Electronic Supplementary Information

for

Reverse-CD mimics with flexible linkages offer adaptable cavity sizes for guest encapsulation

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Electronic Supplementary Material (ESI) for Chemical Communications
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1) Materials and methods

Chemicals and solvents were purchased from sigma Aldrich and used directly. TLC analyses were done using precoated TLC silica gel 60 F254 (Merck) plates. Chromatograms were visualized under UV light and by dipping plates into chromic acid solution followed by heating. Melting points were recorded on a Stuart, SMP 30 melting point apparatus. NMR spectra were recorded on an Avance III-500 (Bruker) NMR spectrometer. IR spectra were recorded by preparing KBr pellets, using IR Prestige-21 (Shimadzu) spectrometer. Elemental analyses were done on Elementar, vario MICRO cube elemental analyzer. Axima CFRplus MALDI-TOF spectrometer (Shimadzu Biotech) was used to analyze molecular masses of cyclic oligomeric compounds. HRMS was recorded using MICRO-Q TOF mass spectrometer in the ESI mode. Guest binding studies were done using $^1$H NMR in D$_2$O and isothermal titration calorimetry (MicroCal iTC200) at room temperature (30 °C). Single crystal X-ray intensity data was collected on a Bruker KAPPA APEX-II diffractometer in omega and phi scan mode, MoKα = 0.71073 Å at 298 K.

2) Synthesis of R-CD analogs

![Scheme S1. Synthesis of R-CD analogs. a) NaOAc, Ac$_2$O, 60 °C, 12h, 90%; b) Me$_3$SiN$_3$, SnCl$_4$, DCM, rt, Ar, 12h, 95%; c) i) NaOMe, MeOH, rt, ii) PhCH(OMe)$_2$, TsOH, MeCN, rt, j) NaOAc, Ac$_2$O, 60 °C, 12h, 90%]

*Scheme S1.* Synthesis of R-CD analogs. a) NaOAc, Ac$_2$O, 60 °C, 12h, 90%; b) Me$_3$SiN$_3$, SnCl$_4$, DCM, rt, Ar, 12h, 95%; c) i) NaOMe, MeOH, rt, ii) PhCH(OMe)$_2$, TsOH, MeCN, rt,
Ar, 24h, 83% (2 steps); d) BnBr, NaH, DMF, 0 °C-rt, 3h, 90%; e) Et₃SiH, CF₃COOH, (CF₃CO)₂O, DCM, 0 °C-rt, 5h, 78%; f) Propargyl bromide, NaH, DMF, -15 °C, 2h, 87%; g) Cul, DIPEA, THF, Ar, rt, 24h, 90%; h) Pd/C (w/w 10%), HCOONH₄, EtOAc:EtOH:H₂O (v/v/v 2:2:1), 50 °C, 20h (>90%).

**a) Synthesis of diol 7:** To a solution of 2,3,4,5-tetra-O-acetyl-β-galactosylazide (6)¹ (8.75 g, 23.46 mmol) in MeOH (100 mL), NaOMe (150 mg) was added and the mixture was stirred at room temperature. The reaction was followed by TLC. At about an hour, TLC showed the completion of the reaction with the formation of a new single polar spot. The reaction mixture was filtered through Dowex-200 (H⁺) resin. The filtrate was evaporated under reduced pressure and the residue was further dried under high vacuum. The residue was then dissolved in dry acetonitrile (100 mL). To this p-toluenesulfonic acid (223 mg, 1.17 mmol) and benzaldehydedimethylacetal (17.6 mL, 117.29 mmol) were added and the mixture was stirred at rt for 24h by which time the TLC showed completion of reaction. The reaction was quenched by adding triethylamine (1 mL), solvent was evaporated using a rotary evaporator under reduced pressure and the crude mixture thus obtained was dissolved in ethyl acetate. The solution was washed with distilled water, the organic layer was separated and the aqueous layer was re-extracted with ethyl acetate (2 x 50 mL). The combined organic layer was washed with brine and dried over anhyd. Na₂SO₄ and evaporated under reduced pressure. The crude solid thus obtained was purified by column chromatography using a mixture of ethylacetate and petroleum ether (3:2 v/v) as eluent to obtain pure diol 7 (5.56g, 83%) as a colorless solid. Melting point: 134-136 °C. ¹H NMR (CDCl₃, 500 MHz) δ 7.41 (m, 2H, C₆H₅), 7.30 (m, 3H, C₆H₅), 5.43 (s, 1H, PhCH), 4.45 (d, J = 8.5 Hz, H-1), 4.25 (d, J = 12.5 Hz, H-6a), 4.08 (m, 1H, H-4), 3.95 (d, J = 12.5 Hz, H-6b), 3.62-3.53 (m, 2H, H-2& H-3), 3.43 (m, 1H, H-5), 3.20 (br, 1H, -OH), 3.06 (br, 1H, -OH). ¹³C NMR (CDCl₃, 125 MHz) δ 137.38, 129.41,
128.35, 126.40 (C₆H₅), 101.46 (PhCH), 90.27 (C-1), 75.11 (C-4), 72.81 (C-3), 71.07 (C-2), 68.89 (C-6), 68.38 (C-5). IR (KBr): 2120 cm⁻¹ (azide); 3378 cm⁻¹ (OH) and 3535 cm⁻¹ (OH). Elemental analysis, calculated for C₁₃H₁₅N₃O₅ C = 53.24, H = 5.16, N = 13.38; Found C = 53.49, H = 5.21, N = 13.38.

