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Two distinct anion-binding modes and their relative stabilities

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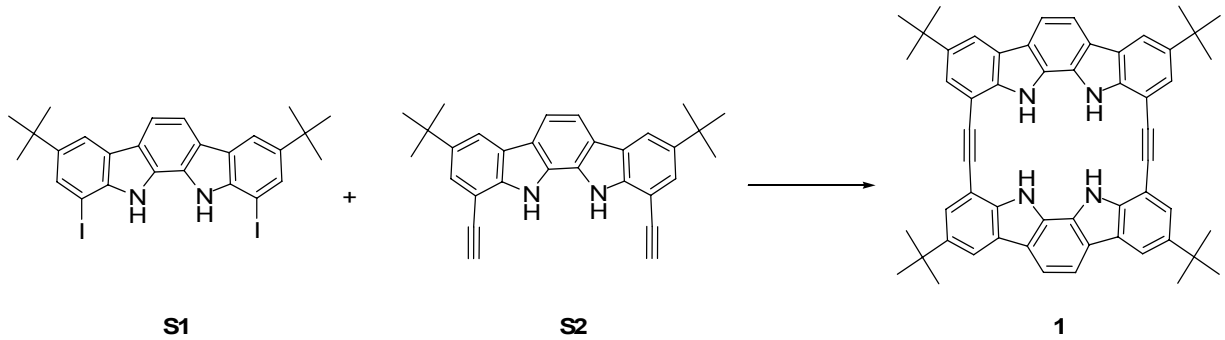
Contents

1. Synthesis
2. Computer Modeling
3. Binding Studies
4. ^{1}H NMR Studies
5. X-ray Crystallographic Analysis

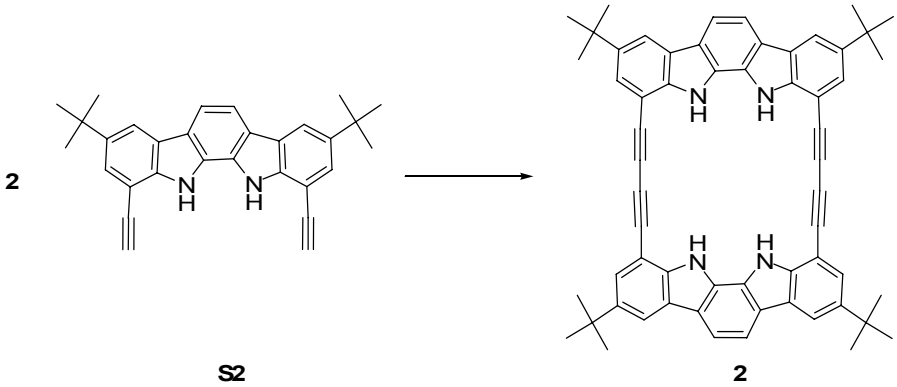
1. Synthesis



Compounds **S1** and **S2** were prepared following the procedures described previously.[1]

Macrocycle **1**: Copper-free Sonogashira-type coupling between **S1** and **S2** was carried out by following the method described by Soheili et. al.[2] In a glovebox, **S1** (0.30 g, 0.48 mmol), DABCO (0.11 g, 2.0 equiv) and $(AllylPdCl)_2$ (9 mg, 0.05 equiv) were placed in a Schlenk flask, and degassed CH_3CN (150 mL) and toluene (30 mL) were added. Then, $P(t\text{-}Bu)_3$ (24 mg, 0.25 equiv) and compound **S2** (0.20 g, 0.48 mmol) were sequentially added. The solution was stirred for 2.5 d at room temperature and was concentrated. The residue was taken up in CH_2Cl_2, washed with deionized water, and concentrated. After purified by column chromatography (silica gel, CH_2Cl_2/acetone, 100:1), the product was repeatedly washed with deionized water, aceotonitrile and methanol to give **1** as an off-white solid. Yields were in between 15% and 70%, depending on the washing times with organic solvents and on the quality of reagents and solvents used for the reaction. Mp > 300 °C; ^1H NMR (400 MHz, acetone-d_6, 25 °C): δ (ppm) 10.80 (s, 4H, NH), 8.37 (s, 4H, ArH), 8.08 (s, 4H, ArH), 7.83 (s, 4H, ArH), 1.55 ppm (s, 36H, *t*-Bu); ^{13}C NMR (126 MHz, DMSO, 298 K): δ (ppm) 137.3, 126.1, 125.1, 123.4, 119.8, 112.1, 108.1, 83.5, 79.7, 33.5, 30.7, 25.1 ppm; IR (thin film) 3362 cm^{-1} (NH); HRMS-FAB (m/z) calcd for $C_{56}H_{52}N_4$ 780.4192, found 780.4192.

[1] K.-J. Chang, D. Moon, M. S. Lah and K.-S. Jeong, *Angew. Chem. Int. Ed.,* 2005, **44**, 7926-7929.
[2] A. Soheili, J. Albaneze-Walker, J. A. Murry, P. G. Dormer and D. L. Hughes, *Org. Lett.*, 2003, **5**, 4191-4194.



Macrocycle **2**: **S2** (1.7 g, 3.9 mmol) was dissolved in pyridine (50 mL) and $Cu(OAc)_2{\cdot}H_2O$ (1.8 g, 9.0 mmol) was added,[3] and the mixture was stirred overnight (31 h) at room temperature. After filtration through Celite, the filtrate was concentrated. The residue was taken up in CH_2Cl_2, washed with saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated. After purified by column chromatography (silica gel, CH_2Cl_2), the product was repeatedly washed with deionized water, aceotonitrile and methanol to give **2** as a yellow solid (1.0 g, 61%): Mp > 300 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 298 K) δ (ppm) 8.75 (s, 4H, NH), 8.22 (s, 4H, ArH), 7.98 (s, 4H, ArH), 7.72 (s, 4H, ArH), 1.50 ppm (s, 36H, *t*-Bu); ^{13}C NMR (100 MHz, CD_2Cl_2, 298 K) δ (ppm) 143.5, 139.6, 126.6, 125.5, 124.31, 122.4, 118.6, 112.9, 103.6, 79.4, 77.8, 34.8, 31.7 ppm; IR (thin film) 3350 cm^{-1} (NH); HRMS (FAB) *m/z* calcd for $C_{60}H_{52}N_4$ 828.4192, found 828.4190.

