Supporting Information

Double-layered alcohol: controlling the macroscopic organization of small molecules through the self-assembly of their receptors

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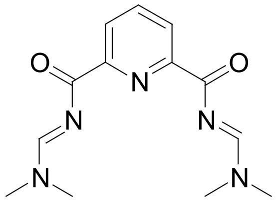
A. Synthesis

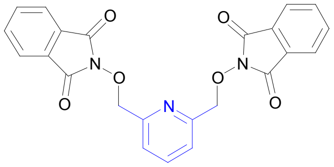
A.1: Materials and Methods:

Commercially available compounds were used as received. Anhydrous diethyl ether, dichloromethane, tetrahydrofurane, acetonitrile, toluene were dried by passing through an activated alumina column. All reactions were performed under Argon (Ar) unless stated otherwise. Deuterated solvents were used as received, except for $CDCl_3$ which was sometimes neutralized by passing through a short column of basic alumina (such treated $CDCl_3$ will be signaled below by an asterisk, *i. e.* '$CDCl_3$*'). ^{1}H NMR and ^{13}C NMR were performed using 300 MHz, 400 MHz and 500 MHz Bruker instruments. Peak listings for all NMR spectra are given in ppm and referenced against the solvent residual signal. Thin layer chromatography (TLC) analysis was performed on silica gel with a pore diameter of 60 Å or activated basic Aluminum oxide with a pore diameter of 58 Å. Column chromatography was performed on silica gel with a particle size of 40-63 μm and a pore diameter of 60 Å.

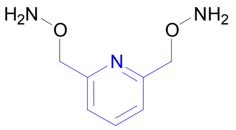


Bis(*N'*,*N'*-dimethylformamidyl-*N*-acyl)-2,6-pyridine (**3**):[1] Pyridyl-2,6-dicarboxamide (11 mmol, 1.0 equiv) was mixed with *N,N*-dimethylformamide dimethyl-acetal (DMF-DMA, 35 mmol, 3.2 equiv) in dimethyl sulfoxide (20 mL). The reaction was heated at 85 °C for 3.5 hours while the methanol by-product distilled off. After cooling to room temperature, the white precipitate was filtered and washed with diethyl ether. The resulting *N,N*-dimethylformamidine product (74 %) was then used without further purification. ^{1}H NMR (CDCl$_3$*, 500 MHz, 25 °C) 8.59 (s, 2 H), 8.31 (d, ^3J = 7.5 Hz, 2 H), 7.82 (t, ^3J = 7.5 Hz, 1 H), 3.16 (br s, 6 H), 3.11 (br s, 6 H). ^{13}C NMR (CDCl$_3$*, 125 MHz, 25 °C) 176.0, 161.3, 153.5, 137.0, 126.5, 41.3, 35.4. EI$^+$-HRMS: calc. for $C_{13}H_{17}N_5O_2$: 275.1382; found: 275.1382 [M]$^+$, 232.0981 [M-Me$_2$N-H]$^+$, 220.0929 [M-Me$_2$N-H-C]$^+$, 205.0839 [M-Me$_2$N-H-C-NH]$^+$. EA calc. for $C_{13}H_{17}N_5O_2$: %C 56.71, %H 6.22, %N 25.44; found %C 56.38, %H 6.20, %N 25.22. Mp decomposed around 204 °C.

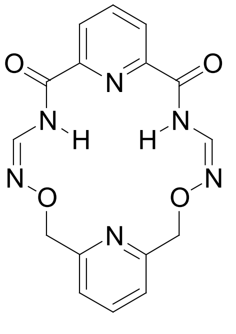
Py(CH$_2$ONPht)$_2$:[2] Sodium hydride suspension in mineral oil (60%, 1.24 g, 31 mmol, 2.8 eq) was washed with hexanes under argon, and suspended in dry DMF under argon. *N*-hydroxyphthalimide (4.24 g, 26 mmol, 2.4 eq) was then added portionwise as a solid, as the mixture was stirred in an ice/water bath. 2,6-Dibromomethylpyridine (3.0 g, 11 mmol, 1.0 eq) was then added at once and the mixture was stirred at 60 ºC for 21 hours under argon. Water was then added at room temperature, the precipitate filtered and washed with copious amounts of water. The solid was then dissolved in dichloromethane and washed with water The organic layer was isolated, dried on sodium sulphate and concentrated in vacuo to give a white solid (3.83 g, 81 %). ^{1}H NMR (300 MHz; CDCl$_3$; 25 ºC): 7.7-7.9 (m, 11 H), 5.26 (s, 4H).



Py(CH$_2$ONH$_2$)$_2$:[2] Py(CH$_2$ONPht)$_2$ (3.83 g, 8.9 mmol, 1.0 eq) was suspended in 95% ethanol (150 mL). Most of the reagent was dissolved by heating gently, and hydrazine hydrate (1.1 mL, 22 mmol, 2.5 eq) was added. The mixture was then heated at 80 ºC for 4 hours. Back to room temperature, the suspension was concentrated in vacuo to give a white solid which was taken up in diethyl ether (80 mL). The precipitate was filtered and washed with more diethyl ether (6 × 50 mL). The combined filtrates were concentrated in vacuo to give 1.53 g of a crude oil which was purified by column chromatography (silica gel, 100:1:5 Et$_2$O/Et$_3$N/CH$_3$OH) to give of a colourless oil (1.12 g, 6.63 mmol, 73 %). ^{1}H NMR (300 MHz; CDCl$_3$*; 25 ºC): 7.72 (t, $^3J = 7.8$ Hz, 1 H), 7.32 (d, $^3J = 7.8$ Hz, 2 H), 5.61 (s, 4 H), 4.83 (s, 4 H). ^{13}C NMR (CDCl$_3$*, 125 MHz, 25 °C) 157.6, 137.2, 120.7, 78.4. R$_f$ (SiO$_2$, 100:1:15 Et$_2$O/Et$_3$N/CH$_3$OH) = 0.25; $C_7H_{11}N_3O_2 \cdot 0.45\ H_2O$: calc. %C 47.42, %H 6.77, %N 23.70; found %C 47.66, %H 6.83, %N 23.31.



Macrocycle 1:[2] Bis-reactive **Py(CH$_2$ONH$_2$)$_2$** nucleophile (18.4 mg, 0.108 mmol, 1.0 eq) and bis-reactive electrophile **3** (29.9 mg, 0.108 mmol, 1.0 eq) were mixed in 2 mL of anhydrous dichloromethane in the presence of acetic acid (24.7 µL, 0.43 mmol, 4.0 eq). The solution was stirred at room temperature for 3 days, and washed with saturated aqueous potassium bicarbonate (2 mL). The aqueous layer was extracted with dichloromethane and the combined organic layers were dried over sodium sulphate, concentrated in vacuo and purified by preparative TLC with 2:100 MeOH/ CH$_2$Cl$_2$ as an eluent to give pure **1** (10 mg, 26%). ^{1}H NMR (CDCl$_3$*, 500 MHz, 25 °C) 10.63 (d, $^3J = 10$ Hz, 2 H), 8.48 (d, $^3J = 7.5$ Hz, 2 H), 8.11 (t, $^3J = 7.5$ Hz, 1 H), 7.86 (d, $^3J = 10$ Hz, 2 H), 7.75 (t, $^3J = 7.5$ Hz, 1 H), 7.31 (d, $^3J = 7.5$ Hz, 2 H), 5.29 (s, 4 H). ^{1}H NMR (CD$_3$OD, 300 MHz, 25°C, low solubility) 8.65 (dd, $^3J = 7.8$ Hz, $^3J = 8$ Hz, 2 H), 8.27 (dd, $^3J = 7.4$ Hz, $^3J = 8.2$ Hz, 1 H), 7.93 (t, $^3J = 7.7$ Hz, 1 H), 7.89 (s, 1 H), 7.48 (d, $^3J = 7.6$ Hz, 2 H), 5.31 (s, 4 H). ^{13}C NMR (CDCl$_3$*, 100 MHz, 25 °C) 162.0, 155.7, 148.1, 137.9, 134.3, 127.6, 122.6, 76.7. Mp: 200 °C (dec.). See details of crystal structures further in supporting information.



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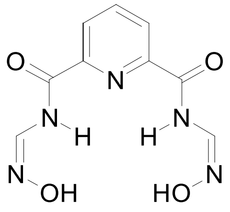
Macrocycle 2:

N^2,N^6-bis((Z)-(hydroxyimino)methyl)pyridine-2,6-dicarboxamide (4): Bis(*N',N'*-dimethylformamidyl-*N*-acyl)-2,6-pyridine (**3**) (3.09 g, 11.2 mmol) was mixed with a suspension of hydroxylamine hydrochloride (1.716 g, 24.7 mmol, 2.2 equiv.) in anhydrous dichloromethane (100 mL). Acetic acid (1.28 mL, 22 mmol, 2 equiv.) was then added at once and the suspension was stirred for 5 hours. The resulting white precipitate was collected, with a small amount of dichloromethane then recrystallized in hot ethanol to give 2.10 g (76%) of the



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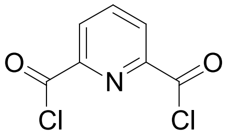
desired product as a white needle-like solid.^{1}H NMR (DMSO-d$_6$, 400 MHz, 25 °C) 11.10 (s, 2 H), 10.71 (d, ^3J = 10.0 Hz, 2 H), 8.36 (m, 2 H), 8.31 (m, 1 H), 7.74 (d, ^3J = 10.0 Hz, 2 H). ^{13}C NMR (DMSO-d$_6$, 100 MHz, 25 °C) 160.9, 147.6, 140.2, 133.1, 126.6. ESI$^+$ HRMS: calc. for $C_9H_9N_5O_4 \cdot H^+$: 252.0732, found: 252.0739. EA calc. for $C_9H_9N_5O_4$.1.1 H_2O: %C 39.89, %H 4.17, %N 25.84, found %C 40.25, %H 3.79, %N 25.53. Mp 183-185 °C. The inclusion of water is confirmed by the crystal structure (see below).

<u>Macrocycle 1</u>: A sodium hydride suspension (85.3 mg, 60% in mineral oil, 2.1 mmol, 2.8 equiv.) was washed with hexanes under argon, and suspended in dry DMF (12 mL) under argon. **4** (191 mg, 0.761 mmol) was then added and the yellow suspension stirred for an hour at room temperature. 2,6-Bis(bromomethyl)-pyridine (202 mg, 0.761 mmol, 1.0 equiv.) was then added at once. The yellow solution was stirred for 24 hours at room temperature, whereupon water (20 mL) was poured and the resulting light yellow precipitate was collected and purified by column chromatography (silica gel, 100:5 CH_2Cl_2 / MeOH, first fraction, R_f = 0.17) to give 156 mg (0.44 mmol, 58%) of macrocycle **1** as a white solid. ^{1}H NMR ($CDCl_3$*, 500 MHz, 25°C) 10.63 (d, ^3J = 10 Hz, 2 H), 8.48 (d, ^3J = 7.5 Hz, 2 H), 8.11 (t, ^3J = 7.5 Hz, 1 H), 7.86 (d, ^3J = 10 Hz, 2 H), 7.75 (t, ^3J = 7.5 Hz, 1 H), 7.31 (d, ^3J = 7.5 Hz, 2 H), 5.29 (s, 4 H). ^{13}C NMR ($CDCl_3$ with 2 drops of CD_3OD, 150 MHz, 25 °C) 162.6, 155.6, 148.0, 138.9, 138.1, 135.2, 127.3, 122.2, 76.1. Mp 200 °C (dec.). ESI$^+$HRMS: calc. for $C_{16}H_{14}N_6O_4 \cdot H^+$: 355.1154, found: 355.1151. EA calc. for $C_{16}H_{14}N_6O_4$.2.55 H_2O: %C 48.01, %H 4.81, %N 21.00; found %C 48.17, %H 4.61, %N 20.80.