b) Synthesis of dibenzyl ether 8: To a cooled solution (0 °C) of the diol 7 (3.0 g, 10.23 mmol) in dry DMF (30 mL), sodium hydride (1.435 g, 35.84 mmol) was added in portions and stirred for 10 minutes at 0 °C. To this, benzyl bromide (3.65 mL, 30.72 mmol) was added dropwise and the mixture was stirred further for half an hour at 0 °C and then warmed to room temperature. Reaction was monitored by TLC and it was complete after 3h. The reaction mixture was quenched with ice cold water and the solvent was evaporated under reduced pressure. The residue was dissolved in chloroform and the solution was washed successively with distilled water and brine, organic layer was dried over anhyd. Na₂SO₄ and evaporated under reduced pressure. The crude solid thus obtained was chromatographed using 15% ethyl acetate in petroleum ether as eluent to yield dibenzyl ether 8 as a colorless solid (4.32 g, 90%). Melting point: 119-120 °C. \(^1\)H NMR (CDCl₃, 500 MHz) δ 7.47 (d, J = 7 Hz, 2H, o-Hs of a phenyl ring), 7.31-7.21 (m, 13H, C₆H₅), 5.40 (s, 1H, PhCH), 4.77 (s, 2H, OCH₂Ph), 4.67 (s, 2H, OCH₂Ph), 4.55 (d, J = 8.5 Hz, 1H, H-1), 4.24 (d, J = 12.5 Hz, 1H, H-6a), 4.06 (d, J = 3.5 Hz, 1H, H-4), 3.93 (d, J = 12.5 Hz, 1H, H-6b), 3.72 (t, J = 9.5 Hz, 8.5 Hz, 1H, H-2), 3.51 (dd, J = 9.5 Hz, 3.5 Hz, 1H, H-3), 3.33 (br, 1H, H-5). \(^{13}\)C NMR (CDCl₃, 125 MHz) δ 138.17, 138.08, 137.71, 129.11, 128.45, 128.41, 128.25, 128.19, 127.87, 127.84, 127.80, 126.48, 101.42 (PhCH), 90.36 (C-1), 79.68 (C-3), 77.66 (C-2), 75.61 (OCH₂Ph), 73.43 (C-4), 71.88 (OCH₂Ph), 69.00 (C-6), 68.26 (C-5). IR (KBr): 2108 cm⁻¹ (azide). Elemental analysis,
c) **Synthesis of tribenzyl ether 9:** To a cooled solution (0 °C) of the dibenzyl ether 8 (4.3 g, 9.091 mmol) in dry DCM (100 mL), triethylsilane (7.24 mL, 45.46 mmol) and trifluoroacetic anhydride (3.79 mL, 27.27 mmol) were added. To this cooled solution, trifluoroacetic acid (3.53 mL, 45.46 mmol) was added dropwise and the reaction mixture was gradually allowed to warm to room temperature. The reaction was completed after 5h (TLC) and was quenched with saturated aqueous sodium bicarbonate solution. DCM layer was separated and aqueous layer was extracted with chloroform. The combined organic layer was dried over anhyd. Na₂SO₄ and evaporated under reduced pressure. The crude solid thus obtained was purified by column chromatography using 15% ethyl acetate in petroleum ether as eluent to obtain tribenzyl ether 9 (3.35 g, 78%) as a colorless solid. Melting point: 134-136 °C. ¹H NMR (CDCl₃, 500 MHz) δ 7.29-7.21 (br m, 15H, 3 X C₆H₅), 4.78-4.69 (m, 2H, OCH₂Ph), 4.67-4.59 (m, 2H, OCH₂Ph), 4.51 (s, 2H, 6-OCH₂Ph), 4.50 (d, J = 9 Hz, H-1), 3.98 (m, 1H, H-4), 3.73-3.65 (m, 2H, H-6a& H-6b), 3.57-3.52 (m, 2H, H-2& H-5), 3.45 (dd, J = 9 Hz, 3.0 Hz, H-3), 2.51 (br, 1H, 4-OH). ¹³C NMR (CDCl₃, 125 MHz) δ 137.92, 137.76, 137.55, 128.60, 128.52, 128.46, 128.35, 128.22, 128.11, 127.94, 127.90, 90.28 (C-1), 80.93 (C-3), 78.16 (C-2), 75.53 (OCH₂Ph), 75.23 (C-5), 73.84, 72.34 (2 X OCH₂Ph), 69.01 (C-6), 66.68 (C-4). Elemental analysis, calculated for C₂₇H₂₉N₃O₅, C = 68.19, H = 6.15, N = 8.84; Found C = 68.01, H = 6.14, N = 8.63.

