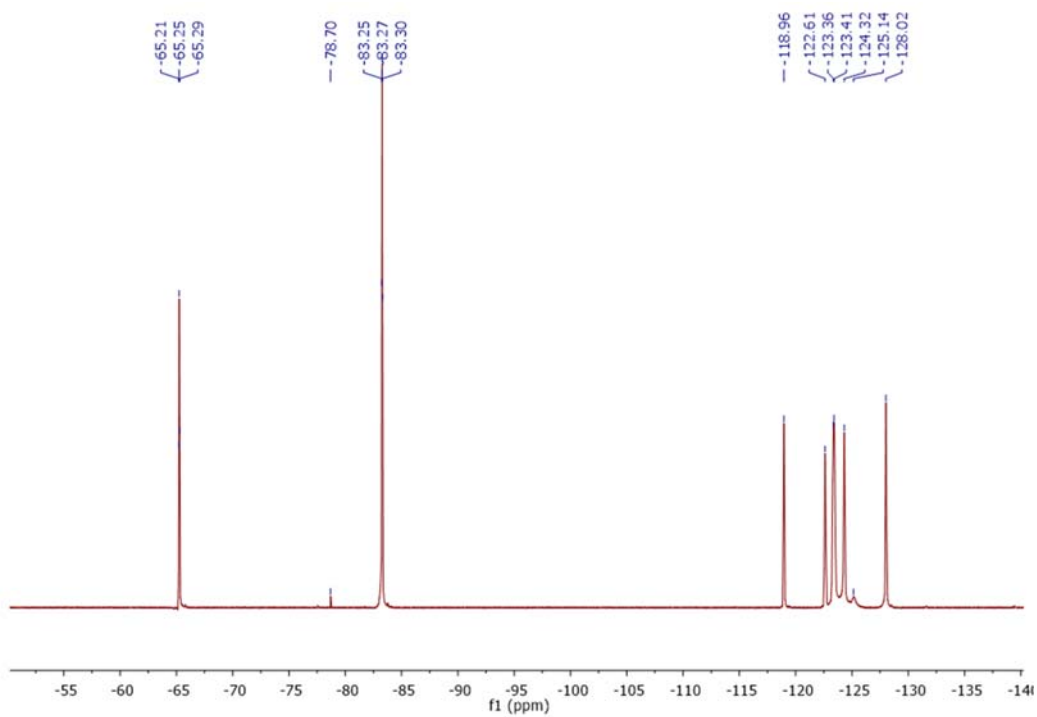


Figure S11.  $^{19}\text{F-NMR}$  spectrum of Eu2 in  $\text{DMSO-}d_6$ .

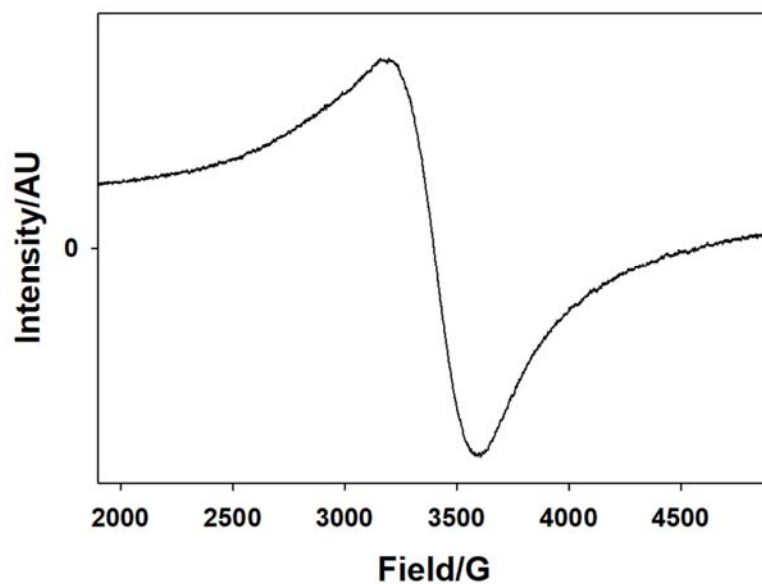


**Figure S12.**  $^{19}\text{F}$ -NMR spectrum of **Eu1** nanoemulsion in phosphate-buffered saline (1 $\times$ ) with 10% v/v  $\text{D}_2\text{O}$ .



