Supporting Information

General: All reactions were carried out under argon and with rigid exclusion of humidity.

Dilithium-bis-(5,5'ethylphosphonato)-6,6'-dihydroxy-3,3,3',3'-tetramethyl-1,1'-spiro-bis-indane 1: To a solution of **1** (0.3 mmol) in dry methylbutylketone (15mL) lithium bromide (0.6 mmol) was added and the mixture was heated to reflux for 1 h. The white precipitate was filtered, suspended in diethylether and sonicated for 0.5 h. The solid was filtered again and dried under reduced pressure at 130°C over phosphorus pentoxide. Yield 95%.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.79 (POCH$_2$CH$_3$, t, 6H, $^{3}J_{HH}$ = 14.5 Hz); 1.01 (SpiroCH$_3$, s, 6H); 1.07 (SpiroCH$_3$, s, 6H); 1.87 (SpiroCH$_2$, d, 2H, $^{2}J_{HH}$ = 13.2 Hz); 1.99 (SpiroCH$_2$, d, 2H, $^{2}J_{HH}$ = 13.2 Hz); 3.38 (POCH$_2$CH$_3$, m, 4H); 5.69 (arom. H, d, 2H, $^{4}J_{HP}$ = 4.4 Hz); 6.94 (arom. H, d, 2H, $^{3}J_{HP}$ = 12.6 Hz).

^{13}C NMR (126 MHz, DMSO-d_6): δ = 14.13; 16.86 (d, $^{3}J_{CP}$= 7.3 Hz); 22.03; 25.70; 30.03; 30.84; 32.10; 42.69; 57.34; 59.13; 59.26 (d, $^{1}J_{CP}$= 42.5 Hz); 110.17 (d, $^{3}J_{CP}$= 10.9 Hz); 125.43 (d, $^{2}J_{CP}$= 6.07 Hz); 141.34 (d, $^{3}J_{CP}$= 12.1 Hz); 154.21; 160.15 (d, $^{2}J_{CP}$= 7.28 Hz).

^{31}P{^{1}H}-NMR (202 MHz, DMSO-d_6): δ = 13.85 ppm.

FAB-MS:

assignment	m/z	intensity [%]
M^+	537	100

IR (cm^{-1}): 2956, 2903, 1508, 1474, 1418, 1363, 1184, 1125, 1041, 946, 780.

To get an analytically pure sample the lithium salt was protonated with HCl, filtered and the resulting bisphosphonic acid dried under reduced pressure:

Elemental analysis **(1)**:

element	calculated	found	deviation
C	57.25 %	57.90 %	- 0.65
H	6.53 %	7.00 %	- 0.47

Dilithium-bis-(5,5'-ethylphosphonato)-6,6'-(2,4,5-trimethyl-1,3-benzyloxy)-3,3,3',3'-tetra-methyl-1,1'-spirobisindane 2: To a solution of **2** (0.3 mmol) in dry acetonitrile (15mL) lithium bromide (0.6 mmol) was added and the mixture was heated to reflux for 100 h. The white precipitate was filtered, suspended in diethylether and sonicated for 0.5 h. The solid was filtered again and dried under reduced pressure at 130°C over phosphorus pentoxide. Yield 90%.

