Electronic Supplementary Material (ESI) for ChemComm.

Tuning the Allosteric Sequestration of Anticancer Drugs for Developing Cooperative Nano-Antidotes

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SUPPORTING INFORMATION

General Information

All solvents were dried before use. All materials were obtained from commercial suppliers and used without further purification. Analytical thin-layer chromatography (TLC) was performed on silica-gel plates w/UV254. ^{1}H NMR and ^{13}C NMR spectra were recorded on 400, 600, 700 and 850 MHz spectrophotometers. UV-Vis spectra were measured using Shimadzu UV-2401PC spectrophotometer. Fluorescence spectra were recorded with Shimadzu RF-5301. Dynamic light scattering (DLS) measurements were completed with Zetasizer NanoZS instrument (ZEN3600). Transmission electron microscopy (TEM) images were recorded with FEI Tecnai G2 Spirit TEM microscope working at 80 kV.

Experimental Results

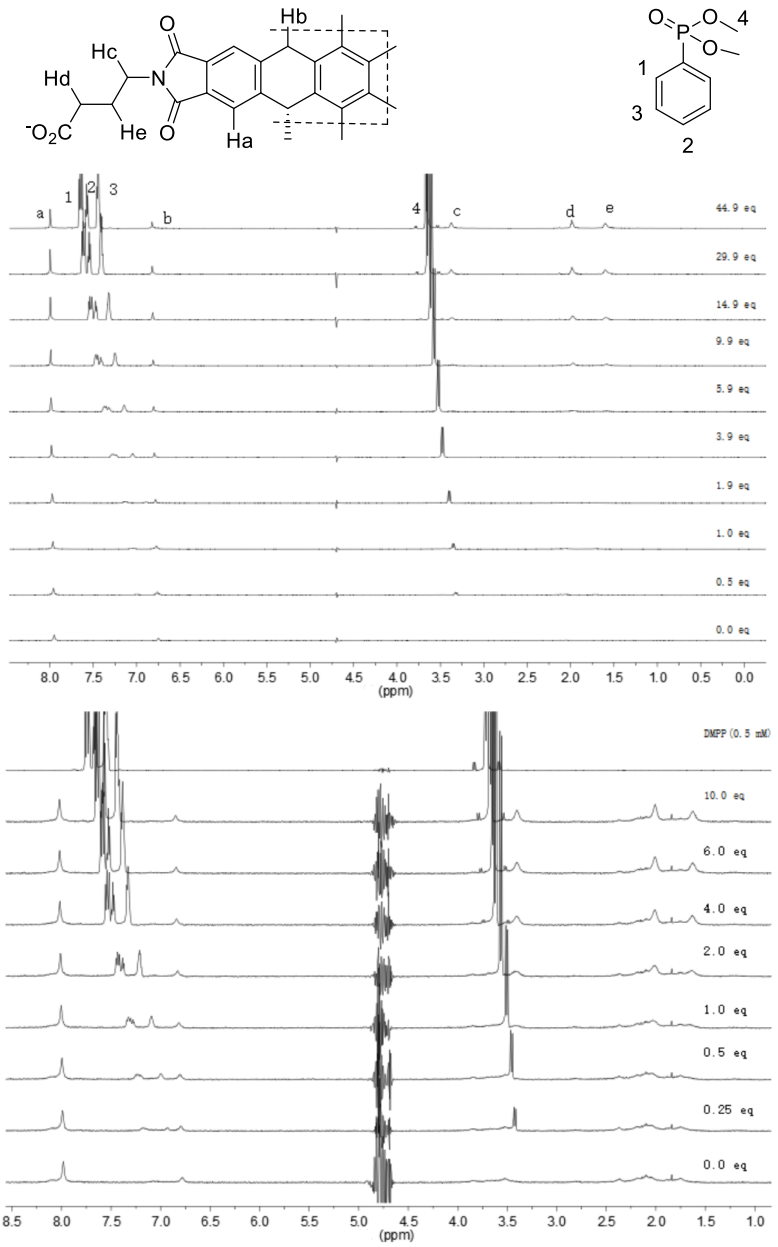


Figure S1. ^{1}H NMR spectra (298 K, 600 MHz) of 0.3 mM basket $\mathbf{1}^{6-}$ (top) and 0.468 mM basket $\mathbf{1}^{6-}$ (bottom) obtained upon an incremental addition of a standard 50.0 mM solution of DMPP **2** (10 mM phosphate buffer at pH = 7.0 $\pm$ 0.1).

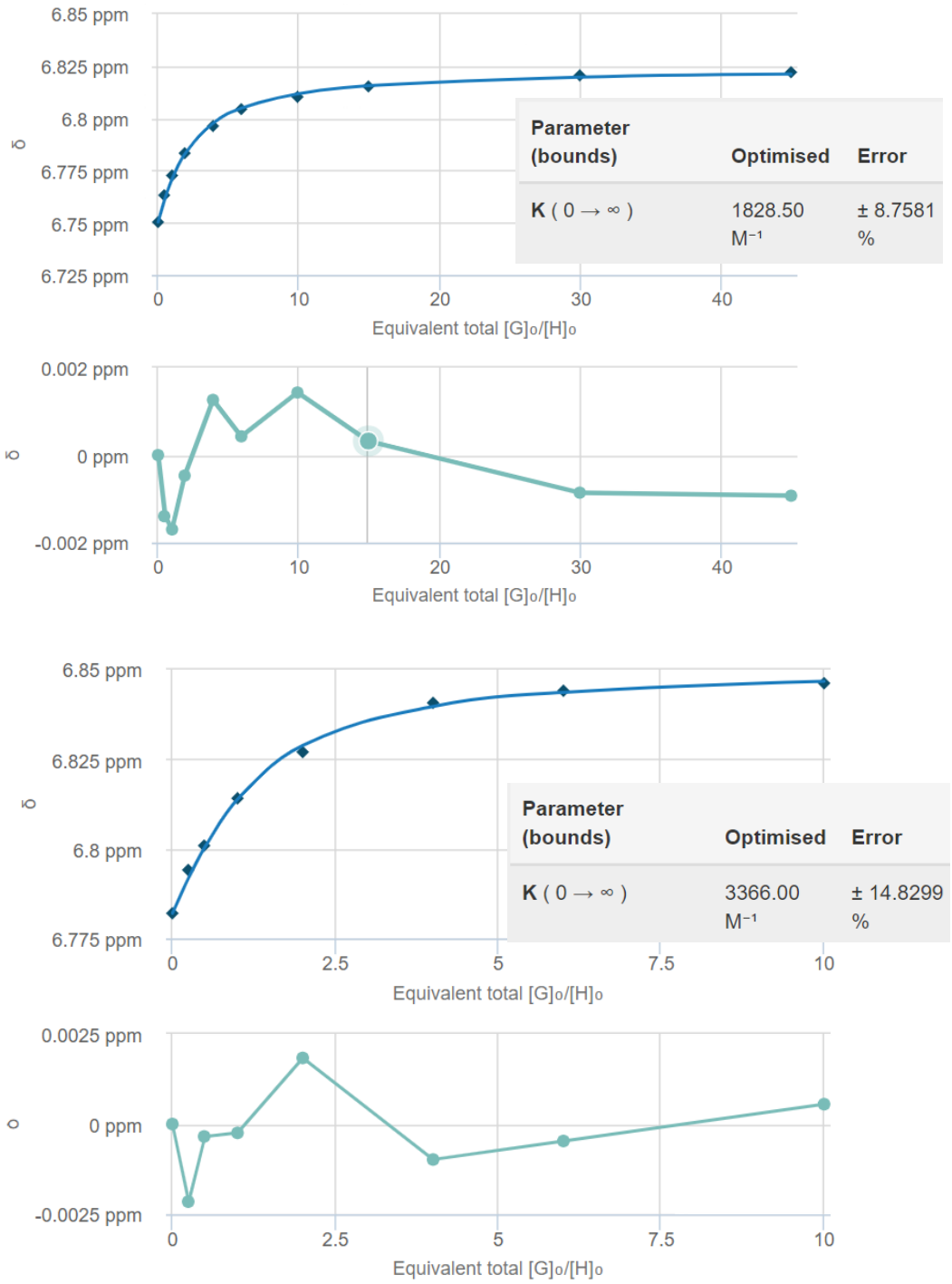


Figure S2. ^{1}H NMR titration experiments were repeated two times. A change in the chemical shift of $\mathbf{H_b}$ resonance from 0.3 mM basket $\mathbf{1}^{6-}$ and 0.468 mM basket $\mathbf{1}^{6-}$ (Figure S1; 10 mM phosphate buffer at pH = 7.0 ± 0.1) as a function of the increasing concentration of **2** was subjected to nonlinear least-square analysis using 1:1 binding model (see: supramolecular.org) giving K_1 = 1829 M^{-1} and K_1 = 3366 M^{-1}. The reported value is mean ± standard deviation: $K_1 = 2.6 \pm 1.1 \cdot 10^3$ M^{-1}.

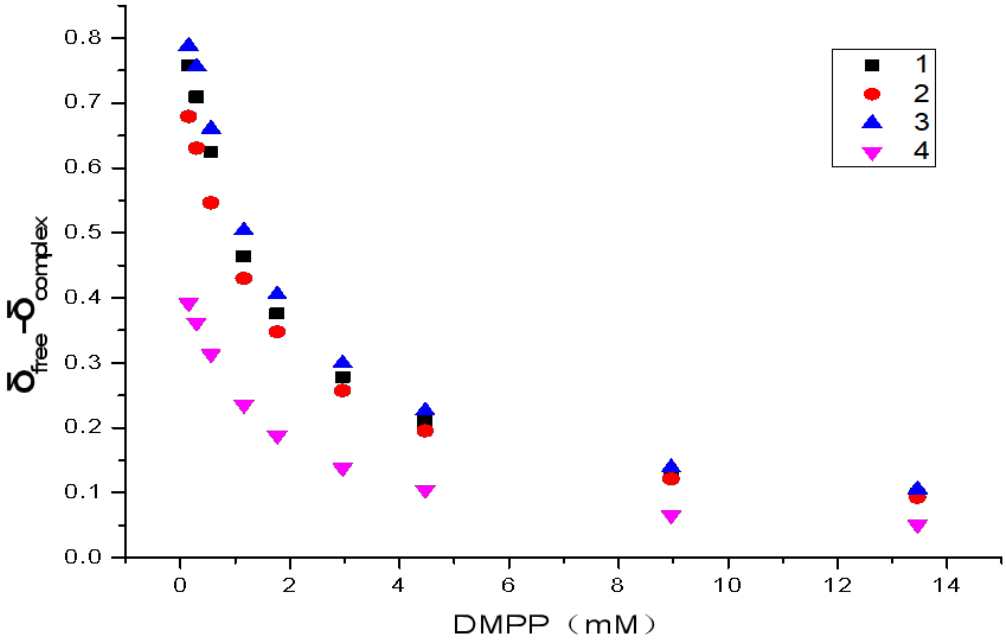


Figure S3. A plot showing magnetic perturbations of $\mathbf{H}_{1\text{-}4}$ nuclei from DMPP **2** observed during ^{1}H NMR supramolecular titration (Figure S1); note that OCH_3 resonances ($\mathbf{H}_4$, pink) were the least shielded.

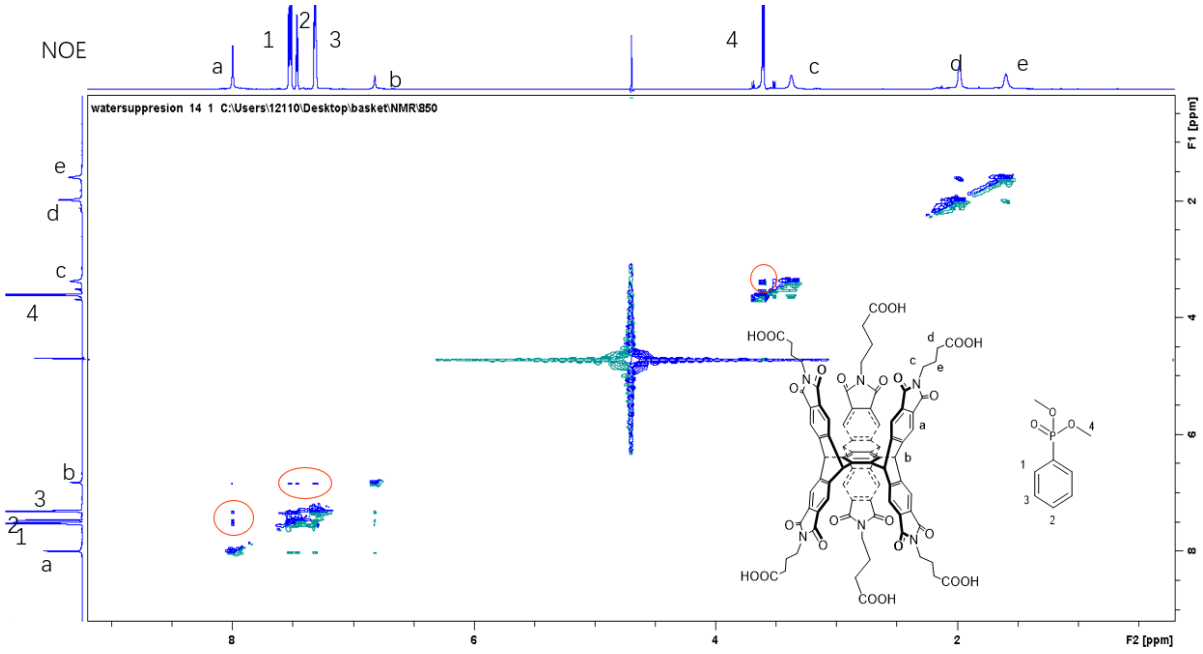


Figure S4. ^{1}H-^{1}H NOESY NMR (298 K, 850 MHz) spectrum of 8.0 mM solution of DMPP **2** and 0.4 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1). The observed host-guest NOEs ($\mathbf{H}_b$ vs $\mathbf{H}_{1/2/3}$, $\mathbf{H}_a$ vs $\mathbf{H}_{1/2/3}$ and $\mathbf{H}_c$ vs $\mathbf{H}_4$ are circled.

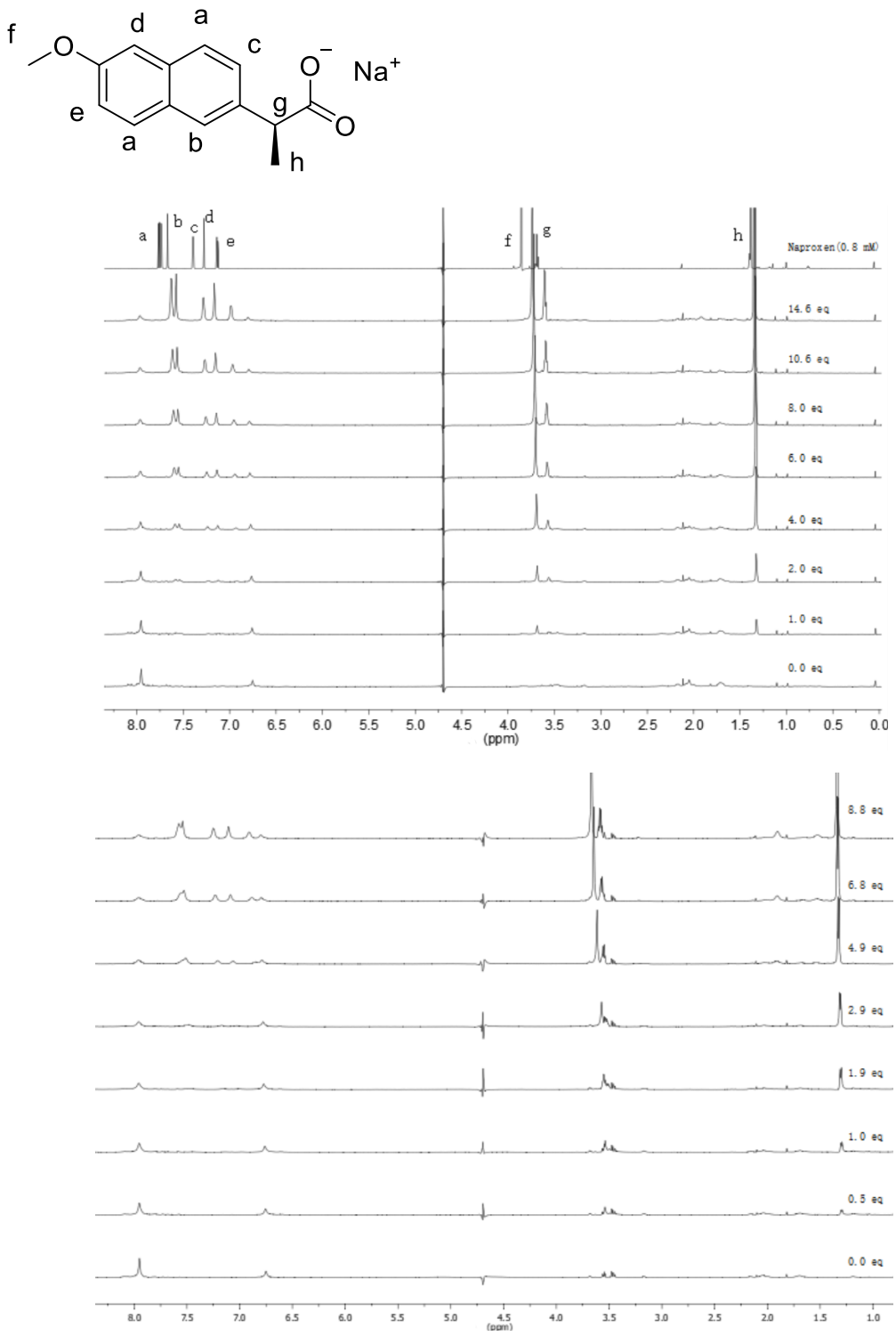
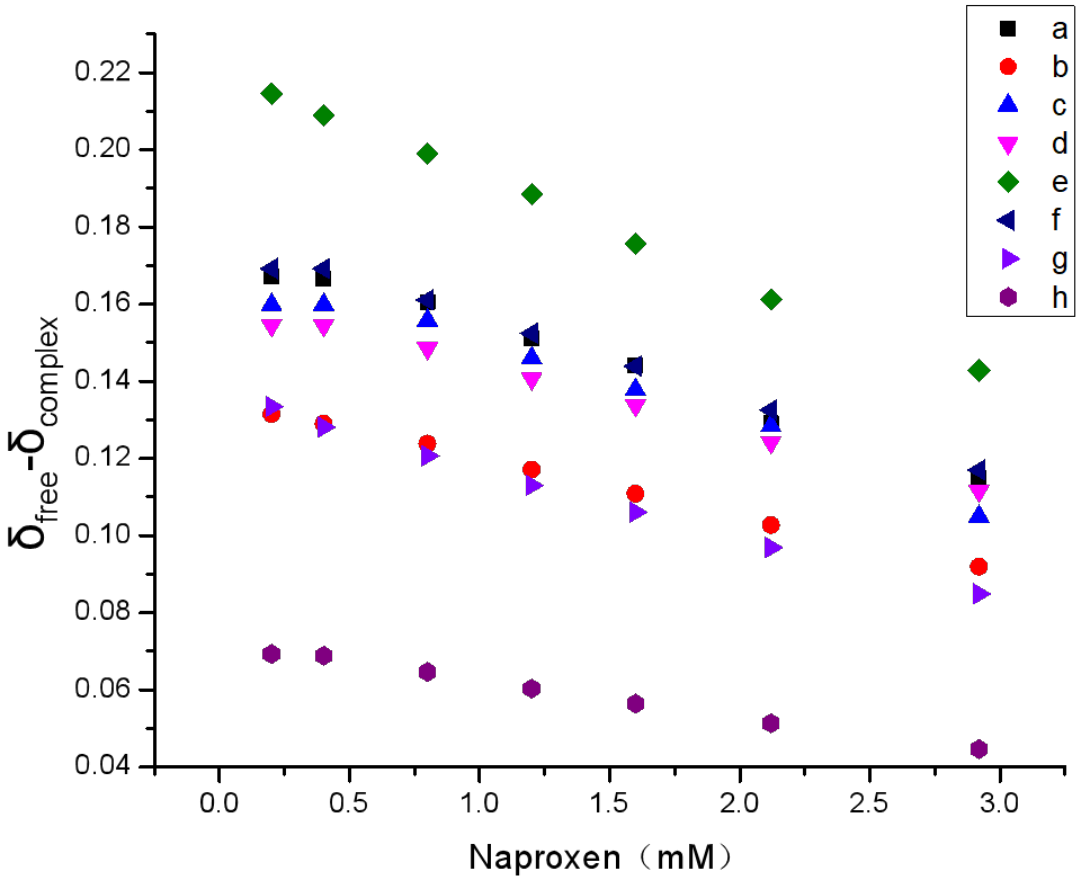


Figure S5. (Top) ^{1}H NMR spectra (298 K, 850 MHz) of 0.2 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of a standard 40.0 mM solution of naproxen $\mathbf{3}^{-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1), (Bottom) ^{1}H NMR spectra (298 K, 600 MHz) of 0.536 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of a standard 40.0 mM solution of naproxen $\mathbf{3}^{-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1).



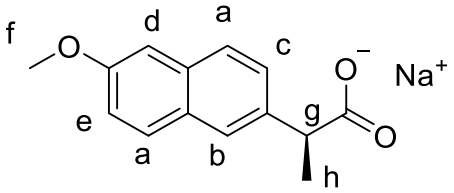


Figure S6. A plot showing magnetic perturbations of proton nuclei from naproxen **3**$^{-}$ observed during ^{1}H NMR supramolecular titration (Figure S5); note that $\mathbf{H}_{b/g/h}$ resonances were the least shielded.

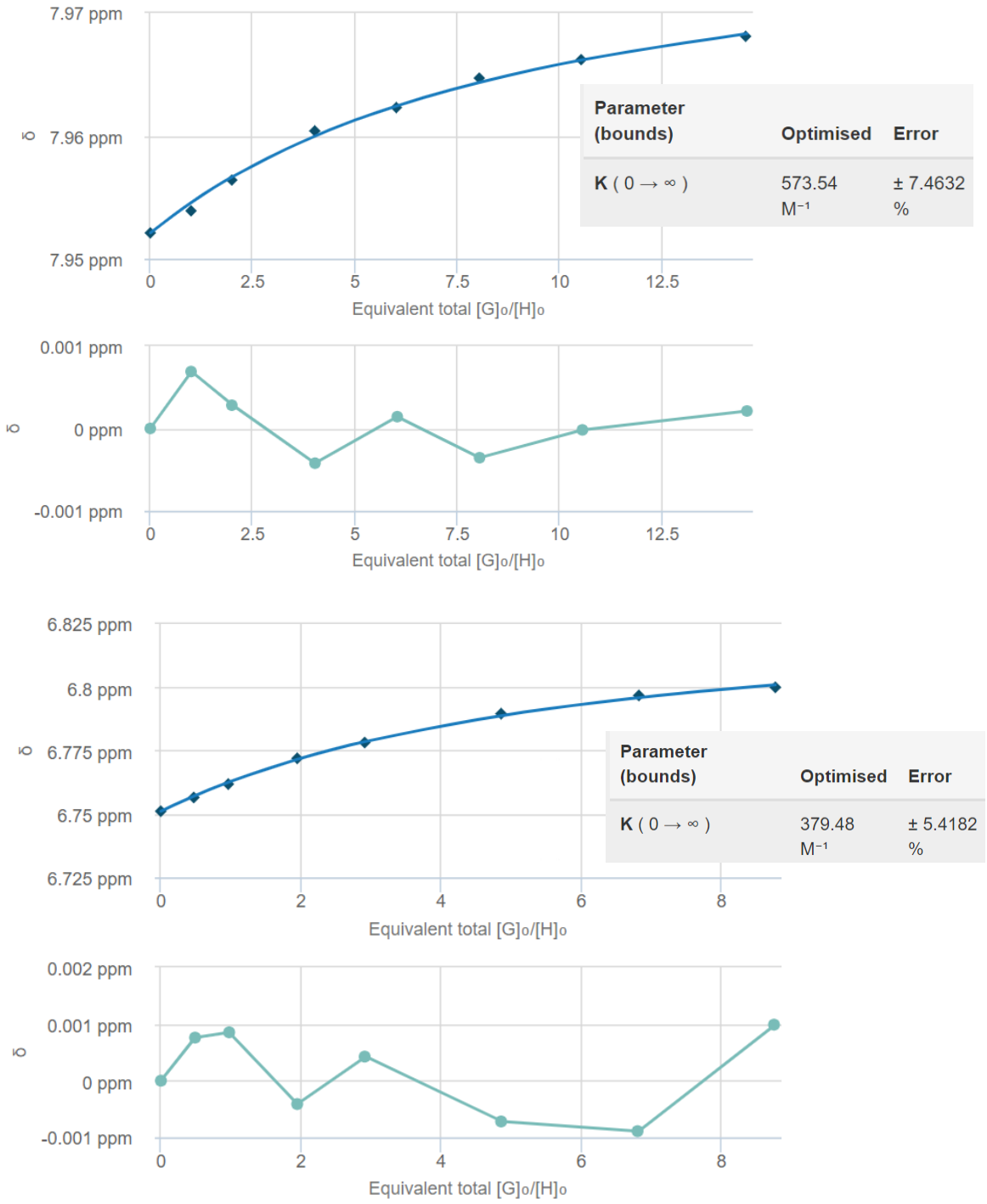


Figure S7. ^{1}H NMR titration experiments (Figure S5) were repeated two times (top and bottom). A change in the chemical shift of $\mathbf{H}_b$ resonance from 0.2 mM basket $\mathbf{1}^{6-}$ and 0.5 mM basket $\mathbf{1}^{6-}$ (Figure S5; 10 mM phosphate buffer at pH = 7.0 ± 0.1) as a function of the increasing concentration of naproxen $\mathbf{3}^{-}$ was subjected to nonlinear least-square analysis using 1:1 binding model (see: supramolecular.org) giving K_1 = 573 M^{-1} and K_1 = 379 M^{-1} and a random distribution of residues. The reported value is mean ± standard deviation: $K_1 = 4.8 \pm 1.4 \cdot 10^2$ M^{-1}.