d) **Synthesis of 1:** To a cooled solution (-15 °C) of tribenzyl ether 9 (3.3 g, 6.98 mmol) in dry DMF (30 mL), sodium hydride (558 mg, 13.95 mmol) was added in portions and
stirred at the same temperature for 10 minutes. Propargyl bromide (0.933 mL, 10.47 mmol) was then added dropwise and stirred at the same temperature till the reaction was complete (2h). The reaction mass was quenched with ice cold water and the solvent was evaporated under reduced pressure. The crude mixture was dissolved in chloroform and washed with distilled water and brine. The organic layer was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure using a rotary evaporator. The crude solid thus obtained was chromatographed using 8% ethylacetate in petroleum ether as eluent to yield 1 (3.1 g, 87%) as a colorless solid. This has to be stored as a solution in organic solvent such as THF, chloroform or should be made fresh just before use. Melting point: 84-85 °C. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ 7.28-7.21 (m, 15H, 3xC$_6$H$_5$), 4.77-4.62 (m, 4H, 2xOCH$_2$Ph), 4.54 (d, $J = 8.45$ Hz, 1H, H-1), 4.50 (s, 2H, 6-OCH$_2$Ph), 4.42 (d of AB q, $J = 39.85$ Hz, 16.05 Hz, 2.15 Hz, 2H, OCH$_2$CCH), 4.06 (d, $J = 2.3$ Hz, 1H, H-4), 3.70-3.68 (m, 1H, H-6a), 3.62-3.59 (m, 3H, H-2, H-5 & H-6b), 3.48-3.46 (dd, $J = 9.6$ Hz, 2.6Hz, 1H, H-3), 2.33 (s, 1H, CCH). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ 138.03, 137.91, 137.83, 128.50, 128.46, 128.40, 128.16, 127.90, 127.88, 127.84, 127.83, 127.75 (ArC), 90.49 (C-1), 82.38 (C-3), 80.04 (C-5), 78.82 (CCH) 75.66 (C-2), 75.57 (OCH$_2$Ph), 74.97 (CCH), 73.72, 73.11 (2XOCH$_2$Ph), 71.96 (C-4), 68.94 (C-6), 59.36 (-OCH$_2$CCH). IR (KBr): 2116 cm$^{-1}$ (azide), 3240 cm$^{-1}$ (alkyne). Elemental analysis calculated for C$_{30}$H$_{31}$N$_3$O$_5$, C = 70.16, H = 6.08, N = 8.18; Found C = 70.24, H = 6.05, N = 8.09.

e) Cyclooligomerization of monomer 1: A solution of the azide 1 (1.0 g, 1.94 mmol), CuI (185.6 mg, 0.97 mmol) and diisopropylethylamine (6.8 mL, 38.98 mmol) in dry THF (50 mL) was stirred at rt. TLC showed completion of the reaction after 24h. THF was evaporated under reduced pressure. The crude mass thus obtained was dissolved in
chloroform and filtered through a small bed of silica (~5 cm). The IR spectrum of crude product of cyclization has shown absence of azide and alkyne signals suggesting that the starting material was consumed completely and converted into cyclic products. The MALDI spectrum of the crude reaction mass showed the presence of dimer to heptamer. The colorless crude solid was purified by flash column chromatography using a mixture of ethylacetate and petroleum ether (2:3 v/v) as the eluent. Cyclic dimer 10 (151 mg, 15%), cyclic trimer 11 (215 mg, 22%), cyclic tetramer 12 (150 mg, 15%) and cyclic pentamer 13 (50 mg, 5%) were obtained as colorless solids in pure form and the higher cyclic oligomers (330 mg, 33%) were obtained as a mixture. The $^1$H NMR spectra of these cyclic compounds were found to be different from each other.

