Supplementary Material

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1 General information about materials, methods and instrumentation

1.1 Materials, reagents and solvents

All reagents and solvents were purchased from commercial suppliers. Macrocyclic host compounds were used only as (R,R)-cycHC\[n\] enantiomers and were synthesized in our laboratory from (R,R)-cyclohexanourea according to procedures described in literature (Aav et al., 2013; Prigorchenko et al., 2015; Kaabel et al., 2019).

1.2 Sample preparation

All the solutions were prepared using Hamilton® Gastight syringes, those syringes was also used for all the additions during titrations. For the precise measurement of higher volumes (over 1 ml) was used the mass of solvent and its density instead of volumetric glassware. Samples were weighed on a microbalance with an accuracy of 6 μg (Radwag® MYA 11.4Y, Poland).

1.3 NMR measurements

$^1$H NMR (400 MHz) and $^{19}$F NMR (376.5 MHz) spectra were recorded on Bruker Avance III spectrometer, using a Bruker BBO probe equipped with a z-gradient coil. Chemical shifts were referenced to residual proton solvent peak ($\delta(^1H) =3.34$ ppm in CD$_3$OD-$d_4$ and $\delta(^1H) =7.26$ ppm in CDC$_3$) or to TMS (0.00 ppm) as internal standard. All chemical shifts are reported in ppm units. The data was analyzed using the program MNova (Mestrelab).

As an internal reference for the fluorine signal position in $^{19}$F NMR of 9, we added hexafluorobenzene 19; however, it appeared that presence of reference inside the samples was not necessary as we did not observed fluctuations in reference $\delta$ between individual spectra.

1.4 Anion binding with cycHC[6]

Binding of anions to cycHC[6] was tested in CD$_3$OD-$d_4$ (0.8 mM cycHC[6]) and CDCl$_3$ (1.2 mM cycHC[6]) by addition of salt excess to the macrocycle solution. Tetrabutylammonium (TBA) chloride and bromide have been added as a solid compound. Specific excess of salt was determined from integration of NMR signals against known concentration of macrocycle. $^1$H NMR was measured shortly before and after a salt addition and then after 18 h. Dissolution of weakly soluble cycHC[6] in methanol was achieved by employing repeatedly heating and sonification.

1.5 Screening of potential guests in chloroform

Chemical shifts changes of cycHC[8] (ca 2.5 mM) proton signals induced by addition of 0.5, 5 and 40 equiv of guests (1-9) were investigated by $^1$H NMR in CDCl$_3$. Guests were added as a solutions of known concentration (typically 300-400 mM).

1.6 Test of hydrogen bond formation

$^1$H NMR of pentafluorophenol (50 mM) in CDCl$_3$ was measured before and after the addition of solid cycHC[8] (20 mg), which provided solution containing roughly 0.5 eq of macrocycle.
1.7 Titration experiments in chloroform

All NMR titrations were performed at constant concentration of guest (2 mM for qualitative comparison titrations) in a sample throughout the whole experiment, that was achieved by dissolution of titrant (cycHC[n]) in the solution of guest. ¹H or ¹⁹F NMR was used according to the guest’s structure with a preference to use ¹⁹F NMR as it usually provided larger changes in chemical shift.

1.8 DFT calculations of partial atomic charges

The structures of the guests were built using the Avogadro molecular editor (Hanwell et al., 2012) and pre-optimised with the MMFF94 force field (Halgren, 1996). Density functional theory (DFT) with the functional B3LYP-D (D3BJ dispersion model) (Lee et al., 1988; Becke, 1992; Stephens et al., 1994; Ehrlich et al., 2011; Grimme et al., 2011; Vosko et al., 2011) in combination with the 6-311G** basis set (Frisch et al., 1984) was used to re-optimise the structures and the frequency calculations were used to confirm that the found structures were at a minimum. All DFT calculations were performed with NWChem 6.8 program package. (Aprà et al., 2020) The wavefunction from the DFT calculations was analysed by Multiwfn (Lu and Chen, 2012b) and the partial charges were found using the Hirshfeld charges model (Hirshfeld, 1977; Lu and Chen, 2012a). Mercury 4.2.0 (Macrae et al., 2006, 2008, 2020) was used to visualize the structures of molecules for Figure 5 in the main text.

1.9 Job's plot experiments

Continuous variation method was conducted at total concentration 10 mM for trifluoroacetic acid (guest 16) and cycHC[8] and at total concentration 20 mM for 16 and cycHC[6]. It means that we prepared solutions of a same concentration for both compounds used at particular experiment and then prepared set of NMR samples varying the ratios between the two compounds, therefore the total concentration in every sample is same.

1.10 Binding strength evaluation

Stepwise association constants were evaluated (Bindfit) and simulated (Bindsim) using online tools at supramolecular.org (Thordarson, 2011; Hibbert and Thordarson, 2016) and by our 3:1 binding model, which we introduced in previous publication (Ustrnul et al., 2019). In Bindfit we used 2:1 NMR binding model with "full flavor", which do not assume any specific relation: (i) between chemical shifts of HG and HG₂; (ii) between stepwise association constants (K₁, K₂). The 3:1 binding model was adapted to studied system of HB donors and macrocycle using following constrains: (i) \( K_{1obs} > K_{2obs} > K_{3obs} \) and (ii) and \( \delta_{HG1}, \delta_{HG2}, \delta_{HG3} \geq \delta_{EXPmax} - 5 (\delta_{EXPmax} - \delta_{EXPmin}) \); to prevent the chemical shift \( \delta \) of complexed guest (HGₙ) from diverging extremely from experimentally observed values.

The titration data were fitted using NumPy (1.10.2) and SciPy (0.18.1) libraries of Python 3. The script allows for simultaneous fitting of several datasets, which significantly improves stability of the fit results. This is essential in the case of 1:3 and 1:4 binding calculations. The leastsq function (implementation of the Levenberg-Marquadt algorithm) was used to determine the parameter set including the association constants \( K_1, K_2, \) and \( K_3 \) that minimizes \( \chi^2 = \sum [f(x_i) - y_i]^2 \), where \( f(x_i) \) is the theoretical value of the traced quantity (chemical shift) for a given pair of the host and guest concentration \( x_i = (c_{host0,i}, c_{guest0,i}) \); \( y_i \) is the corresponding experimental value. The concentrations of the free host and guest molecules as well as their complexes are calculated.
numerically (function `scipy.fsolve`), using the definition of the binding constants and the mass balance equations.

2 Structures of hosts and guest used in the study

![Chemical structures](image)

**Scheme 1.** Structures of macrocyclic hosts and small guest molecules used in the study.
Figure S1. $^1$H NMR spectra of free cycHC[6] in MeOD-$d_4$ (0.8 mM) and in the presence of chloride (8 equiv) and bromide (5 equiv) anions from tetrabutylammonium salts (cation signals assigned with asterisk). Measured 18 h after the salt addition.
Figure S2. $^1$H NMR spectra of free cycHC[6] in CDCl$_3$ (1.2 mM) and in the presence of tetrabutylammonium chloride (12 equiv) (cation signals assigned with asterisk).
Screening of potential guests (1-9) in chloroform

Figure S3. $^1$H NMR spectra of free cycHC[8] (2.5 mM) in CDCl$_3$ and in the presence of guestst 1-9 (40 equiv). Rest of the macrocycle's signals did not shifted or was covered with signals of guest. Additional signal in spectra with guest 8 corresponds to –OH group proton.
Figure S4. (A) $^1$H NMR spectra of free pentafluorophenol (10) in CDCl$_3$ (60 mM) and (B) in the presence of 0.5 eq of cycHC[8] (30 mM). Downfield shift of acidic proton correspond with formation of hydrogen bond to macrocycle.
5 NMR titrations, Job plots and the data evaluation

5.1 Cooperativity evaluation criterions for cycHC\[n\]

Let's define a stepwise association constant \(K_i\) for an interaction between a substrate (host) M having \(m\) identical, independent binding sites and a ligand (guest) L having 1 binding site (Ercolani, 2003).

\[
\begin{align*}
M + L & \rightleftharpoons K_1 ML \\
ML + L & \rightleftharpoons K_2 ML_2 \\
& \quad \vdots \\
ML_{i-1} + L & \rightleftharpoons K_i ML_i \\
ML_{m-1} + L & \rightleftharpoons K_m ML_m
\end{align*}
\]

Evaluation of stepwise association constants has to take in count the number of equal binding sites on same molecule of host (Ercolani, 2003; Thordarson, 2011). It can be derived what should be the ratio of stepwise association constants in systems with no cooperativity and this ratio can be used as a criterion to asses cooperativity. For a two-step binding it is generally know that non-cooperative system exhibits ratio of stepwise constants according equation \(K_1 = 4K_2\).

Here is a general equation for ratio between any two consecutive \(K_i\) in system \(ML_m\):

\[
\frac{K_{i+1}}{K_i} = \frac{i(m-i)}{(i+1)(m-i+1)}
\]

If the ratio \(K_{i+1}/K_i\) is satisfied with determined association constants then the system is noncooperative or statistical. If the ratio value is higher than it would be for statistical system then we speak about positive cooperativity. If the ratio value is lower than it would be for statistical system then we speak about negative cooperativity.

The \(K_{i+1}/K_i\) ratios for noncooperative binding of guest to \textbf{cycHC[6]} \((m = 6)\) based on equation above:

\[
\begin{align*}
K_2/K_1 &= 5/12 \\
K_3/K_2 &= 8/15 \\
K_4/K_3 &= 9/16 \\
K_5/K_4 &= 8/15 \\
K_6/K_5 &= 5/12
\end{align*}
\]

The \(K_{i+1}/K_i\) ratios for noncooperative binding of guest to \textbf{cycHC[8]} \((m = 8)\) based on equation above:

\[
\begin{align*}
K_2/K_1 &= 7/16 \\
K_3/K_2 &= 12/21 \\
K_4/K_3 &= 15/24 \\
K_5/K_4 &= 16/25 \\
K_6/K_5 &= 15/24 \\
K_7/K_6 &= 12/21 \\
K_8/K_7 &= 7/16
\end{align*}
\]
5.2 Normalization of titration curves

For the normalization of titration curves was used following formula:

\[ N_x = 1 - \frac{\delta_x - \delta_y}{\delta_0 - \delta_y} \]

Where
\( N_x \) is normalized value of chemical shift at \( x \) equivalents of cycHC[\( n \)]
\( \delta_x \text{ equiv} \) is chemical shift of guest at \( x \) equivalents of cycHC[\( n \)]
\( \delta_0 \text{ equiv} \) is chemical shift of guest at 0 equivalents of cycHC[\( n \)]
\( \delta_y \text{ equiv} \) is chemical shift of guest at \( X \) equivalents of cycHC[\( n \)], which is point for which we normalize a titration curve

5.3 NMR titration data for association constants evaluation

Following NMR data for trifluoroacetic acid 16 (Table S13-S17) and methanesulfonic acid 18 (Table S19-S22) were used for qualitative comparison between binding of trifluoroacetic acid 16 with cycHC[6] and cycHC[8] and for qualitative comparison between binding of cycHC[6] with guest 16 and 18. All of these data for 16 and 18 were also used for evaluation of first three apparent stepwise association constants with our 3:1 binding model (Ustrnul et al., 2019). Following constrains were used to improve a chance for a binding model to converge: (i) \( K_{1\text{obs}} > K_{2\text{obs}} > K_{3\text{obs}} \) and (ii) \( \delta_{HG1}, \delta_{HG2}, \delta_{HG3} \geq \delta_{\text{EXPmax}} - 5(\delta_{\text{EXPmax}} - \delta_{\text{EXPmin}}) \); to prevent the chemical shift \( \delta \) of complexed guest (HG\( x \)) from diverging extremely from experimentally observed values.