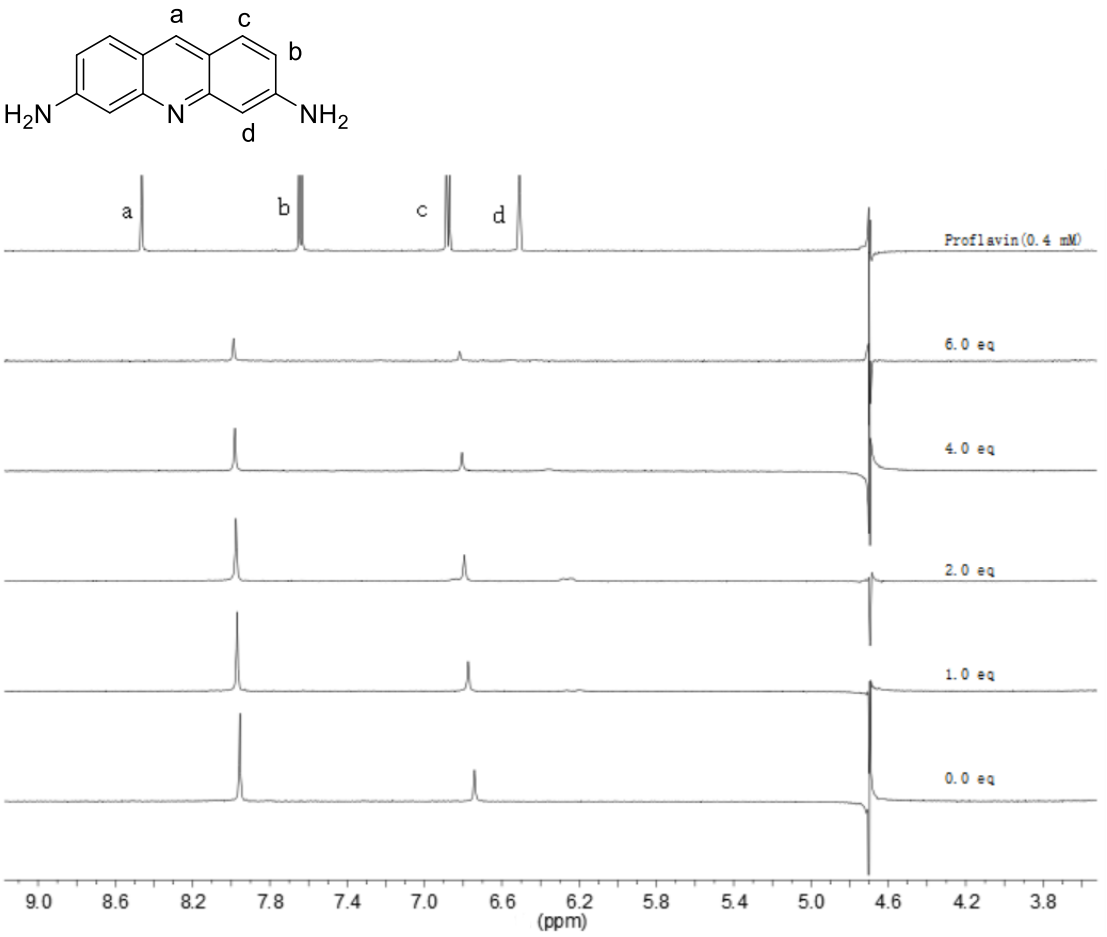


Figure S8. ^{1}H NMR spectra (298 K, 600 MHz) of 0.05 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of a standard 6.2 mM solution of proflavine $\mathbf{4}^{+}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1).

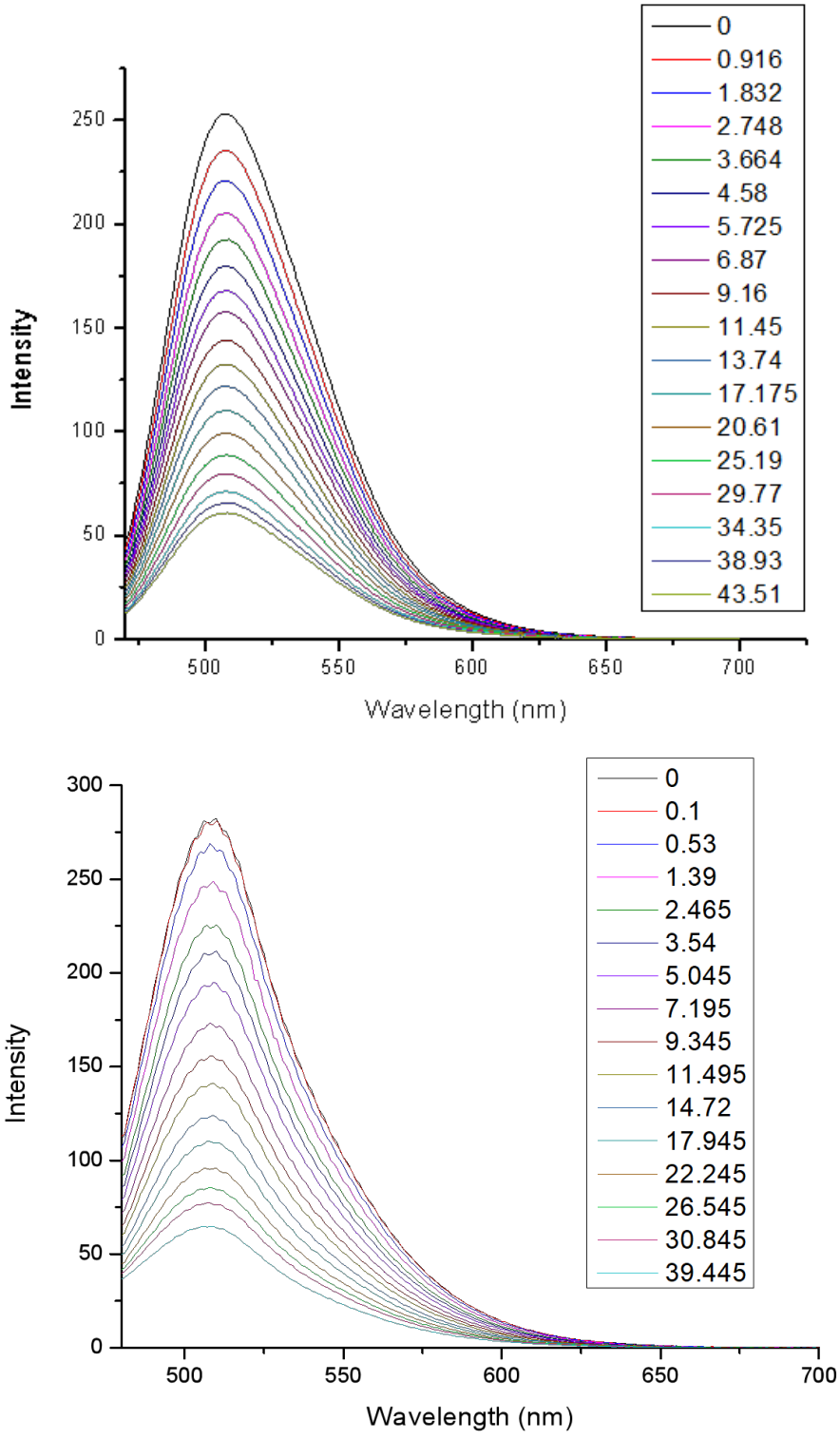


Figure S9. Fluorescence spectra of 2.0 μM solution of proflavine **4** (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of 458.0 μM solution of basket $\mathbf{1}^{6-}$; increasing concentrations (μM) of $\mathbf{1}^{6-}$ are shown in the inset.

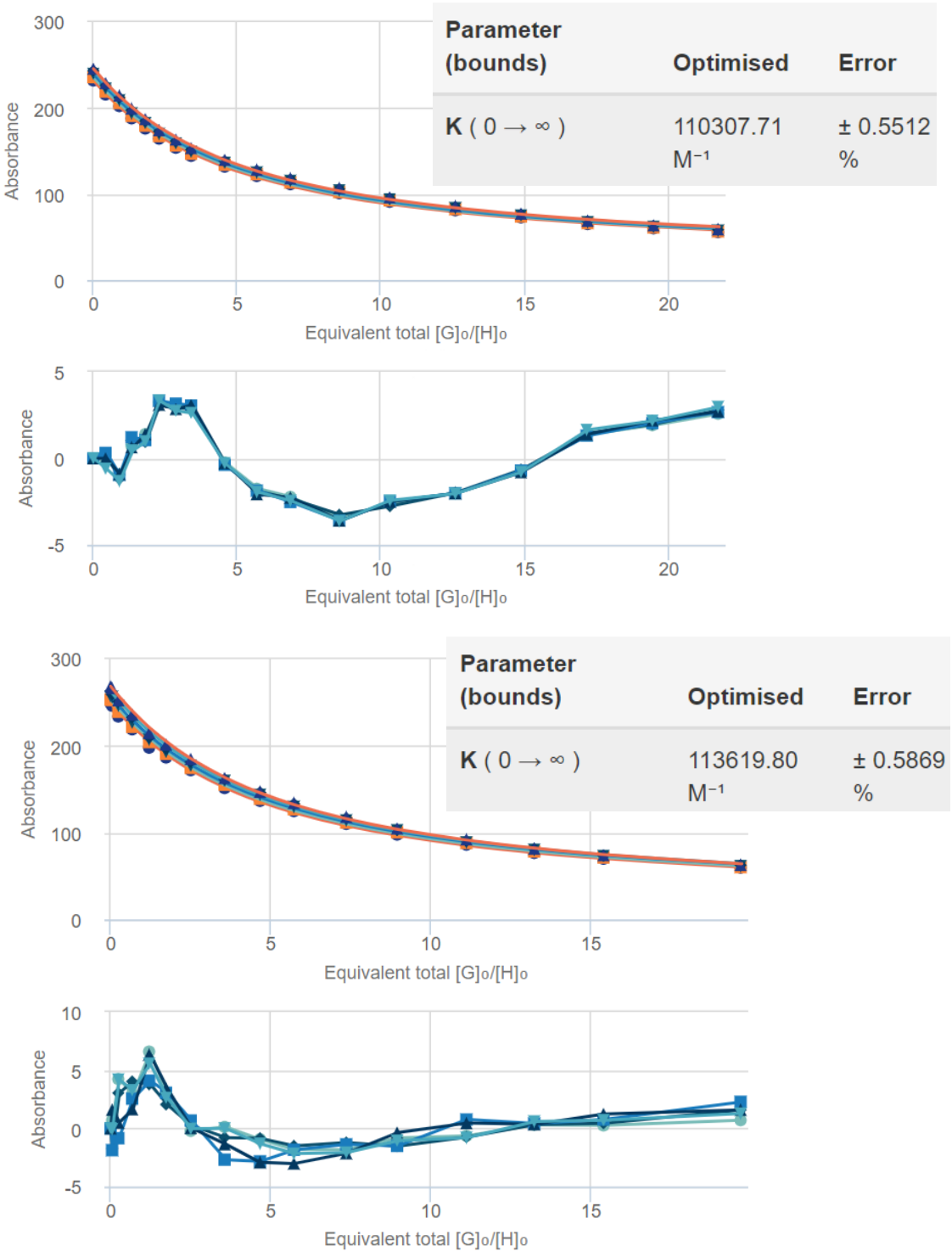


Figure S10. Fluorescence titration experiments were repeated two times (top and bottom; Figure S9). A change in the emission intensity of proflavine **4**$^{+}$ as a function of the increasing concentration of basket **1**$^{6-}$ was subjected to global (498–518 nm) nonlinear least-square analysis using 1:1 binding model (see supramolecular.org) giving K_1 = 110308 M^{-1} and K_1 = 113620 M^{-1}. The reported value is mean ± standard deviation: $K_1 = 1.12 \pm 0.02 \cdot 10^5$ M^{-1}.

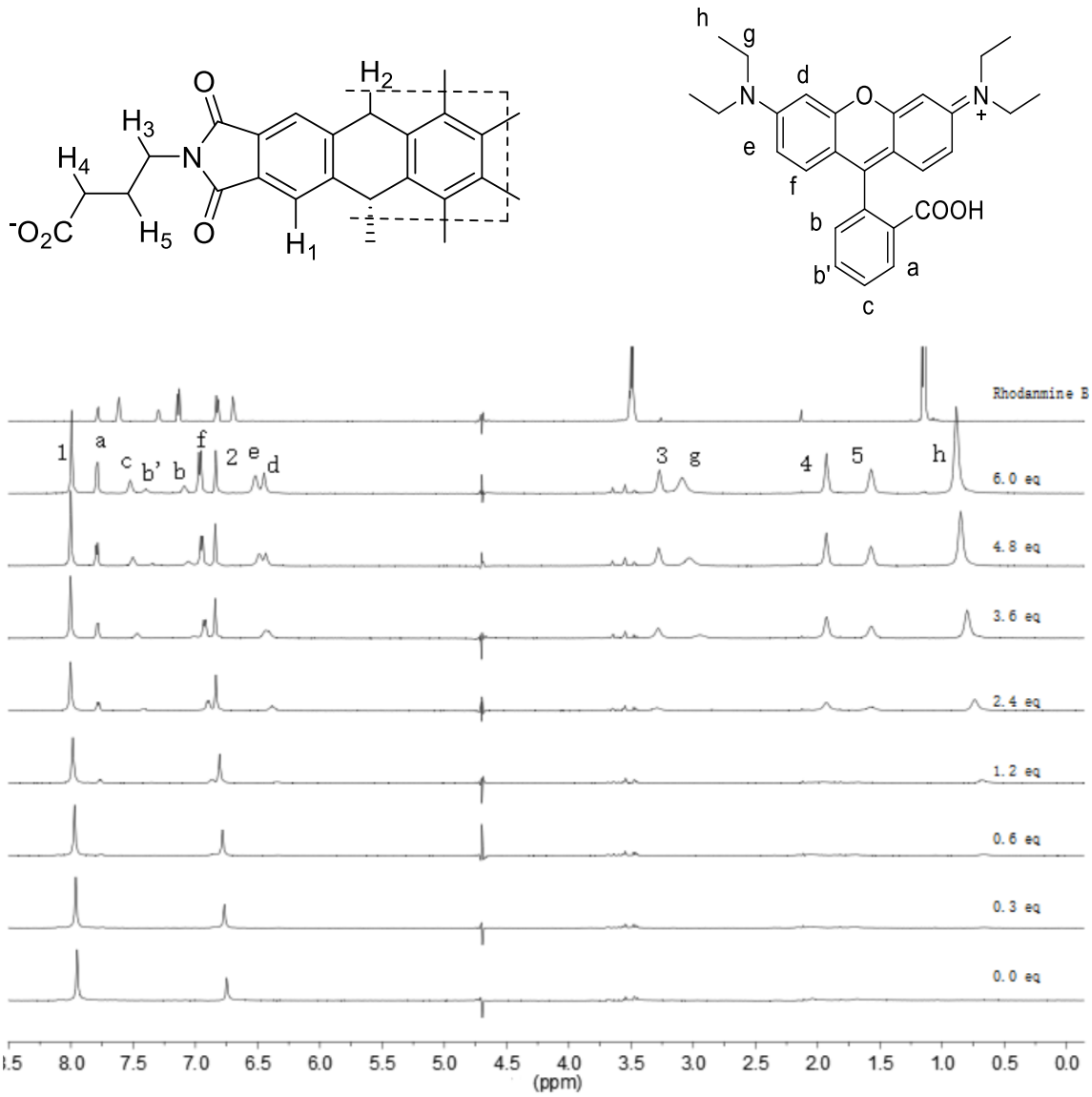


Figure S11. ^{1}H NMR spectra (298 K, 600 MHz) of 0.26 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 $\pm$ 0.1) obtained upon an incremental addition of a standard 11.5 mM solution of RhB **6** (10 mM phosphate buffer at pH = 7.0 $\pm$ 0.1).

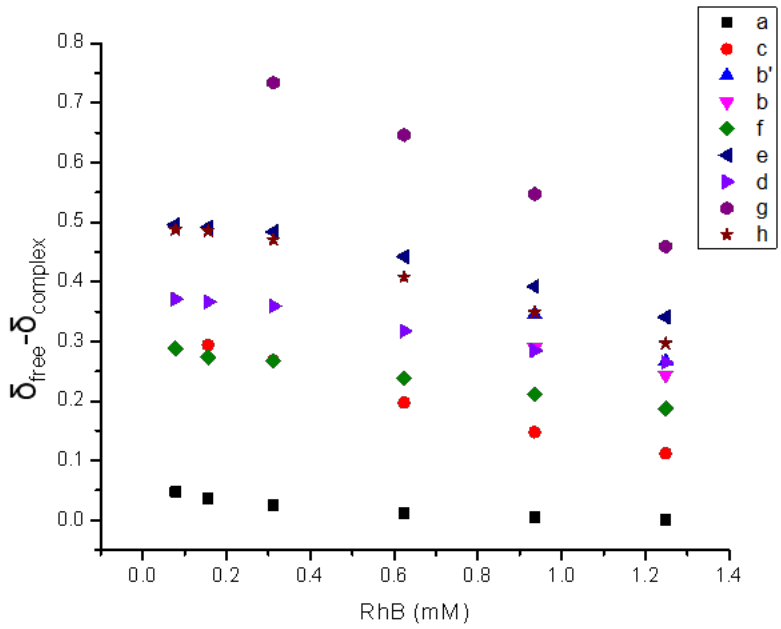


Figure S12. A plot showing magnetic perturbations of proton nuclei from RhB **6** observed during ^{1}H NMR supramolecular titration (Figure S11); note that $\mathbf{H}_{a/c/f/b/b'}$ resonances were the least shielded.

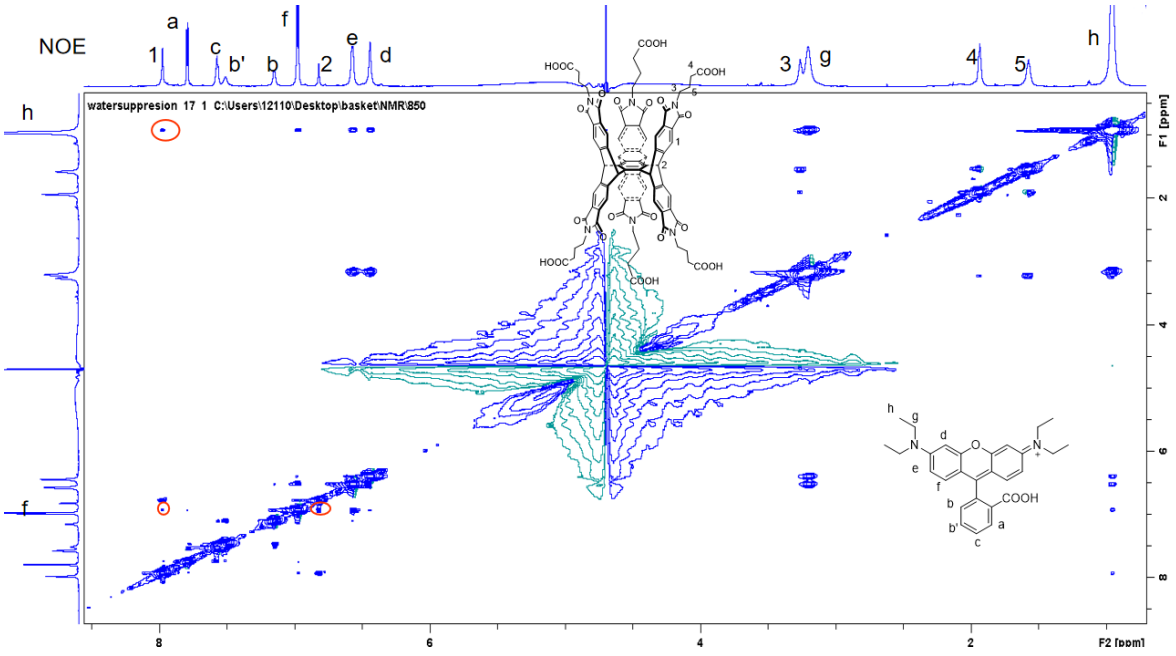


Figure S13. ^{1}H-^{1}H NOESY NMR (298 K, 850 MHz) spectrum of 1.8 mM solution of RhB **6** and 0.3 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1). The observed host-guest NOEs ($\mathbf{H}_h$ vs $\mathbf{H}_1$ and $\mathbf{H}_f$ vs $\mathbf{H}_1$) are circled.

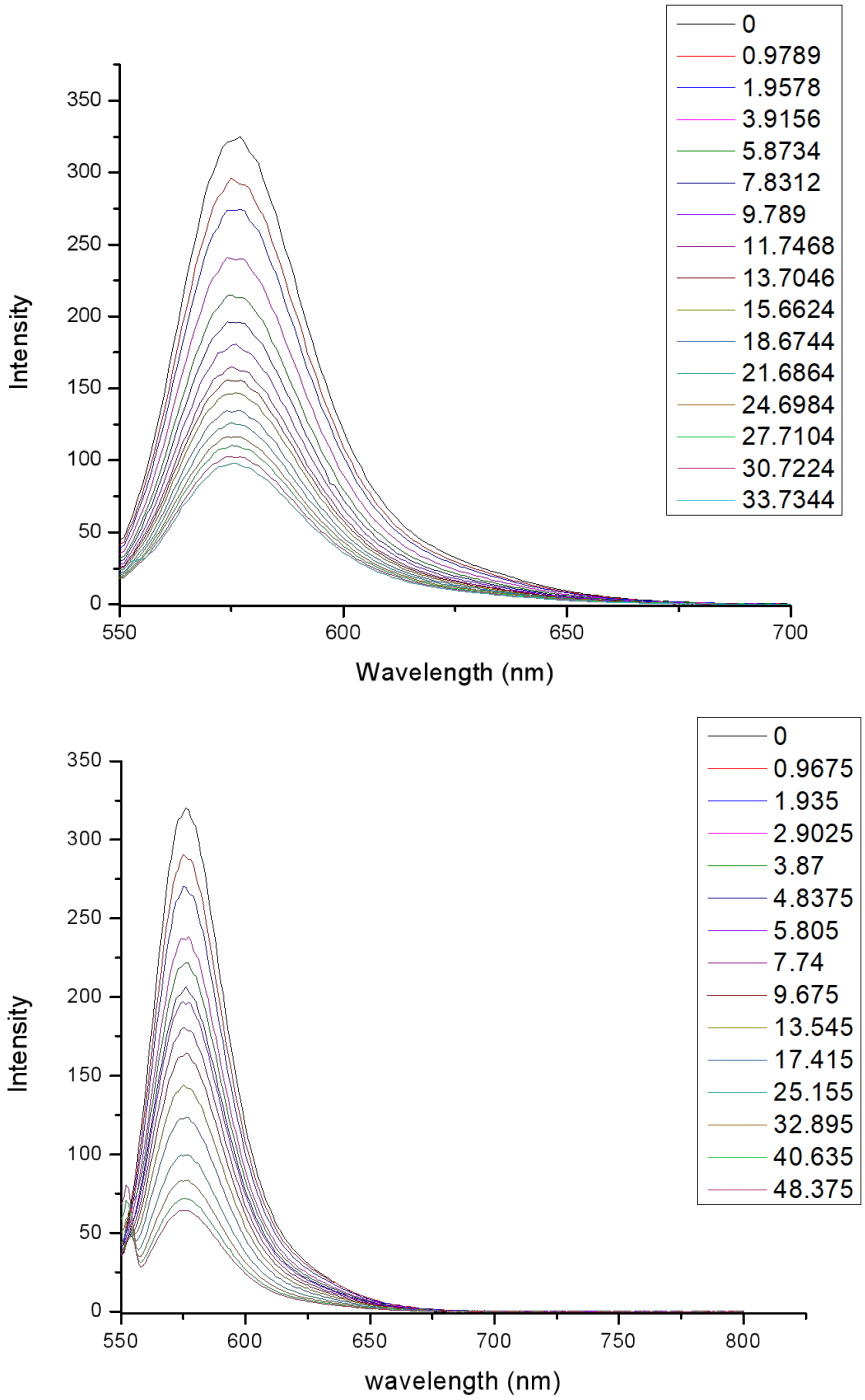


Figure S14. Fluorescence spectra of 2.0 μM solution of RhB **6** (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of 356.4 μM solution of basket $\mathbf{1}^{6-}$; increasing concentrations (μM) of $\mathbf{1}^{6-}$ are shown in the inset.

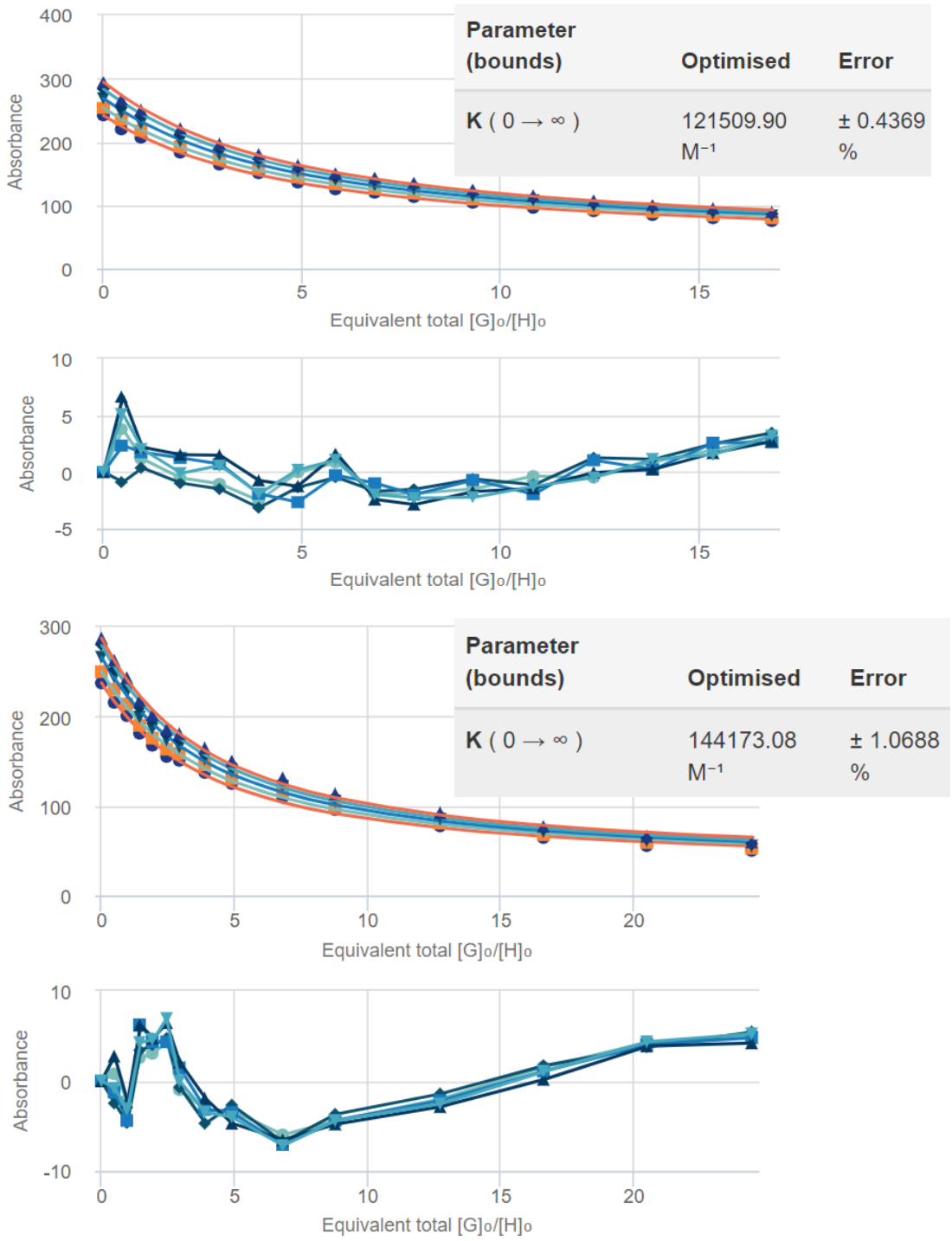


Figure S15. Fluorescence titration experiments were repeated two times (top and bottom; Figure S14). A change in the emission intensity of RhB **6** as a function of the increasing concentration of basket $\mathbf{1}^{6-}$ was subjected to global (566-586 nm) nonlinear least-square analysis using 1:1 binding model (see supramolecular.org) giving K_1 = 121510 M^{-1} and K_1 = 144173 M^{-1}. The reported value is mean ± standard deviation: $K_1 = 1.3 \pm 0.2 \cdot 10^5$ M^{-1}.

