

ESI : Parker ; *Chem. Commun.*, 2006

1. Experimental

2. NMRD and VT 17-O (2.1T) NMR profiles for 4, 5 and 6

3. Sample low and high-resolution electrospraymass spectra for 4 and 5.

1. Experimental

General. CH₂Cl₂ distilled from CaH₂. THF distilled from Na/benzophenone. NEt₃ distilled from CaH₂. Anhydrous nitromethane was purchased from Fluka. Gel filtration chromatography was performed with Biogel P-6 gel fine (column 2.5 cm x 98 cm) eluting with water at 0.7 mL min⁻¹. Detection was performed with a Knauer Differential Refractometer. Glucose and galactose pentabenzoate were prepared according to F. W. Lichtenthaler, E. Kaji and S. Weprek *J. Org. Chem.* 1985, 50, 3505-3515.

Tris(β-D-glucopyranosyloxymethyl)-methylamine, 2

Prepared according to the method described by P. R. Ashton, S. E. Boyd, C. L. Brown, N. Jayaraman, S. A. Nepogodiev and J. F. Stoddart *Chem. Eur. J.* **1996**, 2, 1115-1128. Analytical data were in agreement with those reported in the literature.

Glu₁₂GdgDOTA, 4

To a suspension of GdgDOTA (16 mg, 18 μmol) and NEt₃ (13 μL, 115 μmol) in DMF (1 mL) was added *O*-benzotriazol-1-yl-*N, N, N', N'*-tetramethyluronium tetrafluoroborate (37 mg, 115 μmol) and the mixture allowed to stir for few minutes. The amine tris(β-D-glucopyranosyloxymethyl)methylamine (88 mg, 132 μmol) was added to the reaction, and the mixture allowed to stir overnight at 40 °C under an atmosphere of dry argon. The pH of the reaction was then measured to be approximately 4 and further NEt₃ (30 μL) was added until the pH was around 8. Further *O*-benzotriazol-1-yl-*N, N, N', N'*-tetramethyluronium tetrafluoroborate was added (40 mg) and the reaction left to stir at 40 °C for a further 2.5 h. The reaction was then partitioned between water (10 mL) and CH₂Cl₂ (10 mL). The aqueous layer was washed with CH₂Cl₂ (2 x 10 mL) and freeze-dried to afford a white solid.

Purification by gel-filtration chromatography (Biogel P-6) afforded a colourless solid (25 mg, 43%) as a fluffy white powder after lyophilization.

ES-MS: $[M]^{2-} = 1601.05$, $[M]^{3-} = 1067.35$.

HRMS (ES⁻) calcd. for C₁₁₆H₁₉₆N₈O₈₄ Gd $[M]^{2-}$: 1601.0242; found 1601.0243.

N^α-(Benzyloxycarbonyl)-N-[tris(hydroxymethyl)methyl]glycinamide

Hydroxybenzotriazole (1.35 g, 9.99 mmol) was added to a solution of carbobenzyloxyglycine (2.00 g, 9.56 mmol) and 1,3-dicyclohexylcarbodiimide (2.06 g, 9.98 mmol) in DMF (20 mL). When all reagents were dissolved, TRIS (2.32 g, 19.15 mmol) was added. The reaction mixture was stirred overnight at room temperature under an atmosphere of argon. After completion of the reaction (TLC), DMF was removed under vacuum and the white solid obtained was dissolved in EtOH (20 mL). The white slurry was filtered and the filtrate evaporated to dryness. The product was purified by column chromatography (SiO₂, CH₂Cl₂ / MeOH 1%→CH₂Cl₂ / MeOH 5%) to yield a white solid (0.86 g, 28%).

ES-MS: m/z 335 $[M + Na]^+$, 647 $[2 \times M + Na]^+$

HRMS (ES⁺) calcd. for C₁₄H₂₀N₂O₆ $[M + Na]^+$: 335.1214; found 335.1214

δ_H (DMSO, 300 MHz): 3.51 (6H, d, $J = 6.0$ Hz, CH₂OH), 3.62 (2H, d, $J = 6.0$ Hz, CH₂NH), 4.69 (3H, t, $J = 6.0$ Hz, OH), 5.02 (2H, s, CH₂Ph), 7.13 (5H, bs, Ph-H), 7.32 (1H, s, C_(quat)NH), 7.44 (1H, m, CH₂NH).

δ_C (DMSO, 75 MHz): 44.2 (CH₂NHCO), 61.0 (CH₂OH), 62.40 (CH₂C(quat)), 66.8 (CH₂Ph), 127.7, 128.0, 128.4 (Ph-C), 136.9 (Ph-C(quat)), 158.0 (COCH₂NH), 171.6 (COOCH₂Ph).

N^α-(Benzyloxycarbonyl)-N-[tris(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyloxymethyl)methyl]glycinamide

AgOTf (0.50 g, 1.94 mmol) was activated by dissolving in anhydrous PhCH₃ (10 mL) and the solvent was removed under vacuum. This procedure was repeated a further two times. A mixture of **7** (0.147 g, 0.47 mmol), AgOTf and 2,4,6-collidine (190 μL, 1.44 mmol) in CH₂Cl₂ (4.4 mL) and MeNO₂ (4.4 mL) was stirred at -30 °C. A solution of 2,3,4,6-tetra-O-benzoyl-α-D-glucopyranosyl bromide (1.10 g, 1.67 mmol) in CH₂Cl₂ (4.4 mL) was added dropwise over 20 min to this suspension. Stirring was continued for 30 min at the same temperature and then the reaction mixture was for 2 h at 0 °C, then overnight at room temperature. After completion of the reaction (TLC), C₅H₅N (1.0 mL) was added to the

reaction mixture, which was left to stir for 30 min and then diluted with CH₂Cl₂ (20 mL) before being filtered through Celite. The filtrate was washed successively with aqueous Na₂S₂O₃ solution (1 M, 2 x 50 mL), aqueous HCl solution (0.1 M, 2 x 50 mL), saturated aqueous NaHCO₃ solution (2x50 mL) and H₂O (2x50 mL). The organic phase was dried over Na₂SO₄ and the solvent was removed in *vacuo* to afford crude product, the TLC of which showed a main product (R_f (EtOAc/Hex 3:7) = 0.2; H₂SO₄) and few other minor components. The main product was separated by column chromatography (SiO₂, EtOAc / Hex, 3:7) to afford the product as a white foamy solid (0.47 g, 49%).