Note:
Even if we would be adding a guest to the macrocycle, we could not easily distinguish between complexes of different stoichiometry, which would eventually lead to large errors in evaluating stepwise \( K_a \). Moreover, the number of variables in the evaluation process, which has to be fitted simultaneously, grows exponentially with the increasing stoichiometry, hence obtaining reliable values of all six or eight stepwise association constants for cycHC[6] or cycHC[8] is very difficult. Determination of all \( K_a \) would require excessive amount of experimental data from wide range of concentrations, which can be often impossible to do, for example due to a limited solubility of host or guest.
5.4 NMR titration data

Table S1. $^1$H NMR titration data for 2 mM thiophenol (guest 6) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest 6 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1, ppm | H1 normalized at 10 equiv |
|-----|--------------------------|---------------------------|-------------------|---------|--------------------------|
| 1   | 1.98E-03                 | 0.00E+00                  | 0.00              | 7.2321  | 0.0000                   |
| 2   | 1.98E-03                 | 9.90E-04                  | 0.50              | 7.2317  | 0.0506                   |
| 3   | 1.98E-03                 | 2.03E-03                  | 1.02              | 7.2318  | 0.0380                   |
| 4   | 1.98E-03                 | 4.02E-03                  | 2.03              | 7.2305  | 0.2025                   |
| 5   | 1.98E-03                 | 5.98E-03                  | 3.01              | 7.2298  | 0.2911                   |
| 6   | 1.98E-03                 | 7.96E-03                  | 4.01              | 7.2292  | 0.3671                   |
| 7   | 1.98E-03                 | 9.95E-03                  | 5.01              | 7.2283  | 0.4810                   |
| 8   | 1.98E-03                 | 1.19E-02                  | 6.02              | 7.2273  | 0.6076                   |
| 9   | 1.98E-03                 | 1.39E-02                  | 7.01              | 7.2267  | 0.6835                   |
| 10  | 1.98E-03                 | 1.59E-02                  | 8.01              | 7.2258  | 0.7975                   |
| 11  | 1.98E-03                 | 1.79E-02                  | 9.01              | 7.2251  | 0.8861                   |
| 12  | 1.98E-03                 | 1.98E-02                  | 10.01             | 7.2242  | 1.0000                   |
| 13  | 1.98E-03                 | 2.18E-02                  | 11.00             | 7.2236  | 1.0759                   |
Table S2. $^{19}$F NMR titration data for 2 mM 3-(trifluoromethyl)phenol (guest 9) with cycHC[6], in CDCl$_3$ in presence of hexafluorobenzene (19) and corresponding spectra below.

