SUPPORTING INFORMATION

Per(6-guanidino-6-deoxy)cyclodextrins: Synthesis, characterisation and binding behaviour toward selected small molecules and DNA.

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Experimental Section

General. The 1D and 2D NMR spectra were acquired at 500 MHz in DMSO-d_6 or D_2O, as indicated. Some ^{13}C NMR spectra were acquired on an AC 250 instrument at 62.9 MHz. The 2D spectra COSY and HSQC were acquired using the pulse sequences provided by the instrument's software employing gradient selection. Dimethylformamide (DMF) was dried over CaH_2 for 48 h and then distilled under reduced pressure. Cyclodextrins were dried under vacuum at 80 ºC overnight. Triphenyl phosphine was freshly recrystallized from hexane. *N,N*-Diisopropylethylamine (DIPEA) and pyrazole-1*H*-carboxamidine hydrochloride were used as received.

REFERENCES ARE NUMBERED AS IN THE MAIN TEXT.

***Hexakis*(6-bromo-6-deoxy)-α-cyclodextrin (1a)**. It was prepared according to ref. 4a in 86% yield (presence of ~2% residual Ph_3PO); mp = 195-197 ºC; lit[7a] mp = 222 ºC; mp lit[7c] mp = 195-196 ºC; ^1H (DMSO-d_6, 500 MHz) δ 5.81 (d, J = 6.8 Hz, 6H, OH2), 5.66 (d, J = 2.2 Hz, 6H,

OH3), 4.94 (d, J = 2.7 Hz, 6H, H1), 3.92-3.98 (m, 12H, H5, H6), 3.81 (t, J = 8.4, 6H, H3), 3.74 (dd, J = 17.6 Hz, J = 6.6 Hz, 6H, H6'), 3.42 (t, J = 8.9 Hz, 6H, H4), 3.35 –3.32 (m, 6H, H2) ppm; ^{13}C (DMSO-d_6, 125 MHz) δ 102.75 (C1), 85.59 (C4), 73.37 (C3), 72.53 (C2), 71.52 (C5), 35.68 (C6) ppm, in agreement with the corresponding lit.[7a] data.

***Heptakis*(6-bromo-6-deoxy)-β-cyclodextrin (1b)**. It was prepared according to ref. 4a in 85% yield (presence of ~5% residual Ph_3PO); mp = 212 ºC**;** lit[7a] mp =214 ºC; lit[7c] mp =205-206 ºC; lit[7d] mp =300 ºC; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 6.02 (d, J = 6.4 Hz, 7H, OH2), 5.89 (br s, 7H, OH3), 4.98 (d, J = 2.9 Hz, 7H, H1), 4.00 (d, J = 10.3 Hz, 7H, H6), 3.82 (t, J = 7.9 Hz, 7H, H5), 3.69 - 3.62 (m, 14H, H6', H3), 3.40- 3.34 (m, 14H, H2, H4) ppm; ^{13}C (DMSO-d_6, 62.9 MHz) δ 102.08 (C1), 84.59 (C4), 72.25 (C3), 72.03(C2), 70.98 (C5), 34.42 (C6) ppm, in agreement with the corresponding lit.[7a] data.

***Octakis*(6-bromo-6-deoxy)-γ-cyclodextrin (1c)**. It was prepared according to ref. 4a in 86% yield (presence of ~2% residual Ph_3PO); mp = 196-198 ºC; lit[5c] mp = 201-202 ºC; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 6.00 (d, J = 6.4 Hz, 8H, OH2,), 5.97 (br s, 8H, OH3), 5.01 (d, J = 2.6 Hz, 8H, H1), 3.98 (d, J = 10.0 Hz, 8H, H6), 3.81 (t, J = 8.0 Hz, 8H, H5), 3.68 (dd, J = 8.0 Hz, J = 10.0 Hz, 8H, H6'), 3.61 (t, J = 8.8 Hz, 8H, H3), 3.40-3.34 (m, 16H, H2, H4) ppm; ^{13}C (DMSO-d_6, 125 MHz) δ 101.9 (C1), 83.93 (C4), 72.15 (C2), 72.06 (C3), 70.89 (C5), 34.26 (C6-Br) ppm, in agreement with the corresponding lit.[7e] data.

***Hexakis*(6-azido-6-deoxy)-α-cyclodextrin (2a).** It was prepared according to ref. 8 in 98% yield; mp = 235-236 ºC; ^{1}H NMR (DMSO-d_6, 298K, 500 MHz) δ 5.65 (d, J = 7.0 Hz,, 6H, OH2), 5.47 (d, J = 2.4 Hz, 6H, OH3), 4.88 (d, J = 3.3 Hz, 6H, H1), 3.84-3.75 (m, 6H, H5), 3.77-3.70 (m, 12H, H6, H3), 3.58 (dd, J = 13.2 Hz , J = 7.0 Hz, 6H, H6'), 3.42-3.30 (m, 12H, H2, H4, partially overlapping with the residual HDO signal) ppm; ^{13}C NMR (DMSO-d_6, 125

MHz) δ 101.79 (C1), 83.41 (C4), 72.72 (C3), 71.59 (C2), 70.41 (C5), 51.37 (C6) ppm, in agreement with the corresponding lit.[1,7e] data.**;** IR (KBr pellet): 3368 (br, str, OH); 2920 (str, CH.); 2097 (str, -N_3); 1654 (str) cm-[1].

