Electronic supplementary information

Highly Effective Binding of Neutral Dinitriles by Simple Pillar[5]arenes

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Contents

Materials and methods.

All of the guests were commercially available and used as received. AlkP5A hosts[1] (MeP5A, EtP5A, BuP5A and OctP5A) were prepared by condensation of the corresponding 1,4-dialkoxybenzene with paraformaldehyde and $BF_3{\cdot}O(C_2H_5)_2$ as a catalyst. ^{1}H NMR, ^{13}C NMR and 2D NOESY spectra were recorded on a Bruker AV500 instrument.

Copies of ^{1}H NMR and ^{13}C NMR spectra of hosts.

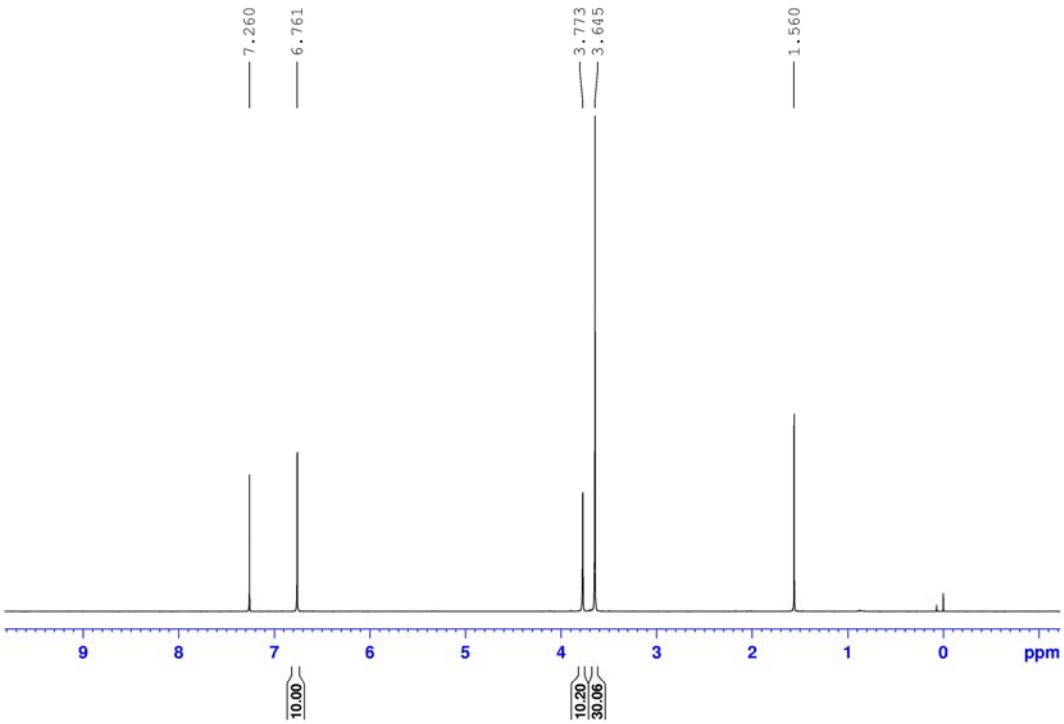

Figure S1. ^{1}H NMR spectrum (500 MHz) of MeP5A in $CDCl_3$.

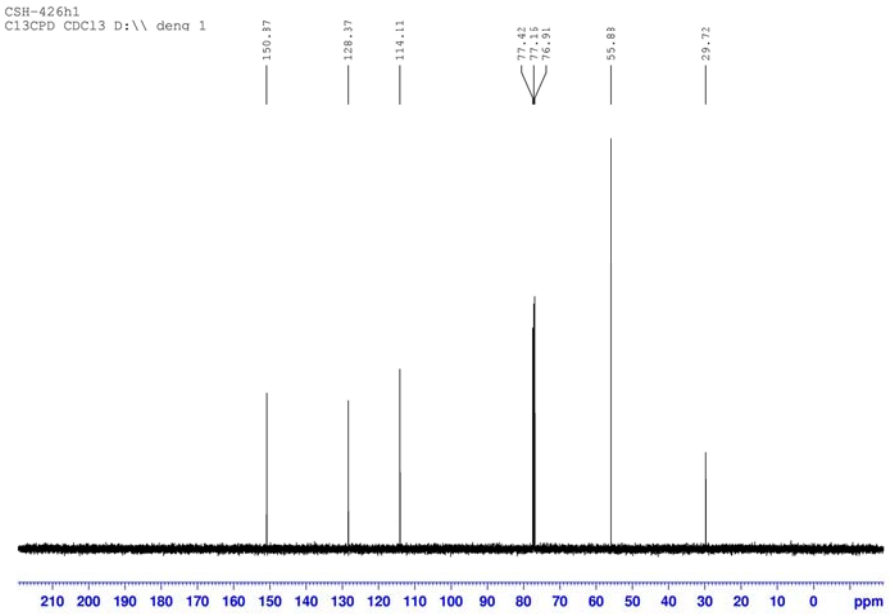

Figure S2. ^{13}C NMR spectrum (125 MHz) of MeP5A in $CDCl_3$.

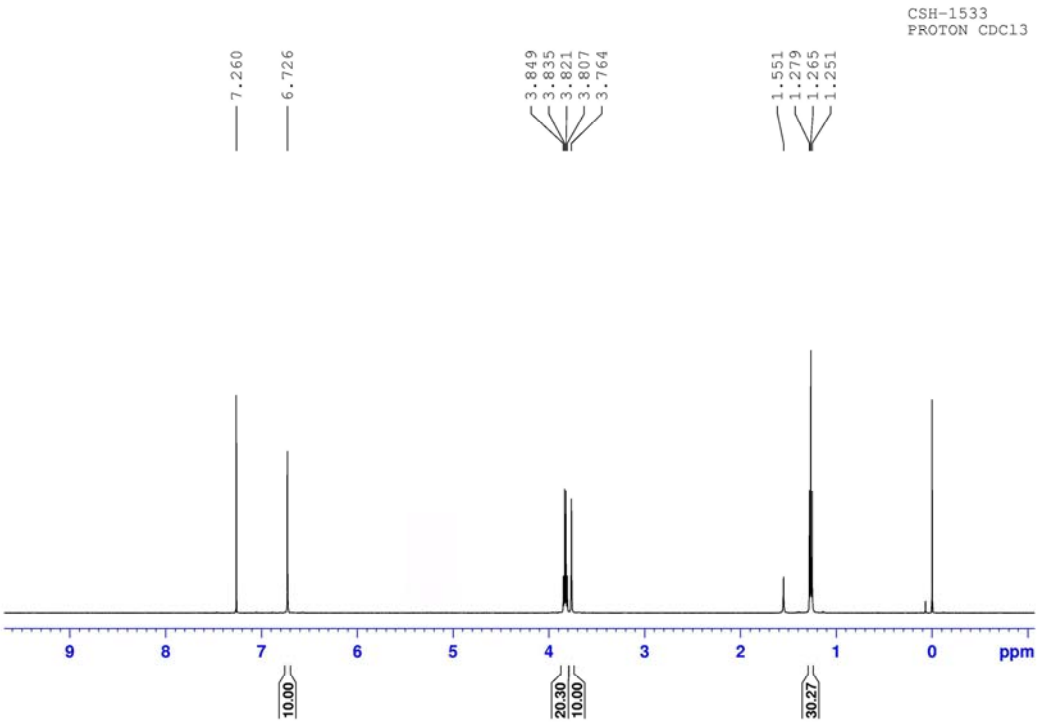

Figure S3. ^{1}H NMR spectrum (500 MHz) of EtP5A in $CDCl_3$.

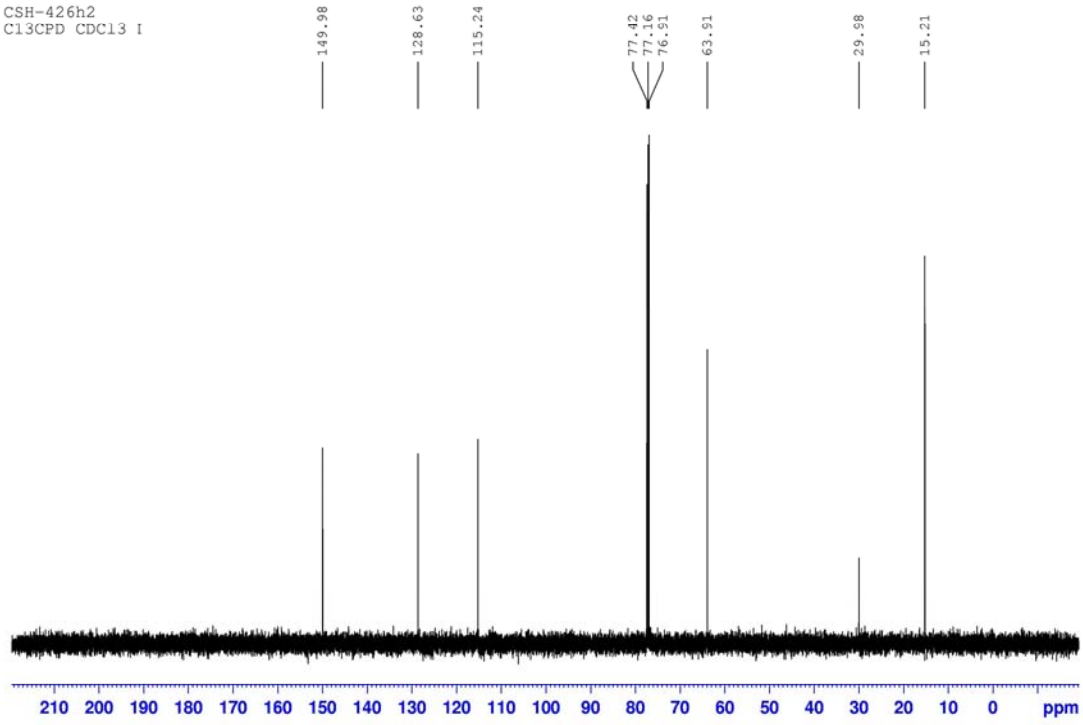

Figure S4. ^{13}C NMR spectrum (125 MHz) of EtP5A in $CDCl_3$.

