ELECTRONIC SUPPLEMENTARY INFORMATION

Highly Fluorinated Cyclodextrins and their Host-Guest Interactions

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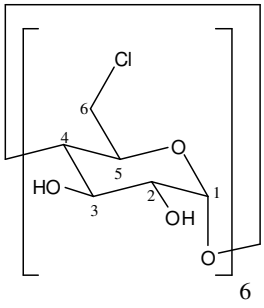
Synthesis

Synthesis of 6-chloro-6-deoxy-cyclodextrins 1a – 1c

The synthesis of perchlorinated cyclodextrins was accomplished as described by Guillo et al.[1] To a solution of 1 eq of cyclodextrin dissolved in DMF, 5.2 eq methylsulfonylchloride per glycose unit of the cyclodextrin is added and stirred at 65 °C for 4 d. The solution is concentrated, the residue is dissolved in methanol and neutralized with 3 M sodium methoxide. The product was precipitated in ice water, filtered out and washed with methanol. The product was vacuum-dried at 55 °C and was obtained as white solid.

Hexakis-(6-chloro-6-deoxy)-α-cyclodextrin 1a

Cyclodextrin **1a** was synthesized as described above with α-cyclodextrin (10.52 g, 10.81 mmol) and methylsulfonyl chloride (26.01, 335.6 mmol).



1a

Empirical formula (MW in g/mol): $C_{36}H_{54}O_{24}Cl_6$ (1083.52)

Yield: 78 % (9.19 g, 8.48 mmol)

MS (ESI, MeOH): 560,04 $[M + Ca]^{2+}$, 1103.10 $[M + Na]^+$,2183.22 $[2 M + Na]^+$

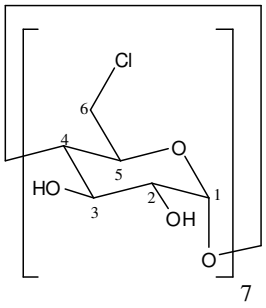
^{1}H NMR (400 MHz, DMSO) δ 5.76 (d, *J* = 5.4, 1H, 2-OH), 5.59 (s, 1H, 3-OH), 4.92 (d, *J* = 3.2, 1H, 1-H), 4.13 – 3.89 (m, 2H, 5-H, 3-H), 3.90 – 3.71 (m, 2H, 4-H, 2-H), 3.44 (t, *J* = 8.9, 1H, 6a-H), 3.36 (s, 2H, 6b-H).

^{13}C NMR (101 MHz, DMSO) δ 101.92 (1-C), 83.60 (4-C), 72.65 (3-C), 71.64 (2-C), 70.83 (5-C), 45.30 (6-C).

[1] F. Guillo, B. Hamelin, L. Jullien, J. Canceill, J. M. Lehn, L. de Robertis and H. Driguez, *Bull. Soc. Chim. Fr.*, 1995, **132**, 857.

Heptakis-(6-chloro-6-deoxy)-β-cyclodextrin 1b

Cyclodextrin **1b** was synthesized as described above with β-cyclodextrin (10.04 g, 8.81 mmol) and methylsulfonyl chloride (24.8, 230 mmol).



1b

Empirical formula (MW in g/mol): $C_{42}H_{63}O_{28}Cl_7$ (1264.10)

Yield: 89 % (9.86 g, 7.80 mmol)

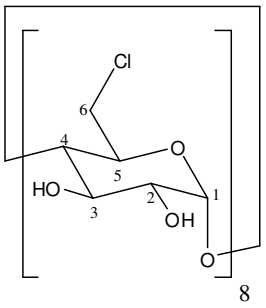
MS (ESI, MeOH): 1287.12 $[M + Na]^+$, 1919.19 $[3 M + 2 Na]^{2+}$

^{1}H NMR (300 MHz, DMSO) δ 6.00 (d, *J* = 6.6, 1H, 2-OH), 5.85 (d, *J* = 1.5, 1H, 3-OH), 4.96 (d, *J* = 3.5, 1H, 1-H), 4.13 – 4.02 (m, 1H, 5-H), 3.91 – 3.70 (m, 2H, 3-H, 4-H), 3.60 (dt, *J* = 8.5, 6.9, 1H, 6a-H), 3.42 – 3.29 (m, 3H, 2-H, 6b-H).

^{13}C NMR (75 MHz, DMSO) δ 102.08 (1-C), 83.62 (4-C), 72.48 (3-C), 72.02 (2-C), 71.21 (5-C), 45.00 (6-C).

Octakis-(6-chloro-6-deoxy)-γ-cyclodextrin 1c

Cyclodextrin **1c** was synthesized as described above with γ-cyclodextrin (10.11 g, 7.79 mmol) and methylsulfonyl chloride (25.28, 325.78 mmol).



1c

Empirical formula (MW in g/mol): $C_{48}H_{72}O_{32}Cl_8$ (1444.69)

Yield: 84 % (9.49 g, 6.57 mmol)

MS (ESI, MeOH): 743.07 $[M + 2 Na]^{2+}$, 1467.13 $[M + Na]^+$

^{1}H NMR (300 MHz, DMSO) δ 6.01 (s, 2H, 2,3-OH), 4.98 (d, *J* = 3.7, 1H, 1-H), 4.02 (d, *J* = 9.9, 1H, 6a-H), 3.91 – 3.74 (m, 2H, 5-H), 3.60 (t, *J* = 9.2, 1H, 3-H), 3.37 (dd, *J* = 10.0, 7.8, 2H, 6b-H).

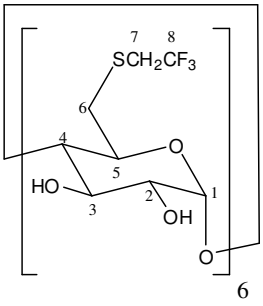
^{13}C NMR (101 MHz, DMSO) δ 102.04 (1-C), 83.00 (4-C), 72.36 (3-C), 72.22 (2-C), 71.14 (5-C), 45.01 (6-C).

Synthesis of fluorinated cyclodextrins 2a – 2c

The synthesis of the 2,2,2-trifluoroethanethio-substituted cyclodextrins **2a** – **2c** from perchlorinated cyclodextrins **1a** – **1c** was performed according to the following procedure: 3 eq 2,2,2-trifluoroethanethiol per glycose unit of the cyclodextrin was dissolved in dry DMF at 0 °C and treated with 3 eq of a 60% dispersion of sodium hydride in mineral oil. After stirring for 30 min a solution of **1a** – **1c** in the minimal amount of DMF was added dropwise. The solution was stirred for 5 d at 70 °C. The solvent is concentrated and poured on water. The precipitation was collected by centrifugion, dissolved in DMF again and precipitated two times from diethyl ether. The product was vacuum-dried at 60 °C and obtained as light beige solid.

Hexakis-(6-deoxy-6-trifluoroethanethio)-α-cyclodextrin 2a

Cyclodextrin **2a** was synthesized as described above with 2,2,2-trifluoroethanethiol (0.15 mL, 1.69 mmol), 60 % sodium hydride suspension in mineral oil (67 mg, 1.66 mmol) and **1a** (0.11 g, 0.10 mmol).



2a

Empirical formula (MW in g/mol):	$C_{48}H_{66}O_{24}F_{18}S_6$ (1516.38)
Yield:	57 % (90 mg, 0.058 mmol)
MS (ESI, MeOH):	800.08 $[M + Ca]^{2+}$, 1583.19 $[M + Na]^+$
Elemental analysis	($C_{48}H_{66}O_{24}F_{18}S_6$)
Calculated [%]:	C, 36.92; H, 4.26; N, 0.0
Determined [%]:	C, 36.62; H, 4.18; N, 0.0

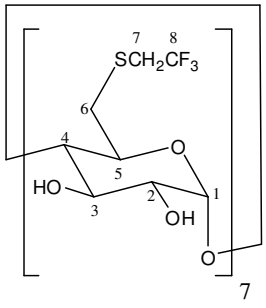
^{1}H NMR (300 MHz, DMSO) δ 5.74 (d, *J* = 6.1, 1H, 2-OH), 5.58 (s, 1H, 3-OH), 4.90 (s, 1H, 1-H), 3.88 (s, 1H, 5-H), 3.72 (d, *J* = 6.6, 1H, 3-H), 3.60 – 3.29 (m, 4H, 4, 7, 2-H), 3.16 (d, *J* = 12.7, 1H, 6a-H), 3.01 (d, *J* = 6.3, 1H, 6b-H).

^{13}C NMR (75 MHz, DMSO) δ 126.42 (q, *J* = 266.3, 1C, 8-C), 101.80 (1-C), 84.60 (4-C), 72.78 (3-C), 71.69 (2-C), 71.31 (5-C), 34.13 – 33.31 (6,7-C).

