Supporting Information

Dissection of the Polar and Non-Polar Contributions to Aromatic Stacking Interactions in Solution

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1. General methods

All $^1$H NMR spectra were recorded at 298 K on a Bruker 500 MHz Advance TCI Cryoprobe and on Bruker 500MHz Avance III HD Smart Probe. All the $^1$H NMR spectra were referenced to residual isotopic impurity if CD$_3$CN (1.98 ppm). The following abbreviations are used in reporting the multiplicity for NMR resonances: s=single, d=doublet, t= triplet and m= multiplet. The NMR data were processed using Bruker Topspin 3.5 pl2 and MestReNova 12.0.0. Low resolution electrospray ionization mass spectrometry LRMS (ESI-MS) experiments were carried out in positive mode with Agilent Technologies LC/MSD Trap SL AGILENT instrument (mobile phase Acetonitrile). MS peak intensity for each analysis is reported as monoisotopic mass and the data were processed with Data Explorer 4.2. Chemicals were purchased from Sigma Aldrich, TCI, or Apollo Scientific and used without further purification.
2. Synthesis and Characterization

Compounds 1 has been synthesized and fully characterized (1H NMR, MS analysis) accordingly to: C. Bravin, E. Badetti, F.A. Scaramuzzo, G. Licini, C. Zonta. *J. Am. Chem. Soc.* 2017; 139, 6456-6460.

2.1. General procedure for encapsulation of reference compounds

To 500 µl (0.5 µmol) of a solution 0.001 M in CD$_3$CN of cage 1 were added 60 µl (1.2 µmol) of a solution 0.01 M in CD$_3$CN of a different reference compound carboxylate triethylammonium salt 2a, 2h in a NMR tube. The mixture was checked via 1H NMR (1H NMR yield >95% based on internal standard p-xylene). No equilibration time is needed.

(2a-2a)@1 1H NMR (500 MHz, CD$_3$CN) δ (ppm): 9.18 (d, 6H, J=2.0 Hz PyrH), 8.42 (s, 6H, NH$_{imm}$), 8.33 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 7.89 (d, 12H, J=8.5 Hz, ArH), 7.72 (d, 12H, J=8.5 Hz, ArH), 7.67 (d, 6H, J=8.0 Hz, PyrH), 4.30 (s, 12H, CH$_2$), 3.93 (s, 12H, CH$_2$eda), 1.36 (m, 4H, CH$_2$β, Hex), 1.27 (m, 4H, CH$_2$γ, Hex), 1.24 (m, 4H, CH$_2$δ, Hex). 0.67 (m, 6H, CH$_3$), 0.67 (m, 6H, CH$_3$ Hex). 4H, CH$_3$ of Hex are hidden by solvent peak.

ESI-MS (m/z): [M]$^{2+}$ calcd. for [C$_{96}$H$_{94}$N$_{14}$O$_4$Zn$_2$]$^{2+}$, 819.4 found; 819.3

(2b-2b)@1 1H NMR (500 MHz, CD$_3$CN) δ (ppm): 9.21 (d, 6H, J=2.0 Hz PyrH), 8.40 (s, 6H, NH$_{imm}$), 8.32 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 7.89 (d, 12H, J=8.5 Hz, ArH), 7.73 (d, 12H, J=8.5 ArH),...
7.67 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 4.29 (s, 12H, CH₂), 3.93 (s, 12H, CH₂eda), 0.97 (d, 12H, CH₃ of sBu), 4H, CH₂α and 2H, CH₃ of sBu are hidden by solvent peak.

ESI-MS (m/z): [M]²⁺ calcd. for [C₉₄H₉₀Ni₄O₄Zn₂]²⁺, 805.4 found; 805.3

(2c-2c)@1 ¹H NMR (500 MHz, CD3CN) δ (ppm): 9.19 (d, 6H, J=2.0 Hz PyrH), 8.49 (s, 6H, NHimm), 8.37 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 7.93 (d, 12H, J=8.5 Hz, ArH), 7.79 (d, 12H, J=8.5 ArH), 7.67 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 4.36 (s, 12H, CH₂), 3.91 (s, 12H, CH₂eda), 1.27 (s, 18H, CH₃ of tBu).

ESI-MS (m/z): [M]²⁺ calcd. for [C₉₄H₉₀Ni₄O₄Zn₂]²⁺, 805.3 found; 805.3

(2d-2d)@1 ¹H NMR (500 MHz, CD3CN) δ (ppm): 9.18 (d, 6H, J=2.0 Hz PyrH), 8.39 (s, 6H, NHimm), 8.31 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 7.88 (d, 12H, J=8.5 Hz, ArH), 7.72 (d, 12H, J=8.5 ArH), 7.66 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 4.28 (s, 12H, CH₂), 3.93 (s, 12H, CH₂eda), 1.03 (s, 18H, CH₃ of neoP), 2H, CH₂α of neoP are hidden by solvent peak.

ESI-MS (m/z): [M]²⁺ calcd. for [C₉₆H₉₆Ni₄O₄Zn₂]²⁺, 819.3 found; 819.3

(2e-2e)@1 ¹H NMR (500 MHz, CD3CN) δ (ppm): 9.21 (d, 6H, J=2.0 Hz PyrH), 8.39 (s, 6H, NHimm), 8.31 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 7.88 (d, 12H, J=8.5 Hz, ArH), 7.73 (d, 12H, J=8.5 ArH), 7.67 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 4.28 (s, 12H, CH₂), 3.93 (s, 12H, CH₂eda), 1.67 (m, 4H, CH₂ of cHex), 1.50 (m, 10H, CH₂ of cHex), 1.32 (m, 6H, CH₂ of cHex), 2H, CH₂α of cHex are hidden by solvent peak.