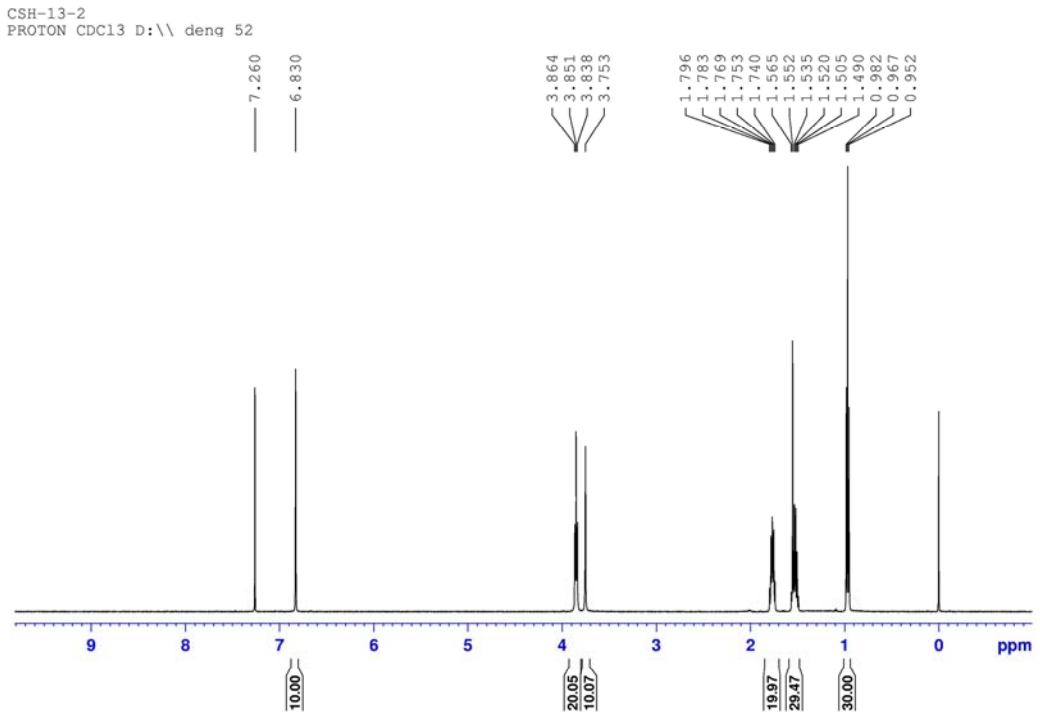

Figure S5. ^{1}H NMR spectrum (500 MHz) of BuP5A in $CDCl_3$.

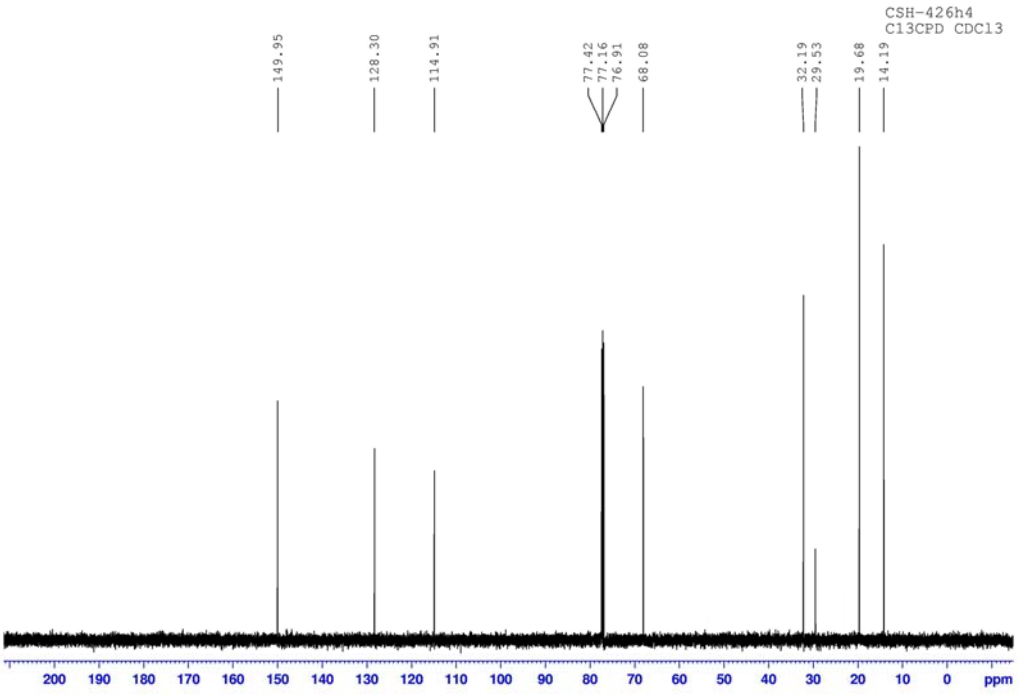

Figure S6. ^{13}C NMR spectrum (125 MHz) of BuP5A in $CDCl_3$.

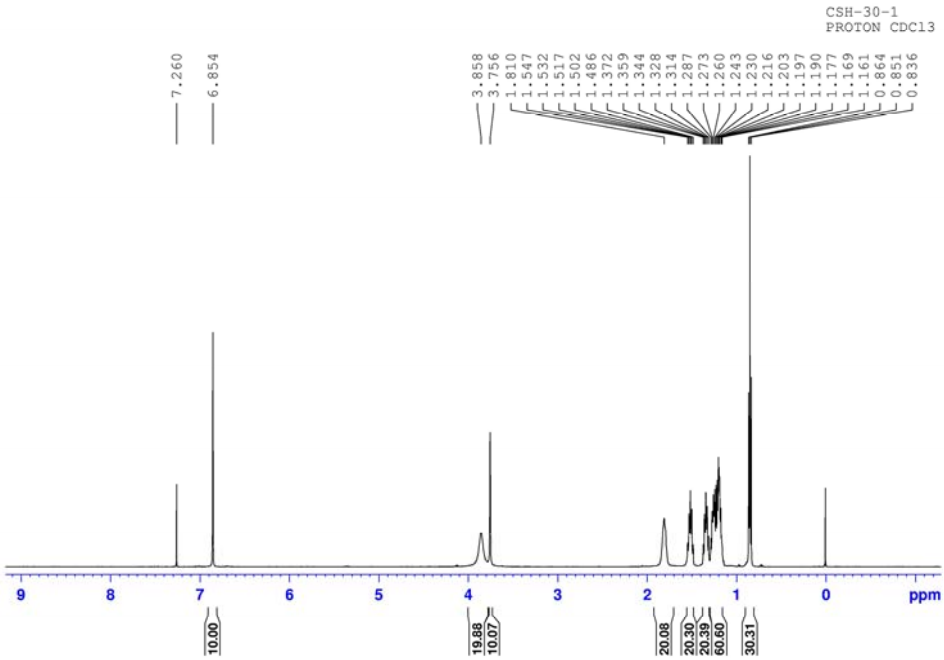

Figure S7. ^{1}H NMR spectrum (500 MHz) of OctP5A in $CDCl_3$.

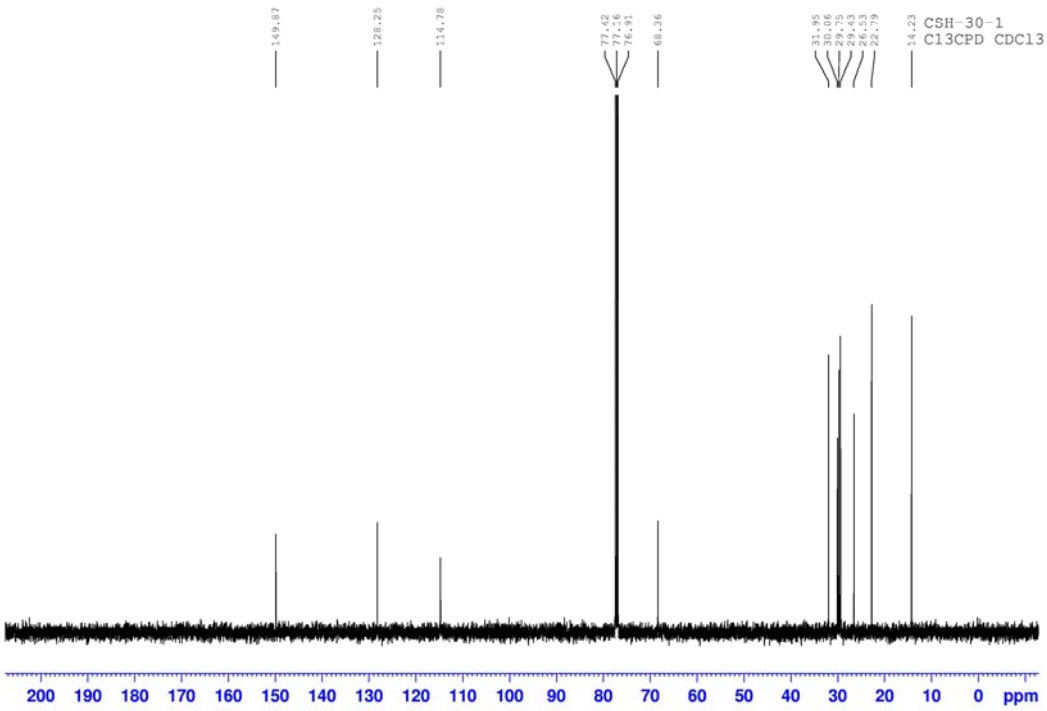

Figure S8. ^{13}C NMR spectrum (125 MHz) of OctP5A in $CDCl_3$.

^{1}H NMR spectra of guests in the absence and presence of AlP5As.