^{19}F NMR (282 MHz, DMSO) δ -65.52 (t, *J* = 10.4, 3F).

Heptakis-(6-deoxy-6-trifluoroethanethio)-β-cyclodextrin 2b

Cyclodextrin **2b** was synthesized as described above with 2,2,2-trifluoroethanethiol (3.7 mL, 41.5 mmol), 60 % sodium hydride suspension in mineral oil (1 g, 41.5 mmol) and **1b** (2.5 g, 1.98 mmol).



2b

Empirical formula (MW in g/mol):	$C_{56}H_{77}O_{28}F_{21}S_7$ (1820.23)
Yield:	88 % (3.17g, 1.74 mmol)
MS (ESI, MeOH):	930.10 $[M + Ca]^{2+}$, 1843.22 $[M + Na]^+$
Elemental analysis	($C_{56}H_{77}O_{28}F_{21}S_7$)
Calculated [%]:	C, 36.92; H, 4.26; N, 0.0
Determined [%]:	C, 36.57; H, 4.11; N, 0.0

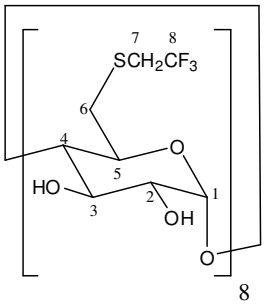
^{1}H NMR (600 MHz, DMSO) δ 5.98 (d, *J* = 6.8, 1H, 2-OH), 5.86 (d, *J* = 1.9, 1H, 3-OH), 4.93 (d, *J* = 3.2, 1H, 1-H), 3.89 – 3.77 (m, 1H, 5-H), 3.61 (t, *J* = 9.1, 1H, 3-H), 3.50 – 3.39 (m, 3H, 4-, 7-H), 3.39 – 3.34 (m, 1H, 2-H), 3.17 (d, *J* = 12.3, 1H, 6a-H), 3.00 (dd, *J* = 14.2, 7.2, 1H, 6b-H).

^{13}C NMR (151 MHz, DMSO) δ 126.33 (q, *J* = 276.45, 8-C), 102.05 (1-C), 84.22 (4-C), 72.38 (3-C), 72.06(2-C), 71.49 (5-C), 34.32 – 33.71 (6-, 7-C).

^{19}F NMR (564 MHz, DMSO) δ -65.70 (t, *J* = 10.5, 3F).

Octakis-(6-deoxy-6-trifluoroethanethio)-γ-cyclodextrin 2c

Cyclodextrin **2c** was synthesized as described above with 2,2,2-trifluoroethanethiol (0.15 mL, 1.66 mmol), 60 % sodium hydride suspension in mineral oil (40 mg, 1.66 mmol) and **1c** (98 mg, 0.068 mmol).



2c

Empirical formula (MW in g/mol)	$C_{64}H_{88}O_{32}F_{24}S_8$ (2080.26)
Yield:	82 % (0.12 g, 0.055 mmol)
MS (ESI, MeOH):	1060.11 [M + Ca]2+,
	2103.25 [M + Na]+
Elemental analysis	(C64H88O32F24S8)
Calculated [%]:	C, 36.92; H, 4.26; N, 0.0
Determined [%]:	C, 36.91; H, 4.22; N, 0.0

^{1}H NMR (300 MHz, DMSO) δ 5.97 (s, 2H, 2,3-OH), 4.96 (d, *J* = 3.0, 1H, 1-H), 4.01 – 3.72 (m, 1H, 5-H), 3.57 (t, *J* = 9.2, 1H, 3-H), 3.43 (dd, *J* = 14.7, 6.9, 4H, 4,7,2-H), 3.17 (d, *J* = 12.4, 1H, 6a-H), 2.99 (dd, *J* = 13.7, 7.1, 1H, 6b-H).

^{13}C NMR (75 MHz, DMSO) δ 102.09 (1-C), 83.91 (4-C), 72.31 (3-C), 72.13 (2-C) 71.63 (5-C), 33.91 (6+7-C).

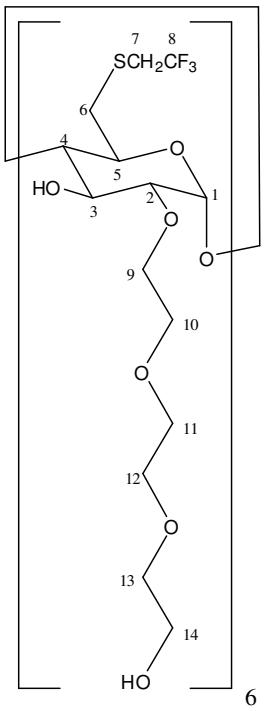
^{19}F NMR (282 MHz, DMSO) δ -65.63 (t, *J* = 10.4, 3F).

Synthesis of fluorinated cyclodextrins 3a – 3c

Fluorinated cyclodextrins **3a** – **3c** were synthesized according to the following procedure: cyclodextrin **2a** – **2c** was solved in dry DMF and treated with 1.5 eq sodium hydride per glycose unit of the cyclodextrin. After stirring for 1 h at room temperature, 3 eq triethylene glycol toluenesulfonate ester per glycose unit was added dropwise. The mixture was stirred for 2 d at room temperature. The solvent was removed and the raw product purified by size eclusion chromatography on a Sephadex LH-20 column. The product was dried at 60 °C in vacuum and obtained as brown highly viscous oil.

Hexakis-(2-O-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl), 6-deoxy-6-trifluoroethanethio)-α-cyclodextrin 3a

Cyclodextrin **3a** was synthesized as described above with **2a** (0.2 g, 0.13 mmol), sodium hydride (46 mg, 1.18 mmol) and triethylene glycol toluenesulfonate ester (0.95 g, 3.14 mmol).



3a

Empirical Formula (MW in g/mol): $C_{84}H_{138}F_{18}O_{42}S_6$ (2354.33)

Yield: 100 % (0.31g, 0.13 mmol)

MS (ESI, MeOH): 1397.93 $[M_{EO27} + 2\ Na]^{2+}$, 1331.90 $[M_{EO24} + 2\ Na]^{2+}$, 1265.86 $[M_{EO21} + 2\ Na]^{2+}$, 1199.32 $[M_{EO18} + 2\ Na]^{2+}$, 1133.28 $[M_{EO15} + 2\ Na]^{2+}$, 1067.24 $[M_{EO12} + 2\ Na]^{2+}$, 2243.58 $[M_{EO15} + Na]^{+}$, 2375.66 $[M_{EO18} + Na]^{+}$, 2508.74 $[M_{EO21} + Na]^{2+}$

Elemental analysis ($C_{84}H_{138}O_{42}F_{18}S_6$)

Calculated [%]: C, 42.85; H, 5.91; N, 0.0

Determined [%]: C, 43.05; H, 5.75; N, 0.0

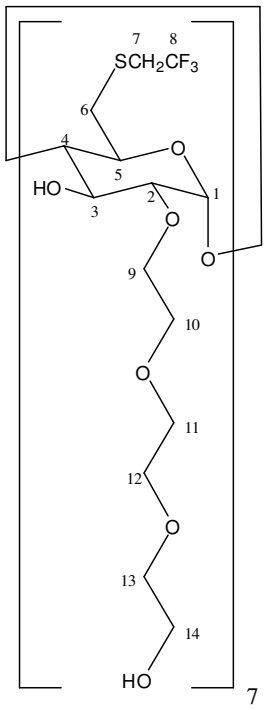
^{1}H NMR (300 MHz, CDCl3) δ 4.90 (d, J = 22.9, 1H, 1-H), 4.82 – 4.55 (m, 1H, 3-OH), 4.02 (dd, J = 18.0, 9.8, 2H, 3-H, 5-H), 3.92 – 3.71 (m, 2H, 14-H), 3.56 (dd, J = 18.7, 6.4, 11H, 9-H, 10-H), 3.45 – 3.30 (m, 2H, 2-H, 4-H), 3.20 (dd, J = 27.2, 18.0, 4H, 6a-H, 7-H), 2.90 (dd, J = 14.7, 5.3, 1H, 6b-H).

^{13}C NMR (75 MHz, CDCl3) δ 126.09 (q, J = 276.1, 8-C), 101.00 (1-C), 86.17 (4-C), 80.54 (2-C), 77.65 - 70.39 (9-C, 10-C, 11-C, 12-C, 13-C), 61.65 (14-C), 35.39 - 34.36 (6-C, 7-C).

^{19}F NMR (282 MHz, $CDCl_3$) δ -66.38 (t, *J* = 9.9, 3F).