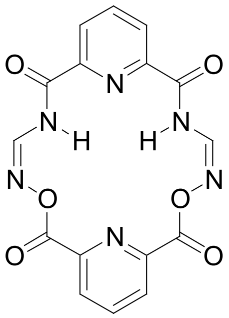
1

2,6-Pyridinedicarboxylic acid chloride (Py(COCl)₂): The acyl chloride was synthesized from dipicolinic acid using thionyl chloride under reflux condition. Thionyl chloride (20 mL, 0.28 mol) was added to pre-dried dipicolinic acid (2.1 g, 0.01 mol) and the reaction mixture was refluxed under argon for 13 h. The excess thionyl chloride was distilled off, purged with argon and dried under membrane pump to give pyridine-2,6-dicarbonyl dichloride (**Py(COCl)₂**, 2.5 g) as a pinkish solid in 96% yield.



Py(COCl)₂

<u>Macrocycle 2</u>: To a solution of **4** (50.0 mg, 0.20 mmol) in anhydrous DMF (4.0 mL) under argon, was added 4-dimethylaminopyridine (DMAP, 48.6 mg, 0.4 mmol, 2 equiv.) and lithium chloride (8.4 mg, 0.2 mol, 1 equiv.). The mixture was stirred for 30 min. 2,6-Pyridinedicarboxylic acyl chloride (40.6 mg, 0.20 mmol, 1.0 equiv.) was then added at 0 ºC. The mixture was stirred for 10 min at 0 ºC and then allowed to warm to room temperature, and stirred overnight. The resulting white precipitate was filtered, and washed with diethyl ether and purified by chromatography on silica gel, to yield macrocycle **2** (46.0 mg, 61 % yield) as a white powder.



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A single crystal was obtained by slow diffusion of diethyl ether into a solution of **2** in a mixture of chloroform and methanol to form colorless cube-like crystals (see crystal data below). ^{1}H NMR (CDCl$_3$* with 3-4 drops of CD$_3$OD, 600 MHz, 25 °C) 12.9 (d, $^{3}J = 9.3$ Hz, 2 H), 8.56 (d, $^{3}J = 7.8$ Hz, 2 H), 8.46 (d, $^{3}J = 7.8$ Hz, 2 H), 8.27 (s, 2 H), 8.20 (t, $^{3}J = 7.8$ Hz, 2 H), 8.12 (t, $^{3}J = 7.8$ Hz, 2 H). ^{13}C NMR (CDCl$_3$* with 3-4 drops of CD$_3$OD, 150 MHz, 25 °C) 163.0, 160.9, 147.5, 146.6, 140.3, 140.1, 139.4, 130.6, 128.2. ESI^{+}-HRMS: calc. for $C_{16}H_{10}N_6O_6$: 382.2874; found: 383.0749 [M·H]$^{+}$, 405.0541 [M·Na]$^{+}$, 787.1257 [2M·Na]$^{+}$. Mp ~220 ° C (dec.). EA calc. for $C_{16}H_{10}N_6O_6$ 1.5 CH_3OH: %C 48.84, %H 3.75, %N 19.53; found %C 48.81, %H 3.50, %N 19.52.

References:

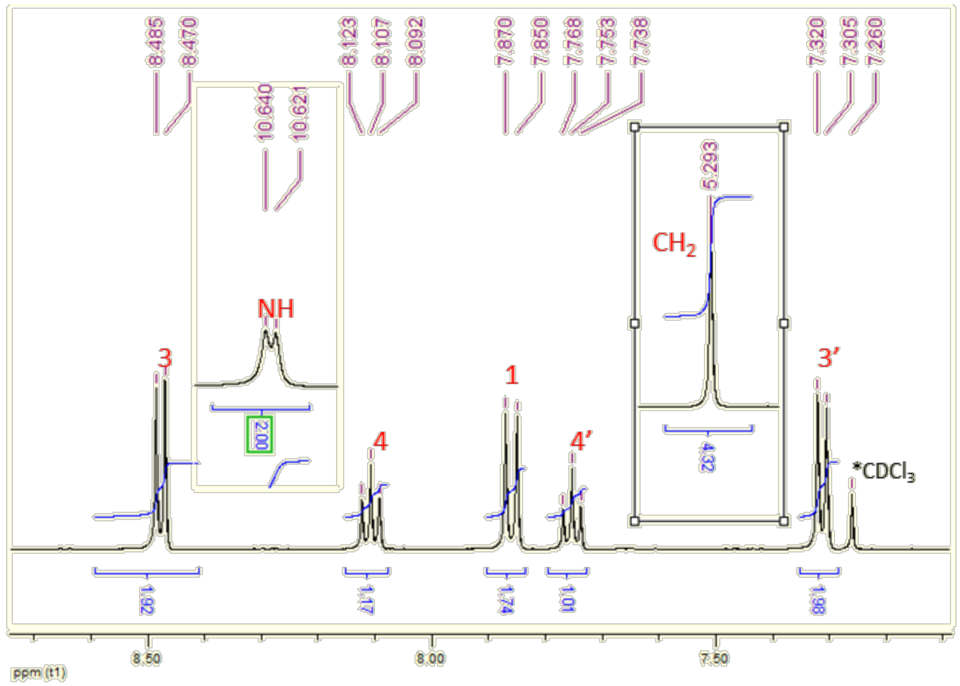
[1] Weiwen Zhao, Ruiyao Wang, Nicholas Mosey, Anne Petitjean, *Org. Lett*. 2011, **13**, 5160-5163.

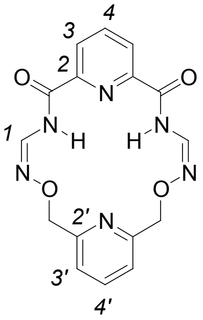
[2] Weiwen, Zhao, Ruiyao Wang, Anne Petitjean, *Org. Biomol. Chem.* 2011, ***9***, 7647-7651.

B. NMR data for macrocycles 1 and 2

Macrocycle 1

^{1}H NMR ($CDCl_3$*, 500 MHz, 25°C)





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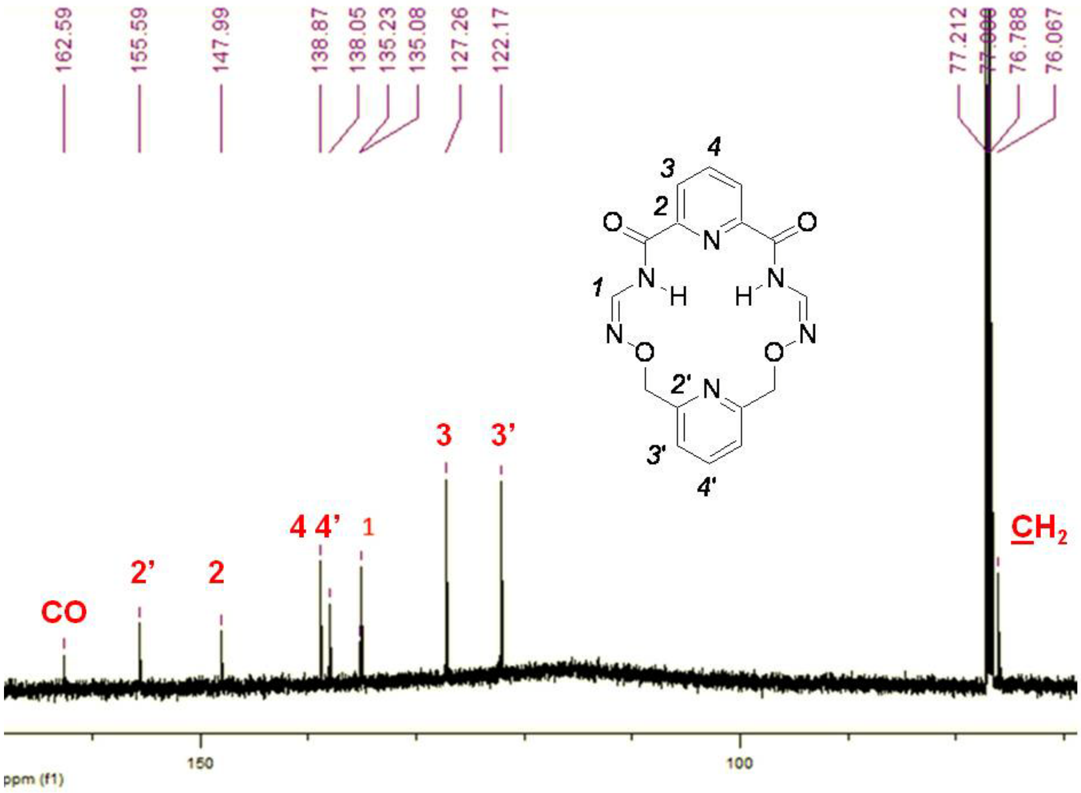
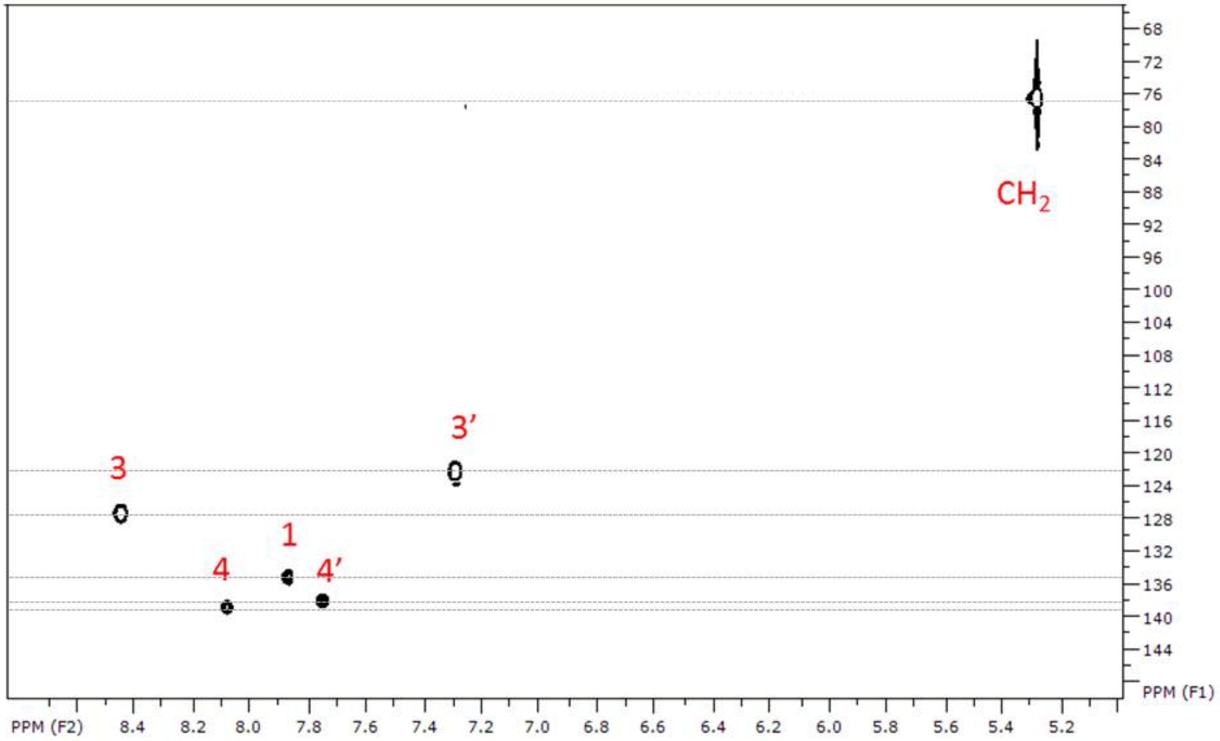
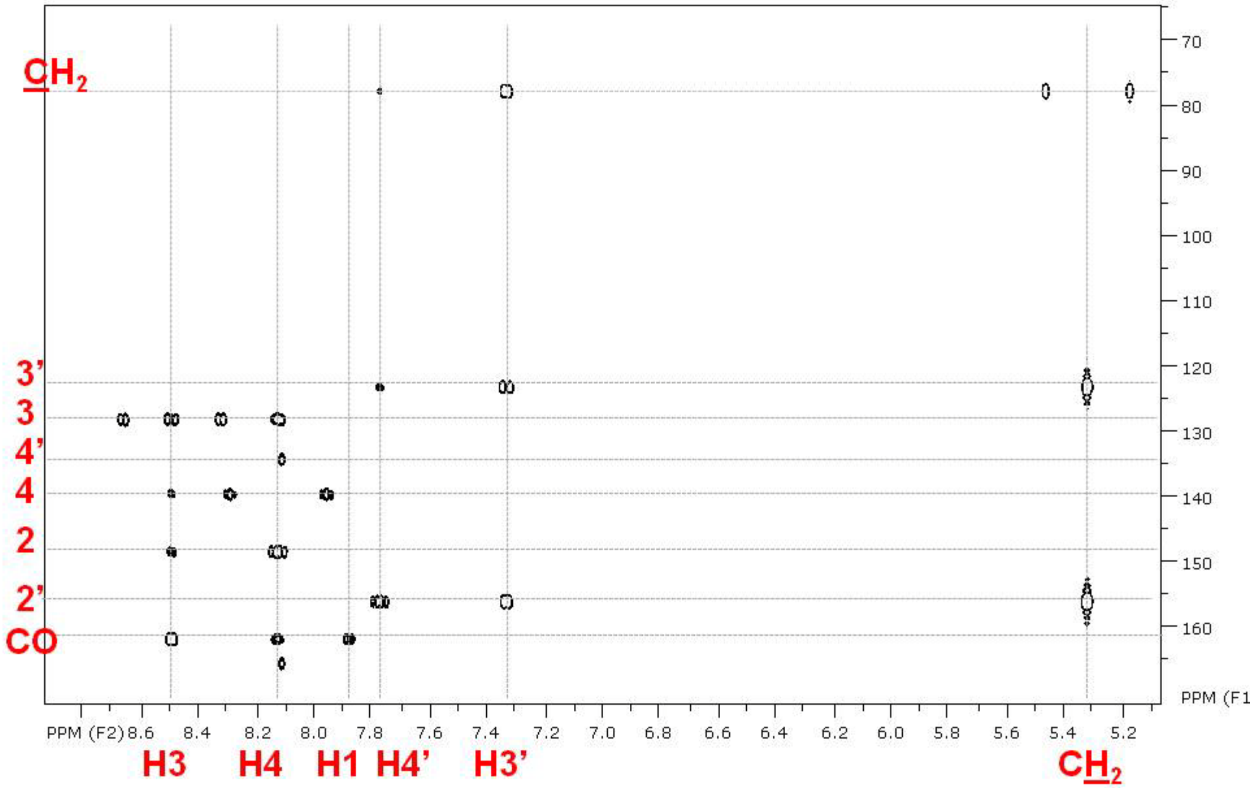
^{13}C NMR ($CDCl_3$ with 3-4 drops of CD_3OD, 150 MHz, 25°C)