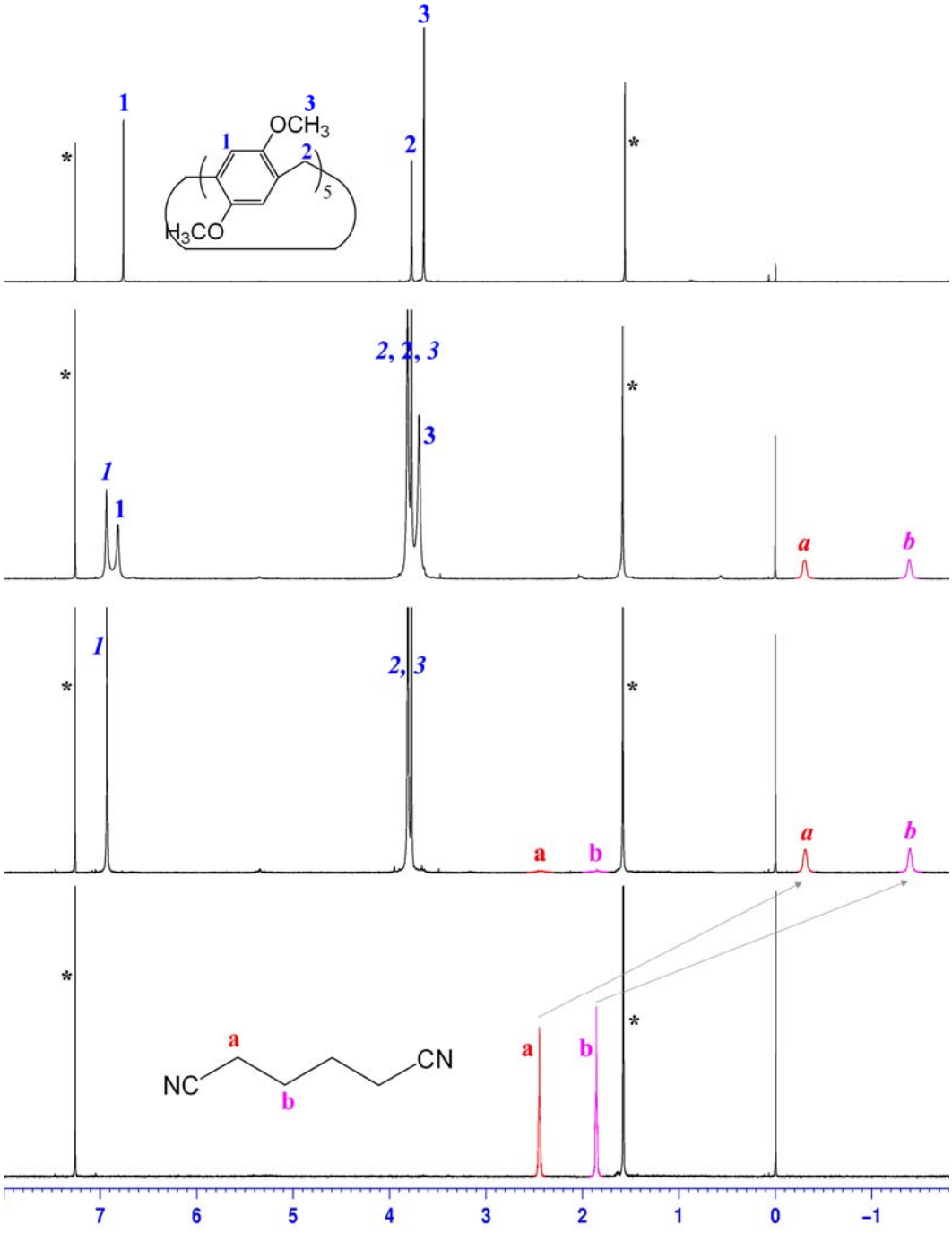

Figure S9. ^{1}H NMR spectra of dinitrile **2** (7.2 mM, 500 MHz, $CDCl_3$) in the presence of increasing amounts of MeP5A; from bottom to top: 0.0, 0.9, and 1.7 equivalents. For comparison, the spectrum of the uncomplexed MeP5A is shown at the top. The peaks marked with an asterisk are due to solvent/water. Italics represent complexed host and guest.

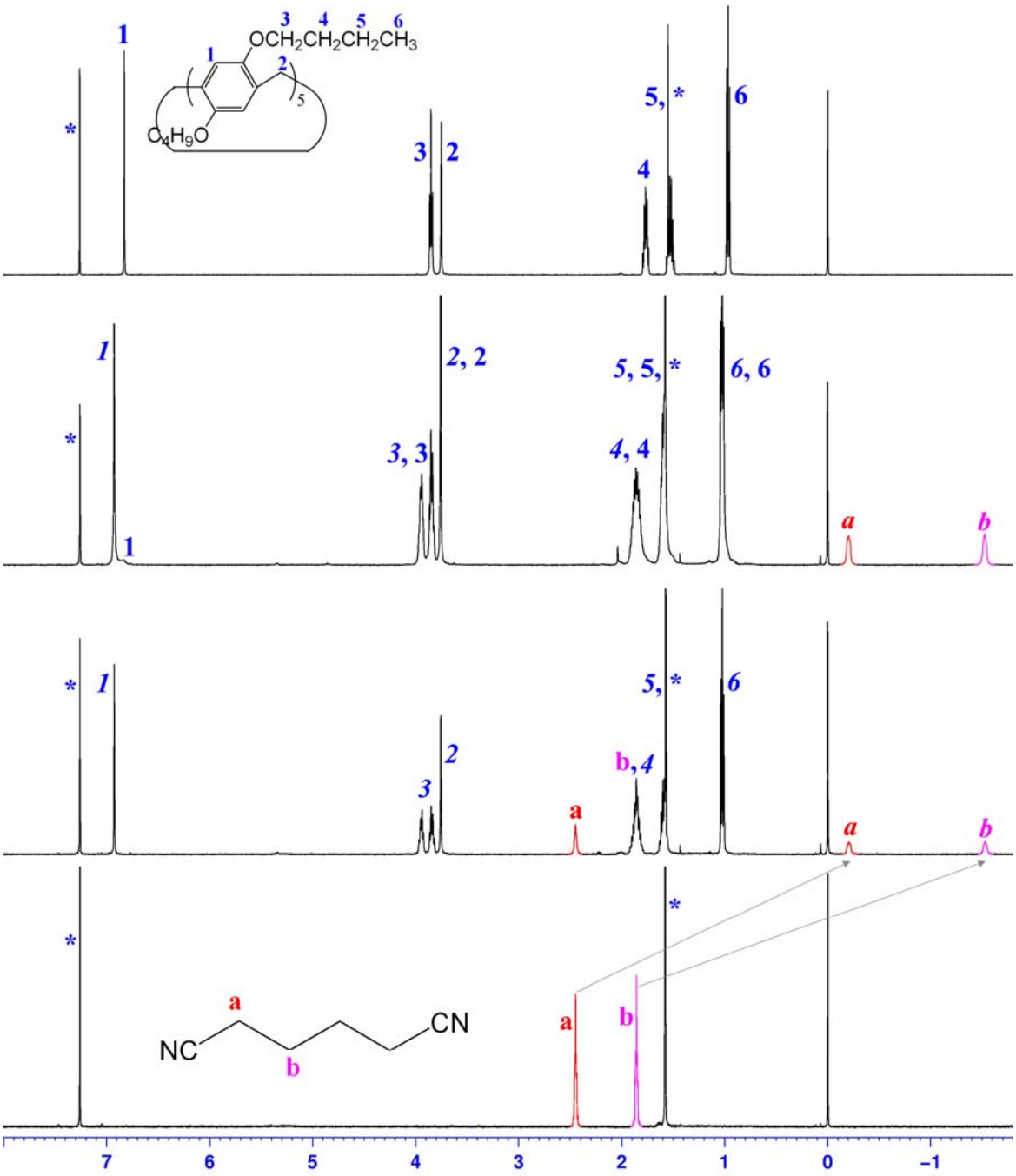

Figure S10. ^{1}H NMR spectra of dinitrile **2** (7.2 mM, 500 MHz, $CDCl_3$) in the presence of increasing amounts of BuP5A; from bottom to top: 0.0, 0.5, and 1.1 equivalents. For comparison, the spectrum of the uncomplexed BuP5A is shown at the top. The peaks marked with an asterisk are due to solvent/water. Italics represent complexed host and guest.

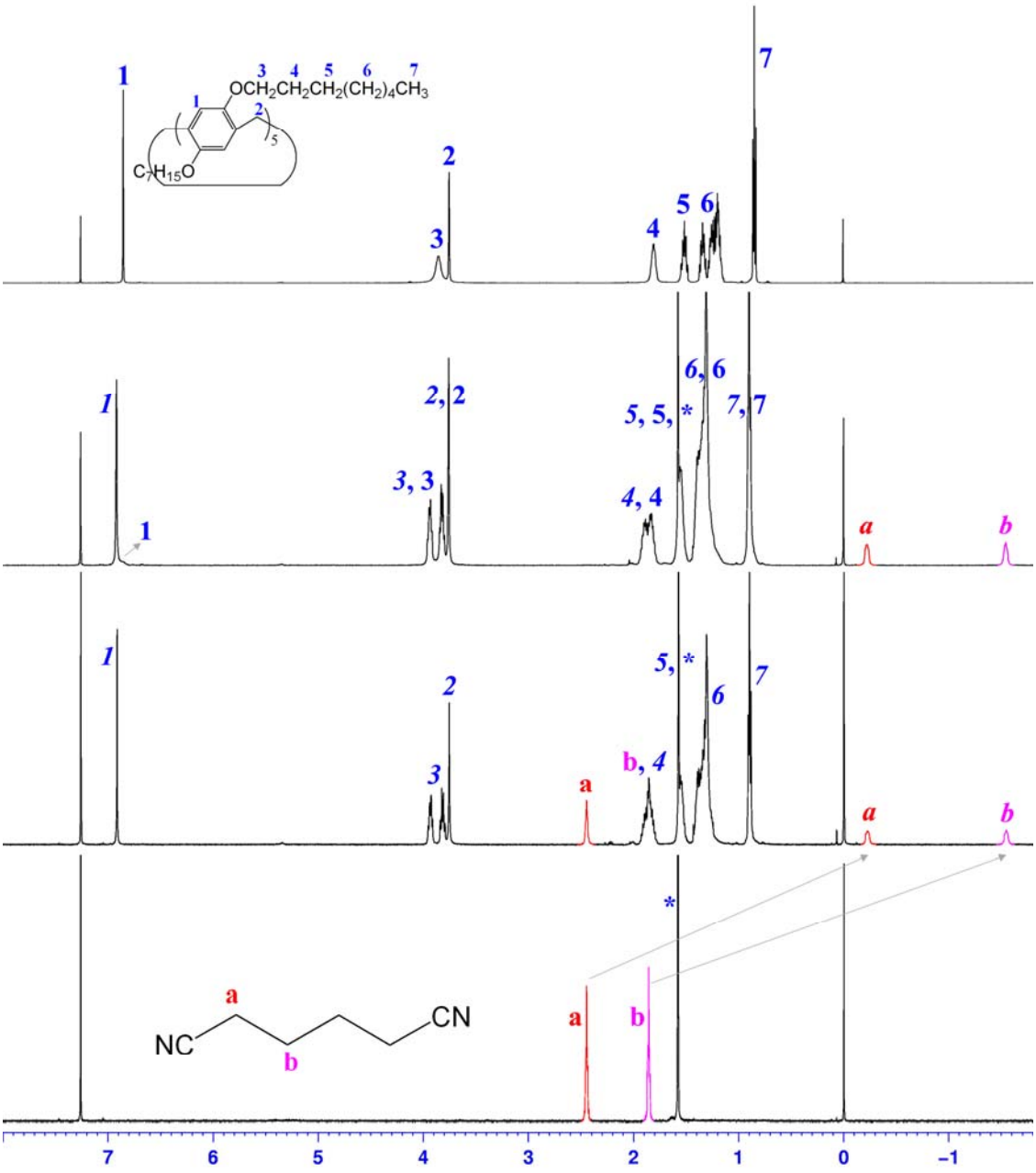

Figure S11. ^{1}H NMR spectra of dinitrile **2** (7.2 mM, 500 MHz, $CDCl_3$) in the presence of increasing amounts of OctP5A; from bottom to top: 0.0, 0.4, and 1.1 equivalents. For comparison, the spectrum of the uncomplexed OctP5A is shown at the top. The peaks marked with an asterisk are due to solvent/water. Italics represent complexed host and guest.

