Synthesis and Relaxivity Studies of a DOTA-based Nanomolecular Chelator Assembly Supported by an Icosahedral Closo-B$_{12}^{2-}$ -Core for MRI: A Click Chemistry Approach

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Supporting Information (SI)

$^1$H, $^{13}$C, $^{11}$B NMR, HRMS Spectra 2-26

IR spectra of closomer 4, 11 and CA-1 27-29

Determination of hydration number (q) 30

Comparison of relaxivity 31

Dynamic Light Scattering Analysis of CA-1 32

HPLC analysis of CA-1 33
Chemical Formula: C₉H₁₅ClO₃
Exact Mass: 206.0710
Applied Biosystems Mariner System 5268

Mariner Spec /1:32 ASC [BP = 321.0, 266]

[M+Na]^+

Chemical Formula: C_9H_{15}IO_3
Exact Mass: 298.0066
Applied Biosystems Mariner System 5268

Mariner Spec /1:40 (T/0.00:0.69) ASC[BP = 707.6, 1400]

[M+Na]^+

Chemical Formula: C_{35}H_{59}N_{4}O_{9}

Exact Mass: 684.4673
Applied Biosystems Mariner System 5268

Mariner Spec / 1:34 ASC [BP = 539.3, 108]

Chemical Formula: C_{23}H_{46}N_{4}O_{9}
Exact Mass: 516.2795

[M+Na]^+

[M+H]^+

[2M+Na]^+

[2M+2Na]^+
$[\text{M+Na}]^+$

Chemical Formula: $C_{23}H_{37}GdN_{4}O_{9}$

Exact Mass: 671.1796

$[3\text{M+2Na}]^{2+}$

$[2\text{M+Na}]^+$
Applied Biosystems Mariner System 5219

Mariner Spec /1:24 ASC[BP = 706.4, 35]

Chemical Formula: C_{23}H_{39}DyN_{4}O_{9}^+
Exact Mass: 677.1847

unidentified

\[ [\text{M+Na}]^+ \]
\[ [\text{M+2Na}]^+ \]
\[ [3\text{M+2Na}]^{2+} \]
\[ [4\text{M+2Na}]^{2+} \]
\[ [5\text{M+2Na}]^{2+} \]
B12-bromoacetic ester
B11 CDC13 {C:Bruker\TOPSPIN} goswami 10
B12-bromoacetic ester
proton CDCl$_3$ (C:\Bruker\TOPSPIN) goswami 9
B12-bromoacetic ester
C13 CDC13 \{C:\Bruker\TOPSPIN\} goswami 10
Chemical Formula: $C_{24}H_{24}B_{12}Br_{12}O_{24}$
Molecular Weight: 1785.0130
Various multiple charged species

$M^{9+}$ species

Starting ligand

Chemical Formula: $C_{444}H_{792}B_{12}N_{84}O_{132}$
Average Molecular Weight: 9549.2549

$+Na$
Chemical Formula: \( \text{C}_{26}\text{H}_{48}\text{Gd}_{12}\text{N}_{34}\text{O}_{132} \)
Ave. Mass: 4692.2286 \([\text{M}^2^-]\)
Determination of Hydration number (q) for DO3A Dy³⁺ complex 10

Varying concentrations of 10 and DyCl₃.6H₂O over the range 10-80 mmol dm⁻³ were prepared in 80% D₂O-H₂O and the pH of the solutions was adjusted to pH 7.0. The ¹⁷O NMR experiments were performed at 400 MHz using a Bruker Avance instrument at RT with the deuterium signal locked. A graph was plotted between the d.i.s. (Δδ) and the concentration for both 10 and the DyCl₃.6H₂O solutions and slope was obtained. The Δδ value for a complex with the general formula, Dy(ligand)ₙ(H₂O)ₚ, is given by the following relation;

\[ \Delta \delta = \frac{q \Delta [\text{Dy(ligand)}]_n[H_2O]}{[H_2O]} \]  

The slope of a plot of the d.i.s. versus the Dy³⁺ concentration is proportional to the q value of the complex (Figure). The q value was obtained by linearly fitting the Δδ value and was found to be 2 for complex 10.

From the graph, which fit well to a straight line, the slope was calculated. From relation I, the slope of the graph can be equated with the following;

\[ \text{Slope} = q \Delta/[H_2O] \]

From the graph, the slope was calculated as,

\[ \text{Slope} = -375 \text{ ppm dm}^3 \text{ mol}^{-1} \]

For DyCl₃, the value of q was assumed to be 9, because the coordination number of Dy(III) in such complexes known to be 9. Hence, the value of Δ/[H₂O] is calculated as follows:

\[ \Delta/[H_2O] = -375 \text{ ppm dm}^3 \text{ mol}^{-1} /9 \]

\[ \Delta/[H_2O] = -41.7 \text{ ppm dm}^3 \text{ mol}^{-1} \]

From this calculation, a value of q for the DOTA-Dy³⁺ complex 10 is calculated as follows:

For complex 10, \( \text{Slope} = \frac{q \Delta}{[H_2O]} \), or

\[ q = \frac{\text{slope}}{(\Delta/[H_2O])} \] or \( q = -40.6/-41.7 \), hence

\[ q = 1 \]
Figure. Comparison of the per-Gd $r_1$ values of CA-1, ligand 9 and Omniscan.
Dynamic Light Scattering Analysis of CA-1
1mM solutions;
Standard: Gold nanoparticles (20 nm)
SE-HPLC analysis of CA-1

- **Column:**
  - BioSep-SEC-S2000 (Phenomenex)
  - 250 X 2.0mm
- **Mobile phase:**
  - PBS, pH 6.6
  - Flow rate: 0.1 ml/min
- **Detector:**
  - UV-256 nm
- **Injection:**
  - 5.0 mg/ml PBS stock solution
  - 5ul injection