^{1}H-^{13}C HSQC(CDCl$_3$*, 600 MHz, 25°C)

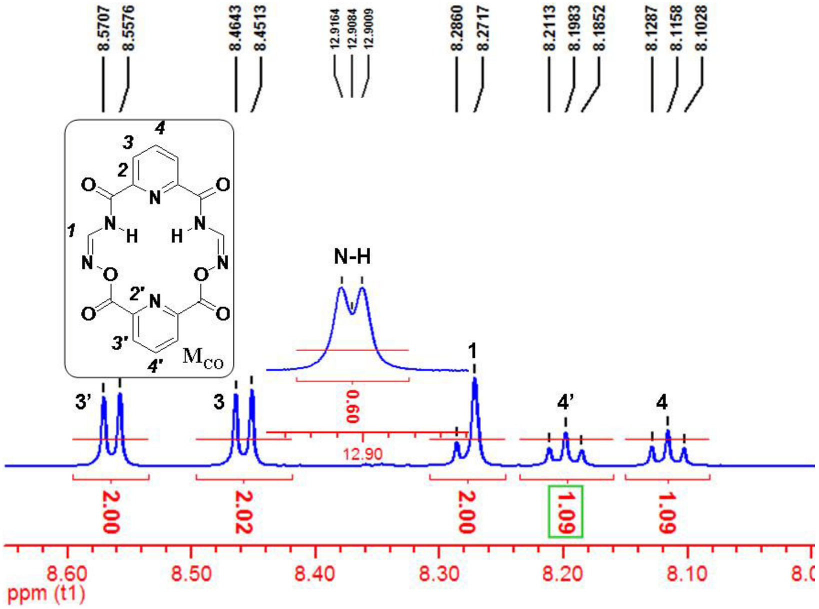


^{1}H-^{13}C HMBC (CDCl$_3$*, 500 MHz, 25°C)

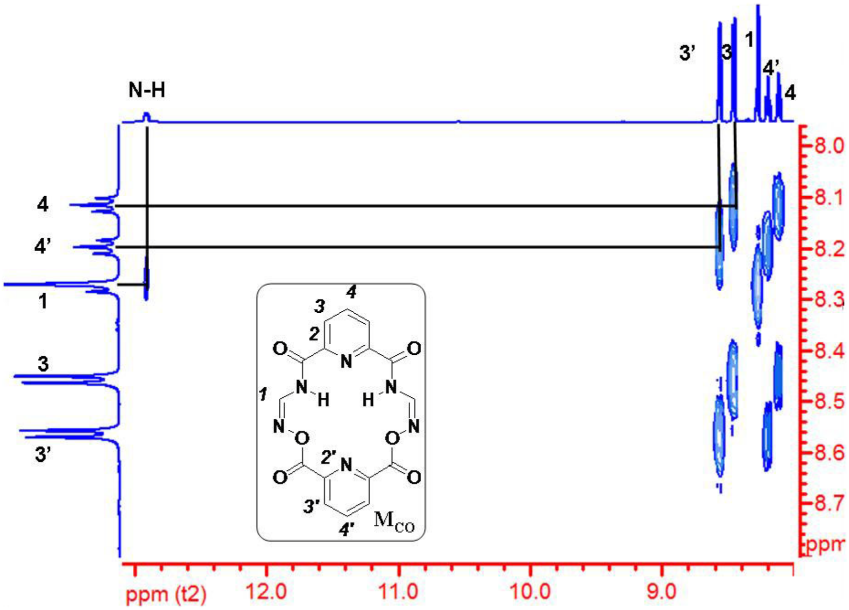


<u>Macrocycle **2**</u>:

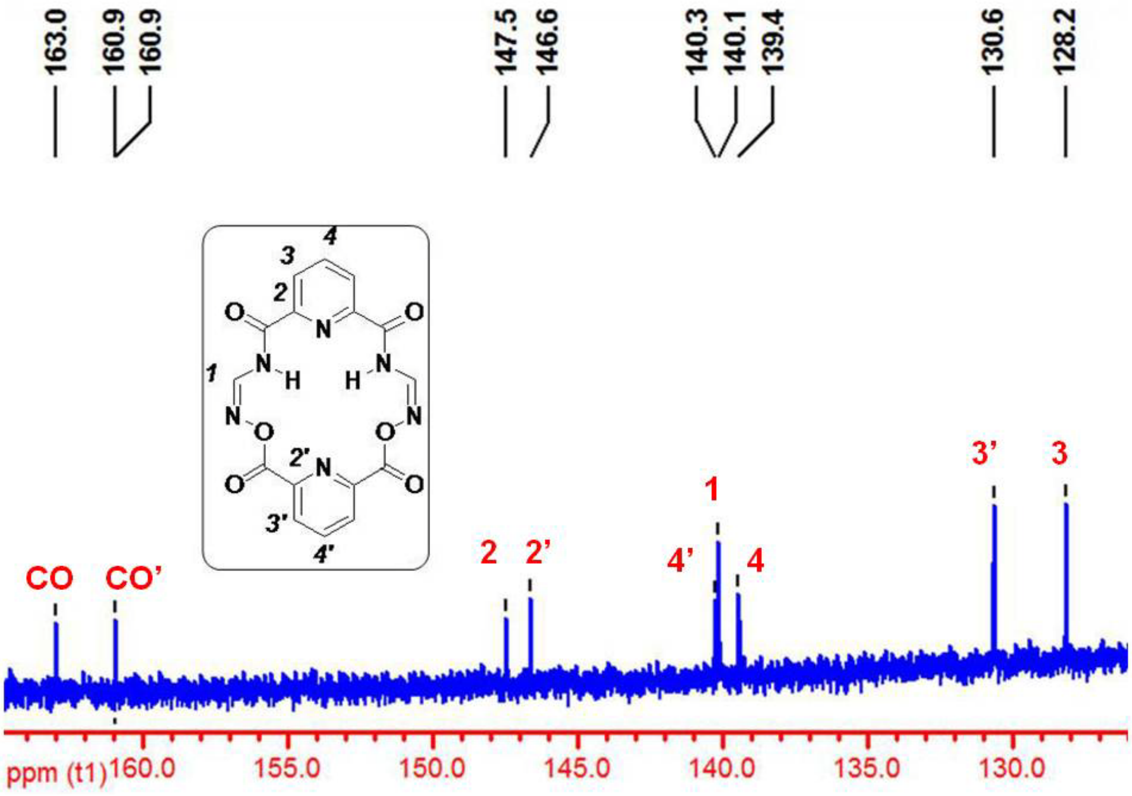
^{1}H NMR (CDCl$_3$* and CD$_3$OD, 600 MHz, 25 °C)