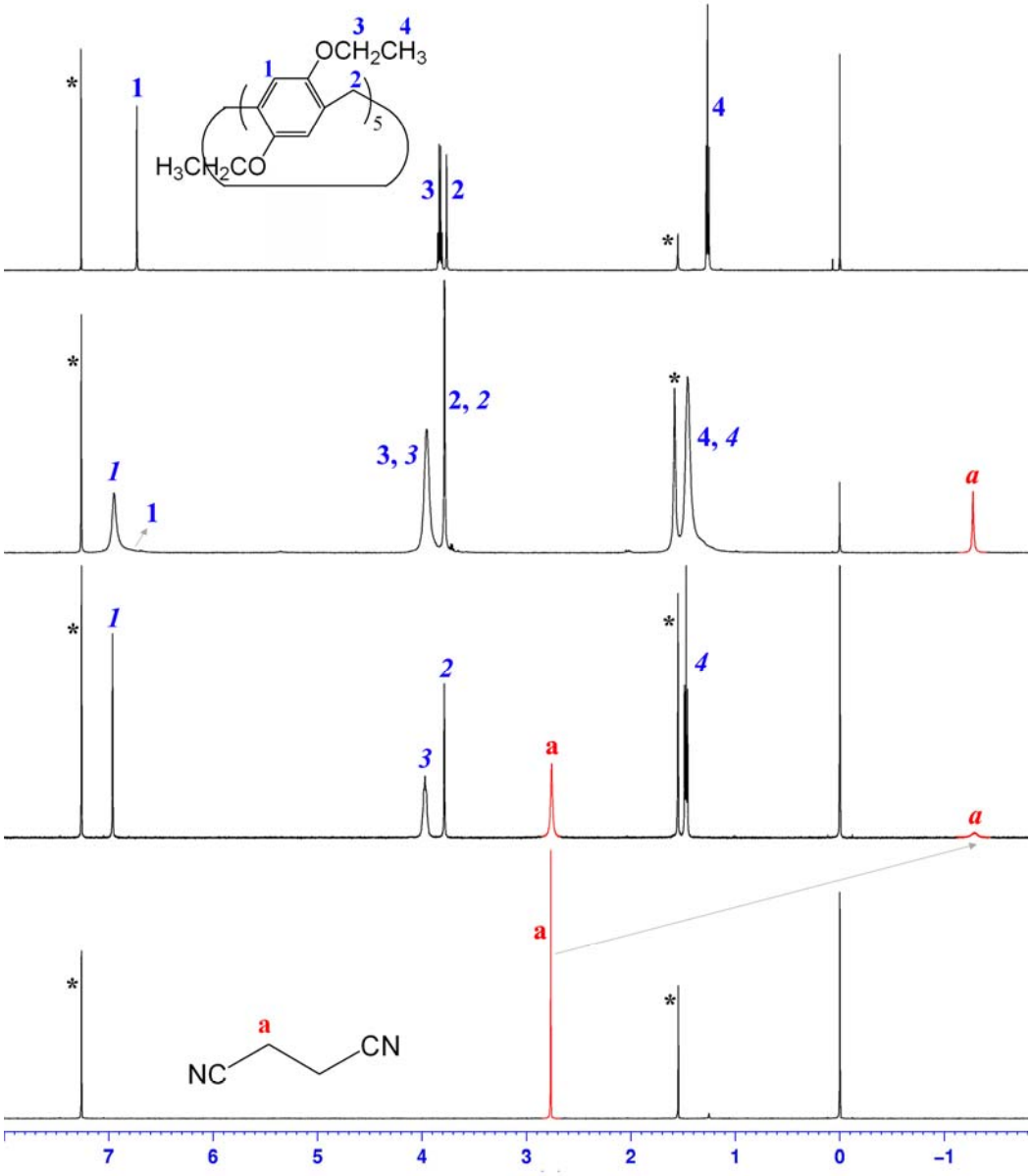

Figure S12. ^{1}H NMR spectra of dinitrile **1** (7.8 mM, 500 MHz, $CDCl_3$) in the presence of increasing amounts of EtP5A; from bottom to top: 0.0, 0.2, and 1.1 equivalents. For comparison, the spectrum of the uncomplexed EtP5A is shown at the top. The peaks marked with an asterisk are due to solvent/water. Italics represent complexed host and guest.

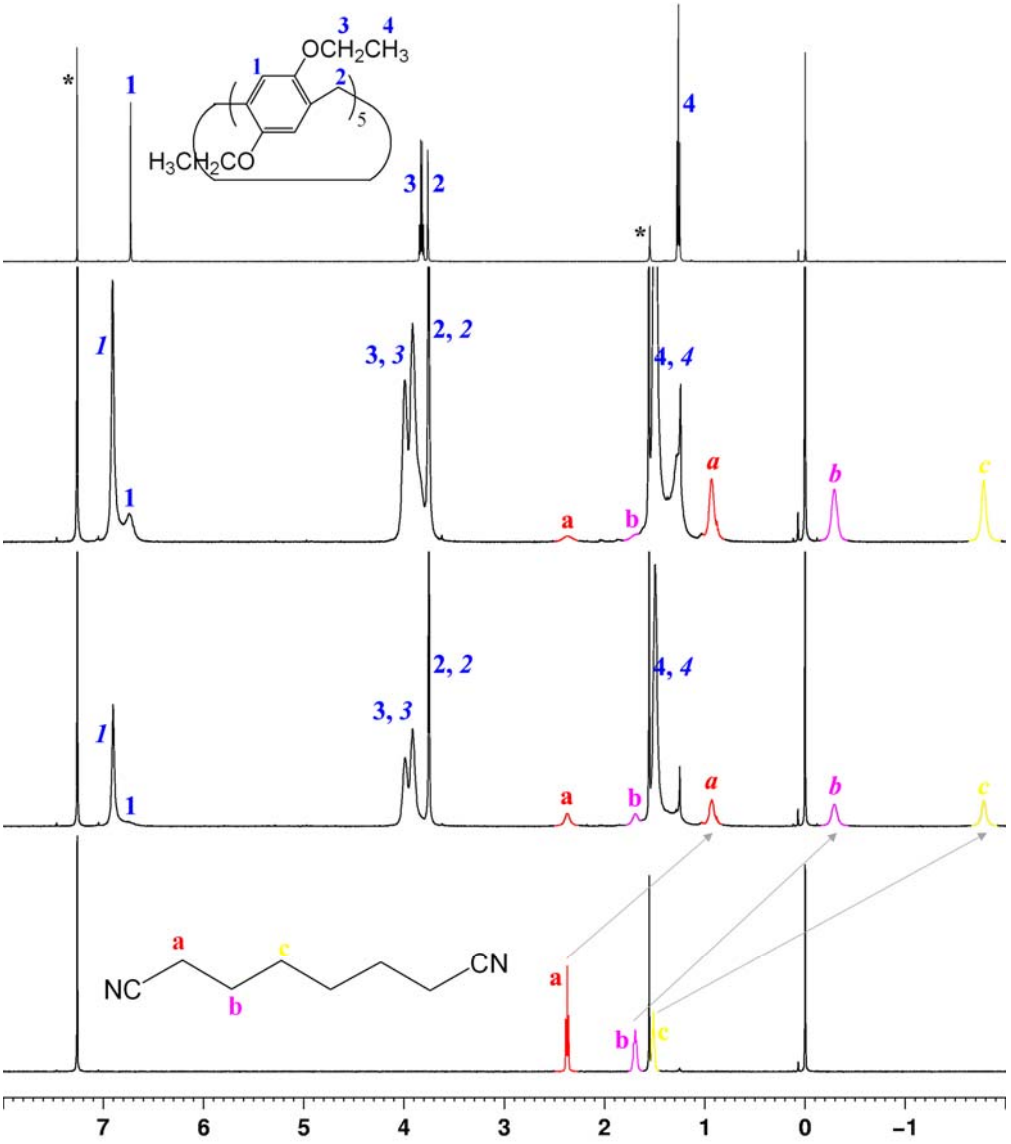

Figure S13. ^{1}H NMR spectra of dinitrile **3** (5.0 mM, 500 MHz, $CDCl_3$) in the presence of increasing amounts of EtP5A; from bottom to top: 0.0, 0.8, and 1.2 equivalents. For comparison, the spectrum of the uncomplexed EtP5A is shown at the top. The peaks marked with an asterisk are due to solvent/water. Italics represent complexed host and guest.