| Nr. | Guest 9 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | F1, ppm | F1 normalized at 10 equiv |
|-----|--------------------------|---------------------------|------------------|--------|--------------------------|
| 1   | 1.97E-03                 | 0.00E+00                  | 0.00             | -62.8125 | 0.0000                  |
| 2   | 1.97E-03                 | 9.81E-04                  | 0.50             | -62.8044 | 0.0904                  |
| 3   | 1.97E-03                 | 1.94E-03                  | 0.98             | -62.7962 | 0.1819                  |
| 4   | 1.97E-03                 | 3.90E-03                  | 1.98             | -62.7827 | 0.3326                  |
| 5   | 1.97E-03                 | 5.88E-03                  | 2.98             | -62.7718 | 0.4542                  |
| 6   | 1.97E-03                 | 7.86E-03                  | 3.99             | -62.7609 | 0.5759                  |
| 7   | 1.97E-03                 | 9.84E-03                  | 4.99             | -62.7528 | 0.6663                  |
| 8   | 1.97E-03                 | 1.18E-02                  | 5.99             | -62.7447 | 0.7567                  |
| 9   | 1.97E-03                 | 1.38E-02                  | 6.99             | -62.7392 | 0.8181                  |
| 10  | 1.97E-03                 | 1.57E-02                  | 7.99             | -62.7338 | 0.8783                  |
| 11  | 1.97E-03                 | 1.77E-02                  | 8.99             | -62.7284 | 0.9386                  |
| 12  | 1.97E-03                 | 1.97E-02                  | 9.99             | -62.7229 | 1.0000                  |
| 13  | 1.97E-03                 | 2.16E-02                  | 10.98            | -62.7175 | 1.0603                  |
| 14  | 1.97E-03                 | 2.38E-02                  | 12.05            | -62.7148 | 1.0904                  |
Table S3. $^{19}$F NMR titration data for 2 mM pentafluorophenol (guest 10) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest 10 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | F1, ppm | F1 normalized at 10 equiv | F2, ppm | F3, ppm |
|-----|---------------------------|---------------------------|-------------------|--------|--------------------------|--------|--------|
| 1   | 2.04E-03                  | 0.00E+00                  | 0.00              | -163.402 | 0.0000                  | -163.455 | -168.031 |
| 2   | 2.04E-03                  | 1.03E-03                  | 0.50              | -163.357 | 0.1125                  | -163.543 | -168.182 |
| 3   | 2.04E-03                  | 2.04E-03                  | 1.00              | -163.319 | 0.2062                  | -163.622 | -168.313 |
| 4   | 2.04E-03                  | 3.07E-03                  | 1.51              | -163.283 | 0.2949                  | -163.694 | -168.433 |
| 5   | 2.04E-03                  | 4.09E-03                  | 2.01              | -163.252 | 0.3730                  | -163.757 | -168.539 |
| 6   | 2.04E-03                  | 6.13E-03                  | 3.01              | -163.197 | 0.5083                  | -163.865 | -168.719 |
| 7   | 2.04E-03                  | 8.17E-03                  | 4.01              | -163.152 | 0.6201                  | -163.954 | -168.868 |
| 8   | 2.04E-03                  | 1.22E-02                  | 6.01              | -163.084 | 0.7881                  | -164.086 | -169.090 |
| 9   | 2.04E-03                  | 1.63E-02                  | 8.01              | -163.035 | 0.9103                  | -164.184 | -169.252 |
| 10  | 2.04E-03                  | 2.04E-02                  | 10.02             | -162.999 | 1.0000                  | -164.255 | -169.371 |
| 11  | 2.04E-03                  | 2.45E-02                  | 12.02             | -162.968 | 1.0761                  | -164.315 | -169.471 |
| 12  | 2.04E-03                  | 2.86E-02                  | 14.02             | -162.944 | 1.1368                  | -164.363 | -169.552 |
| 13  | 2.04E-03                  | 3.26E-02                  | 16.02             | -162.924 | 1.1854                  | -164.398 | -169.610 |
| 14  | 2.04E-03                  | 3.67E-02                  | 18.02             | -162.907 | 1.2283                  | -164.435 | -169.673 |
| 15  | 2.04E-03                  | 3.93E-02                  | 19.29             | -162.897 | 1.2525                  | -164.453 | -169.703 |
Table S4. $^1$H NMR titration data for 2 mM 4-chlorothiophenol (guest 11) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest 11 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1, ppm | H1 normalized at 10 equiv |
|-----|--------------------------|---------------------------|-------------------|--------|--------------------------|
| 1   | 1.97E-03                 | 0.00E+00                  | 0.00              | 7.2067 | 0.0000                   |
| 2   | 1.97E-03                 | 9.94E-04                  | 0.49              | 7.2061 | 0.0759                   |
| 3   | 1.97E-03                 | 1.96E-03                  | 0.99              | 7.2061 | 0.0759                   |
| 4   | 1.97E-03                 | 3.91E-03                  | 1.98              | 7.2051 | 0.2025                   |
| 5   | 1.97E-03                 | 5.92E-03                  | 2.99              | 7.2044 | 0.2911                   |
| 6   | 1.97E-03                 | 7.89E-03                  | 3.98              | 7.2036 | 0.3924                   |
| 7   | 1.97E-03                 | 9.86E-03                  | 4.98              | 7.2029 | 0.4810                   |
| 8   | 1.97E-03                 | 1.18E-02                  | 5.98              | 7.2019 | 0.6076                   |
| 9   | 1.97E-03                 | 1.38E-02                  | 6.98              | 7.2013 | 0.6835                   |
| 10  | 1.97E-03                 | 1.58E-02                  | 7.99              | 7.2004 | 0.7975                   |
| 11  | 1.97E-03                 | 1.78E-02                  | 8.99              | 7.1997 | 0.8861                   |
| 12  | 1.97E-03                 | 1.97E-02                  | 10.00             | 7.1988 | 1.0000                   |
| 13  | 1.97E-03                 | 2.17E-02                  | 11.01             | 7.1982 | 1.0759                   |
| 14  | 1.97E-03                 | 2.39E-02                  | 11.56             | 7.1975 | 1.1646                   |
Table S5. $^1$H NMR titration data for 2 mM benzoic acid (guest 12) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest 12 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1, ppm | H1 normalized at 10 equiv | H2, ppm | H3, ppm |
|-----|---------------------------|---------------------------|-------------------|---------|--------------------------|---------|---------|
| 1   | 1.97E-03                  | 0.00E+00                  | 0.00              | 8.0947  | 0.0000                   | 7.6167  | 7.4799  |
| 2   | 1.97E-03                  | 9.94E-04                  | 0.50              | 8.0928  | 0.0640                   | 7.6148  | 7.4784  |
| 3   | 1.97E-03                  | 1.96E-03                  | 1.00              | 8.0909  | 0.1279                   | 7.6129  | 7.4771  |
| 4   | 1.97E-03                  | 3.91E-03                  | 1.98              | 8.0873  | 0.2492                   | 7.6090  | 7.4738  |
| 5   | 1.97E-03                  | 5.92E-03                  | 3.00              | 8.0837  | 0.3704                   | 7.6051  | 7.4708  |
| 6   | 1.97E-03                  | 7.89E-03                  | 4.00              | 8.0807  | 0.4714                   | 7.6017  | 7.4684  |
| 7   | 1.97E-03                  | 9.86E-03                  | 5.00              | 8.0779  | 0.5657                   | 7.5983  | 7.4662  |
| 8   | 1.97E-03                  | 1.18E-02                  | 6.00              | 8.0778  | 0.5690                   | 7.5982  | 7.4661  |
| 9   | 1.97E-03                  | 1.38E-02                  | 7.00              | 8.0724  | 0.7508                   | 7.5922  | 7.4614  |
| 10  | 1.97E-03                  | 1.58E-02                  | 8.00              | 8.0697  | 0.8418                   | 7.5895  | 7.4590  |
| 11  | 1.97E-03                  | 1.78E-02                  | 9.01              | 8.0675  | 0.9158                   | 7.5867  | 7.4571  |
| 12  | 1.97E-03                  | 1.97E-02                  | 10.00             | 8.0650  | 1.0000                   | 7.5839  | 7.4549  |
| 13  | 1.97E-03                  | 2.17E-02                  | 11.00             | 8.0629  | 1.0707                   | 7.5818  | 7.4532  |
| 14  | 1.97E-03                  | 2.39E-02                  | 12.12             | 8.0603  | 1.1582                   | 7.5788  | 7.4509  |
**Table S6.** $^1$H NMR titration data for 2 mM bromoacetic acid (guest 13) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest 13 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1, ppm | H1 normalized at 10 equiv |
|-----|---------------------------|---------------------------|-------------------|---------|--------------------------|
| 1   | 1.99E-03                  | 0.00E+00                  | 0.00              | 3.8999  | 0.0000                   |
| 2   | 1.99E-03                  | 9.98E-04                  | 0.50              | 3.8948  | 0.1063                   |
| 3   | 1.99E-03                  | 1.99E-03                  | 1.00              | 3.8903  | 0.2000                   |
| 4   | 1.99E-03                  | 3.00E-03                  | 1.51              | 3.8862  | 0.2854                   |
| 5   | 1.99E-03                  | 3.99E-03                  | 2.01              | 3.8826  | 0.3604                   |
| 6   | 1.99E-03                  | 5.98E-03                  | 3.01              | 3.8763  | 0.4917                   |
| 7   | 1.99E-03                  | 7.96E-03                  | 4.00              | 3.8711  | 0.6000                   |
| 8   | 1.99E-03                  | 1.20E-02                  | 6.00              | 3.8629  | 0.7708                   |
| 9   | 1.99E-03                  | 1.59E-02                  | 8.00              | 3.8567  | 0.9000                   |
| 10  | 1.99E-03                  | 1.99E-02                  | 10.00             | 3.8519  | 1.0000                   |
| 11  | 1.99E-03                  | 2.39E-02                  | 12.00             | 3.8479  | 1.0833                   |
| 12  | 1.99E-03                  | 2.79E-02                  | 14.01             | 3.8443  | 1.1583                   |
| 13  | 1.99E-03                  | 3.19E-02                  | 16.01             | 3.8413  | 1.2208                   |
| 14  | 1.99E-03                  | 3.59E-02                  | 18.01             | 3.8386  | 1.2771                   |
| 15  | 1.99E-03                  | 4.56E-02                  | 22.90             | 3.8329  | 1.3958                   |
Table S7. $^{19}$F NMR titration data for 2 mM 2,3,4,5-tetrafluorobenzoic acid (guest 14) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest 14 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | F1, ppm | F1 normalized at 10 equiv | F2, ppm | F3, ppm | F4, ppm |
|-----|--------------------------|---------------------------|-------------------|--------|-------------------------|--------|--------|--------|
| 1   | 2.03E-03                 | 0.00E+00                  | 0.00              | -132.812 | 0.0000                  | -137.262 | -145.321 | -152.754 |
| 2   | 2.03E-03                 | 1.02E-03                  | 0.50              | -132.933 | 0.1046                  | -137.343 | -145.524 | -152.835 |
| 3   | 2.03E-03                 | 2.03E-03                  | 1.00              | -133.048 | 0.2044                  | -137.463 | -145.687 | -152.894 |
| 4   | 2.03E-03                 | 3.05E-03                  | 1.50              | -133.153 | 0.2955                  | -137.463 | -145.836 | -152.947 |
| 5   | 2.03E-03                 | 4.06E-03                  | 2.00              | -133.248 | 0.3778                  | -137.515 | -145.971 | -152.997 |
| 6   | 2.03E-03                 | 6.09E-03                  | 3.00              | -133.410 | 0.5184                  | -137.604 | -146.200 | -153.080 |
| 7   | 2.03E-03                 | 8.13E-03                  | 4.00              | -133.541 | 0.6321                  | -137.676 | -146.385 | -153.147 |
| 8   | 2.03E-03                 | 1.22E-02                  | 6.01              | -133.735 | 0.8008                  | -137.783 | -146.657 | -153.246 |
| 9   | 2.03E-03                 | 1.63E-02                  | 8.01              | -133.869 | 0.9176                  | -137.857 | -146.845 | -153.316 |
| 10  | 2.03E-03                 | 2.03E-02                  | 10.00             | -133.964 | 1.0000                  | -137.910 | -146.977 | -153.365 |
| 11  | 2.03E-03                 | 2.44E-02                  | 12.00             | -134.038 | 1.0641                  | -137.951 | -147.080 | -153.403 |
| 12  | 2.03E-03                 | 2.84E-02                  | 14.00             | -134.095 | 1.1134                  | -138.984 | -147.159 | -153.433 |
| 13  | 2.03E-03                 | 3.25E-02                  | 15.99             | -134.139 | 1.1513                  | -138.009 | -147.221 | -153.457 |
| 14  | 2.03E-03                 | 3.66E-02                  | 17.99             | -134.175 | 1.1829                  | -138.030 | -147.272 | -153.476 |
| 15  | 2.03E-03                 | 3.91E-02                  | 19.25             | -134.195 | 1.2003                  | -138.042 | -147.300 | -153.487 |
**Table S8.** $^{19}$F NMR titration data for 2 mM $R$-Mosher's acid (guest $R$-15) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest R-15 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | F1, ppm | F1 normalized at 10 equiv | F1 normalized at 11 equiv |
|-----|-----------------------------|---------------------------|-------------------|---------|--------------------------|--------------------------|
| 1   | 2.03E-03                    | 0.00E+00                  | 0.00              | -70.650 | 0.0000                   | 0.0000                   |
| 2   | 2.03E-03                    | 1.02E-03                  | 0.50              | -70.737 | 0.1412                   | 0.1369                   |
| 3   | 2.03E-03                    | 2.02E-03                  | 1.00              | -70.810 | 0.2589                   | 0.2511                   |
| 4   | 2.03E-03                    | 4.07E-03                  | 2.01              | -70.923 | 0.4411                   | 0.4277                   |
| 5   | 2.03E-03                    | 6.08E-03                  | 3.00              | -71.009 | 0.5785                   | 0.5609                   |
| 6   | 2.03E-03                    | 8.11E-03                  | 4.01              | -71.073 | 0.6824                   | 0.6616                   |
| 7   | 2.03E-03                    | 1.02E-02                  | 5.01              | -71.124 | 0.7648                   | 0.7414                   |
| 8   | 2.03E-03                    | 1.22E-02                  | 6.01              | -71.165 | 0.8313                   | 0.8060                   |
| 9   | 2.03E-03                    | 1.42E-02                  | 7.01              | -71.198 | 0.8844                   | 0.8574                   |
| 10  | 2.03E-03                    | 1.62E-02                  | 8.00              | -71.226 | 0.9294                   | 0.9010                   |
| 11  | 2.03E-03                    | 1.82E-02                  | 9.01              | -71.251 | 0.9687                   | 0.9392                   |
| 12  | 2.03E-03                    | 2.03E-02                  | 10.01             | -71.270 | 1.0000                   | 0.9695                   |
| 13  | 2.03E-03                    | 2.23E-02                  | 11.01             | -71.289 | 1.0314                   | 1.0000                   |
Table S9. Second independent $^{19}$F NMR titration data for 2 mM R-Mosher’s acid (guest R-15) with cycHC[6], in CDCl₃.

| Nr. | Guest R-15 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | F₁, ppm | F₁ normalized at 11 equiv |
|-----|-----------------------------|-----------------------------|-------------------|---------|--------------------------|
| 1   | 2.03E-03                    | 0.00E+00                    | 0.00              | -70.666 | 0.0000                   |
| 2   | 2.03E-03                    | 1.01E-04                    | 0.05              | -70.676 | 0.0156                   |
| 3   | 2.03E-03                    | 2.01E-04                    | 0.10              | -70.684 | 0.0291                   |
| 4   | 2.03E-03                    | 3.02E-04                    | 0.15              | -70.692 | 0.0428                   |
| 5   | 2.03E-03                    | 4.02E-04                    | 0.20              | -70.700 | 0.0561                   |
| 6   | 2.03E-03                    | 1.02E-03                    | 0.50              | -70.748 | 0.1351                   |
| 7   | 2.03E-03                    | 2.03E-03                    | 1.00              | -70.815 | 0.2449                   |
| 8   | 2.03E-03                    | 4.05E-03                    | 2.00              | -70.921 | 0.4196                   |
| 9   | 2.03E-03                    | 6.07E-03                    | 2.99              | -71.001 | 0.5501                   |
| 10  | 2.03E-03                    | 1.01E-02                    | 4.99              | -71.112 | 0.7335                   |
| 11  | 2.03E-03                    | 1.42E-02                    | 6.99              | -71.185 | 0.8531                   |
| 12  | 2.03E-03                    | 1.82E-02                    | 8.99              | -71.236 | 0.9380                   |
| 13  | 2.03E-03                    | 2.23E-02                    | 10.99             | -71.274 | 1.0000                   |
| 14  | 2.03E-03                    | 2.64E-02                    | 12.99             | -71.304 | 1.0487                   |
| 15  | 2.03E-03                    | 3.07E-02                    | 15.12             | -71.328 | 1.0887                   |

Table S10. $^{19}$F NMR titration data for 2 mM S-Mosher’s acid (guest S-15) with cycHC[6], in CDCl₃.