ES-MS: *m/z* 2071 [*M* + Na]⁺, 4119 [2×*M* + Na]⁺

HRMS (ES⁺) calcd. for C₁₁₆H₉₈N₂O₃₃ [*M* + 2Na]²⁺: 1046.2918; found 1046.2935

δ_H (CDCl₃, 300 MHz): 3.50 (3H, d, ²J_{CH_a,CH_b} = 10.0 Hz, C_(quat)CH_a), 3.60 – 3.70 (5H, m, H-5), 4.16 (3H, d, ³J_{1,2} = 9.0 Hz, H-1), 4.24 (3H, d, ²J_{CH_a,CH_b} = 10.0 Hz, C_(quat)CH_b), 4.38 (3H, dd, ³J_{5,6a} = 4.5 Hz, ²J_{6a,6b} = 12.0 Hz, H-6a), 4.54 (3H, app.d, ²J_{6a,6b} = 12.0 Hz, H-6b), 5.18 (2H, s, CH₂Ph), 5.35 (4H, app.t, ³J_{1,2} ~ ³J_{2,3} = 8.5 Hz, H-2 and CH₂NH), 5.55 (3H, app. t, ³J_{3,4} ~ ³J_{4,5} = 9.5 Hz, H-4), 5.69 (3H, app. t, ³J_{2,3} ~ ³J_{3,4} = 9.5 Hz, H-3), 6.01 (1H, s, NH carbamate), 7.28 – 8.06 (60H, m, Ph-H).

δ_C (CDCl₃, 75 MHz): 58.4 (C_(quat)), 59.3 (CH₂NHCO), 61.9 (C-6), 65.9 (CH₂Ph), 66.9 (C_(quat)CH₂), 68.5 (C-4), 70.9 (C-5), 71.0 (C-2), 71.5 (C-3), 100.3 (C-1), 127.3 – 128.9 (Ph ring carbons), 132.1 (PhC_(quat)), 164.0 (COCH₂NH), 165.0 (COOCH₂Ph).

***N*^α-(Benzyloxycarbonyl)-*N*-[tris(β-*D*-glucopyranosyloxymethyl)-methyl]glycinamide**

A solution of *N*-α-(benzyloxycarbonyl)-*N*-[tris(2,3,4,6-tetra-*O*-benzoyl-β-*D*-glucopyranosyloxymethyl)methyl]glycinamide (0.47g, 0.23 mmol) in 0.10 M methanolic NaOMe (20 mL) was stirred at room temperature overnight. The solution was treated with Amberlite IR-120(PLUS) ion-exchange resin, filtered and the solvents were removed *in vacuo*. The resulting solids were partitioned between H₂O (20 mL) and Et₂O (15 mL). The aqueous layer was washed with further Et₂O (3 x 15 mL) and then freeze-dried to obtain the product as a fluffy white powder (0.16 g, 87%).

ES-MS: *m/z* 821 [*M* + Na]⁺, 1619 [2×*M* + Na]⁺

HRMS (ES⁺) calcd. for C₃₂H₅₀N₂O₂₁ [*M* + Na]⁺: 821.2798; found 821.2791

δ_H (D₂O, 500 MHz): 3.11 (3H, app. t, *J* = 7.5 Hz, H-2), 3.19 – 3.32 (9H, m, H-3, H-4, H-5), 3.55 (3H, dd, ³J_{5,6a} = 5.5 Hz, ²J_{6a,6b} = 12.0 Hz, H-6a) 3.66 (2H, s, CH₂NHCO), 3.74 (3H, dd,

H-5, $^3J_{5,6b} = 2.0$ Hz, $^2J_{6a,6b} = 12.0$ Hz, H-6b), 3.78 (3H, d, $^2J_{\text{CHa,CHb}} = 10.5$ Hz, C(quat)CH_a), 4.08 (3H, d, $^2J_{\text{CHa,CHb}} = 10.5$ Hz, C(quat)CH_b), 4.28 (3H, d, $^3J_{1,2} = 8.0$ Hz, H-1), 5.00 (2H, s, CH₂Ph), 7.29 (5H, m, Ph-H).

δ_C (D₂O, 125.67 MHz): 44.1 (Gly-CH₂), 59.1 (C(quat)), 60.8 (C-6), 67.6 (CH₂Ph), 67.7 (C(quat)CH₂), 69.8 (C-4), 73.2 (C-2), 75.6 (C-3), 76.1 (C-5), 103.1 (C-1), 127.9-128.6 (Ph ring carbons), 157.8 (COCH₂NH), 172.2 (Gly-CO).

N-[Tris(β -D-glucopyranosyloxymethyl)methyl]glycinamide, **3**

A suspension of N^α-(benzyloxycarbonyl)-N-[tris(β -D-glucopyranosyloxymethyl)-methyl]glycinamide (0.47 g, 0.23 mmol) in 10 mL of H₂O/ EtOH (1:1) and Pd(OH)₂/C (0.17 g) was hydrogenolysed overnight using a hydrogenator (40 psi H₂). The reaction mixture was filtered over Celite, the solvent was evaporated under reduced pressure and the residue was dissolved in H₂O (15 mL) and freeze-dried to afford a white powder (0.146 g, 96%).

