Inclusion Complexes of C$_{ethyl}$-2-Methylresorcinarene and Pyridine *N*-oxides: Breaking C-I⋯O-N⁺ Halogen Bond by Host-Guest Complexation

Rakesh Puttreddy[a], Ngong Kodiah Beyeh[a,b]* and Kari Rissanen[a]*

[a] University of Jyvaskyla, Department of Chemistry, Nanoscience Center, P. O. Box 35, FI-40014 University of Jyvaskyla, Finland
[b] Aalto University School of Science, Department of Applied Physics, P.O. Box 11100, FI-00076 AALTO, Finland. Fax: +358 9 855 4019; Tel: +358 9 47001

Supporting Information

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I General information

The C_{ethyl}-2-Methylresorcinarene **1** was synthesized according to procedures.[1] 2-Methylpyridine *N*-oxide (2MePyNO), 3-methylpyridine *N*-oxide (3MePyNO), 4-methoxypyridine *N*-oxide (4MeOPyNO), N-methylmorpholine *N*-oxide (NMO) were purchased from Sigma Aldrich and 2-iodopyridine N-oxide (2IPyNO) was synthesized according to procedure.[2] All the solvents used for syntheses and crystal growth are reagent grade, and are used as received. All the complexes were taken in a small round bottom flask and dried under vacuum at 30-40°C overnight before characterizing by elemental analyses. Infrared spectra were recorded using Bruker instrument by pressing a small amount of the sample on the diamond ATR Prism. ^{1}H NMR spectra were recorded on a Bruker Advance DRX 400 (400 MHz for ^{1}H) spectrometer. All signals are given as δ values in ppm using residual solvent signals as the internal standard.