| Nr. | Guest S-15 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | F₁, ppm | F₁ normalized at 11 equiv |
|-----|-----------------------------|-----------------------------|-------------------|---------|--------------------------|
| 1   | 2.01E-03                    | 0.00E+00                    | 0.00              | -70.655 | 0.0000                   |
| 2   | 2.01E-03                    | 1.06E-04                    | 0.05              | -70.665 | 0.0167                   |
| 3   | 2.01E-03                    | 2.12E-04                    | 0.11              | -70.674 | 0.0313                   |
| 4   | 2.01E-03                    | 3.18E-04                    | 0.16              | -70.683 | 0.0459                   |
| 5   | 2.01E-03                    | 4.24E-04                    | 0.21              | -70.691 | 0.0590                   |
| 6   | 2.01E-03                    | 1.02E-03                    | 0.51              | -70.737 | 0.1344                   |
| 7   | 2.01E-03                    | 2.03E-03                    | 1.01              | -70.805 | 0.2461                   |
| 8   | 2.01E-03                    | 4.05E-03                    | 2.01              | -70.912 | 0.4220                   |
| 9   | 2.01E-03                    | 6.05E-03                    | 3.01              | -70.992 | 0.5526                   |
| 10  | 2.01E-03                    | 1.01E-02                    | 5.01              | -71.103 | 0.7350                   |
| 11  | 2.01E-03                    | 1.41E-02                    | 7.01              | -71.177 | 0.8555                   |
| 12  | 2.01E-03                    | 1.81E-02                    | 9.00              | -71.228 | 0.9385                   |
| 13  | 2.01E-03                    | 2.22E-02                    | 11.00             | -71.265 | 1.0000                   |
| 14  | 2.01E-03                    | 2.62E-02                    | 13.00             | -71.294 | 1.0475                   |
| 15  | 2.01E-03                    | 3.22E-02                    | 15.99             | -71.325 | 1.0990                   |
Table S11. $^1$H NMR titration data for 2 mM R-Mosher's acid (guest R-15) with cycHC[6], in CDCl$_3$

| Nr. | Guest R-15 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1, ppm | H1 normalized at 4 equiv |
|-----|----------------------------|----------------------------|--------------------|---------|-------------------------|
| 1   | 1.88E-03                   | 0.00E+00                   | 0.00               | 7.456   | 0.0000                  |
| 2   | 1.88E-03                   | 9.24E-05                   | 0.05               | 7.455   | 0.0072                  |
| 3   | 1.88E-03                   | 1.85E-04                   | 0.10               | 7.455   | 0.0179                  |
| 4   | 1.88E-03                   | 2.76E-04                   | 0.15               | 7.455   | 0.0323                  |
| 5   | 1.88E-03                   | 3.74E-04                   | 0.20               | 7.454   | 0.0466                  |
| 6   | 1.88E-03                   | 5.61E-04                   | 0.30               | 7.453   | 0.0860                  |
| 7   | 1.88E-03                   | 7.48E-04                   | 0.40               | 7.452   | 0.1254                  |
| 8   | 1.88E-03                   | 9.39E-04                   | 0.50               | 7.451   | 0.1649                  |
| 9   | 1.88E-03                   | 1.32E-03                   | 0.70               | 7.449   | 0.2401                  |
| 10  | 1.88E-03                   | 1.88E-03                   | 1.00               | 7.446   | 0.3369                  |
| 11  | 1.88E-03                   | 2.63E-03                   | 1.40               | 7.443   | 0.4588                  |
| 12  | 1.88E-03                   | 3.75E-03                   | 2.00               | 7.438   | 0.6165                  |
| 13  | 1.88E-03                   | 5.63E-03                   | 3.00               | 7.432   | 0.8315                  |
| 14  | 1.88E-03                   | 7.50E-03                   | 4.00               | 7.428   | 1.0000                  |
| 15  | 1.88E-03                   | 9.29E-03                   | 4.95               | 7.424   | 1.1290                  |

Table S12. $^1$H NMR titration data for 2 mM S-Mosher's acid (guest S-15) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest S-15 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1, ppm | H1 normalized at 4 equiv |
|-----|----------------------------|----------------------------|--------------------|---------|-------------------------|
| 1   | 2.18E-03                   | 0.00E+00                   | 0.00               | 7.455   | 0.0000                  |
| 2   | 2.18E-03                   | 1.05E-04                   | 0.05               | 7.455   | 0.0132                  |
| 3   | 2.18E-03                   | 2.16E-04                   | 0.10               | 7.454   | 0.0329                  |
| 4   | 2.18E-03                   | 3.27E-04                   | 0.15               | 7.454   | 0.0526                  |
| 5   | 2.18E-03                   | 4.37E-04                   | 0.20               | 7.453   | 0.0724                  |
| 6   | 2.18E-03                   | 6.56E-04                   | 0.30               | 7.452   | 0.1118                  |
| 7   | 2.18E-03                   | 8.73E-04                   | 0.40               | 7.451   | 0.1513                  |
| 8   | 2.18E-03                   | 1.09E-03                   | 0.50               | 7.449   | 0.1908                  |
| 9   | 2.18E-03                   | 1.53E-03                   | 0.70               | 7.447   | 0.2664                  |
| 10  | 2.18E-03                   | 2.19E-03                   | 1.00               | 7.444   | 0.3684                  |
| 11  | 2.18E-03                   | 3.06E-03                   | 1.40               | 7.440   | 0.4868                  |
| 12  | 2.18E-03                   | 4.37E-03                   | 2.00               | 7.436   | 0.6382                  |
| 13  | 2.18E-03                   | 6.55E-03                   | 3.00               | 7.429   | 0.8454                  |
| 14  | 2.18E-03                   | 8.74E-03                   | 4.00               | 7.425   | 1.0000                  |
| 15  | 2.18E-03                   | 9.61E-03                   | 4.40               | 7.423   | 1.0559                  |
Table S13. $^{19}$F NMR titration data for 2 mM trifluoroacetic acid (guest 16) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest 16 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | F1, ppm | F1 normalized at 10 equiv | F1 normalized at 9 equiv | F1 normalized at 5 equiv | F1 normalized at 1 equiv |
|-----|--------------------------|---------------------------|-------------------|--------|--------------------------|--------------------------|--------------------------|--------------------------|
| 1   | 2.00E-03                 | 0.00E+00                  | 0.00              | -75.577 | 0.0000                   | 0.0000                   | 0.0000                   | 0.0000                   |
| 2   | 2.00E-03                 | 4.87E-04                  | 0.24              | -75.641 | 0.2247                   | 0.2267                   | 0.2434                   | 0.3810                   |
| 3   | 2.00E-03                 | 9.90E-04                  | 0.49              | -75.687 | 0.3873                   | 0.3907                   | 0.4196                   | 0.6565                   |
| 4   | 2.00E-03                 | 1.49E-03                  | 0.74              | -75.720 | 0.5004                   | 0.5048                   | 0.5420                   | 0.8482                   |
| 5   | 2.00E-03                 | 1.98E-03                  | 0.99              | -75.745 | 0.5899                   | 0.5951                   | 0.6390                   | 1.0000                   |
| 6   | 2.00E-03                 | 2.56E-03                  | 1.28              | -75.766 | 0.6626                   | 0.6684                   | 0.7178                   | 1.1232                   |
| 7   | 2.00E-03                 | 3.18E-03                  | 1.59              | -75.783 | 0.7223                   | 0.7287                   | 0.7824                   | 1.2244                   |
| 8   | 2.00E-03                 | 3.99E-03                  | 1.99              | -75.797 | 0.7735                   | 0.7804                   | 0.8380                   | 1.3113                   |
| 9   | 2.00E-03                 | 6.00E-03                  | 2.99              | -75.818 | 0.8462                   | 0.8537                   | 0.9167                   | 1.4345                   |
| 10  | 2.00E-03                 | 8.00E-03                  | 3.99              | -75.833 | 0.8975                   | 0.9054                   | 0.9722                   | 1.5214                   |
| 11  | 2.00E-03                 | 1.00E-02                  | 4.99              | -75.840 | 0.9231                   | 0.9313                   | 1.0000                   | 1.5649                   |
| 12  | 2.00E-03                 | 1.20E-02                  | 5.97              | -75.848 | 0.9529                   | 0.9614                   | 1.0323                   | 1.6155                   |
| 13  | 2.00E-03                 | 1.40E-02                  | 6.97              | -75.852 | 0.9656                   | 0.9741                   | 1.0460                   | 1.6369                   |
| 14  | 2.00E-03                 | 1.60E-02                  | 7.97              | -75.856 | 0.9786                   | 0.9872                   | 1.0601                   | 1.6589                   |
| 15  | 2.00E-03                 | 1.80E-02                  | 8.97              | -75.859 | 0.9912                   | 1.0000                   | 1.0738                   | 1.6804                   |
| 16  | 2.00E-03                 | 2.00E-02                  | 9.97              | -75.862 | 1.0000                   | 1.0089                   | 1.0833                   | 1.6952                   |
| 17  | 2.00E-03                 | 2.20E-02                  | 10.97             | -75.862 | 1.0000                   | 1.0089                   | 1.0833                   | 1.6952                   |
| 18  | 2.00E-03                 | 2.48E-02                  | 12.39             | -75.865 | 1.0126                   | 1.0216                   | 1.0970                   | 1.7167                   |
**Table S14.** $^{19}$F NMR titration data for 2 mM trifluoroacetic acid (guest 16) with cycHC[8], in CDCl₃.

| Nr. | Guest 16 concentration, M | cycHC[8] concentration, M | molar ratio, equiv | F1, ppm | F1 normalized at 5 equiv |
|-----|---------------------------|---------------------------|-------------------|---------|-------------------------|
| 1   | 1.99E-03                  | 0.00E+00                  | 0.00              | -75.608 | 0.0000                  |
| 2   | 1.99E-03                  | 5.01E-04                  | 0.25              | -75.665 | 0.2692                  |
| 3   | 1.99E-03                  | 9.95E-04                  | 0.50              | -75.706 | 0.4615                  |
| 4   | 1.99E-03                  | 1.50E-03                  | 0.75              | -75.733 | 0.5895                  |
| 5   | 1.99E-03                  | 2.10E-03                  | 1.06              | -75.755 | 0.6920                  |
| 6   | 1.99E-03                  | 2.71E-03                  | 1.36              | -75.769 | 0.7563                  |
| 7   | 1.99E-03                  | 3.51E-03                  | 1.77              | -75.785 | 0.8333                  |
| 8   | 1.99E-03                  | 5.54E-03                  | 2.79              | -75.804 | 0.9230                  |
| 9   | 1.99E-03                  | 7.56E-03                  | 3.81              | -75.815 | 0.9745                  |
| 10  | 1.99E-03                  | 9.58E-03                  | 4.82              | -75.820 | 1.0000                  |
| 11  | 1.99E-03                  | 1.16E-02                  | 5.82              | -75.826 | 1.0255                  |
| 12  | 1.99E-03                  | 1.36E-02                  | 6.84              | -75.828 | 1.0383                  |
| 13  | 1.99E-03                  | 1.56E-02                  | 7.86              | -75.828 | 1.0383                  |
| 14  | 1.99E-03                  | 1.76E-02                  | 8.85              | -75.831 | 1.0510                  |
| 15  | 1.99E-03                  | 1.96E-02                  | 9.85              | -75.831 | 1.0510                  |
| 16  | 1.99E-03                  | 2.04E-02                  | 10.25             | -75.831 | 1.0510                  |