Heptakis-(2-O-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl), 6-deoxy-6-trifluoroethanethio)-β-cyclodextrin 3b

Cyclodextrin **3b** was synthesized as described above with **2b** (95 mg, 0.052 mmol), sodium hydride (13.2 mg, 0.55 mmol) and triethylene glycol toluenesulfonate ester (0.45 g, 1.46 mmol).



3b

Empirical Formula (MW in g/mol): $C_{98}H_{161}F_{21}O_{49}S_7$ (2744.78)

Yield: 108 % (0.14 g, 0.06 mmol)

MS (ESI, MeOH): 893.89 $[M_{EO18} + 3\ Na]^{3+}$, 938.25 $[M_{EO21} + 3\ Na]^{3+}$, 982.28 $[M_{EO24} + 3\ Na]^{3+}$, 1026.64 $[M_{EO27} + 3\ Na]^{3+}$, 1070.33 $[M_{EO30} + 3\ Na]^{3+}$, 1114.68 $[M_{EO33} + 3\ Na]^{3+}$ 1263.31 $[M_{EO15} + 2\ Na]^{2+}$, 1329.84 $[M_{EO18} + 2\ Na]^{2+}$, 1395.88 $[M_{EO21} + 2\ Na]^{2+}$, 1462.42 $[M_{EO24} + 2\ Na]^{2+}$, 1528.46 $[M_{EO27} + 2\ Na]^{2+}$, 1593.99 $[M_{EO30} + 2\ Na]^{2+}$

Elemental analysis ($C_{98}H_{161}O_{49}F_{21}S_7$)

Calculated [%]: C, 42.85; H, 5.91; N, 0.0

Determinded [%]: C, 42.63; H, 6.12; N, 0.0

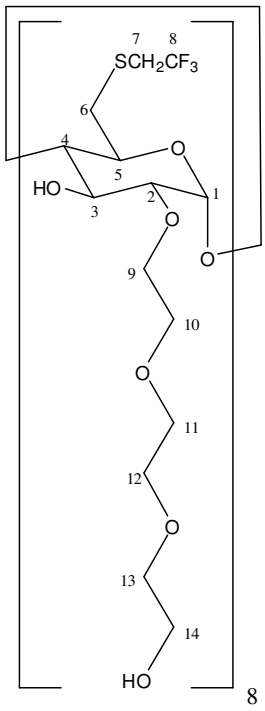
^{1}H NMR (300 MHz, CDCl3) δ 4.99 (d, J = 3.2, 1H, 1-H), 4.91 (s, 1H, 3-OH), 4.11 (dd, J = 7.4, 3.6, 2H, 3-H, 5-H), 3.84 (dd, J = 17.9, 9.9, 5H, 14-H), 3.74 – 3.50 (m, 20H, 9-H, 10-H, 11-H, 12-H, 13-H), 3.40 (dt, J = 12.8, 6.4, 3H, 2-H, 4-H), 3.20 (dd, J = 17.2, 7.6, 6H, 6a-H, 7-H), 2.93 (dd, J = 14.1, 6.7, 1H, 6b-H).

^{13}C NMR (75 MHz, CDCl3) δ 126.14 (q, J = 276.1, 8-C), 101.37 (1-C), 85.76 (4-C), 81.08 (2-C), 73.17 - 70.49 (3-C, 5-C, 9-C, 10-C, 11-C, 12-C, 13-C), 61.78 (14-C), 35.51 - 34.29 (6-C, 7-C).

^{19}F NMR (282 MHz, $CDCl_3$) δ -66.64 (t, *J* = 9.7, 3F).

Octakis-(2-O-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl), 6-deoxy-6-trifluoroethanethio)-γ-cyclodextrin 3c

Cyclodextrin **3c** was synthesized as described above with **2c** (113 mg, 0.054 mmol), sodium hydride (15.6 mg, 0.65 mmol) and triethylene glycol toluenesulfonate ester (0.53 g, 1.74 mmol).



3c

Empirical Formula (MW in g/mol): $C_{112}H_{184}F_{24}O_{56}S_8$ (3139,11)

Yield: 78 % (133 mg, 0.04 mmol)

MS (ESI, MeOH): 981.23 $[M_{EO18} + 3\ Na]^{3+}$, 1024.93$[M_{EO21} + 3\ Na]^{3+}$, 1069.29 $[M_{EO24} + 3\ Na]^{3+}$, 1113.32 $[M_{EO27} + 3\ Na]^{3+}$, 1157.34 $[M_{EO30} + 3\ Na]^{3+}$, 1201.36 $[M_{EO33} + 3\ Na]^{3+}$, 1393.82 $[M_{EO15} + 2\ Na]^{2+}$, 1459.86 $[M_{EO18} + 2\ Na]^{2+}$, 1525.90 $[M_{EO21} + 2\ Na]^{2+}$, 1592.44 $[M_{EO24} + 2\ Na]^{2+}$, 1658.48 $[M_{EO27} + 2\ Na]^{2+}$

Elemental analysis	($C_{112}H_{184}O_{56}F_{24}S_8$)
Calculated [%]:	C, 42.85; H, 5.91; N, 0.0
Determined [%]:	C, 42.81; H, 5.97; N, 0.0

^{1}H NMR (300 MHz, CDCl3) δ 5.05 (d, J = 3.4, 1H, 1-H), 4.93 (s, 1H, 3-OH), 4.19 – 3.99 (m, 1H, 3-H), 3.99 – 3.48 (m, 13H, 5-H, 9-H, 10-H, 11-H, 12-H, 13-H, 14-H), 3.41 (s, 3H, 2-H, 4-H), 3.19 (dd, J = 18.9, 9.4, 3H, 6a-H, 7-H), 3.00 – 2.89 (m, 1H, 6b-H).

^{13}C NMR (101 MHz, CDCl3) δ 126.12 (dd, J = 552.6, 276.7, 8-C), 100.99 (1-C), 84.81 (4-C), 81.27 (2-C), 72.94 - 70.31, 61.67 (14-C), 35.36 - 34.18 (6-C, 7-C).

^{19}F NMR (282 MHz, $CDCl_3$) δ -66.67 (t, *J* = 9.7, 3F).

Isothermal Titration Calorimetry

Isothermal titration calorimetry (ITC) was performed on a *Nano-Isothermal Titration Calorimeter III (Model CSC 5300)* made by *Calorimetry Sciences Corporation* (USA). Analyte solutions for ITC measurements were prepared with destilled and deionized water and degassed for 20 min at room temperature. The guest solution (10-fold excess) was titrated into the cyclodextrin solution. 20 injections of 10 µL were performed with an interval of 300 s. The stirring rate was 300 rpm. The data were fitted to a 1:1 model (2:1 in case of diflunisal and **3c**) using a spread sheet method.[2]

Table S1: Analyte solutions for ITC with α-cyclodextrin **3a**.

compound	M [$^{g}/_{mol}$]	n [mmol]	m [mg]	c [mM]
CD 3a	2354,33	0,0551	129,7	5,509
p-fluorophenol	112,1	0,275	31	55,09
p-trifluoromethylphenol	162,11	0,275	44,8	55,09
m-trifluormethylphenol	162,11	0,275	44,7	55,09
phenol	94,11	0,25	23,4	50
p-cresol	108,14	0,275	29,7	55

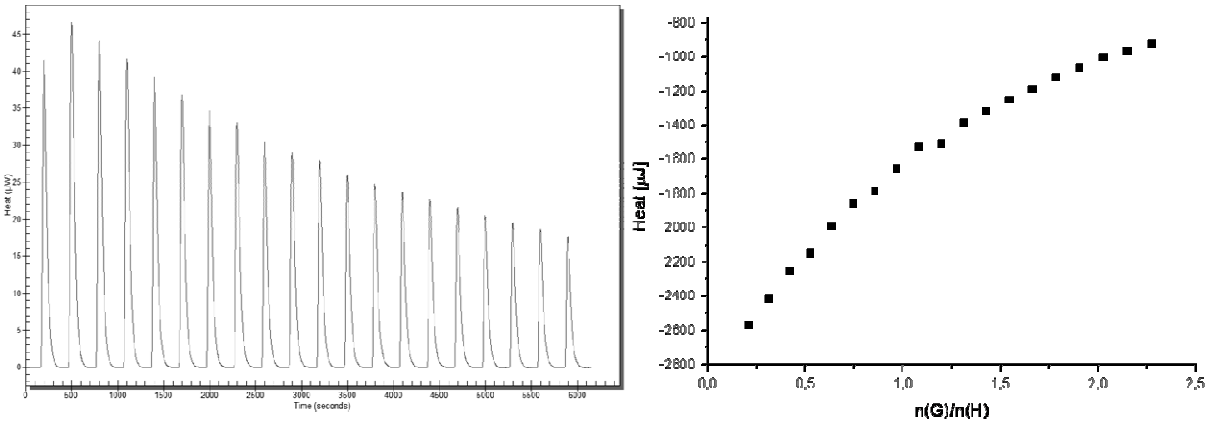


Figure S1: ITC of **3a** with p-fluorophenol.