**Cyclic dimer 10:** Melting Point: 141-142 °C. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ 7.77 (s, 1H, triazol-H), 7.45-7.29 (m, 10H, ArH), 7.23-7.19 (m, 2H, ArH), 7.13-7.11 (m, 3H, ArH), 5.89 (d, $J = 7.8$ Hz, 1H, H-1), 5.19 (d, $J = 11.5$ Hz, 1H, PhCH$_2$), 4.83 (ABq, $J = 11.5$, 25.35 Hz, 2H, PhCH$_2$), 4.75 (d, $J = 11.5$ Hz, 1H, PhCH$_2$), 4.56 (d, $J = 10.75$ Hz, 1H, PhCH$_2$), 4.50 (s, 2H, PhCH$_2$), 4.24 (d, $J = 10.75$ Hz, 1H, PhCH$_2$), 4.19 (d, $J = 1.9$ Hz, 1H, H-4), 4.00 (dd, $J = 7.95$, 9.3 Hz, 1H, H-2), 3.86-3.84 (m, 1H, H-5), 3.81 (dd, $J = 2$, 9.4 Hz, 1H, H-3), 3.59-3.57 (m, 1H, H-6a), 3.56-3.50 (m, 1H, H-6b). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ 148.25 (C-8), 137.6, 137.3, 136.9, 128.68, 128.57, 128.42, 128.35, 128.18, 128.11, 128.02, 127.97, 127.93, 120.01 (C-9), 87.91 (C-1), 82.14 (C-3), 79.69 (C-2), 75.19, 74.74 (C-5), 73.62, 72.52, 71.75 (C-4), 67.70 (C-6), 66.18 (C-7). Elemental analysis calculated for C$_{60}$H$_{62}$N$_6$O$_{10}$, C = 70.16, H = 6.08, N = 8.18; Found C = 70.01, H = 6.36 N = 8.50. $m/z$ calculated for C$_{60}$H$_{62}$N$_6$O$_{10}$Na [M+Na]$^+$ 1050.158; found, 1050.53.
**Cyclic trimer 11**: Melting Point: 90-91 °C. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ 7.77 (s, 1H, triazol-$H$), 7.38-7.28 (m, 10H, Ar$H$), 7.18-7.16 (m, 3H, Ar$H$), 6.97-6.95 (m, 2H, Ar$H$), 5.72 (d, $J = 9.1$ Hz, 1H, H-1), 5.23 (d, $J = 12.0$ Hz, 1H, PhCH$_2$), 4.81 (d, $J = 12.0$ Hz, 1H, PhCH$_2$), 4.79 (ABq, $J = 11.7$, 34.25 Hz, 2H, PhCH$_2$), 4.45 (s, 2H, PhCH$_2$), 4.41 (d, $J = 10.75$ Hz, 1H, PhCH$_2$), 4.16 (t, $J = 9.2$ Hz, 1H, H-2), 4.10 (d, $J = 2.3$ Hz, 1H, H-4), 4.03 (d, $J = 10.75$ Hz, 1H, PhCH$_2$), 3.88 (t, $J = 6.6$ Hz, 1H, H-5), 3.79 (dd, $J = 2.7$, 9.35 Hz, 1H, H-3), 3.65-3.58 (m, 2H, H-6a & H-6b). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ 146.28 (C-8), 137.61, 137.38, 137.18, 128.59, 128.51, 128.31, 128.15, 128.10, 128.01, 127.99, 127.87, 127.78, 119.95 (C-9), 88.09 (C-1), 82.37 (C-3), 77.84 (C-2), 76.15 (C-4 or C-5), 76.02 (C-5 or C-4), 74.79, 73.73, 72.97, 68.45 (C-7), 67.69 (C-6). Elemental analysis calculated for C$_{90}$H$_{93}$N$_9$O$_{15}$, C = 70.16, H = 6.08, N = 8.18; Found C = 70.35, H = 6.27, N = 8.42. m/z calculated for C$_{90}$H$_{93}$N$_9$O$_{15}$Na $[M+Na]^+$ 1563.75; found, 1565.65.