II ^{1}H NMR experiments

A 10 mM stock solution of C_{ethyl}-2-methylresorcinarene and 20 mM stock solution of the guests (2MePyNO, 3MePyNO, 4MeOPyNO, NMO, and 2IPyNO) were prepared in CD_3OD. For the pure host, 300 µL of the stock solution was measured to NMR tube and diluted with 150 µL of CD_3OD to give a 6.6 mM sample concentration. For the pure guests, 150 µL of the stock solution was measured to NMR tube and diluted with 300 µL of CD_3OD to give a 6.6 mM sample concentration. For a 1:1 host-guest mixture, 300 µL of the host and 150 µL of the guests were measured to give a 6.6 mM concentration of both the host and the guests. The spectra were calibrated using the CD_3OD signal ($δ_{CD3}$ = 3.31 ppm) as internal standard.
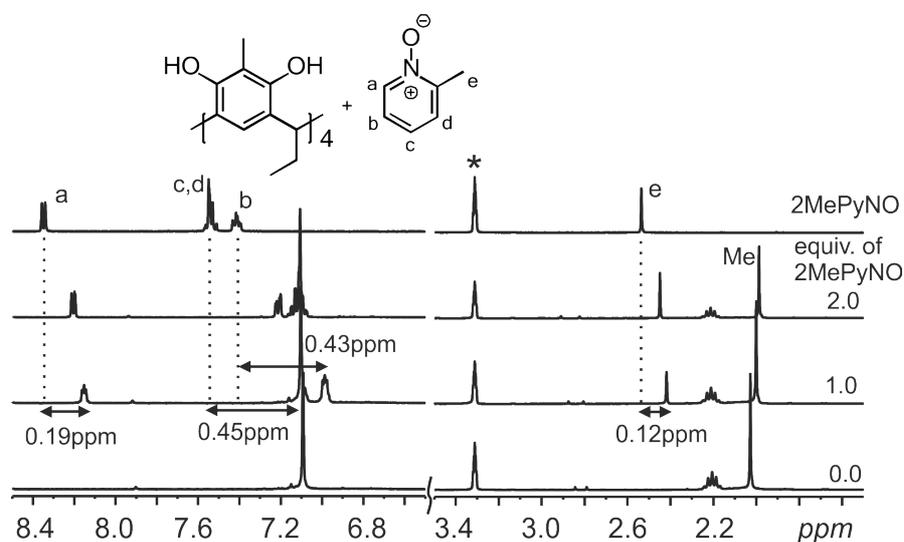
Fig. S1. Selected region of the ^{1}H NMR (CD_3OD, room temperature) after the addition of up to 2 equivalents of 2MePyNO to host **1**. Stars represent the residual CD_3OD. The shift changes of the guest signals in ppm are highlighted.
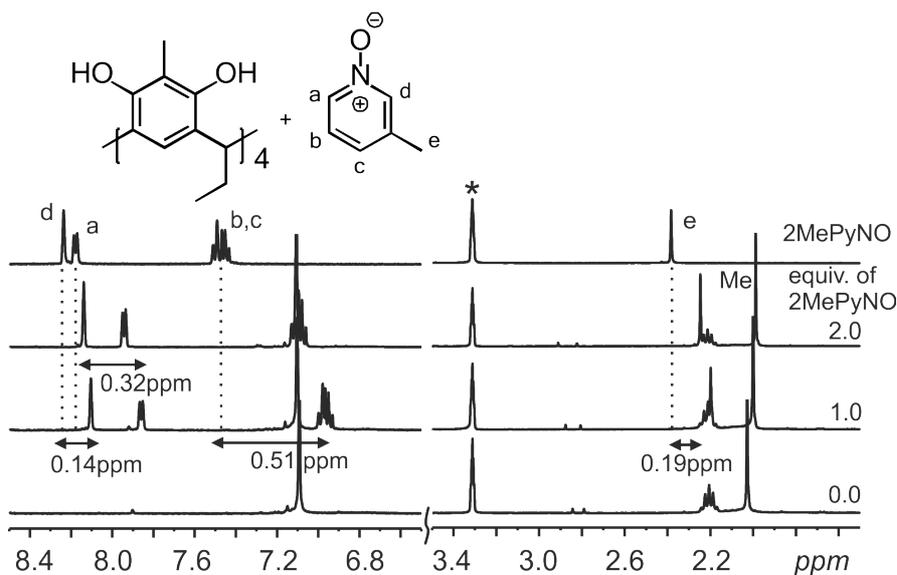
Fig. S2. Selected region of the ¹H NMR (CD₃OD, room temperature) after the addition of up to 2 equivalents of 3MePyNO to host **1**. Stars represent the residual CD₃OD. The shift changes of the guest signals in ppm are highlighted.
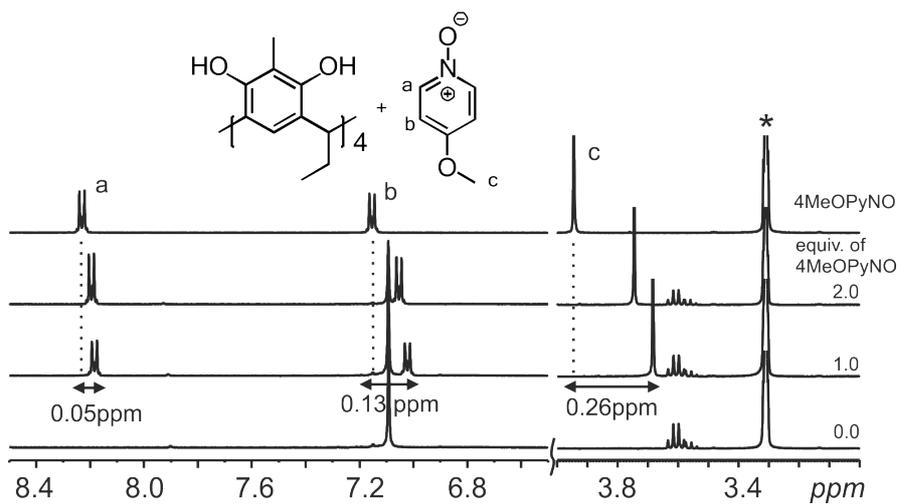
Fig. S3. Selected region of the ¹H NMR (CD₃OD, room temperature) after the addition of up to 2 equivalents of 4MeOPyNO to host **1**. Stars represent the residual CD₃OD. The shift changes of the guest signals in ppm are highlighted.