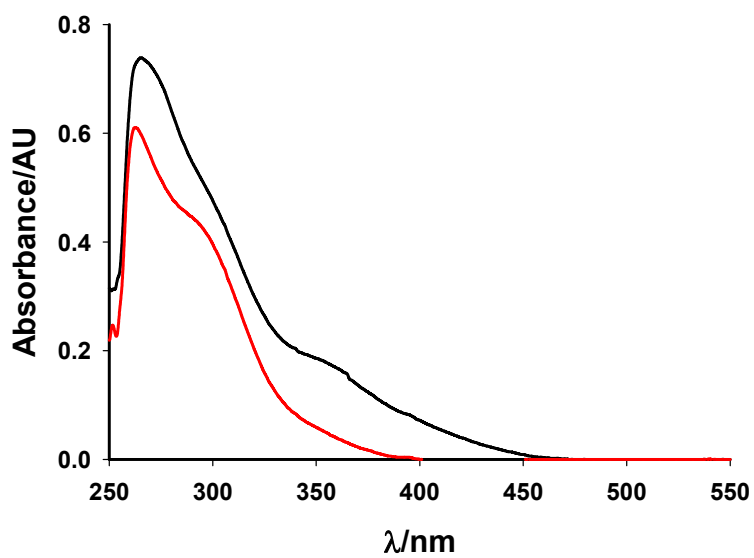
**Figure S13.**  $^{19}\text{F}$ -NMR spectrum of **Eu2** nanoemulsion in phosphate-buffered saline (1 $\times$ ) with 10% v/v  $\text{D}_2\text{O}$ .

## EPR Spectra



**Figure S14.** EPR spectrum of **Eu2** in degassed 1H,1H-perfluorooctylalcohol/*n*-perfluorooctyl bromide (20% w/w).

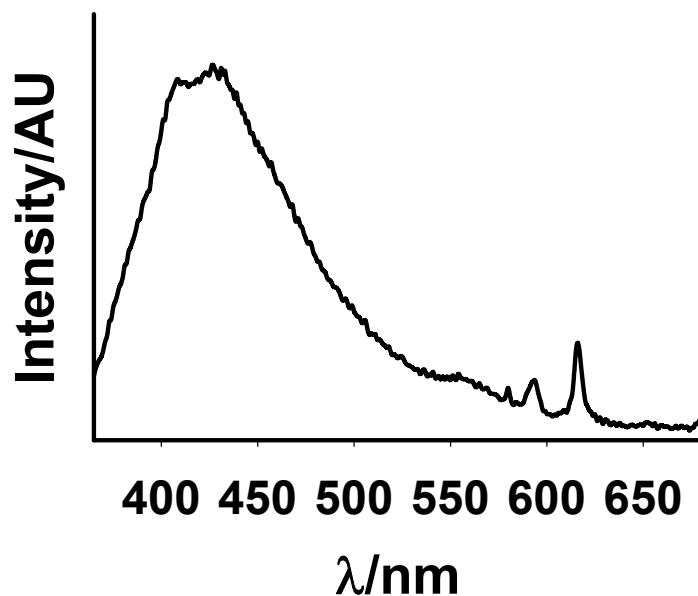
## UV-visible Spectra



**Figure S15.** UV-visible absorbance spectra of **Eu1** (—) and **Eu2** (—) in degassed 1H,1H-perfluorooctylalcohol/*n*-perfluorooctyl bromide (20% w/w).