[3] G. Eglinton and A. R. Galbraith, *J. Chem. Soc.*, 1959, 889-896; K. Sonogashira, *in Comprehensive Organic Synthesis* (Eds. B. M. Trost, E. Fleming, G. Patterden), Pergamon, Oxford, 1991, Vol. 3, pp. 551-561.

2. Computer Modeling

Energy-minimized structures of **1** and **2** were obtained from MacroModel[4] 7.1 program on a Silicon Graphics Indigo2 IMPACT workstation. The structures was generated with MMFF* force field [5] via 1000 separated search steps in Monte Carlo conformational search. [6]

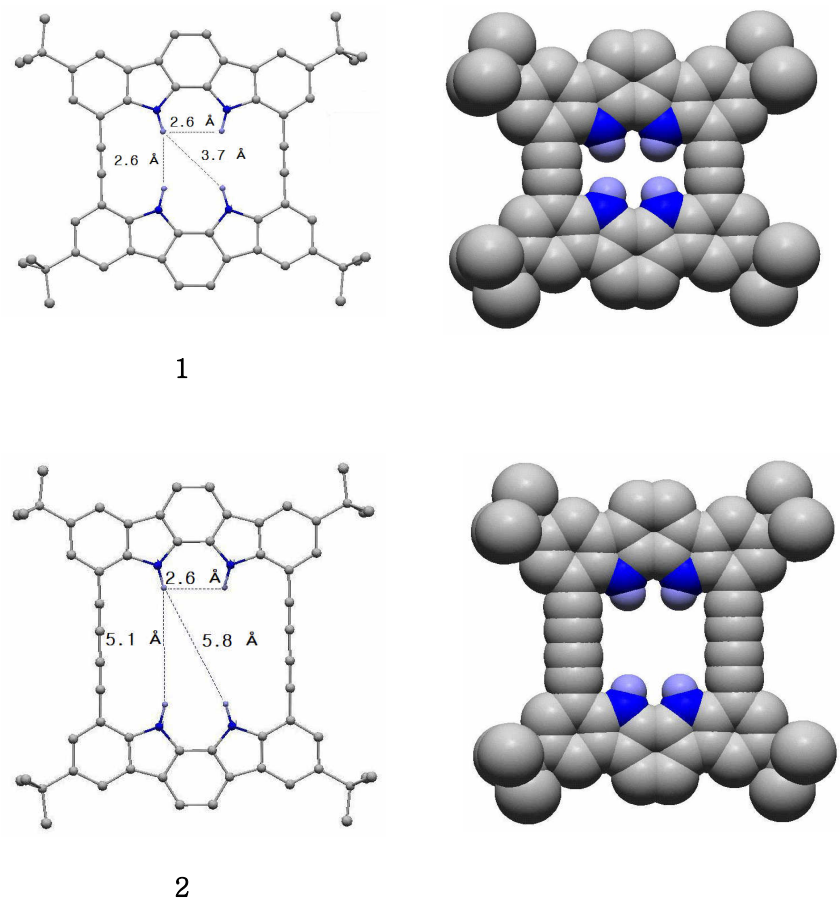


Figure S1. Energy-minimized structures of macrocycle **1** and **2**

[4] F. Mohamedi, N. G. T. Richards, W. C. H. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson and W. C. Still, *J. Comp. Chem*., 1990, **11**, 440-467.
[5] T. A. Halgren, *J. Comp. Chem*., 1996, **17**, 490-519.
[6] M. Saunders, K. N. Houk, Y. D. Wu, W. C. Still, M. Lipton, G. Chang and W. C. Guida, *J. Am. Chem. Soc.,* 1990, 112, 1419-1427.

3. Binding Studies

Titrations: The titration experiments were conducted using UV-visible spectroscopy and were all duplicated at 23 ± 1 ^{o}C in 10% (v/v) MeOH in acetone. The stock solution (2.0×10^{-5} M) of **1** or **2** was first prepared. Using this solution as a solvent, a stock solution ($6.0 \times 10^{-4} – 6.0 \times 10^{-1}$ M, depending on the binding affinity) of an anion was prepared. A 2.0 mL of **1** or **2** was transferred to a UV cell, and an initial absorption spectrum was taken. To this solution were added small portions of the anion solution (10 μL initially, then 20-50 μL, and finally 100-200 μL), and the spectrum was recorded after each addition and 12-22 data points were obtained. Upon addition of an anion, the UV-visible spectra were gradually changed, showing multiple isosbestic points at wavelengths. The association constants (K_a) were determined by nonlinear curve fitting of the titration curves,[7] plotting the absorbance change at two different wavelengths against equivalents of an anion added.

Job's plots:[8] Stock solutions of the macrocycle (7.0×10^{-5} M) and an anion (7.0×10^{-5} M) were separately prepared in 10% MeOH in acetone. The UV-visible spectrum was taken for each of 10 different solutions containing total 1.5 mL of the macrocycle and an anion in the following ratios: 1.50:0, 1.35:0.15, 1.20:0.30, 1.05:0.45, 0.90:0.60, 0.75:0.75, 0.60:0.90, 0.45:1.05, 0.30:1.20, and 0.15:1.35. Job's plots were constructed by plotting $[HG]\cdot\alpha$ against mol fraction of the macrocycle (see below).