**Table S15.** Second independent $^{19}$F NMR titration data for 2 mM trifluoroacetic acid (guest 16) with cycHC[8], in CDCl₃.

| Nr. | Guest 16 concentration, M | cycHC[8] concentration, M | molar ratio, equiv | F1, ppm | F1 normalized at 5 equiv | F1 normalized at 1 equiv |
|-----|---------------------------|---------------------------|-------------------|---------|-------------------------|-------------------------|
| 1   | 1.90E-03                  | 0.00E+00                  | 0.00              | -75.442 | 0.0000                  | 0.0000                  |
| 2   | 1.90E-03                  | 9.44E-05                  | 0.05              | -75.468 | 0.0719                  | 0.1046                  |
| 3   | 1.90E-03                  | 1.90E-04                  | 0.10              | -75.487 | 0.1250                  | 0.1819                  |
| 4   | 1.90E-03                  | 2.85E-04                  | 0.15              | -75.507 | 0.1820                  | 0.2648                  |
| 5   | 1.90E-03                  | 3.81E-04                  | 0.20              | -75.526 | 0.2357                  | 0.3430                  |
| 6   | 1.90E-03                  | 5.71E-04                  | 0.30              | -75.560 | 0.3308                  | 0.4813                  |
| 7   | 1.90E-03                  | 7.62E-04                  | 0.40              | -75.589 | 0.4100                  | 0.5964                  |
| 8   | 1.90E-03                  | 9.54E-04                  | 0.50              | -75.612 | 0.4762                  | 0.6928                  |
| 9   | 1.90E-03                  | 1.33E-03                  | 0.70              | -75.649 | 0.5797                  | 0.8434                  |
| 10  | 1.90E-03                  | 1.91E-03                  | 1.00              | -75.688 | 0.6874                  | 1.0000                  |
| 11  | 1.90E-03                  | 2.67E-03                  | 1.40              | -75.720 | 0.7777                  | 1.1314                  |
| 12  | 1.90E-03                  | 3.81E-03                  | 2.00              | -75.750 | 0.8599                  | 1.2510                  |
| 13  | 1.90E-03                  | 5.71E-03                  | 3.00              | -75.776 | 0.9334                  | 1.3580                  |
| 14  | 1.90E-03                  | 7.62E-03                  | 4.00              | -75.790 | 0.9732                  | 1.4158                  |
| 15  | 1.90E-03                  | 9.53E-03                  | 5.00              | -75.800 | 1.0000                  | 1.4548                  |
| 16  | 1.90E-03                  | 1.62E-02                  | 8.52              | -75.810 | 1.0291                  | 1.4972                  |
Figure S5. $^{19}$F NMR titration data for trifluoroacetic acid 16 (2 mM) in the presence of growing concentration of cycHC[6] (purple) and cycHC[8] (red and green) normalized at ca 5 equiv. Experimental datapoints from Table S13, Table S14, Table S15 are assigned with circles, the dotted lines are shown to guide the eye. More pronounced curves for titrations with cycHC[8] are suggesting stronger binding caused by larger amount of available binding sites (carbonyl groups) on cycHC[8] in comparison with cycHC[6].
Table S16. $^{19}$F NMR titration data for 18 mM trifluoroacetic acid (guest 16) with cycHC[6], in CDCl$_3$

| Nr. | Guest 16 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | F1, ppm | F1 normalized at 1.2 equiv | F1 normalized at 1 equiv |
|-----|---------------------------|----------------------------|-------------------|---------|---------------------------|-------------------------|
| 1   | 1.82E-02                  | 0.00E+00                   | 0.00              | -75.569 | 0.0000                    | 0.0000                  |
| 2   | 1.82E-02                  | 3.75E-04                   | 0.02              | -75.604 | 0.1232                    | 0.1255                  |
| 3   | 1.82E-02                  | 7.47E-04                   | 0.04              | -75.635 | 0.2283                    | 0.2324                  |
| 4   | 1.82E-02                  | 1.12E-03                   | 0.06              | -75.660 | 0.3151                    | 0.3209                  |
| 5   | 1.82E-02                  | 1.49E-03                   | 0.08              | -75.681 | 0.3876                    | 0.3946                  |
| 6   | 1.82E-02                  | 1.85E-03                   | 0.10              | -75.706 | 0.4710                    | 0.4796                  |
| 7   | 1.82E-02                  | 2.22E-03                   | 0.12              | -75.717 | 0.5108                    | 0.5201                  |
| 8   | 1.82E-02                  | 2.77E-03                   | 0.15              | -75.739 | 0.5836                    | 0.5942                  |
| 9   | 1.82E-02                  | 3.67E-03                   | 0.20              | -75.764 | 0.6704                    | 0.6826                  |
| 10  | 1.82E-02                  | 4.59E-03                   | 0.25              | -75.779 | 0.7212                    | 0.7344                  |
| 11  | 1.82E-02                  | 5.49E-03                   | 0.30              | -75.790 | 0.7611                    | 0.7749                  |
| 12  | 1.82E-02                  | 7.31E-03                   | 0.40              | -75.812 | 0.8369                    | 0.8521                  |
| 13  | 1.82E-02                  | 9.12E-03                   | 0.50              | -75.826 | 0.8843                    | 0.9004                  |
| 14  | 1.82E-02                  | 1.09E-02                   | 0.60              | -75.836 | 0.9169                    | 0.9336                  |
| 15  | 1.82E-02                  | 1.46E-02                   | 0.80              | -75.846 | 0.9530                    | 0.9703                  |
| 16  | 1.82E-02                  | 1.82E-02                   | 1.00              | -75.855 | 0.9821                    | 1.0000                  |
| 17  | 1.82E-02                  | 2.18E-02                   | 1.20              | -75.860 | 1.0000                    | 1.0182                  |
| 18  | 1.82E-02                  | 2.55E-02                   | 1.40              | -75.864 | 1.0148                    | 1.0332                  |
| 19  | 1.82E-02                  | 2.91E-02                   | 1.60              | -75.867 | 1.0254                    | 1.0440                  |
| 20  | 1.82E-02                  | 3.27E-02                   | 1.79              | -75.869 | 1.0326                    | 1.0514                  |
| 21  | 1.82E-02                  | 3.59E-02                   | 1.97              | -75.872 | 1.0402                    | 1.0591                  |
Table S17. $^{19}$F NMR titration data for 18 mM trifluoroacetic acid (guest 16) with cycHC[8], in CDCl$_3$

| Nr. | Guest 16 concentration, M | cycHC[8] concentration, M | molar ratio, equiv | F1, ppm | F1 normalized at 1.2 equiv | F1 normalized at 1 equiv |
|-----|--------------------------|---------------------------|-------------------|---------|---------------------------|-------------------------|
| 1   | 1.82E-02                 | 0.00E+00                  | 0.00              | -75.562 | 0.0000                    | 0.0000                  |
| 2   | 1.82E-02                 | 3.62E-04                  | 0.02              | -75.597 | 0.1298                    | 0.1308                  |
| 3   | 1.82E-02                 | 7.31E-04                  | 0.04              | -75.629 | 0.2480                    | 0.2500                  |
| 4   | 1.82E-02                 | 1.09E-03                  | 0.06              | -75.654 | 0.3424                    | 0.3451                  |
| 5   | 1.82E-02                 | 1.46E-03                  | 0.08              | -75.677 | 0.4289                    | 0.4323                  |
| 6   | 1.82E-02                 | 1.83E-03                  | 0.10              | -75.696 | 0.4998                    | 0.5038                  |
| 7   | 1.82E-02                 | 2.19E-03                  | 0.12              | -75.711 | 0.5550                    | 0.5594                  |
| 8   | 1.82E-02                 | 2.73E-03                  | 0.15              | -75.729 | 0.6222                    | 0.6271                  |
| 9   | 1.82E-02                 | 3.65E-03                  | 0.20              | -75.754 | 0.7165                    | 0.7222                  |
| 10  | 1.82E-02                 | 4.56E-03                  | 0.25              | -75.770 | 0.7755                    | 0.7816                  |
| 11  | 1.82E-02                 | 5.47E-03                  | 0.30              | -75.783 | 0.8228                    | 0.8293                  |
| 12  | 1.82E-02                 | 7.29E-03                  | 0.40              | -75.799 | 0.8818                    | 0.8887                  |
| 13  | 1.82E-02                 | 9.13E-03                  | 0.50              | -75.809 | 0.9213                    | 0.9286                  |
| 14  | 1.82E-02                 | 1.10E-02                  | 0.60              | -75.816 | 0.9448                    | 0.9523                  |
| 15  | 1.82E-02                 | 1.46E-02                  | 0.80              | -75.824 | 0.9765                    | 0.9842                  |
| 16  | 1.82E-02                 | 1.83E-02                  | 1.00              | -75.828 | 0.9922                    | 1.0000                  |
| 17  | 1.82E-02                 | 2.19E-02                  | 1.20              | -75.830 | 1.0000                    | 1.0079                  |
| 18  | 1.82E-02                 | 2.50E-02                  | 1.37              | -75.832 | 1.0078                    | 1.0158                  |
Figure S6. $^{19}$F NMR titration data for trifluoroacetic acid 16 (18.2 mM) in the presence of growing concentration of cycHC[6] (purple) and cycHC[8] (green) normalized at 1.2 equiv. Experimental datapoints from Table S16, Table S17 are assigned with circles, the dotted lines are shown to guide the eye. More pronounced curve for titration with cycHC[8] is suggesting stronger binding caused by larger amount of available binding sites (carbonyl groups) on cycHC[8] in comparison with cycHC[6]. Results corresponds to data obtained at 2 mM concentration of 16 (Figure S5).
Figure S7. $^{19}$F NMR titration data for different concentrations of trifluoroacetic acid 16 in the presence of growing concentration of cycHC[6] (red, purple) and cycHC[8] (blue, green) normalized at 1.0 equiv. Experimental datapoints from Table S13, Table S15, Table S16, Table S17 are assigned with circles, the dotted lines are shown to guide the eye. Graph illustrates the change in the shape of titration curves related to roughly one order of magnitude difference in concentration of titrated compound (here 16). Significant difference is caused by different proportion of formed complex as a natural consequence of constant value of binding constants at all concentrations.
Table S18. $^1$H NMR titration data for 2 mM S-camphorsulfonic acid (guest 17) with cycHC[6], in CDCl$_3$ and corresponding spectra below.