ESI-MS (m/z): [M]²⁺ calcd. for [C₉₈H₉₈Ni₄O₄Zn₂]²⁺, 831.3 found; 831.4

(2f-2f)@1 ¹H NMR (500 MHz, CD3CN) δ (ppm): 9.18 (d, 6H, J=2.0 Hz PyrH), 8.40 (s, 6H, NHimm), 8.30 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 7.88 (d, 12H, J=8.5 Hz, ArH), 7.71 (d, 12H, J=8.5 ArH), 7.66 (d, 6H, J=8.0 Hz, J=8.5 Hz, PyrH), 4.29 (s, 12H, CH₂), 3.94 (s, 12H, CH₂eda), 2.07 (m, 4H, CH₂α, cHexMe are partially hidden by solvent peak), 1.80 (m, 10H, CH₂, cHexMe), 1.50 (m, 10H, CH₂, cHexMe).

ESI-MS (m/z): [M]²⁺ calcd. for [C₁₀₀H₉₆Ni₄O₄Zn₂]²⁺, 845.4 found; 843.3

(2g-2g)@1 ¹H NMR (500 MHz, CD3CN) δ (ppm): 9.19 (d, 6H, J=2.0 Hz PyrH), 8.42 (s, 6H, NHimm), 8.33 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 7.90 (d, 12H, J=8.5 Hz, ArH), 7.74 (d, 12H, J=8.5 Hz, ArH), 7.65 (d, 6H, J=8.0 Hz, PyrH), 4.30 (s, 12H, CH₂), 3.92 (s, 12H, CH₂eda), 1.68 (m, 8H, CH₂, cPen), 1.62 (m, 4H, CH₂, cPen), 1.44 (m, 4H, CH₂, cPen). 2H, CH₂α of cPen are hidden by solvent peak.

ESI-MS (m/z): [M]²⁺ calcd. for [C₉₆H₉₆Ni₄O₄Zn₂]²⁺, 817.3 found; 817.3
(2h-2h@1) $^1$H NMR (500 MHz, CD$_3$CN) $\delta$ (ppm): 9.16 (d, 6H, J=2.0 Hz PyrH), 8.39 (s, 6H, NH$_{imm}$), 8.30 (dd, 6H, J=8.0 Hz, J=2.0 Hz, PyrH), 7.88 (d, 12H, J=8.5 Hz, ArH), 7.71 (d, 12H, J=8.5 Hz, ArH), 7.66 (d, 6H, J=8.0 Hz, PyrH), 4.28 (s, 12H, CH$_2$), 3.94 (s, 12H, CH$_2$eda), 1.43 (m, 8H, CH$_2$, cPenMe), 1.33 (m, 2H, CH$_2$, cPenMe), 1.23 (m, 8H, CH$_2$, cPenMe). 4H, CH$_{2n}$ of cPenMe are hidden by solvent peak.

ESI-MS (m/z): [M]$^{2+}$ calcd. for [C$_{98}$H$_{94}$N$_{14}$O$_4$Zn$_2$]$^{2+}$, 831.4 found; 831.3
2.2. General procedure for competition experiments

To 500 µl (0.5 µmol) of a solution 0.001 M in CD$_3$CN of cage 1 were added 10 µl (0.1 µmol) of a 0.01 M mixed solution of two guests of the carboxylate series 2a, 2h and benzoate series 3a, 3e were introduced. The mixture was monitored with $^1$H NMR ($^1$H NMR yield >95% based on internal standard p-xylene). No equilibration time is needed.
3. Results and discussion

3.1.1 $^1$H NMR determination of binding stoichiometry and binding constant along the titration points for (2a-2a)@1

Figure S1. $^1$H NMR inclusion components. Addition of Hexanoate 2a to cage 1 in CD$_3$CN. a) Preformed cage 1 (0.001 M cage). b) - e) Addition of sub-stoichiometric amounts (0.21-1.67 equiv) of 2a results in the formation of a new species which could be attributed to 1:2 H:G complex. f) Addition of 2.45 equiv of 2a totally shift the system to the new species (2a-2a)@1. Counter anions are perchlorates.
3.1.2 \( ^1H \) NMR determination of binding stoichiometry and binding constant along the titration points for \((2b-2b)@1\)

![Figure S2. \( ^1H \) NMR inclusion components. Addition of Isovalerate 2b to cage 1 in CD₃CN. a) Preformed cage 1 (0.001 M cage). b) - c) Addition of sub-stoichiometric amounts (0.44-1.78 equiv) of 2b results in the formation of a new species which could be attributed to 1:2 H:G complex. d) Addition of 2.67 equiv of 2b totally shift the system to the new species \((2b-2b)@1\). Counter anions are perchlorates.](image-url)
3.1.3 $^1$H NMR determination of binding stoichiometry and binding constant along the titration points for $(2c-2c)@1$

**Figure S3.** $^1$H NMR inclusion components. Addition of Pivalate 2c to cage 1 in CD$_3$CN. a) Preformed cage 1 (0.001 M cage). b) - e) Addition of sub-stoichiometric amounts (0.21-1.78 equiv) of 2c results in the formation of a new species which could be attributed to 1:2 H:G complex. f) Addition of 2.59 equiv of 2c totally shift the system to the new species $(2c-2c)@1$. Counter anions are perchlorates.
3.1.4 $^1$H NMR determination of binding stoichiometry and binding constant along the titration points for (2d-2d)$\@$1