III Solid state analysis

III.a Synthesis of complexes

1. Synthesis of 2MePyNO@1

To a solution of C_{ethyl}-2-Methylresorcinarene **1** (25 mg, 0.0380 mmol) in methanol (4 ml) was added a methanol (2 ml) solution of 2MePyNO (4.0 mg, 0.0380 mmol) at room temperature. The solution was left at room temperature and subjected to slow evaporation to give brown colour crystals. IR v_{max} cm^{-1}: 3270, 2964, 2930, 2872, 1456, 1298, 1201, 1107, 847, 764, 562. Elemental Analysis: Calculated for $C_{40}H_{48}O_8.2(C_5H_5NO)$: C 71.37; H 7.14; N 3.20. Found for $C_{40}H_{48}O_8.2(C_5H_5NO)$: C 70.91; H 7.56; N 3.78.

2. Synthesis of 3MePyNO@1

To a solution of C_{ethyl}-2-Methylresorcinarene **1** (44 mg, 0.0670 mmol) in methanol (7 ml) was added a methanol (2 ml) solution of 3MePyNO (7.3 mg, 0.0670 mmol) at room temperature. The solution was left at room temperature and subjected to slow evaporation to give brown colour crystals. IR v_{max} cm^{-1}: 3311, 2957, 2868, 1604, 1455, 1264, 1156, 1016, 943, 788, 746, 674, 557, 491. Elemental Analysis: The crystals were stable only for few hours and turns to semi-crystalline (or gummy) material, which gave unsatisfactory results.

3. Synthesis of 4MeOPyNO@1

To a solution of C_{ethyl}-2-Methylresorcinarene **1** (28 mg, 0.0426 mmol) in methanol (4 ml) was added a methanol (2 ml) solution of 4MeOPyNO (5.3 mg, 0.0426 mmol) at room temperature. The solution was left at room temperature and subjected to slow evaporation to give brown colour crystals. IR v_{max} cm^{-1}: 3310, 3040, 2878, 1622, 1493, 1292, 1011, 848, 753, 584, 521, 462. Elemental Analysis: Calculated for $C_{40}H_{48}O_8.C_6H_7NO_2.2(CH_3OH)$: C 68.14; H 7.51; N 1.66. Found for $C_{40}H_{48}O_8.C_6H_7NO_2 (H_2O)$: C 69.22, H 6.89; N 1.52

4. Synthesis of NMO@1

To a solution of C_{ethyl}-2-Methylresorcinarene **1** (25 mg, 0.0380 mmol) in methanol (4 ml) was added a methanol (2 ml) solution of NMO (4.5 mg, 0.0380 mmol) at room temperature. The solution was left at room temperature and subjected to slow evaporation to give huge brown colour plate like crystals. IR v_{max} cm^{-1}: 3216, 2929, 2872, 2352, 1446, 1114, 1079, 856, 719, 623, 498. Elemental Analysis: Calculated for $C_{40}H_{48}O_8.2(C_5H_{11}NO_2).2(CH_3OH)$: C 65.39; H 8.23; N 2.93. Found for $C_{40}H_{48}O_8.2(C_5H_{11}NO_2)$: C 67.01; H 7.89; N 3.74

5. Syntheses of 2-IPyNO@1

To a solution of C_{ethyl}-2-Methylresorcinarene **1** (10 mg, 0.0152 mmol) in methanol (4 ml) was added a methanol (2 ml) solution of 2IPyNO (3.4 mg, 0.0152 mmol) at room temperature. The solution was left at room temperature and subjected to slow evaporation to give brown colour crystals. IR v_{max} cm^{-1}: 3216, 2961, 2868, 1601, 1457, 1199, 1110, 1076, 833, 761, 566, 504. Elemental Analysis: Calculated for $2(C_{40}H_{48}O_8).2(C_5H_4INO).6H_2O$: C 58.00; H 6.27; N 1.50. Found for $2(C_{40}H_{48}O_8).2(C_5H_4INO).4H_2O$: C .59.12; H 6.20; N 1.99