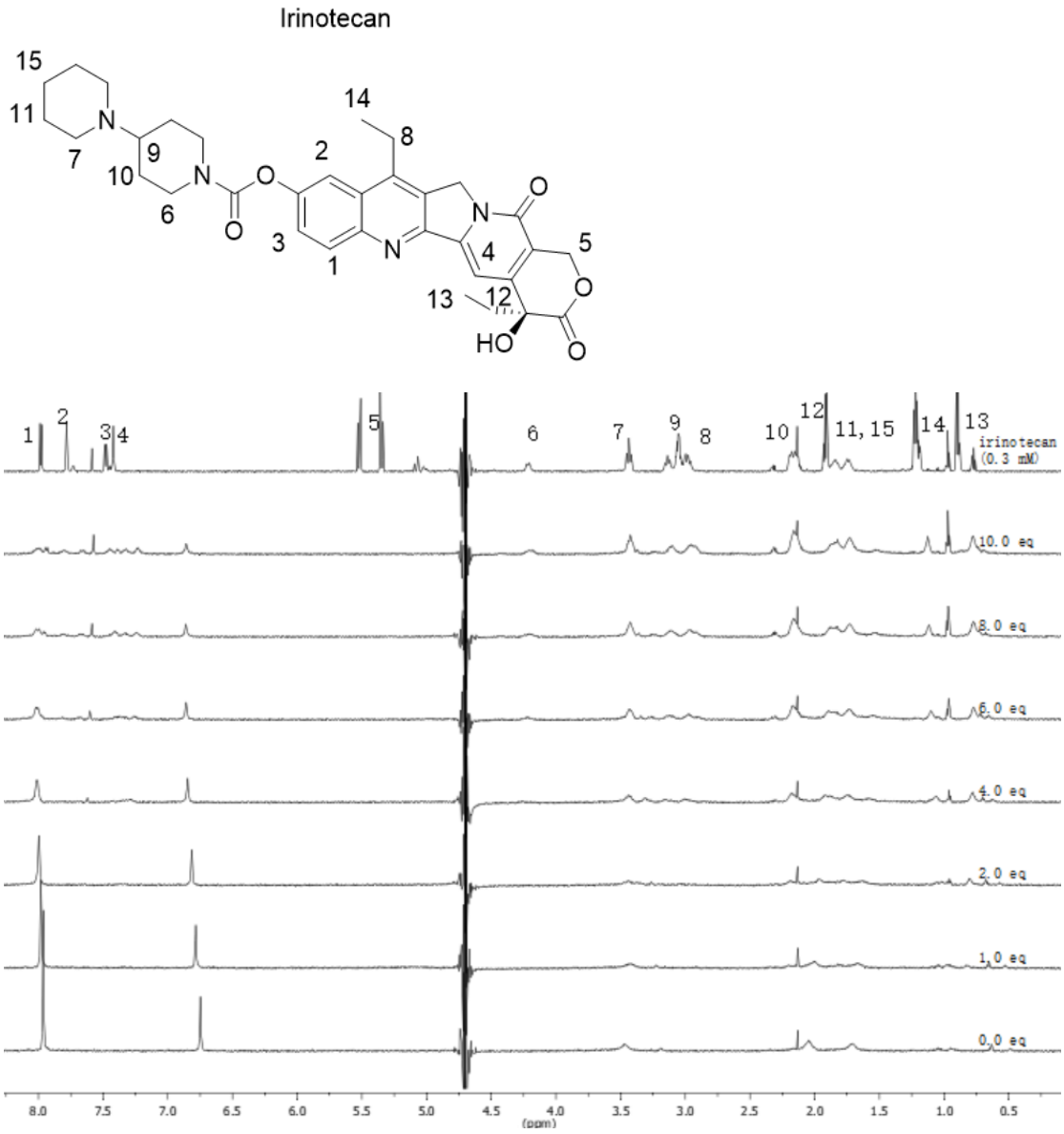


Figure S16. ^{1}H NMR spectra (298 K, 700 MHz) of 0.05 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of a standard 3.6 mM solution of irinotecan $\mathbf{7}^{+}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1).

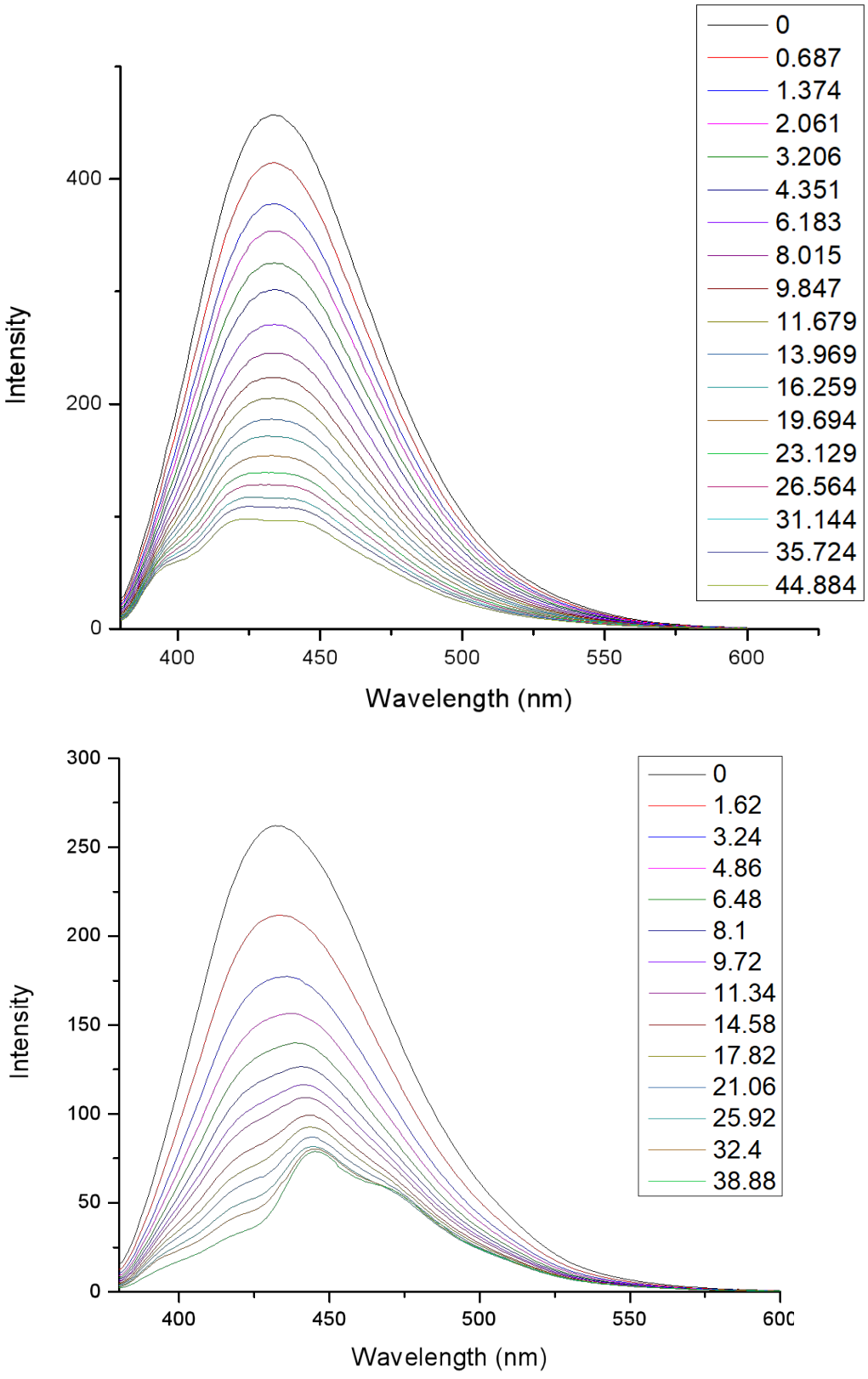


Figure S17. Fluorescence spectra of 3.0 μM solution of irinotecan $\mathbf{7}^{+}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of 400.5 μM solution of basket $\mathbf{1}^{6-}$; increasing concentrations (μM) of $\mathbf{1}^{6-}$ are shown in the inset.

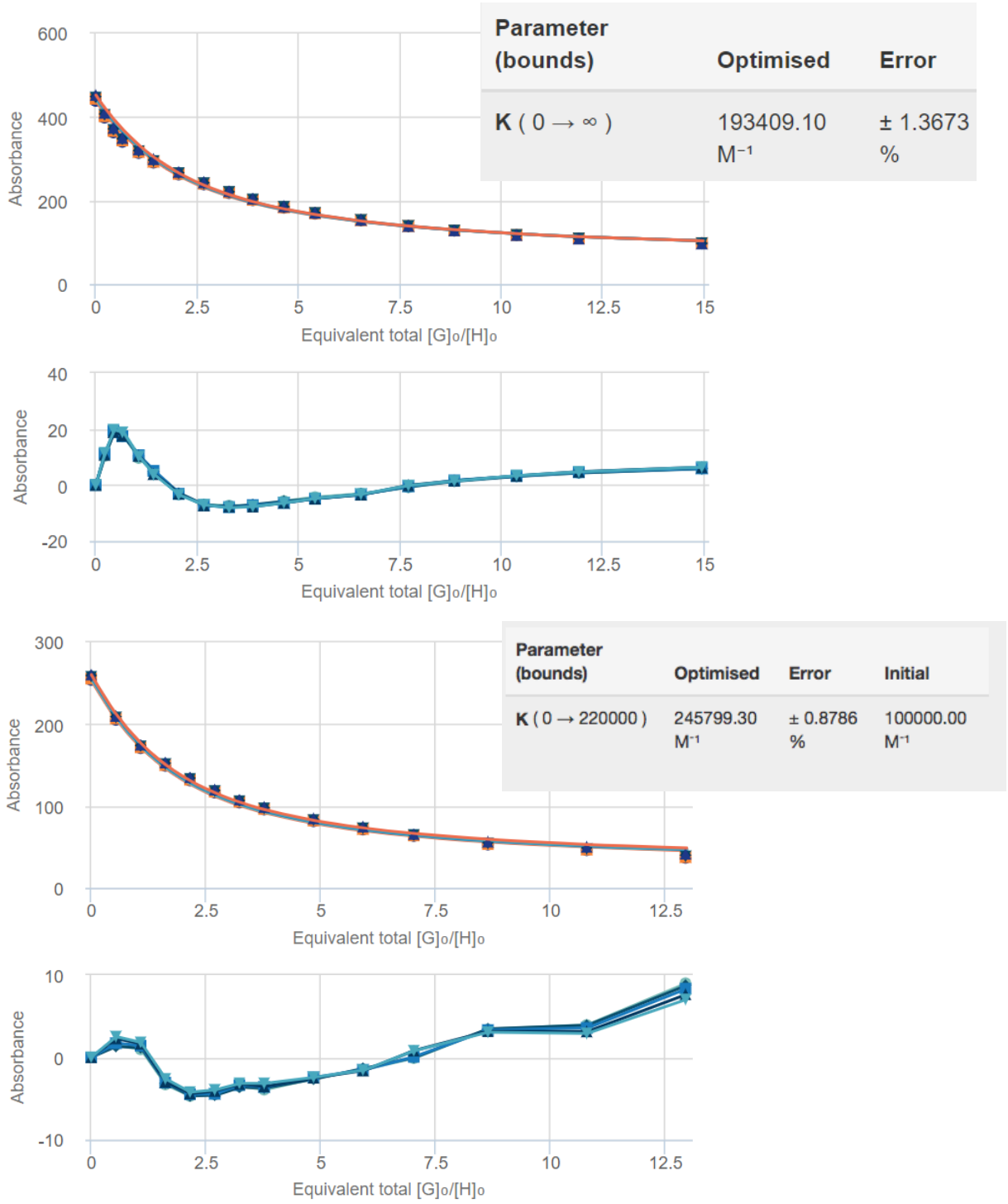


Figure S18. Fluorescence titration experiments were repeated two times (top and bottom; Figure S17). A change in the emission intensity of irinotecan **7** as a function of the increasing concentration of basket $\mathbf{1}^{6-}$ was subjected to global (425-445 nm) nonlinear least-square analysis using 1:1 binding model (see supramolecular.org) giving K_1 = 193409 M^{-1} and K_1 = 245799 M^{-1}. The reported value is mean ± standard deviation: $K_1 = 2.2 \pm 0.4 \cdot 10^5$ M^{-1}.

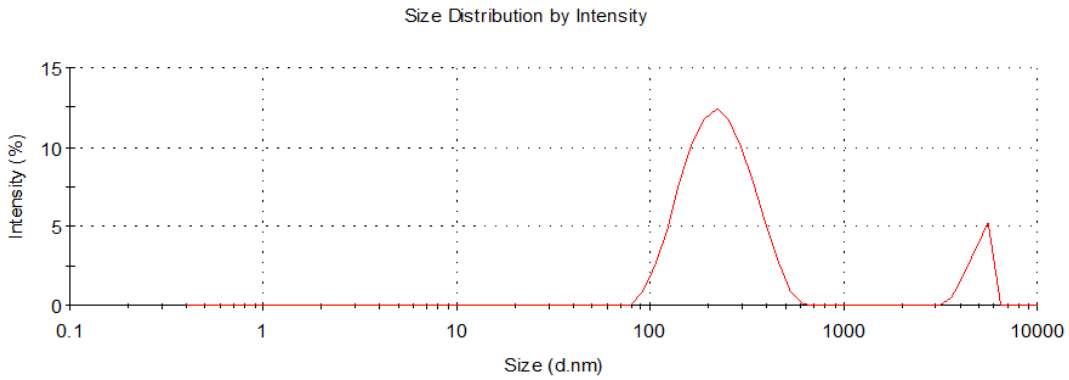


Figure S19. The size distribution of particles in the solution (10 mM phosphate buffer at pH=7.0) of $\mathbf{1}^{6-}$ (0.2 mM) and DMPP **2** (0.2 mM) was obtained from DLS measurement at 298 K.

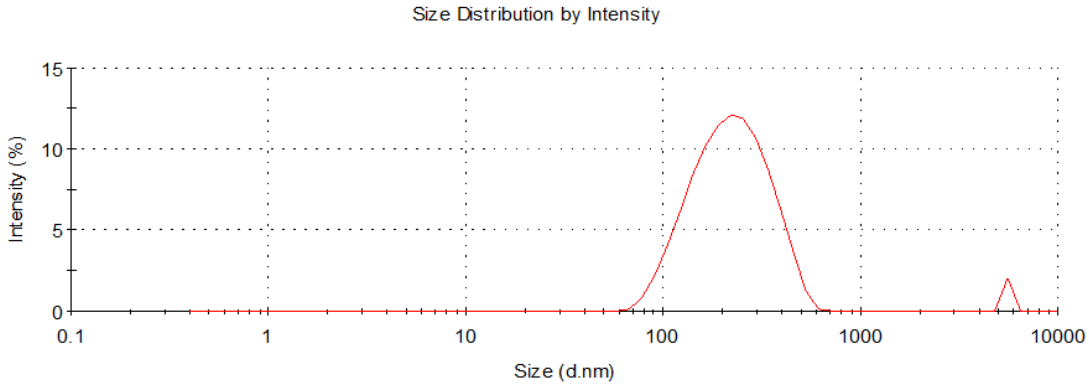


Figure S20. The size distribution of particles in the solution (10 mM PBS at pH=7.0) of $\mathbf{1}^{6-}$ (0.2 mM) and naproxen $\mathbf{3}^{-}$ (0.2 mM) was obtained from DLS measurement at 298 K.

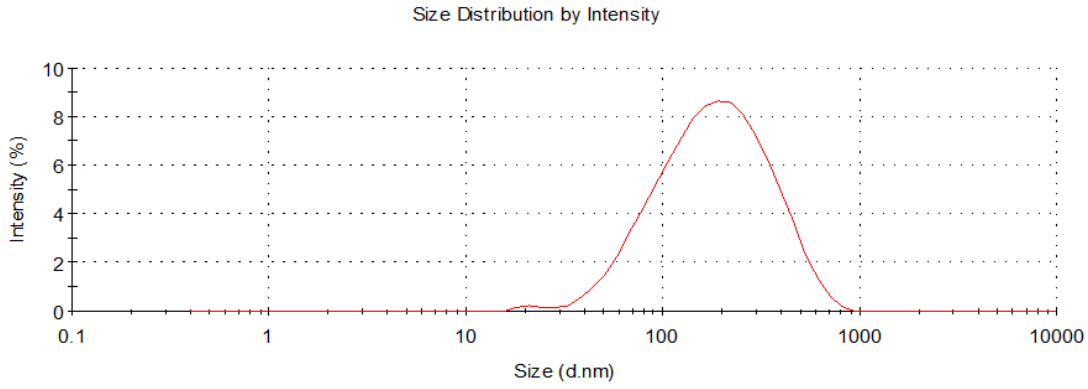


Figure S21. The size distribution of particles in the solution (10 mM PBS at pH=7.0) of $\mathbf{1}^{6-}$ (0.2 mM) and RhB **6** (0.2 mM) was obtained from DLS measurement at 298 K.

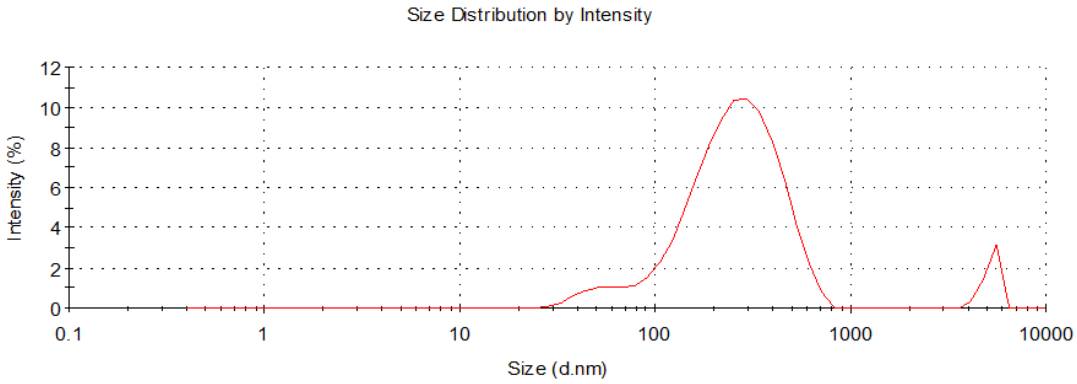


Figure S22. The size distribution of particles in the solution (10 mM PBS at pH=7.0) of $\mathbf{1}^{6-}$ (0.2 mM) and irinotecan $\mathbf{7}^{+}$ (0.2 mM) was obtained from DLS measurement at 298 K.

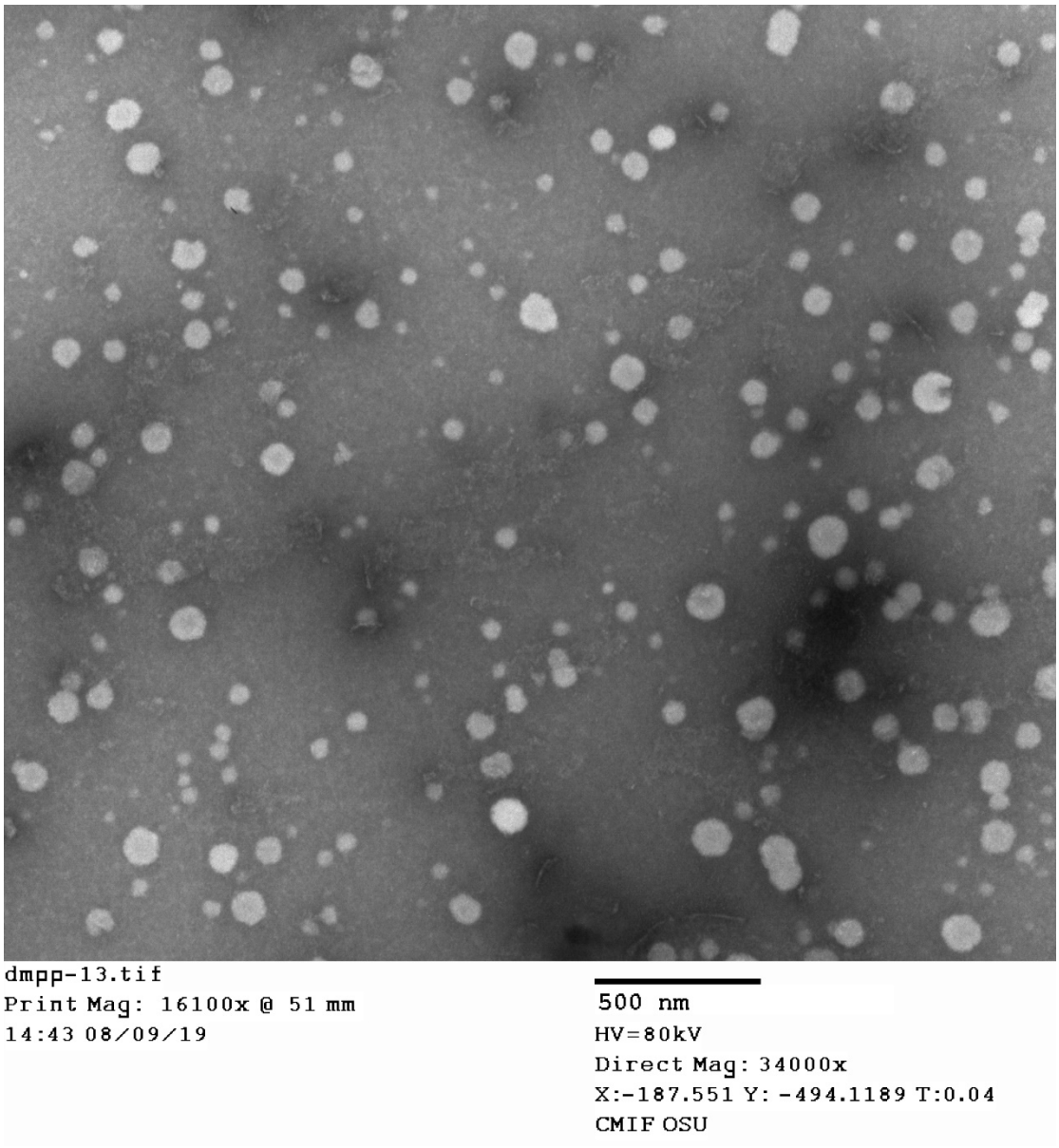


Figure S23. TEM image of 10 mM PBS solution (pH=7.0) of $\mathbf{1}^{6-}$ (0.3 mM) and DMPP **2** (0.3 mM) deposited on a copper grid and stained with uranyl acetate.

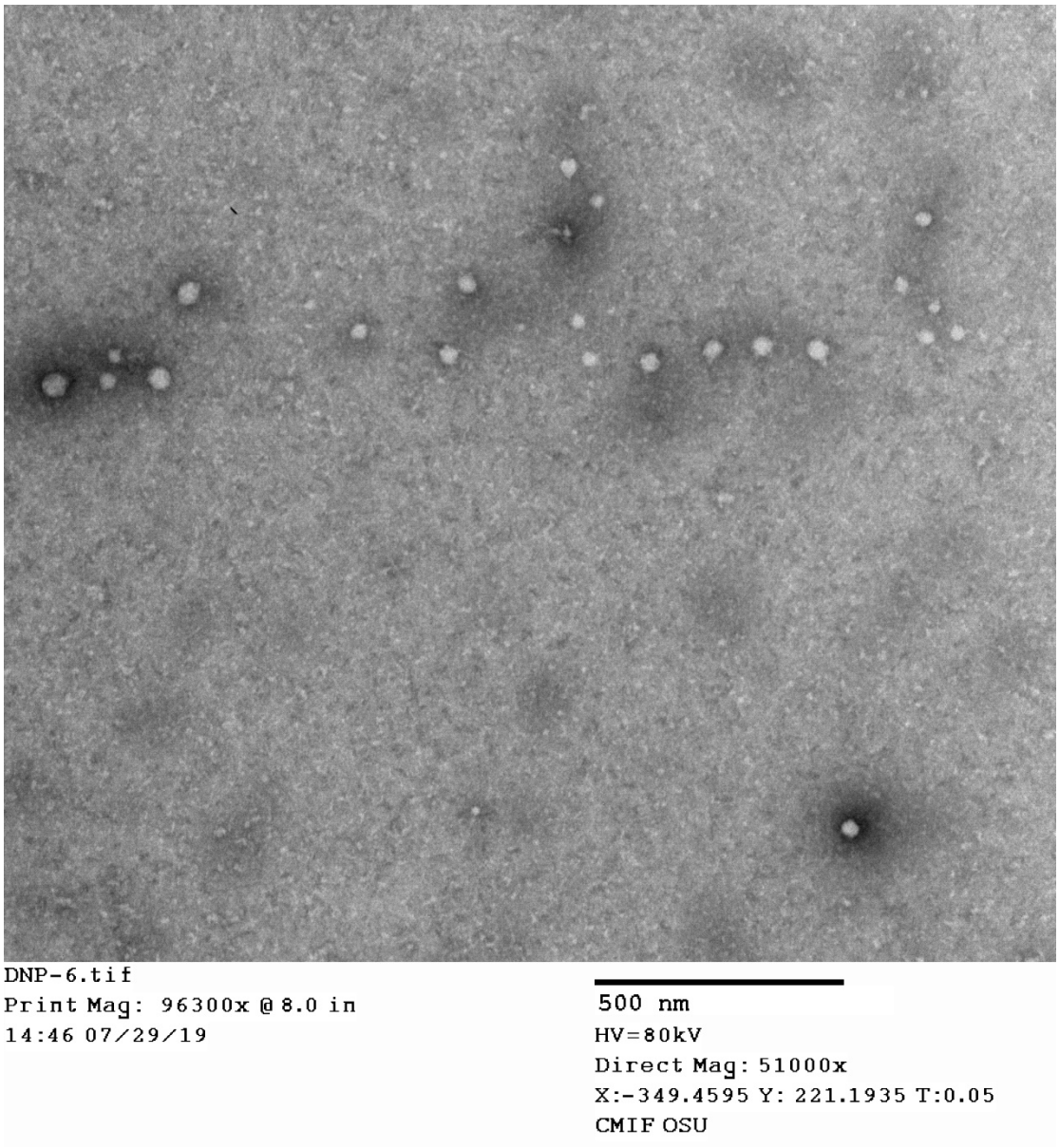


Figure S24. TEM image of 10 mM PBS solution (pH=7.0) of $\mathbf{1}^{6-}$ (0.3 mM) and naproxen $\mathbf{3}^{-}$ (0.3 mM) deposited on a copper grid and stained with uranyl acetate.

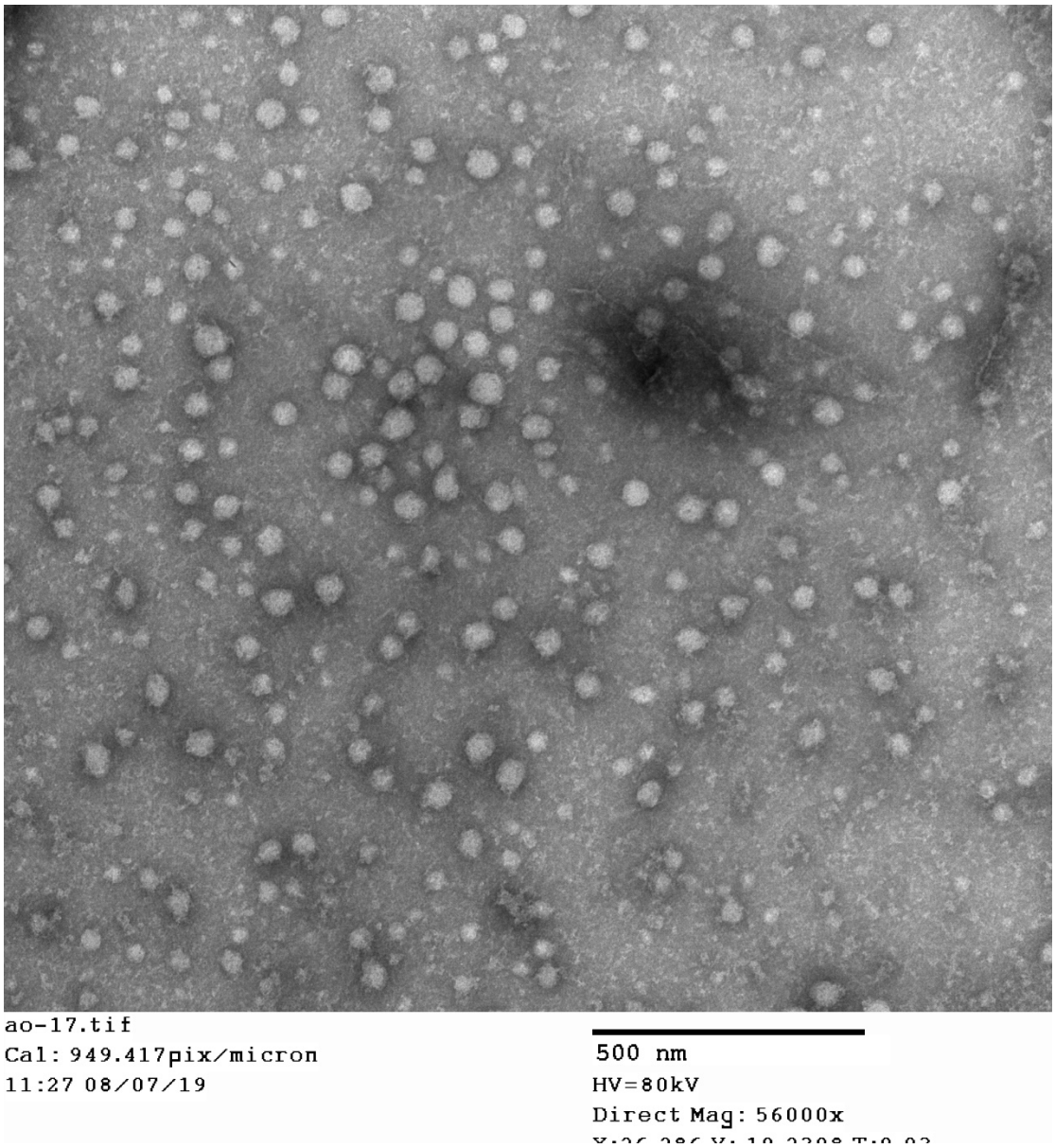


Figure S25. TEM image of 10 mM PBS solution (pH=7.0) of 1 (0.1 mM) and $\mathbf{4}^{+}$ (0.1 mM) at deposited on a copper grid and stained with uranyl acetate.