**Cyclic tetramer 12**: Melting Point: 96-97 °C. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ 7.60 (s, 1H, triazol-$H$), 7.48 (br, 2H, Ar$H$), 7.4-7.33 (m, 3H, Ar$H$), 7.25-7.2 (m, 6H, Ar$H$), 7.14-7.12 (m, 2H, Ar$H$), 7.01 (br, 2H, Ar$H$), 5.63 (d, $J = 9.0$ Hz, 1H, H-1), 5.05-4.97 (m, 2H), 4.83 (br, 2H), 4.61 (d, $J = 10.9$ Hz, 1H), 4.23-4.16 (m, 4H, H-2, H-4), 4.10 (d, $J = 11.65$ Hz, 1H), 3.79 (br, 1H, H-3), 3.73 (br, 1H, H-5), 3.30 (br, 2H, H-6a & H-6b). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ 145.5 (C-8), 137.72, 137.52, 137.25, 128.61, 128.5, 128.37, 128.32, 128.01, 127.89, 127.83, 121.01 (C-9), 88.01 (C-1), 82.99 (C-3), 77.55 (C-2), 76.16 (C-5), 73.34, 73.27, 72.84 (C-4), 67.84 (C-6), 65.98 (C-7). Elemental analysis calculated for C$_{120}$H$_{124}$N$_{12}$O$_{20}$, C = 70.16, H = 6.08, N = 8.18; Found C = 69.85, H = 6.43, N = 8.37. m/z calculated for C$_{120}$H$_{125}$N$_{12}$O$_{20}$ $[M+H]^+$ 2053.91; found, 2054.39.
Cyclic pentamer 13: Melting point: 110-111°C. $^1$H NMR (CDCl$_3$, 500 MHz) δ 7.48 (s, 1H), 7.38-7.37 (br, 2H), 7.30-7.23 (m, 3H), 7.14-7.07 (m, 6H), 7.03-7.01 (m, 2H), 6.91 (br, 2H), 5.51 (d, $J = 9$ Hz, 1H, H-1), 4.93 (d, $J = 12.5$ Hz, 1H), 4.87 (d, $J = 11.5$ Hz, 1H), 4.72 (d, $J = 11.6$ Hz, 2H), 4.13-4.06 (m, 4H), 3.99 (d, $J = 11.75$ Hz, 1H), 3.69 (dd, $J = 2.35$ Hz, 9.35 Hz, 1H), 3.62 (t, $J = 6.2$ Hz, 1H), 3.19 (d, $J = 6.6$ Hz, 1H). $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 145.00, 137.66, 137.47, 137.20, 128.62, 128.37, 128.04, 127.99, 127.93, 127.85, 127.83, 121.40, 88.14, 82.91, 77.37, 76.16, 74.92, 73.31, 72.87, 67.84, 65.49. m/z calculated for C$_{150}$H$_{155}$N$_{15}$O$_{25}$K [M+K]$^+$ 2605.10; found, 2610.46.

Figure S1: $^1$H NMR Comparison of (A) Crude product after the cyclization reaction with (B) Cyclic dimer 10, (C) Cyclic trimer 11, (D) Cyclic tetramer 12 and (E) Cyclic pentamer 13.
Figure S2: MALDI spectra of the crude product of the cyclization reaction, showing the presence of dimer to heptamer.

f) **General procedure for the debenzylation of the cyclic galactomers**: To a solution of cyclic dimer 10 (550 mg, 0.536 mmol) in mixture of ethylacetate:ethanol:water (10 mL, v/v/v 2:2:1) in a pressure tube, Pd/C (10% w/w, 3.41 g, 3.216 mmol) and ammonium formate (4.05 g, 64.33 mmol) were added. The tube was closed tightly and was heated to 50 °C for 20h. After 20h, the reaction mixture was cooled to room temperature and was diluted with methanol (10 mL) and water (10 mL). The reaction mixture was filtered and the filtrate was evaporated under reduced pressure. The residue was then re-dissolved in milli-Q water and was further purified by dialysis using Spectra-phor dialyzer (MWCO 100Da).

**Cyclic dimer 2**: Melting point: 122-123 °C. [α]D = +17.5° (c 0.3, water). \(^1\)H NMR (D2O, 500 MHz) δ 8.36 (s, 1H), 5.69 (d, J = 9.1 Hz, 1H, H-1), 4.90 (d, J = 11.9 Hz, 1H, H7a), 4.79 (d, J = 11.9 Hz, 1H, H7b), 4.14 (t, J = 9.55 Hz, 1H, H-2), 4.08 (br, 1H, H-4), 4.00-3.99 (m, 2H, H-3 & H-5), 3.64-3.56 (m, 2H, H-6a & H-6b). \(^1\)C NMR (D2O, 125 MHz) δ 144.63 (C-8), 123.95 (C-9), 88.17 (C1), 77.99 (C-5), 77.30 (C-4), 73.47 (C-3), 70.06 (C-
Cyclic trimer 3: Melting point: 76-77 °C. $[\alpha]_D = +5.0^\circ$ (c 0.2, water). $^1$H NMR (D$_2$O, 500 MHz) $\delta$ 8.37 (s, 1H, triazol-H), 5.71 (d, $J = 9.5$ Hz, 1H, H-1), 5.05 (d, $J = 12$ Hz, 1H, H-7a), 4.76 (d, $J = 12$ Hz, 1H, H-7b), 4.13 (t, $J = 9.5$ Hz, 1H, H-2), 4.05 (br, 1H, H-4), 4.01-3.97 (m, 2H, H-3 & H-5), 3.64-3.56 (m, 2H, H-6a & H-6b). $^{13}$C NMR (D$_2$O, 125 MHz) $\delta$ 145.68 (C-8), 122.53 (C-9), 88.08 (C-1), 78.75 (C-4 or C-5), 78.02 (C-5 or C-4), 73.28 (C-3), 69.80 (C-2), 67.40 (C-7), 60.53 (C-6). HRMS (ES) calcd. for C$_{27}$H$_{39}$N$_9$O$_{15}$[M]+ 729.2566; found, 729.2559.