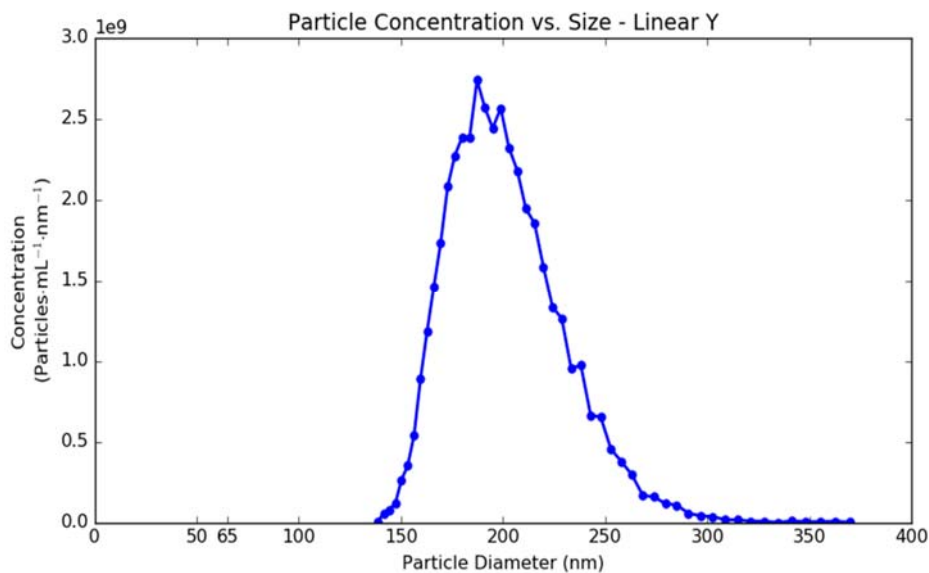


## Luminescence Spectra



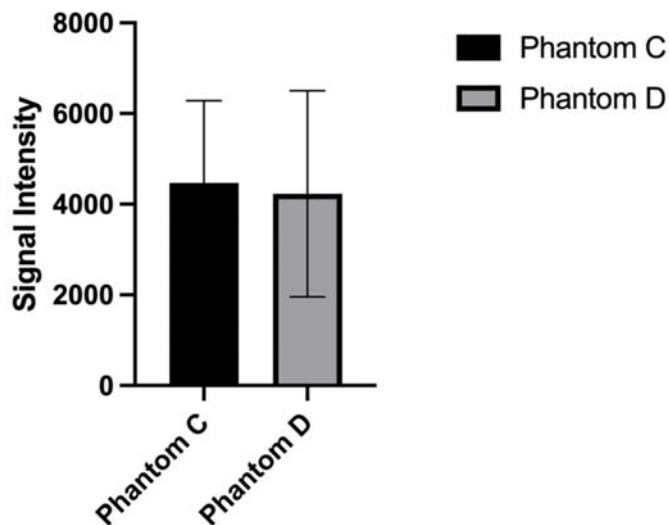
**Figure S16.** Luminescence emission from 5d–4f transition of **Eu2** in degassed 1H,1H-perfluorooctylalcohol/*n*-perfluorooctyl bromide (20% w/w).

## Particle Size Analysis



**Figure S17.** Particle size analysis of loaded nanoemulsion in phosphate-buffered saline (1x). Lines between points are a guide for the eyes.

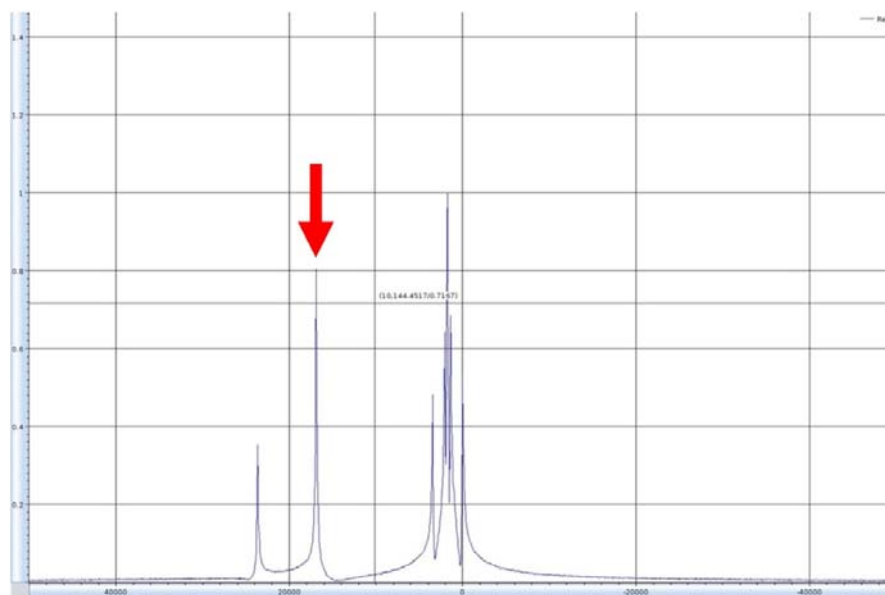
## Statistical Analysis of Signal Intensities Between C and D in Figure 5