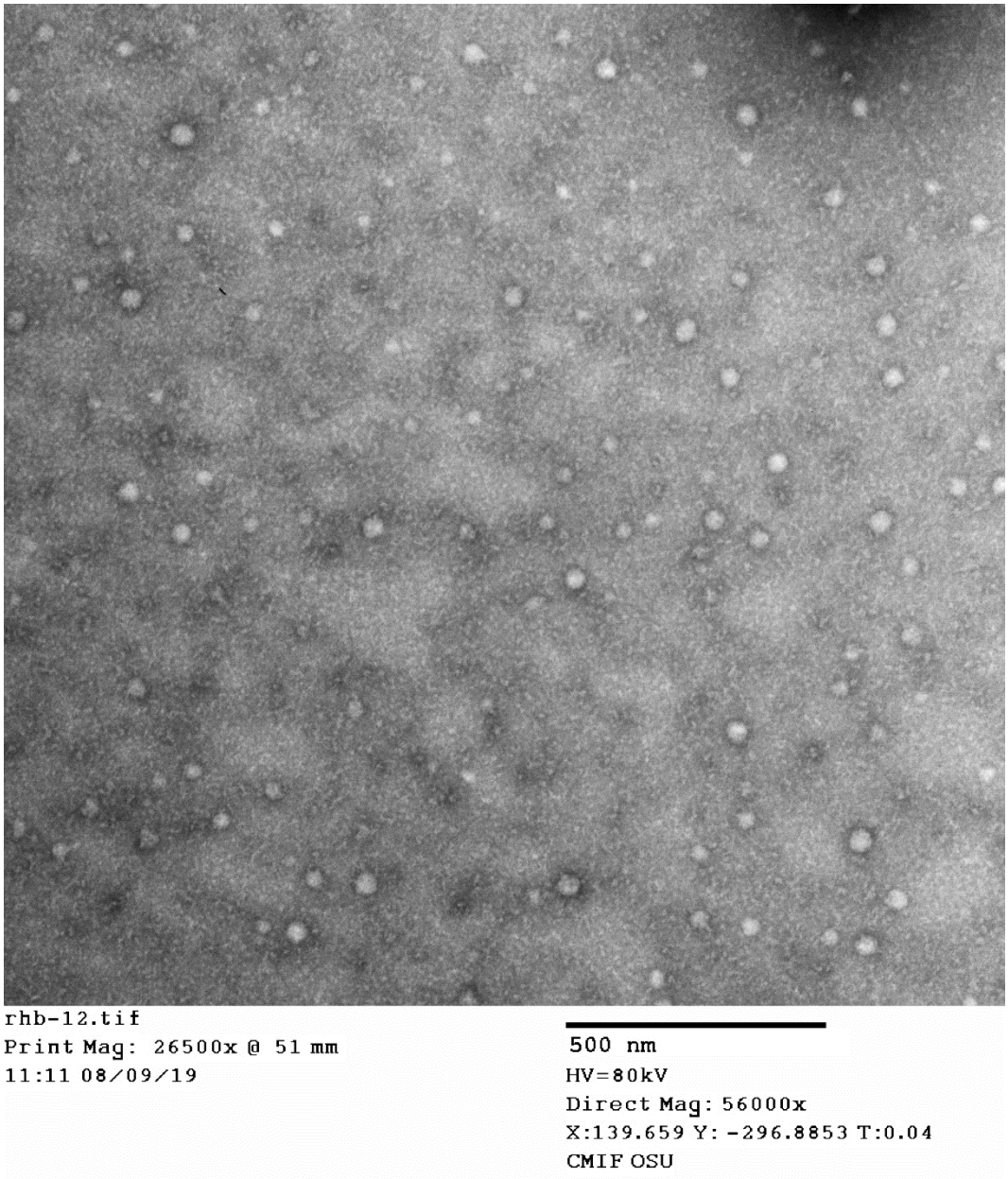


Figure S26. TEM image of 10 mM PBS solution (pH=7.0) of $\mathbf{1}^{6-}$ (0.2 mM) and RhB **6** (0.2 mM) deposited on a copper grid and stained with uranyl acetate.

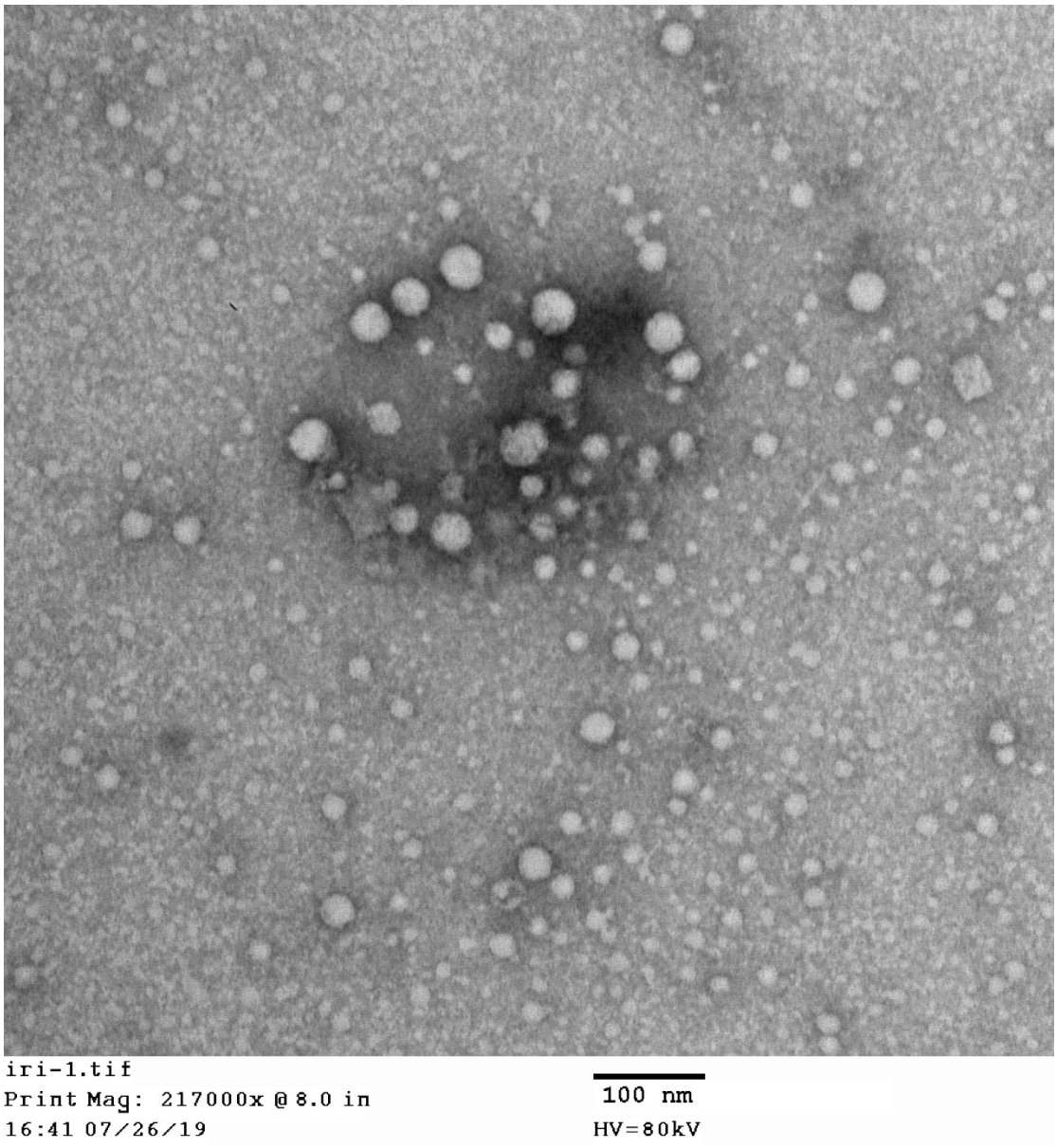


Figure S27. TEM image of a 10 mM PBS solution (pH=7.0) of $\mathbf{1}^{6-}$ (0.2 mM) and irinotecan $\mathbf{7}^{+}$ (0.2 mM) deposited on a copper grid and stained with uranyl acetate.

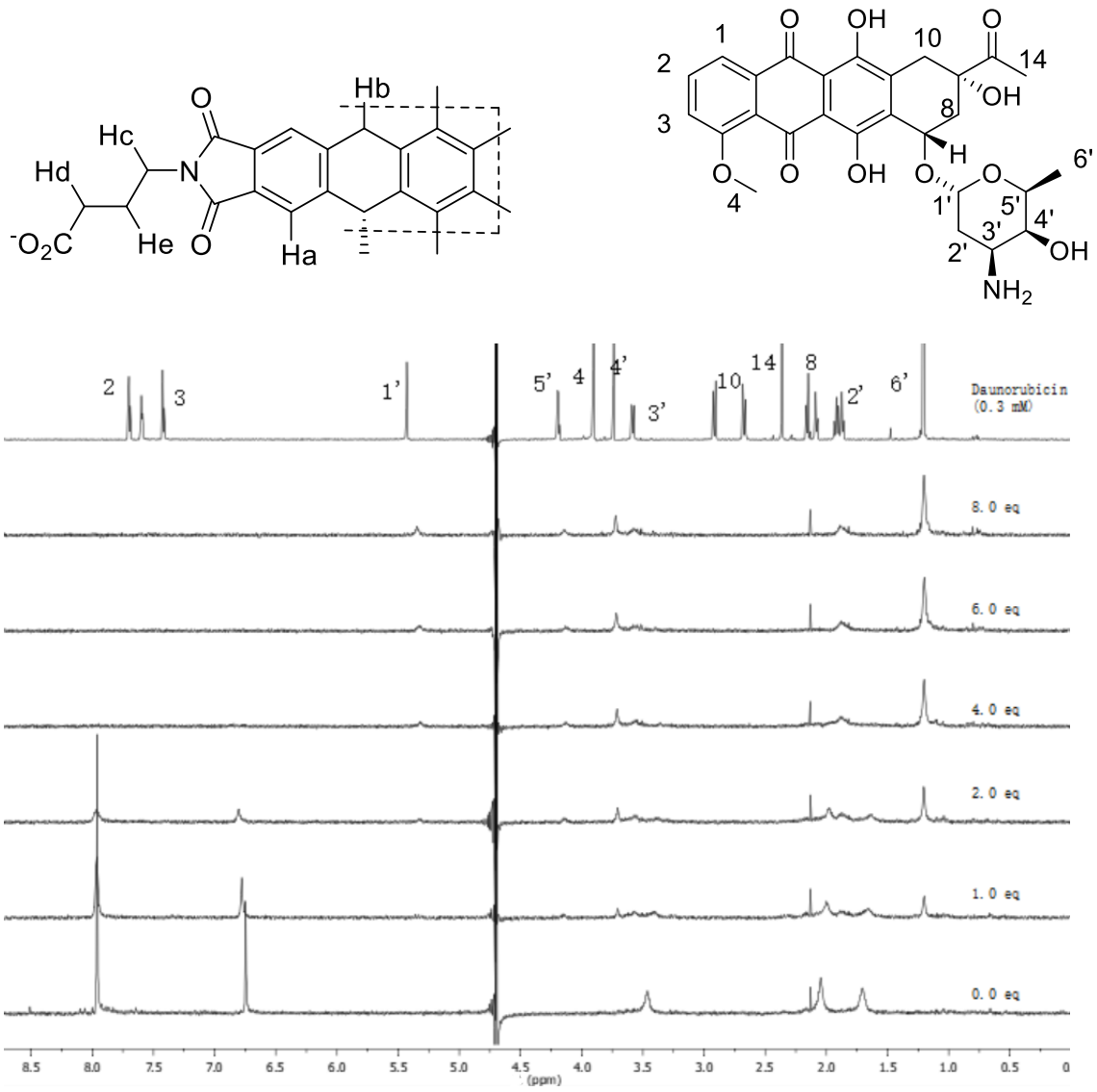


Figure S28. ^{1}H NMR spectra (298 K, 850 MHz) of 0.04 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of a standard 4.5 mM solution of daunorubicin $\mathbf{9}^{+}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1).

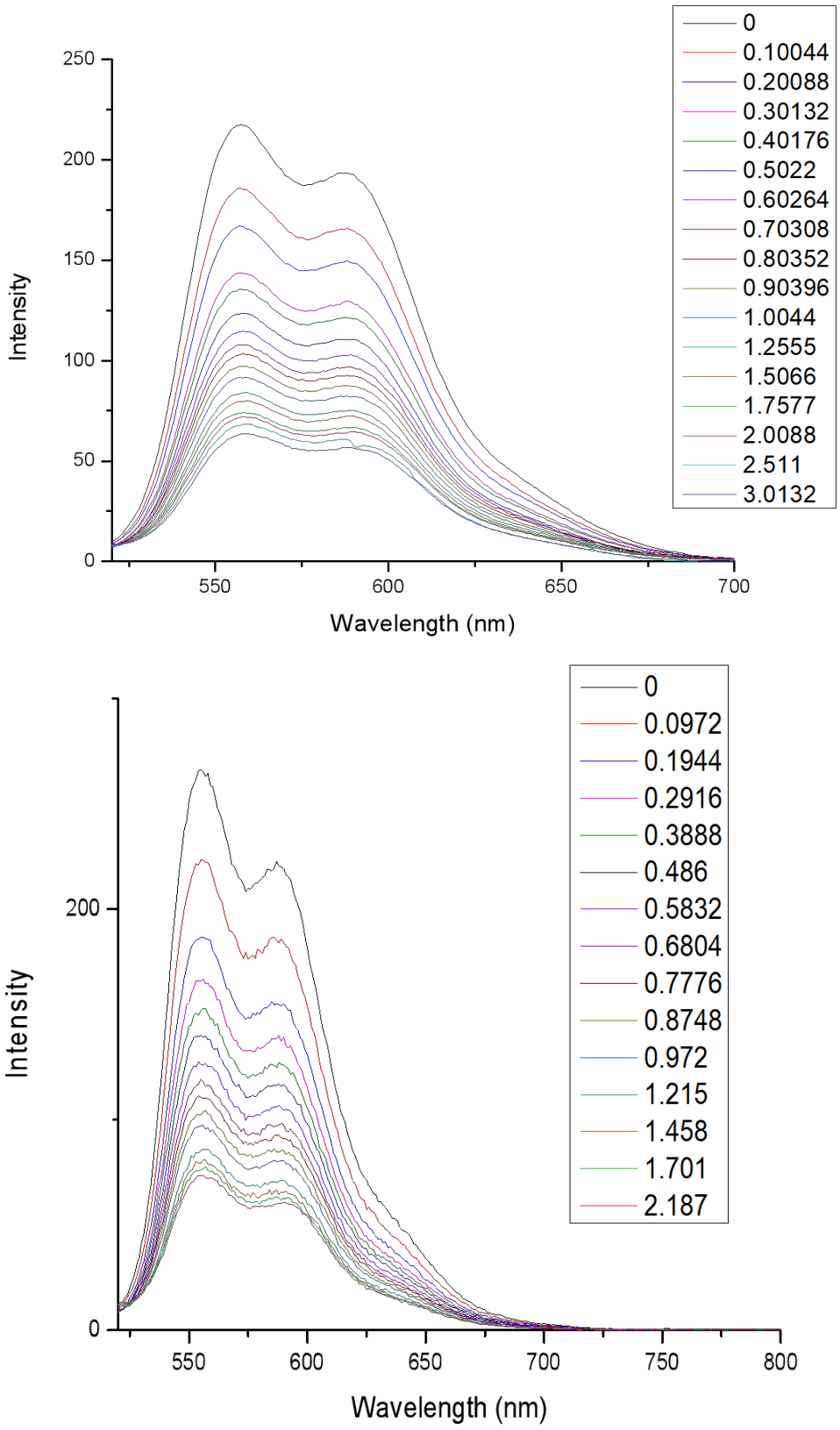


Figure S29. Fluorescence spectra of 1.0 μM solution of daunorubicin $\mathbf{9}^{+}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of 50.0 μM solution of basket $\mathbf{1}^{6-}$; increasing concentrations (μM) of $\mathbf{1}^{6-}$ are shown in the inset.

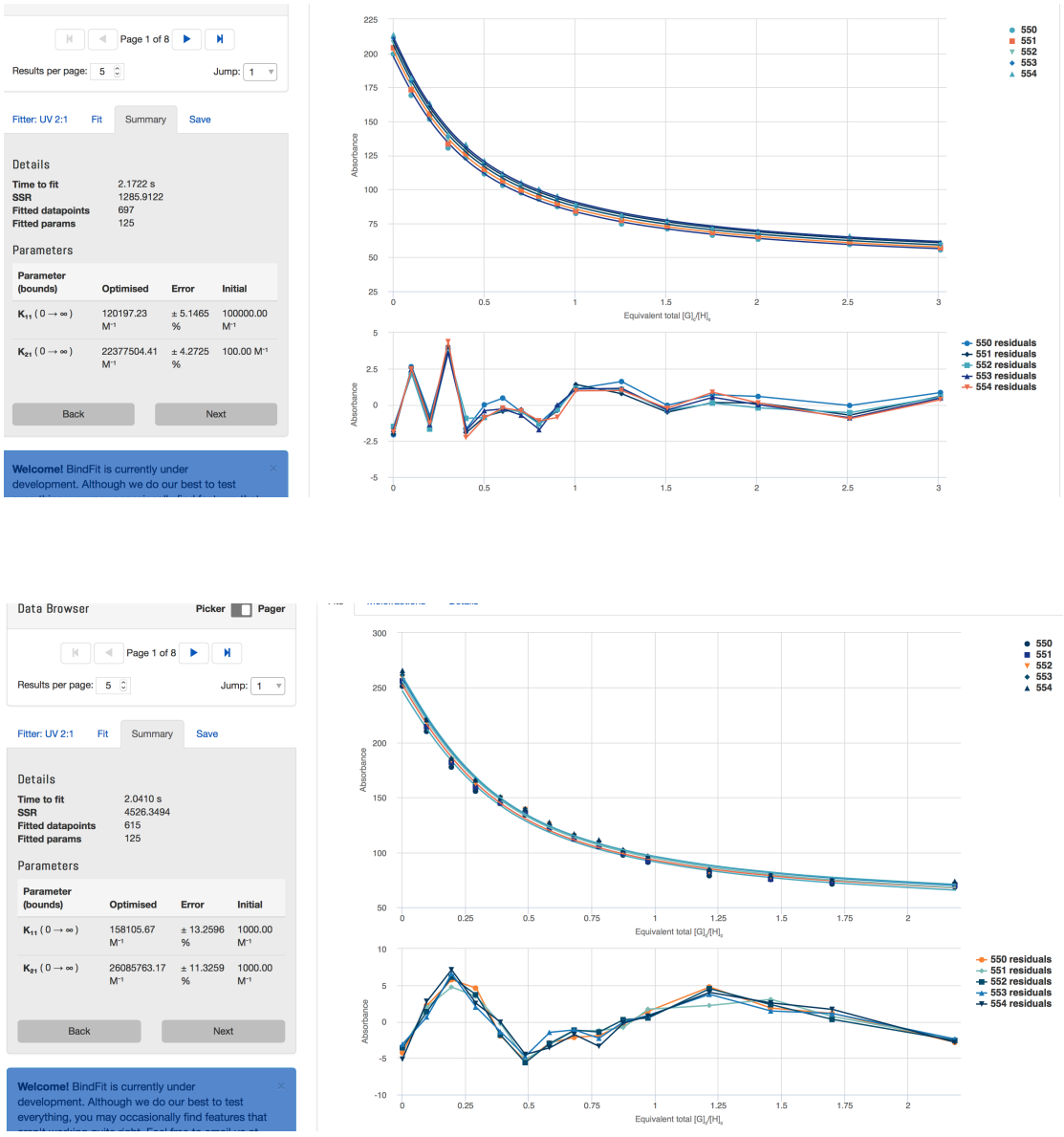


Figure S30. Fluorescence titration experiments were repeated two times (top and bottom; Figure S29). A change in the emission intensity of daunorubicin $\mathbf{9}^{+}$ as a function of the increasing concentration of basket $\mathbf{1}^{6-}$ was subjected to global (550-590 nm) nonlinear least-square analysis using 2:1 binding model (see supramolecular.org) giving $K_1 = 1.4 \pm 0.3 \cdot 10^5$ M^{-1} and $K_2 = 2.4 \pm 0.1 \cdot 10^7$ M^{-1}; the reported value is mean $\pm$ standard deviation.

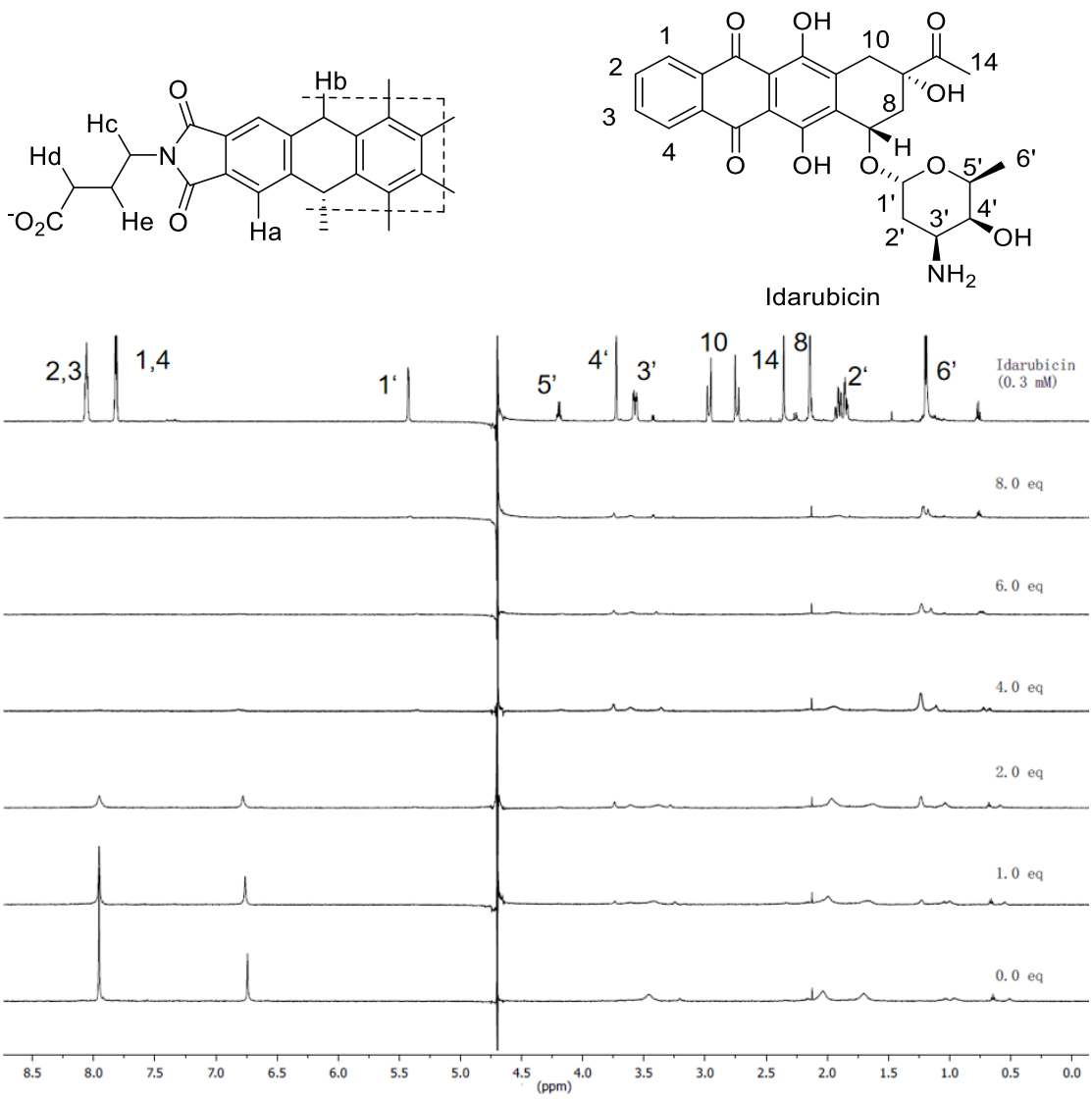


Figure S31. ^{1}H NMR spectra (298 K, 600 MHz) of 0.04 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of a standard 4.5 mM solution of idarubicin $\mathbf{10}^{+}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1).