Cyclic tetramer 4: Melting point: 145-146 °C. $[\alpha]_D = +2.66^\circ$ (c 0.3, water). $^1$H NMR (D$_2$O, 500 MHz) $\delta$ 8.34 (s, 1H), 5.67 (d, $J = 9.05$ Hz, 1H, H-1), 5.01 (d, $J = 11.8$ Hz, 1H, H-7a), 4.77 (br, 1H, H-7b), 4.12 (t, $J = 9.6$ Hz, 1H, H-2), 4.09 (br, 1H, H-4), 3.98-3.96 (m, 1H, H-3 & H-5), 3.63-3.55 (m, 1H, H6a & H-6b). $^{13}$C NMR (D$_2$O, 125 MHz) $\delta$ 144.63, 123.97, 88.15, 77.96, 77.27, 73.45, 70.04, 65.87, 60.54. HRMS (ES) calcd. for C$_{36}$H$_{52}$N$_{12}$O$_{20}$[M]+ 972.3421; found, 972.3417.

3) Optimization of dimer 2, trimer 3 and tetramer 4

The dimer 2, trimer 3 and tetramer 4 were optimized for their possible low energy structures using quantum mechanical techniques using B3LYP/6-311+G(d,p)$^2$ and M05-2X/6-311+G(d,p) levels of theory (Guassian09$^3$).
Figure S3. Minimum energy (DFT- M05-2X) structures of (A) dimer 2, (B) trimer 3 and (C) tetramer 4.

### Dimer 2/ M05-2X/6-311+G(d,p)

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Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2013
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S17
4) Crystal structure of trimer 3

Trimer 3 (50 mg) was crystallized from ethanol:chloroform mixture (7:3, v/v). The rectangular plate type crystals were analyzed using single crystal X-ray diffraction. X-ray intensity data measurements of freshly grown crystal of 3 were carried out at 298K on a Bruker-KAPPA APEX II CCD diffractometer with graphite-monochromatized (MoKα = 0.71073 Å) radiation. The X-ray generator was operated at 50 kV and 30 mA. The X-ray data collection was monitored by SMART program (Bruker, 2003). All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2003). SHELX-97 was used for structure solution and full matrix least-squares refinement on F2. Molecular and packing diagrams were generated using ORTEP-3 and Mercury-3. Geometrical calculations were performed using SHELXTL (Bruker, 2003) and PLATON. The asymmetric unit contains two molecules of trimer 3 and nine water molecules.

Crystal data for 3: CCDC 960369 (C27H39N9O15)2(H2O)9, M = 1620.61, colorless rectangular plate type, 0.2 x 0.15 x 0.1 mm³, Monoclinic, space group P21, a = 14.434, b = 14.233, c = 17.487 Å, V = 3589.9 Å³, Z = 2, T = 296(2) K, 2θ max = 50.00°, D calc (g cm⁻³) = 1.483, F(000) = 1680, μ (mm⁻¹) = 0.128, 12068 reflections collected, 6604 unique reflections (R int = 0.1243), multi-scan absorption correction, T min = 0.975, T max = 0.987, number of parameters = 1003, number of restraints = 3, GoF = 1.036, R1 = 0.0663, wR2 = 0.2090, R
indices based on 7341 reflections with I > 2s(I) (refinement on F2). \( \Delta \rho_{\text{max}} = 0.083, \Delta \rho_{\text{min}} = -0.010 \) (eÅ\(^{-3}\)).

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We have carried out VT-NMR studies of trimer 3 and tetramer 4 in both D$_2$O and CD$_3$OD. As temperature increased H-2 proton, located inside the ring, shifted slightly downfield (up to 0.05 ppm) whereas triazolyl proton shifted up-field (up to 0.07 ppm). However large shifts are not observed. The flexible nature of these compounds (rotation of triazolyl ring and conformational flexibility of O-CH2 linkages) may be allowing multiple conformations of similar energies. The time averaged spectra of several interconvertible conformations may not show a remarkable difference in NMR signals.

Figure S5: Temperature variable $^1$H NMR spectral overlay of cyclic trimer 3 in CD$_3$OD.
**Figure S6**: Temperature variable \(^1\)H NMR spectral overlay of cyclic tetramer 4 in CD\(_3\)OD.
Figure S7: Temperature variable $^1$H NMR spectral overlay of cyclic trimer 3 in D$_2$O.
Figure S8: Temperature variable $^1$H NMR spectral overlay of cyclic tetramer 4 in D$_2$O.