III.b X-ray analysis

1. General information

Data for 2MePyNO@**1**, 3MePyNO@**1**, 4MeOPyNO@**1** and NMO@**1** were collected at 170 K on Bruker-Nonius Kappa CCD diffractometer with an APEX-II detector and graphite monochromatized Mo-Kα (λ = 0.71073 Å) radiation. The data for **2-IPyNO@1** was collected at 120 K on a dual source Agilent SuperNova diffractometer with an Atlas detector using mirror-monochromated Cu-Kα radiation (λ = 1.54184 Å). Single crystal X-ray data for 2IPyNO was collected at 123 K using Agilent SuperNova single-source diffractometer with an Atlas EoS CCD detector using mirror-monochromated Mo-$K\alpha$ (λ = 0.71073 Å) radiation. The data collection and reduction carried on Agilent SuperNova diffractometer were done using the program *CrysAlisPro*[3] and for the data obtained from Bruker Nonius Kappa diffractometer were performed using the program *COLLECT*[4] and *HKL DENZO AND SCALEPACK*[5], respectively. The intensities were corrected for absorption using the Gaussian face-index absorption correction method[3] for 2IPyNO@**1**, and the intensities for 2MePyNO@**1**, 3MePyNO@**1**, 4MeOPyNO@**1** and NMO@**1** were corrected for absorption using SADABS[6] with multi-scan absorption correction type method. All the structures were solved with direct methods (SHELXS)[7] and refined by full-matrix least squares on F^2 using the OLEX2,[8] which utilizes the SHELXL-2013 module.[7] No attempt was made to locate the hydrogens for disordered solvent molecules, and for some hydrogen atoms involved in hydrogen bonds were introduced from difference Fourier maps. Constraints, restraints and masking are used where appropriate for disordered models.

2. X-Ray Structure Refinement Details for 3MePyNO@1

Direct methods of phase determination followed by four Fourier cycles of refinement led to Fourier electron difference map of the asymmetry unit of the unit cell. All the non-hydrogen atoms were identified, including the 50:50 occupied out-of-cavity 3MePyNO molecules in the asymmetric unit. There were two out-cavity methanol molecules in the asymmetric unit with large thermal parameters indicating probable disordered at two positions. Using constraint EADP and restraint ISOR commands show significant increase in the R-factor. Convergence and R-factor was followed throughout the structure solution, with prime importance given to disordered host and guest molecules. The in-cavity 3MePyNO also has high thermal movement. As a result, the C-O distances for two methanol molecules are restrained using DFIX command followed by continous four Fourier cycles of refinement till the convergence was achieved. It is important to note that the data collected for this structure was of poor quality associated with high thermal movement, especially for 3MePyNO and solvent molecules. As a result, no attempt was made either to constraint or restraint the thermal movement of solvent molecules. The H-atoms were included in the refinement in calculated positions on the riding atoms using ADD H command in Olex2. The final refinement converged at R_1 = 0.0979 and wR_2 = 0.2502 for intensities I>2(I). The largest peak/hole in the final difference map was 0.928/-0.367 e/Å^3.

3. X-Ray Structure Refinement Details for 4MeOPyNO@1

Direct methods of phase determination followed by four Fourier cycles of refinement led to an electron density map from which most of the non-hydrogen atoms were found for a host and in-cavity guest molecule, and two out-cavity methanol molecules in the asymmetry unit of the unit cell. All the non-hydrogen atoms for host and guest molecules were solved without any disorder problem; however, the out-cavity methanol molecules have shown large displacement parameter indicating disorder. For the first methanol molecule, despite of high displacement parameters, no constraint EADP and restraint ISOR were used, however, the C-O distances was restrained using DFIX command. No attempt was made to locate the hydrogen atoms from Fourier difference map, and all the H-atoms were included in the refinement in the calculated positions on the riding atoms using ADD H command in Olex2. The final refinement converged at $R_1 = 0.0543$ and $wR_2 = 0.1222$ for intensities I>2(I). The largest peak/hole in the final difference map was 0.568/-0.652 e/Å^3.