***Heptakis*(6-azido-6-deoxy)-β-cyclodextrin** (**2b**); It was prepared according to ref. 8; Yield 96% mp = 241-242 ºC; lit.[3a] mp = 240-245 ºC (dec); ^{1}H NMR (DMSO-d_6, 298K, 500 MHz) δ 5.90 (br s, 14H, OH2), 5.75 (br s, 14H, OH3), 4.91 (d, J = 2.7 Hz, 7H, H1), 3.78 (d, J = 12.3 Hz, 7H, H6), 3.73 (t, J = 9.3 Hz, 7H, H3), 3.60 (m, 14H, H6', H5), 3.37 (m, 7H, H2), partially overlapping with 3.34 (m, 7H, H4) ppm; ^{13}C NMR (DMSO-d_6, 298K, 125 MHz) δ 102.15 (C1), 83.12 (C4), 72.77 (C5), 71.95 (C2), 70.31 (C3), 51.22 (C6-N_3) ppm, in agreement with lit.[8] ^{13}C NMR data in the same solvent; IR (KBr pellet): 3377 (br, str O-H); 2920 (str, C-H.); 2099 (str, -N_3); 1654 (str) cm^{-1}.

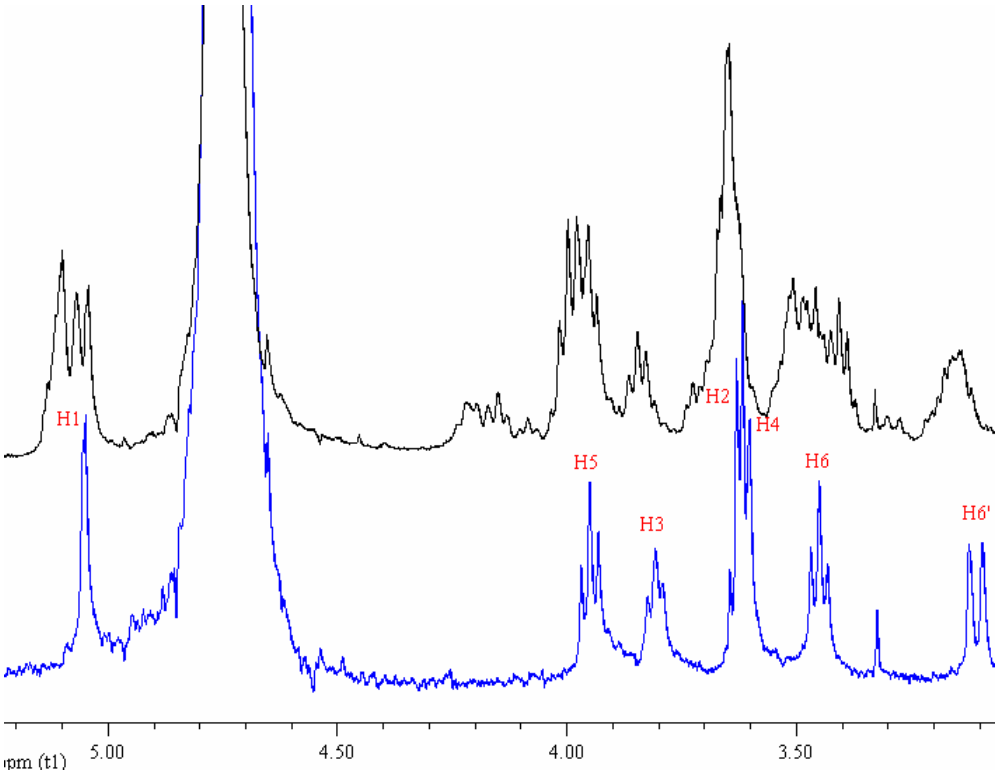
***Octakis*(6-azido-6-deoxy)-γ-cyclodextrin** (**2c**). It was prepared according to ref. 8 in 75% yield; mp = 210-212 ºC**;** ^{1}H NMR (DMSO-d_6, 298K, 500 MHz) δ 5.92 (d, J = 7.2 Hz, 8H, OH2), 5.86 (d, J = 2.0 Hz, 8H, OH3), 4.94 (d, J = 3.5 Hz, 8H, H1), 3.74 (m, 8H, H5), 3.73 (d, J = 11.6 Hz, 8H, H6), 3.58 (8H, H6') overlapping with 3.57 (H3, 8H), 3.39 (m, 8H, H2), overlapping with 3.35 (t, J = 8.8 Hz, 8H, H4) ppm; ^{13}C NMR (DMSO-d_6, 298K, 125 MHz) δ 101.9 (C1), 82.44 (C4), 72.25 (C3), 72.01 (C2), 70.20 (C5), 51.07 (C6-N_3) ppm, in agreement with lit.[3a, 7e] data. IR (KBr pellet): 3358 (br, str, OH); 2916 (str, CH.); 2098 (str, -N_3); 1654 (str) cm^{-1}.

***Hexakis*(6-amino-6-deoxy)-α-cyclodextrin** (**3a**). It was prepared according to ref. 8 in 70% yield (free base); mp = 389-390 ºC (dec); ^{1}H NMR (D_2O/DCl, 298K, 500 MHz) δ 5.16 (d, J = 3.2 Hz, 6H, H1), 4.19 (m, 6H, H5), 4.01 (t, J = 9.0 Hz, 6H, H3), 3.67 (dd, J = 3.1 Hz, J = 10.5 Hz, 6H, H2), 3.59 (t, J = 9.0 Hz, 6H, H4), 3.44 (dd, J = 3.0 Hz, J = 13.5 Hz, 6H, H6), 3.26 (dd,