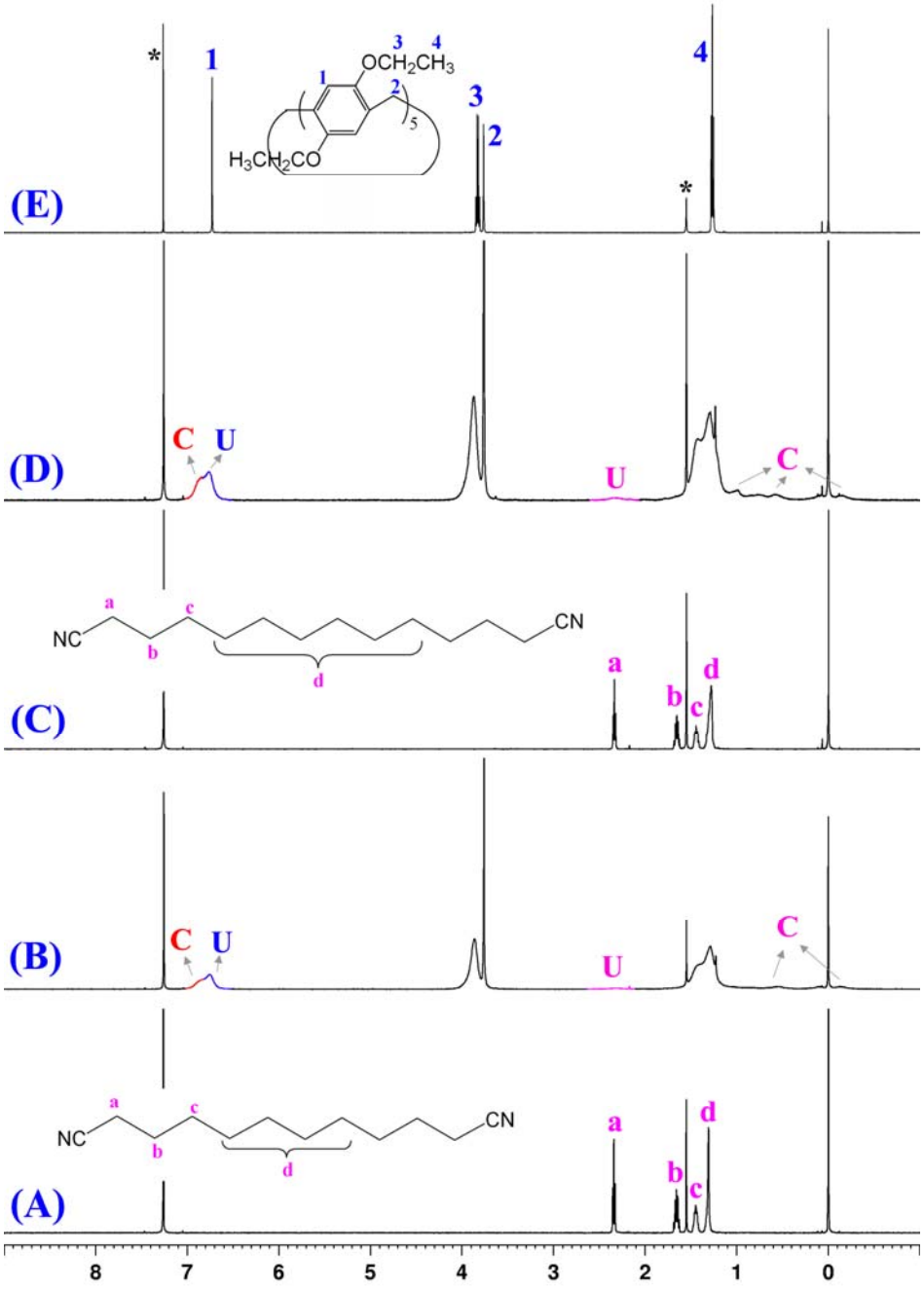

Figure S14. ^{1}H NMR spectra (500 MHz) of the long dinitrile **4**/**5** in the absence and presence of about 1.1 equivalent of EtP5A in $CDCl_3$. (A), **4**; (B) **4** + EtP5A; (C), **5**; (D) **5** + EtP5A; (E), EtP5A. The concentrations of guests and EtP5A host were 4.6-5.7 mM. "C" and "U" represent complexed and uncomplexed host/guest, respectively. Asterisk = solvent/water.

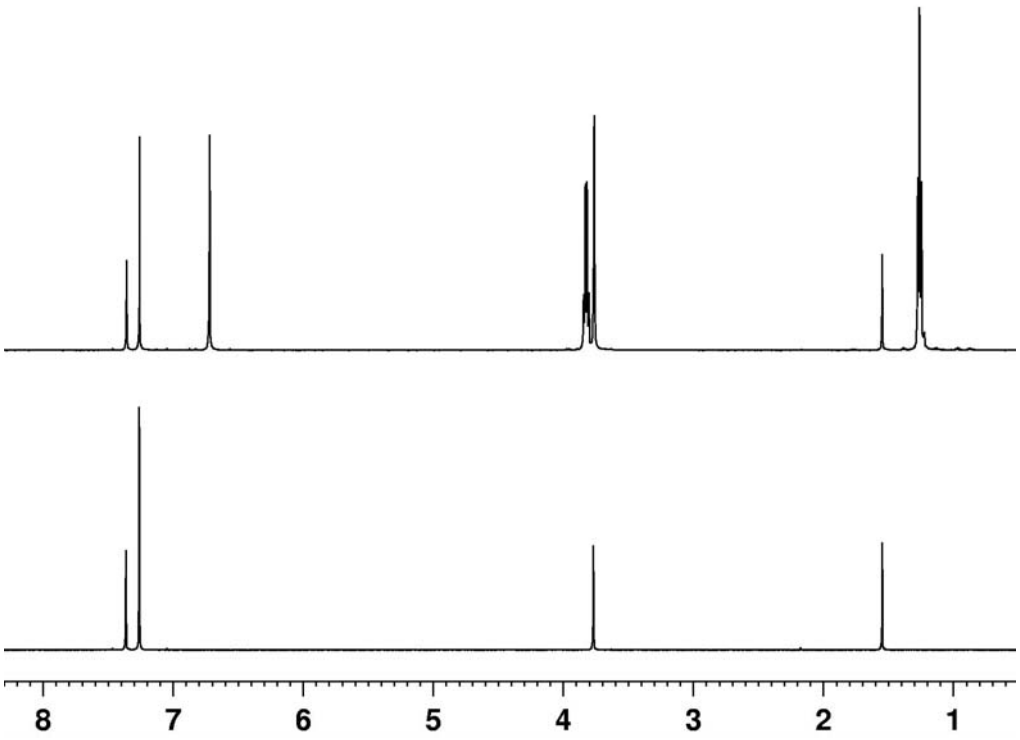

Figure S15. ^{1}H NMR spectra of 1,4-phenylenediacetonitrile **6** (5.3 mM, 500 MHz, $CDCl_3$) in the absence (bottom) and presence (top) of 1.1 equivalent of EtP5A. No obvious NMR changes were observed, indicating that EtP5A did not form inclusion complex with the guest or at least had very weak interactions.

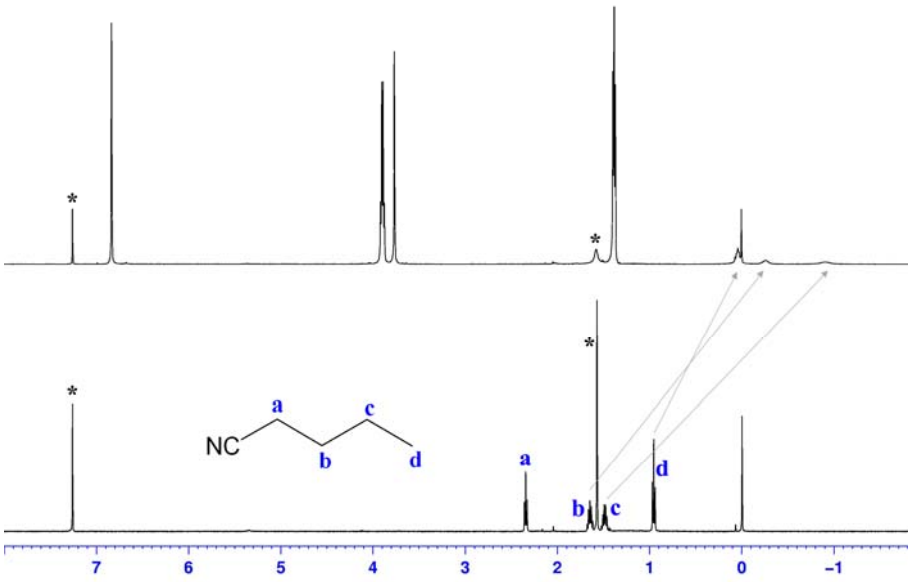

Figure S16. ^{1}H NMR spectra of mono-nitrile **7** (7.5 mM, 500 MHz, $CDCl_3$) in the absence (bottom) and presence (top) of 1.3 equivalent of EtP5A. The peaks marked with an asterisk are due to solvent/water.

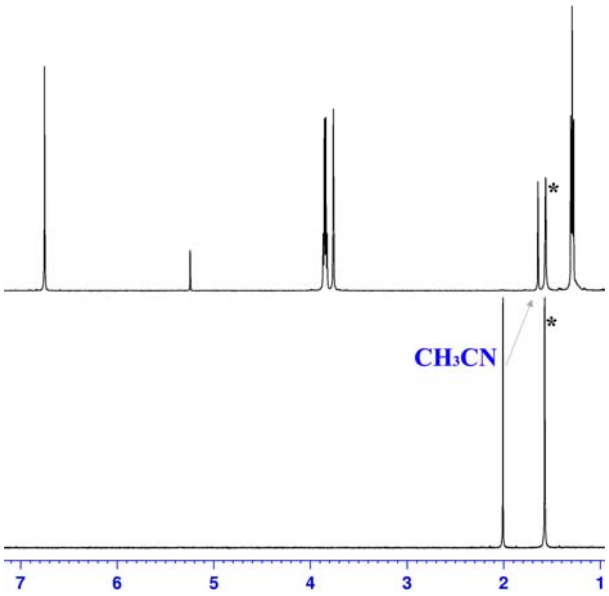

Figure S17. ^{1}H NMR spectra of mono-nitrile **8** (6.1 mM, 500 MHz, $CDCl_3$) in the absence (bottom) and presence (top) of 0.8 equivalent of EtP5A. The peaks marked with an asterisk are due to water.

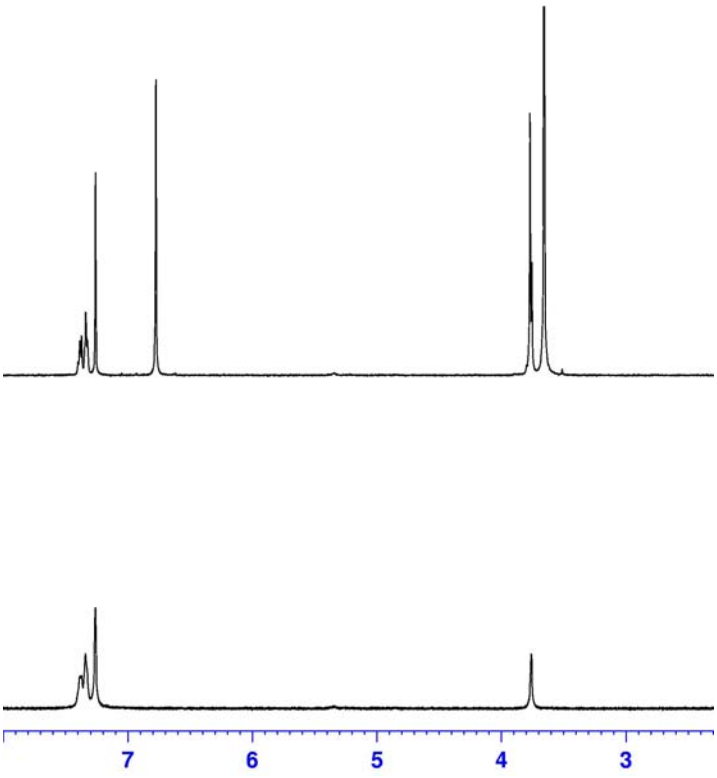

Figure S18. ^{1}H NMR spectra of mono-nitrile **9** (6.0 mM, 500 MHz, $CDCl_3$) in the absence (bottom) and presence (top) of 0.8 equivalent of MeP5A. No obvious NMR changes were observed, indicating that MeP5A did not form inclusion complex with the guest or at least had very weak interactions.