6) **Binding studies of cyclic trimer 3 and cyclic tetramer 4**

a) **Binding studies of trimer 3 with 3-butyn-1-ol and benzoic acid**

The binding of trimer 3 with 3-butyn-1-ol and benzoic acid were studied using MicroCal iTC200 and $^1$H NMR. All reagents were dissolved in milliQ water (for ITC experiments). The host, cyclic trimer 3 was taken in the cell and guest was loaded in the pipette. The first injection was 0.5 μL and the subsequent injections were 2 μL per 4 sec. and the duration between the injections was 180 sec. The interaction between host and guest led to release of energy and gradually decreased upon saturation. The blank titration (host vs water, same mode of addition with same interval) was subtracted from guest titration data and the resultant data was fitted using one-site binding curve in Microcal origin 7.0 software. As binding shows weak interaction of these guests with the host (trimer 3); the stoichiometry value was fixed for N = 1 and the data points were fitted. The association constants for the
interaction of 3 with 3-but-yn-1-ol and benzoic acid were found to be \( \sim 7 \text{ M}^{-1} \) and \( 3550 \text{ M}^{-1} \) respectively. These values were confirmed by repeated experiments. Apart from the ITC, we have monitored the guest binding ability of trimer 3 with above mentioned guests using \(^1\text{H}\) NMR titration experiments. The guest and host were dissolved in D\(_2\)O and \(^1\text{H}\) NMR spectra were recorded while titrating against guest. The spectra were calibrated with the external standard (1,4-dioxan in fused capillary tube). Both 3-but-yn-1-ol and benzoic acid have shown up field (\( \sim 0.02-0.1 \text{ ppm} \)) in their respective protons during the titration with cyclic trimer 3.

**Trimer 3 with 3-but-yn-1-ol**

The trimer 3 was taken in the cell (10.28 mM, 200 μL) in milliQ-water and 3-but-yn-1-ol (500 mM, 40 μL) was loaded in the pipette for ITC experiment.

\[ \begin{align*}
\text{Data: Data1_NDH} \\
\text{Model: OneSite} \\
\text{Chi}^2/\text{DoF} = 2.052 \\
N & = 1.00 \pm 0 \text{ Sites} \\
K & = 6.69 \pm 0.525 \text{ M}^{-1} \\
\Delta H & = -785.7 \pm 41.34 \text{ cal/mol} \\
\Delta S & = 1.19 \text{ cal/mol/deg}
\end{align*} \]

*Figure S9:* ITC profile for the binding of trimer 3 with 3-but-yn-1-ol.
**Figure S10:** $^1$H NMR titration of trimer 3 with 3-but-yn-1-ol.
Trimer 3 with 1-Butanol

The trimer 3 was taken in the cell (10.28 mM, 200 μL) in milliQ-water and 1-butanol (500 mM, 40 μL) was loaded in the pipette for ITC experiment.

Figure S11: ITC profile for the binding of trimer 3 with 1-butanol.
Figure S12: $^1$H NMR titration of trimer 3 with 1-butanol.
Cyclic Trimer with Propargyl Alcohol

The trimer 3 was taken in the cell (10.28 mM, 200 μL) in milliQ-water and propargyl alcohol (500 mM, 40 μL) was loaded in the pipette for ITC experiment.

![ITC profile for the binding of trimer 3 with propargyl alcohol.](image)

**Figure S13**: ITC profile for the binding of trimer 3 with propargyl alcohol.
Figure S14: $^1$H NMR titration of trimer 3 with propargyl alcohol.
Trimer 3 with Benzoic acid

The trimer 3 was taken in the cell (0.05 mM, 200 μL) in milliQ-water and benzoic acid (3.43 mM, 40 μL) was loaded in the pipette for ITC experiment.

**Figure S15**: ITC profile of the binding of trimer 3 with benzoic acid.
Figure S16: $^1$H NMR titration of trimer 3 with benzoic acid.
b) Binding studies of tetramer 4 with benzoic acid and phenol

The binding of tetramer 4 was examined using benzoic acid and the experiment was carried out at a constant temperature (30 °C) using MicroCal iTC200 and $^1$H NMR. The tetramer 4 was taken in the cell (0.463 mM, 200 μL) in milliQ-water and benzoic acid (4.63 mM, 40 μL) was loaded in the pipette. The first injection was 0.5 μL and the remaining injections were 2 μL per 4 sec. and the duration between the injections was 180 sec. The interaction between the host and guest led to release of energy and gradually decreased. The blank titration (Host vs water) was subtracted from substrate titration data and the resultant data was fitted using one-site binding curve in Microcal origin 7.0 software which showed a sigmoidal curve with a binding constant of ~30400 M$^{-1}$ for stoichiometry 1:1 (N = 0.91). The $^1$H NMR titration has shown up field shift of the guest protons.