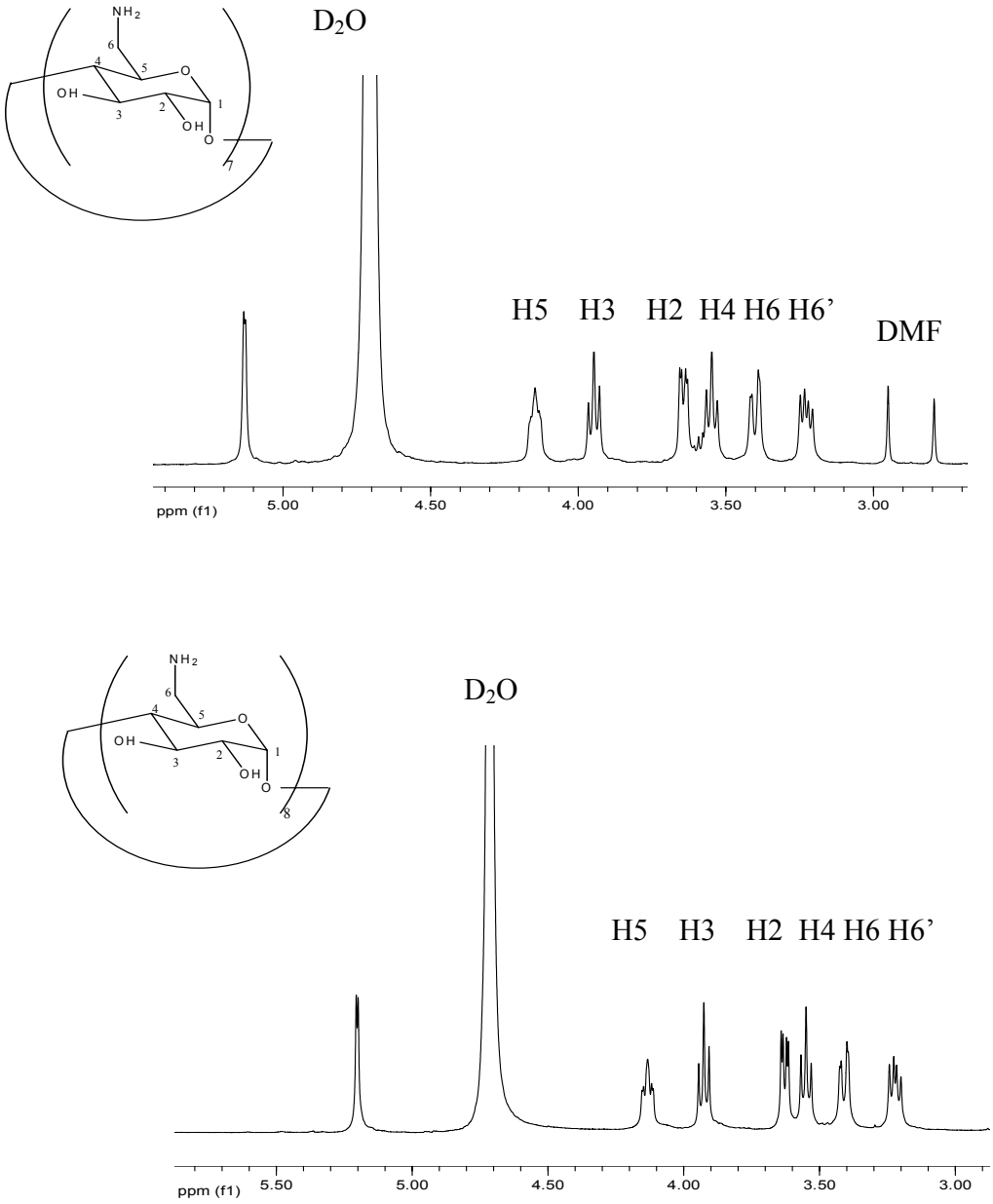
J = 6.5 Hz, *J* = 13.5 Hz, 6H, H6') ppm; ^{13}C (D_2O/DCl, 125 MHz) δ 101.6 (C1), 82.67 (C4), 72.82 (C3), 71.60 (C2), 68.40 (C5), 40.56 (C6-NH_2) ppm, in agreement with lit.[3a] data; ^{1}H NMR (DMSO-d_6, 298K, 500 MHz) δ 8.26 (br s, disappears with D_2O, NH_2), 5.62 (br m, diminishes with D_2O, 12H, OH2, OH3), 5.08 (d, *J* = 2.6 Hz, 6H, H1), 4.26 (br t, *J* = 8 Hz, 6H, H5), 3.86 (t, *J* = 9.5 Hz, 6H, H3), 3.54 (t, *J* = 9.2 Hz, 6H, H4), 3.45 (dd, *J* = 2.7 Hz, *J* = 9.7 Hz, 6H, H2), 3.39 (d, *J* = 12.9 Hz, 6H, H6), 3.01 (m, 6H, H6') ppm.

***Heptakis*(6-amino-6-deoxy)-β-cyclodextrin (3b).** It was prepared according to ref. 8 in 61% yield (free base); mp =392 ºC (dec) ^{1}H NMR (D_2O/ DCl, 298K, 500 MHz) δ 5.13 (d, *J* = 3.0 Hz, 7H, H1), 4.15 (m, 7H, H5), 3.95 (t, *J* = 9.7 Hz, 7H, H3), 3.64 (dd, *J* = 9.7 Hz, *J* = 3.0 Hz, 7H, H2), 3.55 (t, *J* = 9.5 Hz, 7H, H4), 3.40 (dd, *J* = 13.3 Hz, *J* = 2.6 Hz, 7H, H6), 3.23 (dd, *J* = 13.3 Hz, *J* = 6.7 Hz, 7H, H6') ppm; ^{13}C (D_2O/DCl, 125 MHz) δ 100.9 (C1), 81.65 (C4), 71.52 (C3), 71.12 (C2), 67.39 (C5), 39.52 (C6-NH_2) ppm, in agreement with lit.[3a] data. ^{1}H NMR (DMSO-d_6, 298K, 500 MHz) δ 8.23 (br s, NH_2), 5.93 (d, *J* = 6.60 Hz, 6H, OH2), 5.84 (br s, 6H, OH3) 5.05 (br s, 6H, H1), 4.04 (t, *J* = 8,1 Hz, 6H, H5), 3.64 (t, *J* = 9.2 Hz, 6H, H3), 3.49 (t, *J* = 8.8 Hz, 6H, H4), 3.42 (br s, 6H, H2), 3.30 (H6 hidden under HDO peak), 3.03 (m, 6H, H6') ppm.