[2] J. Huskens, H. van Bekkum and J. A. Peters, Computers & Chemistry, 1995, 19, 409.

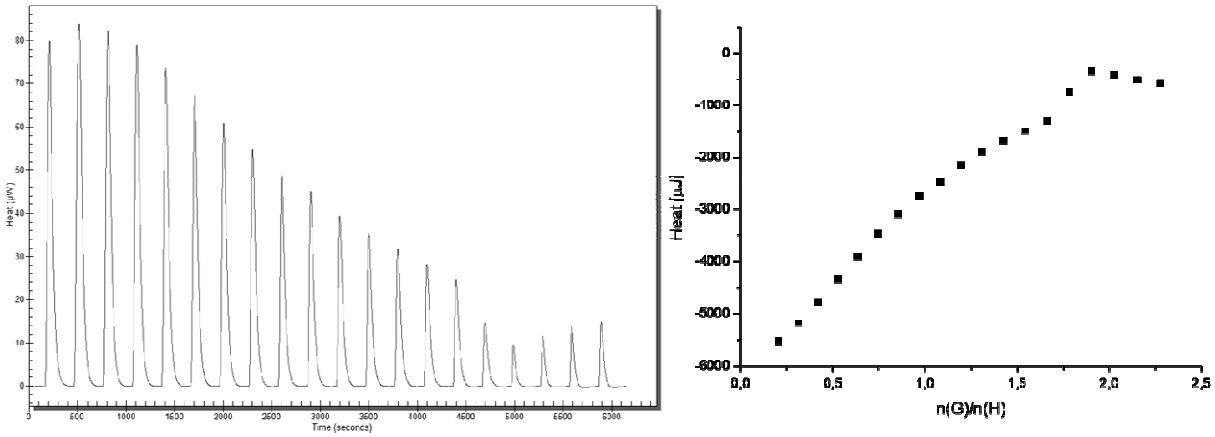


Figure S2: ITC of **3a** with p-trifluoromethylphenol.

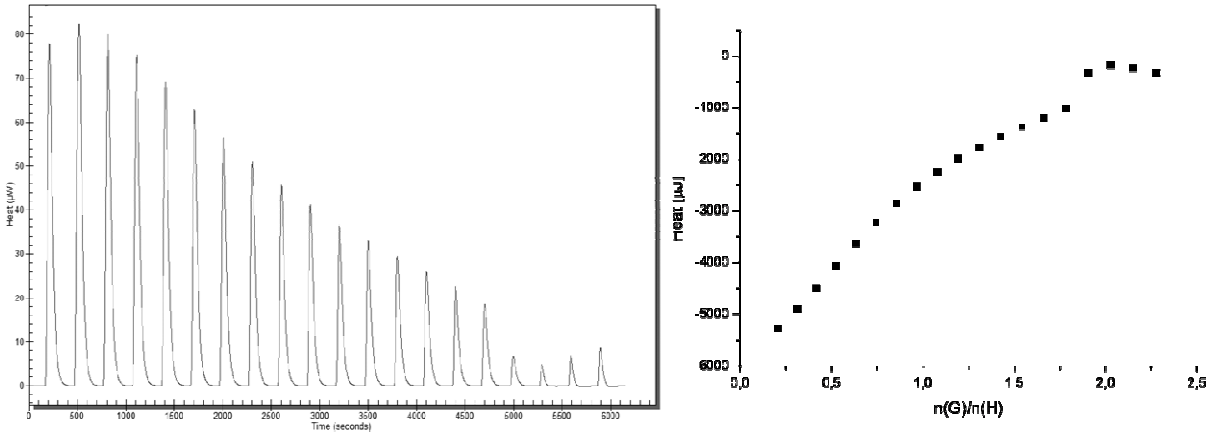


Figure S3: ITC data of **3a** with m-trifluoromethylphenol.

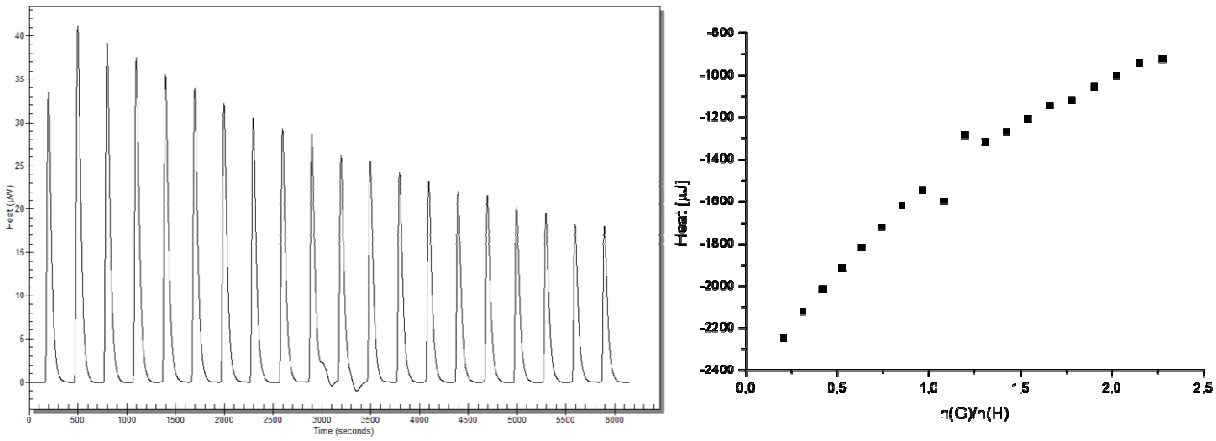


Figure S4: ITC of **3a** with phenol.

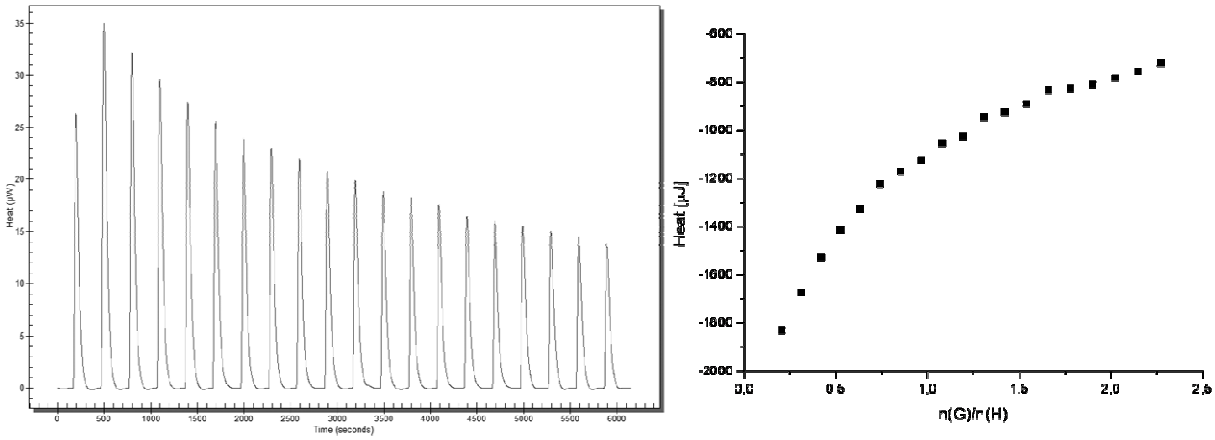


Figure S5: ITC of **3a** with p-cresol.