ES-MS: m/z 687 [$M + \text{Na}$]⁺, 1351 [$2 \times M + \text{Na}$]⁺.

HRMS (ES⁺) calcd. for C₂₄H₄₄N₂O₁₉ [$M + \text{Na}$]⁺: 687.2430; found 687.2426

δ_H (D₂O, 500 MHz): 3.14 (3H, app. t, $^3J_{1,2} = 8.5$ Hz, H-2), 3.22 (3H, app. t, $^3J_{3,4} = 9.5$ Hz, H-4), 3.28–3.34 (8H, m, H-3, H-5, CH₂NH₂), 3.55 (3H, d, $^2J_{6a,6b} = 12.5$ Hz, H-6a), 3.76 (3H, d, $^2J_{6a,6b} = 12.5$ Hz, H-6b), 3.79 (3H, d, $^2J_{\text{CHa,CHb}} = 10.0$ Hz, C(quat)CH_a), 4.12 (3H, d, $^2J_{\text{CHa,CHb}} = 10.0$ Hz, C(quat)CH_b), 4.31 (3H, d, $^3J_{1,2} = 7.5$ Hz, H-1).

δ_C (D₂O, 125.67 MHz): 42.9 (Gly-CH₂), 57.5 (C(quat)), 60.8 (C-6), 67.8 (C(quat)CH₂), 69.9 (C-4), 73.2 (C-2), 75.7 (C-3), 76.1 (C-5), 100.1 (C-1), 172.3 (CONH).

Analytical data in good agreement with P. R. Ashton *et al.* *Chem. Eur. J.* **1996**, *2*, 1115-1128.

Glu₁₂**glyGdgDOTA, 5**

To a suspension of GdgDOTA (15 mg, 0.017 mmol) in *N*-methylmorpholine (12 μ L, 0.11 μ mol) and DMF (0.82 mL) was added *O*-benzotriazol-1-yl-*N, N', N'*-tetramethyluronium tetrafluoroborate (40 mg, 0.12 mmol) and the mixture allowed to stir for few minutes. A solution of the amine *N*-[tris(β -D-glucopyranosyloxymethyl)methyl]glycinamide (70 mg, 0.13 mmol) was added to the reaction, and the mixture allowed to stir overnight at 40 °C under an atmosphere of argon. The reaction was portioned between water (10 mL) and CH₂Cl₂ (10 mL). The aqueous layer was washed with CH₂Cl₂ (10 mL) and freeze-dried. The

crude of the reaction is a mixture of the fully substituted tetra-amide (major product) and the under-substituted triamide and diamide (minor products). Purification by gel-filtration chromatography afforded the pure tetra-substituted product (19 mg, 32%), as confirmed by electrospray analysis.

ES-MS: $[M]^{2-} = 1715.07$.

HRMS (ES⁻) calcd. for C₁₂₄H₂₀₄N₁₂O₈₈ Gd $[M]^{2-}$: 1715.0712; found 1715.0716.

(TRIS)₄GdgDOTA, 6

To a suspension of GdgDOTA (109 mg, 126 μmol) in NEt₃ (105 μL, 0.75 mmol) and DMF (2.0 mL) was added *O*-benzotriazol-1-yl-*N, N, N', N'*-tetramethyluronium tetrafluoroborate (247 mg, 0.77 mmol) and the mixture allowed to stir for few minutes. Tris(hydroxymethyl)methylamine (200 mg, 1.65 mmol) was added and the mixture allowed to stir overnight at 40 °C under an atmosphere of argon. The reaction was portioned between water (20 mL) and CH₂Cl₂ (20 mL). The aqueous layer was washed with CH₂Cl₂ (20 mL) and freeze-dried. Purification by gel-filtration chromatography afforded the pure tetra-substituted product (83 mg, 52%), as confirmed by electrospray analysis.

ES-MS: $[M]^{-} = 1258.4$

HRMS (ES⁻) calcd. for C₄₄H₇₆N₈O₂₄ Gd $[M]^{-}$: 629.2112; found 629.2113.

***N^α*-(Benzyloxycarbonyl)-*N*-[tris(2,3,4,6-tetra-*O*-benzoyl-β-*D*-galactopyranosyloxymethyl)methyl]glycinamide**

AgOTf (1.006 g, 3.92 mmol) was activated by dissolving in anhydrous PhCH₃ (10 mL) and the solvent then removed under vacuum. This procedure was repeated a further two times. A mixture of *N^α*-(benzyloxycarbonyl)-*N*-[tris(hydroxymethyl)methyl]glycinamide (300 mg, 961 μmol), AgOTf and 2,4,6-collidine (444 μL, 3.36 mmol) in CH₂Cl₂ (7 mL) and MeNO₂ (7 mL) was stirred at approximately -30 °C under an argon atmosphere. A solution of 2,3,4,6-tetra-*O*-benzoyl-α-*D*-galactopyranosyl bromide (2.22 g, 3.37 mmol) in CH₂Cl₂ (7 mL) was added dropwise over 20 min to the reaction mixture. Stirring was continued for 30 min at the same temperature and the reaction mixture then stirred for 2 h at 0 °C, then overnight at room temperature. The reaction mixture was then diluted with CH₂Cl₂ (100 mL) before being filtered through Celite. The filtrate was washed successively with aqueous Na₂S₂O₃ solution (1 M, 2 x 100 mL), aqueous HCl solution (1 M, 100 mL), saturated aqueous NaHCO₃ solution (100 mL) and H₂O (100 mL). The organic phase was dried over MgSO₄ and the solvent was

removed in *vacuo* to afford crude product. The main product was separated by column chromatography (SiO₂, EtOAc / Hex, 3:7 to 4:7) to yield the title compound (1.26 g, 64%) as a foamy white solid.