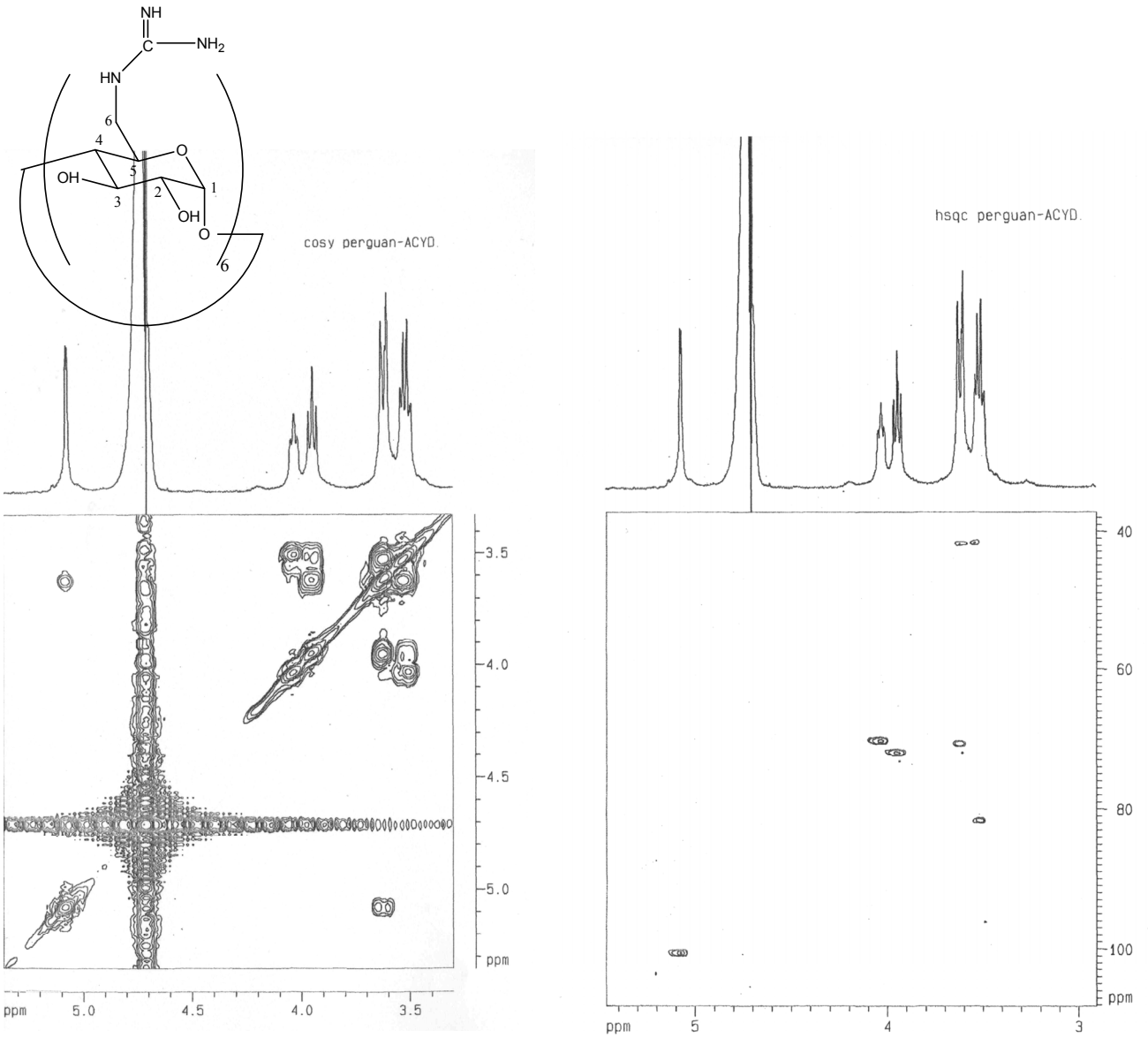
***Octakis*(6-amino-6-deoxy)-γ-cyclodextrin (3c)**. It was prepared according to ref. 8 in 75% yield (free base); mp = 396-397 ºC (dec) ^{1}H NMR (D_2O/ DCl, 298K, 500 MHz) δ 5.20 (d, *J* = 3.5 Hz, 8H, H1), 4.13 (m, 8H, H5), 3.93 (t, *J* = 9.7 Hz, 8H, H3), 3.63 (dd, *J* = 9.7 Hz, *J* = 3.5 Hz, 8H, H2), 3.55 (t, *J* = 9.5 Hz, 8H, H4), 3.41 (dd, *J* = 13.5 Hz, *J* = 2.5 Hz, 8H, H6), 3.22 (dd, *J* = 13.5 Hz, *J* = 8.3 Hz, 8H, H6') ppm; ^{13}C (D_2O/DCl, 125 MHz) δ 99.88 (C1), 80.35 (C4), 71.23 (C3), 71.00 (C2), 67.01 (C5), 39.55 (C6-NH_2) ppm, in agreement with lit.[3a] data.