Figure S4. $^1$H NMR inclusion components. Addition of 3,3-dimethylbutyrate 2d to cage 1 in CD$_3$CN. a) Preformed cage 1 (0.001 M cage). b) - e) Addition of sub-stoichiometric amounts (0.21-1.78 equiv) of 2d results in the formation of a new species which could be attributed to 1:2 H:G complex. f) Addition of 2.60 equiv of 2d totally shift the system to the new species (2d-2d)$\@$1. Counter anions are perchlorates.
3.1.5  $^1$H NMR determination of binding stoichiometry and binding constant along the titration points for $(2e-2e)@1$

**Figure S5.** $^1$H NMR inclusion components. Addition of cyclohexanecarboxylate $2e$ to cage 1 in CD$_3$CN. a) Preformed cage 1 (0.001 M cage). b) - e) Addition of sub-stoichiometric amounts (0.42-1.90 equiv) of $2e$ results in the formation of a new species which could be attributed to 1:2 H:G complex. f) Addition of 2.66 equiv of $2e$ totally shift the system to the new species $(2e-2e)@1$. Counter anions are perchlorates.
3.1.6  $^1$H NMR determination of binding stoichiometry and binding constant along the titration points for (2f-2f)@1

Figure S6. $^1$H NMR inclusion components. Addition of 2-cyclohexylacetate 2f to cage 1 in CD$_3$CN. a) Preformed cage 1 (0.001 M cage). b) - e) Addition of sub-stoichiometric amounts (0.21-1.80 equiv) of 2f results in the formation of a new species which could be attributed to 1:2 H:G complex. f) Addition of 2.61 equiv of 2f totally shift the system to the new species (2f-2f)@1. Counter anions are perchlorates.
3.1.7 $^1$H NMR determination of binding stoichiometry and binding constant along the titration points for (2g-2g)@1

**Figure S7.** $^1$H NMR inclusion components. Addition of cyclopentanecarboxylate 2g to cage 1 in CD$_3$CN. a) Preformed cage 1 (0.001 M cage). b) - e) Addition of sub-stoichiometric amounts (0.21-1.82 equiv) of 2g results in the formation of a new species which could be attributed to 1:2 H:G complex. f) Addition of 2.62 equiv of 2g totally shift the system to the new species (2g-2g)@1. Counter anions are perchlorates.
3.1.8 $^1$H NMR determination of binding stoichiometry and binding constant along the titration points for (2h-2h)@1

Figure S8. $^1$H NMR inclusion components. Addition of 2-cyclopentylacetate 2h to cage 1 in CD$_3$CN. a) Preformed cage 1 (0.001 M cage), b) - e) Addition of sub-stoichiometric amounts (0.20-1.72 equiv) of 2h results in the formation of a new species which could be attributed to 1:2 H:G complex. f) Addition of 2.54 equiv of 2h totally shift the system to the new species (2h-2h)@1. Counter anions are perchlorates.
3.2 Identification of the binding species of 2a–2h

3.2.1. Identification of the 1:2 (Host:Guest) binding species of 2a-2h

Guests series 2a-2h led to the formation of a 1:2 Host:Guest (H:G) inclusion complexes. Therefore, it was possible to obtain the global binding constant $K_B = (K_1 \cdot K_2)$ for the species (2a, 2h-2a, 2h)@1 considering the process with a of double encapsulation of two guests within the same cage. (Table S1).

| Guest                     | $K_B = (K_1 \cdot K_2)$ [M$^{-2}$] |
|---------------------------|--------------------------------------|
| hexanoate 2a              | 11.57±0.11                           |
| isovaleriate 2b           | 14.29±0.17                           |
| pivalate 2c               | 12.30±0.23                           |
| 2-dimethylbutyrate 2d     | 8.64±0.09                            |
| cyclohexanecarboxylate 2e | 17.46±0.30                           |
| 2-cyclohexylacetate 2f    | 21.59±0.46                           |
| cyclopentanecarboxylate 2g| 18.72±0.30                           |
| 2-cyclopentylacetate 2h   | 25.34±0.46                           |

Table S1. Binding constant values $K_B$ of homo species obtained by titration experiment of carboxylates. The values are expressed as (1·10$^6$ M$^{-2}$).
3.3. $^1$H NMR of $\alpha$-pyridine proton ring of filled cages in competition experiments

The $^1$H NMR spectra for the competition experiments with aliphatic carboxylates chosen as a reference compounds are shown below in Figures S9-S16. The magnified region between 9.5 and 9.0 ppm displays the range of $\alpha$-pyridine protons of the cage, which contains two guests in ratio 1:1. The coloured dots represent the carboxylates coordinated within the cage in each competition experiment.
3.3.1. $^1$H NMR titration for the competition experiment of all possible combination of guests 2a and 3a, 3e.

Figure S9. $^1$H NMR experiment for the competition experiment of all possible combination of guests 2a-3a, 3e.
3.3.2. $^1$H NMR titration for the competition experiment of all possible combination of guests 2b and 3a, 3e

**Figure S10.** $^1$H NMR experiment for the competition experiment of all possible combination of guests 2b-3a, 3e.
3.3.3. $^1$H NMR titration for the competition experiment of all possible combination of guests 2c and 3a, 3e

Figure S11. $^1$H NMR experiment for the competition experiment of all possible combination of guests 2c-3a, 3e.
3.3.4. $^1$H NMR titration for the competition experiment of all possible combination of guests 2d and 3a, 3e.

Figure S12. $^1$H NMR experiment for the competition experiment of all possible combination of guests 2d-3a, 3e.
3.3.5. $^1$H NMR titration for the competition experiment of all possible combination of guests 2e and 3a, 3e.

Figure S13. $^1$H NMR experiment for the competition experiment of all possible combination of guests 2e-3a, 3e.
3.3.6. $^1$H NMR titration for the competition experiment of all possible combination of guests 2f and 3a, 3e.