Table S2: Analyte solutions for ITC with β-cyclodextrin **3b**.

compound	M [$^{g}/_{mol}$]	n [mmol]	m [mg]	c [mM]
CD **3b**	2744,78	0,055	151	5,5
p-fluorophenol	112,1	0,275	30,8	55
p-trifluoromethylphenol	162,11	0,275	44,7	55
CD **3b**	2744,78	0,05	137,3	5
m-trifluormethylphenol	162,11	0,275	40,5	50
phenol	94,11	0,25	23,4	50
p-cresol	108,14	0,25	27,1	50
CD **3b**	2744,78	0,008	22,9	1,67
4-(trifluoromethyl)cyclo-hexanecarboxylic acid	196,17	0,25	49	16,7
CD **3b**	2744,78	0,0096	26,4	1,6
4-methylcyclo-hexanecarboxylic acid	142,196	0,08	11,4	16
CD **3b**	2744,78	0,015	41,8	3
diflunisal	250,198	0,15	37,8	30

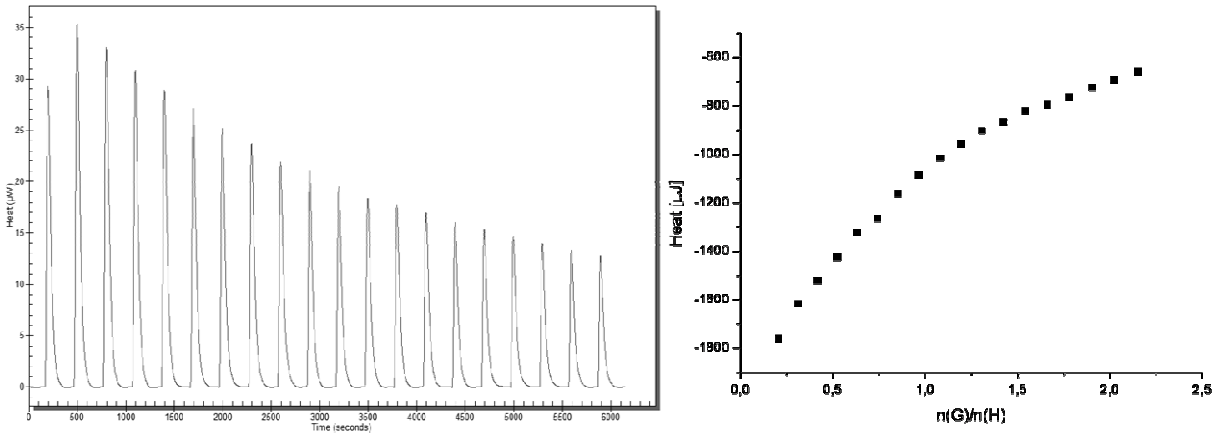


Figure S6: ITC of **3b** with p-fluorophenol.

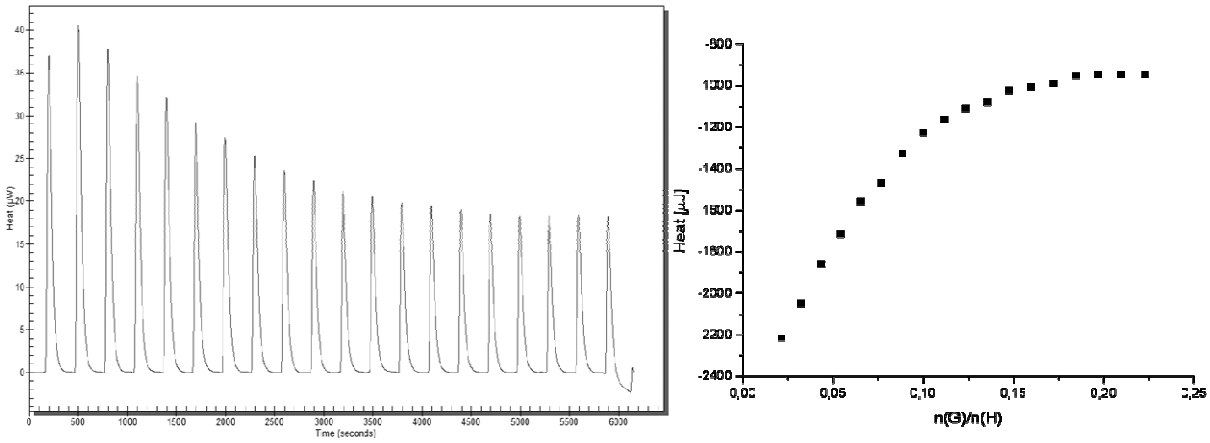


Figure S7: ITC of **3b** with p-trifluoromethylphenol.

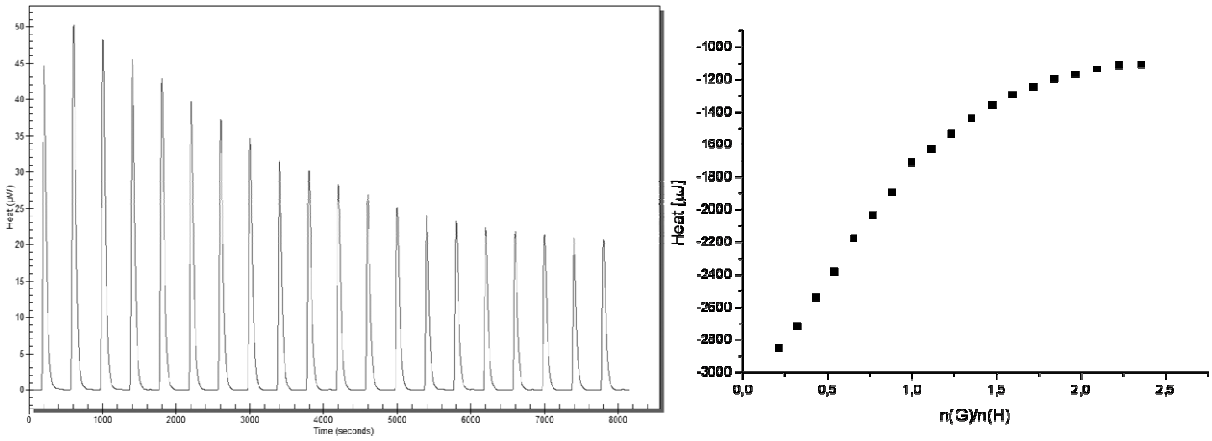


Figure S8: ITC of **3b** with m-trifluoromethylphenol.

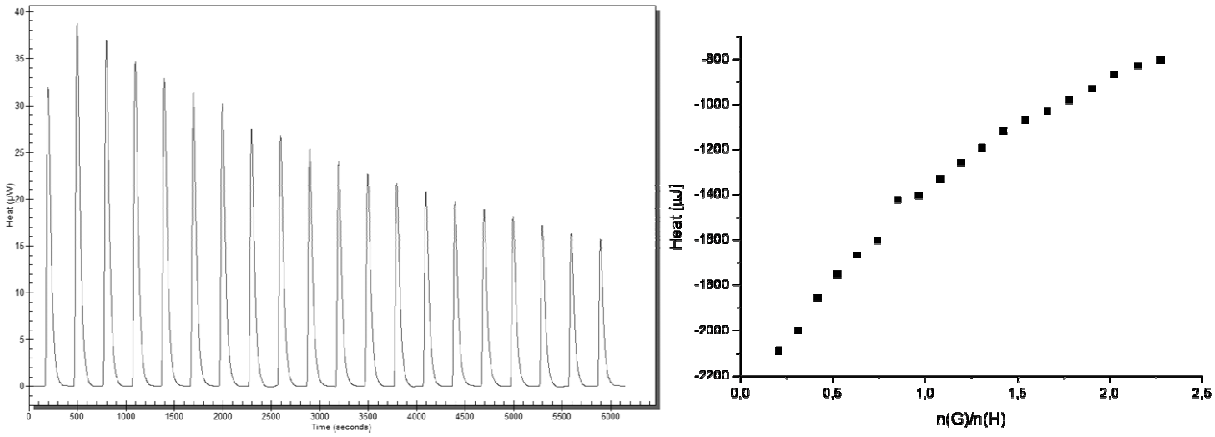


Figure S9: ITC of **3b** with phenol.

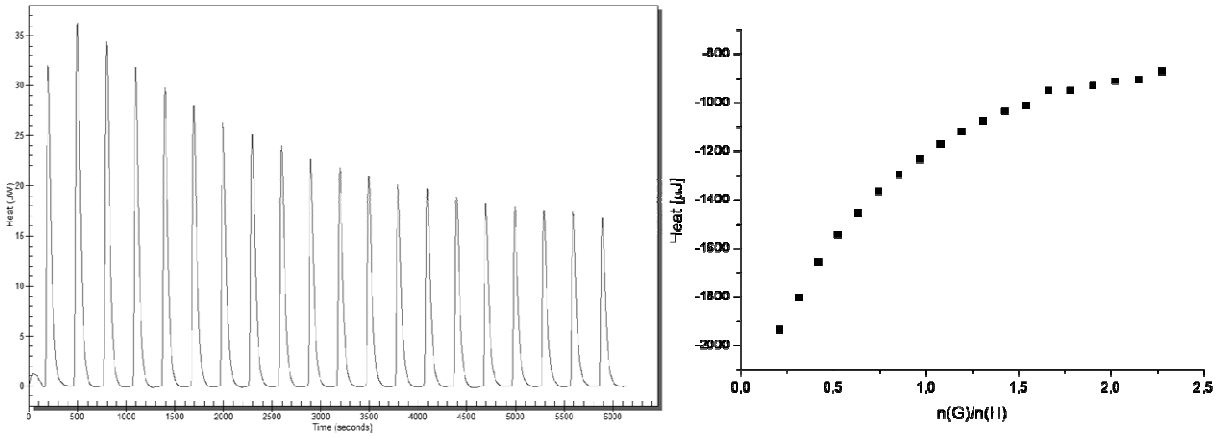


Figure S10: ITC of **3b** with p-cresol.