4. X-Ray Structure Refinement Details for NMO@1

Direct methods of phase determination followed by four Fourier cycles of refinement led to an electron density map from which most of the non-hydrogen atoms were found for one host, two NMO guest molecules, and two methanol molecules in the asymmetry unit of the unit cell. Isotropic refinement followed by anisotropic refinement of the non-hydrogen atoms led conclusion that one of the carbon atoms of the methanol molecule has high thermal movement suggesting disorder over two positions. Using constraint EADP and restraint ISOR commands show significant increase in the R-factor, and leaves a largest peak/hole in the final difference map of 1.20/-2.40 e/Å^3. As a result, the C-O distances for one of the methanol molecule was restrained using DFIX command, and ISOR command for second methanol molecule are used with continous four Fourier cycles of refinement till the convergence was achieved. No attempt was made to locate the hydrogen atoms from Fourier difference map, and all the H-atoms were included in the refinement in the calculated positions on the riding atoms using ADD H command in Olex2. The final refinement converged at $R_1 = 0.0743$ and $wR_2 = 0.1897$ for intensities I>2(I). The largest peak/hole in the final difference map was 0.461/-0.927 e/Å^{-3}.

5. X-Ray Structure Refinement Details for 2-IPyNO@1

Direct methods of phase determination followed by four Fourier cycles of refinement led to an electron density map from which most of the non-hydrogen atoms were found for a host and in-cavity guest molecules, and six out-cavity methanol molecules in the asymmetry unit of the unit cell. All the non-hydrogen atoms for host and guest molecules were solved without any disorder problem; however, the final model has large residual electron density of 3.11eÅ^{-3} and 2.69eÅ^{-3} close to oxygen and iodine of 2IPyNO guest molecule. No attempt was made to resolve the large residual peaks, and to locate the hydrogen atoms from Fourier difference map. Hydrogen atoms on water molecules were fixed using DFIX command based on donor-acceptor principle, while all the other hydrogen atoms were included in the refinement in the calculated positions on the riding atoms using ADD H command in Olex2. The final refinement converged at $R_1 = 0.0722$ and $wR_2 = 0.1809$ for intensities I>2(I). The largest peak/hole in the final difference map was 2.883/-1.658 e/Å^3.