Figure S14. $^1$H NMR experiment for the competition experiment of all possible combination of guests 2f-3a, 3e.
3.3.7. $^1$H NMR titration for the competition experiment of all possible combination of guests 2g and 3a, 3e

Figure S15. $^1$H NMR experiment for the competition experiment of all possible combination of guests 2g, 3a, 3e.
3.3.8. $^1$H NMR titration for the competition experiment of all possible combination of guests 2h and 3a, 3e

Figure S16. $^1$H NMR experiment for the competition experiment of all possible combination of guests 2h-3a, 3e.
3.4. Binding constant determination of the homo and hetero co-encapsulated species and $^1$H NMR of a pyridine proton ring of filled cages in competition experiments

From the $^1$H NMR competition experiments, it was possible to calculate the binding constants of homo and hetero species using the procedure described in Carlo Bravin, Giulia Licini, Christopher A. Hunter and Cristiano Zonta Chem. Sci., 2019, 10, 1466-1471.

By the integration of each peak related to the filled species and the cage 1 it was possible to determine the binding constant for each homo by each competition experiment species (Table S2). The integrals are defined via fitting of the characteristic peaks when partial overlap is present. The presence of 1:1 inclusion species were taken into account when considering the binding constant calculation for the 2:1 inclusion species. Then it was possible to obtain the binding constant for the hetero species, which are reported in Table S4. The integral peaks are referred to internal standard p-xylene and their values are reported with the error calculated repeating the experiments three times. The binding constants obtained for the homo species for each competition experiment and the binding constants obtained for hetero species of benzoates are in agreement with the values reported by the titration experiments. The guests are described as in the legend below. Statistical correction for the hetero-complexes is taken into account.

### Binding constant for homo species obtained by competition experiment

| Competition experiment | Guest X | Guest Y | Binding constant for the Homo species (X-X) | Binding constant for the Homo species (Y-Y) | Binding constant for the Hetero species (X-Y) |
|------------------------|---------|---------|---------------------------------------------|---------------------------------------------|---------------------------------------------|
| 1                      | NO$_2$  | Cl      | 43.76±4.63                                 | 24.52±2.44                                  | 27.63±2.42                                  |
| 2                      | NO$_2$  | Me      | 42.94±4.31                                 | 18.78±2.33                                  | 26.27±2.13                                  |
| 3                      | NO$_2$  | OMe     | 47.29±4.01                                 | 12.99±1.25                                  | 25.00±1.09                                  |
| 4                      | NO$_2$  | N(Me)$_2$ | 43.00±4.24                               | 4.96±1.2                                    | 20.34±0.20                                  |
| 5                      | NO$_2$  | Hex     | 40.23±4.42                                 | 8.53±1.98                                   | 11.48±2.86                                  |
| 8                      | NO$_2$  | sBu     | 41.04±2.78                                 | 15.83±0.02                                  | 27.67±0.33                                  |
| 9                      | NO$_2$  | tBu     | 35.63±1.16                                 | 13.53±0.59                                  | 33.23±0.36                                  |
| 10                     | NO$_2$  | neoP    | 29.91±4.80                                 | 7.96±0.58                                   | 23.11±2.99                                  |
| 11                     | NO$_2$  | cHex    | 40.36±0.12                                 | 17.34±0.04                                  | 25.53±0.11                                  |
| 12                     | NO$_2$  | cHexMe  | 40.93±0.67                                 | 21.44±0.29                                  | 27.18±0.23                                  |
| 13                     | NO$_2$  | cPen    | 38.79±0.54                                 | 18.12±0.23                                  | 25.70±0.06                                  |
| 14                     | NO$_2$  | cPenMe  | 40.60±0.24                                 | 24.35±0.78                                  | 29.11±1.06                                  |
| 15                     | Cl      | Me      | 26.87±2.58                                 | 17.00±1.33                                  | 16.30±3.63                                  |
| 16                     | Cl      | OMe     | 23.60±2.44                                 | 9.81±1.01                                   | 13.65±0.24                                  |
| 17                     | Cl      | N(Me)$_2$ | 23.46±2.11                                | 4.62±0.87                                   | 11.74±2.79                                  |
| 18                     | Cl      | Hex     | 21.27±2.19                                 | 11.04±1.08                                  | 10.63±2.23                                  |
| 21                     | Cl      | sBu     | 22.94±0.40                                 | 14.87±0.24                                  | 28.72±0.03                                  |
| 22                     | Cl      | tBu     | 21.37±0.14                                 | 14.73±0.04                                  | 26.67±0.45                                  |
| 23                     | Cl      | neoP    | 23.80±2.15                                 | 9.34±1.60                                   | 23.53±1.39                                  |
| 24                     | Cl      | cHex    | 22.15±0.57                                 | 17.06±0.03                                  | 26.10±0.45                                  |
| 25                     | Cl      | cHexMe  | 21.73±0.49                                 | 21.12±0.52                                  | 26.87±0.49                                  |
| 26                     | Cl      | cPen    | 22.69±0.02                                 | 18.41±0.21                                  | 25.67±0.17                                  |
| 27                     | Cl      | cPenMe  | 22.21±0.01                                 | 24.86±0.02                                  | 27.30±0.20                                  |
| 28                     | Me      | OMe     | 17.83±2.13                                 | 10.95±1.00                                  | 13.82±0.82                                  |
| 29                     | Me      | N(Me)$_2$ | 18.44±2.01                                | 4.23±0.67                                   | 8.05±0.22                                   |
| 30                     | Me      | Hex     | 19.56±1.66                                 | 11.88±1.11                                  | 10.60±1.58                                  |
Table S2. Binding constant values obtained in each competition experiment for the homo species and hetero species. The values are expressed as $(1 \cdot 10^6$ M$^{-2})$