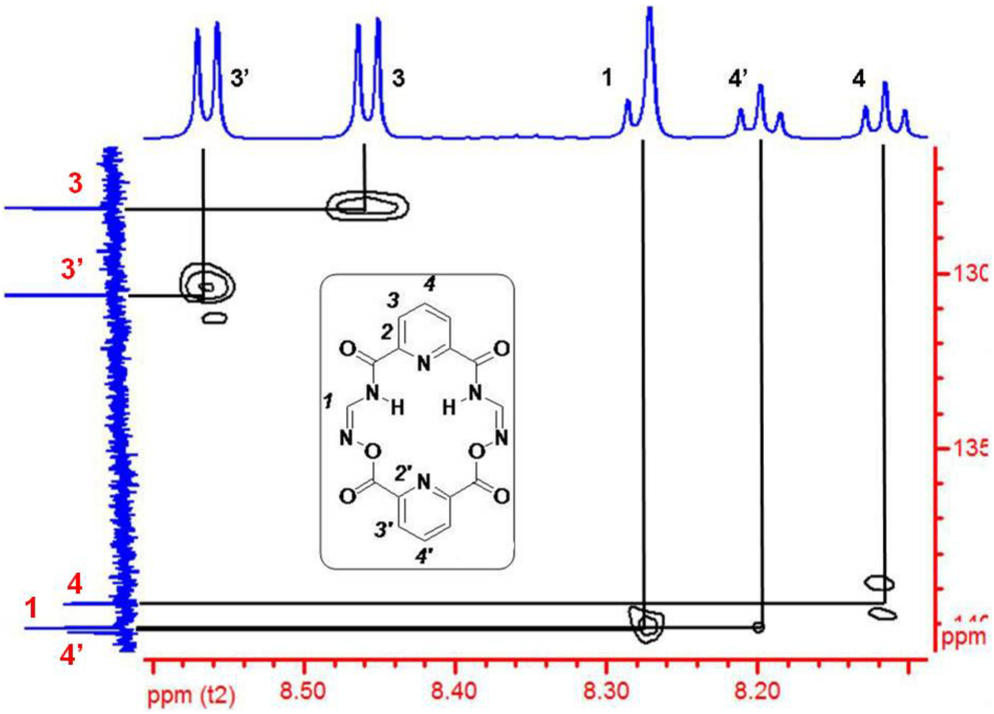
^{1}H-^{1}H COSY (CDCl$_3$* and CD$_3$OD, 600 MHz, 25 °C)



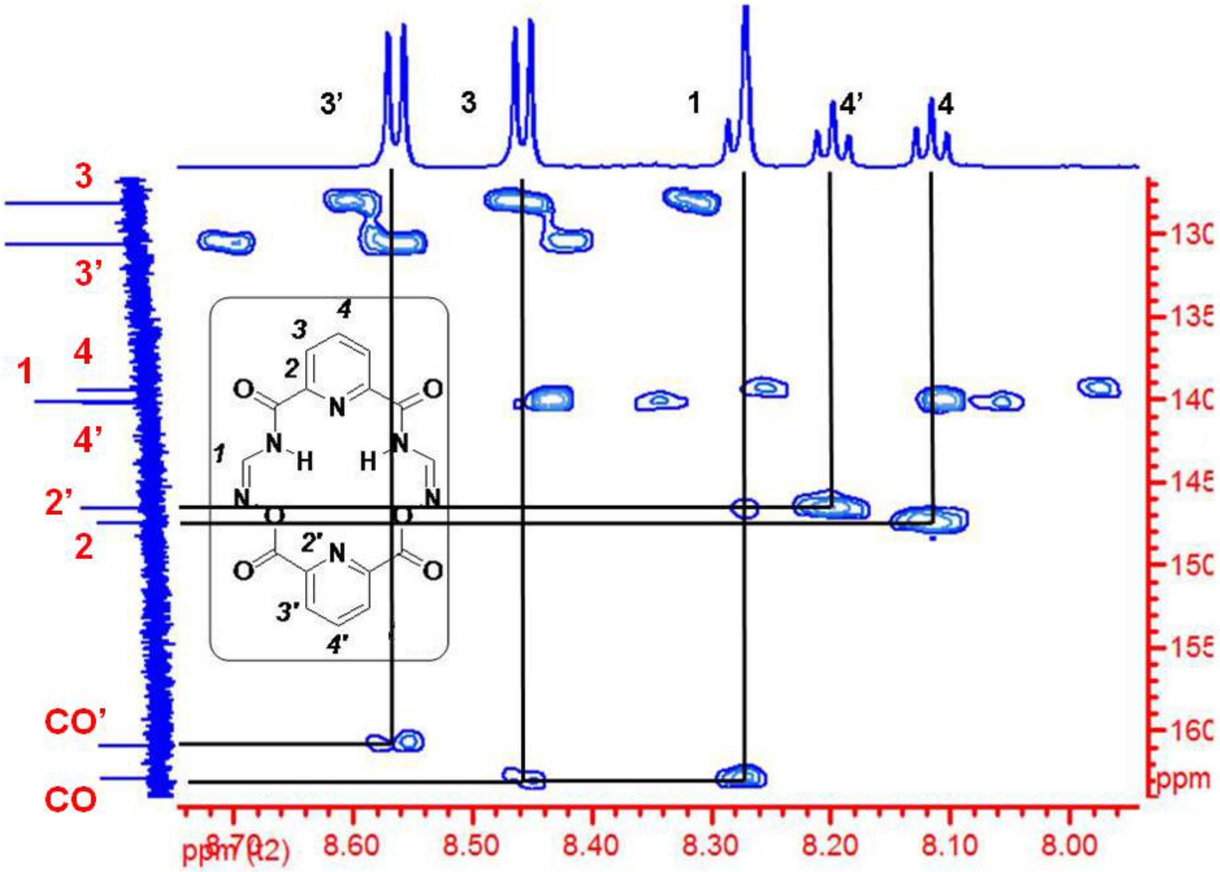
^{13}C NMR ($CDCl_3$* and CD_3OD, 150 MHz, 25 °C)



^{1}H-^{13}C HSQC ($CDCl_3$* and CD_3OD, 600 MHz, 25 °C)

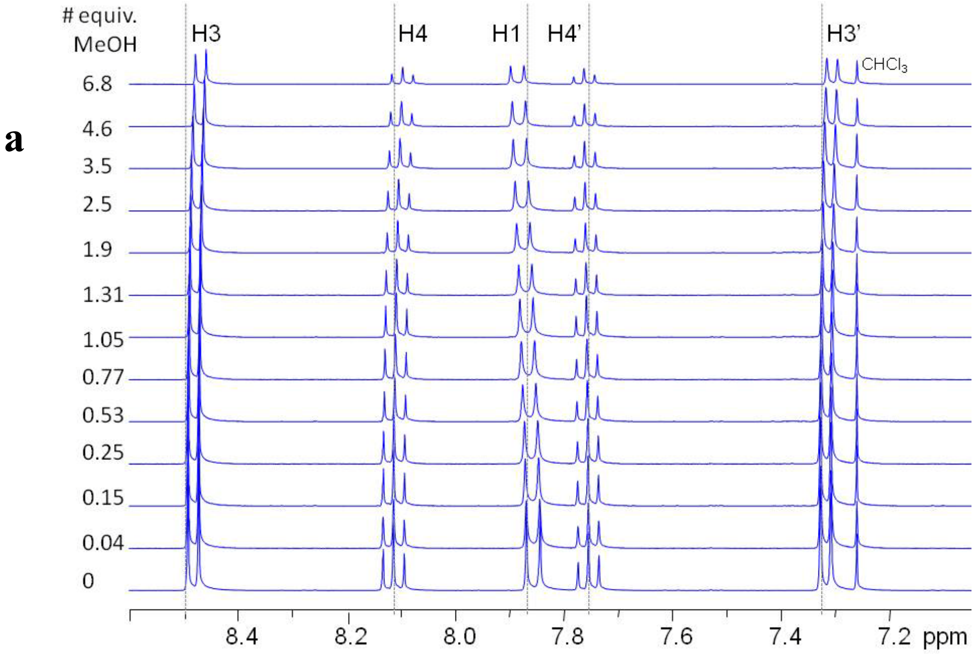


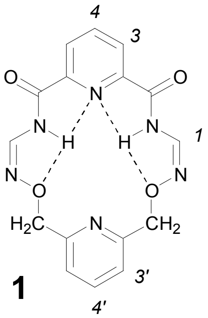
^{1}H-^{13}C HMBC ($CDCl_3$* and CD_3OD, 600 MHz, 25 °C)



C. ^{1}H NMR titrations of 1 with HO$^-$ containing species

C.1. CH_3OH substrate induces chemical shift changes consistent with the mode of binding observed in the solid state. For instance, H4' moves downfield, consistent with the corresponding pyridine nitrogen ('bottom' pyridine) binding an electrodeficient species. On the contrary, H4 moves upfield, consistent with the proton of the NH fragment becoming less electrodeficient (donation by the MeOH oxygen). Finally, the NH signal moves downfield, consistent with H-bonding to an additional heteroatom. However, binding is very weak (signals keep changing after addition of 7 equiv.; due to small chemical shift differences, an accurate determination of the binding constant is not possible; it is however estimated to be of the order of 35 M^{-1}).