Table S1. Crystal data and X-Ray experimental details for 2MePyNO@1 - 2IPyNO

	2MePyNO@1	3MePyNO@1	4MeOPyNO@1	NMO@1	2IPyNO@1	2IPyNO
Chemical formula	$C_{52}H_{62}N_2O_{10}$	$C_{107}H_{135}N_4O_{23}$	$C_{48}H_{63}NO_{12}$	$C_{52}H_{78}N_2O_{14}$	$C_{45}H_{58}INO_{12}$	C_5H_4INO
M_r	875.03	1845.18	845.99	955.16	931.82	220.99
Temperature (K)	170.0	170.0	170.0	170.0	120.0	123.0
Crystal system, space group	Monoclinic, $P2_1/n$	Triclinic P-1	Triclinic P-1	Monoclinic $P2_1/c$	Triclinic P-1	Monoclinic $P2_1/n$
a, b, c (Å)	12.559(3) 24.734(5) 14.682(3)	11.929(2) 12.698(3) 17.705(4)	9.1360(18) 11.097(2) 22.784(5)	12.672(3) 24.549(5) 16.932(3)	12.4821(3) 15.6440(5) 23.8049(7)	8.3971(2) 8.3248(3) 9.1806(3)
α, β, γ (°)	90 90.28(3) 90	76.17(3) 75.84(3) 84.38(3)	92.12(3) 96.27(3) 103.65(3)	90 103.57(3) 90	95.809(3) 99.751(2) 106.037(2)	90 91.672(3) 90
Volume (Å³)	4560.7(16)	2522.8(10)	2226.5(8)	5120.1(19)	4348.8(2)	641.49(3)
Z	4	1	2	4	4	4
Density (Calculated) mg/m³	1.274	1.215	1.262	1.239	1.423	2.288
Absorption Coefficient (mm⁻¹)	0.088	0.085	0.090	0.089	6.310	4.890
F(000)	1872	989	908	2064	1936	408