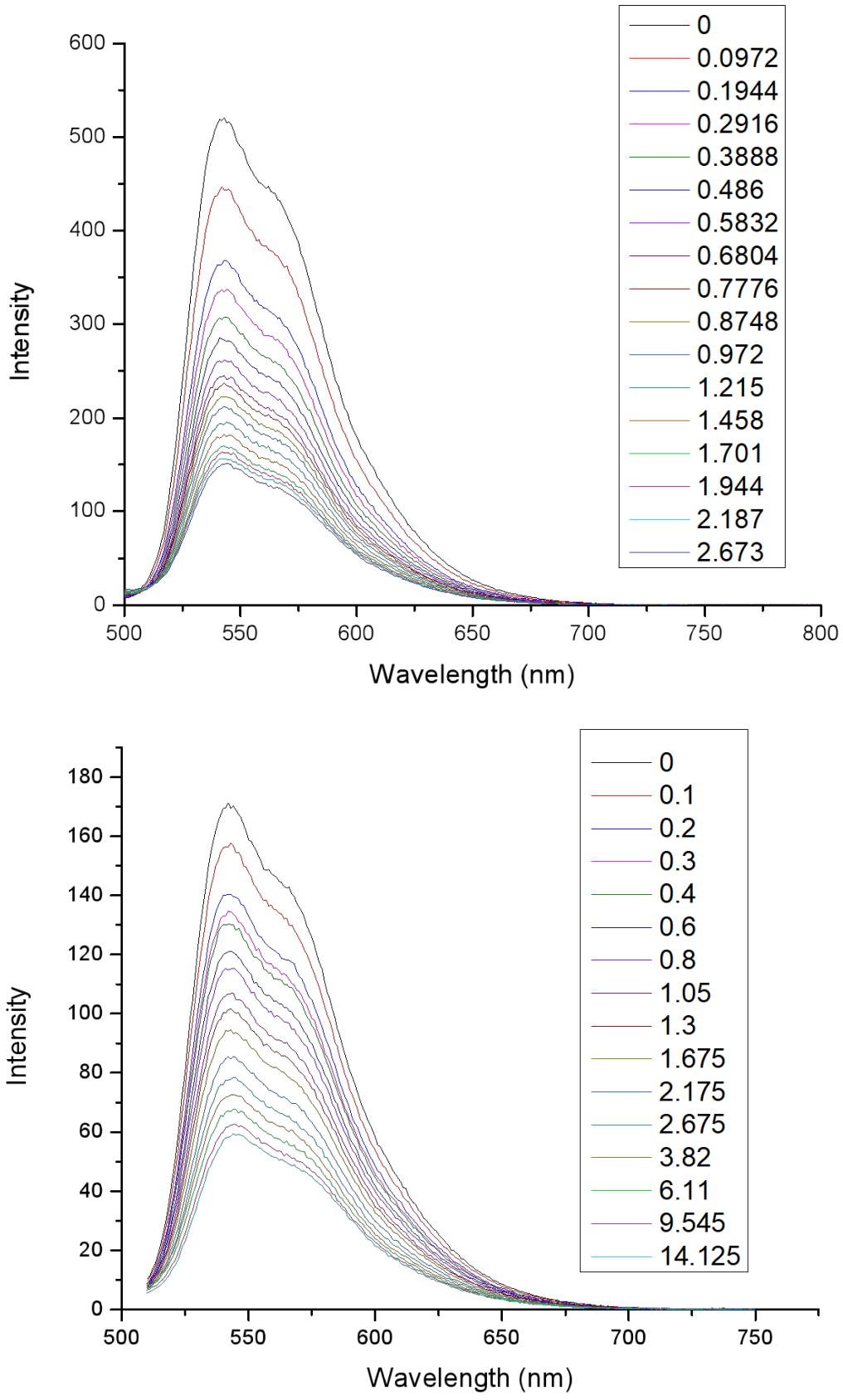


Figure S32. Fluorescence spectra of 1.0 μM solution of idarubicin $\mathbf{10}^{+}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of 50.0 μM solution of basket $\mathbf{1}^{6-}$; increasing concentrations (μM) of $\mathbf{1}^{6-}$ are shown in the inset.

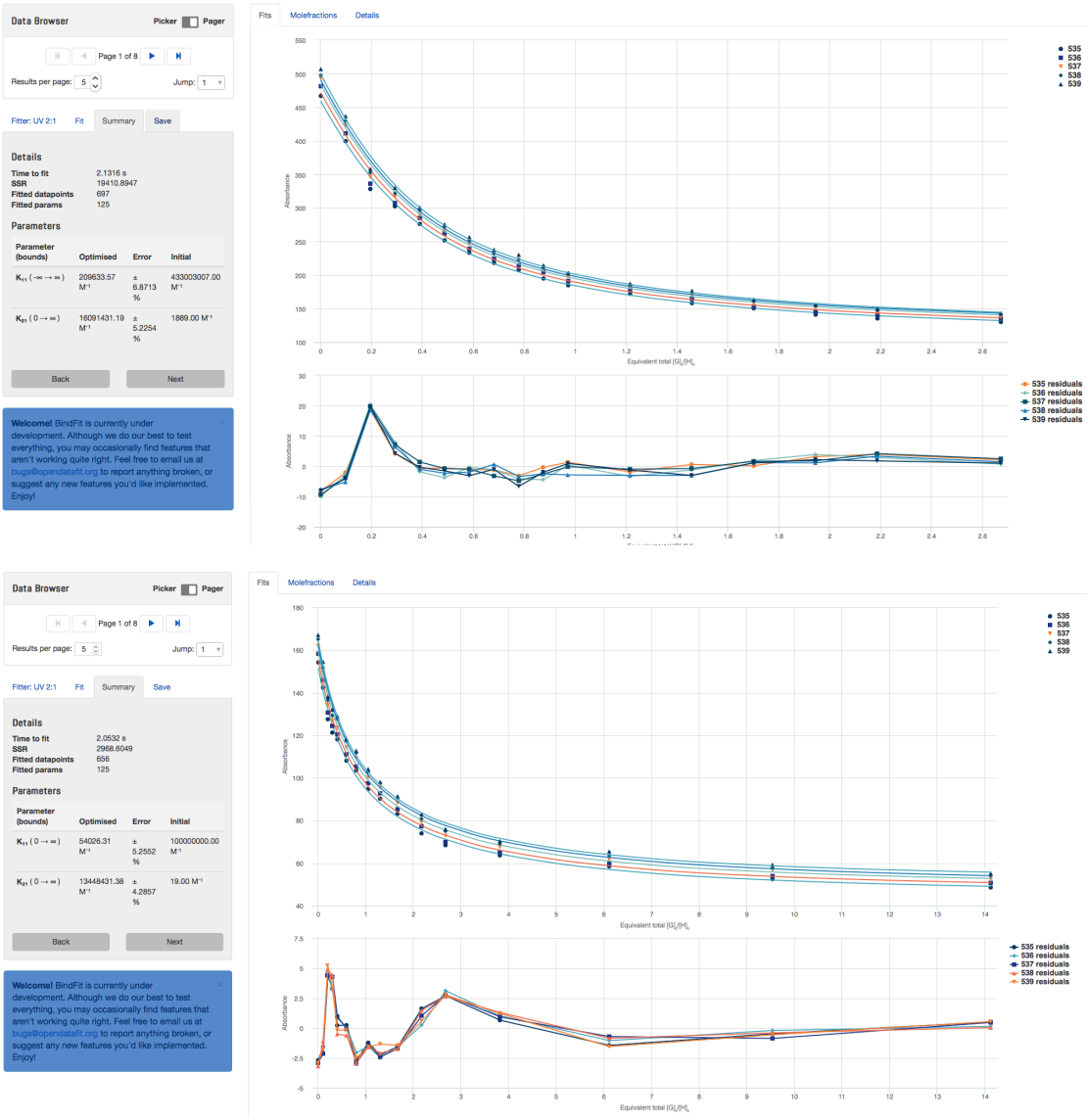


Figure S33. Fluorescence titration experiments were repeated two times (top and bottom; Figure S32). A change in the emission intensity of idarubicin **10**$^{+}$ as a function of the increasing concentration of basket **1**$^{6-}$ was subjected to global (535-575 nm) nonlinear least-square analysis using 2:1 binding model (see supramolecular.org) giving $K_1 = 1.3 \pm 0.9 \cdot 10^5$ M^{-1}and $K_2 = 1.5 \pm 0.2 \cdot 10^7$ M^{-1}; the reported value is mean $\pm$ standard deviation.

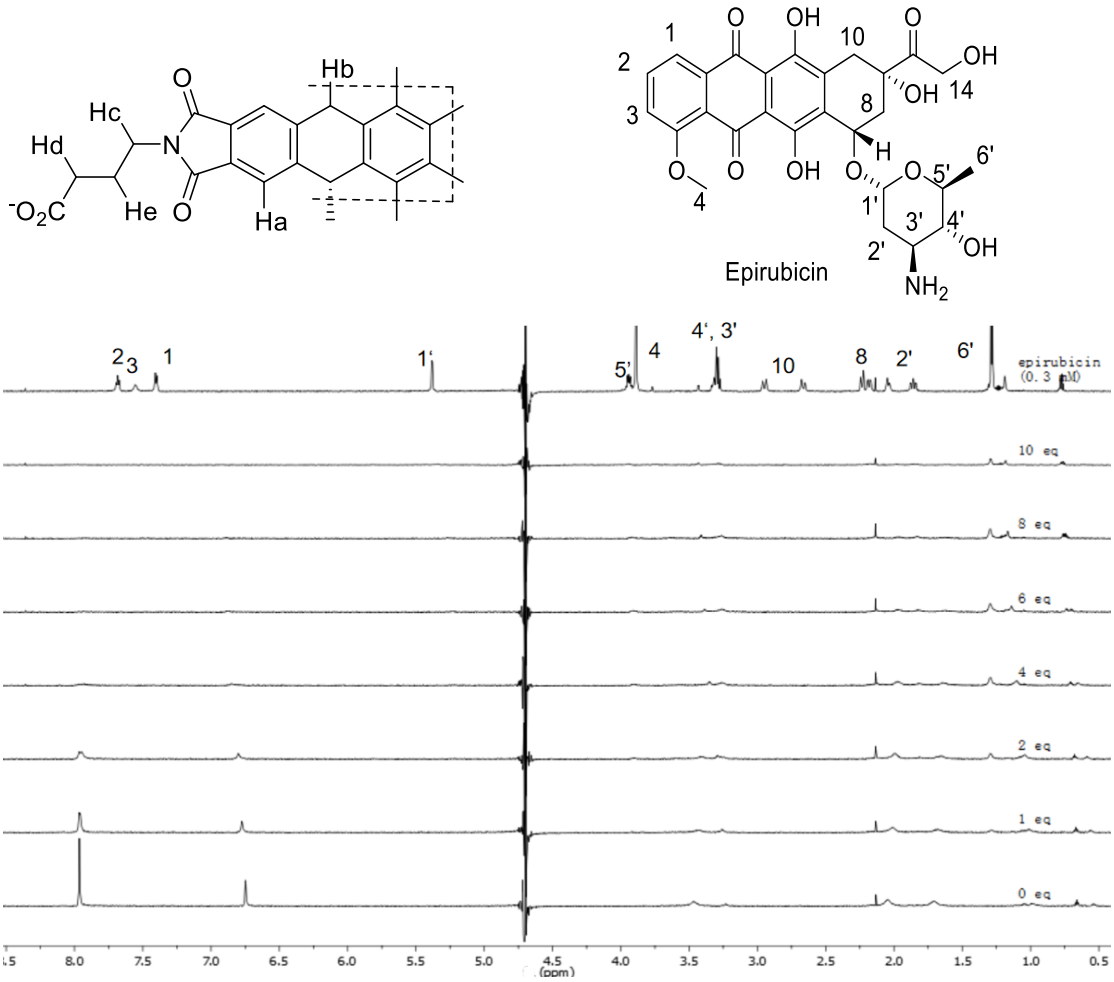
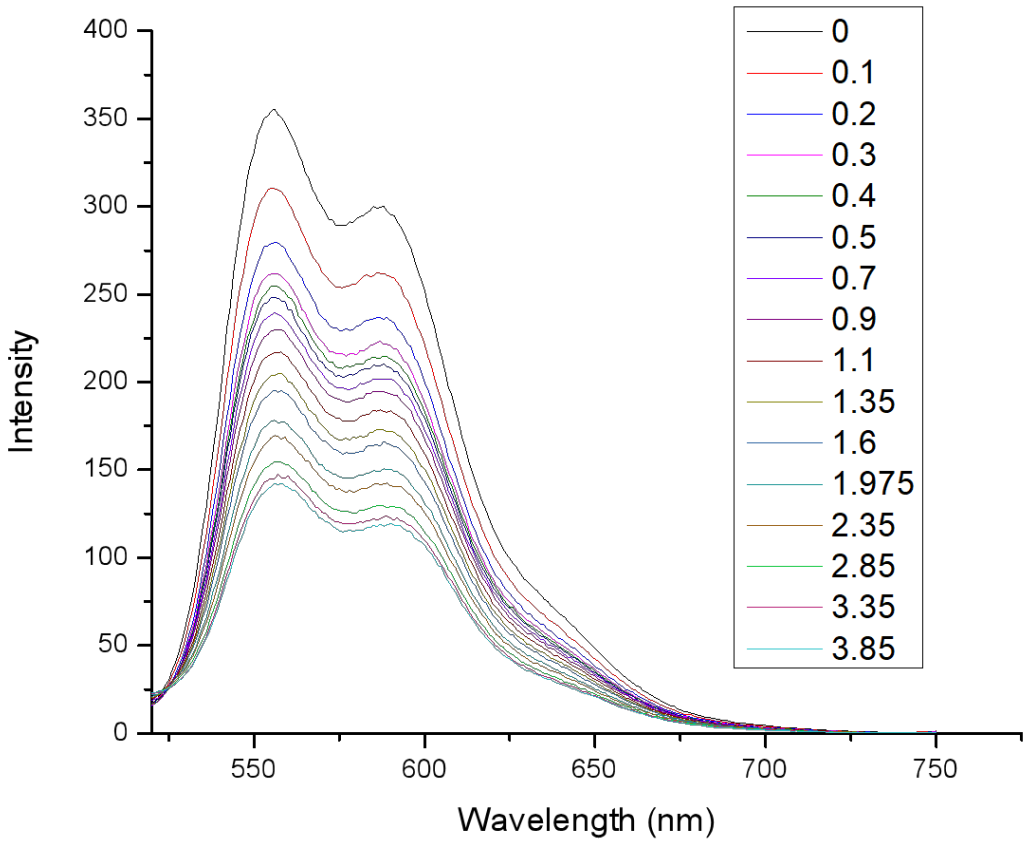


Figure S34. ^{1}H NMR spectra (298 K, 700 MHz) of 0.04 mM basket $\mathbf{1}^{6-}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of a standard 4.5 mM solution of epirubicin $\mathbf{11}^{+}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1).



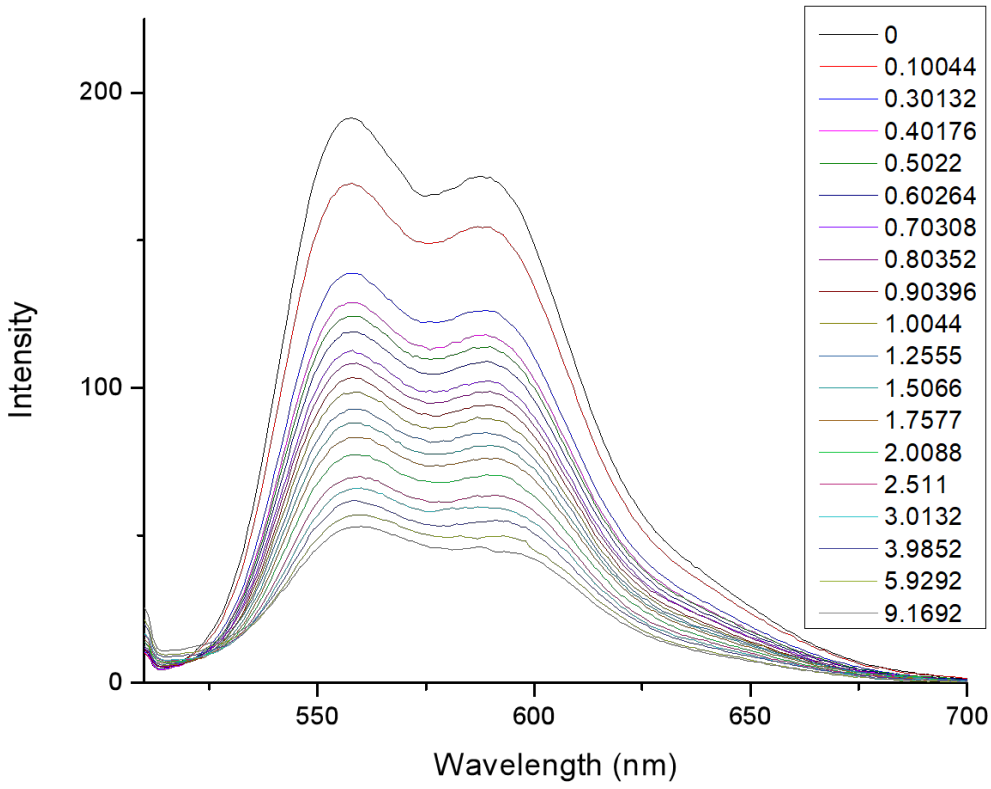


Figure S35. Fluorescence spectra of 1.0 μM solution of epirubicin $\mathbf{11}^{+}$ (10 mM phosphate buffer at pH = 7.0 ± 0.1) obtained upon an incremental addition of 50.0 μM solution of basket $\mathbf{1}^{6-}$; increasing concentrations (μM) of $\mathbf{1}^{6-}$ are shown in the inset.

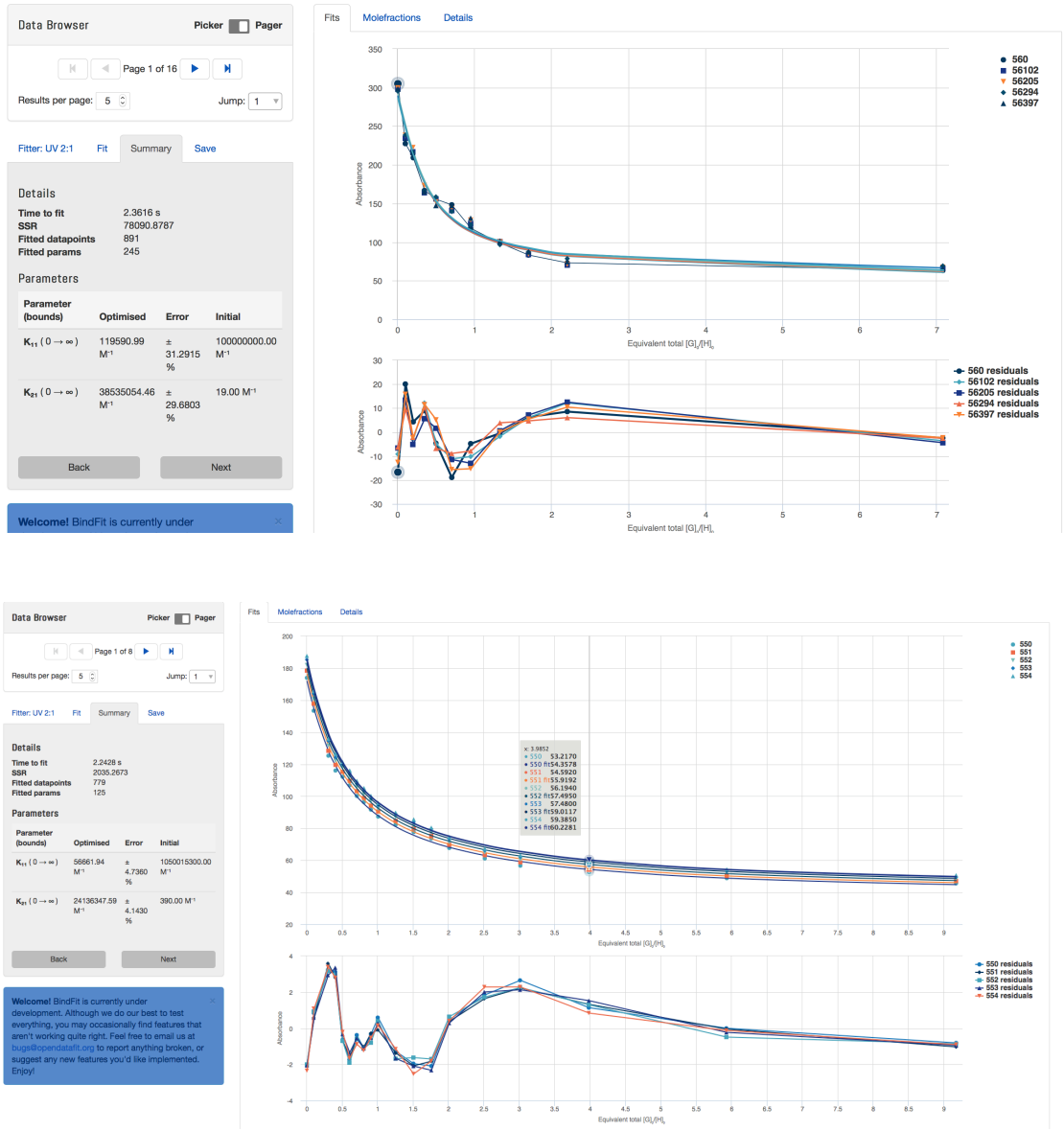


Figure S36. Fluorescence titration experiments were repeated two times (top and bottom; Figure S35). A change in the emission intensity of epirubicin **11**$^{+}$ as a function of the increasing concentration of basket **1**$^{6-}$ was subjected to global (550-590 nm) nonlinear least-square analysis using 2:1 binding model (see supramolecular.org) giving $K_1 = 9 \pm 4 \cdot 10^4$ M^{-1} and $K_2 = 3 \pm 1 \cdot 10^7$ M^{-1}; the reported value is mean $\pm$ standard deviation.

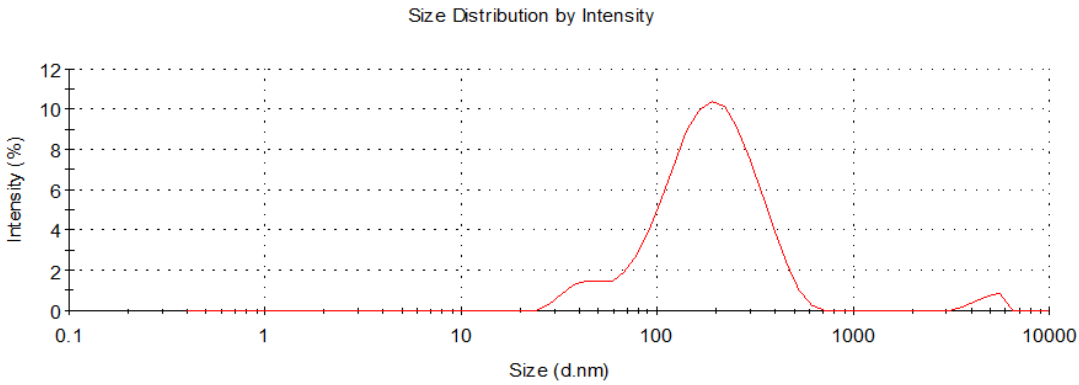


Figure S37. The size distribution of particles in the solution (10 mM PBS at pH=7.0) of $\mathbf{1}^{6-}$ (0.1 mM) and daunorubicin $\mathbf{9}^{+}$ (0.1 mM) was obtained from DLS measurement at 298 K.

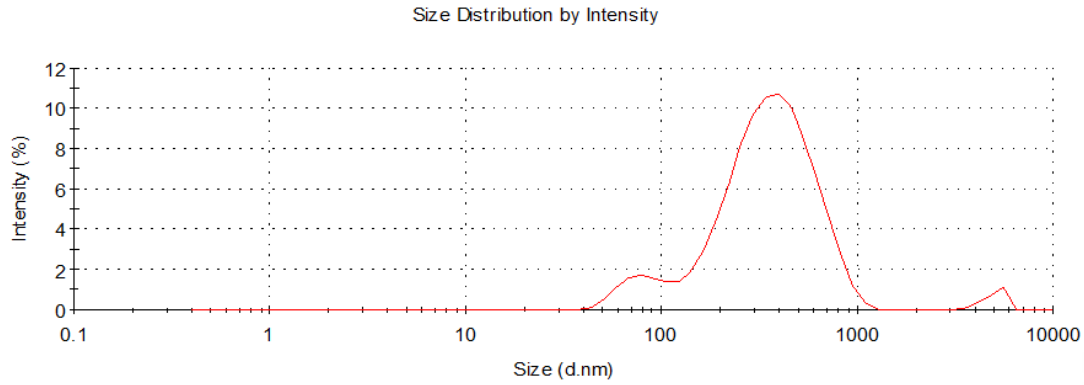


Figure S38. The size distribution of particles in the solution (10 mM PBS at pH=7.0 of $\mathbf{1}^{6-}$ (0.1 mM) and idarubicin $\mathbf{10}^{+}$ (0.1 mM) was obtained from DLS measurement at 298 K.

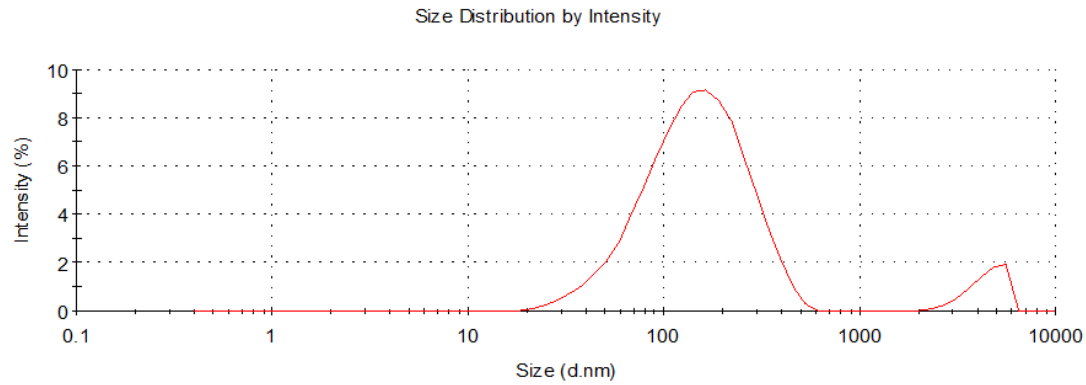


Figure S39. The size distribution of particles in the solution (10 mM PBS at pH=7.0) of $\mathbf{1}^{6-}$ (0.1 mM) and epirubicin $\mathbf{11}^{+}$ (0.1 mM) was obtained from DLS measurement at 298 K.

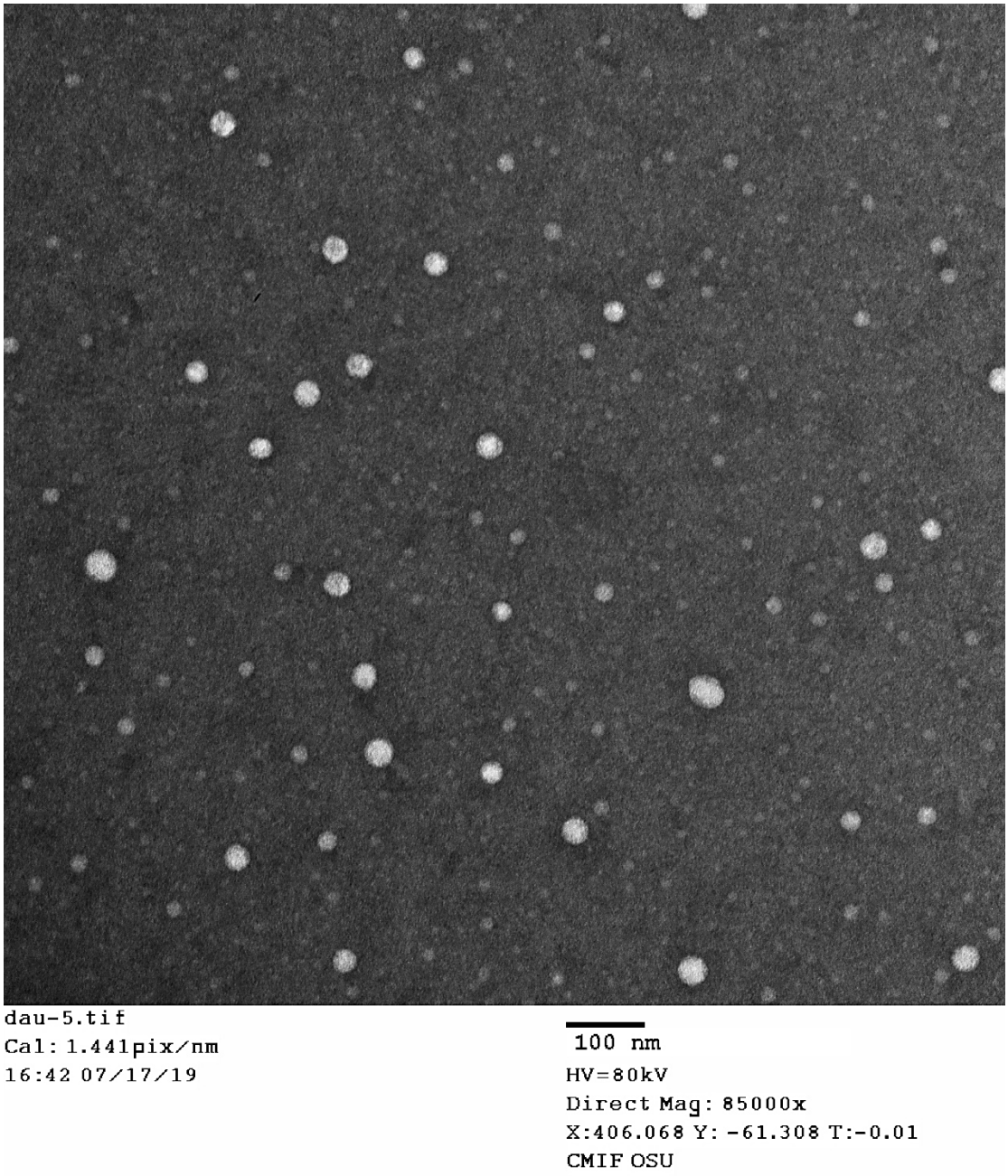


Figure S40. TEM image of 10 mM PBS solution (pH=7.0) of $\mathbf{1}^{6-}$ (0.1 mM) and daunorubicin $\mathbf{9}^{+}$ (0.1 mM) deposited on a copper grid and stained with uranyl acetate.