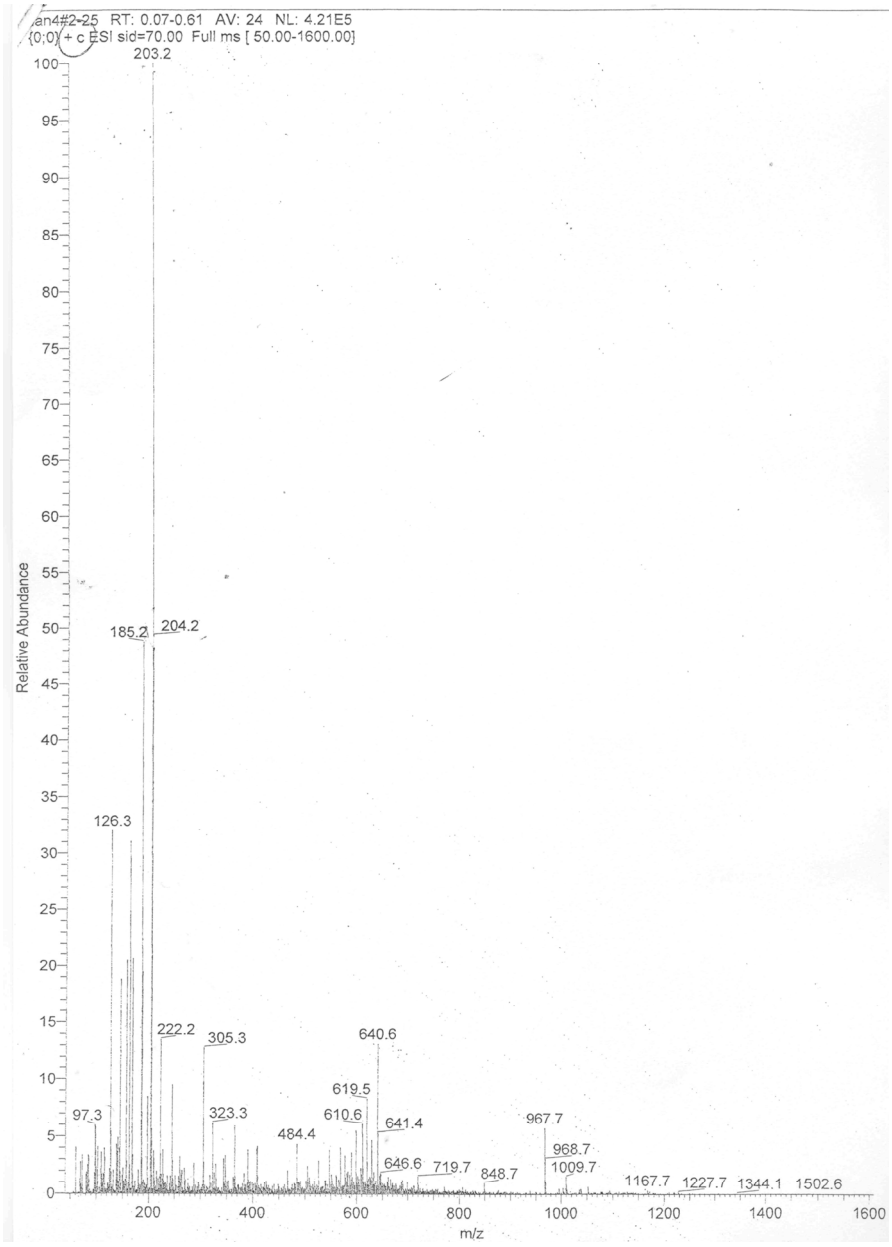
Supporting Figure 1. *Bottom*: ^{1}H NMR spectrum of *hexakis*(6-amino-6-deoxy)-α-cyclodextrin hydrochloride (**3a)** in D_2O at pH ~3 (DCl) , corresponding to a symmetrical α-cyclodextrin derivative i.e. fully aminated in the primary side and protonated. *Top*: ^{1}H NMR spectrum of **3a** in D_2O at pH 7 showing complete breaking of the symmetry. The ^{13}C spectrum was the same in both cases.