**Average binding constant values from all the experiments for Homo species**

| Reference | Binding constant for the Homo species (X-X) |
|-----------|------------------------------------------|
| NO$_2$-NO$_2$ | 38.05±2.23 |
| Cl-Cl | 22.45±0.72 |
| Me-Me | 16.45±0.75 |
| OMe-OMe | 11.92±1.58 |
| N(Me)$_2$- N(Me)$_2$ | 8.64±0.85 |

Table S3. Average binding constant values obtained from the titration experiments of homo species with different reference compounds. The values are expressed as $(1 \cdot 10^6$ M$^{-2})$
Binding constant values from all the experiments for Hetero species

|        | NO₂   | Cl    | Me    | OMe   | N(Me)₂ | Ref   |
|--------|-------|-------|-------|-------|--------|-------|
| Hex    | 11.48±2.86 | 10.63±1.23 | 10.60±1.58 | 10.61±2.58 | 10.98±0.44 | 10.17±0.76 |
| sBu    | 27.67±0.33 | 28.72±0.03 | 26.97±0.44 | 26.07±0.58 | 26.17±0.35 | 15.69±0.54 |
| tBu    | 33.27±0.36 | 26.67±0.46 | 26.10±0.14 | 27.57±0.23 | 30.13±0.94 | 18.52±5.12 |
| neoP   | 23.11±2.99 | 23.52±1.40 | 23.68±1.78 | 24.08±1.03 | 21.97±0.25 | 11.56±2.58 |
| cHex   | 25.53±0.11 | 26.10±0.45 | 24.87±0.19 | 23.91±0.24 | 24.05±1.37 | 18.32±0.99 |
| cHexMe | 27.18±0.23 | 26.87±0.49 | 27.02±0.16 | 26.47±0.25 | 26.08±0.04 | 19.00±2.80 |
| cPen   | 25.70±0.06 | 25.67±0.17 | 25.17±0.09 | 23.77±0.53 | 26.10±0.41 | 19.00±0.54 |
| cPenMe | 29.11±1.06 | 27.30±0.20 | 26.88±0.06 | 25.93±0.07 | 25.52±1.05 | 24.71±0.35 |

Table S4. Binding constant values obtained from the titration experiments of hetero species with different reference compounds. The values are expressed as (1·10⁶ M⁻²).

After the binding constant determination for each cage filled species, it was possible to obtain the corresponding ΔG° using the Gibbs equation and consequently these values were used for ΔΔG° calculation in the DMC (Table S5).

ΔG° values

|        | NO₂   | Cl    | Me    | OMe   | N(Me)₂ | Ref   |
|--------|-------|-------|-------|-------|--------|-------|
| Hex    | -43.41±1.15 | -42.43±1.24 | -42.31±1.39 | -42.18±1.21 | -41.67±1.11 | -40.26±1.08 |
| sBu    | -43.58±0.32 | -42.14±0.10 | -41.29±0.21 | -40.40±0.18 | -38.08±0.98 | -40.99±0.24 |
| tBu    | -43.51±0.15 | -42.10±0.39 | -41.34±0.91 | -40.42±0.14 | -38.07±0.55 | -41.24±0.12 |
| neoP   | -43.43±0.68 | -42.16±0.55 | -41.23±0.97 | -40.46±0.46 | -38.07±0.69 | -41.23±0.42 |
| cHex   | -43.57±0.14 | -42.12±0.15 | -41.28±0.10 | -40.40±0.81 | -38.05±0.16 | -41.39±0.10 |
| cHexMe | -43.58±0.79 | -42.11±0.13 | -41.28±0.19 | -40.41±0.92 | -38.07±0.43 | -42.07±0.48 |
| cPen   | -43.55±0.13 | -42.14±0.11 | -41.27±0.11 | -40.42±0.12 | -38.03±0.64 | -41.50±0.29 |
| cPenMe | -43.58±0.28 | -42.12±0.33 | -41.26±0.27 | -40.41±0.10 | -38.03±0.32 | -42.17±0.21 |

Table S5. ΔG° values obtained using the Gibbs equation from binding constant displayed in Table S4. The values are expressed in (kJ/mol)
3.5. Correlation of the experimental aromatic stacking interactions in function of the Hammett constant

Aromatic stacking energies (kJ mol\(^{-1}\)) measured for the guest with substituent X (y-axis) plotted as a function of the Hammett constant \(\sigma_Y\) of the guest with substituent Y (x-axis).

3.5.1. Hammett correlation plots of benzoates 3a-3e aromatic stacking interactions with hexanoate 2a as a reference compound

Figure S17. Plot of the linear fittings and fitting parameters for the DMC data using hexanoate 2a as reference compound.
3.5.2. Hammett correlation plots of benzoates 3a-3e aromatic stacking interactions with sorbate 2b as a reference compound

| Series  | Slope     | Intercept | R²     |
|---------|-----------|-----------|--------|
| N(Me)₂  | -2.12±0.02 | 0.41±0.16 | 0.991  |
| OMe     | -1.58±0.01 | -0.48±0.01| 0.889  |
| Me      | -1.56±0.02 | -0.71±0.02| 0.860  |
| Cl      | -1.34±0.02 | -0.92±0.03| 0.938  |
| NO₂     | -1.00±0.01 | -2.09±0.16| 0.845  |