HRMS (ES⁺) calcd. for C₁₁₆H₉₈O₃₃N₂Na₂ [M + 2Na]²⁺: 1046.2908; found 1046.2907.

¹H NMR (500 MHz, CDCl₃): δ = 3.59 (2H, d, *J* = 10.5 Hz, glyCH₂), 3.58 - 3.67 (3H, m, C_{quat}CH_a), 3.78 (3H, t, *J* = 7.0 Hz, H-5), 4.15 (3H, d, ³*J*_{1,2} = 7.0 Hz, H-1), 4.36 - 4.40 (6H, m, H-6a, C_{quat}CH_b), 4.55 (3H, dd, ³*J*_{5,6a} = 6.5 Hz, ²*J*_{6a,6b} = 11.0 Hz, H-6b), 5.11 (1H, d, ²*J*_{CHa,CHb} = 12.5 Hz, PhCH_a), 5.16 (1H, d, ²*J*_{CHa,CHb} = 12.5 Hz, PhCH_b), 5.24 (1H, bs, NH), 5.42 (3H, dd, ³*J*_{3,4} = 3.5 Hz, ³*J*_{2,3} = 10.5 Hz, H-3), 5.65 (3H, dd, ³*J*_{1,2} = 7.0 Hz, ³*J*_{2,3} = 10.5 Hz, H-2), 5.87 (3H, app. t, ³*J*_{3,4} ≈ ³*J*_{4,5} = 3.5 Hz, H-4), 6.00 (1H, bs, NH), 7.27 - 8.08 (65H, band, 13 x Ph).

¹³C NMR (125 MHz, CDCl₃): δ = 44.6 (glyCH₂), 61.8 (C-6), 67.2 (PhCH₂), 68.1 (C-4, C_{quat}CH₂), 70.1 (C-2), 71.3 (C-3), 71.4 (C-5), 102.0 (C-1), 125.1 - 134.1 (Ph ring carbons), 156.5 (urethane C=O), 165.1, 165.7, 165.8, 166.1 (PhCO), 169.0 (NHCO).

Proton and carbon assignments confirmed by COSY and HSQC experiments.

N^α-(Benzyloxycarbonyl)-*N*-[tris(β-*D*-galactopyranosyloxymethyl)-methyl]glycinamide

A solution of *N*-α-(benzyloxycarbonyl)-*N*-[tris(2,3,4,6-tetra-*O*-benzoyl-β-*D*-galactopyranosyloxymethyl)methyl]glycinamide (1.26 g, 0.616 mmol) in 0.1 M methanolic NaOMe (50 mL) was stirred at room temperature overnight. It was then neutralized with Amberlite IR-120(PLUS) ion-exchange resin, filtered and the solvents were removed *in vacuo*. The resulting solids were partitioned between H₂O (20 mL) and Et₂O (15 mL). The aqueous layer was washed with further Et₂O (3 x 15 mL) and then freeze-dried to obtain the product as a fluffy white powder (433 mg, 88%).

HRMS (ES⁺) calcd. for C₃₂H₅₀O₂₁N₂Na [M + Na]⁺: 821.2789; found 821.2785.

¹H NMR (500 MHz, H₂O): δ = 3.37 (3H, app. t, ³*J*_{1,2} ≈ ³*J*_{2,3} = 8.0 Hz, H-2), 3.46 - 3.51 (6H, m, H-3, H-5), 3.56 - 3.64 (6H, m, H-6a, H-6b), 3.68 (2H, s, glyCH₂), 3.74 (3H, d, *J* = 3.0 Hz, H-4), 3.82 (3H, d, ²*J*_{CHa, CHb} = 10.5 Hz, C_{quat}CH_a), 4.10 (3H, d, C_{quat}CH_b), 4.22 (3H, d, ³*J*_{1,2} = 8.0 Hz, H-1), 5.01 (2H, s, PhCH₂), 7.26 - 7.33 (5H, m, Ph-H).

^{13}C NMR (125 MHz, H_2O): $\delta = 44.1$ (gly CH_2), 60.1 (C_{quat}), 61.1 (C-6), 67.4 ($\text{C}_{\text{quat}}\text{CH}_2$), 68.7 (C-4), 70.9 (C-2), 72.7, 75.3 (C-3, C-5), 103.7 (C-1), 127.8, 128.5, 129.0, 136.5 (Ph ring carbons), 158.6 (C=O urethane), 172.0 (C=O glycine).

Proton and carbon assignments confirmed by COSY and HSQC experiments.

N-[Tris(β -D-galactopyranosyloxymethyl)-methyl]glycinamide

A suspension of N^{α} -(Benzyloxycarbonyl)-*N*-[tris(β -D-galactopyranosyloxymethyl)-methyl]glycinamide (433 mg, 0.54 mmol) in H_2O / EtOH (10 mL, 1:1) and 20%Pd(OH) $_2$ /C (85 mg) was hydrogenated at room temperature overnight using a Parr hydrogenator (40 psi H_2). The reaction mixture was filtered over Celite, the solvent was evaporated in *vacuo* and the residue was dissolved in H_2O (15 mL) and freeze-dried to afford a white powder (360 mg, 100%).