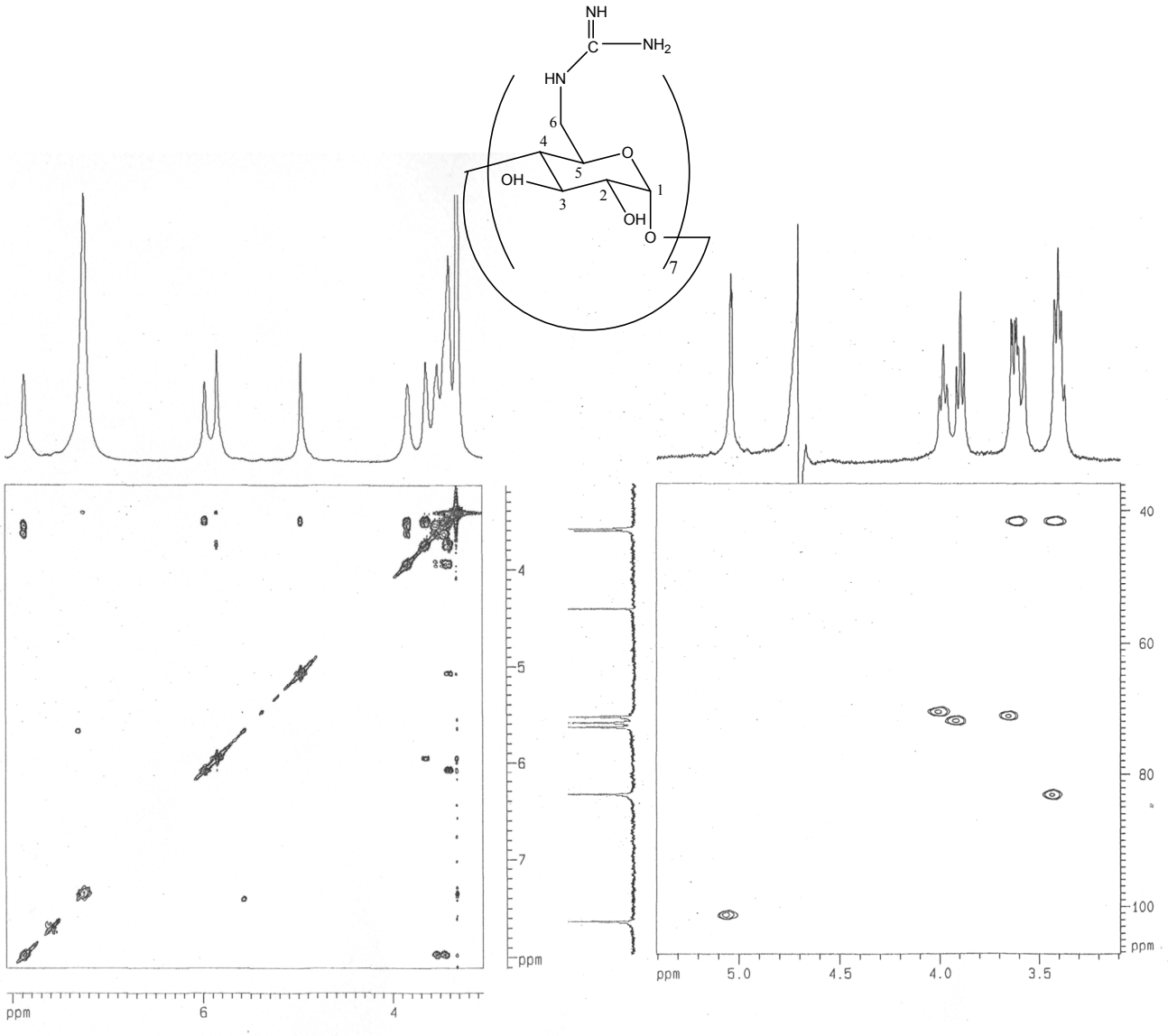
Supporting Figure 2. *Top*: ^{1}H NMR spectrum of *heptakis*(6-amino-6-deoxy)-β-cyclodextrin hydrochloride (**3b)** in D_2O. *Bottom*: ^{1}H NMR spectrum of *octakis*(6-amino-6-deoxy)-γ-cyclodextrin hydrochloride (**3c).**



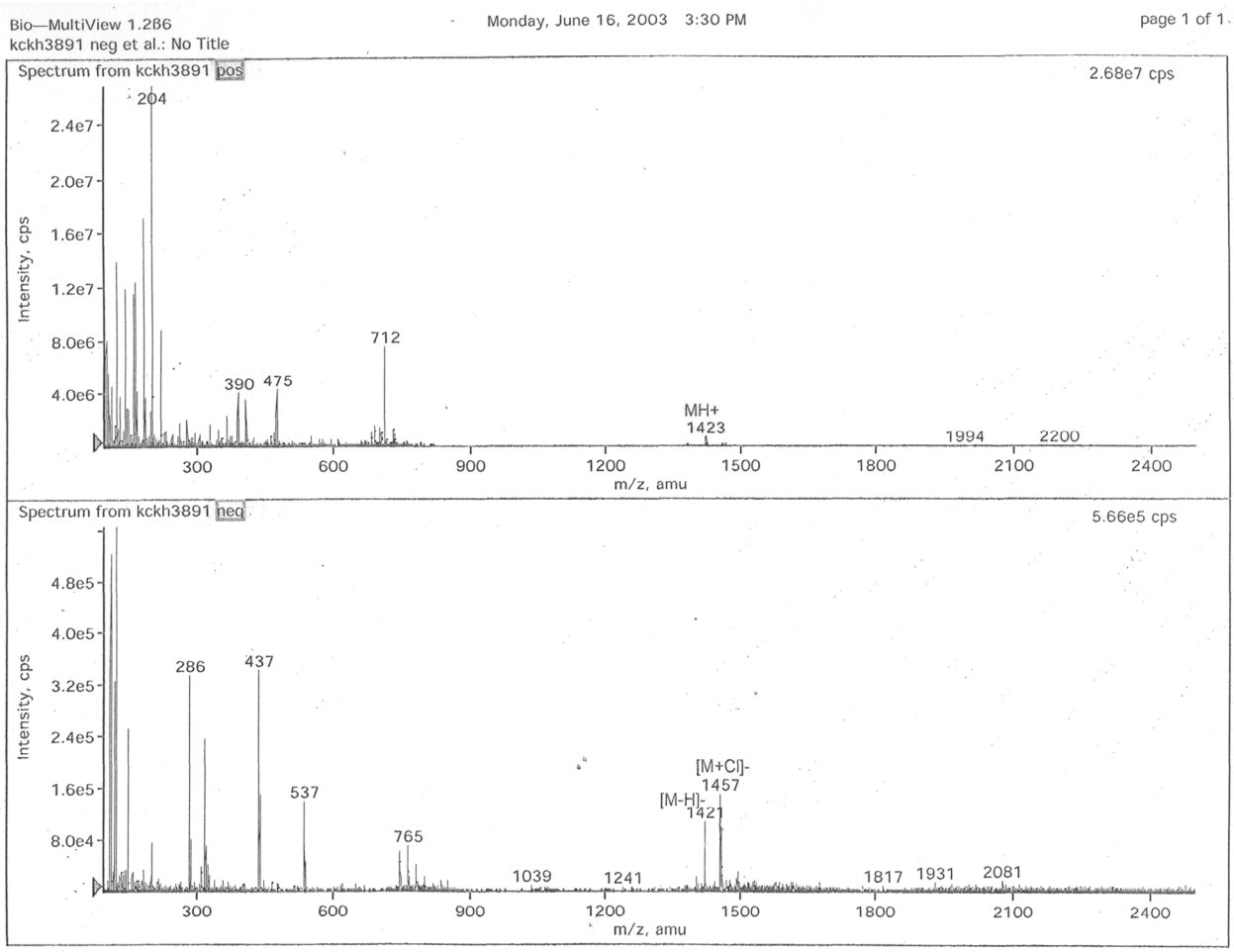
Supporting figure 3. *Left*: Partial ^{1}H-^{1}H correlation, and *Right*: Partial ^{1}H-^{13}C correlation NMR spectrum of *hexakis*(6-guanidino-6-deoxy)-α-cyclodextrin hydrochloride (**4a),** in D_2O.