$$A = A_H + A_{HG} \quad \cdots\cdots \quad (1)$$

Here, A is the observed UV absorbance of the each solution, and A_H and A_{HG} are corresponding to the UV absorbance of the free macrocycle and its complex, respectively. According to Beer-Lambert's law and by substituting $\alpha = \frac{\varepsilon_{HG}}{\varepsilon_H} - 1 = \frac{\Delta\varepsilon_{HG}}{\varepsilon_H}$, the equation (1) becomes

$$[HG]\alpha = \frac{A}{b\varepsilon_H} - [H]_0 \quad \cdots\cdots \quad (2)$$

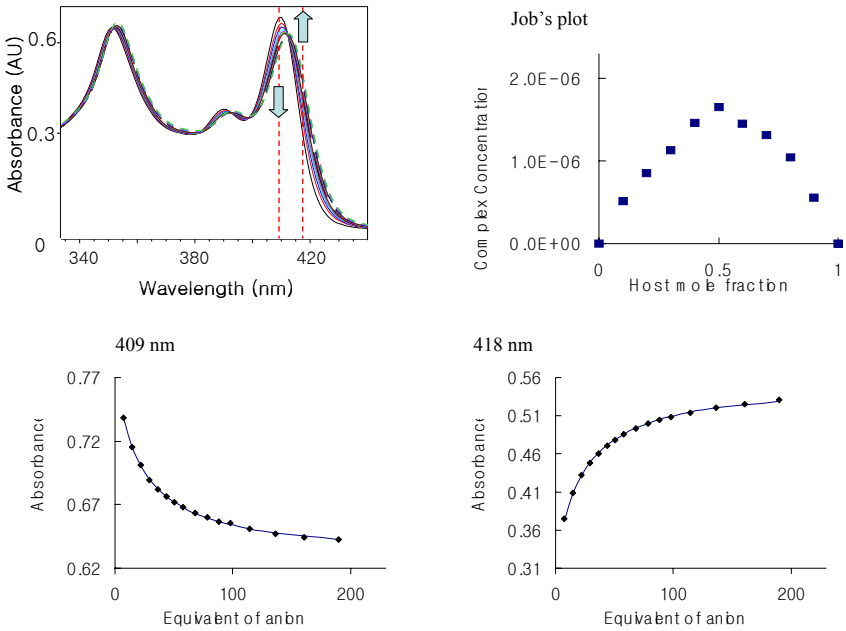
[7] J. R Long, R. S. Drago, *J. Chem. Edu.*, 1982, **59**, 1037-1039.

[8] (a) K. A. Connors, *Binding Constants*, John Wiley & Sons, New York, 1987, pp. 24–28; (b) H.-J. Schneider, A. K. Yatsimirsky, Principle and Methods in Supramolecular Chemsitry, John Wiley & Sons, New York, 2000, pp. 148–149.

[Representative Titration Data] - The association constants reported in Table 1 are all the average ones from duplicated experiments and thus the figures are slightly different in some anions.

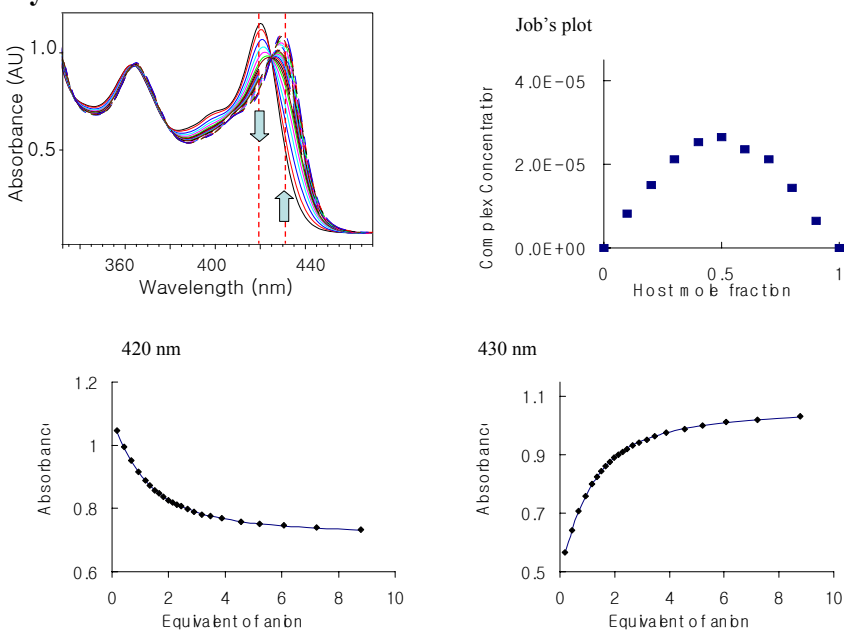
a) Azide

(i) with macrocyle 1



In titration curves, theoretical lines were generated by fitting with $K_a = 2.4 \times 10^3$ M^{-1} (409 nm) and 2.2×10^3 M^{-1} (418 nm), respectively.

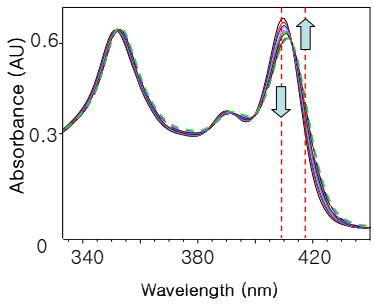
(ii) with macrocyle 2

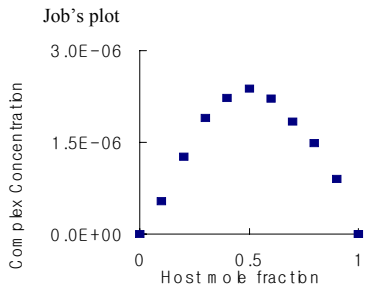


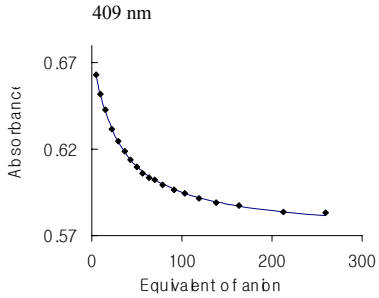
In titration curves, theoretical lines were generated by fitting with $K_a = 7.6 \times 10^4$ M^{-1} (420 nm) and 8.2×10^4 M^{-1} (430 nm), respectively.