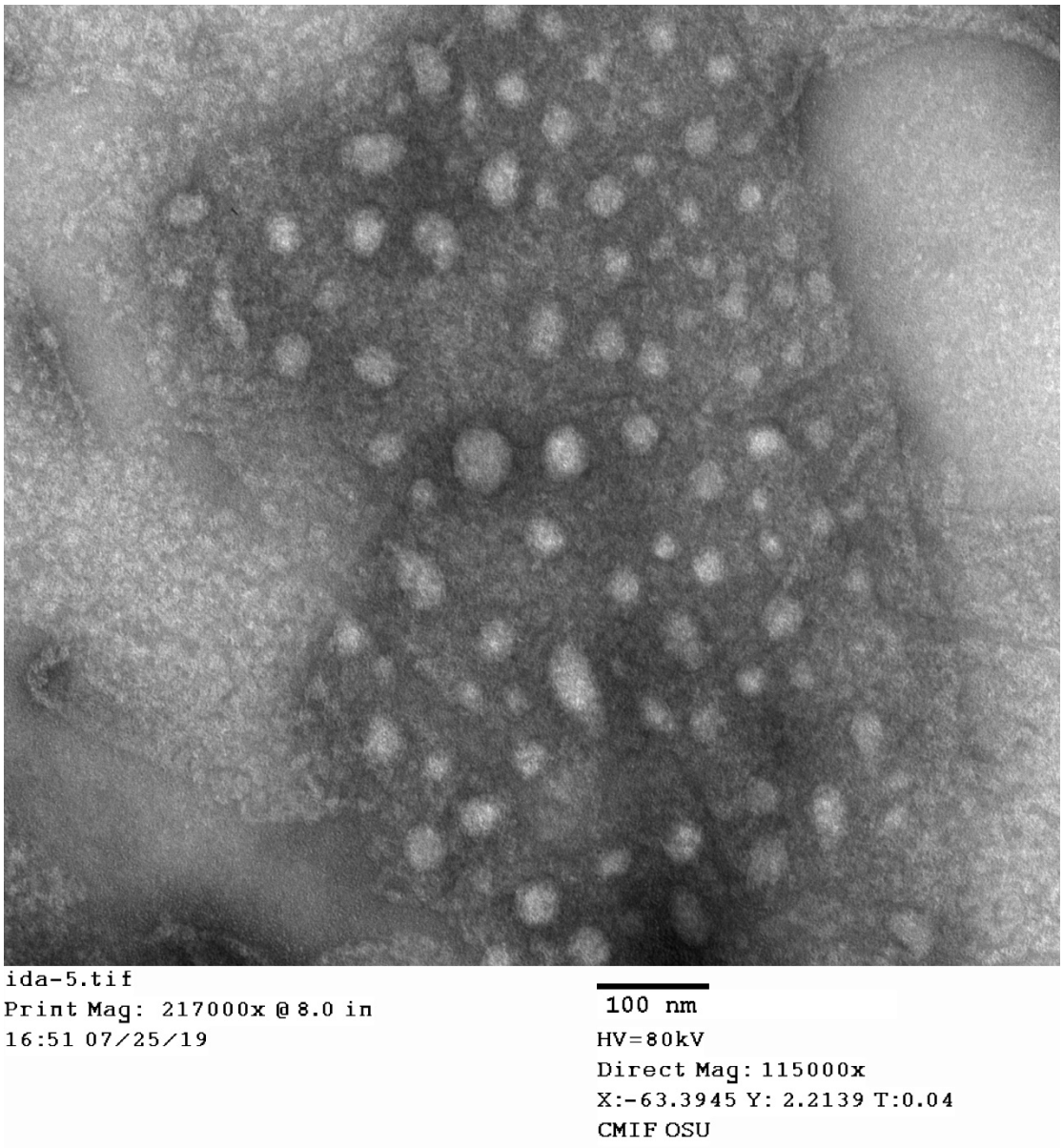


Figure S41. TEM image of 10 mM PBS solution (pH=7.0) of $\mathbf{1}^{6-}$ (0.1 mM) and idarubicin $\mathbf{10}^{+}$ (0.1 mM) deposited on a copper grid and stained with uranyl acetate.

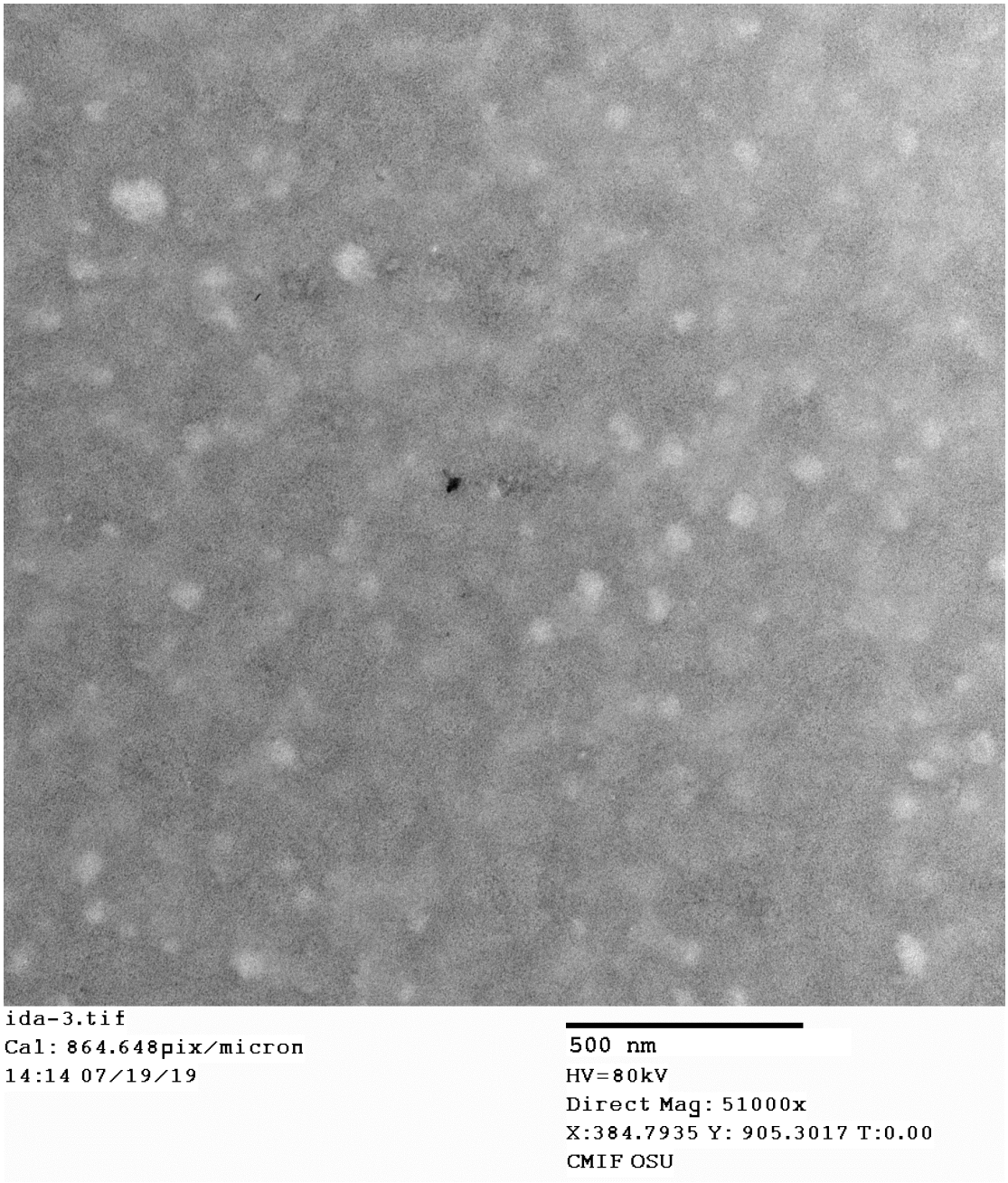


Figure S42. TEM image of 10 mM PBS solution (pH=7.0) of $\mathbf{1}^{6-}$ (0.1 mM) and epirubicin $\mathbf{11}^{+}$ (0.1 mM) deposited on a copper grid and stained with uranyl acetate.

X-Ray crystallography

The single crystal X-ray diffraction studies were carried out on a Bruker Kappa Photon II CPAD diffractometer equipped with Mo K_α radiation (λ = 0.71073 Å). A 0.348 x 0.191 x 0.154 mm piece of a colorless block was mounted on a MiTeGen Micromount with CHRISTO-LUBE MCG 1024 oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ϖ scans. Crystal-to-detector distance was 60 mm using variable exposure time (2s-20s) depending on θ with a scan width of 1.0°. Data collection was 99.8% complete to 25.00° in θ. A total of 242352 reflections were collected covering the indices, -16<=h<=16, -30<=k<=30, -20<=l<=20. 10767 reflections were found to be symmetry independent, with a R_{int} of 0.0425. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be $P2_1/m$. The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model for refinement.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Due to solvent disorder, Platon SQUEEZE was used to remove the electron density from the lattice due to the disordered solvent contribution. Solvent appeared to be a mixture of DMSO and Dichloromethane. One void was found with approximately 585 electrons. Crystallographic data are summarized in Table S1.

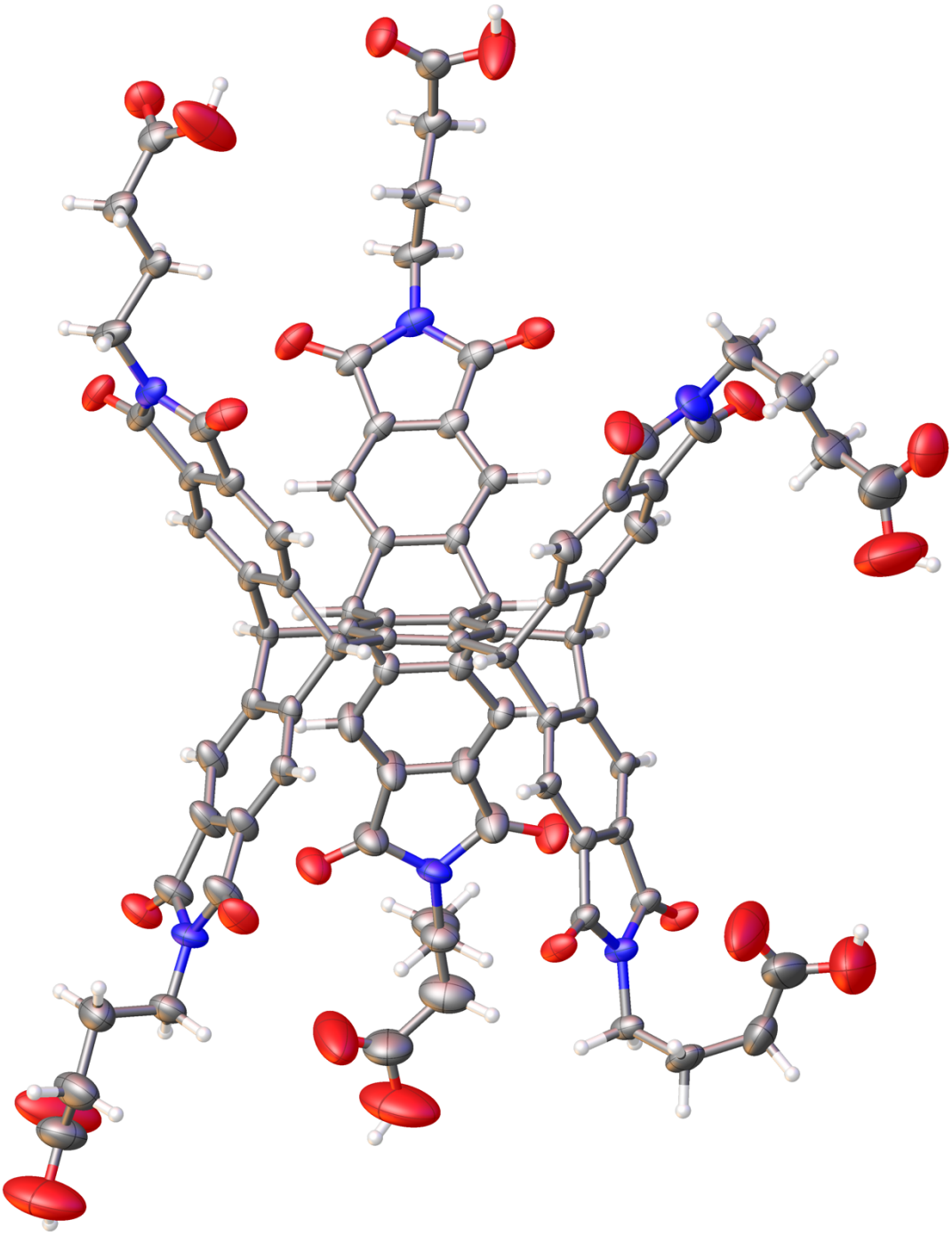


Figure S43. Solid-State structure of **1** (ORTEP).

Table S1. Crystal data and structure refinement for **1**.

Report date	2019-11-18	
Identification code	WK_GABA	
Empirical formula	C85.01 H62.56 Cl0.94 N6 O24.27 S0.27	
Molecular formula	C84 H60 N6 O24, 0.27(C2 H6 O S), 0.48(C H2 Cl2)	
Formula weight	1598.56	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/m 1	
Unit cell dimensions	a = 13.0085(6) Å	α= 90°.
	b = 24.5621(10) Å	β= 92.839(2)°.
	c = 16.7777(7) Å	γ = 90°.
Volume	5354.2(4) $Å^3$	
Z	2	
Density (calculated)	0.992 Mg/m^3	
Absorption coefficient	0.101 mm^{-1}	
F(000)	1658	
Crystal size	0.348 x 0.191 x 0.154 mm^3	
Crystal color, habit	Colorless Block	
Theta range for data collection	2.827 to 25.999°.	
Index ranges	-16<=h<=16, -30<=k<=30, -20<=l<=20	
Reflections collected	242352	
Independent reflections	10767 [R(int) = 0.0425, R(sigma) = 0.0138]	
Completeness to theta = 25.000°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.2627 and 0.2269	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10767 / 153 / 742	
Goodness-of-fit on F^2	1.090	
Final R indices [I>2sigma(I)]	R1 = 0.0879, wR2 = 0.2481	
R indices (all data)	R1 = 0.1042, wR2 = 0.2844	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.777 and -0.894 $e.Å^{-3}$	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **1**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	-9911(2)	9891(1)	6595(2)	49(1)
O(3)	-11375(2)	9013(1)	4418(2)	49(1)
O(6)	-1073(2)	8430(1)	6471(2)	41(1)
N(1)	-10857(2)	9539(1)	5512(2)	38(1)
N(4)	-827(3)	7500	6401(2)	33(1)
C(1)	-9991(2)	9592(1)	6019(2)	38(1)
C(2)	-9204(2)	9221(1)	5698(2)	32(1)
C(3)	-8181(2)	9150(1)	5945(2)	30(1)
C(4)	-7610(2)	8801(1)	5497(2)	26(1)
C(5)	-6469(2)	8683(1)	5641(2)	24(1)
C(6)	-5977(2)	8817(1)	4856(2)	27(1)
C(7)	-5168(2)	9177(1)	4777(2)	31(1)
C(8)	-4787(3)	9222(1)	4023(2)	41(1)
C(9)	-3955(3)	9580(2)	3737(2)	53(1)
C(10)	-10727(2)	9150(1)	4919(2)	37(1)
C(11)	-9639(2)	8956(1)	5036(2)	31(1)
C(12)	-9083(2)	8599(1)	4586(2)	30(1)
C(13)	-8056(2)	8523(1)	4829(2)	28(1)
C(14)	-7297(2)	8156(1)	4422(2)	26(1)
C(15)	-6409(2)	8526(1)	4203(2)	30(1)
C(16)	-6016(3)	8571(1)	3450(2)	42(1)
C(17)	-5190(3)	8924(2)	3380(2)	49(1)
C(19)	-6844(2)	7780(1)	5075(2)	22(1)
C(20)	-6376(2)	8069(1)	5728(2)	22(1)
C(21)	-5879(2)	7789(1)	6344(2)	21(1)
C(22)	-5270(2)	8032(1)	7059(2)	24(1)
C(23)	-5752(2)	7785(1)	7785(2)	28(1)
C(24)	-6187(3)	8084(1)	8384(2)	42(1)
C(27)	-4198(2)	7788(1)	7011(2)	25(1)
C(28)	-3302(2)	8079(1)	6904(2)	27(1)
C(29)	-2422(2)	7783(1)	6784(2)	28(1)
C(30)	-1387(2)	7969(1)	6549(2)	31(1)
C(31)	-11799(2)	9846(1)	5617(3)	47(1)

O(2)	-3466(2)	9926(1)	4096(2)	52(1)
O(4)	-4545(7)	8829(4)	2020(5)	54(2)
O(5)	-7103(4)	8434(2)	10000(2)	68(1)
O(7)	-14653(4)	9335(3)	6808(4)	53(1)
O(8)	-13758(7)	9759(4)	7755(3)	122(3)
O(9)	-2420(12)	9648(9)	662(8)	165(7)
O(10)	-1260(10)	10248(6)	555(8)	179(6)
O(11)	-4865(8)	7500	12732(5)	89(2)
O(12)	-3823(8)	7500	11736(9)	182(6)
N(2)	-3730(7)	9390(4)	2952(6)	40(2)
N(3)	-7204(5)	7500	10187(3)	59(2)
C(18)	-4508(7)	9027(3)	2681(4)	47(2)
C(25)	-6541(4)	7781(2)	9019(3)	42(1)
C(26)	-6983(4)	7972(3)	9768(3)	55(1)
C(32)	-12426(3)	9560(2)	6260(3)	40(1)
C(33)	-13324(3)	9920(2)	6450(3)	42(1)
C(34)	-14006(4)	9644(2)	7015(3)	43(1)
C(35)	-2909(8)	9604(4)	2483(5)	46(2)
C(36)	-3234(6)	10119(4)	2052(5)	63(2)
C(37)	-2344(8)	10362(4)	1609(6)	78(3)
C(38)	-2013(8)	10022(5)	912(7)	82(3)
C(39)	-7476(7)	7500	11026(4)	66(2)
C(40)	-6555(9)	7354(5)	11582(6)	68(3)
C(41)	-5641(9)	7675(5)	11436(6)	68(3)
C(42)	-4740(10)	7500	11993(9)	103(4)
O(4B)	-4984(10)	9007(6)	1963(6)	74(3)
O(5B)	-7882(10)	8418(5)	9605(8)	63(3)
O(7B)	-14390(20)	9365(15)	6956(18)	53(1)
O(8B)	-13560(30)	9528(15)	8014(15)	122(3)
O(9B)	-2220(20)	9291(15)	975(16)	226(12)
O(10B)	-2090(20)	8416(9)	1280(16)	270(12)
O(11B)	-7820(30)	7500	12700(16)	189(11)
O(12B)	-9240(30)	7500	13323(15)	189(11)
N(2B)	-4095(9)	9545(5)	2928(7)	49(2)
N(3B)	-8082(13)	7500	9706(11)	52(4)
C(18B)	-4943(16)	9185(7)	2641(10)	47(2)
C(25B)	-6908(13)	7780(8)	8821(10)	42(1)
C(26B)	-7675(11)	7966(7)	9411(8)	49(3)

C(32B)	-12803(12)	9633(6)	5905(12)	40(1)
C(33B)	-12632(12)	9635(6)	6806(12)	42(1)
C(34B)	-13589(14)	9498(7)	7240(12)	43(1)
C(35B)	-3408(11)	9827(5)	2390(6)	59(3)
C(36B)	-2291(13)	9616(5)	2525(9)	81(4)
C(37B)	-2154(15)	9024(7)	2322(12)	123(6)
C(38B)	-2130(20)	8932(13)	1490(20)	167(9)
C(39B)	-8913(15)	7500	10291(10)	54(5)
C(40B)	-8390(20)	7500	11107(12)	92(9)
C(41B)	-9220(30)	7500	11720(14)	128(10)
C(42B)	-8830(30)	7500	12605(14)	189(11)
O(13)	-91(8)	7347(9)	8137(5)	169(8)
O(14)	985(10)	7898(7)	8744(8)	176(6)
C(43)	204(3)	7455(4)	6100(3)	33(1)
C(44)	1057(5)	7350(3)	6718(5)	52(2)
C(45)	1209(7)	7763(4)	7382(6)	73(2)
C(46)	601(8)	7701(7)	8080(8)	109(5)
S(1S)	-10221(18)	7490(20)	10102(10)	195(8)
O(1S)	-9670(30)	6965(19)	9970(20)	152(14)
C(3S)	-10380(30)	7520(40)	11139(14)	143(12)
C(4S)	-11370(40)	7460(40)	9490(40)	143(12)
Cl(1S)	-4552(14)	7500	12422(12)	134(3)
Cl(2S)	-5549(10)	7500	10788(8)	134(3)
C(1S)	-5694(17)	7500	11805(11)	68(3)
Cl(3S)	-10540(10)	7848(8)	10238(8)	195(8)
C(2S)	-11220(60)	7500	9440(40)	143(12)

Table S3. Bond lengths [Å] and angles [°] for **1**.

O(1)-C(1)	1.213(4)
O(3)-C(10)	1.208(4)
O(6)-C(30)	1.213(3)
N(1)-C(1)	1.383(4)
N(1)-C(10)	1.396(5)
N(1)-C(31)	1.456(4)
N(4)-C(30)#1	1.393(3)
N(4)-C(30)	1.393(3)
N(4)-C(43)	1.460(5)
C(1)-C(2)	1.490(4)
C(2)-C(3)	1.385(4)
C(2)-C(11)	1.383(4)
C(3)-H(3)	0.9500
C(3)-C(4)	1.381(4)
C(4)-C(5)	1.520(4)
C(4)-C(13)	1.412(4)
C(5)-H(5)	1.0000
C(5)-C(6)	1.529(4)
C(5)-C(20)	1.521(3)
C(6)-C(7)	1.385(4)
C(6)-C(15)	1.402(4)
C(7)-H(7)	0.9500
C(7)-C(8)	1.386(4)
C(8)-C(9)	1.492(5)
C(8)-C(17)	1.385(5)
C(9)-O(2)	1.205(4)
C(9)-N(2)	1.441(10)
C(9)-N(2B)	1.363(13)
C(10)-C(11)	1.497(4)
C(11)-C(12)	1.384(4)
C(12)-H(12)	0.9500
C(12)-C(13)	1.390(4)
C(13)-C(14)	1.524(4)
C(14)-H(14)	1.0000
C(14)-C(15)	1.528(4)
C(14)-C(19)	1.528(3)

C(15)-C(16)	1.391(4)
C(16)-H(16)	0.9500
C(16)-C(17)	1.391(5)
C(17)-C(18)	1.527(7)
C(17)-C(18B)	1.445(16)
C(19)-C(19)#1	1.377(5)
C(19)-C(20)	1.417(3)
C(20)-C(21)	1.375(3)
C(21)-C(21)#1	1.420(5)
C(21)-C(22)	1.526(3)
C(22)-H(22)	1.0000
C(22)-C(23)	1.523(4)
C(22)-C(27)	1.524(3)
C(23)-C(23)#1	1.401(6)
C(23)-C(24)	1.387(4)
C(24)-H(24)	0.9500
C(24)-H(24A)	0.9500
C(24)-C(25)	1.396(6)
C(24)-C(25B)	1.43(2)
C(27)-C(27)#1	1.412(5)
C(27)-C(28)	1.388(4)
C(28)-H(28)	0.9500
C(28)-C(29)	1.380(4)
C(29)-C(29)#1	1.392(5)
C(29)-C(30)	1.493(4)
C(31)-H(31B)	0.9900
C(31)-H(31A)	0.9900
C(31)-H(31D)	0.9900
C(31)-H(31C)	0.9900
C(31)-C(32)	1.553(5)
C(31)-C(32B)	1.508(15)
O(4)-C(18)	1.209(11)
O(5)-C(26)	1.214(7)
O(7)-C(34)	1.173(8)
O(8)-H(8)	0.8400
O(8)-C(34)	1.299(8)
O(9)-C(38)	1.130(16)
O(10)-H(10)	0.8400

O(10)-C(38)	1.299(13)
O(11)-C(42)	1.259(16)
O(12)-H(12A)	0.8400
O(12)-H(12A)#1	0.8400
O(12)-C(42)	1.289(17)
N(2)-C(18)	1.407(12)
N(2)-C(35)	1.456(12)
N(3)-C(26)	1.393(7)
N(3)-C(26)#1	1.393(7)
N(3)-C(39)	1.468(8)
C(25)-C(25)#1	1.378(11)
C(25)-C(26)	1.484(7)
C(32)-H(32A)	0.9900
C(32)-H(32B)	0.9900
C(32)-C(33)	1.511(6)
C(33)-H(33A)	0.9900
C(33)-H(33B)	0.9900
C(33)-C(34)	1.493(7)
C(35)-H(35A)	0.9900
C(35)-H(35B)	0.9900
C(35)-C(36)	1.506(12)
C(36)-H(36A)	0.9900
C(36)-H(36B)	0.9900
C(36)-C(37)	1.527(12)
C(37)-H(37A)	0.9900
C(37)-H(37B)	0.9900
C(37)-C(38)	1.516(15)
C(39)-H(39A)	0.9900
C(39)-H(39A)#1	0.9900
C(39)-H(39B)#1	0.9900
C(39)-H(39B)	0.9900
C(39)-C(40)	1.525(14)
C(39)-H(40C)#1	1.05(2)
C(39)-H(40D)#1	1.05(2)
C(40)-H(40A)	0.9900
C(40)-H(40B)	0.9900
C(40)-C(41)	1.457(16)
C(40)-H(1SA)#1	1.417(16)

C(40)-H(1SB)#1	0.93(2)
C(41)-H(41A)	0.9900
C(41)-H(41B)	0.9900
C(41)-C(42)	1.524(17)
C(41)-H(1SA)#1	1.12(2)
O(4B)-C(18B)	1.22(2)
O(5B)-C(26B)	1.19(2)
O(7B)-C(34B)	1.17(3)
O(8B)-H(8B)	0.8400
O(8B)-C(34B)	1.30(3)
O(9B)-C(38B)	1.24(4)
O(10B)-H(10B)	0.8400
O(10B)-C(38B)	1.32(3)
O(11B)-C(42B)	1.32(2)
O(12B)-H(12B)#1	0.8400
O(12B)-H(12B)	0.8400
O(12B)-C(42B)	1.345(19)
N(2B)-C(18B)	1.48(2)
N(2B)-C(35B)	1.474(14)
N(3B)-C(26B)#1	1.364(19)
N(3B)-C(26B)	1.364(19)
N(3B)-C(39B)	1.496(17)
C(25B)-C(25B)#1	1.38(4)
C(25B)-C(26B)	1.51(2)
C(32B)-H(32C)	0.9900
C(32B)-H(32D)	0.9900
C(32B)-C(33B)	1.52(3)
C(33B)-H(33C)	0.9900
C(33B)-H(33D)	0.9900
C(33B)-C(34B)	1.51(2)
C(35B)-H(35C)	0.9900
C(35B)-H(35D)	0.9900
C(35B)-C(36B)	1.55(2)
C(36B)-H(36C)	0.9900
C(36B)-H(36D)	0.9900
C(36B)-C(37B)	1.50(2)
C(37B)-H(37C)	0.9900
C(37B)-H(37D)	0.9900