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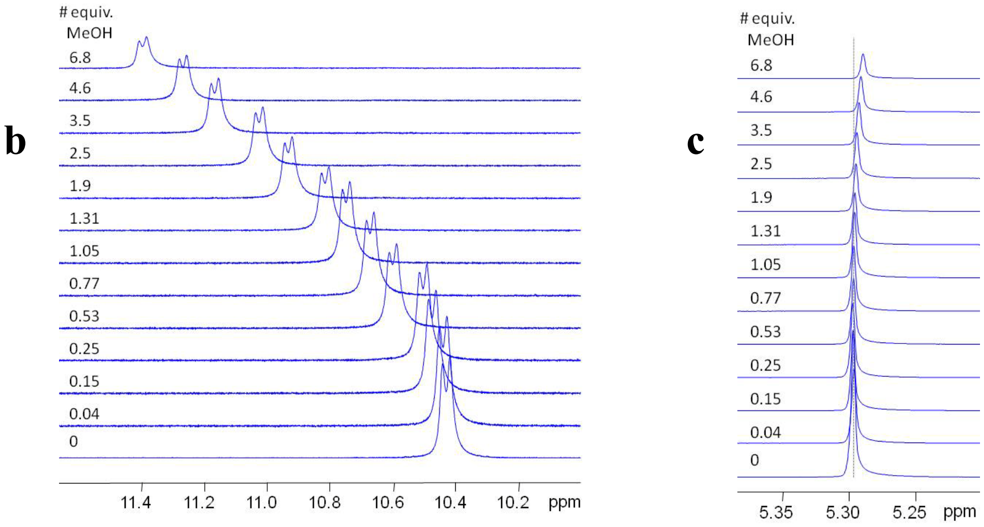
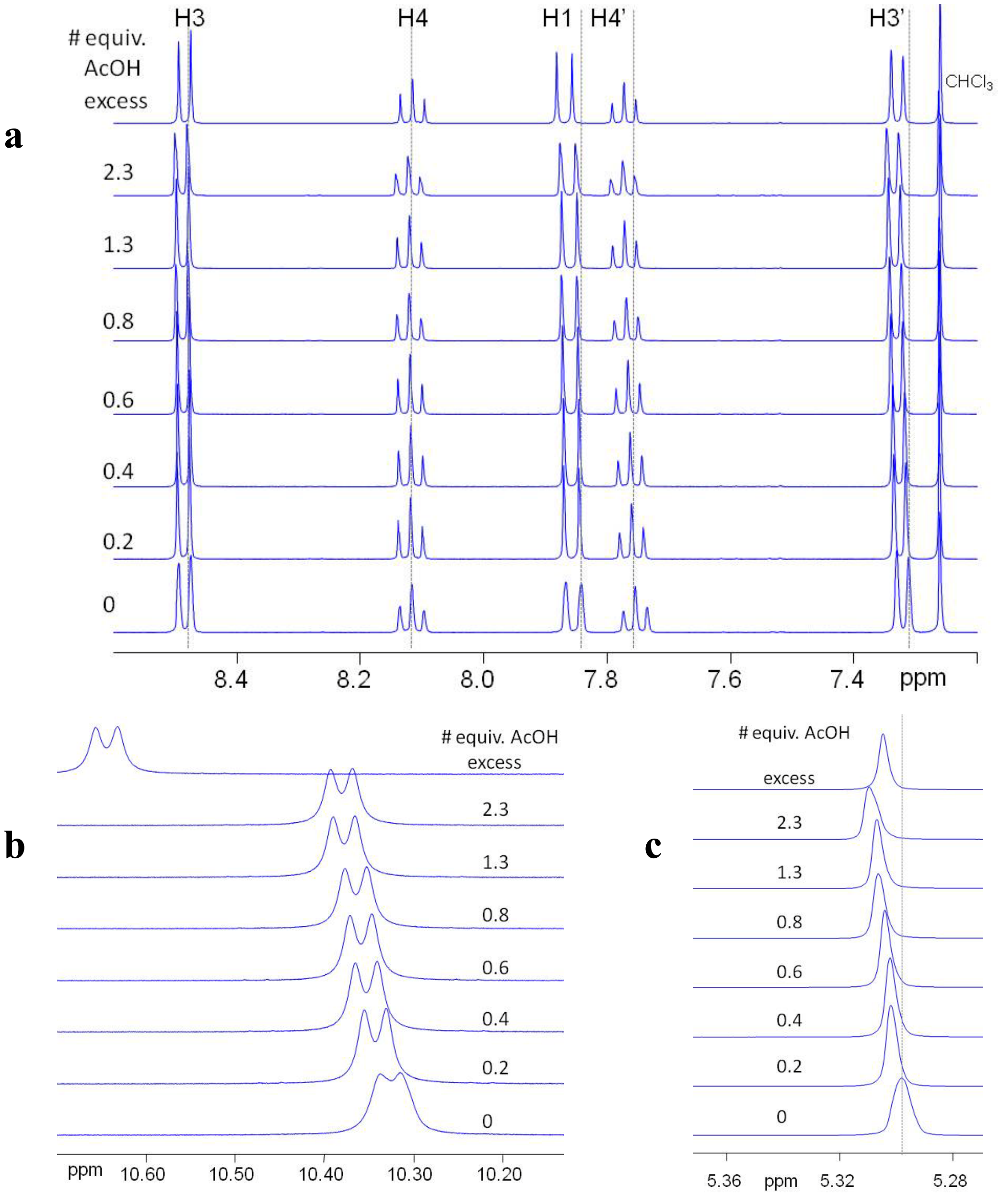


Figure S1: ^{1}H NMR titration of **1** (15-24 mM) with MeOH in $CDCl_3$ (400 MHz, 25 °C); a) Aromatic region; b) NH signal, c) CH_2 signal. Vertical grey dotted lines have been added to guide the eye with regards to chemical shift changes.

C.2. CH_3COOH substrate induces fairly similar chemical shift changes as with MeOH. The amide NH is deshielded, consistent with H-bonding. The pyridyl proton H4' (on the 'bottom' pyridine) moves downfield, which suggests that it binds an electrodeficient species (equivalent of protonation here, considering the acidity of AcOH). H4 and H3 of the pyridyl-bis-amide fragment seem unaffected. Once again, binding is fairly weak (signals keep changing after addition of 7 equiv.; due to small chemical shift differences, an accurate determination of the binding constant is not possible; it is however estimated to be of the order of 400 M^{-1}).



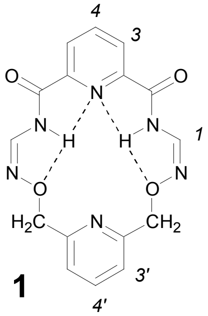


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Figure S2: ^1H NMR titration of **1** (17-25 mM) with CH_3COOH in $CDCl_3$ (400 MHz, 25 °C); a) Aromatic region; b) NH signal, c) CH_2 signal. Vertical grey dotted lines have been added to guide the eye with regards to chemical shift changes.

D. Crystallographic data

D.1. Structure of **1**.CH_3OH [CCDC 874203]

A crystal of the compound (colorless, block-shaped, size 0.20 × 0.15 × 0.12 mm) was mounted on a glass fiber with grease and cooled to -93 °C in a stream of nitrogen gas controlled with Cryostream Controller 700. Data collection was performed on a Bruker SMART APEX II X-ray diffractometer with graphite-monochromated Mo K_α radiation (λ = 0.71073 Å), operating at 50 kV and 30 mA over 2θ ranges of 3.76 ~ 52.00º. No significant decay was observed during the data collection. Data were processed on a PC using the Bruker AXS Crystal Structure Analysis Package:[1] Data collection: APEX2 (Bruker, 2006); cell refinement: SAINT (Bruker, 2005); data reduction: SAINT (Bruker, 2005); structure solution: XPREP (Bruker, 2005) and SHELXTL (Bruker, 2000); structure refinement: SHELXTL; molecular graphics: SHELXTL; publication materials: SHELXTL. Neutral atom scattering factors were taken from Cromer and Waber.[2] The crystal is monoclinic space group $P2_1$/n, based on the systematic absences, *E* statistics and successful refinement of the structure. The structure was solved by direct methods. Full-matrix least-square refinements minimizing the function $\sum w\ (F_o^2 - F_c^2)^2$ were applied to the compound. All non-hydrogen atoms were refined anisotropically. The H atom of OH from MeOH was located from difference Fourier maps. All of the other H atoms were placed in geometrically calculated positions, with C-H = 0.95 (aromatic), 0.99(CH_2), and 0.88(N-H) Å, and refined as riding atoms, with Uiso(H) = 1.2 Ueq(C or N). The methyl group of MeOH was refined with AFIX 137, which allowed the rotation of the methyl group whilst keeping the C-H distances and X-C-H angles fixed. Convergence to final R_1 = 0.0405 and wR_2 = 0.0933 for 2336 (I>2σ(I)) independent reflections, and R_1 = 0.0681 and wR_2 = 0.1084 for all 3451 (R(int) = 0.0357) independent reflections, with 259 parameters and 0 restraints, were achieved.[3] The largest residual peak and hole to be 0.157 and – 0.146 e/Å^3, respectively. Crystallographic data, atomic coordinates and equivalent isotropic displacement parameters, bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates and isotropic displacement parameters, torsion angles and H-bonding information are given in Table S1 to S7. The molecular structure and the cell packing are shown in Figure S3.

[1] Bruker AXS Crystal Structure Analysis Package: Bruker (2000). SHELXTL. Version 6.14. Bruker AXS Inc., Madison, Wisconsin, USA; Bruker (2005). XPREP. Version 2005/2. Bruker AXS Inc., Madison, Wisconsin, USA;

Bruker (2005). SAINT. Version 7.23A. Bruker AXS Inc., Madison,Wisconsin, USA; Bruker (2006). APEX2. Version 2.0-2. Bruker AXS Inc., Madison, Wisconsin, USA.

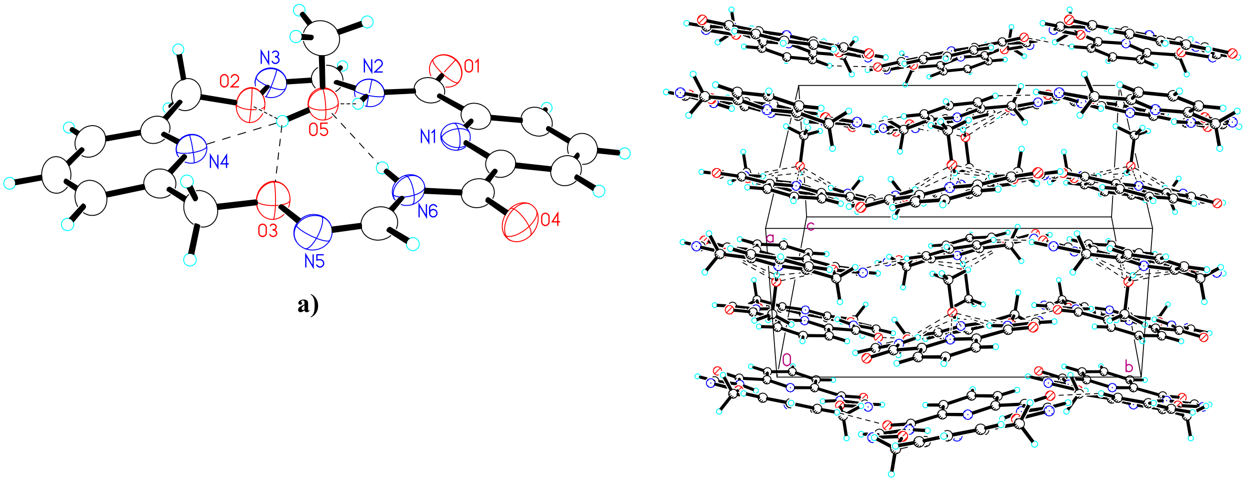
[2] Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, UK, 1974; Vol. 4, Table 2.2 A.

[3] $R1 = \sum ||Fo| - |Fc|| / \sum |Fo|$

$$wR_2 = \{\sum [w\,(Fo^2 - Fc^2)^2] / \sum [w(Fo^2)^2]\}^{1/2}$$

$$(w = 1 / [\sigma^2(Fo^2) + (0.0476P)^2 + 0.134P], \text{ where } P = [\mathrm{Max}\,(Fo^2, 0) + 2Fc^2] / 3)$$

Figure S3. a) molecular Structure (displacement ellipsoids for non-H atoms are shown at the 50% probability level and H atoms are represented by circles of arbitrary size. The solvent molecules and the anions are omitted for clarity); b) crystal cell packing.



a)

b)

Table S1. Crystal data and structure refinement for ap19

Identification code	ap19	
Empirical formula	C17 H18 N6 O5	
Formula weight	386.37	
Temperature	180(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 7.5319(8) Å	α= 90°.
	b = 15.1775(19) Å	β= 98.919(3)°.
	c = 15.610(2) Å	γ = 90°.
Volume	1762.8(4) Å^3	
Z	4	
Density (calculated)	1.456 Mg/m^3	
Absorption coefficient	0.110 mm^{-1}	
F(000)	808	
Crystal size	0.20 x 0.15 x 0.12 mm^3	
Theta range for data collection	1.88 to 26.00°.	
Index ranges	-9<=h<=8, -18<=k<=14, -17<=l<=19	
Reflections collected	9428	
Independent reflections	3451 [R(int) = 0.0357]	
Completeness to theta = 26.00°	99.5 %	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9869 and 0.9782	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3451 / 0 / 259	
Goodness-of-fit on F^2	1.038	
Final R indices [I>2sigma(I)]	R1 = 0.0405, wR2 = 0.0933	
R indices (all data)	R1 = 0.0681, wR2 = 0.1084	
Extinction coefficient	0.0046(8)	
Largest diff. peak and hole	0.157 and -0.146 e.Å^{-3}	