^1H NMR (500 MHz, H_2O): $\delta = 3.36 - 3.41$ (5H, H-2, gly CH_2), 3.48 – 3.54 (6H, m, H-3, H-5), 3.57 – 3.67 (6H, H-6a, H-6b), 3.77 (3H, d, $J = 3.0$ Hz, H-4), 3.81 (3H, d, $^2J_{\text{CH}_a, \text{CH}_b} = 10.5$ Hz, $\text{C}_{\text{quat}}\text{CH}_a$), 4.14 (3H, d, $^2J_{\text{CH}_a, \text{CH}_b} = 10.5$ Hz, $\text{C}_{\text{quat}}\text{CH}_b$), 4.25 (3H, d, $^3J_{1,2} = 7.5$ Hz, H-1).

^{13}C NMR (125 MHz, H_2O): $\delta = 42.6$ (gly CH_2), 60.1 (C_{quat}), 61.1 (C-6), 67.8 ($\text{C}_{\text{quat}}\text{CH}_2$), 68.7 (C-4), 70.8 (C-2), 72.7, 75.3 (C3, C5), 103.7 (C-1), 171.1 (C=O glycine).

Proton and carbon assignments confirmed by COSY and HSQC experiments.

HRMS (ES^+) calcd. for $\text{C}_{24}\text{H}_{44}\text{O}_{19}\text{N}_2\text{Na}$ [$\text{M} + \text{Na}$] $^+$: 687.2430; found 687.2428

Gal $_{12}$ glyGdgDOTA

To a suspension of GdgDOTA (19 mg, 22 μmol) and NEt_3 (18 μL , 129 μmol) in DMF (1 mL) was added *O*-benzotriazol-1-yl-*N, N, N', N'*- tetramethyluronium tetrafluoroborate (40 mg, 134 μmol) and the mixture allowed to stir for few minutes. The amine *N*-[tris(β -D-galactopyranosyloxymethyl)-methyl]glycinamide (88 mg, 132 μmol) was added to the reaction, and the mixture allowed to stir overnight at 40 $^{\circ}\text{C}$ under an atmosphere of dry argon. The pH of the reaction was then measured to be approximately 4 and further NEt_3 (30 μL) was added until the pH was around 8. Further *O*-benzotriazol-1-yl-*N, N, N', N'*- tetramethyluronium tetrafluoroborate was added (35 mg) and the reaction left to stir at 40 $^{\circ}\text{C}$ for a further 2.5 h. The reaction was then partitioned between water (10 mL) and CH_2Cl_2 (10 mL). The aqueous layer was washed with CH_2Cl_2 (2 x 10 mL) and freeze-dried to afford

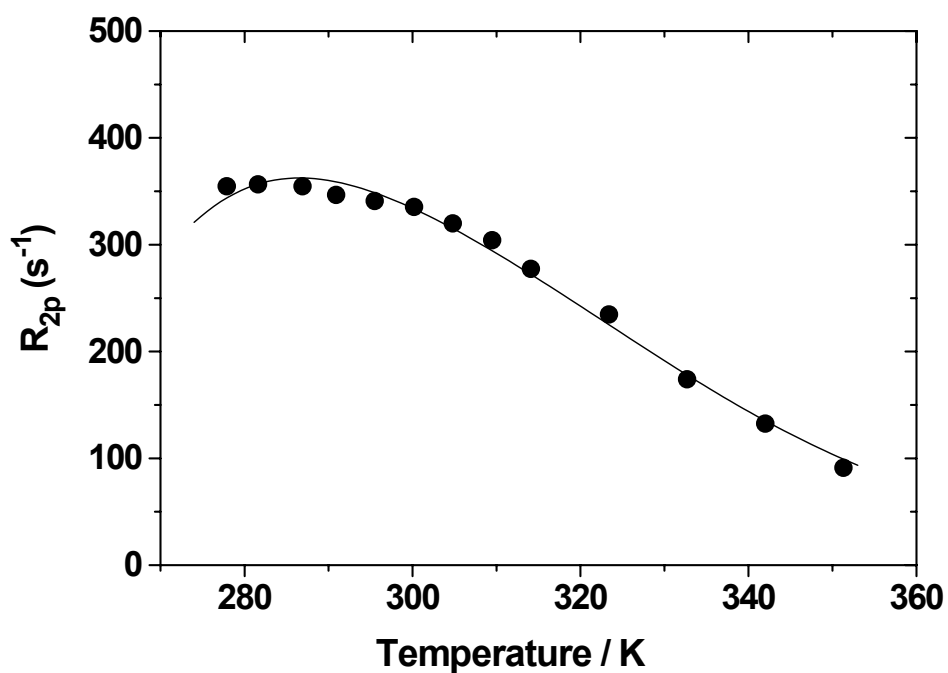
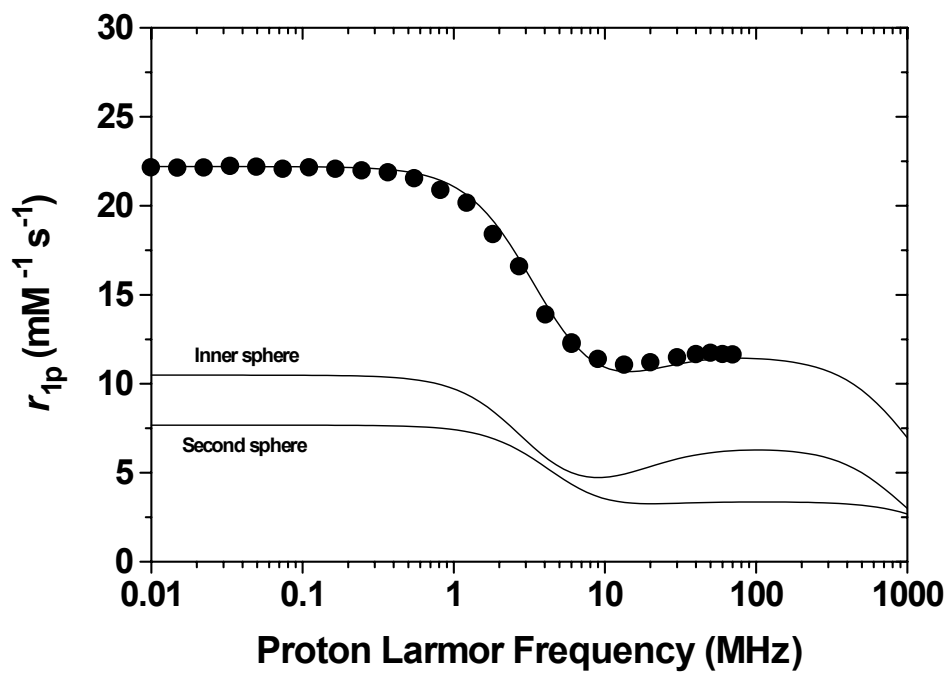
white solids. Purification by gel-filtration chromatography (Biogel P-6) afforded the pure product (32 mg, 42%) as a fluffy white powder after lyophilization, as confirmed by electrospray analysis.