**Figure S18.** Plot of the linear fittings and fitting parameters for the DMC data using isovaleriate 2b as reference compound.
3.5.3. Hammett correlation plots of benzoates 3a-3e aromatic stacking interactions with pivalate 2c as a reference compound

| Series | Slope   | Intercept | $R^2$ |
|--------|---------|-----------|-------|
| N(Me)$_2$ | -2.10±02 | 0.65±0.17 | 0.985 |
| OMe    | -1.56±0.01 | -0.45±0.01 | 0.885 |
| Me     | -1.53±0.01 | -0.91±0.03 | 0.767 |
| Cl     | -1.31±0.02 | -1.21±0.03 | 0.809 |
| NO$_2$ | -0.94±0.01 | -1.74±0.20 | 0.939 |

Figure S19. Plot of the linear fittings and fitting parameters for the DMC data using pivalate 2c as reference compound.
3.5.4. Hammett correlation plots of benzoates 3a-3e aromatic stacking interactions with 3,3-dimethylbutyrate 2d as a reference compound

| Series | Slope       | Intercept  | $R^2$  |
|--------|-------------|------------|--------|
| N(Me)$_2$ | -2.21±0.03  | 0.47±0.27  | 0.986  |
| OMe    | -1.66±0.01  | -0.19±0.26 | 0.929  |
| Me     | -1.65±0.01  | -0.55±0.35 | 0.925  |
| Cl     | -1.44±0.01  | -0.94±0.32 | 0.881  |
| NO$_2$ | -1.01±0.01  | -2.06±0.27 | 0.890  |

Figure S20. Plot of the linear fittings and fitting parameters for the DMC data using 3,3-dimethylbutyrate 2d as reference compound.
3.5.5. Hammett correlation plots of benzoates 3a-3e aromatic stacking interactions with cyclohexanecarboxylate 2e as a reference compound

| Series | Slope   | Intercept | \( R^2 \) |
|--------|---------|-----------|-----------|
| N(Me)\(_2\) | -2.13±0.02 | -0.41±0.05 | 0.993 |
| OMe   | -1.58±0.02 | -1.30±0.04 | 0.897 |
| Me    | -1.56±0.02 | -1.52±0.03 | 0.869 |
| Cl    | -1.33±0.01 | -1.76±0.06 | 0.936 |
| NO\(_2\) | -1.00±0.02 | -2.90±0.02 | 0.858 |

Figure S21. Plot of the linear fittings and fitting parameters for the DMC data using cyclohexanecarboxylate 2e as reference compound.
3.5.6. Hammett correlation plots of benzoates 3a-3e aromatic stacking interactions with 2-cyclohexylacetate 2f as a reference compound

| Series | Slope   | Intercept | $R^2$ |
|--------|---------|-----------|-------|
| N(Me)$_2$ | -2.18±0.03 | -0.72±0.08 | 0.995 |
| OMe     | -1.64±0.03 | -1.57±0.17 | 0.930 |
| Me      | -1.62±0.03 | -1.83±0.15 | 0.902 |
| Cl      | -1.40±0.5  | -2.20±0.16 | 0.911 |
| NO$_2$  | -1.06±0.04 | -3.26±0.15 | 0.909 |

**Figure S22.** Plot of the linear fittings and fitting parameters for the DMC data using 2-cyclohexylacetate 2f as reference compound.
3.5.7. Hammett correlation plots of benzoates 3a – 3e aromatic stacking interactions with cyclopentanecarboxylate 2g as a reference compound

| Series | Slope   | Intercept | $R^2$ |
|--------|---------|-----------|-------|
| N(Me)$_2$ | -2.26±0.02 | -0.27±0.05 | 0.996 |
| OMe    | -1.69±0.02 | -1.40±0.04 | 0.905 |
| Me     | -1.65±0.02 | -1.49±0.03 | 0.903 |
| Cl     | -1.45±0.02 | -1.89±0.06 | 0.942 |
| NO$_2$ | -1.10±0.02 | -2.96±0.02 | 0.911 |

**Figure S23.** Plot of the linear fittings and fitting parameters for the DMC data using cyclopentanecarboxylate 2g as reference compound.
3.5.8. Hammett correlation plots of benzoates \textbf{3a-3e} aromatic stacking interactions with 2-cyclopentylacetate \textbf{2h} as a reference compound

| Series     | Slope  | Intercept | R$^2$ |
|------------|--------|-----------|-------|
| N(Me)$_2$  | -2.06±0.04 | -0.83±0.02 | 0.997 |
| OMe       | -1.50±0.02 | -1.68±0.01 | 0.917 |
| Me        | -1.48±0.05 | -1.90±0.02 | 0.880 |
| Cl        | -1.25±0.05 | -2.23±0.03 | 0.892 |
| NO$_2$    | -0.92±0.05 | -3.16±0.08 | 0.902 |

**Figure S24.** Plot of the linear fittings and fitting parameters for the DMC data using 2-cyclopentylacetate \textbf{2h} as reference compound.
3.6. Hammett plot of slopes and intercept values of $\Delta \Delta G^\circ$ correlation

After the correlation of the $\Delta \Delta G^\circ$ values with of Hammett constant for each substituent it was possible to determine a correlation between the slope (Figure S25,S27,S29,S31,S33,S35,S37,S39) and intercept (Figure S26,S28,S30,S32,S34,S36,S38) values for each substituent. The fitting values define the coefficient for equation (1) which are reported in Table S6. The points obtained were then fitted with the equation:

$$\Delta \Delta G^\circ = a \sigma_x \sigma_y - b \sigma_x - c \sigma_y - d$$

(1)

Figure S25. Correlation plot of Slopes (kJ mol$^{-1}$) ($\Delta \Delta G^\circ$) for each substituent against Hammett constant for hexanoate 2a.