Table S2. Atomic coordinates (× 10^4) and equivalent isotropic displacement parameters (Å^2 × 10^3) for ap19. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	3292(2)	6998(1)	157(1)	49(1)
O(2)	446(2)	6474(1)	2615(1)	44(1)
O(3)	-690(2)	3508(1)	2582(1)	44(1)
O(4)	1296(2)	2481(1)	30(1)	50(1)
O(5)	1716(2)	4809(1)	2243(1)	40(1)
N(1)	2134(2)	4759(1)	408(1)	35(1)
N(2)	2023(2)	6349(1)	1228(1)	37(1)
N(3)	1023(2)	7281(1)	2291(1)	43(1)
N(4)	-758(2)	5054(1)	3411(1)	36(1)
N(5)	-745(2)	2644(1)	2226(1)	44(1)
N(6)	807(2)	3322(1)	1174(1)	37(1)
C(1)	2082(2)	3990(1)	-19(1)	36(1)
C(2)	2544(2)	3909(1)	-840(1)	44(1)
C(3)	3085(3)	4644(1)	-1245(1)	47(1)
C(4)	3169(2)	5442(1)	-811(1)	43(1)
C(5)	2693(2)	5468(1)	9(1)	36(1)
C(6)	2718(2)	6336(1)	473(1)	37(1)
C(7)	1753(2)	7141(1)	1623(1)	41(1)
C(8)	50(3)	6625(1)	3455(1)	45(1)
C(9)	-918(2)	5854(1)	3771(1)	36(1)
C(10)	-1893(3)	5992(1)	4434(1)	42(1)
C(11)	-2759(3)	5288(1)	4748(1)	48(1)
C(12)	-2637(3)	4470(1)	4378(1)	44(1)
C(13)	-1635(2)	4378(1)	3719(1)	36(1)
C(14)	-1488(3)	3470(1)	3345(1)	43(1)
C(15)	14(3)	2638(1)	1552(1)	42(1)
C(16)	1385(2)	3198(1)	396(1)	38(1)
C(17)	3408(3)	4695(1)	2763(1)	55(1)

Table S3. Bond lengths [Å] and angles [°] for ap19.

O(1)-C(6)	1.227(2)	C(2)-H(2A)	0.9500
O(2)-C(8)	1.409(2)	C(3)-C(4)	1.385(3)
O(2)-N(3)	1.4189(18)	C(3)-H(3A)	0.9500
O(3)-C(14)	1.417(2)	C(4)-C(5)	1.382(3)
O(3)-N(5)	1.4221(18)	C(4)-H(4A)	0.9500
O(4)-C(16)	1.227(2)	C(5)-C(6)	1.502(2)
O(5)-C(17)	1.411(2)	C(7)-H(7A)	0.9500
O(5)-H(5H)	0.90(3)	C(8)-C(9)	1.503(2)
N(1)-C(1)	1.342(2)	C(8)-H(8A)	0.9900
N(1)-C(5)	1.344(2)	C(8)-H(8B)	0.9900
N(2)-C(6)	1.363(2)	C(9)-C(10)	1.374(2)
N(2)-C(7)	1.380(2)	C(10)-C(11)	1.380(3)
N(2)-H(2B)	0.8800	C(10)-H(10A)	0.9500
N(3)-C(7)	1.270(2)	C(11)-C(12)	1.379(3)
N(4)-C(13)	1.349(2)	C(11)-H(11A)	0.9500
N(4)-C(9)	1.350(2)	C(12)-C(13)	1.375(2)
N(5)-C(15)	1.272(2)	C(12)-H(12A)	0.9500
N(6)-C(16)	1.365(2)	C(13)-C(14)	1.507(2)
N(6)-C(15)	1.375(2)	C(14)-H(14A)	0.9900
N(6)-H(6A)	0.8800	C(14)-H(14B)	0.9900
C(1)-C(2)	1.385(3)	C(15)-H(15A)	0.9500
C(1)-C(16)	1.498(3)	C(17)-H(17A)	0.9800
C(2)-C(3)	1.375(3)	C(17)-H(17B)	0.9800
		C(17)-H(17C)	0.9800

C(8)-O(2)-N(3)	108.15(12)	O(2)-C(8)-H(8B)	109.4
C(14)-O(3)-N(5)	107.49(12)	C(9)-C(8)-H(8B)	109.4
C(17)-O(5)-H(5H)	109.9(16)	H(8A)-C(8)-H(8B)	108.0
C(1)-N(1)-C(5)	116.93(16)	N(4)-C(9)-C(10)	122.88(16)
C(6)-N(2)-C(7)	120.12(15)	N(4)-C(9)-C(8)	118.99(16)
C(6)-N(2)-H(2B)	119.9	C(10)-C(9)-C(8)	118.11(16)
C(7)-N(2)-H(2B)	119.9	C(9)-C(10)-C(11)	119.15(18)
C(7)-N(3)-O(2)	110.15(14)	C(9)-C(10)-H(10A)	120.4
C(13)-N(4)-C(9)	117.11(16)	C(11)-C(10)-H(10A)	120.4
C(15)-N(5)-O(3)	109.86(14)	C(12)-C(11)-C(10)	118.78(19)

C(16)-N(6)-C(15)	119.85(15)
C(16)-N(6)-H(6A)	120.1
C(15)-N(6)-H(6A)	120.1
N(1)-C(1)-C(2)	123.05(17)
N(1)-C(1)-C(16)	117.87(16)
C(2)-C(1)-C(16)	118.97(16)
C(3)-C(2)-C(1)	119.19(18)
C(3)-C(2)-H(2A)	120.4
C(1)-C(2)-H(2A)	120.4
C(2)-C(3)-C(4)	118.69(19)
C(2)-C(3)-H(3A)	120.7
C(4)-C(3)-H(3A)	120.7
C(5)-C(4)-C(3)	118.57(18)
C(5)-C(4)-H(4A)	120.7
C(3)-C(4)-H(4A)	120.7
N(1)-C(5)-C(4)	123.54(17)
N(1)-C(5)-C(6)	117.41(16)
C(4)-C(5)-C(6)	119.00(16)
O(1)-C(6)-N(2)	122.83(17)
O(1)-C(6)-C(5)	120.25(17)
N(2)-C(6)-C(5)	116.88(15)
N(3)-C(7)-N(2)	128.60(17)
N(3)-C(7)-H(7A)	115.7
N(2)-C(7)-H(7A)	115.7
O(2)-C(8)-C(9)	111.20(14)
O(2)-C(8)-H(8A)	109.4
C(9)-C(8)-H(8A)	109.4
C(12)-C(11)-H(11A)	120.6
C(10)-C(11)-H(11A)	120.6
C(13)-C(12)-C(11)	119.06(17)
C(13)-C(12)-H(12A)	120.5
C(11)-C(12)-H(12A)	120.5
N(4)-C(13)-C(12)	123.01(17)
N(4)-C(13)-C(14)	119.28(16)
C(12)-C(13)-C(14)	117.70(16)
O(3)-C(14)-C(13)	110.74(14)
O(3)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14A)	109.5
O(3)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	108.1
N(5)-C(15)-N(6)	129.08(17)
N(5)-C(15)-H(15A)	115.5
N(6)-C(15)-H(15A)	115.5
O(4)-C(16)-N(6)	122.33(17)
O(4)-C(16)-C(1)	120.50(17)
N(6)-C(16)-C(1)	117.14(15)
O(5)-C(17)-H(17A)	109.5
O(5)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
O(5)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5

Table S4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for ap19. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	54(1)	38(1)	58(1)	12(1)	14(1)	-4(1)
O(2)	64(1)	26(1)	47(1)	-2(1)	19(1)	-9(1)
O(3)	60(1)	24(1)	50(1)	-2(1)	15(1)	-5(1)
O(4)	62(1)	33(1)	54(1)	-10(1)	5(1)	5(1)
O(5)	46(1)	32(1)	43(1)	-2(1)	10(1)	-3(1)

N(1)	32(1)	34(1)	38(1)	2(1)	2(1)	4(1)
N(2)	39(1)	28(1)	43(1)	6(1)	5(1)	-2(1)
N(3)	50(1)	26(1)	54(1)	2(1)	8(1)	-7(1)
N(4)	38(1)	30(1)	40(1)	0(1)	4(1)	0(1)
N(5)	50(1)	25(1)	57(1)	-4(1)	8(1)	-4(1)
N(6)	41(1)	26(1)	42(1)	-4(1)	3(1)	0(1)
C(1)	31(1)	38(1)	39(1)	-3(1)	-1(1)	7(1)
C(2)	40(1)	46(1)	44(1)	-8(1)	1(1)	6(1)
C(3)	42(1)	60(1)	39(1)	2(1)	5(1)	6(1)
C(4)	37(1)	48(1)	44(1)	10(1)	5(1)	4(1)
C(5)	30(1)	37(1)	41(1)	8(1)	2(1)	5(1)
C(6)	32(1)	35(1)	43(1)	9(1)	1(1)	1(1)
C(7)	43(1)	27(1)	53(1)	4(1)	6(1)	-5(1)
C(8)	55(1)	36(1)	46(1)	-7(1)	11(1)	-7(1)
C(9)	38(1)	33(1)	36(1)	-2(1)	0(1)	1(1)
C(10)	48(1)	38(1)	41(1)	-4(1)	4(1)	4(1)
C(11)	54(1)	49(1)	42(1)	1(1)	15(1)	3(1)
C(12)	48(1)	41(1)	44(1)	7(1)	12(1)	-1(1)
C(13)	34(1)	33(1)	38(1)	6(1)	2(1)	1(1)
C(14)	49(1)	32(1)	50(1)	4(1)	15(1)	-2(1)
C(15)	46(1)	27(1)	51(1)	-4(1)	4(1)	-2(1)
C(16)	34(1)	34(1)	43(1)	-4(1)	-3(1)	8(1)
C(17)	49(1)	61(1)	53(1)	8(1)	6(1)	3(1)

Table S5. Hydrogen coordinates (× 10^4) and isotropic displacement parameters (Å^2 × 10^3) for ap19.

	x	y	z	U(eq)
H(5H)	860(40)	4881(16)	2582(17)	84(9)
H(2B)	1747	5852	1465	44
H(6A)	942	3838	1433	44
H(2A)	2488	3352	-1121	53
H(3A)	3395	4605	-1811	57
H(4A)	3546	5962	-1071	52
H(7A)	2168	7650	1360	50
H(8A)	-707	7159	3451	54

H(8B)	1181	6731	3858	54
H(10A)	-1970	6564	4672	51
H(11A)	-3427	5367	5211	57
H(12A)	-3237	3977	4576	52
H(14A)	-753	3090	3779	52
H(14B)	-2700	3205	3210	52
H(15A)	37	2084	1272	50
H(17A)	3788	5252	3053	82
H(17B)	4291	4515	2398	82
H(17C)	3319	4240	3199	82

Table S6. Torsion angles [°] for ap19.