ES-MS: $[M]^{2-} = 1715$, $[M]^{3-} = 1143$ (tetraamide product).

HRMS (ES⁻) calcd. for $C_{124}H_{204}N_{12}O_{88}$ $[M]^{2-}$: 1715.0712; found 1715.0714.

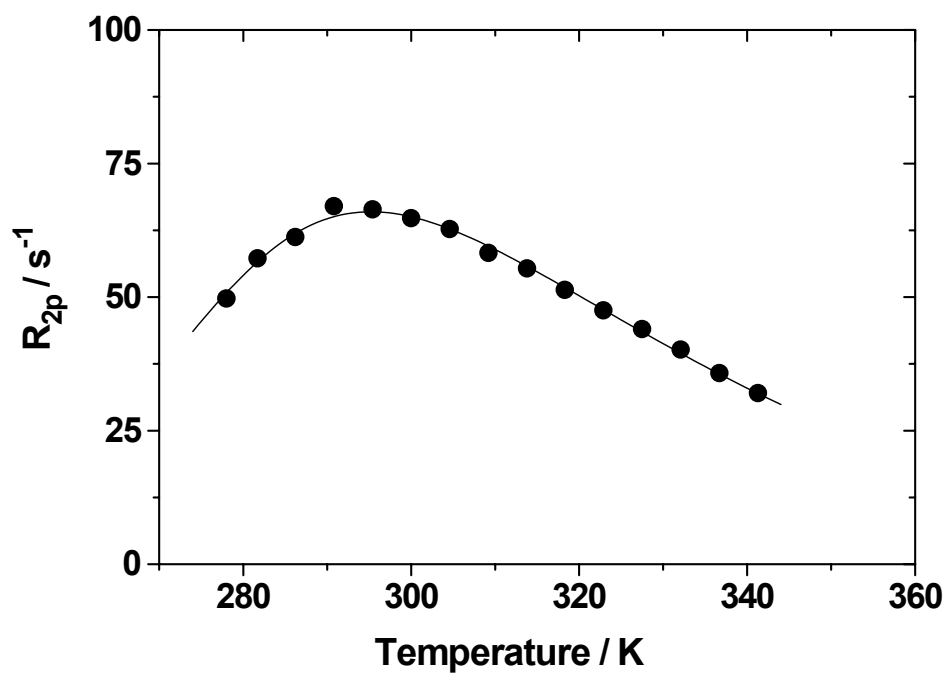
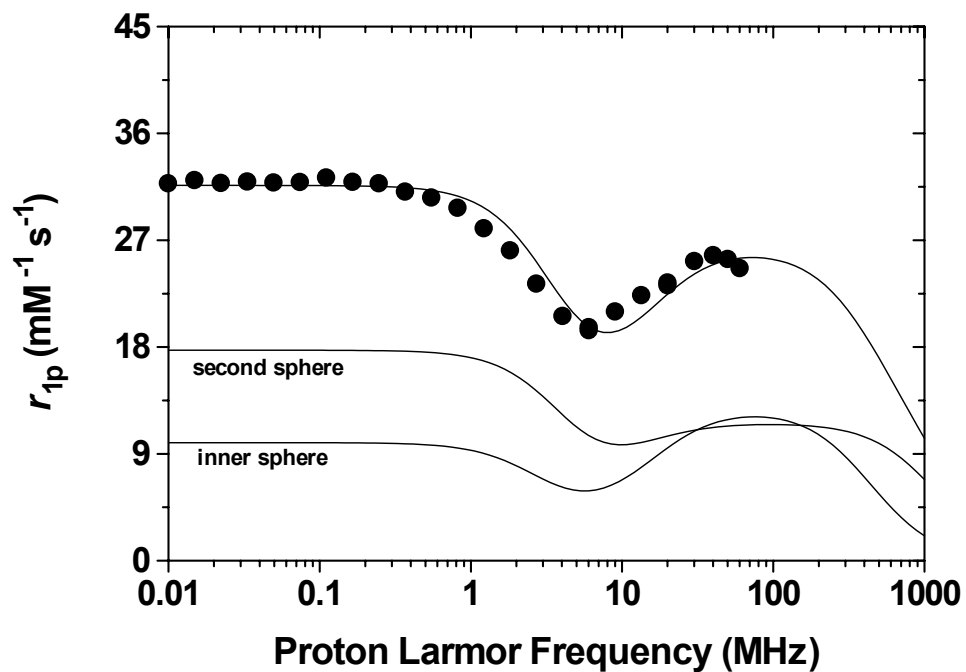
2. NMRD and VT 17-O (2.1 T) Profiles