| Nr. | Guest 17 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1, ppm | H1 normalized at 10 equiv | H2, ppm |
|-----|---------------------------|---------------------------|-------------------|---------|--------------------------|---------|
| 1   | 2.00E-03                  | 0.00E+00                  | 0.00              | 3.1317  | 0.0000                   | 0.9878  |
| 2   | 2.00E-03                  | 1.01E-03                  | 0.50              | 3.1297  | 0.0743                   | 0.9860  |
| 3   | 2.00E-03                  | 2.01E-03                  | 1.00              | 3.1282  | 0.1301                   | 0.9845  |
| 4   | 2.00E-03                  | 3.00E-03                  | 1.50              | 3.1266  | 0.1896                   | 0.9832  |
| 5   | 2.00E-03                  | 4.01E-03                  | 2.00              | 3.1253  | 0.2379                   | 0.9818  |
| 6   | 2.00E-03                  | 6.01E-03                  | 3.00              | 3.1227  | 0.3346                   | 0.9790  |
| 7   | 2.00E-03                  | 8.03E-03                  | 4.01              | 3.1196  | 0.4498                   | 0.9763  |
| 8   | 2.00E-03                  | 1.20E-02                  | 6.01              | 3.1148  | 0.6283                   | 0.9711  |
| 9   | 2.00E-03                  | 1.60E-02                  | 8.02              | 3.1102  | 0.7993                   | 0.9661  |
| 10  | 2.00E-03                  | 2.01E-02                  | 10.02             | 3.1048  | 1.0000                   | 0.9612  |
| 11  | 2.00E-03                  | 2.41E-02                  | 12.03             | 3.0990  | 1.2156                   | 0.9563  |
| 12  | 2.00E-03                  | 2.81E-02                  | 14.03             | 3.0927  | 1.4498                   | 0.9517  |
| 13  | 2.00E-03                  | 3.21E-02                  | 16.03             | 3.0897  | 1.5613                   | 0.9470  |
| 14  | 2.00E-03                  | 3.61E-02                  | 18.03             | 3.0828  | 1.8178                   | 0.9428  |
| 15  | 2.00E-03                  | 4.32E-02                  | 21.57             | 3.0740  | 2.1450                   | 0.9352  |
Table S19. $^1$H NMR titration data for ca 0.4 mM methanesulfonic acid (guest 18) with cycHC[6], in CDCl$_3$. Concentration of 18 obtained from comparison of signals integration with cycHC[6].

| Guest 18 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1, ppm | H1 recalc. to start from 0 | normalization around 5 eq | normalization around 9 eq |
|---------------------------|---------------------------|-------------------|---------|---------------------------|--------------------------|--------------------------|
| 5.50E-04                  | 0.00E+00                  | 0.00              | 3.0952  | 0.0000                    | 0.0000                   | 0.0000                   |
| 5.50E-04                  | 2.01E-04                  | 0.37              | 3.0733  | 0.0219                    | 0.2486                   | 0.2186                   |
| 4.18E-04                  | 3.02E-04                  | 0.72              | 3.0587  | 0.0365                    | 0.4143                   | 0.3643                   |
| 3.55E-04                  | 4.02E-04                  | 1.13              | 3.0473  | 0.0479                    | 0.5437                   | 0.4780                   |
| 3.42E-04                  | 6.03E-04                  | 1.77              | 3.0332  | 0.0620                    | 0.7037                   | 0.6188                   |
| 3.15E-04                  | 8.05E-04                  | 2.55              | 3.0232  | 0.0720                    | 0.8173                   | 0.7186                   |
| 3.15E-04                  | 1.01E-03                  | 3.19              | 3.0161  | 0.0791                    | 0.8978                   | 0.7894                   |
| 2.98E-04                  | 1.41E-03                  | 4.73              | 3.0071  | 0.0881                    | 1.0000                   | 0.8792                   |
| 3.09E-04                  | 2.01E-03                  | 6.52              | 3.0003  | 0.0949                    | 1.0772                   | 0.9471                   |
| 3.10E-04                  | 2.82E-03                  | 9.10              | 2.9950  | 0.1002                    | 1.1373                   | 1.0000                   |
| 3.04E-04                  | 4.01E-03                  | 12.93             | 2.9900  | 0.1052                    | 1.1941                   | 1.0499                   |
| 3.04E-04                  | 6.03E-03                  | 19.83             | 2.9854  | 0.1098                    | 1.2463                   | 1.0958                   |
| 3.20E-04                  | 8.05E-03                  | 25.18             | 2.9832  | 0.1120                    | 1.2713                   | 1.1178                   |
| 3.22E-04                  | 1.05E-02                  | 32.59             | 2.9824  | 0.1128                    | 1.2804                   | 1.1257                   |
**Figure S8.** NMR titration data for trifluoroacetic acid 16 (2 mM, green) and methanesulfonic acid 18 (ca 0.4 mM, purple) in the presence of growing concentration of cycHC[6] normalized at 9 equiv. Experimental datapoints from Table S13, Table S19 are assigned with circles, the dotted lines are shown to guide the eye. Although, titration curve of 16 is more pronounced than curve of 18 the concentration of 18 is roughly five-times lower, which has strong impact on the titration curve shape (proportion of formed complex as seen in Figure S7). Hence, we can speculate that cycHC[6] binds 18 similarly or rather stronger than 16.
Table S20. $^1$H NMR titration data for ca 2.2 mM methanesulfonic acid (guest 18) with cycHC[6], in CDCl$_3$. Concentration of 18 obtained from comparison of signals integration with cycHC[6].

| Guest 18 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1 ppm | H1 recalc. to start from 0 | normalization around 5 eq |
|--------------------------|---------------------------|------------------|--------|----------------------------|--------------------------|
| 1.36E-03                 | 0.00E+00                  | 0.00             | 3.1085 | 0.0000                     | 0.0000                   |
| 1.36E-03                 | 5.19E-04                  | 0.38             | 3.0563 | 0.0522                     | 0.4254                   |
| 1.61E-03                 | 1.04E-03                  | 0.65             | 3.0339 | 0.0746                     | 0.6080                   |
| 1.87E-03                 | 1.56E-03                  | 0.84             | 3.0217 | 0.0868                     | 0.7074                   |
| 1.98E-03                 | 2.09E-03                  | 1.06             | 3.0143 | 0.0942                     | 0.7677                   |
| 2.24E-03                 | 2.61E-03                  | 1.17             | 3.0090 | 0.0995                     | 0.8109                   |
| 2.36E-03                 | 3.13E-03                  | 1.33             | 3.0053 | 0.1032                     | 0.8411                   |
| 2.50E-03                 | 3.65E-03                  | 1.46             | 3.0024 | 0.1061                     | 0.8647                   |
| 2.50E-03                 | 4.17E-03                  | 1.67             | 2.9999 | 0.1086                     | 0.8851                   |
| 2.50E-03                 | 5.21E-03                  | 2.09             | 2.9965 | 0.1120                     | 0.9128                   |
| 2.50E-03                 | 6.26E-03                  | 2.50             | 2.9939 | 0.1146                     | 0.9340                   |
| 2.49E-03                 | 8.33E-03                  | 3.35             | 2.9904 | 0.1181                     | 0.9625                   |
| 2.56E-03                 | 1.04E-02                  | 4.06             | 2.9879 | 0.1206                     | 0.9829                   |
| 2.60E-03                 | 1.25E-02                  | 4.82             | 2.9858 | 0.1227                     | 1.0000                   |
| 2.49E-03                 | 1.84E-02                  | 7.40             | 2.9814 | 0.1271                     | 1.0359                   |

Table S21. $^1$H NMR titration data for ca 0.3 mM methanesulfonic acid (guest 18) with cycHC[6], in CDCl$_3$. Concentration of 18 obtained from comparison of signals integration with standard (1,2,4,5-tetrachloro-3-nitrobenzene) having constant concentration throughout titration.

| Guest 18 concentration, M | cycHC[6] concentration, M | molar ratio, equiv | H1 ppm | H1 recalc. to start from 0 | normalization around 5 eq |
|--------------------------|---------------------------|------------------|--------|----------------------------|--------------------------|
| 2.48E-04                 | 0.00E+00                  | 0.00             | 3.0739 | 0.0000                     | 0.0000                   |
| 2.20E-04                 | 3.53E-05                  | 0.16             | 3.0692 | 0.0047                     | 0.0646                   |
| 2.25E-04                 | 7.03E-05                  | 0.31             | 3.0626 | 0.0113                     | 0.1554                   |
| 2.44E-04                 | 1.17E-04                  | 0.48             | 3.0548 | 0.0191                     | 0.2627                   |
| 2.70E-04                 | 1.74E-04                  | 0.64             | 3.0488 | 0.0251                     | 0.3453                   |
| 3.12E-04                 | 2.31E-04                  | 0.74             | 3.0438 | 0.0301                     | 0.4140                   |
| 3.44E-04                 | 3.45E-04                  | 1.01             | 3.0372 | 0.0367                     | 0.5048                   |
| 3.48E-04                 | 4.61E-04                  | 1.33             | 3.0316 | 0.0423                     | 0.5818                   |
| 3.85E-04                 | 5.76E-04                  | 1.50             | 3.0272 | 0.0467                     | 0.6424                   |
| 3.98E-04                 | 6.91E-04                  | 1.74             | 3.0228 | 0.0511                     | 0.7029                   |
| 4.18E-04                 | 9.19E-04                  | 2.20             | 3.0172 | 0.0567                     | 0.7799                   |
| 4.61E-04                 | 1.38E-03                  | 2.99             | 3.0096 | 0.0643                     | 0.8845                   |
| 4.56E-04                 | 1.84E-03                  | 4.03             | 3.0046 | 0.0693                     | 0.9532                   |
| 4.80E-04                 | 2.30E-03                  | 4.79             | 3.0012 | 0.0727                     | 1.0000                   |
| 4.70E-04                 | 2.53E-03                  | 5.38             | 2.9993 | 0.0746                     | 1.0261                   |
| 4.77E-04                 | 2.70E-03                  | 5.67             | 2.9980 | 0.0759                     | 1.0440                   |
Table S22. $^1$H NMR titration data for ca 0.8 mM methanesulfonic acid (guest 18) with cycHC[8], in CDCl₃. Concentration of 18 obtained from comparison of signals integration with cycHC[8].