^{1}H NMR (500 MHz, methanol-d$_4$): δ = 1.20 (SpiroCH$_3$, s, 3H); 1.32 (POCH$_2$CH$_3$, t, 3H, $^{3}J_{HH}$ = 14.5 Hz); 1.35 (POCH$_2$CH$_3$, t, 3H, $^{3}J_{HH}$ = 14.5 Hz); 1.36 (SpiroCH$_3$, s, 6H); 1.37 (SpiroCH$_3$, s, 3H); 1.63 (arom. CH$_3$, s, 3H); 1.81 (SpiroCH$_2$, d, 1H, $^{2}J_{HH}$ = 12.6 Hz); 1.92 (SpiroCH$_2$, d, 1H, $^{2}J_{HH}$ = 12.7 Hz); 2.30 (SpiroCH$_2$, d, 1H, $^{2}J_{HH}$ = 12.6 Hz); 2.40 (SpiroCH$_2$, d, 1H, $^{2}J_{HH}$ = 12.0 Hz); 2.41 (arom. CH$_3$, s, 3H); 2.57 (arom. CH$_3$, s, 3H); 3.84 (POCH$_2$CH$_3$, m, 1H); 3.93 (POCH$_2$CH$_3$, m, 1H) 3.98 (POCH$_2$CH$_3$, m, 2H); 5.28 ppm (ArCH$_2$OAr, dd, 2H, $^{2}J_{HH}$ = 95.2 Hz); 5.29 (ArCH$_2$OAr, d, 2H, $^{2}J_{HH}$ = 22.05 Hz); 5.53 (arom. H, d, 1H, $^{4}J_{HP}$ = 5.1 Hz); 6.04 (arom. H, d, 1H, $^{4}J_{HP}$ = 5.1 Hz); 6.83 ppm (arom. H, s, 1H); 7.54 (arom. H, d, 1H, $^{3}J_{HP}$ = 13.9 Hz); 7.78 ppm (arom. H, d, 1H, $^{3}J_{HP}$ = 13.3 Hz).

^{13}C NMR (126 MHz, methanol-d$_4$): δ = 14.88; 17.11 (m); 19.84; 21.80; 31.02; 31.39; 31.70; 43.93; 44.00; 58.91; 59.12; 59.71; 61.08 (d, $^{2}J_{CP}$= 6.06 Hz); 61.26 (d, $^{2}J_{CP}$= 6.06 Hz); 65.35; 72.24; 109.46 (d, $^{3}J_{CP}$= 9.72 Hz); 121.64 (d, $^{3}J_{CP}$= 10.9 Hz); 123.63 (d, $^{1}J_{CP}$= 175.93 Hz); 129.38 (d, $^{2}J_{CP}$= 6.07 Hz); 129.61 (d, $^{2}J_{CP}$= 6.07 Hz); 130.31;132.23; 132.32; 132.35; 138.01; 139.63; 141.07; 143.61 (d, $^{3}J_{CP}$= 13.3 Hz); 149.70 (d, $^{3}J_{CP}$= 13.36 Hz); 153.77 (d, $^{4}J_{CP}$= 2.43 Hz); 154.49; 158.76 (d, $^{2}J_{CP}$= 2.42 Hz); 160.90 (d, $^{2}J_{CP}$= 2.42 Hz).

^{31}P{^{1}H}-NMR (202 MHz, methanol-d$_4$): δ = 12.90 / 14.09.

FAB-MS:

assignment	m/z	intensity [%]
M^+	681	0,6

IR (cm^{-1}): 2956, 2870, 2900, 1508, 1474, 1396, 1362, 1200, 1185, 1125, 1046, 700, 781.

Elemental analysis (2 + H$_2$O):

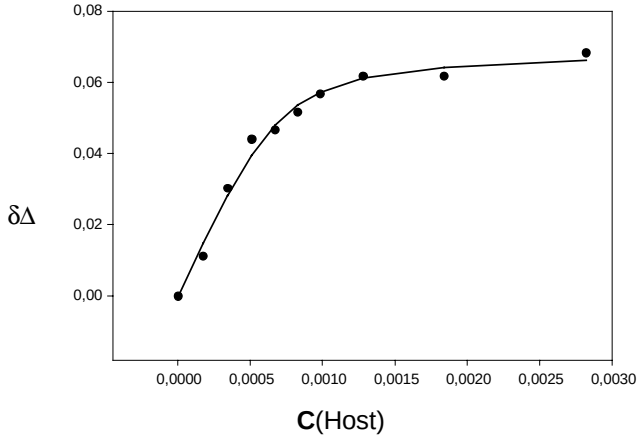
element	calculated	found	deviation
C	61.53 %	61.94 %	- 0.41
H	6.93 %	6.73 %	- 0.15