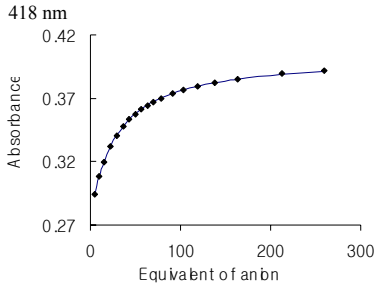
b) Chloride (a halide)

(i) with macrocyle 1



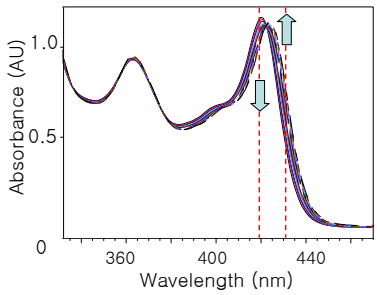


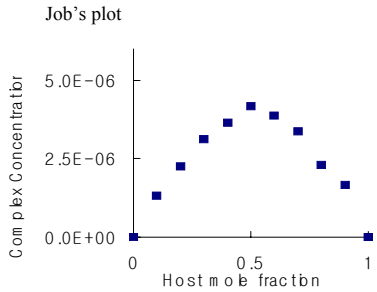


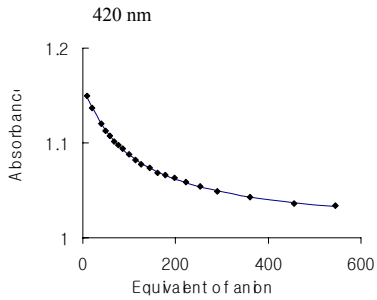


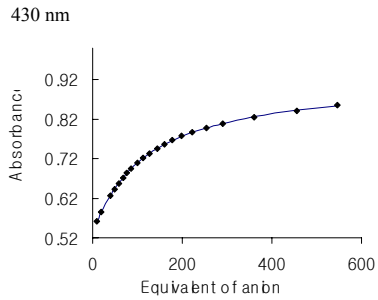
In titration curves, theoretical lines were generated by fitting with $K_a = 1.8 \times 10^3$ M^{-1} (409 nm) and 1.9×10^3 M^{-1} (418 nm), respectively.

(ii) with macrocyle 2





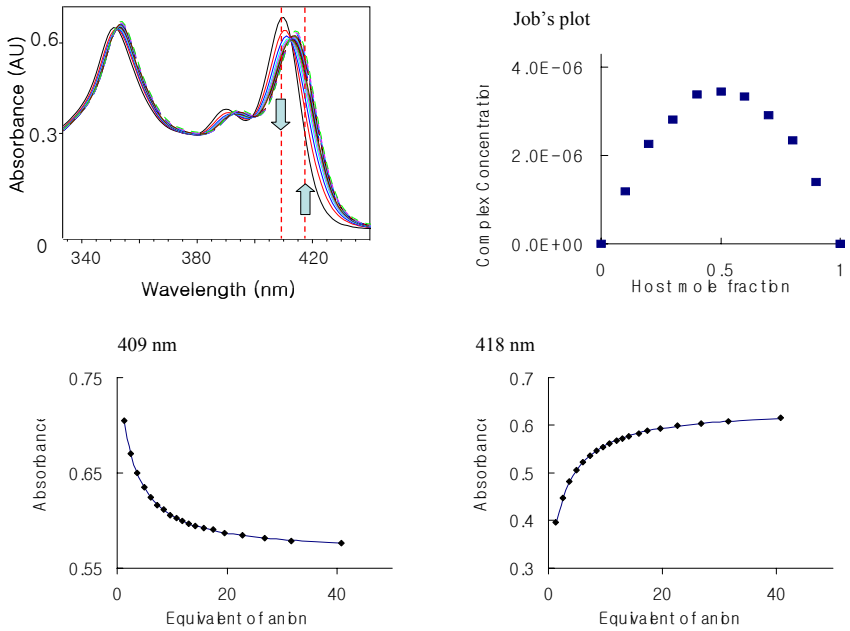




In titration curves, theoretical lines were generated by fitting with $K_a = 4.2 \times 10^2$ M^{-1} (420 nm) and 4.3×10^2 M^{-1} (430 nm), respectively.

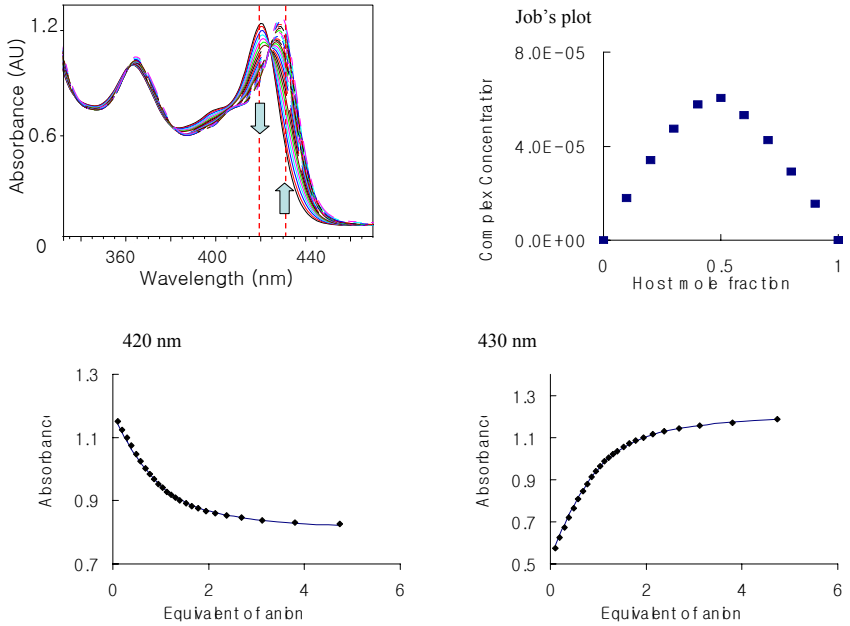
c) Acetate (an oxyanion)

(i) with macrocyle 1



In titration curves, theoretical lines were generated by fitting with $K_a = 2.1 \times 10^4$ M^{-1} (409 nm) and 1.7×10^4 M^{-1} (418 nm), respectively.

(ii) with macrocyle 2



In titration curves, both theoretical lines were generated by fitting with $K_a = 1.8 \times 10^5$ M^{-1} (420 nm, 430 nm).