C(8)-O(2)-N(3)-C(7)	166.09(16)	O(2)-C(8)-C(9)-N(4)	22.2(2)
C(14)-O(3)-N(5)-C(15)	-177.77(15)	O(2)-C(8)-C(9)-C(10)	-159.54(16)
C(5)-N(1)-C(1)-C(2)	-1.1(2)	N(4)-C(9)-C(10)-C(11)	-0.3(3)
C(5)-N(1)-C(1)-C(16)	-177.33(15)	C(8)-C(9)-C(10)-C(11)	-178.50(18)
N(1)-C(1)-C(2)-C(3)	0.0(3)	C(9)-C(10)-C(11)-C(12)	-0.9(3)
C(16)-C(1)-C(2)-C(3)	176.25(16)	C(10)-C(11)-C(12)-C(13)	1.1(3)
C(1)-C(2)-C(3)-C(4)	0.7(3)	C(9)-N(4)-C(13)-C(12)	-1.0(2)
C(2)-C(3)-C(4)-C(5)	-0.5(3)	C(9)-N(4)-C(13)-C(14)	-179.49(16)
C(1)-N(1)-C(5)-C(4)	1.4(3)	C(11)-C(12)-C(13)-N(4)	-0.1(3)
C(1)-N(1)-C(5)-C(6)	178.68(15)	C(11)-C(12)-C(13)-C(14)	178.38(18)
C(3)-C(4)-C(5)-N(1)	-0.6(3)	N(5)-O(3)-C(14)-C(13)	-174.88(14)
C(3)-C(4)-C(5)-C(6)	-177.90(16)	N(4)-C(13)-C(14)-O(3)	-11.7(2)
C(7)-N(2)-C(6)-O(1)	7.3(3)	C(12)-C(13)-C(14)-O(3)	169.74(15)
C(7)-N(2)-C(6)-C(5)	-170.31(15)	O(3)-N(5)-C(15)-N(6)	0.1(3)
N(1)-C(5)-C(6)-O(1)	176.77(16)	C(16)-N(6)-C(15)-N(5)	-173.08(18)
C(4)-C(5)-C(6)-O(1)	-5.8(3)	C(15)-N(6)-C(16)-O(4)	-3.2(3)
N(1)-C(5)-C(6)-N(2)	-5.5(2)	C(15)-N(6)-C(16)-C(1)	174.56(15)
C(4)-C(5)-C(6)-N(2)	171.88(16)	N(1)-C(1)-C(16)-O(4)	179.44(16)
O(2)-N(3)-C(7)-N(2)	-0.7(3)	C(2)-C(1)-C(16)-O(4)	3.0(3)
C(6)-N(2)-C(7)-N(3)	175.14(18)	N(1)-C(1)-C(16)-N(6)	1.6(2)
N(3)-O(2)-C(8)-C(9)	168.52(14)	C(2)-C(1)-C(16)-N(6)	-174.80(15)
C(13)-N(4)-C(9)-C(10)	1.2(3)		
C(13)-N(4)-C(9)-C(8)	179.40(16)		

Table S7. Hydrogen bonds for ap19 [Å and °].

D-H...A	**d(D-H)**	**d(H...A)**	**d(D...A)**	**<(DHA)**
O(5)-H(5H)...N(4)	0.90(3)	1.93(3)	2.827(2)	174(2)
O(5)-H(5H)...O(2)	0.90(3)	2.44(2)	2.7935(17)	103.7(18)
O(5)-H(5H)...O(3)	0.90(3)	2.39(2)	2.7864(17)	106.8(18)
N(2)-H(2B)...O(5)	0.88	2.00	2.8523(19)	164.0
N(6)-H(6A)...O(5)	0.88	1.97	2.8273(18)	164.2

D.2. Structure of **2**.CH_3OH [CCDC 874204]

A crystal of the compound (colorless, prism-shaped, size 0.15 × 0.20 × 0.25 mm) was mounted on a glass fiber with grease and cooled to -93 °C in a stream of nitrogen gas controlled with Cryostream Controller 700. Data collection was performed on a Bruker SMART APEX II X-ray diffractometer with graphite-monochromated Mo K_α radiation ($\lambda = 0.71073$ Å), operating at 50 kV and 30 mA over 2θ ranges of 3.86 ~ 52.00º. No significant decay was observed during the data collection. Data were processed on a PC using the Bruker AXS Crystal Structure Analysis Package:[1] Data collection: APEX2 (Bruker, 2010); cell refinement: SAINT (Bruker, 2009); data reduction: SAINT (Bruker, 2009); absorption correction: SADABS (Bruker, 2008); structure solution: XPREP (Bruker, 2008) and SHELXTL (Bruker, 2000); structure refinement: SHELXTL; molecular graphics: SHELXTL; publication materials: SHELXTL. Neutral atom scattering factors were taken from Cromer and Waber.[2] The crystal is monoclinic space group *C*2/m, based on the systematic absences, *E* statistics and successful refinement of the structure. The structure was solved by direct methods. Full-matrix least-square refinements minimizing the function $\sum w\,(F_o^2 - F_c^2)^2$ were applied to the compound. All non-hydrogen atoms were refined anisotropically. For the hydrogen bonded MeOH, the H atoms of the -OH group were located from difference Fourier maps, and refined as riding atoms with Uiso(H) = 1.2 UeqO, while the H atoms of the methyl group were not added. No H atoms on the disordered lattice MeOH were added. All other H atoms were placed in geometrically calculated positions, with C-H = 0.95 (aromatic), and N-H = 0.88 Å, and refined as riding atoms, with Uiso(H) = 1.2 UeqC or N. The -O–N=C-N- part of the molecule and the hydrogen bonded –OH group are disordered. Shelx commands, PART, SAME and SADI were applied to resolve the disorder. Convergence to final $R_1 = 0.0484$ and $wR_2 = 0.1498$ for 1608 (I>2σ(I)) independent reflections, and $R_1 = 0.0537$ and

wR_2 = 0.1617 for all 1864 (R(int) = 0.0175) independent reflections, with 197 parameters and 2 restraints, were achieved.[3] The largest residual peak and hole to be 0.568 and – 0.213 e/Å^3, respectively. Crystallographic data, atomic coordinates and equivalent isotropic displacement parameters, bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates and isotropic displacement parameters, torsion angles and the hydrogen bonding information are given in Tables S8 to 15. The molecular structure and the cell packing are shown in Figure S4.

[1] Bruker AXS Crystal Structure Analysis Package: Bruker (2000). SHELXTL. Version 6.14. Bruker AXS Inc., Madison, Wisconsin, USA; Bruker (2008). SADABS. Version 2008/1. Bruker AXS Inc., Madison, Wisconsin, USA; Bruker (2008). XPREP. Version 2008/2. Bruker AXS Inc., Madison, Wisconsin, USA; Bruker (2009). SAINT. Version 7.68A. Bruker AXS Inc., Madison,Wisconsin, USA; Bruker (2010). APEX2. Version 2010.3-0. Bruker AXS Inc., Madison, Wisconsin, USA.

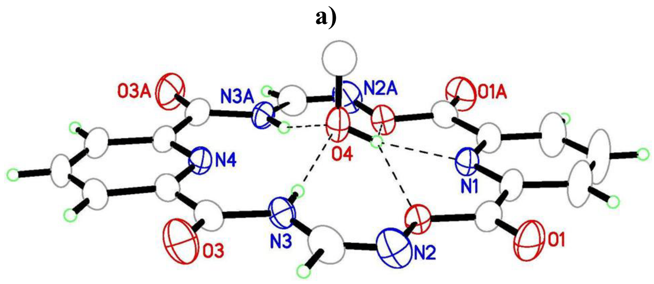
[2] Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, UK, 1974; Vol. 4, Table 2.2 A.

[3] $R_1 = \sum||Fo| - |Fc|| / \sum|Fo|$

$wR_2 = \{\sum[w(Fo^2 - Fc^2)^2] / \sum[w(Fo^2)^2]\}^{1/2}$

$(w = 1 / [\sigma^2(Fo^2) + (0.1054P)^2 + 0.7778P]$, where $P = [\mathrm{Max}(Fo^2, 0) + 2Fc^2] / 3)$

Figure S4. a) Molecular Structure (Displacement ellipsoids for non-H atoms are shown at the 50% probability level and H atoms are represented by circles of arbitrary size).



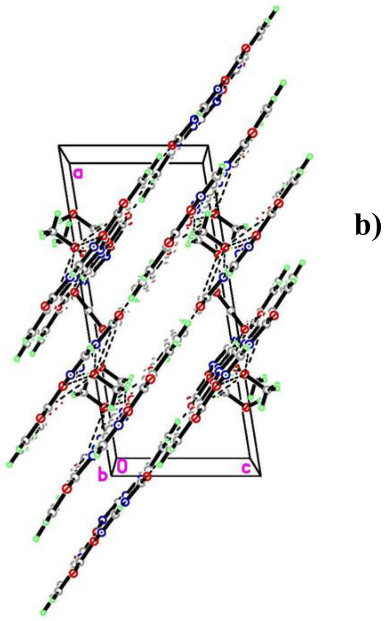


Table S8. Crystal data and structure refinement for ap33b

Identification code	ap33b	
Empirical formula	C17.50 H15 N6 O7.25	
Formula weight	425.36	
Temperature	180(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/m	
Unit cell dimensions	a = 17.5387(3) Å	α= 90°.
	b = 13.3386(2) Å	β= 99.1200(10)°.
	c = 7.87380(10) Å	γ = 90°.
Volume	1818.72(5) Å^3	
Z	4	
Density (calculated)	1.553 Mg/m^3	
Absorption coefficient	0.124 mm^{-1}	
F(000)	880	
Crystal size	0.25 x 0.20 x 0.15 mm^3	
Theta range for data collection	1.93 to 26.00°.	
Index ranges	-12<=h<=21, -16<=k<=16, -9<=l<=9	
Reflections collected	4940	
Independent reflections	1864 [R(int) = 0.0175]	
Completeness to theta = 26.00°	99.2 %	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9816 and 0.9697	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1864 / 2 / 197	
Goodness-of-fit on F^2	1.083	
Final R indices [I>2sigma(I)]	R1 = 0.0484, wR2 = 0.1498	
R indices (all data)	R1 = 0.0537, wR2 = 0.1617	
Extinction coefficient	0.0035(13)	
Largest diff. peak and hole	0.568 and -0.213 e.Å^{-3}	

Table S9. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters (Å$^2 \times 10^3$) for ap33b. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	1873(1)	2634(1)	-3773(2)	48(1)
O(3)	4860(1)	2630(1)	2320(2)	55(1)
O(5)	0	0	0	124(4)
N(1)	2121(1)	0	-3304(2)	31(1)
N(4)	4636(1)	0	1830(2)	31(1)
C(1)	807(2)	0	-5787(5)	82(1)
C(2)	1139(1)	893(2)	-5180(3)	62(1)
C(3)	1797(1)	855(1)	-3931(2)	37(1)
C(4)	2144(1)	1833(1)	-3277(2)	35(1)
O(2)	2804(6)	1771(8)	-2099(17)	28(1)
N(2)	3093(11)	2674(11)	-1480(18)	48(3)
C(5)	3672(9)	2541(10)	-330(20)	42(2)
N(3)	3971(13)	1733(11)	463(17)	31(2)
O(2A)	4050(20)	1718(18)	490(30)	38(5)
N(2A)	3725(15)	2737(16)	-140(30)	37(3)
C(5A)	3180(20)	2620(20)	-1520(50)	49(6)
N(3A)	2743(18)	1580(20)	-2010(50)	37(4)
C(6)	4610(1)	1826(1)	1778(2)	37(1)
C(7)	4970(1)	855(1)	2434(2)	34(1)
C(8)	5650(1)	894(2)	3630(2)	43(1)
C(9)	5991(1)	0	4215(3)	47(1)
C(10)	2608(2)	0	1290(3)	47(1)
C(11)	575(5)	0	-717(14)	104(3)
O(4)	3084(1)	0	-21(2)	38(1)

Table S10. Bond lengths [Å] and angles [°] for ap33b.