NMR titrations: Host-guest complexations

All NMR titrations were carried out with a Bruker DRX 500 (500 MHz) NMR spectrometer in DMSO-d_6. To this end two parent solutions were prepared: One of them contained one equivalent of the guest, dissolved in 8 mL of solvent. The respective host solution contained 1.525 equivalents and was dissolved in 610µl of DMSO. Ten NMR tubes were each filled with the same amount of guest solution (0.8 mL). The increasing amounts of host solution (10-200µl) were injected into these tubes with a mocrosyringe and their NMR spectra were recorded. For the evaluation only sharp NMR signals were used which gave unambiguous chemical shift data during the whole titration. The calculation of association constants was performed by nonlinear regression of the binding isotherms. Table 1-4 summarize all relevant titration data for elected examples of NMR titrations with host **1** and **2**.

Contrary to the diamine guests the spiro hosts **1** and **2** carry aromatic protons. Therefore these signals can be easily assigned and observed during the whole titration. This is the reason, why **1** and **2** were used as analytes, and the host solutions were titrated to them. The diamines gave signals between 0 - 4 ppm, which become superimposed by host signals during the titration. Thus it is very difficult to use them as titrants.

Almost all the chemically induced sifts were low-field shifts, which were feeded into the regression as absolute, positive values in order to get positive Δδ-values.



NMR titration curve for the addition of host molecule **1** to a solution of Cyc (diaminocyclohxane) in DMSO.

Table 1: Host-guest titration of **1** *(3,01mg = 5,6µmol) with* ***Cyc*** *(1,60mg = 8,6µmol)*

Sample	Eq.	Host [µl]	Guest [µl]	δ[a] [ppm]	Δδ [ppm]	δ[b] [ppm]	Δδ [ppm]
0	0	0	800	7.1231	0	5.8813	0
1	0.25	10	800	7.1294	0.0063	5.8926	0.0113
2	0.50	20	800	7.1370	0.0139	5.9116	0.0303
3	0.75	30	800	7.1433	0.0202	5.9254	0.0440
4	1.00	40	800	7.1446	0.0215	5.9280	0.0466
5	1.25	50	800	7.1471	0.0240	5.9330	0.0516
6	1.50	60	800	7.1496	0.0265	5.9381	0.0567
7	2.00	80	800	7.1509	0.0278	5.9431	0.0617
8	3.00	120	800	7.1521	0.0290	5.9431	0.0617
9	5.00	200	800	7.1549	0.0318	5.9496	0.0683
				K_{ass} [l/mol]	11.000	K_{ass} [l/mol]	8.400
				Deviation [%]	35	Deviation [%]	32

[a] proton *ortho* of the phosphonate ester

[b] proton *meta* of the phosphonate ester

Table 2: Host-guest titration of **1** *(5,10mg = 9,5µmol) with* ***His*** *(2,30mg = 9,5µmol)*

Sample	Eq.	Host [µl]	Guest [µl]	δ[a] [ppm]	Δδ [ppm]	δ[b] [ppm]	Δδ [ppm]
0	0	0	800	7.1395	0	5.8990	0
1	0.16	10	800	7.1521	0.0126	5.9166	0.0175
2	0.33	20	800	7.1660	0.0265	5.9406	0.0415
3	0.49	30	800	7.1761	0.0366	5.9582	0.0592
4	0.66	40	800	7.1898	0.0503	5.9807	0.0817
5	0.82	50	800	7.1962	0.0567	5.9948	0.0957
6	0.98	60	800	7.2038	0.0643	6.0074	0.1084
7	1.31	80	800	7.2163	0.0768	6.0275	0.1285
8	1.97	120	800	7.2278	0.0883	6.0490	0.1500
9	3.28	200	800	7.2530	0.1135	6.0528	0.1538
				K_{ass} [l/mol^{-1}]	1.300	K_{ass} [l/mol^{-1}]	2.400
				Deviation [%]	16	Deviation [%]	11

[a] proton *ortho* of the phosphonate ester

[b] proton *meta* of the phosphonate ester

Table 3: Host-guest titration of **2** *(2,50mg = 3,6µmol) with* ***Cyc*** *(1,45mg = 7,8µmol)*