4. ^{1}H NMR studies

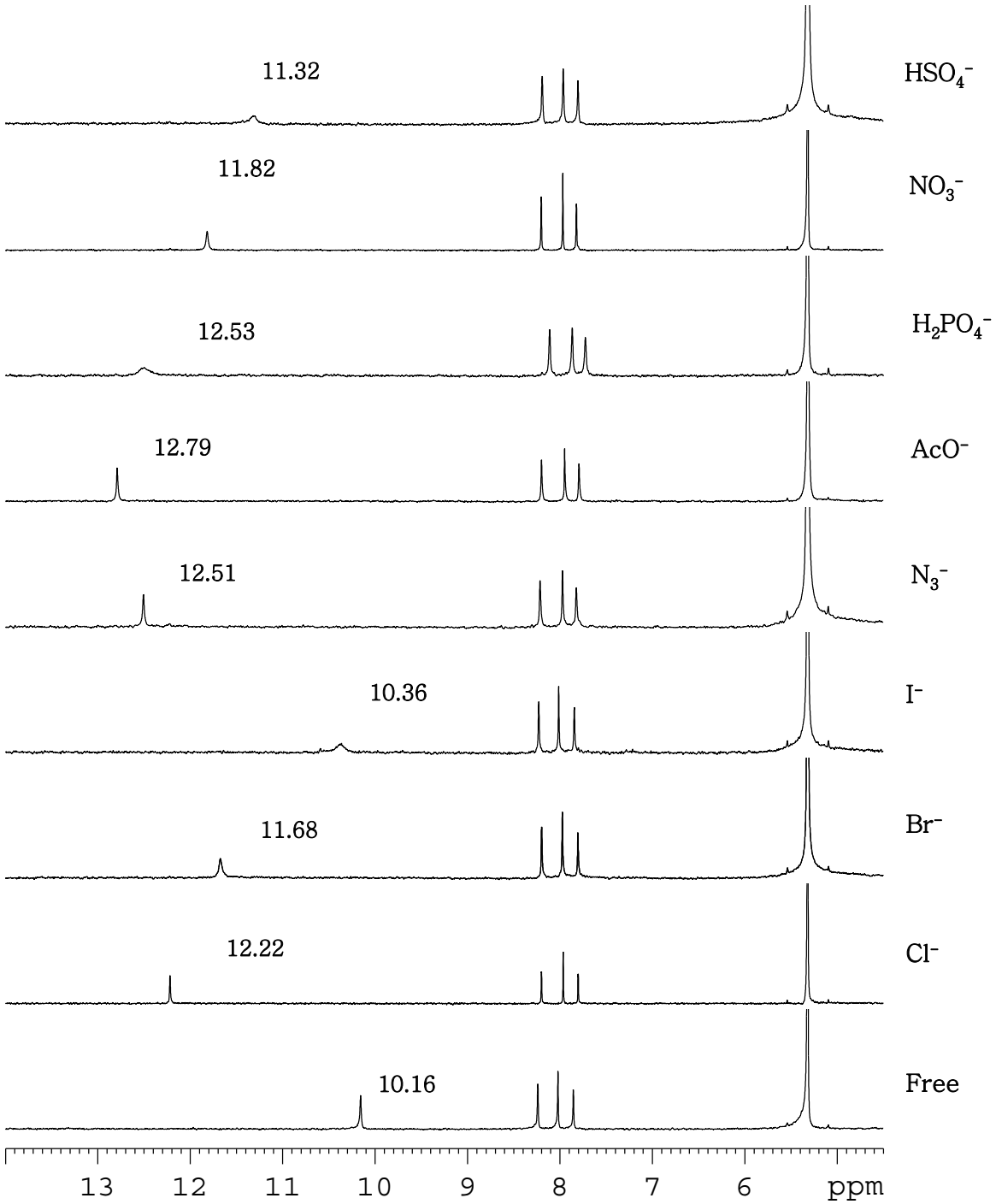


Figure S2. Partial ^{1}H NMR spectra (400 MHz, 1% v/v acetone-d_6/CD_2Cl_2, 25 ^oC) of **1** (0.2 mM) upon addition of anions (3 equiv)