Figure S17: ITC profile of the binding of tetramer 4 with benzoic acid.
Figure S18: $^1$H NMR titration of tetramer 4 with benzoic acid.
Titration of tetramer 4 with phenol

Figure S19: $^1$H NMR titration of tetramer 4 with phenol

c) Anion binding studies with trimer 3 and tetramer 4

The triazole based hosts are known to form inclusion complexes with various anions. We have examined the binding of anions (chloride and bromide) with these CD analogs using $^1$H NMR spectroscopy. However, no evidence of binding could be obtained. This is not surprising as anion recognition in water requires sufficient binding energy to overcome the high hydration energies of anions in water. Though triazole based receptors are known to bind anions, to the best of our knowledge, there are no reports on the anion binding of such ligands in water. The insolvability of our CD analogs in non-polar organic solvents precludes such anion binding studies in such solvents.
Titration of trimer 3 with \( n \)-tetrabutylamminiumchloride

Figure S20: \(^1\)H NMR titration of trimer 3 with \( n \)-tetrabutylammoniumchloride.
Titration of tetramer 4 with \( n \)-tetrabutylamminiumchloride

Figure S21: \(^1\)H NMR titration of tetramer 4 with \( n \)-tetrabutylammoniumchloride.

7) Spectral charts
Figure S22: $^1$H NMR (A) and COSY (B) spectra of compound 7 in CDCl$_3$
Figure S23: $^{13}$C (C), DEPT (D) and HMQC (E) spectra of compound 7 in CDCl$_3$. 
Figure S24: $^1$H NMR (A) and COSY (B) spectra of compound 8 in CDCl$_3$. 
Figure S25: $^{13}$C (C), DEPT (D) and HMQC (E) spectra of compound 8 in CDCl$_3$. 
Figure S26: $^1$H NMR (A) and COSY (B) spectra of compound 9 in CDCl$_3$. 

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Figure S27: $^{13}$C (C), DEPT (D) and HMQC (E) spectra of compound 9 in CDCl$_3$. 
**Figure S28**: $^1$H NMR (A) and COSY (B) spectra of compound 1 in CDCl$_3$. 
Figure S29: $^{13}$C (C), DEPT (D) and HMQC (E) spectra of compound 1 in CDCl$_3$. 
Figure S30: $^1$H NMR (A) spectrum of cyclic dimer 10 in CDCl$_3$. 
Figure S31: COSY and $^{13}$C spectra of cyclic dimer 10 in CDCl$_3$. 
Figure S32: DEPT and HMQC spectra of cyclic dimer 10 in CDCl₃.
Figure S33: HMBC and NOESY spectra of cyclic dimer 10 in CDCl₃.
Figure S34: MALDI spectrum of cyclic dimer 10.
Figure S35: $^1$H NMR spectra of cyclic trimer 11 in CDCl$_3$. 

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Figure S36: COSY and $^{13}$C spectra of cyclic trimer 11 in CDCl₃.
**Figure S37**: DEPT and HMQC spectra of cyclic trimer 11 in CDCl₃.
Figure S38: MALDI spectrum of cyclic trimer 11.
Figure S39: $^1$H NMR spectrum of cyclic tetramer 12 in CDCl$_3$. 
Figure S40: COSY and $^{13}$C spectra of cyclic tetramer 12 in CDCl$_3$. 
**Figure S41**: DEPT and HMQC spectra of cyclic tetramer 12 in CDCl$_3$. 
Figure S42: MALDI spectrum of cyclic tetramer 12.
**Figure S43**: $^1$H NMR spectrum of cyclic pentamer 13 in CDCl$_3$. 
Figure S44: COSY and $^{13}$C spectra of cyclic pentamer 13 in CDCl$_3$. 
Figure S45: DEPT and HMQC spectra of cyclic pentamer 13 in CDCl$_3$. 
Figure S46: $^1$H NMR spectrum of cyclic dimer 2 in D$_2$O
Figure S47: COSY and $^{13}$C spectra of cyclic dimer 2 in D$_2$O
Figure S48: DEPT and HMQC spectra of cyclic dimer 2 in D$_2$O
Figure S49: $^1$H NMR spectrum of cyclic trimer 3 in D$_2$O
Figure S50: COSY and $^{13}$C spectra of cyclic trimer 3 in D$_2$O
Figure S51: DEPT and HMQC spectra of cyclic trimer 3 in D$_2$O
**Figure S52**: $^1$H NMR spectrum of cyclic tetramer 4 in D$_2$O
Figure S53: COSY and $^{13}$C spectra of cyclic tetramer 4 in D$_2$O
Figure S54: DEPT and HMQC spectra of cyclic tetramer 4 in D$_2$O
7. References