Sample	Eq.	Host [µl]	Guest [µl]	δ[a] [ppm]	Δδ [ppm]	δ[b] [ppm]	Δδ [ppm]
0	0	0	800	4.8689	0	5.1539	0
1	0,35	10	800	4.8904	0.0215	5.1980	0.0441
2	0,69	20	800	4.9131	0.0442	5.2409	0.0870
3	1,04	30	800	4.9572	0.0883	5.2812	0.1273
4	1,38	40	800	4.9925	0.1236	5.3039	0.1500
5	1,73	50	800	4.9988	0.1299	5.3127	0.1588
6	2,08	60	800	5.0076	0.1387	5.3203	0.1664
7	2,77	80	800	5.0152	0.1463	5.3291	0.1752
8	4,15	120	800	5.0190	0.1501	5.3341	0.1802
9	6,92	200	800	5.0278	0.1589	5.3404	0.1865
				K_{ass} [l/mol^{-1}]	1160	K_{ass} [l/mol^{-1}]	2040
				Deviation [%]	36	Deviation [%]	20

[a] aromatic proton at the mesitylene bridge

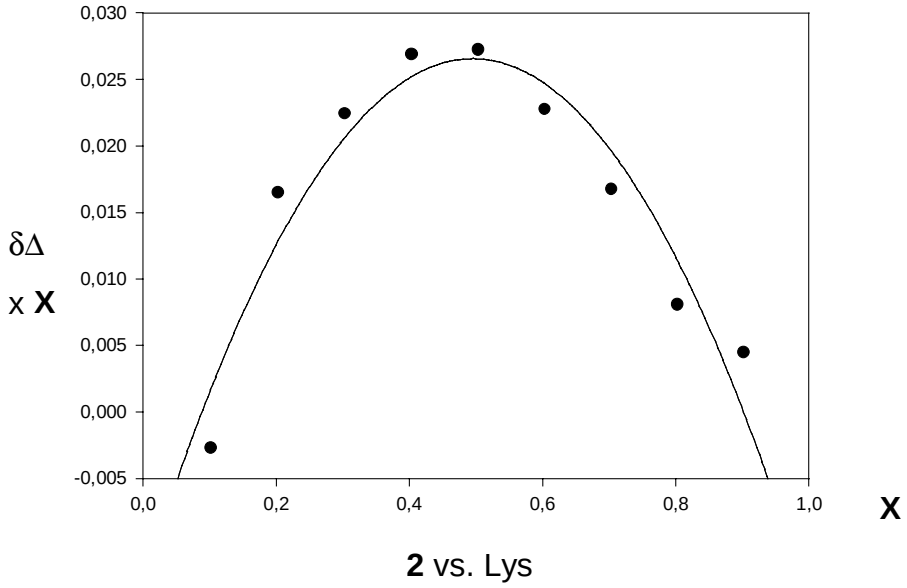
[b] proton α of the aromatic oxygen

Table 4: Host-guest titration of **2** *(2,71mg = 3,9µmol) with* ***Lys*** *(1,05mg = 1,40µmol)*