2D NOESY analysis of 2 with EtP5A.

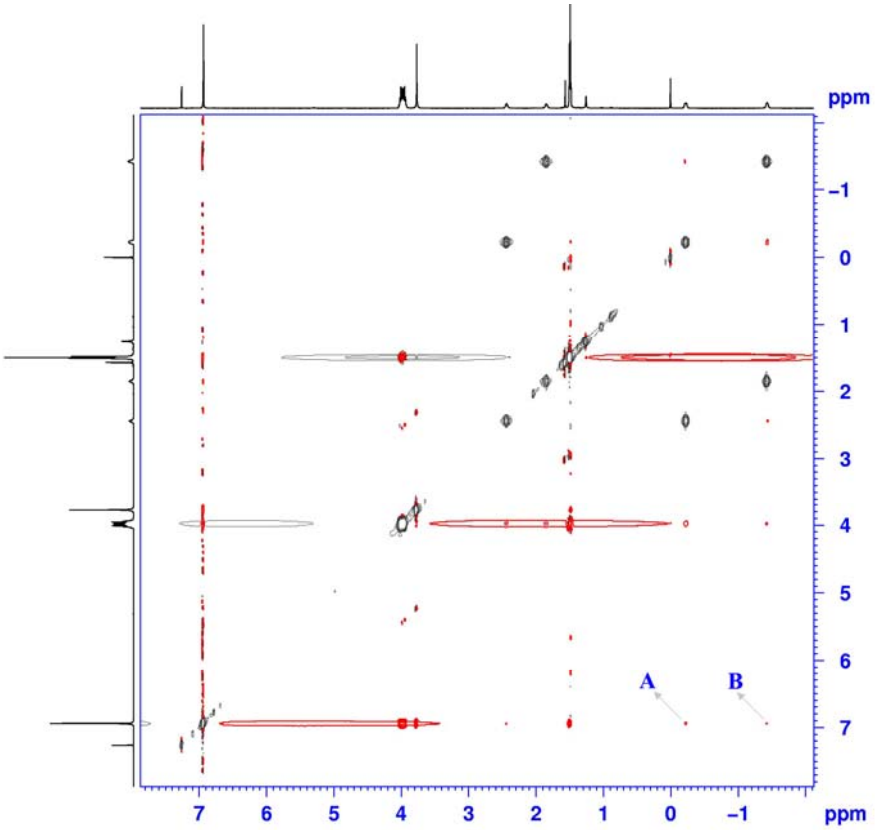

Figure S19. 2D NOESY analysis of **2** with EtP5A in $CDCl_3$ with a mixing time of 300 ms. (500 MHz, 298 K, The concentrations of host and guest are 16.0 and 24.1 mM, respectively)

X-ray crystal data and crystal structure of 2⊂EtP5A complex.

Crystallographic data: colorless, $C_{61}H_{76.50}N_2O_{10}$, *FW* 997.74, Triclinic, space group P-1, a = 13.3784 (19), b = 20.944 (3), c = 21.091 (3), α = 102.210 (2)°, β = 90.345 (2)°, γ = 92.153 (3)°, V = 5771.1 (14) Å^3, Z = 4, D_c = 1.148 g cm^{-3}, T = 173(2) K, μ = 0.077 mm^{-1}, 32311 measured reflections, 20274 independent reflections, 1240 parameters, 30 restraint, F(000) = 2146, R_1 = 0.2483, wR_2 = 0.4505 (all data), R_1 = 0.1671, wR_2 = 0.4015 [$I > 2\sigma(I)$], max. residual density 1.084 e·Å^{-3}, and goodness-of-fit (F^2) = 1.134. CCDC 850074.

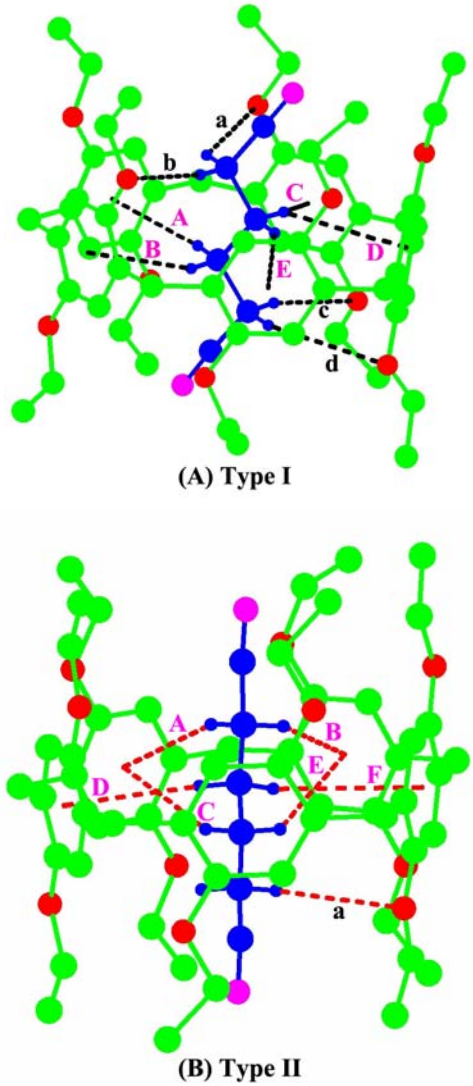

Figure S20. Crystal structure of **2**⊂EtP5A complex. Hydrogens of the host have been omitted for clarity. EtP5A is green, **2** is blue, oxygens are red, and nitrogens are magenta. Dashes represent C−H···π interactions or C−H···O hydrogen bonds. (A) Type I. C−H···π parameters: H···ring centre distances (Å), C−H···ring angles (deg) A, 2.88, 161; B, 2.90, 152; C, 3.08, 146; D, 3.25, 115; E, 2.97, 149. C−H···O hydrogen-bond parameters: H···O distances (Å), C−H···O angles (deg) a, 3.29, 127; b, 2.95, 171; c, 3.28, 169; d, 3.24, 143. (B) Type II.

C−H···π parameters: H···ring centre distances (Å), C−H···ring angles (deg) A, 3.14, 161; B, 3.13, 144; C, 2.97, 155; D, 2.97, 160; E, 3.14, 143; F, 3.18, 138. C−H···O hydrogen-bond parameters: H···O distance (Å), C−H···O angle (deg) a, 3.01, 166.

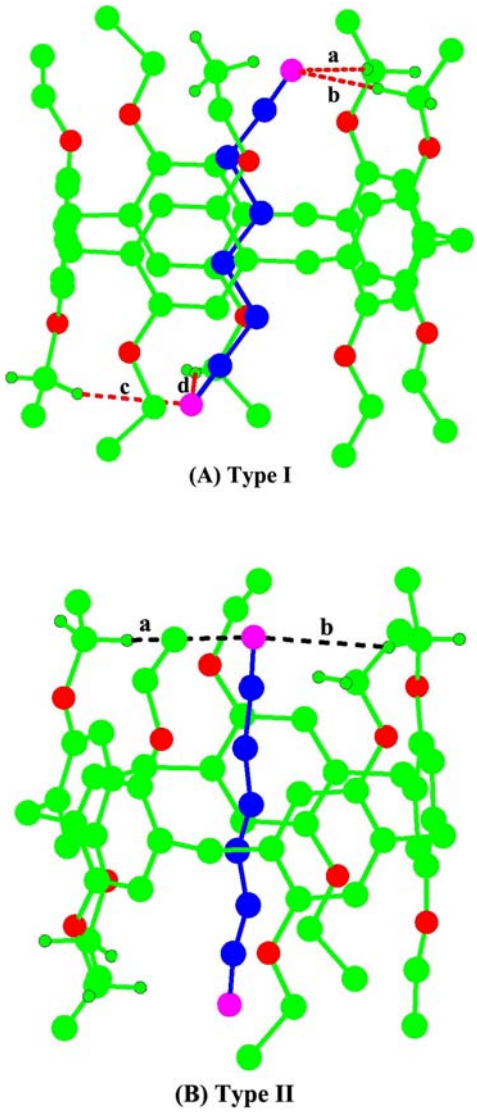

Figure S21. Crystal structure of the interpenetrated complex **2**⊂EtP5A. Hydrogens of the guest have been omitted for clarity. EtP5A is green, **2** is blue, oxygens are red, and nitrogens are magenta. Dashes represent C−H···N hydrogen bonds. (A) Type I. C−H···N hydrogen-bond parameters: H···N distances (Å), C−H···N angles (deg) a, 2.64, 146; b, 2.84, 137; c, 2.72, 149; d, 2.89, 152. (B) Type II. C−H···N hydrogen-bond parameters: H···N distances (Å), C−H···N angles (deg) a, 3.00, 144; b, 3.01, 136.

Job plots.

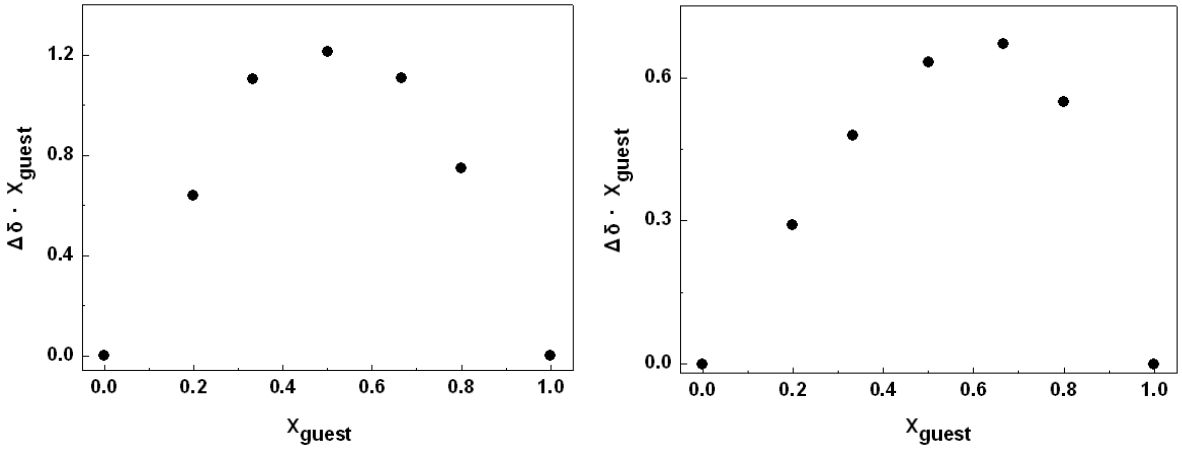

Figure S22. Left: Job plot showing the 1 : 1 stoichiometry of the complex between EtP5A and **7** in $CDCl_3$ by plotting the Δδ in chemical shift of the guest's methylene proton H_b (for proton designations, see Figure S16) observed by ^1H NMR spectroscopy against the mole fraction of dimer (X_{host}). ([host] + [guest] = 12.0 mM). Right: Job plot showing the 1 : 2 stoichiometry of the complex between EtP5A and **8** in $CDCl_3$ by plotting the Δδ in chemical shift of the guest's methyl proton observed by ^1H NMR spectroscopy against the mole fraction of guest (X_{guest}). ([host] + [guest] = 16.0 mM).