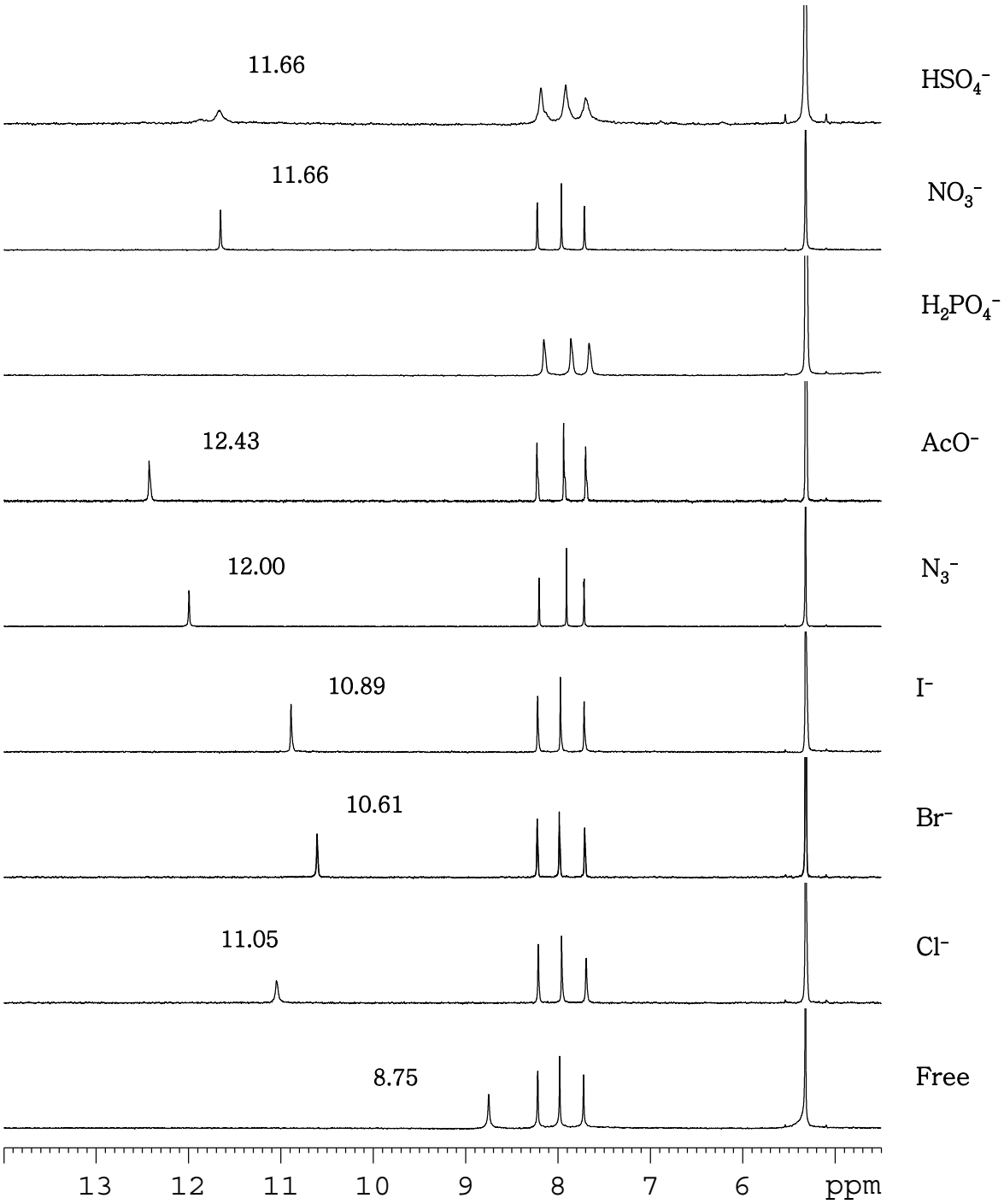


Figure S3. Partial ^{1}H NMR spectra (400 MHz, CD_2Cl_2, 25 ^oC) of **2** (0.8 mM) upon addition of anions (3 equiv). In the case of $H_2PO_4^-$, the NH signal was broadened and disappeared around 12.9 ppm.

5. X-ray crystallographic Analysis

The crystals were coated with paratone oil to prevent the loss of crystallinity upon exposure to air. The diffraction data were measured with synchrotron radiation (λ = 0.70000 Å) using a 4AMXW ADSC Quantum-210 detector with a platinum-coated silicon double-crystal monochromator at the Pohang Accelerator Laboratory, Korea. ADSC Quantum-210 ADX program[9] was used for data collection and the HKL2000 (*Ver*. 0.98.689)[10] was used for cell refinement, reduction, and absorption correction. All structures were solved by direct methods and refined by full-matrix least-squares calculations with the SHELXTL-PLUS software package.[11]

[(tetrabutylammonium)$_3$(**1N$_3$**)$_3$]3.5(diethylether): $C_{230}H_{299}N_{24}O_{3.5}$, fw = 3455.93, triclinic, space group *P*$\bar{1}$, T = 90(2) K, a = 22.506(5) Å, b = 22.564(5) Å, c = 22.614(5) Å, α = 65.145(5)°, β = 85.503(5)°, γ = 80.707(5)°, V = 10283(4) Å^3, Z = 2. ρ_{calc} = 1.116 g/cm^{-3}, μ(synchrotron, λ = 0.70000 Å) = 0.066 mm^{-1}. Three **1** with a statistically disordered *tert*-butyl group, three N_3^- anions, three tetrabutylammonium cations, and four diethyl ether sites were found in an asymmetric unit. Because the geometry of all diethylether sites was behaving badly during the least squares refinement, their refinement was performed with geometry restraints using DFIX and DANG commands. One disordered diethyl ether is located around a crystallographic inversion center. Another disordered one was identified and refined with partial occupancy factors, while one of its disordered methyl residue could not be identified in the difference Fourier map. All non-hydrogen atoms except the atoms in the disordered *tert*-butyl group of **1** and the structural solvent molecules were refined anisotropically. Four hydrogen atoms attached to the nitrogen atoms could be found in the difference Fourier map and were refined with isotropic displacement coefficients, while the remaining hydrogen atoms except the hydrogen atoms on the three structural solvents were assigned isotropic displacement coefficients U(H) = 1.2 (C) or 1.5U (C_{methyl}),

[9] A. J. Arvai, C. Nielsen, ADSC Quantum-210 ADX Program, Area Detector System Corporation; Poway, CA, USA, **1983**.
[10] Z. Otwinowski, W. Minor, in *Methods in Enzymology*, ed. Carter, Jr., C. W.; Sweet, R. M. Academic Press, New York, 1997, vol. 276, part A, pp. 307-326.
[11] G. M. Sheldrick, SHELXTL-PLUS, Crystal Structure Analysis Package; Bruker Analytical X-Ray; Madison, WI, USA, 1997.

and their coordinates were allowed to ride on their respective atoms. Refinement converged to final R1 = 0.0704 (I > 2σ(I)), wR2 = 0.2050 for all data, GOF = 1.072, max./min. residual electron density 1.254 / -0.638 e·Å^3. A summary of the crystal and intensity data is given in Table S1.

[(tetrabutylammonium)(**2**N_3)](hexane): $C_{88}H_{102}N_8$, fw = 1199.72, monoclinic, space group $P2_1/c$, T = 93(2) K, a = 18.459(4) Å, b = 17.029(3) Å, c = 12.014(2) Å, β = 103.43(3)°, V = 3673.2(13) Å^3, Z = 2. ρ_{calc} = 1.085 g/cm^{-3}, μ(synchrotron, λ = 0.70000 Å) = 0.063 mm^{-1}. **2** with a statistically disordered *tert*-butyl group and N_3^- anion were found at one crystallographic inversion center, and a disordered tetrabutylammonium ion were found at another crystallographic inversion center along with a disordered hexane site at the other crystallographic inversion center as an asymmetric unit. Since the C-C bond of the disordered *tert*-butyl group and the geometry of the disordered hexane were behaving badly during the least squares refinement, the refinement was performed with geometry restraints using DFIX and DANG commands. All non-hydrogen atoms except the atoms in all the disordered residues were refined anisotropically. Four hydrogen atoms attached to the nitrogen could be located in the difference Fourier map and were refined with isotropic displacement coefficients while the other hydrogen atoms except the hydrogen atoms on the disordered tetrabutylammonium ion and the disordered hexane were assigned isotropic displacement coefficients U(H) = 1.2 (C) or 1.5U (C_{methyl}), and their coordinates were allowed to ride on their respective atoms. The geometrically restrained methylene hydrogen atoms on the disordered tetrabutylammonium ion and the disordered hexane were allowed to ride on their respective atoms, and the methyl hydrogen atoms were not included in the riding model. Refinement converged to final R1 = 0.0946 (I > 2σ(I)), wR2 = 0.2671 for all data, GOF = 1.070, max./min. residual electron density 0.905 / -0.400 e·Å^3. A summary of the crystal and intensity data is given in Table S2.