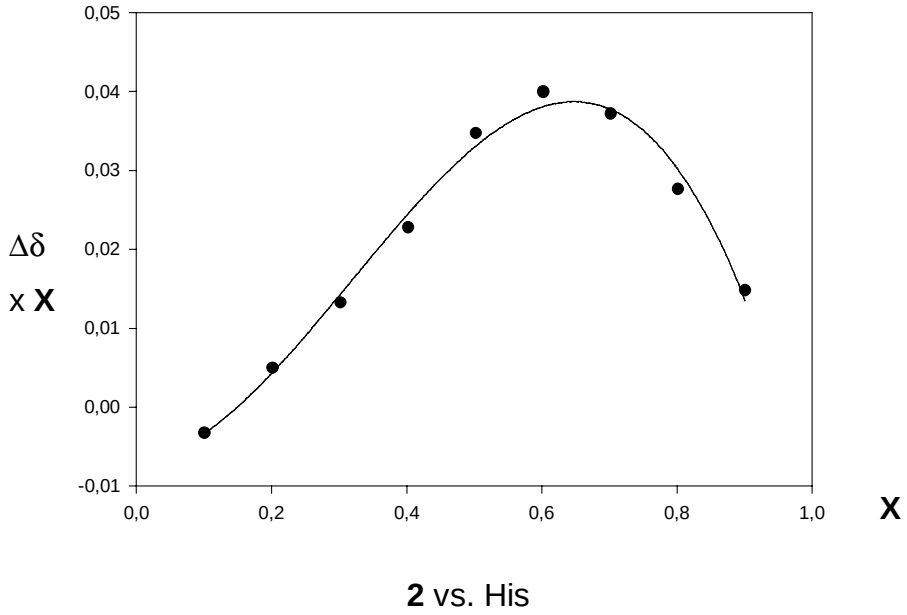
Sample	Eq.	Host [µl]	Guest [µl]	δ [ppm]	Δδ [ppm]
0	0	0	800	5,8458	0,0000
4	0,89	0,035	800	5,9430	0,0972
5	1,02	0,04	800	5,9632	0,1174
6	1,14	0,045	800	5,9707	0,1249
7	1,27	0,05	800	5,9719	0,1261
8	1,78	0,07	800	5,9809	0,1351
9	7,60	0,3	800	5,9984	0,1526
				K_{ass} [l/mol^{-1}]	20.900
				Deviation [%]	26

Job-Plot

Exactly one equivalent of both complex partners is dissolved each in 3.6 mL of DMSO. These parent solutions are combined in varying ratios, reaching from 0:10 to 10:0. NMR spectra are recorded for each mixture, and those proton signals, which could observed as sharp signals throughout the entire experiment, were used for the evaluation of the complex stoichiometry according to Job's method of continuous variations. The experimental data for two representative Job-Plot experiments are summarized in Table 5 and 6.



Job-Plot for the complexation of lysine methyl ester with macrocyclic host molecule **2.**



Job-Plot for the complexation of histidine methyl ester with macrocyclic host molecule **2.**

*Table 5: Job-Plot of **His** (1,33mg = 5,5µmol) with **2** (3,71mg = 5,3µmol)*

Sample	**His** [µl]	**2** [µl]	δ^1 [ppm]	$\Delta\delta$ [ppm]	δ^2 [ppm]	$\Delta\delta$ [ppm]
0	20	0	3.7330	0	2.4574	0
1	80	720	3.7366	-0.0036	2.4512	0.0062
2	160	640	3.7267	0.0063	2.4500	0.0074
3	240	560	3.7141	0.0189	2.4408	0.0166
4	320	480	3.6951	0.0379	2.4354	0.0220
5	400	400	3.6637	0.0693	2.4356	0.0218
6	480	320	3.6334	0.0996	2,43	0.0231
7	560	240	3.6065	0.1235	2.4357	0.0217
8	640	160	3.5956	0.1374	2.4344	0.0230
9	700	80	3.5855	0.1475	2.4357	0.0217

[1] protons of the methyl ester

[2] proton β of the carboxylic ester

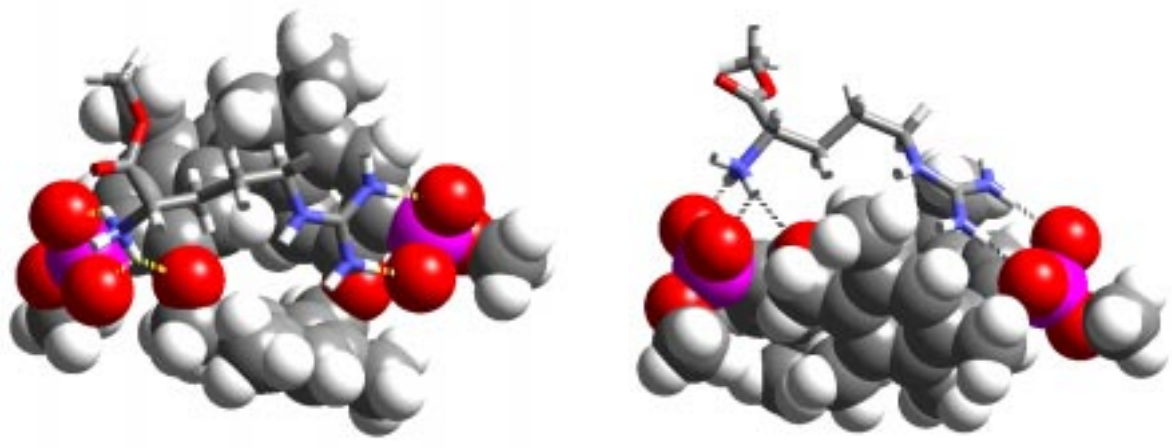
*Table 6: Job-Plot of **Lys** (1,32mg = 5,7µmol) witht **2** (3,90mg = 5,6µmol)*