Cartoon representation of host-guest complexes.

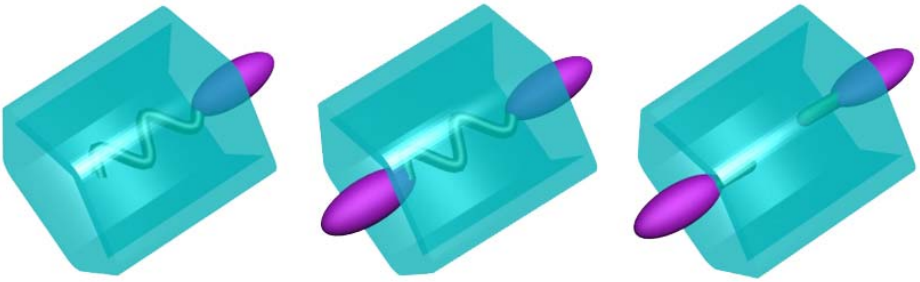

Figure S23. Modes of binding interaction between the investigated nitrile guests and AlkP5A hosts.

Determination of the association constants.

(1). For dinitrile⊂AlkP5A host-guest complexes, chemical exchange is slow on the NMR time scale and peaks are observed for both complexed and uncomplexed species in the NMR spectra. So association constants for these complexes could be determined by integration from a 1 : 1 mixture using the ^{1}H NMR single point method.[S2, S3] (Table 1)

$$K_a = \frac{[P5A{\cdot}G]_c}{[P5A]_{uc}[G]_{uc}}$$

In $CDCl_3$, the forces stabilizing the **2**⊂EtP5A complex are very significant, since the free guest is never observed in the presence of one equivalent of the wheel or more, suggesting very strong binding affinities[S4, S5]. Therefore, $(CD_3)_2CO/CDCl_3$ and DMSO-d_6/$CDCl_3$ mixed solvents are used to obtain the K_a values. As can be seen from Table S1 and Figure S24, in 1:9, 2:8 and 3:7 $(CD_3)_2CO/CDCl_3$ solvent, the free **2** can not be observed in the presence of one equivalent of EtP5A wheel or more either, suggesting very strong interactions. In pure $(CD_3)_2CO$, the K_a value for this complex is calculated to be $(2.4 \pm 0.3) \times 10^3$ M^{-1} (Table S1), which is 14 times higher than our previous reported value of the formation of pseudorotaxane between EtP5A and neutral 1,4-bis(imidazol-1-yl)butane axle [$(1.7 \pm 0.1) \times 10^2$ M^{-1}][S6], and 6.7 times higher than that of the typical *N*,*N*-dibenzylammonium hexafluorophosphate⊂dibenzo-24-crown-8 complex (360 M^{-1})[S7] in the same solvent.

From Table S2 and Figure S25, the association constants decrease with the increase of solvent polarity, i.e., with the increase of DMSO-d_6's proportion. And the values of some selected host-guest complexes were determined in 1:9 DMSO-d_6/$CDCl_3$ solvent, and listed in Table 1 in the manuscript.

Table S1. K_a values for **2**⊂EtP5A complex in $(CD_3)_2CO/CDCl_3$ at 298 K.

Solvent (v : v)	K_a (M^{-1})
$CDCl_3$	*a*
$(CD_3)_2CO/CDCl_3$ 1 : 9	*a*
$(CD_3)_2CO/CDCl_3$ 2 : 8	*a*
$(CD_3)_2CO/CDCl_3$ 3 : 7	*a*
$(CD_3)_2CO$	$(2.4 \pm 0.3) \times 10^3$

[a] The free guest **1** is never observed in the presence of one equivalent of EtP5A host or more, suggesting very strong binding affinities.

Table S2. K_a values for **2**⊂EtP5A complex in DMSO-d_6/$CDCl_3$ at 298 K.

Solvent (v : v)	K_a (M^{-1})
$CDCl_3$	[a]
DMSO-d_6/$CDCl_3$ 1 : 9	$(1.5 \pm 0.3) \times 10^4$
DMSO-d_6/$CDCl_3$ 2 : 8	$(8.1 \pm 0.5) \times 10^3$
DMSO-d_6/$CDCl_3$ 3 : 7	$(7.2 \pm 0.6) \times 10^3$
DMSO-d_6/$CDCl_3$ 5 : 5	$(1.3 \pm 0.2) \times 10^3$
DMSO-d_6	[b]

[a] The free guest **1** is never observed in the presence of one equivalent of EtP5A host or more, suggesting very strong binding affinities. [b] Could not be determined due to the poor solubility of EtP5A in DMSO-d_6.

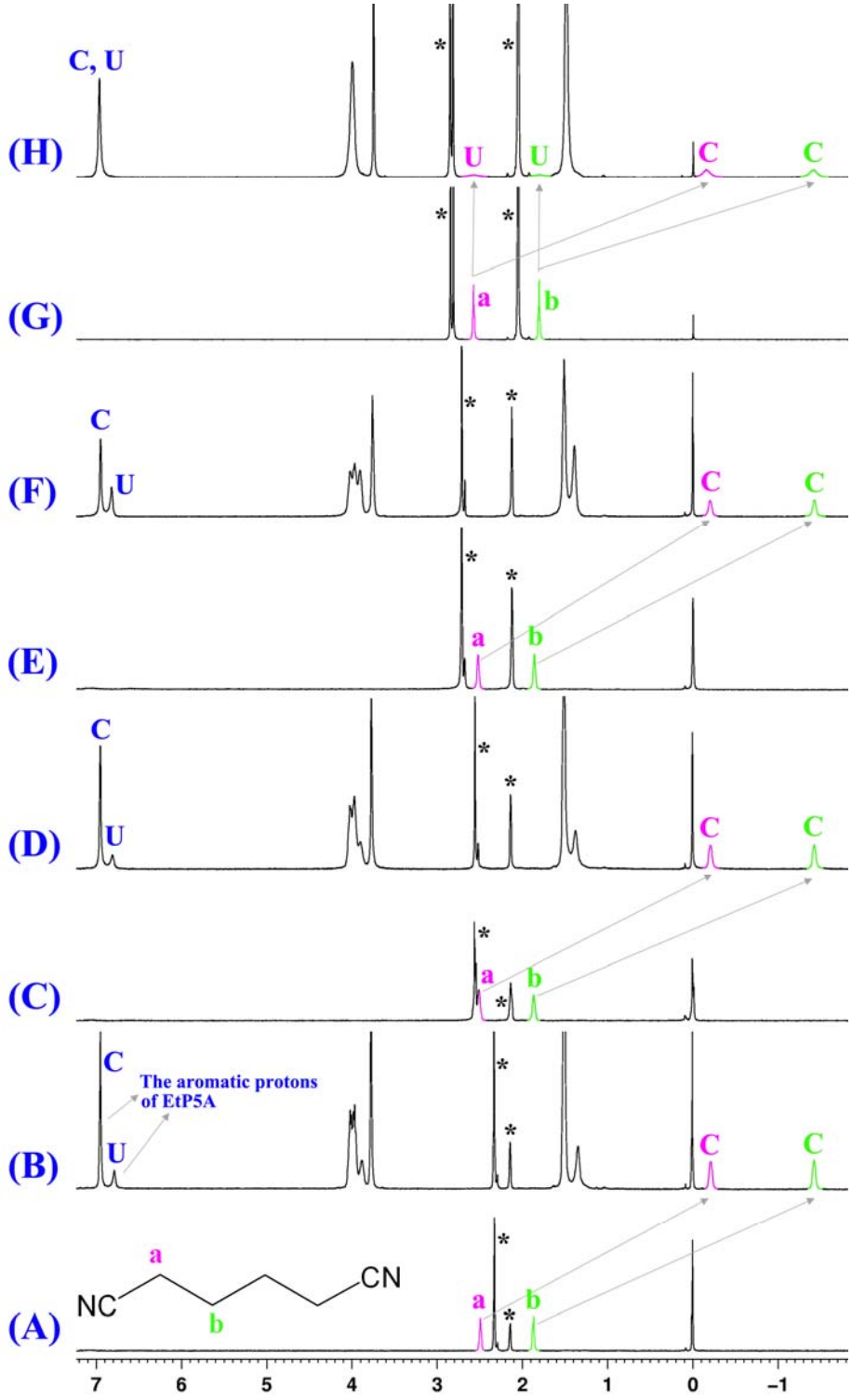

Figure S24. ^{1}H NMR spectra (500 MHz) of dinitriles **2** in the absence and presence of about 1.2 equivalent of EtP5A in 1:9 (v:v) $(CD_3)_2CO/CDCl_3$ [(A), **2**; (B) **2** + EtP5A], 2:8 $(CD_3)_2CO/CDCl_3$ [(C), **2**; (D) **2** + EtP5A], 3:7 $(CD_3)_2CO/CDCl_3$ [(E), **2**; (F) **2** + EtP5A], and pure $(CD_3)_2CO$ [(G), **2**; (H) **2** + EtP5A]. The concentrations of guests and EtP5A host were 4.3−5.6 mM. "C" and "U" represent complexed and uncomplexed host/guest, respectively. Asterisk = solvent/water.