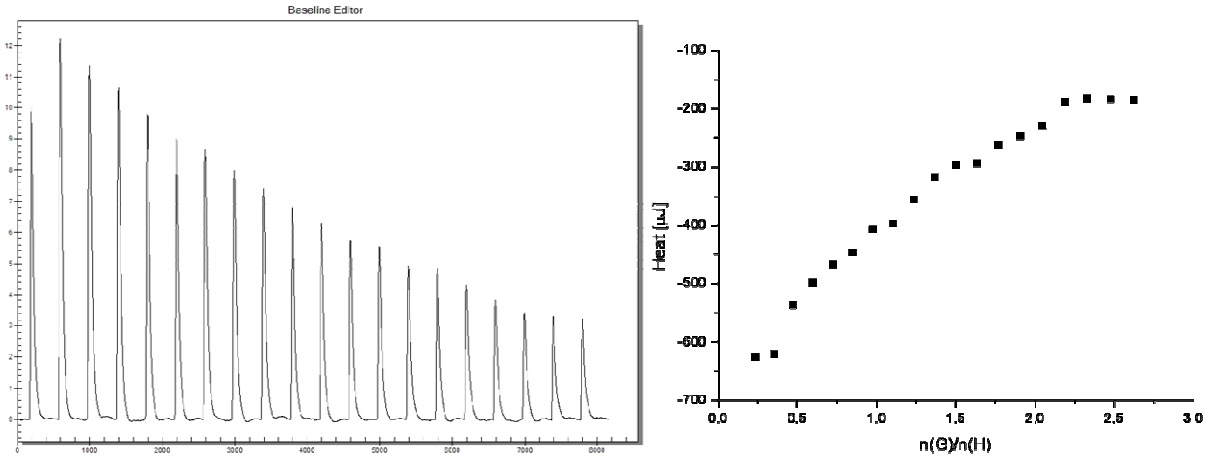


Figure S11: ITC of **3b** with 4-(trifluoromethyl)cyclohexane carboxylic acid.

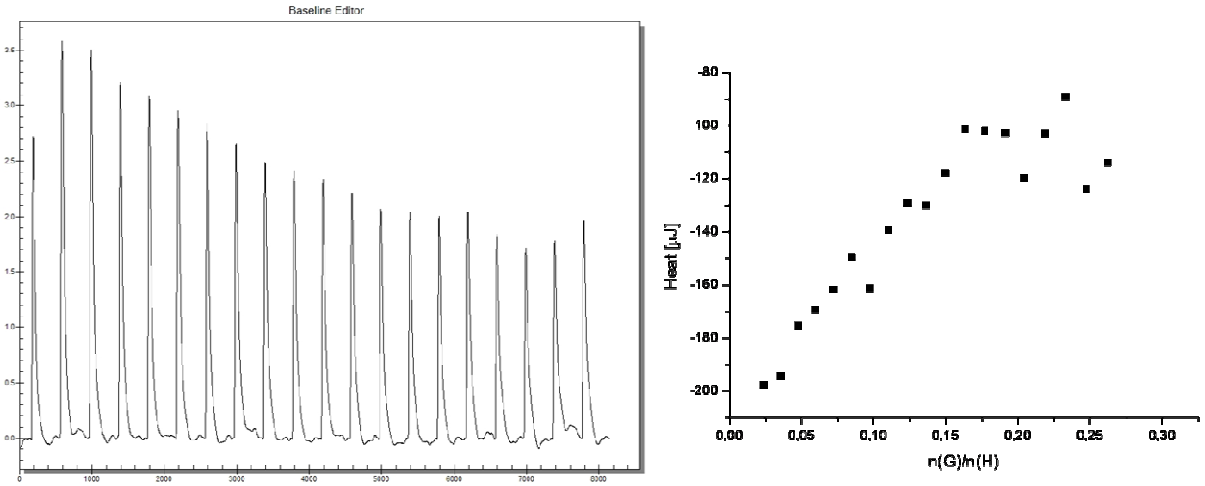


Figure S12: ITC of **3b** with 4-methylcyclohexane carboxylic acid.

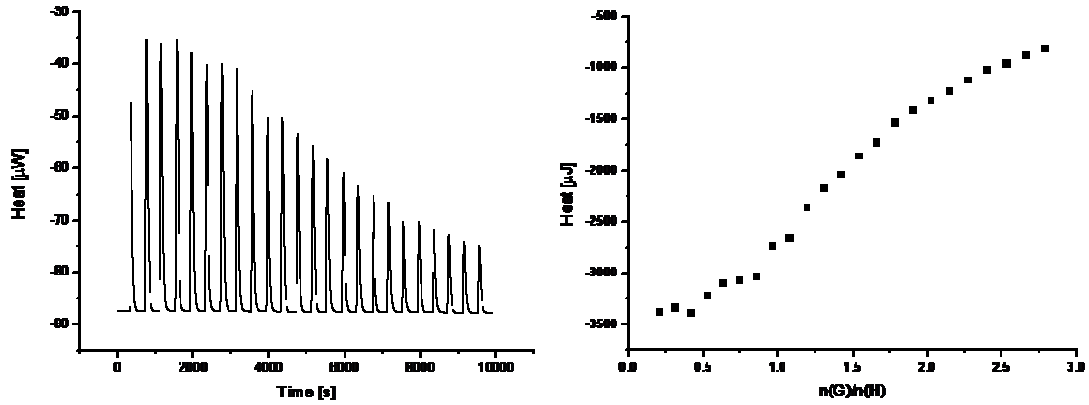


Figure S13: ITC of **3b** with diflunisal in borate buffer at pH 9.

Table S3: Analyte solutions for ITC with γ-cyclodextrin **3c.**

Compound	M [$^{g}/_{mol}$]	n [mmol]	m [mg]	c [mM]
CD **3c**	3139,11	0,01	31,4	1
diflunisal	250,198	0,15	37,9	30

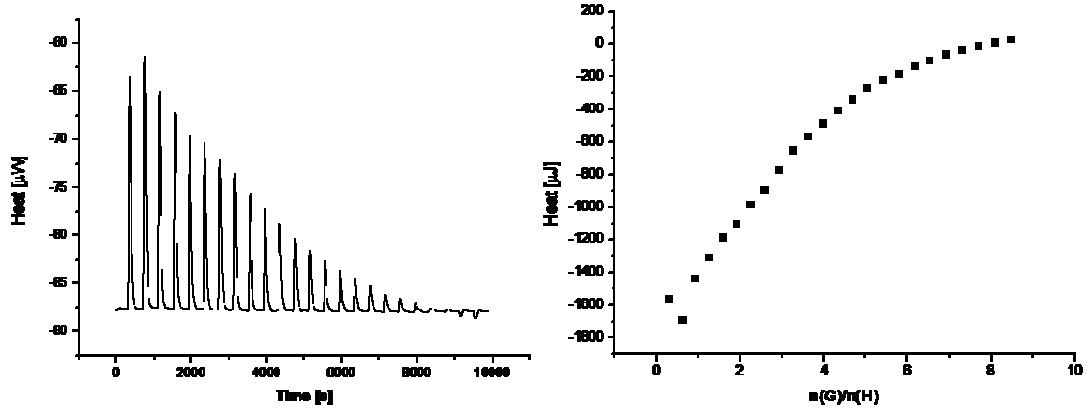


Figure S14: ITC of **3c** with diflunisal in borate buffer at pH 9.

NMR Titration

NMR titration of cyclodextrin 3b with p-trifluoromethylphenol

NMR titration of β-cyclodextrin **3b** with *p*-trifluoromethylphenol is characterized by a fast exchange of free and complexed guest relative to the NMR time-scale. The NMR spectrum displays an average (δ_{obs}) of the shift of free (δ_G) and complexed guests (δ_C):

$$\partial_{obs} = \partial_G(1-x) + x\partial_C \qquad x = \frac{[C]}{[G]_0}$$

$$x = \frac{\partial_{obs} - \partial_G}{\partial_C - \partial_G} \qquad [C] = x[G]_0$$

The shift of complexed guest (δ_C) was obtained from NMR titrations and extrapolation. In view of the small shifts observed in ^{1}H-NMR, only ^{19}F-NMR data (Table S4) were used to determine complex stoichiometry (Job's Plot) and binding constant K_a. Once δ_C is known, the concentration of the complex in equilibrium can be determined and the equilibrium contact K can be calculated according to:

$$K = \frac{[C]}{[G][CD]}$$

$$K = \frac{[C]}{([G]_0 - [C])([CD]_0 - [C])}$$

(with $[G]_0$ = guest concentration and $[CD]_0$ = cyclodextrin concentration)

Table S4: ^{19}F-NMR data for the titration of cyclodextrin **3b** with *p*-trifluoromethylphenol.