Figure S26. Correlation plot of Intercepts (kJ mol$^{-1}$) ($\Delta \Delta G^\circ$) for each substituent against Hammett constant for hexanoate 2a.
Figure S27. Correlation plot of Slopes (kJ mol⁻¹) (ΔΔG°) for each substituent against Hammett constant for Isovaleriate 2b.

Figure S28. Correlation plot of Intercepts (kJ mol⁻¹) (ΔΔG°) for each substituent against Hammett constant for Isovaleriate 2b.
Figure S29. Correlation plot of Slopes (kJ mol\(^{-1}\)) (ΔΔG°) for each substituent against Hammett constant for Pivalate 2c.

Figure S30. Correlation plot of Intercepts (kJ mol\(^{-1}\)) (ΔΔG°) for each substituent against Hammett constant for Pivalate 2c.
**Figure S31.** Correlation plot of Slopes (kJ mol\(^{-1}\)) (ΔΔG°) for each substituent against Hammett constant for 3,3-dimethylbutyrate 2d.

**Figure S32.** Correlation plot of Intercepts (kJ mol\(^{-1}\)) (ΔΔG°) for each substituent against Hammett constant for 3,3-dimethylbutyrate 2d.
**Figure S33.** Correlation plot of Slopes (kJ mol$^{-1}$) ($\Delta\Delta G^\circ$) for each substituent against Hammett constant for cyclohexanecarboxylate 2e.

**Figure S34.** Correlation plot of Intercepts (kJ mol$^{-1}$) ($\Delta\Delta G^\circ$) for each substituent against Hammett constant for cyclohexanecarboxylate 2e.
Figure S35. Correlation plot of Slopes (kJ mol\(^{-1}\)) (ΔΔG°) for each substituent against Hammett constant for 2-cyclohexylacetate 2f.

![Slope Correlation Plot](image1)

\[ y = 0.68x - 1.55 \]
\[ R^2 = 0.975 \]

Figure S36. Correlation plot of Intercepts (kJ mol\(^{-1}\)) (ΔΔG°) for each substituent against Hammett constant for 2-cyclohexylacetate 2f.

![Intercept Correlation Plot](image2)

\[ y = -1.55x - 2.00 \]
\[ R^2 = 0.990 \]
**Figure S37.** Correlation plot of Slopes (kJ mol\(^{-1}\)) (\(\Delta \Delta G^\circ\)) for each substituent against Hammett constant for cyclopentancarboxylate 2g.

**Figure S38.** Correlation plot of Intercepts (kJ mol\(^{-1}\)) (\(\Delta \Delta G^\circ\)) for each substituent against Hammett constant for cyclopentancarboxylate 2g.
Figure S39. Correlation plot of Slopes (kJ mol\(^{-1}\)) (\(\Delta \Delta G^\circ\)) for each substituent against Hammett constant for 2-cyclopentylacetate 2h.

\[
y = 0.69x - 1.41 \\
R^2 = 0.972
\]

Figure S40. Correlation plot of Intercepts (kJ mol\(^{-1}\)) (\(\Delta \Delta G^\circ\)) for each substituent against Hammett constant for 2-cyclopentylacetate 2h.

\[
y = -1.41x - 2.04 \\
R^2 = 0.990
\]
\[ \Delta \Delta G^\circ = a \sigma_x \sigma_y - b \sigma_x - c \sigma_y - d \]  \hspace{1cm} (1)

| Reference compound   | a (\(\sigma_x \sigma_y\)) | b (\(\sigma_x\)) | b (\(\sigma_y\)) | d         |
|----------------------|---------------------------|-------------------|------------------|-----------|
| Hexanoate 2a         | 0.69\(\pm\)0.01          | -1.54\(\pm\)0.04 | -1.54\(\pm\)0.04 | -1.25\(\pm\)0.27 |
| isovaleriate 2b      | 0.67\(\pm\)0.02          | -1.49\(\pm\)0.07 | -1.49\(\pm\)0.07 | -0.84\(\pm\)0.06 |
| pivalate 2c          | 0.70\(\pm\)0.01          | -1.45\(\pm\)0.03 | -1.45\(\pm\)0.03 | -0.81\(\pm\)0.35 |
| 3,3-dimethylbutyrate 2d | 0.72\(\pm\)0.05          | -1.56\(\pm\)0.32 | -1.56\(\pm\)0.32 | -0.74\(\pm\)0.65 |
| cyclohexanecarboxylate 2e | 0.68\(\pm\)0.01          | -1.48\(\pm\)0.14 | -1.48\(\pm\)0.14 | -1.66\(\pm\)0.12 |
| 2-cyclohexylacetate 2f | 0.68\(\pm\)0.00          | -1.55\(\pm\)0.05 | -1.55\(\pm\)0.05 | -2.00\(\pm\)0.07 |
| cyclopentanecarboxylate 2g | 0.70\(\pm\)0.02          | -1.60\(\pm\)0.01 | -1.60\(\pm\)0.01 | -1.70\(\pm\)0.04 |
| 2-cyclopentylacetate 2h | 0.69\(\pm\)0.02          | -1.41\(\pm\)0.21 | -1.41\(\pm\)0.21 | -2.04\(\pm\)0.04 |

Table S6. Coefficients obtained for the equation (1) considering the guests series 2a-2h
3.7. Dissection of polar and non-polar contribution

Description of charge

The Hammett equation to describe how substituents affect the equilibrium constant for the interaction between an aromatic ring with substituent X and another arbitrary aromatic ring is

\[ \log \left( \frac{K_X}{K_H} \right) = \rho \sigma_X \]