Table S1. Crystal data and structure refinement for [(tetrabutylammonium)$_3$(**1N$_3$**)$_3$]3.5(diethyl ether).

Empirical formula	C230 H299 N24 O3.50	
Formula weight	3455.93	
Temperature	90(2) K	
Wavelength	0.70000 Å	
Crystal system	Triclinic	
Space group	$P\bar{1}$	
Unit cell dimensions	a = 22.506(5) Å	α = 65.145(5)°.
	b = 22.564(5) Å	β = 85.503(5)°.
	c = 22.614(5) Å	γ = 80.707(5)°.
Volume	10283(4) Å^3	
Z	2	
Density (calculated)	1.116 Mg/m^3	
Absorption coefficient	0.066 mm^{-1}	
F(000)	3750	
Crystal size	0.40 x 0.20 x 0.15 mm^3	
Theta range for data collection	1.34 to 25.00°.	
Index ranges	0<=h<=27, -26<=k<=27, -27<=l<=27	
Reflections collected	35509	
Independent reflections	35509 [R(int) = 0.0000]	
Completeness to theta = 25.00°	93.6 %	
Absorption correction	Empirical	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	35509 / 28 / 2375	
Goodness-of-fit on F^2	1.072	
Final R indices [I>2sigma(I)]	R1 = 0.0704, wR2 = 0.2050	
R indices (all data)	R1 = 0.1016, wR2 = 0.2274	
Largest diff. peak and hole	1.254 and -0.638 e.Å^{-3}	

Table S2. Crystal data and structure refinement for [(tetrabutylammonium)(**2**N_3)](hexane).

Empirical formula	C82 H102 N8	
Formula weight	1199.72	
Temperature	93(2) K	
Wavelength	0.70000 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 18.459(4) Å	α = 90°.
	b = 17.029(3) Å	β = 103.43(3)°.
	c = 12.014(2) Å	γ = 90°.
Volume	3673.2(13) $Å^3$	
Z	2	
Density (calculated)	1.085 Mg/m^3	
Absorption coefficient	0.063 mm^{-1}	
F(000)	1300	
Crystal size	0.20 x 0.15 x 0.05 mm^3	
Theta range for data collection	2.08 to 24.30°.	
Index ranges	-21<=h<=21, -19<=k<=18, 0<=l<=14	
Reflections collected	10687	
Independent reflections	5867 [R(int) = 0.0209]	
Completeness to theta = 24.30°	93.8 %	
Absorption correction	Empirical	
Max. and min. transmission	0.9968 and 0.9874	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5867 / 10 / 429	
Goodness-of-fit on F^2	1.070	
Final R indices [I>2sigma(I)]	R1 = 0.0946, wR2 = 0.2671	
R indices (all data)	R1 = 0.1135, wR2 = 0.2885	
Extinction coefficient	0.037(5)	
Largest diff. peak and hole	0.905 and -0.400 e.$Å^{-3}$	