(TRIS)₄GdgDOTA, 6



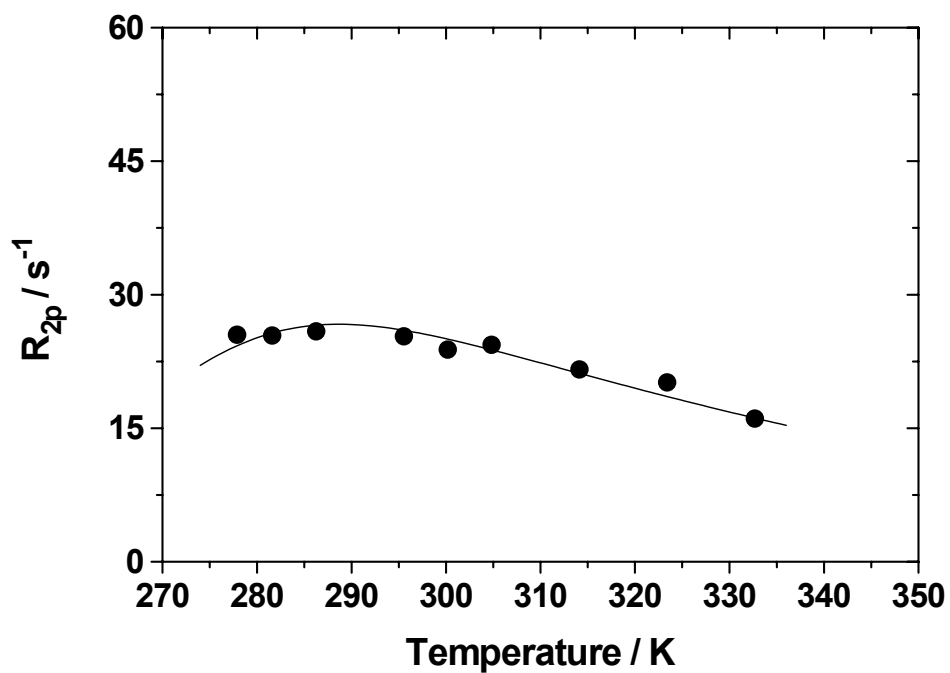
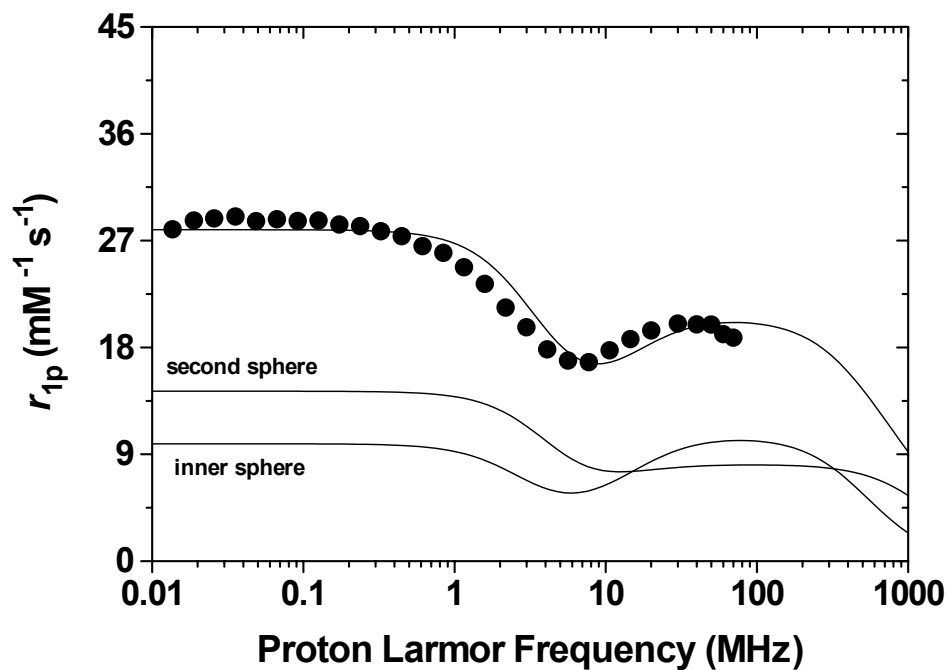
concentration of 6: 32mM