C(37B)-C(38B)	1.41(3)
C(39B)-H(39C)	0.9900
C(39B)-H(39D)	0.9900
C(39B)-C(40B)	1.499(18)
C(40B)-H(40C)	0.9900
C(40B)-H(40D)	0.9900
C(40B)-C(41B)	1.53(2)
C(41B)-H(41C)	0.9900
C(41B)-H(41D)	0.9900
C(41B)-C(42B)	1.546(19)
O(13)-C(46)	1.26(2)
O(14)-H(14A)	0.8400
O(14)-C(46)	1.291(16)
C(43)-H(43A)	0.9900
C(43)-H(43B)	0.9900
C(43)-C(44)	1.503(9)
C(44)-H(44A)	0.9900
C(44)-H(44B)	0.9900
C(44)-C(45)	1.511(11)
C(45)-H(45A)	0.9900
C(45)-H(45B)	0.9900
C(45)-C(46)	1.453(17)
S(1S)-O(1S)	1.50(2)
S(1S)-C(3S)	1.764(19)
S(1S)-C(4S)	1.77(2)
C(3S)-H(3SA)	0.9800
C(3S)-H(3SB)	0.9800
C(3S)-H(3SC)	0.9800
C(4S)-H(4SA)	0.9800
C(4S)-H(4SB)	0.9800
C(4S)-H(4SC)	0.9800
Cl(1S)-C(1S)	1.770(18)
Cl(2S)-C(1S)	1.725(17)
C(1S)-H(1SA)	0.9900
C(1S)-H(1SB)	0.9900
Cl(3S)-Cl(3S)#1	1.71(4)
Cl(3S)-C(2S)	1.78(2)
C(2S)-H(2SB)	0.9900

C(2S)-H(2SA)	0.9900

C(1)-N(1)-C(10)	112.2(3)
C(1)-N(1)-C(31)	122.8(3)
C(10)-N(1)-C(31)	124.9(3)
C(30)#1-N(4)-C(30)	111.7(3)
C(30)#1-N(4)-C(43)	119.8(4)
C(30)-N(4)-C(43)	128.5(4)
O(1)-C(1)-N(1)	125.5(3)
O(1)-C(1)-C(2)	128.6(3)
N(1)-C(1)-C(2)	105.9(3)
C(3)-C(2)-C(1)	129.4(3)
C(11)-C(2)-C(1)	108.5(3)
C(11)-C(2)-C(3)	122.0(3)
C(2)-C(3)-H(3)	121.6
C(4)-C(3)-C(2)	116.7(3)
C(4)-C(3)-H(3)	121.6
C(3)-C(4)-C(5)	125.4(2)
C(3)-C(4)-C(13)	121.4(2)
C(13)-C(4)-C(5)	113.2(2)
C(4)-C(5)-H(5)	113.1
C(4)-C(5)-C(6)	105.7(2)
C(4)-C(5)-C(20)	106.0(2)
C(6)-C(5)-H(5)	113.1
C(20)-C(5)-H(5)	113.1
C(20)-C(5)-C(6)	105.2(2)
C(7)-C(6)-C(5)	124.9(2)
C(7)-C(6)-C(15)	121.9(3)
C(15)-C(6)-C(5)	113.2(2)
C(6)-C(7)-H(7)	121.8
C(6)-C(7)-C(8)	116.5(3)
C(8)-C(7)-H(7)	121.8
C(7)-C(8)-C(9)	129.7(3)
C(17)-C(8)-C(7)	122.0(3)
C(17)-C(8)-C(9)	108.2(3)
O(2)-C(9)-C(8)	128.9(3)
O(2)-C(9)-N(2)	124.0(5)
N(2)-C(9)-C(8)	106.7(5)

N(2B)-C(9)-C(8)	102.7(5)
O(3)-C(10)-N(1)	125.6(3)
O(3)-C(10)-C(11)	128.6(3)
N(1)-C(10)-C(11)	105.7(3)
C(2)-C(11)-C(10)	107.6(3)
C(2)-C(11)-C(12)	122.2(3)
C(12)-C(11)-C(10)	130.2(3)
C(11)-C(12)-H(12)	121.8
C(11)-C(12)-C(13)	116.4(3)
C(13)-C(12)-H(12)	121.8
C(4)-C(13)-C(14)	113.0(2)
C(12)-C(13)-C(4)	121.3(3)
C(12)-C(13)-C(14)	125.6(2)
C(13)-C(14)-H(14)	113.2
C(13)-C(14)-C(15)	105.7(2)
C(13)-C(14)-C(19)	105.8(2)
C(15)-C(14)-H(14)	113.2
C(19)-C(14)-H(14)	113.2
C(19)-C(14)-C(15)	105.2(2)
C(6)-C(15)-C(14)	113.2(2)
C(16)-C(15)-C(6)	121.2(3)
C(16)-C(15)-C(14)	125.5(3)
C(15)-C(16)-H(16)	121.8
C(15)-C(16)-C(17)	116.5(3)
C(17)-C(16)-H(16)	121.8
C(8)-C(17)-C(16)	121.9(3)
C(8)-C(17)-C(18)	107.5(4)
C(8)-C(17)-C(18B)	110.0(7)
C(16)-C(17)-C(18)	130.4(4)
C(16)-C(17)-C(18B)	123.7(8)
C(19)#1-C(19)-C(14)	127.16(13)
C(19)#1-C(19)-C(20)	120.00(14)
C(20)-C(19)-C(14)	112.8(2)
C(19)-C(20)-C(5)	113.1(2)
C(21)-C(20)-C(5)	126.9(2)
C(21)-C(20)-C(19)	120.0(2)
C(20)-C(21)-C(21)#1	119.96(14)
C(20)-C(21)-C(22)	127.0(2)

C(21)#1-C(21)-C(22)	113.01(13)
C(21)-C(22)-H(22)	113.2
C(23)-C(22)-C(21)	104.8(2)
C(23)-C(22)-H(22)	113.2
C(23)-C(22)-C(27)	107.4(2)
C(27)-C(22)-C(21)	104.2(2)
C(27)-C(22)-H(22)	113.2
C(23)#1-C(23)-C(22)	113.44(14)
C(24)-C(23)-C(22)	124.6(3)
C(24)-C(23)-C(23)#1	121.90(19)
C(23)-C(24)-H(24)	122.2
C(23)-C(24)-H(24A)	123.3
C(23)-C(24)-C(25)	115.7(4)
C(23)-C(24)-C(25B)	113.4(8)
C(25)-C(24)-H(24)	122.2
C(25B)-C(24)-H(24A)	123.3
C(27)#1-C(27)-C(22)	113.20(14)
C(28)-C(27)-C(22)	125.4(2)
C(28)-C(27)-C(27)#1	121.12(15)
C(27)-C(28)-H(28)	121.5
C(29)-C(28)-C(27)	117.1(2)
C(29)-C(28)-H(28)	121.5
C(28)-C(29)-C(29)#1	121.80(15)
C(28)-C(29)-C(30)	130.0(2)
C(29)#1-C(29)-C(30)	107.82(15)
O(6)-C(30)-N(4)	124.8(3)
O(6)-C(30)-C(29)	128.8(3)
N(4)-C(30)-C(29)	106.3(2)
N(1)-C(31)-H(31B)	109.9
N(1)-C(31)-H(31A)	109.9
N(1)-C(31)-H(31D)	105.5
N(1)-C(31)-H(31C)	105.5
N(1)-C(31)-C(32)	108.9(3)
N(1)-C(31)-C(32B)	127.4(6)
H(31B)-C(31)-H(31A)	108.3
H(31D)-C(31)-H(31C)	106.0
C(32)-C(31)-H(31B)	109.9
C(32)-C(31)-H(31A)	109.9

C(32B)-C(31)-H(31D)	105.5
C(32B)-C(31)-H(31C)	105.5
C(34)-O(8)-H(8)	109.5
C(38)-O(10)-H(10)	109.5
H(12A)-O(12)-H(12A)#1	28.7
C(42)-O(12)-H(12A)	109.5
C(42)-O(12)-H(12A)#1	109.5(9)
C(9)-N(2)-C(35)	124.3(8)
C(18)-N(2)-C(9)	109.0(6)
C(18)-N(2)-C(35)	126.1(8)
C(26)-N(3)-C(26)#1	112.6(6)
C(26)#1-N(3)-C(39)	123.4(3)
C(26)-N(3)-C(39)	123.4(3)
O(4)-C(18)-C(17)	129.7(7)
O(4)-C(18)-N(2)	123.2(8)
N(2)-C(18)-C(17)	107.0(5)
C(24)-C(25)-C(26)	129.3(5)
C(25)#1-C(25)-C(24)	122.2(3)
C(25)#1-C(25)-C(26)	108.4(3)
O(5)-C(26)-N(3)	125.7(5)
O(5)-C(26)-C(25)	129.0(5)
N(3)-C(26)-C(25)	105.2(5)
C(31)-C(32)-H(32A)	110.0
C(31)-C(32)-H(32B)	110.0
H(32A)-C(32)-H(32B)	108.3
C(33)-C(32)-C(31)	108.7(3)
C(33)-C(32)-H(32A)	110.0
C(33)-C(32)-H(32B)	110.0
C(32)-C(33)-H(33A)	109.4
C(32)-C(33)-H(33B)	109.4
H(33A)-C(33)-H(33B)	108.0
C(34)-C(33)-C(32)	111.0(3)
C(34)-C(33)-H(33A)	109.4
C(34)-C(33)-H(33B)	109.4
O(7)-C(34)-O(8)	124.4(6)
O(7)-C(34)-C(33)	123.1(5)
O(8)-C(34)-C(33)	112.4(5)
N(2)-C(35)-H(35A)	109.3

N(2)-C(35)-H(35B)	109.3
N(2)-C(35)-C(36)	111.5(9)
H(35A)-C(35)-H(35B)	108.0
C(36)-C(35)-H(35A)	109.3
C(36)-C(35)-H(35B)	109.3
C(35)-C(36)-H(36A)	109.4
C(35)-C(36)-H(36B)	109.4
C(35)-C(36)-C(37)	111.1(7)
H(36A)-C(36)-H(36B)	108.0
C(37)-C(36)-H(36A)	109.4
C(37)-C(36)-H(36B)	109.4
C(36)-C(37)-H(37A)	108.7
C(36)-C(37)-H(37B)	108.7
H(37A)-C(37)-H(37B)	107.6
C(38)-C(37)-C(36)	114.3(9)
C(38)-C(37)-H(37A)	108.7
C(38)-C(37)-H(37B)	108.7
O(9)-C(38)-O(10)	121.7(12)
O(9)-C(38)-C(37)	126.0(9)
O(10)-C(38)-C(37)	111.7(11)
N(3)-C(39)-H(39A)#1	109.3(3)
N(3)-C(39)-H(39A)	109.3
N(3)-C(39)-H(39B)#1	109.32(13)
N(3)-C(39)-H(39B)	109.3
N(3)-C(39)-C(40)	111.5(7)
N(3)-C(39)-H(40C)#1	113.9(12)
N(3)-C(39)-H(40D)#1	113.9(12)
H(39A)-C(39)-H(39A)#1	82.5
H(39A)-C(39)-H(39B)#1	27.7
H(39A)#1-C(39)-H(39B)#1	108.0
H(39A)-C(39)-H(39B)	108.0
H(39A)-C(39)-H(40C)#1	12.3
H(39A)#1-C(39)-H(40C)#1	91.7
H(39A)#1-C(39)-H(40D)#1	12.3
H(39A)-C(39)-H(40D)#1	91.7
H(39B)-C(39)-H(39A)#1	27.7
H(39B)-C(39)-H(39B)#1	129.8
H(39B)-C(39)-H(40C)#1	115.1

H(39B)#1-C(39)-H(40C)#1	16.5
H(39B)-C(39)-H(40D)#1	16.5
H(39B)#1-C(39)-H(40D)#1	115.1
C(40)-C(39)-H(39A)	109.3
C(40)-C(39)-H(39A)#1	129.9(5)
C(40)-C(39)-H(39B)#1	84.5(5)
C(40)-C(39)-H(39B)	109.3
C(40)-C(39)-H(40C)#1	97.1(14)
C(40)-C(39)-H(40D)#1	118.9(14)
C(39)-C(40)-H(40A)	109.0
C(39)-C(40)-H(40B)	109.0
C(39)-C(40)-H(1SA)#1	111.3(11)
C(39)-C(40)-H(1SB)#1	163.7(15)
H(40A)-C(40)-H(40B)	107.8
H(40A)-C(40)-H(1SA)#1	66.6
H(40A)-C(40)-H(1SB)#1	68.4
H(40B)-C(40)-H(1SA)#1	138.8
H(40B)-C(40)-H(1SB)#1	58.9
C(41)-C(40)-C(39)	113.1(9)
C(41)-C(40)-H(40A)	109.0
C(41)-C(40)-H(40B)	109.0
C(41)-C(40)-H(1SA)#1	45.9(10)
C(41)-C(40)-H(1SB)#1	82.4(13)
C(40)-C(41)-H(41A)	109.5
C(40)-C(41)-H(41B)	109.5
C(40)-C(41)-C(42)	110.7(9)
C(40)-C(41)-H(1SA)#1	65.2(10)
H(41A)-C(41)-H(41B)	108.1
H(41A)-C(41)-H(1SA)#1	57.2
H(41B)-C(41)-H(1SA)#1	156.7
C(42)-C(41)-H(41A)	109.5
C(42)-C(41)-H(41B)	109.5
C(42)-C(41)-H(1SA)#1	93.2(13)
O(11)-C(42)-O(12)	119.8(14)
O(11)-C(42)-C(41)#1	118.1(11)
O(11)-C(42)-C(41)	118.1(11)
O(12)-C(42)-C(41)	119.4(13)
O(12)-C(42)-C(41)#1	119.4(13)

C(41)#1-C(42)-C(41)	32.7(10)
C(34B)-O(8B)-H(8B)	109.5
C(38B)-O(10B)-H(10B)	109.5
C(42B)-O(12B)-H(12B)	109.5
C(9)-N(2B)-C(18B)	115.0(10)
C(9)-N(2B)-C(35B)	121.7(9)
C(35B)-N(2B)-C(18B)	123.2(11)
C(26B)-N(3B)-C(39B)	123.0(8)
C(26B)#1-N(3B)-C(39B)	123.0(8)
C(17)-C(18B)-N(2B)	100.4(12)
O(4B)-C(18B)-C(17)	129.9(14)
O(4B)-C(18B)-N(2B)	121.2(14)
C(24)-C(25B)-C(26B)	130.6(16)
C(25B)#1-C(25B)-C(24)	121.4(8)
C(25B)#1-C(25B)-C(26B)	107.5(10)
O(5B)-C(26B)-N(3B)	125.9(14)
O(5B)-C(26B)-C(25B)	128.7(16)
N(3B)-C(26B)-C(25B)	105.4(14)
C(31)-C(32B)-H(32C)	111.1
C(31)-C(32B)-H(32D)	111.1
C(31)-C(32B)-C(33B)	103.4(13)
H(32C)-C(32B)-H(32D)	109.0
C(33B)-C(32B)-H(32C)	111.1
C(33B)-C(32B)-H(32D)	111.1
C(32B)-C(33B)-H(33C)	108.9
C(32B)-C(33B)-H(33D)	108.9
H(33C)-C(33B)-H(33D)	107.7
C(34B)-C(33B)-C(32B)	113.3(14)
C(34B)-C(33B)-H(33C)	108.9
C(34B)-C(33B)-H(33D)	108.9
O(7B)-C(34B)-O(8B)	114(3)
O(7B)-C(34B)-C(33B)	127(2)
O(8B)-C(34B)-C(33B)	119(2)
N(2B)-C(35B)-H(35C)	109.6
N(2B)-C(35B)-H(35D)	109.6
N(2B)-C(35B)-C(36B)	110.3(11)
H(35C)-C(35B)-H(35D)	108.1
C(36B)-C(35B)-H(35C)	109.6

C(36B)-C(35B)-H(35D)	109.6
C(35B)-C(36B)-H(36C)	108.7
C(35B)-C(36B)-H(36D)	108.7
H(36C)-C(36B)-H(36D)	107.6
C(37B)-C(36B)-C(35B)	114.2(13)
C(37B)-C(36B)-H(36C)	108.7
C(37B)-C(36B)-H(36D)	108.7
C(36B)-C(37B)-H(37C)	109.0
C(36B)-C(37B)-H(37D)	109.0
H(37C)-C(37B)-H(37D)	107.8
C(38B)-C(37B)-C(36B)	113(2)
C(38B)-C(37B)-H(37C)	109.0
C(38B)-C(37B)-H(37D)	109.0
O(9B)-C(38B)-O(10B)	120(3)
O(9B)-C(38B)-C(37B)	125(3)
O(10B)-C(38B)-C(37B)	115(3)
N(3B)-C(39B)-H(39C)	110.4
N(3B)-C(39B)-H(39D)	110.4
N(3B)-C(39B)-C(40B)	106.8(18)
H(39C)-C(39B)-H(39D)	108.6
C(40B)-C(39B)-H(39C)	110.4
C(40B)-C(39B)-H(39D)	110.4
H(39A)#1-C(40B)-H(39B)#1	101.3
C(39B)-C(40B)-H(40C)	110.1
C(39B)-C(40B)-H(40D)	110.1
C(39B)-C(40B)-C(41B)	108(2)
H(40C)-C(40B)-H(40D)	108.4
C(41B)-C(40B)-H(40C)	110.1
C(41B)-C(40B)-H(40D)	110.1
C(40B)-C(41B)-H(41C)	108.3
C(40B)-C(41B)-H(41D)	108.3
C(40B)-C(41B)-C(42B)	116(3)
H(41C)-C(41B)-H(41D)	107.4
C(42B)-C(41B)-H(41C)	108.3
C(42B)-C(41B)-H(41D)	108.3
O(11B)-C(42B)-O(12B)	109(2)
O(11B)-C(42B)-C(41B)	113(3)
O(12B)-C(42B)-C(41B)	137(3)

C(46)-O(14)-H(14A)	109.5
N(4)-C(43)-H(43A)	108.3
N(4)-C(43)-H(43B)	108.3
N(4)-C(43)-C(44)	115.8(5)
H(43A)-C(43)-H(43B)	107.4
C(44)-C(43)-H(43A)	108.3
C(44)-C(43)-H(43B)	108.3
C(43)-C(44)-H(44A)	108.0
C(43)-C(44)-H(44B)	108.0
C(43)-C(44)-C(45)	117.3(7)
H(44A)-C(44)-H(44B)	107.2
C(45)-C(44)-H(44A)	108.0
C(45)-C(44)-H(44B)	108.0
C(44)-C(45)-H(45A)	107.8
C(44)-C(45)-H(45B)	107.8
H(45A)-C(45)-H(45B)	107.2
C(46)-C(45)-C(44)	117.9(9)
C(46)-C(45)-H(45A)	107.8
C(46)-C(45)-H(45B)	107.8
O(13)-C(46)-O(14)	116.1(13)
O(13)-C(46)-C(45)	123.5(12)
O(14)-C(46)-C(45)	117.0(11)
O(1S)-S(1S)-C(3S)	104.9(17)
O(1S)-S(1S)-C(4S)	105.1(18)
C(3S)-S(1S)-C(4S)	116(3)
S(1S)-C(3S)-H(3SA)	109.5
S(1S)-C(3S)-H(3SB)	109.5
S(1S)-C(3S)-H(3SC)	109.5
H(3SA)-C(3S)-H(3SB)	109.5
H(3SA)-C(3S)-H(3SC)	109.5
H(3SB)-C(3S)-H(3SC)	109.5
S(1S)-C(4S)-H(4SA)	109.5
S(1S)-C(4S)-H(4SB)	109.5
S(1S)-C(4S)-H(4SC)	109.5
H(4SA)-C(4S)-H(4SB)	109.5
H(4SA)-C(4S)-H(4SC)	109.5
H(4SB)-C(4S)-H(4SC)	109.5
Cl(1S)-C(1S)-H(1SA)	108.1

Cl(1S)-C(1S)-H(1SB)	108.1
Cl(2S)-C(1S)-Cl(1S)	116.7(15)
Cl(2S)-C(1S)-H(1SA)	108.1
Cl(2S)-C(1S)-H(1SB)	108.1
H(1SA)-C(1S)-H(1SB)	107.3
Cl(3S)#1-Cl(3S)-C(2S)	61.3(8)
Cl(3S)-C(2S)-Cl(3S)#1	57.4(16)
Cl(3S)#1-C(2S)-H(2SB)	118.0
Cl(3S)-C(2S)-H(2SB)	118.0
Cl(3S)-C(2S)-H(2SA)	118.0
Cl(3S)#1-C(2S)-H(2SA)	118.0
H(2SB)-C(2S)-H(2SA)	115.2

Symmetry transformations used to generate equivalent atoms:

#1 x,-y+3/2,z

Table S4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **1**. 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)	39(1)	34(1)	74(2)	-10(1)	8(1)	1(1)
O(3)	32(1)	38(1)	75(2)	9(1)	-14(1)	0(1)
O(6)	28(1)	22(1)	72(2)	5(1)	6(1)	-3(1)
N(1)	29(1)	24(1)	63(2)	11(1)	4(1)	3(1)
N(4)	25(1)	24(2)	52(2)	0	8(1)	0
C(1)	34(2)	22(1)	60(2)	7(1)	3(1)	-1(1)
C(2)	29(1)	19(1)	47(2)	7(1)	1(1)	-2(1)
C(3)	31(1)	19(1)	40(2)	2(1)	-1(1)	-2(1)
C(4)	28(1)	16(1)	35(1)	4(1)	-6(1)	-2(1)
C(5)	26(1)	17(1)	28(1)	2(1)	-4(1)	-3(1)
C(6)	32(1)	20(1)	30(1)	3(1)	-4(1)	0(1)
C(7)	36(2)	23(1)	34(1)	3(1)	-2(1)	-6(1)
C(8)	51(2)	35(2)	36(2)	3(1)	1(1)	-16(1)
C(9)	69(2)	48(2)	44(2)	2(2)	9(2)	-24(2)
C(10)	26(1)	24(1)	60(2)	16(1)	-4(1)	-3(1)
C(11)	25(1)	20(1)	48(2)	11(1)	-6(1)	-1(1)
C(12)	30(1)	19(1)	39(2)	7(1)	-8(1)	-4(1)
C(13)	30(1)	16(1)	35(1)	6(1)	-6(1)	-2(1)
C(14)	31(1)	20(1)	28(1)	2(1)	-7(1)	-2(1)
C(15)	35(1)	21(1)	32(1)	4(1)	-5(1)	-4(1)
C(16)	61(2)	37(2)	29(1)	1(1)	-2(1)	-16(2)
C(17)	69(2)	48(2)	29(2)	2(1)	6(2)	-23(2)
C(19)	21(1)	19(1)	26(1)	1(1)	-2(1)	-1(1)
C(20)	21(1)	17(1)	26(1)	1(1)	-1(1)	-2(1)
C(21)	18(1)	20(1)	27(1)	-2(1)	0(1)	1(1)
C(22)	22(1)	22(1)	27(1)	-1(1)	-3(1)	1(1)
C(23)	25(1)	33(1)	25(1)	-2(1)	-4(1)	1(1)
C(24)	52(2)	40(2)	35(2)	-2(1)	8(1)	6(1)
C(27)	21(1)	21(1)	31(1)	-2(1)	-5(1)	1(1)
C(28)	23(1)	20(1)	36(1)	0(1)	-3(1)	-1(1)
C(29)	24(1)	22(1)	36(1)	0(1)	-3(1)	-3(1)
C(30)	24(1)	25(1)	43(2)	2(1)	1(1)	1(1)
C(31)	28(2)	29(2)	84(3)	11(2)	11(2)	2(1)

O(2)	61(2)	44(1)	53(1)	0(1)	6(1)	-27(1)
O(4)	67(5)	60(4)	37(3)	-3(3)	16(3)	-14(3)
O(5)	85(3)	82(3)	38(2)	-7(2)	14(2)	23(2)
O(7)	51(4)	49(2)	58(3)	-5(2)	-5(2)	-17(3)
O(8)	140(5)	169(8)	58(4)	-11(3)	10(4)	-105(6)
O(9)	153(11)	251(17)	98(8)	-81(10)	67(8)	-107(12)
O(10)	167(11)	196(13)	187(12)	-4(10)	126(10)	-10(9)
O(11)	94(6)	103(6)	69(4)	0	-25(3)	0
O(12)	73(4)	288(18)	189(11)	0	32(6)	0
N(2)	39(4)	41(4)	42(3)	-1(3)	20(3)	-2(3)
N(3)	64(4)	83(5)	30(3)	0	11(3)	0
C(18)	57(5)	46(4)	41(2)	-1(2)	17(3)	-12(3)
C(25)	43(3)	59(2)	23(2)	-4(2)	-3(2)	6(2)
C(26)	58(3)	79(4)	29(2)	-1(2)	5(2)	10(3)
C(32)	28(2)	26(2)	64(3)	13(2)	4(2)	1(2)
C(33)	33(2)	28(2)	65(3)	3(2)	3(2)	4(2)
C(34)	37(3)	32(2)	60(3)	-5(2)	4(2)	7(2)
C(35)	47(5)	45(4)	50(4)	7(3)	17(4)	-6(4)
C(36)	60(5)	70(5)	60(5)	18(4)	17(4)	12(4)
C(37)	81(6)	68(5)	89(7)	25(5)	34(5)	4(5)
C(38)	67(6)	101(8)	80(6)	6(6)	31(5)	-14(5)
C(39)	64(4)	106(7)	29(3)	0	15(3)	0
C(40)	72(3)	100(9)	32(3)	5(3)	11(3)	-7(4)
C(41)	72(3)	100(9)	32(3)	5(3)	11(3)	-7(4)
C(42)	68(4)	164(13)	76(5)	0	-6(4)	0
O(4B)	100(9)	91(9)	33(4)	-1(5)	7(5)	-50(6)
O(5B)	62(7)	61(7)	69(8)	-13(6)	31(6)	2(6)
O(7B)	51(4)	49(2)	58(3)	-5(2)	-5(2)	-17(3)
O(8B)	140(5)	169(8)	58(4)	-11(3)	10(4)	-105(6)
O(9B)	290(30)	270(20)	124(13)	-55(13)	21(15)	80(20)
O(10B)	310(30)	200(15)	310(20)	-150(15)	90(20)	1(16)
O(11B)	217(14)	300(30)	54(5)	0	47(6)	0
O(12B)	217(14)	300(30)	54(5)	0	47(6)	0
N(2B)	52(7)	45(6)	50(4)	2(4)	17(5)	-17(4)
N(3B)	47(8)	60(11)	51(7)	0	8(7)	0
C(18B)	57(5)	46(4)	41(2)	-1(2)	17(3)	-12(3)
C(25B)	43(3)	59(2)	23(2)	-4(2)	-3(2)	6(2)
C(26B)	38(7)	75(11)	34(7)	-10(7)	0(6)	-2(7)

C(32B)	28(2)	26(2)	64(3)	13(2)	4(2)	1(2)
C(33B)	33(2)	28(2)	65(3)	3(2)	3(2)	4(2)
C(34B)	37(3)	32(2)	60(3)	-5(2)	4(2)	7(2)
C(35B)	76(8)	55(6)	48(5)	14(5)	14(5)	-27(6)
C(36B)	70(8)	81(6)	96(9)	1(6)	31(7)	-25(7)
C(37B)	118(12)	94(7)	161(12)	-32(8)	48(10)	-19(8)
C(38B)	157(19)	175(14)	171(12)	-76(10)	19(14)	35(14)
C(39B)	48(9)	71(14)	43(6)	0	5(6)	0
C(40B)	113(14)	120(30)	41(6)	0	-10(7)	0
C(41B)	216(14)	120(30)	54(5)	0	47(6)	0
C(42B)	217(14)	300(30)	54(5)	0	47(6)	0
O(13)	128(7)	320(20)	58(4)	-28(8)	2(4)	-89(11)
O(14)	125(8)	289(17)	114(6)	-80(9)	2(6)	-35(9)
C(43)	25(1)	24(2)	52(2)	0	8(1)	0
C(44)	23(2)	59(6)	76(4)	-6(3)	2(2)	5(2)
C(45)	47(4)	89(6)	83(4)	-23(4)	-13(3)	-9(4)
C(46)	50(4)	189(15)	89(5)	-33(6)	5(4)	11(5)
S(1S)	134(9)	340(20)	118(6)	12(9)	18(5)	121(11)
O(1S)	60(17)	270(30)	130(30)	0(20)	36(18)	70(20)
C(3S)	91(15)	260(30)	76(11)	0(20)	-8(11)	60(20)
C(4S)	91(15)	260(30)	76(11)	0(20)	-8(11)	60(20)
Cl(1S)	117(7)	168(9)	118(8)	0	9(6)	0
Cl(2S)	117(7)	168(9)	118(8)	0	9(6)	0
C(1S)	72(3)	100(9)	32(3)	5(3)	11(3)	-7(4)
Cl(3S)	134(9)	340(20)	118(6)	12(9)	18(5)	121(11)
C(2S)	91(15)	260(30)	76(11)	0(20)	-8(11)	60(20)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **1**.