^{19}F-NMR								
sample	Δ_{guestt} [ppm]	Δ_{host} [ppm]	$\Delta\ \delta_{guest}$ [ppm]	$\Delta\ \delta_{host}$ [ppm]	n(G) [mmol]	n(H) [mmol]	n(G)/(n(G)+n(H)))	ratio G:H
1	0	-66,81	0	0	0	0,0036	0,000	00:01
2	-60,72	-66,83	0,46	-0,02	0,0003	0,0033	0,083	01:11
3	-60,74	-66,86	0,44	-0,05	0,0006	0,003	0,167	02:10
4	-60,76	-66,89	0,42	-0,08	0,0009	0,0027	0,250	01:03
5	-60,8	-66,91	0,38	-0,1	0,0012	0,0024	0,333	01:02
6	-60,83	-66,94	0,35	-0,13	0,0015	0,0021	0,417	05:07
7	-60,87	-66,97	0,31	-0,16	0,0018	0,0018	0,500	01:01
8	-60,93	-67	0,25	-0,19	0,0021	0,0015	0,583	07:05
9	-60,99	-67,03	0,19	-0,22	0,0024	0,0012	0,667	02:01
10	-61,06	-67,05	0,12	-0,24	0,0027	0,0009	0,750	03:01
11	-61,1	-67,09	0,08	-0,28	0,003	0,0006	0,833	10:02
12	-61,16	-67,16	0,02	-0,35	0,0033	0,0003	0,917	11:01
13	-61,18	0	0	0	0,0036	0	1,000	01:00

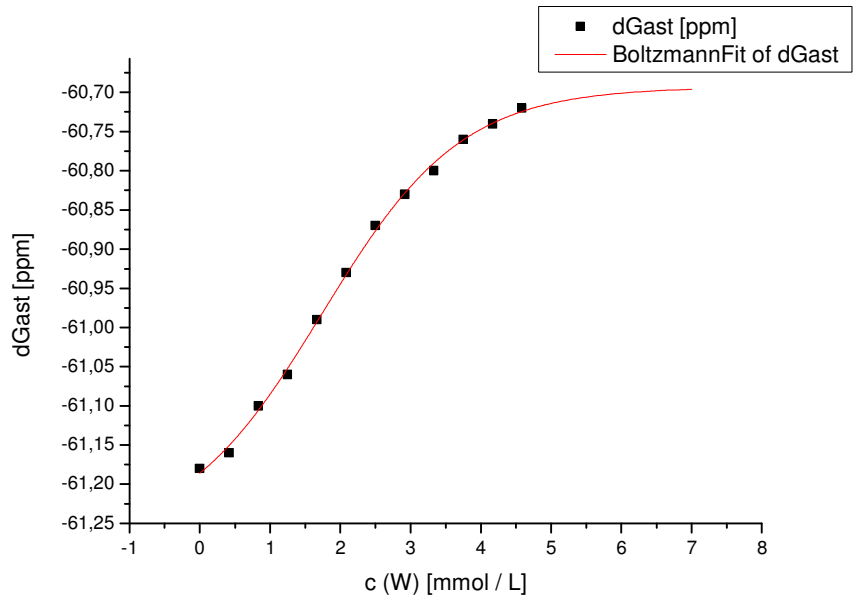


Figure S15: Determination of δ_C.

The shift of the inclusion complex δ_C = -60.7 is obtained from extrapolation of ^{19}F-NMR data (Figure S15). A fit for 1:1 complexation gives a binding constant K_a = 2.06 x 10^3 M^{-1}.

NMR titration of cyclodextrin 3a with p-trifluoromethylphenol

NMR titration of α-cyclodextrin **3a** with *p*-trifluoromethylphenol was carried out as described for **3b**.

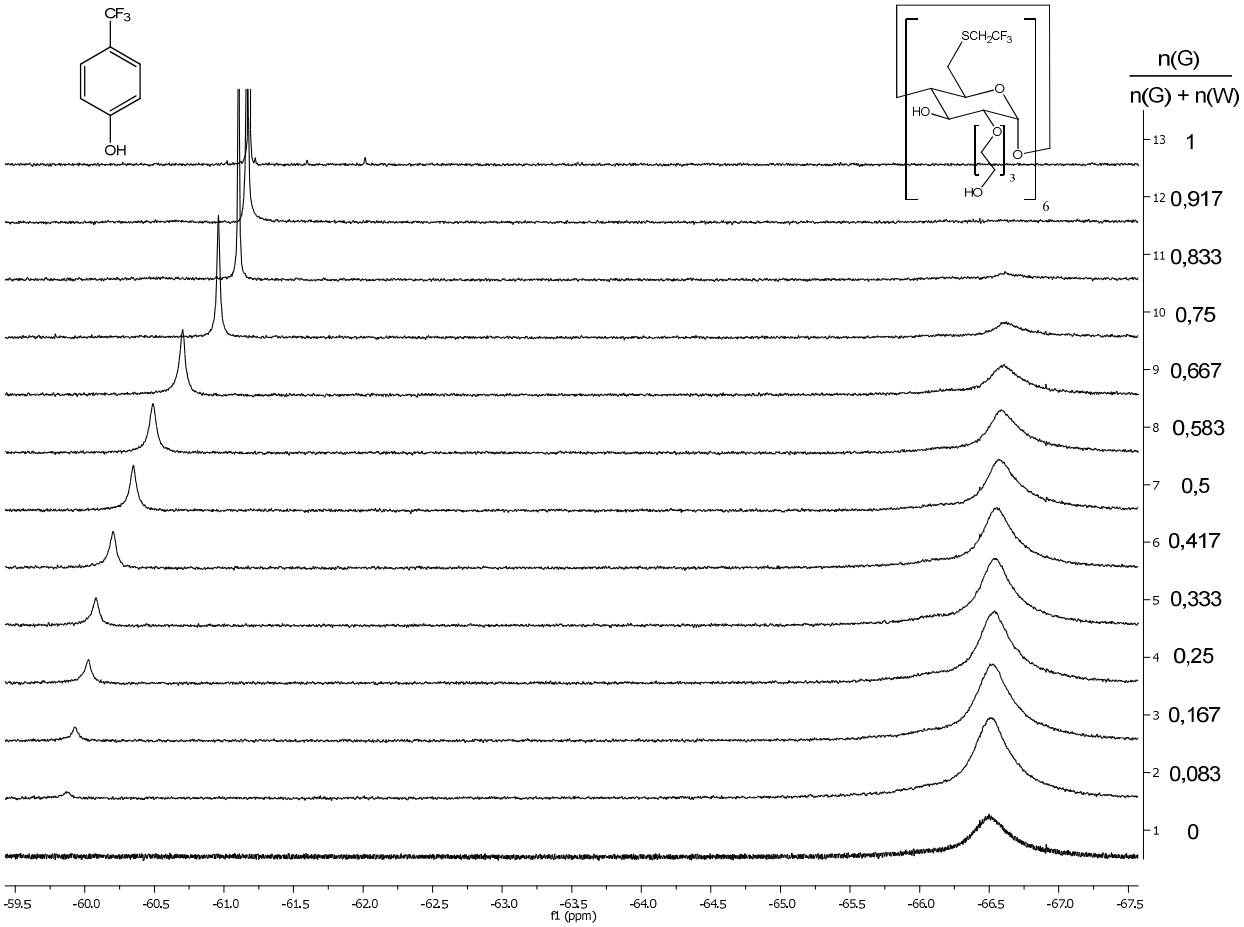


Figure S16: ^{19}F-NMR titration spectra of **2a** with *p*-trifluoromethylphenol.

Table S5: ^{19}F-NMR data for the titration of α-CD **2a** with *p*-trifluoromethylphenol.