We assume that the interaction is entirely electrostatic and can be described by the interaction energy between two point charges to obtain expressions for \( K_H \) and \( K_X \). The electrostatic interaction energy for an aromatic ring with substituent H is described by a charge \( q_H \) a distance \( r \) away from another arbitrary charge \( q_0 \) in a medium of dielectric constant \( \varepsilon \):

\[ -RT \ln(K_H) = \frac{q_0 q_H}{4\pi\varepsilon r} \]

Similarly, the electrostatic interaction energy for an aromatic ring with substituent H is described by a charge \( q_X \) the same distance \( r \) away from the same arbitrary charge \( q_0 \) in the same medium of dielectric constant \( \varepsilon \):

\[ -RT \ln(K_X) = \frac{q_0 q_X}{4\pi\varepsilon r} \]

Substituting into the Hammett equation gives

\[ -log(e)q_0 \frac{4\pi\varepsilon r}{4RT\pi\varepsilon r} (q_X - q_H) = \rho \sigma_X \]

Or

\[ q_X - q_H = \rho' \sigma_X \]

Where \( \rho' \) is a constant:

\[ \rho' = -\frac{log(e)q_0}{4RT\pi\varepsilon r} \rho \]

So the effective charge on a substituted aromatic ring can be defined relative to the charge on an unsubstituted aromatic ring according to Equation (2) in the main text.
4. $^1$H NMR and MS characterization

$(2a-2a)@1$

Figure S41. $^1$H NMR spectrum of inclusion complex G:H$_2$$(2a-2a)@1$ with Hexanoate 2a to cage 1 in CD$_3$CN. p-xylene is used as internal standard 7.095 ppm. Counter anions are perchlorates.

Figure S42. a) ESI-MS spectrum of inclusion complex G:H$_2$$(2a-2a)@1$ with Hexanoate 2a to cage 1 in CH$_3$CN. b) Isotopic pattern of experimental spectrum, c) Isotopic pattern of theoretical spectrum.
Figure S43 \(^1\)H NMR spectrum of inclusion complex G:H\((2b-2b)@1\) with Isovalerate \(2b\) to cage \(1\) in CD\(_3\)CN. p-xylene is used as internal standard 7.095 ppm. Counter anions are perchlorates.

Figure S44. a) ESI-MS spectrum of inclusion complex G:H\((2b-2b)@1\) with Isovalerate \(2b\) to cage \(1\) in CH\(_3\)CN. b) Isotopic pattern of experimental spectrum, c) Isotopic pattern of theoretical spectrum.
(2c-2c)@1

Figure S45. $^1$H NMR spectrum of inclusion complex G:H$_2$(2c-2c)@1 with Pivalate 2c to cage 1 in CD$_3$CN. p-xylene is used as internal standard 7.095 ppm. Counter anions are perchlorates.

Figure S46. a) ESI-MS spectrum of inclusion complex G:H$_2$(2c-2c)@1 with Pivalate 2c to cage 1 in CH$_3$CN. b) Isotopic pattern of experimental spectrum, c) Isotopic pattern of theoretical spectrum.
Figure S47. $^1$H NMR spectrum of inclusion complex G:H$_2$(2d-2d)@1 with 3,3-dimethylbutyrate 2d to cage 1 in CD$_3$CN. P-xylene is used as internal standard 7.095 ppm. Counter anions are perchlorates.

Figure S48. a) ESI-MS spectrum of inclusion complex G:H$_2$(2d-2d)@1 with 3,3-dimethylbutyrate 2d to cage 1 in CH$_3$CN. b) Isotopic pattern of experimental spectrum. c) Isotopic pattern of theoretical spectrum.
Figure S49. $^1$H NMR spectrum of inclusion complex G:H$_2$(2e-2e)$\@1$ with Cyclohexanoate 2e to cage 1 in CD$_3$CN. p-xylene is used as internal standard 7.095 ppm. Counter anions are perchlorates.

Figure S50. a) ESI-MS spectrum of inclusion complex G:H$_2$(2e-2e)$\@1$ with Cyclohexanoate 2e to cage 1 in CH$_3$CN. b) Isotopic pattern of experimental spectrum, c) Isotopic pattern of theoretical spectrum.
**Figure S51.** $^1$H NMR spectrum of inclusion complex $G:H_2(2f-2f)@1$ with 2-cyclohexylacetic acid $2f$ to cage $1$ in CD$_3$CN. Counter anions are perchlorates.

**Figure S52.** a) ESI-MS spectrum of inclusion complex $G:H_2(2f-2f)@1$ with 2-cyclohexylacetic acid $2f$ to cage $1$ in CH$_3$CN. b) Isotopic pattern of experimental spectrum, c) Isotopic pattern of theoretical spectrum.
Figure S53. $^1$H NMR spectrum of inclusion complex G:H$_2$-(2g-2g)@1 with Cyclopentanecarboxylic acid 2g to cage 1 in CD$_3$CN. Counter anions are perchlorates.

Figure S54. a) ESI-MS spectrum of inclusion complex G:H$_2$-(2g-2g)@1 with Cyclopentanecarboxylic acid 2g to cage 1 in CH$_3$CN. b) Isotopic pattern of experimental spectrum. c) Isotopic pattern of theoretical spectrum.
**Figure S55.** $^1$H NMR spectrum of inclusion complex $G:H_2(2h-2h)@1$ with 2-cyclopentylacetate acid $2h$ to cage $1$ in CD$_3$CN. Counter anions are perchlorates.

**Figure S56.** a) ESI-MS spectrum of inclusion complex $G:H_2(2h-2h)@1$ with 2-cyclopentylacetate $2h$ to cage $1$ in CH$_3$CN. b) Isotopic pattern of experimental spectrum, c) Isotopic pattern of theoretical spectrum.