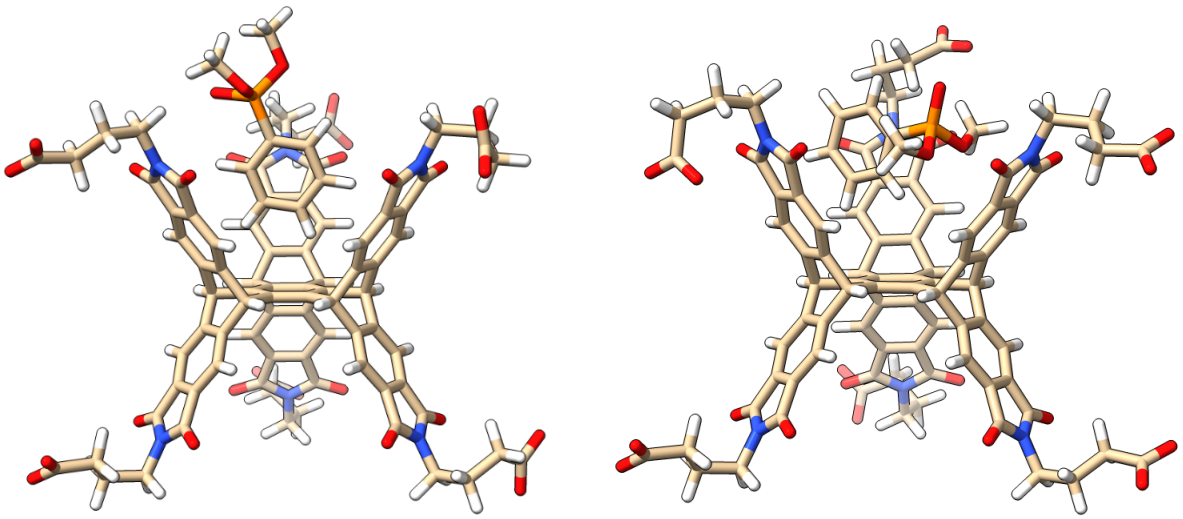
	x	y	z	U(eq)
H(3)	-7887	9333	6400	36
H(5)	-6151	8886	6107	29
H(7)	-4890	9382	5217	38
H(12)	-9387	8416	4134	36
H(14)	-7614	7954	3954	32
H(16)	-6297	8370	3007	51
H(22)	-5270	8439	7062	28
H(24)	-6241	8469	8364	50
H(24A)	-6021	8454	8493	50
H(28)	-3295	8466	6913	32
H(31B)	-12211	9863	5106	56
H(31A)	-11629	10222	5787	56
H(31D)	-11973	10015	5092	56
H(31C)	-11599	10148	5982	56
H(8)	-14199	9627	8049	183
H(10)	-963	10013	284	269
H(12A)	-3400	7585	12109	273
H(32A)	-12680	9203	6059	47
H(32B)	-11983	9497	6749	47
H(33A)	-13063	10264	6689	50
H(33B)	-13725	10009	5950	50
H(35A)	-2714	9327	2089	56
H(35B)	-2297	9680	2840	56
H(36A)	-3474	10387	2441	76
H(36B)	-3814	10038	1666	76
H(37A)	-2549	10727	1410	94
H(37B)	-1746	10409	1991	94
H(39A)	-8036	7234	11098	79
H(39B)	-7733	7865	11168	79
H(40A)	-6742	7409	12141	81
H(40B)	-6392	6963	11515	81
H(41A)	-5789	8065	11521	81

H(41B)	-5456	7627	10875	81
H(8B)	-14015	9325	8191	183
H(10B)	-1572	8363	1013	405
H(12B)	-8803	7392	13671	283
H(32C)	-12945	9261	5703	47
H(32D)	-13383	9874	5734	47
H(33C)	-12087	9369	6959	50
H(33D)	-12385	10000	6979	50
H(35C)	-3427	10223	2491	71
H(35D)	-3648	9762	1829	71
H(36C)	-1834	9836	2198	98
H(36D)	-2069	9672	3092	98
H(37C)	-1504	8891	2586	148
H(37D)	-2727	8813	2534	148
H(39C)	-9352	7173	10216	65
H(39D)	-9352	7827	10216	65
H(40C)	-7950	7827	11178	110
H(40D)	-7950	7173	11178	110
H(41C)	-9661	7175	11625	154
H(41D)	-9661	7825	11625	154
H(14A)	651	7781	9124	264
H(43A)	359	7796	5816	40
H(43B)	200	7156	5704	40
H(44A)	1709	7323	6441	63
H(44B)	932	6991	6964	63
H(45A)	1944	7757	7564	88
H(45B)	1064	8128	7153	88
H(3SA)	-10739	7854	11272	214
H(3SB)	-10794	7203	11296	214
H(3SC)	-9708	7506	11425	214
H(4SA)	-11768	7792	9548	214
H(4SB)	-11198	7414	8931	214
H(4SC)	-11779	7144	9651	214
H(1SA)	-6102	7175	11939	81
H(1SB)	-6102	7825	11939	81
H(2SB)	-10914	7500	8912	171
H(2SA)	-11978	7500	9432	171

Computational Studies

The Monte-Carlo (MC) conformational searches of were completed with the Maestro suite (Schrodinger) using OPLS3e molecular mechanics (MM) force field in implicit water solvent. For each search, we used systematic torsional sampling method with 300 steps per rotatable bond and 50,000 steps overall. The energy window for saving structures was set to 12 kJ/mol.

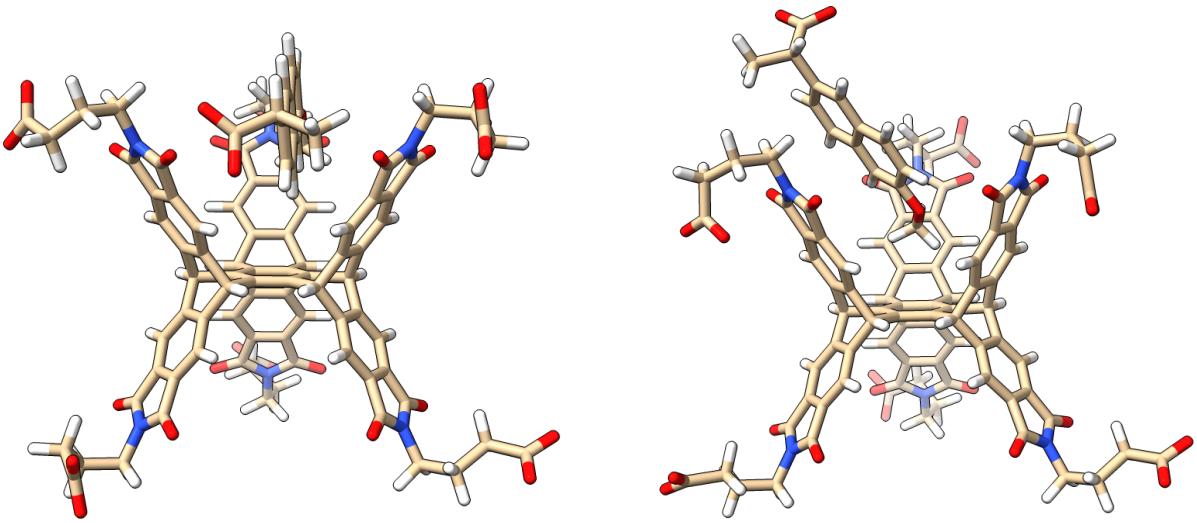
DMPP 2: The starting pose, on the left, consisted of DMPP **2** docked horizontally in the cavity. After the conformational searching procedure, one clusters was found within 5.0 kJ/mol of the global minimum. The lowest energy structure, on the right, found that the guest sat with the phenyl ring between two arms.



Final report:

2961 unique conformations found
2961 minimized with good convergence
Found 156 confs within 1.00 kcal/mol (4.18 kJ/mol) of glob. min.
Found 1183 confs within 2.00 kcal/mol (8.37 kJ/mol) of glob. min.
Found 2961 confs within 3.00 kcal/mol (12.55 kJ/mol) of glob. min.
Global minimum E = -1717.45 found 1 times.

Naproxen 3^-: The starting pose, on the left, consisted of naproxen $\mathbf{3}^-$ docked horizontally in the cavity. After the conformational searching procedure one cluster was found within 5.0 kJ/mol of the global minimum. Through the course of the conformational search, the lowest energy structure, on the right, found that the guest was seated against one arm with one C–H···π contact and the negative carboxyl group pointed up and away from the host's carboxyl groups.



Final report:

2794 unique conformations found

2780 minimized with good convergence

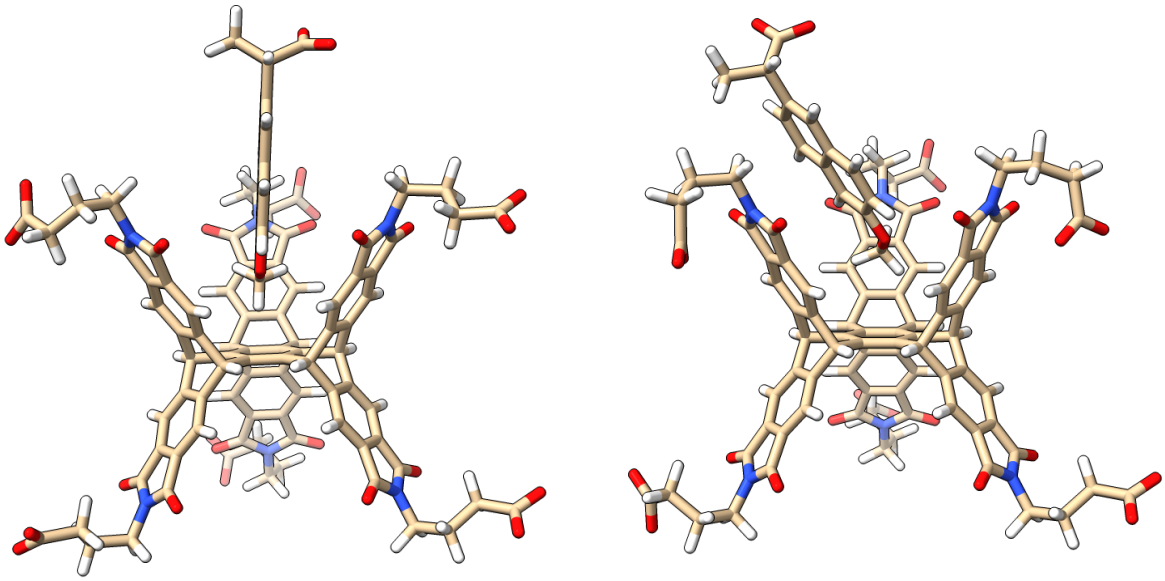
Found 332 confs within 1.00 kcal/mol (4.18 kJ/mol) of glob. min.

Found 1342 confs within 2.00 kcal/mol (8.37 kJ/mol) of glob. min.

Found 2794 confs within 3.00 kcal/mol (12.55 kJ/mol) of glob. min.

Global minimum E = -1895.77 found 5 times.

The starting pose, on the left, consisted of naproxen **3**$^-$ docked vertically in the cavity. After the conformational searching procedure one cluster was found within 5.0 kJ/mol of the global minimum. Through the course of the conformational search, the lowest energy structure, on the right, found that the guest was seated against one arm with one C–H···π contact and the negative carboxyl group pointed up and away from the host's carboxyl groups.



Final report:

564 unique conformations found

563 minimized with good convergence

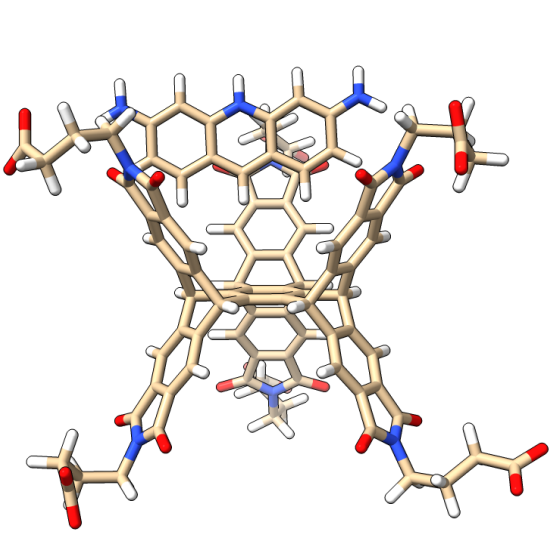
Found 41 confs within 1.00 kcal/mol (4.18 kJ/mol) of glob. min.

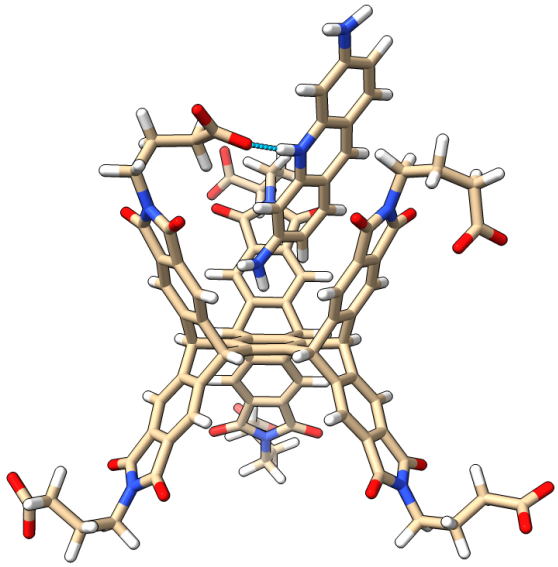
Found 229 confs within 2.00 kcal/mol (8.37 kJ/mol) of glob. min.

Found 564 confs within 3.00 kcal/mol (12.55 kJ/mol) of glob. min.

Global minimum E = -1895.99 found 4 times.

Proflavine 4^+: The starting pose, on the left, consisted of proflavine $\mathbf{4}^+$ docked horizontally in the cavity. After the conformational searching procedure multiple clusters were found within 5.0 kJ/mol of the global minimum. These clusters were found to be redundant and corresponded to the guest bound to different arms. The lowest energy structure, on the right, found that the guest formed one intermolecular hydrogen bond (blue dashed line).

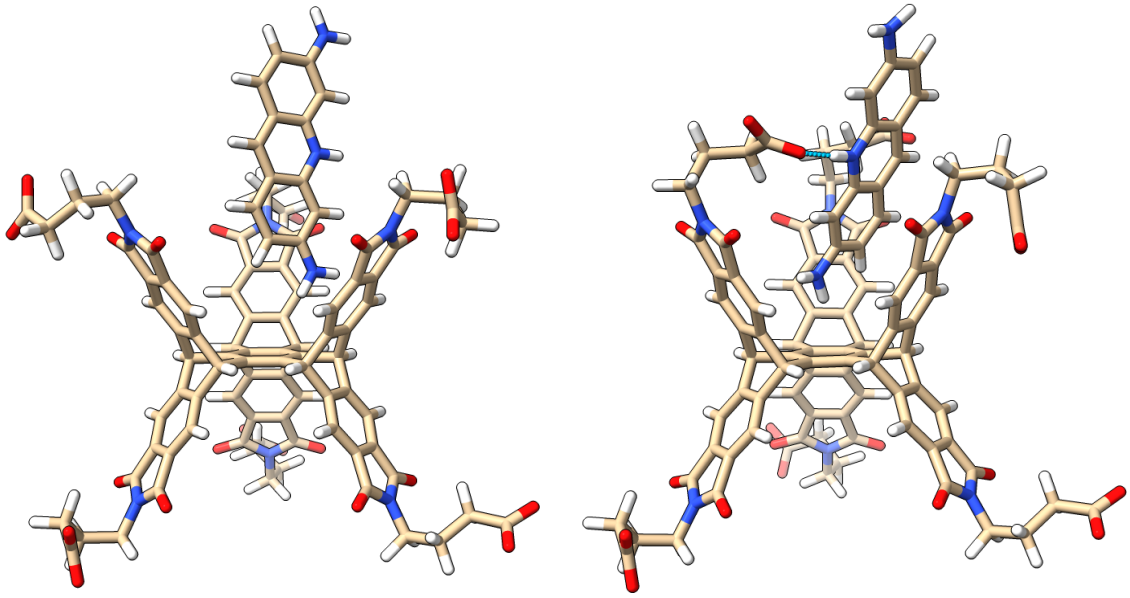




Final report:

1586 unique conformations found
1586 minimized with good convergence
Found 172 confs within 1.00 kcal/mol (4.18 kJ/mol) of glob. min.
Found 714 confs within 2.00 kcal/mol (8.37 kJ/mol) of glob. min.
Found 1586 confs within 3.00 kcal/mol (12.55 kJ/mol) of glob. min.
Global minimum E = -2115.95 found 9 times.

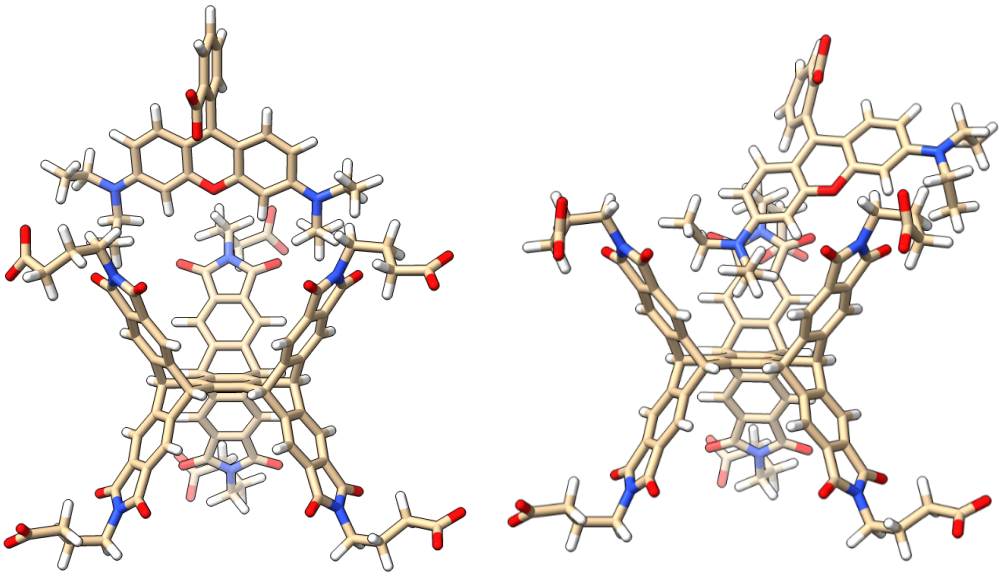
The starting pose, on the left, consisted of proflavine $\mathbf{4}^{+}$ docked horizontally in the cavity. After the conformational searching procedure, one cluster was found within 5.0 kJ/mol of the global minimum. The lowest energy structure, on the right, found that the guest formed one intermolecular hydrogen bond (blue dashed line).



Final report:

1140 unique conformations found
1140 minimized with good convergence
Found 34 confs within 1.00 kcal/mol (4.18 kJ/mol) of glob. min.
Found 213 confs within 2.00 kcal/mol (8.37 kJ/mol) of glob. min.
Found 1140 confs within 3.00 kcal/mol (12.55 kJ/mol) of glob. min.
Global minimum E = -2132.37 found 5 times.

Rhodamine B 6: The starting pose, on the left, consisted of RhB **6** placed horizontally above the cavity. After the conformational searching procedure, one cluster was found within 5.0 kJ/mol of the global minimum. The lowest energy structure, on the right, found that the guest sat with one amine in the cavity with the carboxylate group pointed up and out of the cavity.



Final report:

2350 unique conformations found

2350 minimized with good convergence

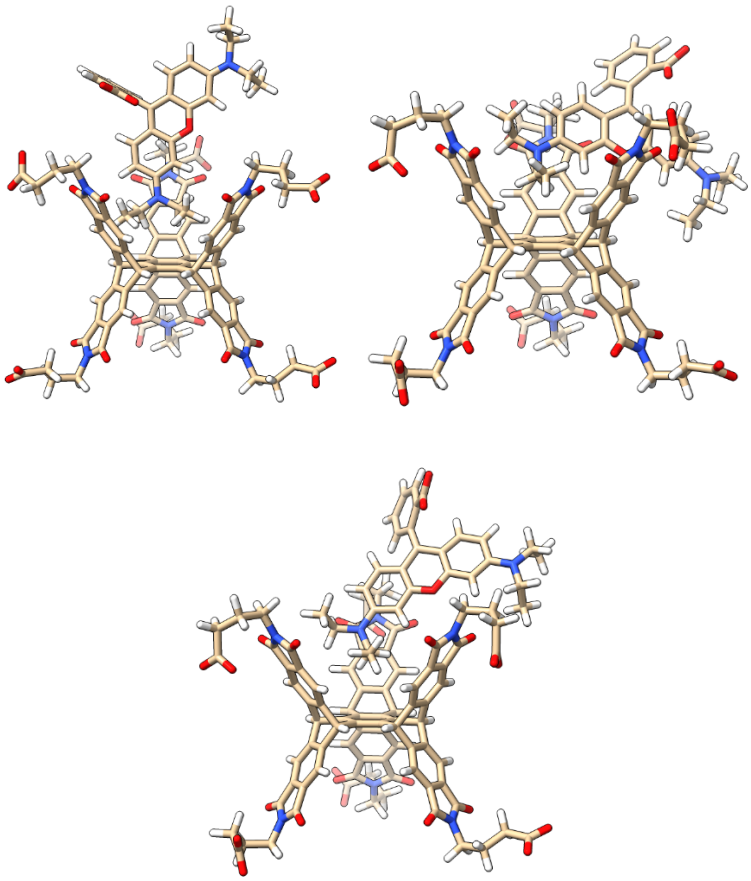
Found 246 confs within 1.00 kcal/mol (4.18 kJ/mol) of glob. min.

Found 1031 confs within 2.00 kcal/mol (8.37 kJ/mol) of glob. min.

Found 2350 confs within 3.00 kcal/mol (12.55 kJ/mol) of glob. min.

Global minimum E = -2066.44 found 2 times.

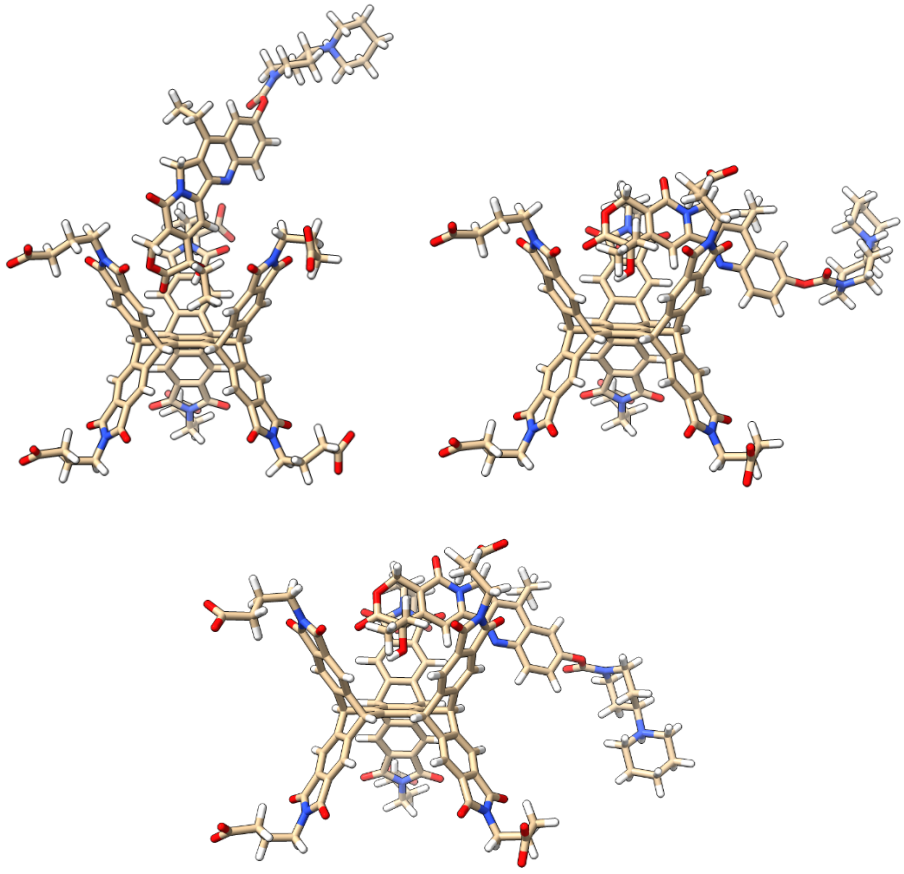
The starting pose, on the top left, consisted of RhB **6** placed vertically in the cavity. After the conformational searching procedure, two clusters were found within 5.0 kJ/mol of the global minimum. The lowest energy cluster, on the top right, found that the guest sat between two arms of the host. The next cluster, close in energy to the last (0.5 kJ/mol), has the guest docked with one amine in the cavity and the carboxylate pointed up and out of the cavity.



Final report:

1386 unique conformations found
1378 minimized with good convergence
Found 327 confs within 1.00 kcal/mol (4.18 kJ/mol) of glob. min.
Found 850 confs within 2.00 kcal/mol (8.37 kJ/mol) of glob. min.
Found 1386 confs within 3.00 kcal/mol (12.55 kJ/mol) of glob. min.
Global minimum E = -2078.63 found 5 times.

Irinotecan $\mathbf{7}^+$: The starting pose, on the top left, consisted of irinotecan $\mathbf{7}^+$ placed vertically in the cavity. After the conformational searching procedure, two clusters were found within 5.0 kJ/mol of the global minimum. The lowest energy cluster, on the top right, showed the guest sitting between two arms of the host with the cyclohexyl ring system pointed up. The next cluster, close in energy to the last (0.5 kJ/mol), has the guest docked between two arms of the host with the cyclohexyl ring system pointed down.



Final report:

3367 unique conformations found
3362 minimized with good convergence
Found 328 confs within 1.00 kcal/mol (4.18 kJ/mol) of glob. min.
Found 2014 confs within 2.00 kcal/mol (8.37 kJ/mol) of glob. min.
Found 3367 confs within 3.00 kcal/mol (12.55 kJ/mol) of glob. min.
Global minimum E = -1434.90 found 17 times.