| Guest 18 concentration, M | cycHC[8] concentration, M | molar ratio, equiv | H1, ppm | H1 recalc to start from 0 | normalization around 5 eq |
|--------------------------|---------------------------|-------------------|---------|--------------------------|--------------------------|
| 6.60E-04                 | 0.00E+00                  | 0.00              | 3.0963  | 0.0000                   | 0.0000                   |
| 6.60E-04                 | 1.02E-04                  | 0.15              | 3.0793  | 0.0170                   | 0.1797                   |
| 6.94E-04                 | 2.04E-04                  | 0.29              | 3.0677  | 0.0286                   | 0.3023                   |
| 7.27E-04                 | 3.05E-04                  | 0.42              | 3.0592  | 0.0371                   | 0.3922                   |
| 7.44E-04                 | 4.06E-04                  | 0.55              | 3.0523  | 0.0440                   | 0.4651                   |
| 7.87E-04                 | 5.13E-04                  | 0.65              | 3.0461  | 0.0502                   | 0.5307                   |
| 7.74E-04                 | 6.19E-04                  | 0.80              | 3.0410  | 0.0553                   | 0.5846                   |
| 8.62E-04                 | 8.24E-04                  | 0.96              | 3.0334  | 0.0629                   | 0.6649                   |
| 8.81E-04                 | 1.24E-03                  | 1.40              | 3.0234  | 0.0729                   | 0.7706                   |
| 8.74E-04                 | 2.06E-03                  | 2.36              | 3.0129  | 0.0834                   | 0.8816                   |
| 8.55E-04                 | 3.09E-03                  | 3.62              | 3.0058  | 0.0905                   | 0.9567                   |
| 8.29E-04                 | 4.12E-03                  | 4.98              | 3.0017  | 0.0946                   | 1.0000                   |
| 8.45E-04                 | 6.18E-03                  | 7.32              | 2.9966  | 0.0997                   | 1.0539                   |
| 7.82E-04                 | 8.26E-03                  | 10.55             | 2.9931  | 0.1032                   | 1.0909                   |
| 8.03E-04                 | 1.03E-02                  | 12.88             | 2.9899  | 0.1064                   | 1.1247                   |

5.5 Evaluation of association constants with 1:1 and 2:1 binding model in Bindfit

Titration data for guests 6, 9, 10, 11, 12, 13, 14, 15 and 17 was not possible to evaluate with 3:1 binding model due to their weak binding strength, therefore, we had to restrict our binding model to fit only $K_{1obs}$ and $K_{2obs}$ for other guests. We employed free online tool Bindfit (supramolecular.org) for comparing the quality of fit with 2:1 and 1:1 binding models (Thordarson, 2011; Hibbert and Thordarson, 2016). Generally, the weakest binding guests 6, 11, 12 and 17 provided unrealistic values of $K_{2obs}$ and could be fitted only with 1:1 binding models. Guests 9, 10, 13, 14 and 15 provided miscellaneous result without any clear trend corresponding to their order in our qualitative comparison. Mostly, it was possible to fit their NMR data with 2:1 and also 1:1 model obtaining similar quality of fit. In some cases (9, 10), both models (2:1 and 1:1) provided reasonable fit; in other cases (13, 14, 15) it meant unrealistic values from 2:1 model and at the same time, regular sinusoidal distribution of residuals for 1:1 model, indicating it as an incorrect model. Overall, the binding between the guests and cycHC[6] cannot be compared in quantitative manner, as the data cannot be evaluated with the same binding model.
### 5.6 Evaluation of association constants with 2:1 and 3:1 binding model

**Table S23.** Summary of observed association constants ($K_{obs}$) from fitting with our script for 3:1 binding model and from fitting with online tool Bindfit (supramolecular.org) for 2:1 binding model.

| guest | macrocycle | fitted data source | guest concentration, mM | 3:1 binding model fitting results | Bindfit 2:1 binding model fitting results$^a$ |
|-------|------------|--------------------|-------------------------|----------------------------------|-------------------------------------------|
|       |            |                    |                         | $K_{1obs}$, M$^{-1}$ | $K_{2obs}$, M$^{-1}$ | $K_{3obs}$, M$^{-1}$ | $K_{1obs}$, M$^{-1}$ | $K_{2obs}$, M$^{-1}$ |
| 1.$^b$ | 16 | cycH[6] | Table S13 | 2.0 | 600±100 | 350±50 | 30±30 | 930±17 | 500±38 |
| 2.$^c$ | 16 | cycH[6] | Table S16 | 18.2 | insufficient quality of fit | 0.04±0.01 | 230 000±22 000 |
| 3. | 16 | cycH[8] | Table S14 | 2.0 | insufficient quality of fit | 350±34 | 550±47 |
| 4. | 16 | cycH[8] | Table S15 | 1.9 | 1 180±20 | 326±17 | 195±20 | 420±57 | 650±83 |
| 5.$^c$ | 16 | cycH[8] | Table S17 | 18.2 | insufficient quality of fit | 0.05±0.01 | 140 000±10 000 |
| 6.$^d$ | 18 | cycH[6] | Table S19 | 0.4 | 1 700±250 | 500±250 | 400±200 | 3 700±470 | 1 400±550 |
| 7.$^d$ | 18 | cycH[6] | Table S20 | 2.2 | insufficient quality of fit | 130±2 | 14 000±270 |
| 8. | 18 | cycH[6] | Table S21 | 0.4 | insufficient quality of fit | 990±37 | 7 300±920 |
| 9. | 18 | cycH[8] | Table S22 | 0.8 | 1 211±150 | 1 175±100 | 470±120 | 240±16 | 11 000±960 |

Notes:  
$^a$ we used 2:1 NMR binding model with "full flavor", which do not assume any specific relation: (i) between chemical shifts of HG and HG$_2$; (ii) between stepwise association constants ($K_1$, $K_2$). We present all obtained values from 2:1 binding model, however, the quality of fit varied from good to insufficient.  
$^b$ Although the value and error of $K_{3obs}$ are same (3:1 binding model), we obtained random distribution of residuals (Figure S10) indicating reliability of overall fit.  
$^c$ Fitting of data from line 2 and 5 for 18.2 mM trifluoroacetic acid (16) by 2:1 model provided insufficient quality of fit with sinusoidal shape of residuals.  
$^d$ Data from line 6 and 7 were fitted simultaneously to improve quality of fit with 3:1 binding model.
Online available Bindfit evaluations for all lines from Table S23 can be found on following web addresses:

Line 1: http://app.supramolecular.org/bindfit/view/b8ae08bd-39dc-426e-a2df-c8ec7c1265a4
Line 2: http://app.supramolecular.org/bindfit/view/1cbea5d1-1702-4636-a0a5-6e47003e09b3
Line 3: http://app.supramolecular.org/bindfit/view/f32f7069-eb39-4bca-8dff-e5f06095064f
Line 4: http://app.supramolecular.org/bindfit/view/294bc989-4d61-42c3-bd2c-54af6e578baa
Line 5: http://app.supramolecular.org/bindfit/view/df10194d-4cab-42c1-98c2-753b97bfefe8
Line 6: http://app.supramolecular.org/bindfit/view/2b583a9b-c797-41a2-ac19-b2a04f82f1cb
Line 7: http://app.supramolecular.org/bindfit/view/5940a110-7a31-433d-9eb1-f998e42e1799
Line 8: http://app.supramolecular.org/bindfit/view/2b90c177-c074-4b06-8f81-959c9180e51e
Line 9: http://app.supramolecular.org/bindfit/view/64b9a9e2-a941-4ce4-8d16-a9d44d007717
Table S24. Experimental and calculated values of chemical shift from 3:1 binding model for titration data, which provided reasonable residuals and apparent association constants ($K_{obs}$). Data from Table S19 and Table S20 were fitted simultaneously and provided one set of $K_{obs}$. Calculated chemical shifts for complexes at specific stoichiometry are at the bottom of the table.

| Table S13 data | Table S15 data | Table S19 data | Table S20 data | Table S22 data |
|----------------|----------------|----------------|----------------|----------------|
| molar ratio, equiv | F1, ppm | F1 FIT (3:1), ppm | residuals, ppm | molar ratio, equiv | F1, ppm | F1 FIT (3:1), ppm | residuals, ppm | molar ratio, equiv | F1, ppm | F1 FIT (3:1), ppm | residuals, ppm | molar ratio, equiv | F1, ppm | F1 FIT (3:1), ppm | residuals, ppm |
| 0.00 | -75.577 | -75.577 | 0.00E+00 | 0.00 | -75.442 | -75.442 | 0.00E+00 | 0.00 | 3.0739 | 3.0739 | 0.00E+00 | 0.00 | 3.0739 | 3.0739 | 0.00E+00 |
| 0.24 | -75.641 | -75.641 | 4.11E-04 | 0.05 | -75.468 | -75.466 | -1.96E-03 | 0.37 | 3.0520 | 3.0460 | 6.01E-03 | 0.38 | 3.0217 | 3.0211 | 6.24E-04 |
| 0.49 | -75.687 | -75.688 | 6.28E-04 | 0.10 | -75.487 | -75.488 | 1.12E-03 | 0.72 | 3.0374 | 3.0352 | 2.17E-03 | 0.65 | 2.9993 | 2.9970 | 2.33E-03 |
| 0.74 | -75.720 | -75.721 | 1.02E-03 | 0.15 | -75.507 | -75.508 | 1.06E-03 | 1.13 | 3.0260 | 3.0265 | -5.11E-04 | 0.84 | 2.9871 | 2.9839 | 3.21E-03 |
| 0.99 | -75.745 | -75.744 | -8.99E-04 | 0.20 | -75.526 | -75.527 | 7.06E-04 | 1.77 | 3.0119 | 3.0135 | -1.64E-03 | 1.06 | 2.9797 | 2.9760 | 3.66E-03 |
| 1.28 | -75.766 | -75.765 | -9.51E-04 | 0.30 | -75.560 | -75.560 | -3.48E-04 | 2.55 | 3.0019 | 3.0041 | -2.16E-03 | 1.17 | 2.9744 | 2.9706 | 3.81E-03 |
| 1.59 | -75.783 | -75.781 | -1.64E-03 | 0.40 | -75.589 | -75.588 | -6.73E-04 | 3.19 | 2.9948 | 2.9970 | -2.23E-03 | 1.33 | 2.9707 | 2.9669 | 3.76E-03 |
| 1.99 | -75.797 | -75.796 | -8.50E-04 | 0.50 | -75.612 | -75.612 | -5.78E-04 | 4.73 | 2.9858 | 2.9871 | -1.33E-03 | 1.46 | 2.9678 | 2.9642 | 3.58E-03 |
| 2.99 | -75.818 | -75.820 | 2.13E-03 | 0.70 | -75.649 | -75.649 | -3.51E-04 | 6.52 | 2.9790 | 2.9781 | 8.80E-04 | 1.67 | 2.9653 | 2.9624 | 2.92E-03 |
| 3.99 | -75.833 | -75.833 | 8.85E-04 | 1.00 | -75.688 | -75.688 | 1.02E-04 | 9.10 | 2.9737 | 2.9771 | 2.61E-03 | 2.09 | 2.9619 | 2.9598 | 2.11E-03 |
| 4.99 | -75.840 | -75.842 | 2.13E-03 | 1.40 | -75.720 | -75.721 | 9.40E-04 | 12.93 | 2.9687 | 2.9653 | 3.43E-03 | 2.50 | 2.9593 | 2.9580 | 1.25E-03 |
| 5.97 | -75.848 | -75.848 | -4.51E-04 | 2.00 | -75.750 | -75.750 | 7.62E-04 | 19.83 | 2.9641 | 2.9602 | 3.85E-03 | 3.35 | 2.9558 | 2.9559 | -7.11E-05 |
| 6.97 | -75.852 | -75.852 | 3.55E-04 | 3.00 | -75.776 | -75.776 | -4.81E-05 | 25.18 | 2.9619 | 2.9599 | 2.00E-03 | 4.06 | 2.9533 | 2.9545 | -1.18E-03 |
| 7.97 | -75.856 | -75.856 | 4.73E-05 | 4.00 | -75.790 | -75.789 | -6.96E-04 | 32.59 | 2.9611 | 2.9597 | 1.37E-03 | 4.82 | 2.9512 | 2.9536 | -2.38E-03 |
| 8.97 | -75.859 | -75.858 | -8.70E-04 | 5.00 | -75.800 | -75.798 | -1.97E-03 | 12.88 | 2.9899 | 2.9919 | -1.97E-03 | 12.88 | 2.9899 | 2.9919 | -1.97E-03 |
| 9.97 | -75.862 | -75.861 | -1.20E-03 | 8.52 | -75.810 | -75.812 | 1.64E-03 | 12.88 | 2.9899 | 2.9919 | -1.97E-03 | 12.88 | 2.9899 | 2.9919 | -1.97E-03 |
| 10.97 | -75.862 | -75.862 | 6.01E-04 | 12.39 | -75.865 | -75.864 | 9.22E-04 | 12.88 | 2.9899 | 2.9919 | -1.97E-03 | 12.88 | 2.9899 | 2.9919 | -1.97E-03 |