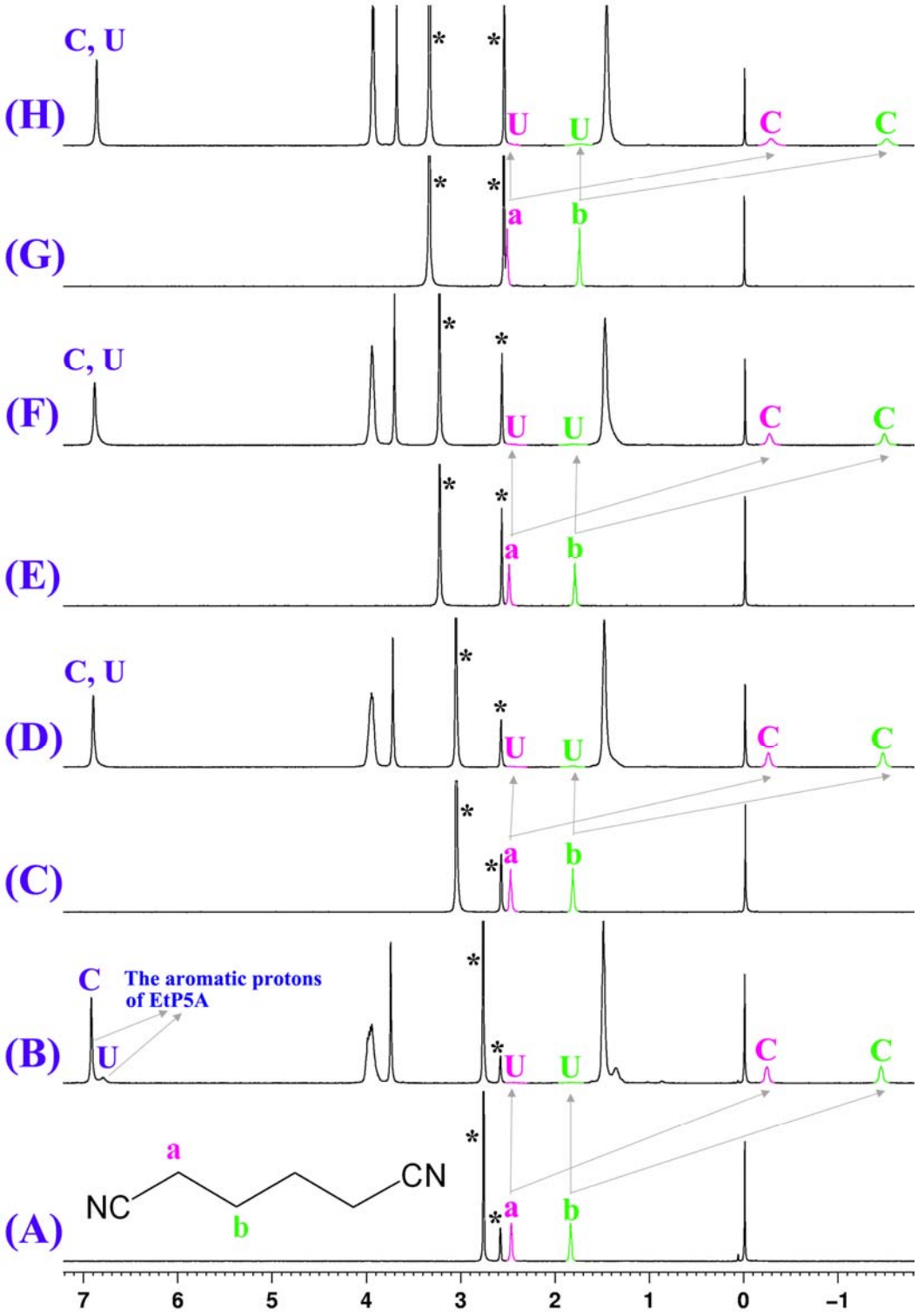

Figure S25. ^{1}H NMR spectra (500 MHz) of dinitriles **2** in the absence and presence of about 1.2 equivalent of EtP5A in 1 : 9 (v : v) DMSO-d_6/$CDCl_3$ [(A), **2**; (B) **2** + EtP5A], 2 : 8 DMSO-d_6/$CDCl_3$ [(C), **2**; (D) **2** + EtP5A], 3 : 7 DMSO-d_6/$CDCl_3$ [(E), **2**; (F) **2** + EtP5A], and 5 : 5 DMSO-d_6/$CDCl_3$ [(G), **2**; (H) **2** + EtP5A]. The concentrations of guests and EtP5A host were 4.1−5.6 mM. "C" and "U" represent complexed and uncomplexed host/guest. Asterisk = solvent/water.

(2). For mono-nitrile **7**, chemical exchange is fast on the NMR time scale (Figure S16). To determine the association constant, NMR titrations were done with solutions which had a constant concentration of AlkP5A and varying concentrations of guest. Using the nonlinear curve-fitting method, the association constant was obtained for each host-guest combination from the following equation[S8]:

$A = (A_\infty/[\mathrm{P5A}]_0)\ (0.5[\mathrm{G}]_0 + 0.5([\mathrm{P5A}]_0+1/K_a)-(0.5\ ([\mathrm{G}]_0^2+(2[\mathrm{G}]_0(1/K_a - [\mathrm{P5A}]_0)) + (1/K_a + [\mathrm{P5A}]_0)^2)^{0.5}))$

Where A is the chemical shift change of aromatic proton (H_1) on AlkP5A host at $[G]_0$, A_∞ is the chemical shift change of H_1 when the host is completely complexed, $[P5A]_0$ is the fixed initial concentration of the AlkP5A host, and $[G]_0$ is the initial concentration of guest. (Figure S26 and S27)

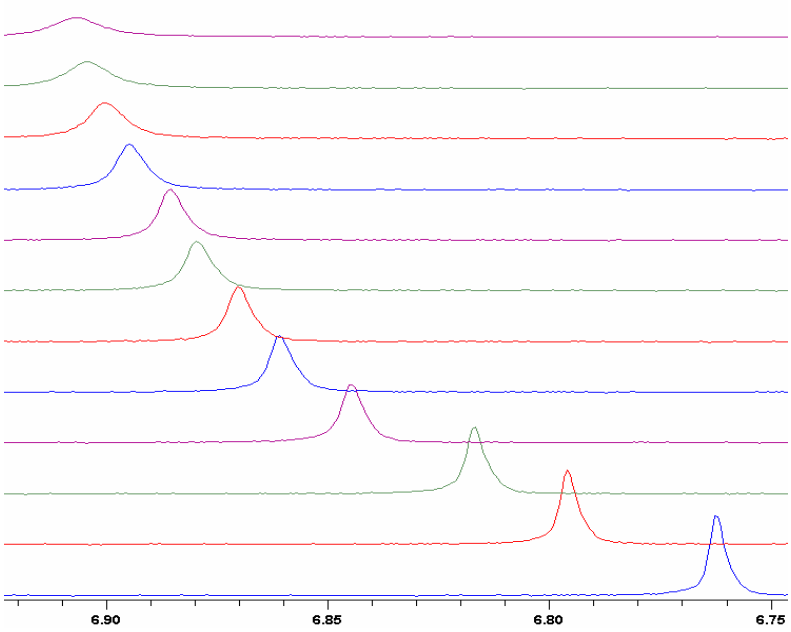

Figure S26. Partial ^{1}H NMR spectra (500 MHz, $CDCl_3$, 298 K) of MeP5A at a concentration of 1.0 mM upon addition of **7**. From bottom to top, the concentration of **7** was 0, 1.0, 2.0, 4.0, 6.2, 8.1, 11.1, 13.9, 19.6, 29.6, 44.4, 89.5 mM.

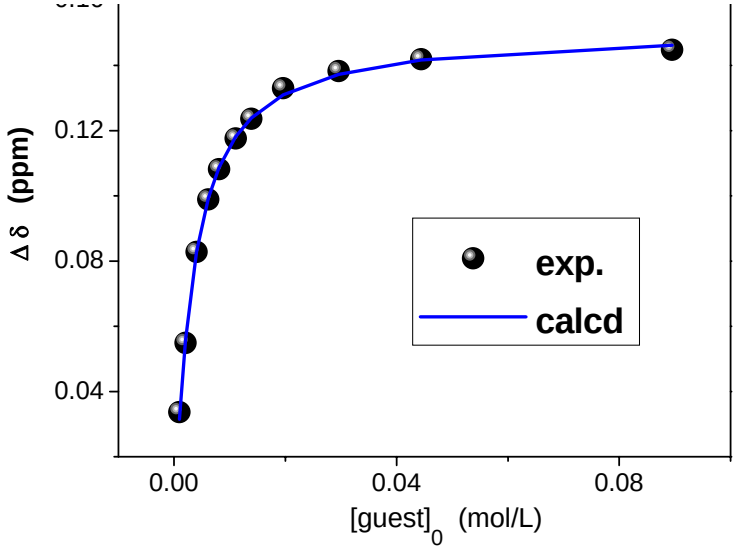

Figure S27. The non-linear curve-fitting (NMR titrations) for the complexation of MeP5A host (1.0 mM) with **7** in $CDCl_3$ at 298 K. The concentration of **7** was 0, 1.0, 2.0, 4.0, 6.2, 8.1, 11.1, 13.9, 19.6, 29.6, 44.4, 89.5 mM.

Table S3. K_a values for mono-nitrile **7**⊂AlkP5A complex in $CDCl_3$ at 298 K.

host	K_a (M^{-1})
MeP5A	$(3.8 \pm 0.3) \times 10^2$
EtP5A	$(4.0 \pm 0.4) \times 10^2$
BuP5A	$(1.9 \pm 0.2) \times 10^2$
OctP5A	$(1.2 \pm 0.2) \times 10^2$

As can be seen from Table S3, The substitution of ten ethyls for ten methyls in EtP5A, affording MeP5A, does not affect the host−guest binding affinity obviously. While the K_a values for BuP5A and OctP5A with this mono-nitrile are decreased by factors of 2.1 and 3.3, respectively, compared with that for EtP5A. This can be ascribed to the steric hindrance of butyl or octyl groups.

(3). For the smallest mono-nitrile acetonitrile (**8**), Job plots indicated the formation of 1:2 host-guest complexes. The average association constants[S8a, S9] are very small (K_{av} < 50 M^{-1}), and can not be calculated accurately.

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[S3] Association constants determined using the ^{1}H NMR single point methods. See: (a) A. B. Braunschweig, C. M. Ronconi, J.-Y. Han, F. Arico, S. J. Cantrill, J. F. Stoddart, S. I. Khan, A. J. P. White, D. J. Williams, *Eur. J. Org. Chem.* **2006**, 1857–1866.; b) S. J. Loeb, J. A. Wisner, *Angew. Chem. Int. Ed.* **1998**, *37*, 2838–2840; c) S. J. Loeb, J. Tiburcio, S. J. Vella, *Org. Lett.* **2005**, *7*, 4923–4926; d) J.-M. Zhao, Q.-S. Zong, T. Han, J.-F. Xiang, C.-F. Chen, *J. Org. Chem.* **2008**, *73*, 6800–6806; e) L. Li, G. J. Clarkson, *Org. Lett.*, **2007**, *9*, 497–500; f) D. Castillo, P. Astudillo, J. Mares, F. J. González, A. Vela, J. Tiburcio, *Org. Biomol. Chem.*, **2007**, *5*, 2252–2256; g) C. Li, Q. Xu, J. Li, F. Yao, X. Jia, *Org. Biomol. Chem.*, 2010, **8**, 1568–1576.

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