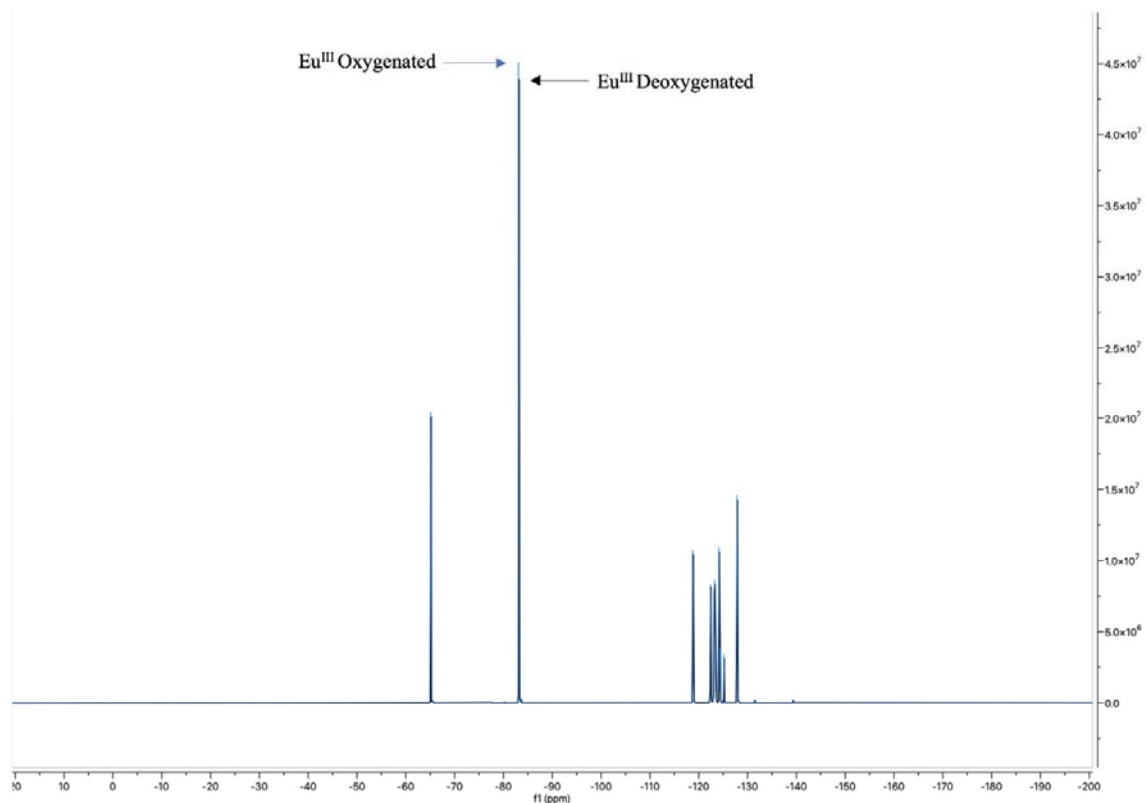
**Figure S18.** Unpaired *t*-test of the signal intensities of image (Phantom) C (Eu2, 50%) and Phantom D (Eu2, 75%) from Figure 5 ( $p = 0.6734$ ) showing no statistical difference.