Values of chemical shift (ppm) of a guest at complexes having stoichiometry 1:1 ($\delta H_{G1}$), 2:1 ($\delta H_{G2}$) and 3:1 ($\delta H_{G3}$)

$\delta H_{G1} = -75.8820 \pm 0.0006$
$\delta H_{G2} = -75.90 \pm 0.03$
$\delta H_{G3} = -75.9 \pm 0.2$

we used constraint:

$\delta H_{G1} = \delta H_{G2} - \delta H_{G3}$

$\delta H_{G1} = 2.9491 \pm 0.004$
$\delta H_{G2} = 2.9373 \pm 0.008$
$\delta H_{G3} = 2.8887 \pm 0.05$

$\delta H_{G1} = 2.9842 \pm 0.001$
$\delta H_{G2} = 2.9842 \pm 0.002$
$\delta H_{G3} = 2.97 \pm 0.05$
Figure S9. Normalization at 4.8 eq for data from Table S19 (0.4 mM guest 18) and Table S20 (2.2 mM guest 18), which were fitted simultaneously by the 3:1 binding model. Normalization of fitted binding isotherm was done using the value of experimentally obtained chemical shift at 4.8 eq.
Figure S10. Fitting of data from Table S13 (2 mM guest 16 titrated by cycHC[6]) with 3:1 binding model (Table S23, line 1). Obtained titration isotherm fits well with experimental points (upper graph), which is supported by random distribution of residuals (lower graph). Fitting provided apparent association constants $K_{1obs} = 600 \pm 100 \text{ M}^{-1}$, $K_{2obs} = 350 \pm 50 \text{ M}^{-1}$ and $K_{3obs} = 30 \pm 30 \text{ M}^{-1}$, which can characterize the system only in this particular experimental conditions. As the quality of fit is similar to results of 2:1 binding model presented in main text of article, the 2:1 model should be assumed as a more reliable.
Figure S11. Fitting of data from Table S14 (2 mM guest 16 titrated by cycHC[8]) with online tool Bindfit (supramolecular.org) for 2:1 binding model (Table 23, line 3). Obtained titration isotherm fits well with experimental points (upper graph), which is supported by random distribution of residuals (lower graph). Fitting provided apparent association constants $K_{1obs} = 353 \pm 34 \text{ M}^{-1}$ and $K_{2obs} = 550 \pm 47 \text{ M}^{-1}$, which can characterize the system only in this particular experimental condition. It can be seen from comparison with following Figure S13, that the same host-guest system could not be fitted at higher concentration of the guest.
Figure S12. Fitting of data from Table S15 (2 mM guest 16 titrated by cycHC[8]) with online tool Bindfit (supramolecular.org) for 2:1 binding model. (Table S23, line 4) Obtained titration isotherm fits reasonably with experimental points (upper graph), which is supported by irregular distribution of residuals (lower graph). Fitting provided apparent association constants $K_{1obs} = 424 \pm 57 \text{ M}^{-1}$ and $K_{2obs} = 653 \pm 83 \text{ M}^{-1}$, which can characterize the system only in this particular experimental conditions. It can be seen from comparison with following Figure S13, that the same host-guest system could not be fitted at higher concentration of the guest.
Figure S13. Fitting of data from Table S17 (18.2 mM guest 16 titrated by cycHC[8]) with online tool Bindfit (supramolecular.org) for 2:1 binding model. Obtained titration isotherm, which does not fit with experimental points (upper graph), and sinusoidal distribution of residuals (lower graph) are evidence that 2:1 binding model is inappropriate for the system. The obtained $K_{1\text{obs}} = 0.05 \pm 0.01$ M$^{-1}$ and $K_{2\text{obs}} = 138436 \pm 9985$ M$^{-1}$ has no physical meaning. Large value of $K_{2\text{obs}}$ in comparison with $K_{1\text{obs}}$ indicates that real stoichiometry of the system could be higher than 2:1.
5.7 NMR data for continuous variation method (Job plot)

Table S25. $^{19}$F NMR data for Job plot experiment at 10 mM total concentration of trifluoroacetic acid (guest 16) and cycHC[8], in CDCl$_3$.

| Nr. | $V$, cycHC[8] (μl) | $V$, 16 (μl) | mole fraction $x_i$ | $\delta$, guest 16 (ppm) | $\Delta\delta$ (ppm) | $\Delta\delta \cdot x_i[16]$ |
|-----|--------------------|--------------|--------------------|-------------------------|------------------|--------------------------|
|     |                    |              | cycHC[8]           | guest 16                |                  |                          |
| 1   | 0                  | 600          | 0                  | -75.4389                | 0.000            | 0                        |
| 2   | 60                 | 540          | 0.1                | -75.6393                | 0.204            | 0.180                    |
| 3   | 120                | 480          | 0.2                | -75.7248                | 0.285            | 0.229                    |
| 4   | 180                | 420          | 0.3                | -75.7654                | 0.326            | 0.229                    |
| 5   | 240                | 360          | 0.4                | -75.7854                | 0.346            | 0.208                    |
| 6   | 300                | 300          | 0.5                | -75.7997                | 0.360            | 0.180                    |
| 7   | 360                | 240          | 0.6                | -75.8105                | 0.371            | 0.149                    |
| 8   | 420                | 180          | 0.7                | -75.8192                | 0.380            | 0.114                    |
| 9   | 480                | 120          | 0.8                | -75.8246                | 0.385            | 0.077                    |
| 10  | 540                | 60           | 0.9                | -75.8294                | 0.390            | 0.039                    |
| 11  | 600                | 0            | 1                  | -75.8294                | 0.390            | 0.039                    |

Table S26. $^{19}$F NMR data for Job plot experiment at 20 mM total concentration of trifluoroacetic acid (guest 16) and cycHC[6], in CDCl$_3$.

| Nr. | $V$, cycHC[6] (μl) | $V$, 16 (μl) | mole fraction $x_i$ | $\delta$, guest 16 (ppm) | $\Delta\delta$ (ppm) | $\Delta\delta \cdot x_i[16]$ |
|-----|--------------------|--------------|--------------------|-------------------------|------------------|--------------------------|
|     |                    |              | cycHC[6]           | guest 16                |                  |                          |
| 1   | 0                  | 520          | 0.00               | -75.5879                | 0.000            | 0                        |
| 2   | 60                 | 480          | 0.11               | -75.7111                | 0.123            | 0.110                    |
| 3   | 65                 | 455          | 0.13               | -75.7205                | 0.132            | 0.116                    |
| 4   | 75                 | 450          | 0.14               | -75.7344                | 0.146            | 0.126                    |
| 5   | 85                 | 425          | 0.17               | -75.7479                | 0.16             | 0.133                    |
| 6   | 100                | 400          | 0.20               | -75.7682                | 0.180            | 0.144                    |
| 7   | 130                | 390          | 0.25               | -75.7846                | 0.196            | 0.148                    |
| 8   | 170                | 340          | 0.33               | -75.8055                | 0.217            | 0.145                    |
| 9   | 250                | 250          | 0.50               | -75.8338                | 0.245            | 0.123                    |
6 Results of DFT calculations of partial atomic charges

Table S27. Calculated values of partial atomic charges on hydrogen bond donating functional groups of guests 6 and 9-18.

| Guest | functional group | Partial charge on O or S | Partial charge H |
|-------|------------------|--------------------------|-----------------|
| 6     | SH               | -0.18534                 | 0.15082114      |
| 9     | OH               | -0.38257                 | 0.35637096      |
| 10    | OH               | -0.34637                 | 0.34536613      |
| 11    | SH               | -0.16992                 | 0.15300263      |
| 12    | OH               | -0.35604                 | 0.34204295      |
| 13    | OH               | -0.60057                 | 0.34158873      |
| 14    | OH               | -0.35474                 | 0.35811029      |
| 15    | OH               | -0.38330                 | 0.38294907      |
| 16    | OH               | -0.35129                 | 0.37697190      |
| 17    | OH               | -0.46568                 | 0.38232675      |
| 18    | OH               | -0.44975                 | 0.38701379      |
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