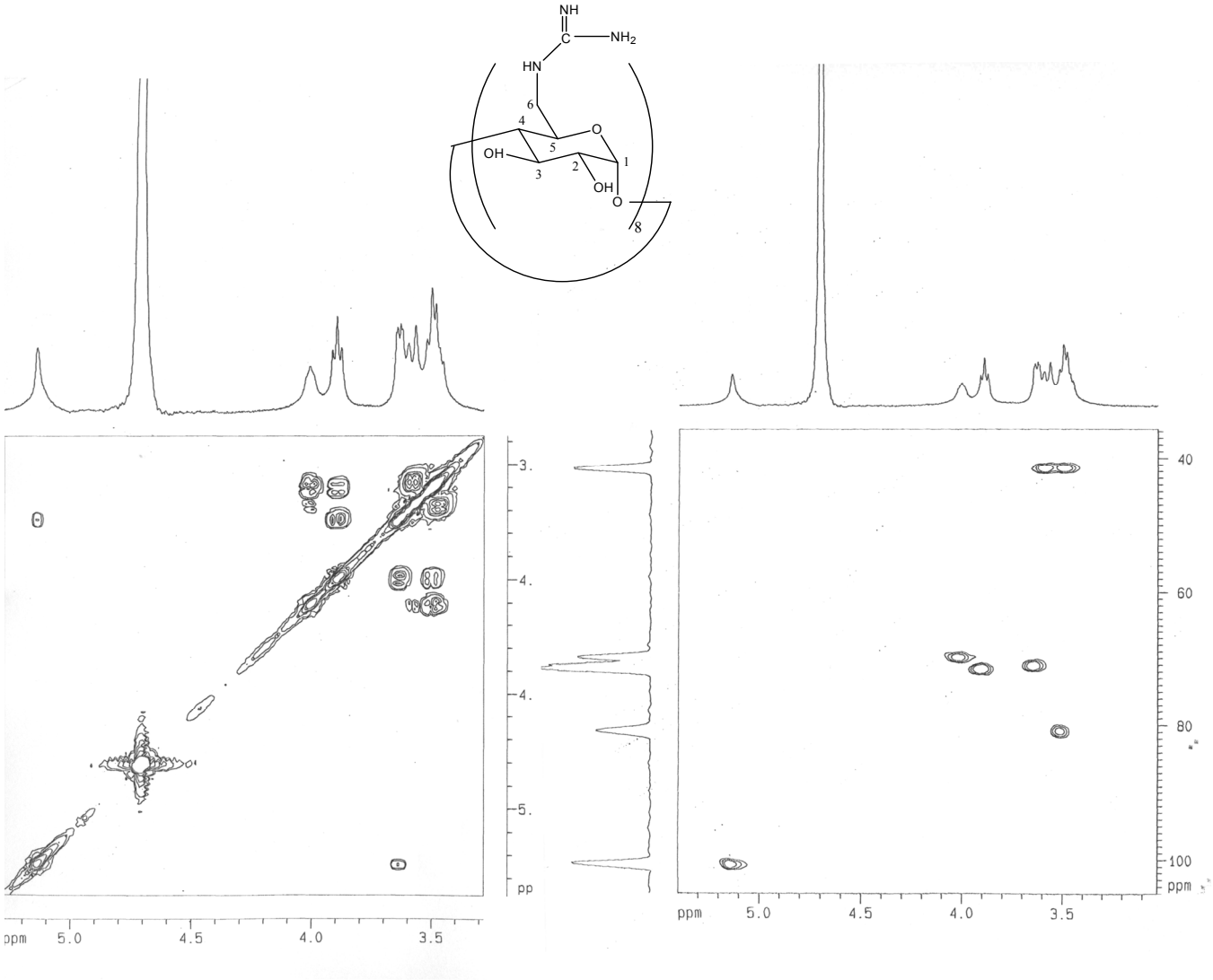
Supporting figure 4. ESI mass spectrum of *hexakis*(6-guanidino-6-deoxy)-α-cyclodextrin hydrochloride (**4a),** in positive mode.