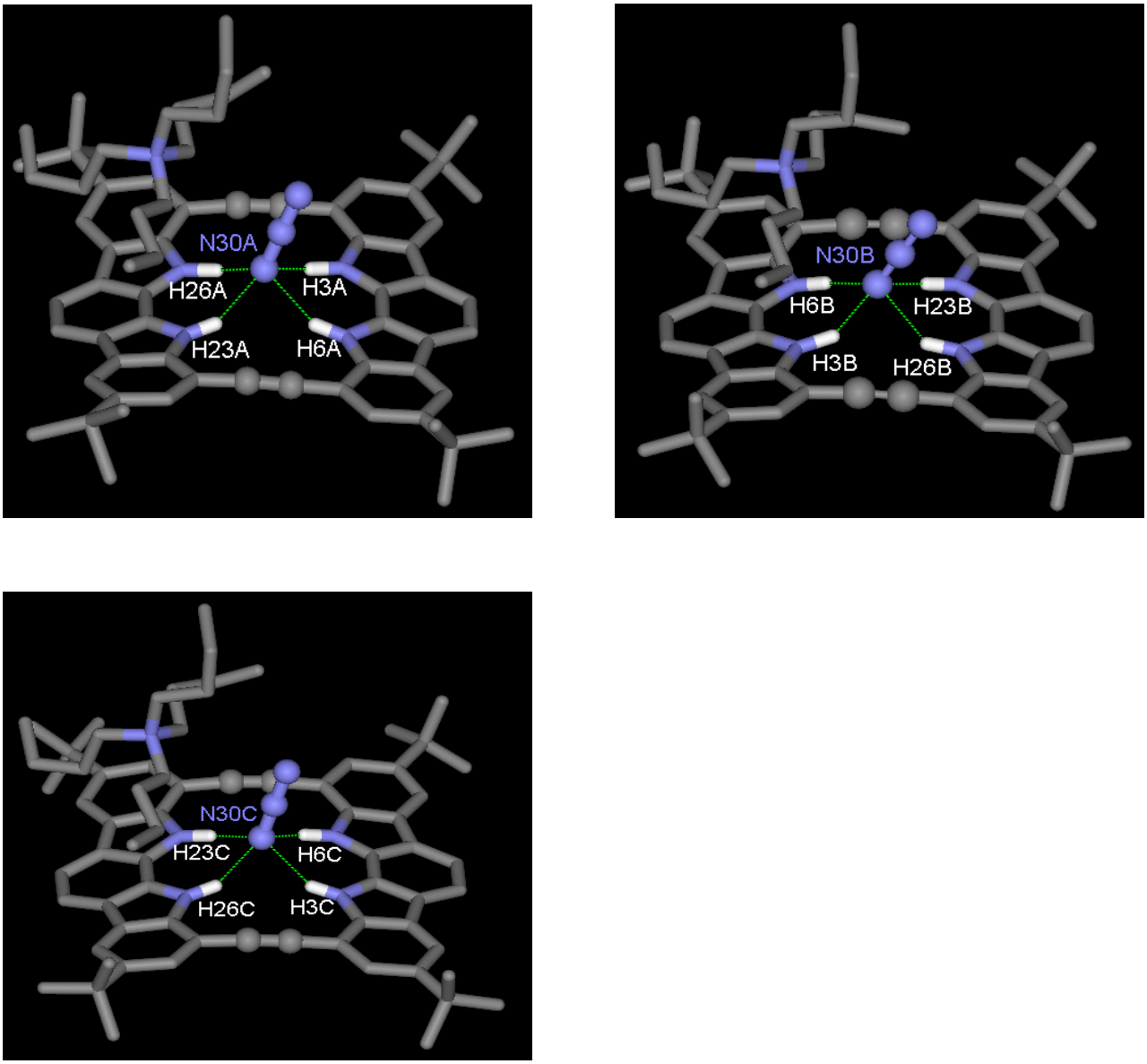


Figure S4. Three independent crystal structures (stick view) of **1**· N_3^- ·Bu_4N^+. For hydrogen-bonding parameters of each crystal, see Table S3.

Table S3. Selected bond parameters of complex **1**·$Bu_4N^+N_3^-$

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(3A)-H(3A)...N(30A)	0.91(3)	2.17(3)	2.922(3)	143(3)
N(6A)-H(6A)...N(30A)	0.90(3)	2.19(3)	2.967(3)	149(3)
N(23A)-H(23A)...N(30A)	0.86(3)	2.15(3)	2.916(3)	143(3)
N(26A)-H(26A)...N(30A)	0.97(3)	2.01(3)	2.884(3)	151(3)
N(30A)-N(31A)		1.184(3)		
N(31A)-N(32A)		1.172(3)		
N(3B)-H(3B)...N(30B)	1.02(3)	2.06(3)	2.911(3)	149(3)
N(6B)-H(6B)...N(30B)	0.89(3)	2.06(3)	2.907(3)	158(3)
N(23B)-H(23B)...N(30B)	0.85(2)	2.23(3)	2.954(3)	150(2)
N(26B)-H(26B)...N(30B)	0.86(3)	2.25(3)	2.946(3)	140(3)
N(30B)-N(31B)		1.197(3)		
N(31B)-N(32B)		1.172(3)		
N(3C)-H(3C)...N(30C)	0.87(2)	2.15(3)	2.934(3)	149(2)
N(6C)-H(6C)...N(30C)	0.89(3)	2.15(3)	2.917(3)	147(3)
N(23C)-H(23C)...N(30C)	0.92(3)	1.99(3)	2.900(3)	162(3)
N(26C)-H(26C)...N(30C)	0.90(3)	2.13(3)	2.937(3)	154(3)
N(30C)-N(31C)		1.192(3)		
N(31C)-N(32C)		1.170(3)		

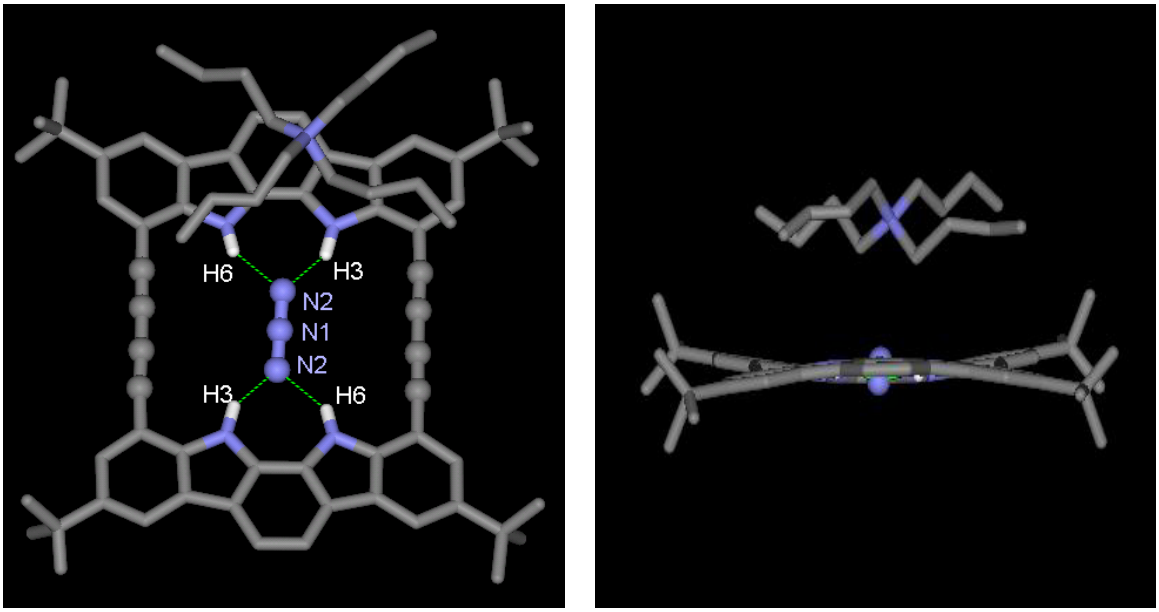


Figure S5. Top and side views of **2**· N_3^-·Bu_4N^+. For hydrogen-bonding parameters, see below (Table S4).

Table S4. Selected bond parameters of complex **2**· N_3^-·Bu_4N^+.

N-H...A	d(D-H)	d(H...A)	d(D...A)	<(NHA)
N(3)-H(3)...N(2A)	0.82(4)	2.11(4)	2.848(4)	150(3)
N(6)-H(6)...N(2A)	0.87(4)	2.05(4)	2.856(4)	153(3)
N(1A)-N(2A)	1.187(3)			