<i>Unpaired t-Test</i>	
<i>P Value</i>	0.6734
<i>P value summary</i>	Not significant
<i>Significantly different (<math>P &lt; 0.05</math>)</i>	no
<i>Two-tailed P value</i>	$t = 0.4240$
<i>Degrees of Freedom</i>	50

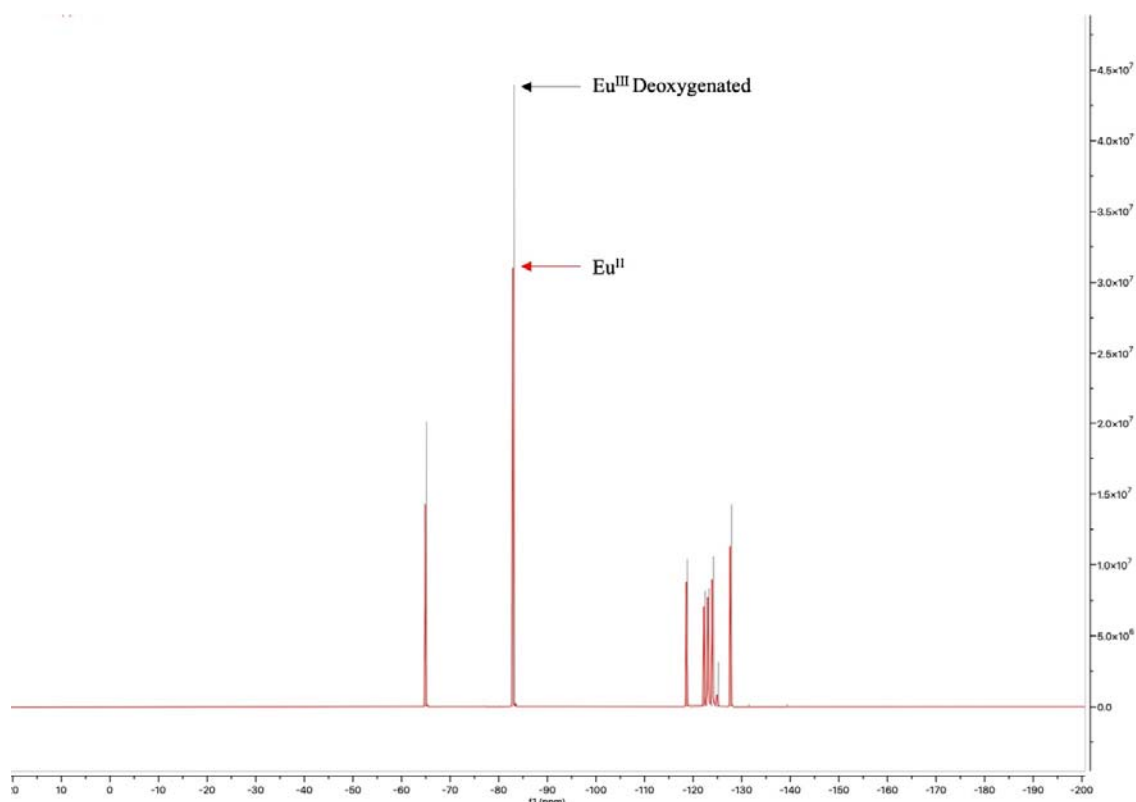
## Chemical Shift Relative Intensity



**Figure S19.** Chemical shift imaging relative intensity of perfluorocarbon emulsions in Figure 4 was set to the frequency of the peak indicated by the red arrow.



**Figure S20.** Overlay of two  $^{19}\text{F}$ -NMR spectra of **Eu1** (4.5 mM) in N-perfluorooctylbromide (80%) and 1H,1H-perfluorooctylalcohol (20%). One spectrum is from degassed sample, and the other spectrum is the first sample after aeration by sparging with air for 3 min. The difference in peak intensity ( $0.1 \times 10^7$ ) between the two samples is more than an order of magnitude smaller than the difference in Figure S21, demonstrating that Eu oxidation, and not the presence of oxygen, is the primary factor responsible for  $^{19}\text{F}$  signal change.



**Figure S21.** Overlay of  $^{19}\text{F}$ -NMR spectra of **Eu1** (4.5 mM) and **Eu2** (4.5 mM) in degassed N-perfluorooctylbromide (80%) and 1H,1H-perfluorooctylalcohol (20%). The difference in peak intensity ( $1.3 \times 10^7$ ) between the two samples is more than an order of magnitude larger than the difference in Figure S20, demonstrating that Eu oxidation, and not the presence of oxygen, is the primary factor responsible for  $^{19}\text{F}$  signal change.