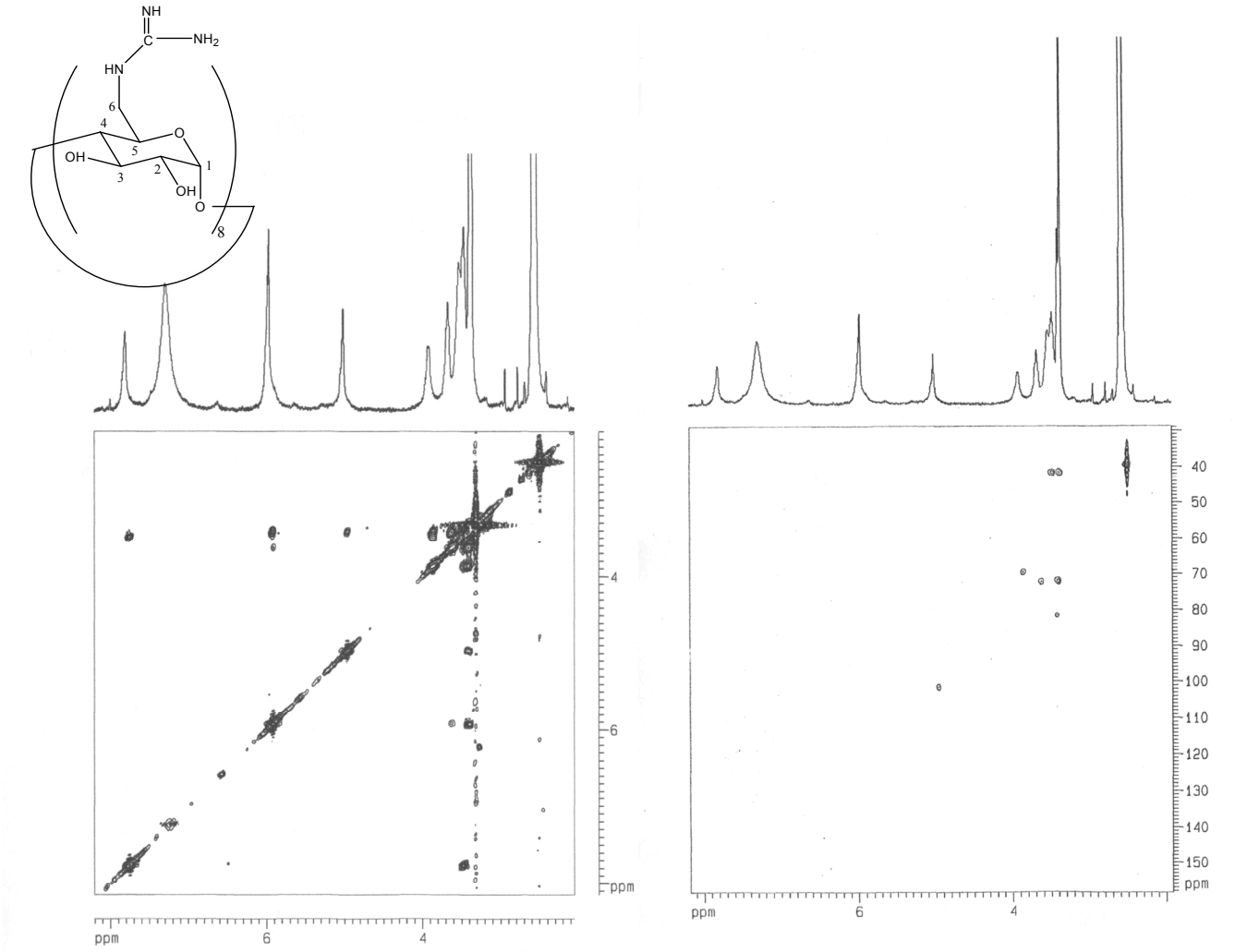
Supporting figure 5. *Left*: Partial ^{1}H-^{1}H correlation NMR spectrum in DMSO-d_6, and *Right*: Partial ^{1}H-^{13}C correlation NMR spectrum in D_2O of *heptakis*(6-guanidino-6-deoxy)-β-cyclodextrin hydrochloride (**4b).**



Supporting figure 6. ESI mass spectrum of *heptakis*(6-guanidino-6-deoxy)-β-cyclodextrin hydrochloride (**4b),** in positive (top) and negative (bottom) mode.



Supporting figure 7 *Left*: Partial ^{1}H-^{1}H correlation NMR spectrum, and *Right*: Partial ^{1}H-^{13}C correlation NMR spectrum in D_2O of oc*takis*(6-guanidino-6-deoxy)-γ-cyclodextrin hydrochloride (**4c**).



Supporting figure 8. *Left*: Partial ^{1}H-^{1}H correlation NMR spectrum, and *Right*: Partial ^{1}H-^{13}C correlation NMR spectrum of oc*takis*(6-guanidino-6-deoxy)-β-cyclodextrin hydrochloride (**4c)** in DMSO-$_{d6}$.

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Table 1: Volumes used for agarose gel electrophoresis.

Lane	Compound	V (µl)	Lane	Compound	V (µl)
1	λHindIII	2	**9**	Calf Thymus DNA	1
2	Calf Thymus DNA	1	**10**	**4b** + DNA	2 +1
3	guanidine.HCl + DNA	10 +1	**11**	**4b** + DNA	5 +1
4	αCD + DNA	10 +1	**12**	**4b** + DNA	10 +1
5	**4a** + DNA	2 +1	**13**	γCD + DNA	10 +1
6	**4a** + DNA	5 +1	**14**	**4c** + DNA	2 +1
7	**4a** + DNA	10 +1	**15**	**4c** + DNA	5 +1
8	βCD + DNA	10 +1	**16**	**4c** + DNA	10 +1