Crystal size (mm³)	0.27 x 0.16 x 0.11	0.18 x 0.09 x 0.07	0.28 x 0.16 x 0.11	0.21 x 0.17 x 0.16	0.12 x 0.07 x 0.06	0.36 x 0.19 x 0.12
θ range for data collection (°)	2.13 to 25.25	1.76 to 25.25	2.04 to 25.25	1.65 to 25.25	3.27 to 66.75	3.30 to 25.24
Reflections collected [R(int)]	32939 [0.0745]	23220 [0.0720]	24718 [0.0343]	62678 [0.1021]	26293 [0.0625]	2242 [0.0344]
Reflections [I>2sigma(I)]	4935	5129	6184	5957	11065	1001
Data completeness (%)	99.9	98.4	99.7	99.9	99.1	99.44
Data/ restraints/ parameters	8253/0/607	8975/70/694	8018/1/596	9271/14/638	15297/4/1098	1149/0/73
Goodness-of-fit on F²	1.014	1.031	1.023	1.031	1.040	1.072
Final R₁ indices [I>2sigma(I)]	$R_1 = 0.0623$ $wR_2 = 0.1372$	$R_1 = 0.0979$ $wR_2 = 0.2502$	$R_1 = 0.0534$ $wR_2 = 0.1222$	$R_1 = 0.0743$ $wR_2 = 0.1897$	$R_1 = 0.0722$ $wR_2 = 0.1807$	$R_1 = 0.0278$ $wR_2 = 0.0692$
Final R indices [all data]	$R_1 = 0.1197$ $wR_2 = 0.1622$	$R_1 = 0.1659$ $wR_2 = 0.2987$	$R_1 = 0.0733$ $wR_2 = 0.1330$	$R_1 = 0.1217$ $wR_2 = 0.2168$	$R_1 = 0.1009,$ $wR_2 = 0.2095$	$R_1 = 0.0313$ $wR_2 = 0.0724$
Largest diff. peak/hole (e.Å⁻³)	0.256/ -0.220	0.928/ -0.367	0.568/ -0.652	0.461/ -0.927	2.883/ -1.664	0.944/ -0.873