(Glu)₁₂GdgDOTA, 4



concentration of 4: 4 mM

(Glu)₁₂glyGdgDOTA, 5



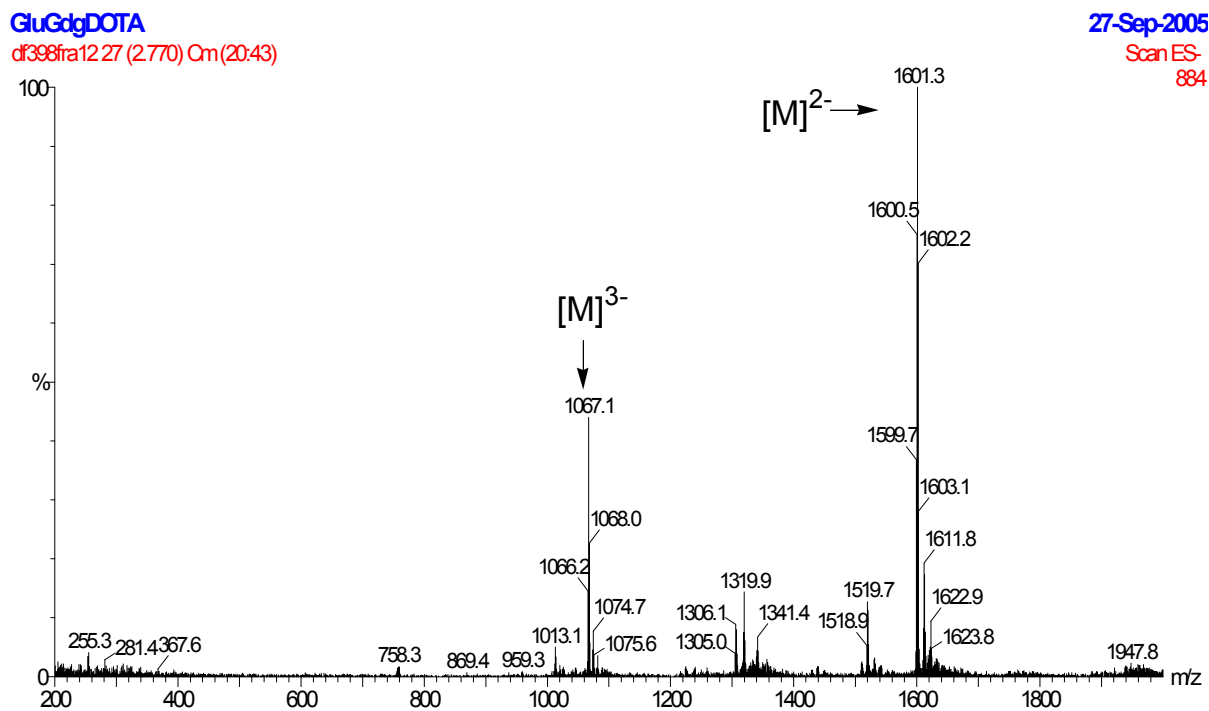
concentration of 5: 3mM

Best fit parameters (25°C) of NMRD and ¹⁷O data

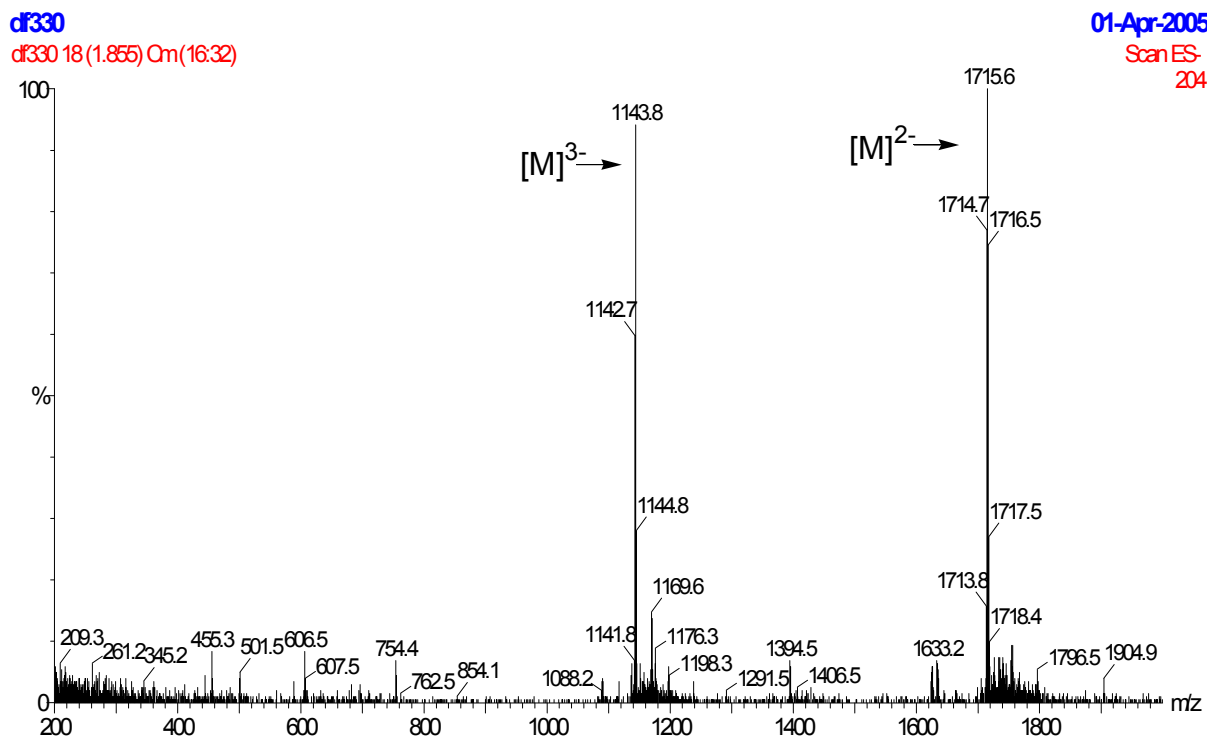
	4	5	6
Δ^2 (s ⁻¹ ; × 10 ⁻¹⁹)	3.7	3.4	3.7
τ_v (ps)	20.0	20.1	13.0
τ_R (ps)	390	318	173
τ_M (ns)	198	221	93
ΔH_M (kJmol ⁻¹)	45.3	46.0	51.0
q	1	1	1
r (Å)	3.0	3.0	3.0
a (Å)	4	4	4
D (cm ² s ⁻¹ ; × 10 ⁻⁵)	2.24	2.24	2.24
q'	8	8	4
r' (Å)	3.70	3.8	3.73
τ_R' (ps)	133	110	81

3. Sample low- and high-resolution electrospray mass spectra for 4 and 5.

Glu₁₂GdgDOTA 4 (Low resolution electrospray mass spectrum).



Glu₁₂glyGdgDOTA 5 (Low resolution electrospray mass spectrum).



Glu₁₂GdgDOTA 4 (High resolution electrospray mass spectrum) .

DF366_050705152149 #1-156 RT: 0.00-4.97 AV: 156 NL: 3.83E3
T: FTMS - c ESI Full ms [400.00-4000.00]