Sample	**Lys** [µl]	**2** [µl]	δ^1 [ppm]	$\Delta\delta$ [ppm]	δ^2 [ppm]	$\Delta\delta$ [ppm]
0	20	0	6.7550	0	4.9029	0
1	80	720	6.7600	-0.0050	4.9131	-0.0102
2	160	640	6.7651	-0.0101	4.9181	-0.0152
3	240	560	6.7789	-0.0239	4.9345	-0.0316
4	320	480	6.7928	-0.0378	4.9534	-0.0505
5	400	400	6,81	-0.0542	4.9798	-0.0769
6	480	320	6,82	-0.0668	5.0038	-0.1009
7	560	240	6,83	-0.0743	5.0214	-0.1185
8	640	160	6,84	-0.0819	5.0391	-0.1362
9	700	80	6,73	0.0265	4.8500	0.0529

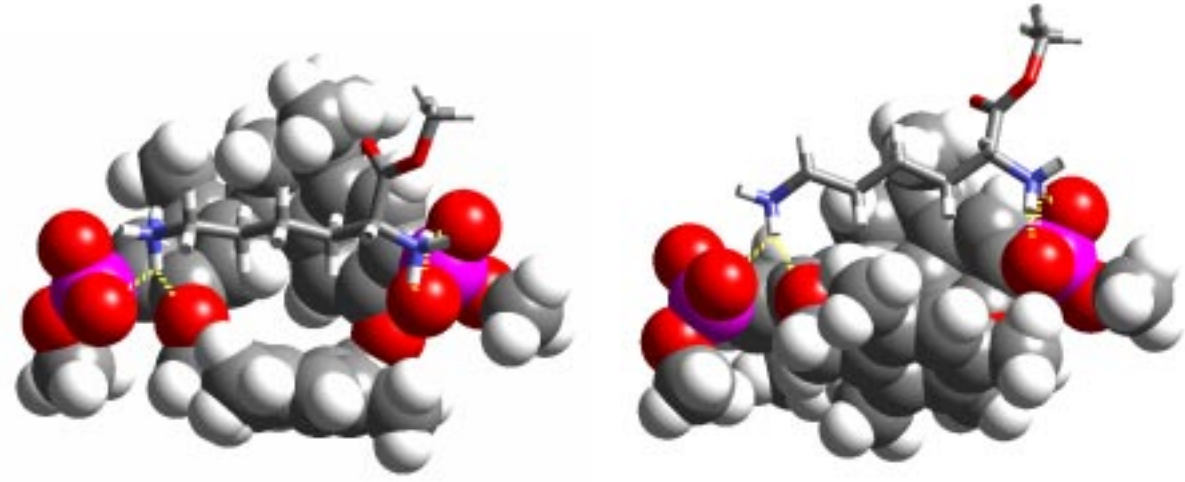
[1] aromatic proton at the mesitylene bridge

[2] proton α-of the aromatic oxygen

Complex structures between macrocyclic host 2 and arginine or lysine according to molecular mechanics calculations



Arginine methyl ester and macrocyclic host **2** - left: top view; right: side view.



Lysine methyl ester and macrocyclic host **2** - left: top view; right: side view.