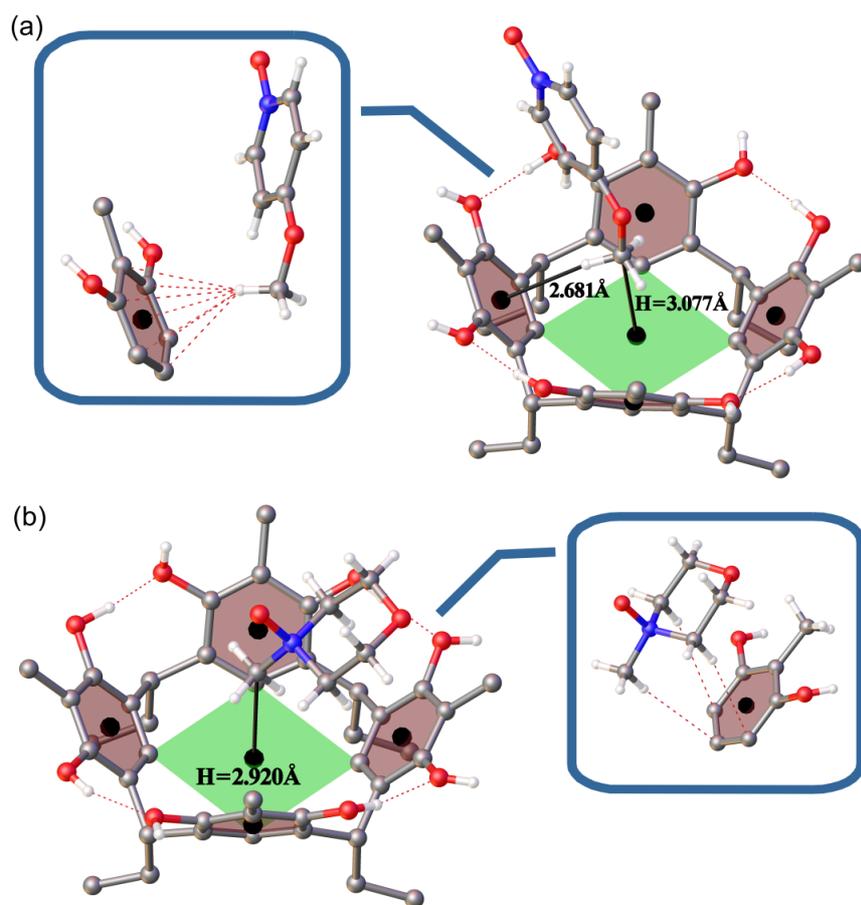
Fig. S4. (a) C–H···π interactions observed in (a) 4MeOPyNO@**1**, and (b) NMO@**1**. In both the figures, selected hydrogen atoms, solvent and guest molecules are omitted for clarity.
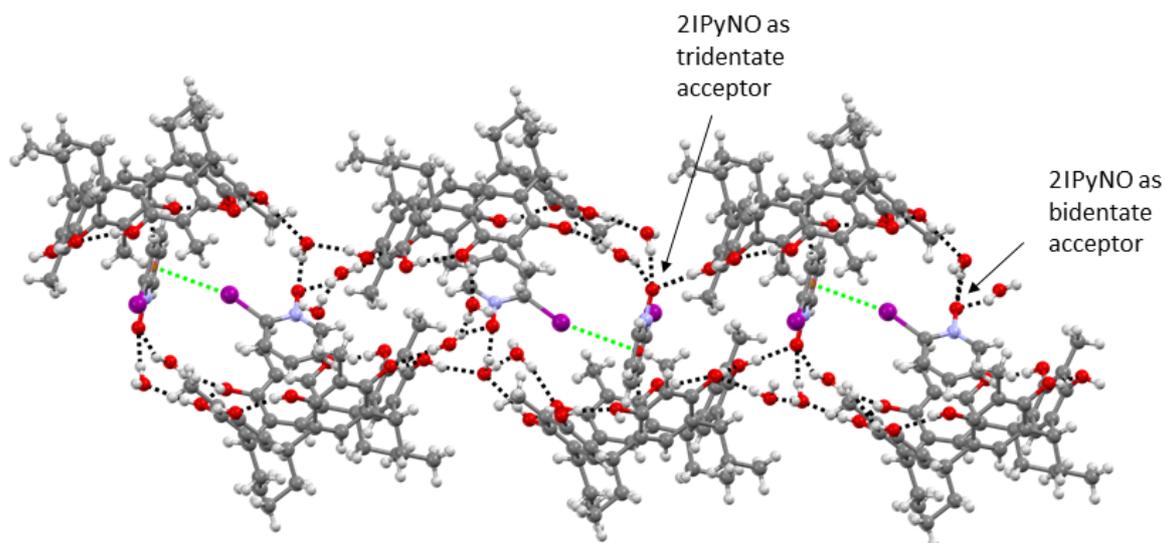
Fig. S5. 2IPyNO guest as bidentate and tridentate hydrogen bond acceptors in 2IPyNO@**1**. Black broken line represents the O–H···O interactions and green broken lines represent C–I···π interactions.
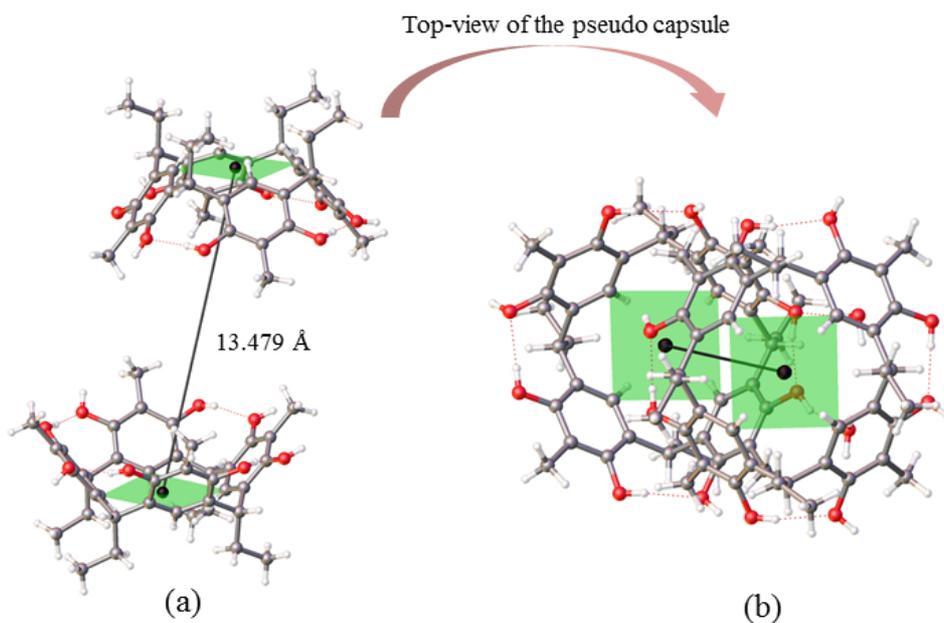
Fig. S6 (a) Side view to show the length of the pseudo capsule 2IPyNO@**1**. Distances are calculated from centroid-to-centroid of bottom ring carbons, and (b) top-view of the capsule. In both the figures, solvent and guest molecules are omitted for clarity.
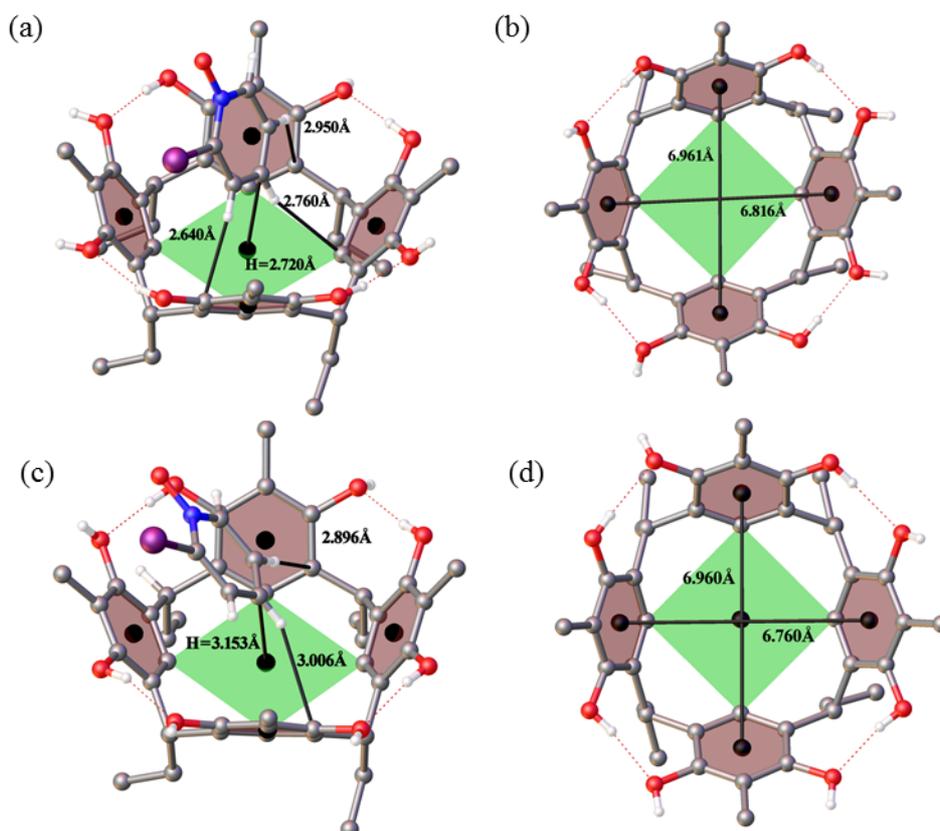
Fig. S7. (a and c) C–H···π interactions in 2IPyNO@**1**, and (b and d) are the respective cavities of the host **1** in 2IPyNO@**1** to highlight the flexibility. In all the figures, selected hydrogen atoms, solvent and guest molecules are omitted for clarity.

IV References

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