O(1)-C(4)	1.2096(19)	C(5)-H(5A)	0.9500
O(3)-C(6)	1.210(2)	N(3)-C(6)	1.405(19)
O(5)-C(11)	1.232(13)	N(3)-H(3A)	0.8800
O(5)-C(11)#1	1.232(13)	O(2A)-C(6)	1.31(3)
N(1)-C(3)#2	1.3339(19)	O(2A)-N(2A)	1.52(4)
N(1)-C(3)	1.3339(19)	N(2A)-C(5A)	1.33(4)
N(4)-C(7)	1.3348(18)	C(5A)-N(3A)	1.60(5)

N(4)-C(7)#2	1.3348(18)	C(5A)-H(5AA)	0.9500
C(1)-C(2)	1.379(3)	N(3A)-H(3AA)	0.8800
C(1)-C(2)#2	1.379(3)	C(6)-C(7)	1.496(2)
C(1)-H(1A)	0.9500	C(7)-C(8)	1.399(2)
C(2)-C(3)	1.393(2)	C(8)-C(9)	1.380(2)
C(2)-H(2A)	0.9500	C(8)-H(8A)	0.9500
C(3)-C(4)	1.495(2)	C(9)-C(8)#2	1.380(2)
C(4)-O(2)	1.366(12)	C(9)-H(9A)	0.9500
C(4)-N(3A)	1.37(3)	C(10)-O(4)	1.426(3)
O(2)-N(2)	1.367(19)	O(4)-H(4H)	0.90(4)
N(2)-C(5)	1.26(2)	O(4)-H(4HA)	0.91(5)
C(5)-N(3)	1.31(3)		

C(11)-O(5)-C(11)#1	180.0(11)	C(6)-O(2A)-N(2A)	110.6(17)
C(3)#2-N(1)-C(3)	117.55(19)	C(5A)-N(2A)-O(2A)	110(2)
C(7)-N(4)-C(7)#2	117.42(18)	N(2A)-C(5A)-N(3A)	123(3)
C(2)-C(1)-C(2)#2	119.6(2)	N(2A)-C(5A)-H(5AA)	118.3
C(2)-C(1)-H(1A)	120.2	N(3A)-C(5A)-H(5AA)	118.3
C(2)#2-C(1)-H(1A)	120.2	C(4)-N(3A)-C(5A)	104.3(19)
C(1)-C(2)-C(3)	118.07(18)	C(4)-N(3A)-H(3AA)	127.9
C(1)-C(2)-H(2A)	121.0	C(5A)-N(3A)-H(3AA)	127.9
C(3)-C(2)-H(2A)	121.0	O(3)-C(6)-O(2A)	123.9(11)
N(1)-C(3)-C(2)	123.33(16)	O(3)-C(6)-N(3)	122.7(6)
N(1)-C(3)-C(4)	119.45(14)	O(2A)-C(6)-N(3)	4(2)
C(2)-C(3)-C(4)	117.22(15)	O(3)-C(6)-C(7)	122.38(15)
O(1)-C(4)-O(2)	121.3(5)	O(2A)-C(6)-C(7)	113.5(11)
O(1)-C(4)-N(3A)	131.9(12)	N(3)-C(6)-C(7)	114.9(6)
O(2)-C(4)-N(3A)	12.1(14)	N(4)-C(7)-C(8)	123.41(16)
O(1)-C(4)-C(3)	122.83(15)	N(4)-C(7)-C(6)	118.66(14)
O(2)-C(4)-C(3)	115.8(4)	C(8)-C(7)-C(6)	117.91(15)
N(3A)-C(4)-C(3)	105.1(12)	C(9)-C(8)-C(7)	118.10(17)
C(4)-O(2)-N(2)	114.5(8)	C(9)-C(8)-H(8A)	121.0
C(5)-N(2)-O(2)	110.0(12)	C(7)-C(8)-H(8A)	121.0
N(2)-C(5)-N(3)	132.3(14)	C(8)#2-C(9)-C(8)	119.5(2)
N(2)-C(5)-H(5A)	113.8	C(8)#2-C(9)-H(9A)	120.2
N(3)-C(5)-H(5A)	113.8	C(8)-C(9)-H(9A)	120.2

C(5)-N(3)-C(6)	119.4(12)	C(10)-O(4)-H(4H)	117(3)
C(5)-N(3)-H(3A)	120.3	C(10)-O(4)-H(4HA)	117(4)
C(6)-N(3)-H(3A)	120.3	H(4H)-O(4)-H(4HA)	126(6)

Symmetry transformations used to generate equivalent atoms: #1 -x,-y,-z #2 x,-y,z

Table S11. Anisotropic displacement parameters (Å^2 × 10^3) for ap33b. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	50(1)	39(1)	53(1)	11(1)	-2(1)	14(1)
O(3)	49(1)	48(1)	62(1)	-18(1)	-6(1)	-15(1)
O(5)	203(14)	115(8)	51(4)	0	15(6)	0
N(1)	28(1)	34(1)	28(1)	0	-1(1)	0
N(4)	26(1)	44(1)	23(1)	0	0(1)	0
C(1)	72(2)	74(2)	78(2)	0	-52(2)	0
C(2)	57(1)	55(1)	61(1)	8(1)	-28(1)	8(1)
C(3)	34(1)	43(1)	31(1)	5(1)	-4(1)	6(1)
C(4)	34(1)	36(1)	34(1)	7(1)	3(1)	8(1)
O(2)	30(2)	13(3)	40(2)	6(2)	-2(2)	0(2)
N(2)	41(4)	38(5)	64(4)	-5(3)	4(3)	0(2)
C(5)	43(3)	19(5)	62(3)	-11(3)	5(3)	-5(3)
N(3)	30(3)	30(4)	31(4)	-8(3)	0(2)	-5(2)
O(2A)	36(8)	30(6)	47(8)	0(5)	0(4)	-4(4)
N(2A)	45(5)	9(7)	54(6)	-5(4)	-2(4)	-5(4)
C(5A)	41(9)	17(6)	87(13)	-15(6)	3(7)	-1(5)
N(3A)	42(5)	16(8)	51(6)	3(5)	0(3)	-9(5)
C(6)	32(1)	45(1)	33(1)	-9(1)	5(1)	-11(1)
C(7)	28(1)	50(1)	24(1)	-5(1)	3(1)	-7(1)
C(8)	30(1)	70(1)	29(1)	-7(1)	2(1)	-11(1)
C(9)	24(1)	87(2)	27(1)	0	-5(1)	0
C(10)	50(1)	36(1)	53(2)	0	5(1)	0
C(11)	71(5)	113(7)	108(8)	0	-49(5)	0
O(4)	36(1)	34(1)	39(1)	0	-11(1)	0

Table S12. Hydrogen coordinates (×10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for ap33b.

	x	y	z	U(eq)
H(1A)	351	0	-6619	98
H(2A)	926	1517	-5600	74
H(5A)	3942	3140	33	50
H(3A)	3774	1139	173	37
H(5AA)	3041	3186	-2236	59
H(3AA)	2861	984	-1572	44
H(8A)	5871	1518	4028	52
H(9A)	6457	0	5015	56
H(4H)	2840(30)	0	-1120(60)	45
H(4HA)	3610(30)	0	340(80)	45

Table S13. Torsion angles [°] for ap33b.

C(2)#2-C(1)-C(2)-C(3)	-1.4(6)
C(3)#2-N(1)-C(3)-C(2)	0.7(3)
C(3)#2-N(1)-C(3)-C(4)	-179.54(11)
C(1)-C(2)-C(3)-N(1)	0.3(4)
C(1)-C(2)-C(3)-C(4)	-179.4(3)
N(1)-C(3)-C(4)-O(1)	-178.96(16)
C(2)-C(3)-C(4)-O(1)	0.8(3)
N(1)-C(3)-C(4)-O(2)	2.5(6)
C(2)-C(3)-C(4)-O(2)	-177.7(6)
N(1)-C(3)-C(4)-N(3A)	-3.3(14)
C(2)-C(3)-C(4)-N(3A)	176.5(14)
O(1)-C(4)-O(2)-N(2)	3.6(14)
N(3A)-C(4)-O(2)-N(2)	-150(10)
C(3)-C(4)-O(2)-N(2)	-177.9(9)
C(4)-O(2)-N(2)-C(5)	176.0(12)
O(2)-N(2)-C(5)-N(3)	-9(3)
N(2)-C(5)-N(3)-C(6)	-176.8(17)
C(6)-O(2A)-N(2A)-C(5A)	177(3)
O(2A)-N(2A)-C(5A)-N(3A)	18(5)
O(1)-C(4)-N(3A)-C(5A)	-13(3)
O(2)-C(4)-N(3A)-C(5A)	18(8)
C(3)-C(4)-N(3A)-C(5A)	172(2)

N(2A)-C(5A)-N(3A)-C(4)	169(3)
N(2A)-O(2A)-C(6)-O(3)	-3(3)
N(2A)-O(2A)-C(6)-N(3)	68(26)
N(2A)-O(2A)-C(6)-C(7)	-178.3(15)
C(5)-N(3)-C(6)-O(3)	6.4(18)
C(5)-N(3)-C(6)-O(2A)	-104(26)
C(5)-N(3)-C(6)-C(7)	-172.3(12)
C(7)#2-N(4)-C(7)-C(8)	1.1(3)
C(7)#2-N(4)-C(7)-C(6)	179.83(11)
O(3)-C(6)-C(7)-N(4)	176.69(16)
O(2A)-C(6)-C(7)-N(4)	-8.4(14)
N(3)-C(6)-C(7)-N(4)	-4.6(8)
O(3)-C(6)-C(7)-C(8)	-4.5(2)
O(2A)-C(6)-C(7)-C(8)	170.4(14)
N(3)-C(6)-C(7)-C(8)	174.2(8)
N(4)-C(7)-C(8)-C(9)	-0.1(3)
C(6)-C(7)-C(8)-C(9)	-178.88(15)
C(7)-C(8)-C(9)-C(8)#2	-0.9(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x,-y,-z   #2 x,-y,z

Table S14. Hydrogen bonds for ap33b [Å and °].

D-H...A	**d(D-H)**	**d(H...A)**	**d(D...A)**	**<(DHA)**
O(4)-H(4H)...O(2)	0.90(4)	2.481(17)	2.871(10)	106.5(11)
O(4)-H(4H)...N(1)	0.90(4)	1.97(4)	2.855(2)	168(4)
N(3)-H(3A)...O(4)	0.88	1.93	2.780(16)	160.6
O(4)-H(4HA)...O(2A)	0.91(5)	2.42(3)	2.84(3)	108.2(14)
N(3A)-H(3AA)...O(4)	0.88	1.79	2.64(3)	160.5

Symmetry transformations used to generate equivalent atoms:

#1 -x,-y,-z   #2 x,-y,z