^{19}F-NMR								
sample	Δ_{guest} [ppm]	Δ_{host} [ppm]	$\Delta\ \delta_{guest}$ [ppm]	$\Delta\ \delta_{host}$ [ppm]	n(G) [mmol]	n(H) [mmol]	n(G)/(n(G)+n(H)))	ratio G:H
1	-	-66,49	-	0	0	0,0036	0	00:01
2	-59,87	-66,51	1,31	-0,02	0,0003	0,0033	0,083	01:11
3	-59,93	-66,52	1,25	-0,03	0,0006	0,003	0,167	02:10
4	-60,02	-66,53	1,16	-0,04	0,0009	0,0027	0,25	01:03
5	-60,08	-66,55	1,1	-0,06	0,0012	0,0024	0,333	01:02
6	-60,2	-66,55	0,98	-0,06	0,0015	0,0021	0,417	05:07
7	-60,35	-66,57	0,83	-0,08	0,0018	0,0018	0,5	01:01
8	-60,49	-66,59	0,69	-0,1	0,0021	0,0015	0,583	07:05
9	-60,7	-66,61	0,48	-0,12	0,0024	0,0012	0,667	02:01
10	-60,96	-66,62	0,22	-0,13	0,0027	0,0009	0,75	03:01
11	-61,11	-66,61	0,07	-0,12	0,003	0,0006	0,833	10:02
12	-61,17	-	0,01	-	0,0033	0,0003	0,917	11:01
13	-61,18	-	0	-	0,0036	0	1	01:00

The complex stoichiometry of **3a** with *p*-trifluoromethylphenol was determined by plotting guest shift signals multiplied by molar amount against ratio of guest and host in a Job's Plot (see Figure S1).

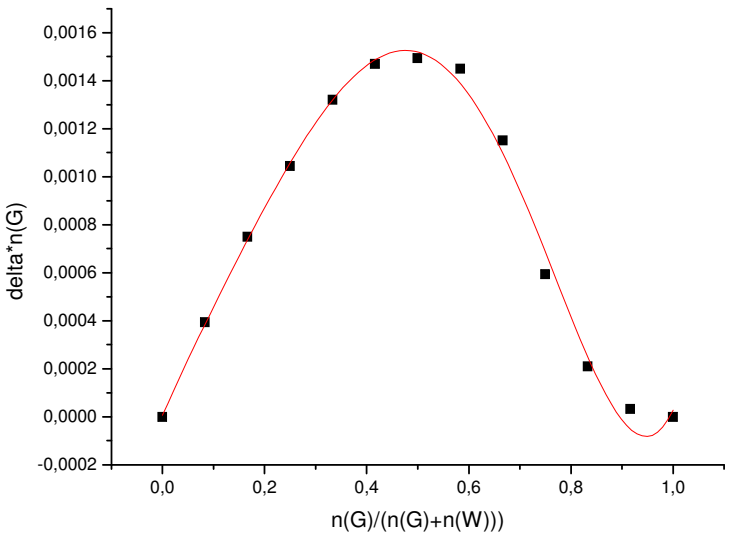


Figure S17: Job's plot for the titration of **3a** with *p*-trifluoromethylphenol.

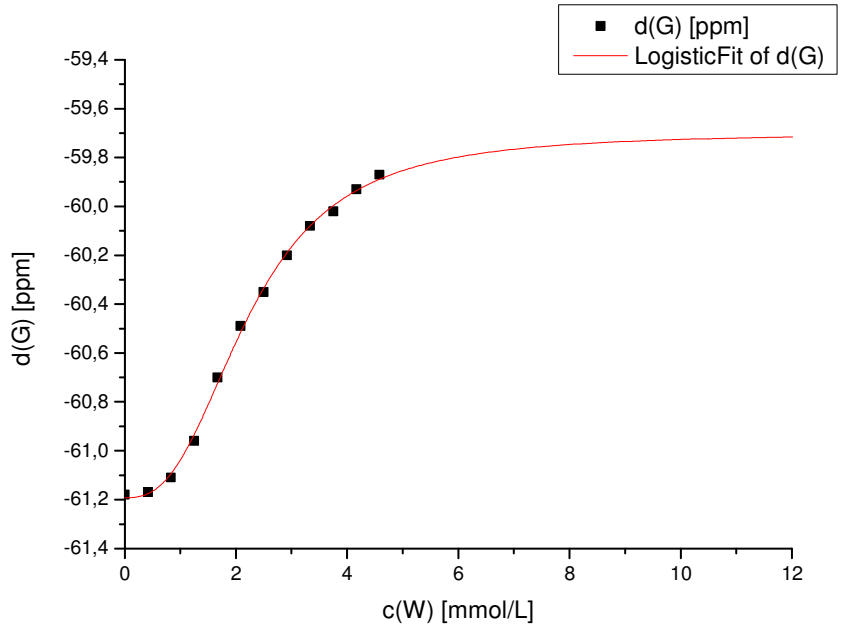


Figure S18: Determination of δ_C by extrapolation of ^{19}F-NMR data.

The ^{19}F-NMR data of **3a** were extrapolated to obtain δ_C = -59.72 ppm (see Figure S18). A fit for 1:1 complexation gives a binding constant K_a = 1.37 x 10^2 M^{-1}.

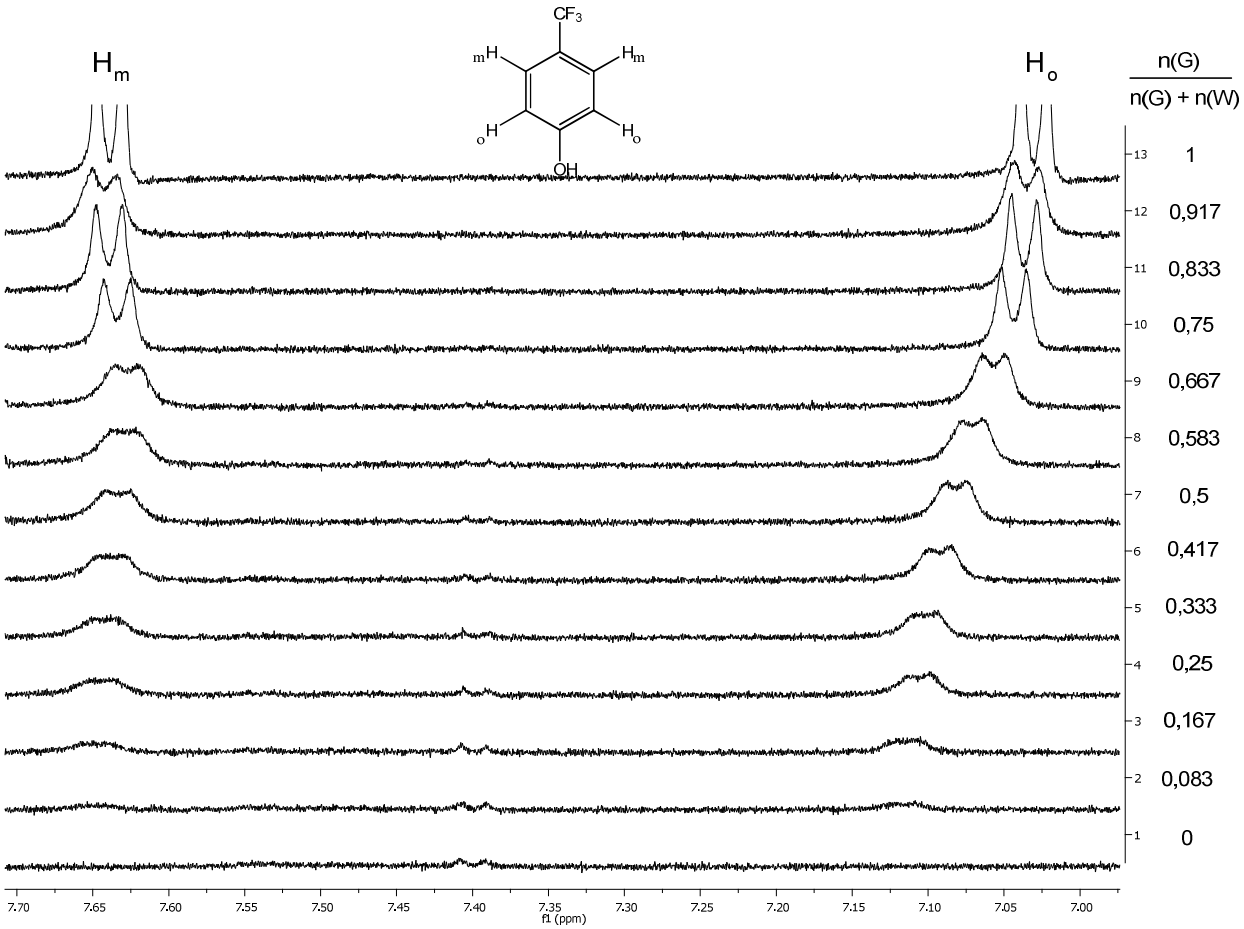


Figure S19: 1H-NMR titration of **3a** with p-trifluoromethylphenol.