Binding of chemical warfare agent simulants as guests in a coordination cage: contributions to binding and a fluorescence-based response

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Supporting Information

Synthesis of the complex $[Cd_8(L^w)_{12}](BF_4)_{16}$.

$Cd(BF_4)_2$ (0.026 g, 0.066 mmol) and L^w (0.050 g, 0.10 mmol) were dissolved in methanol (10 cm^3). The reaction was stirred at room temperature for 16 hours, during which time a white precipitate formed. The solvent was removed under reduced pressure and the solid washed with dichloromethane, diethyl ether and a small amount of cold methanol to afford a white solid $[Cd_8(L^w)_{12}](BF_4)_{16}$. ESMS: m/z 1588 $\{[Cd_8(L^w)_{12}][BF_4]_{11}Na_2\}^{5+}$; 1309 $\{[Cd_8(L^w)_{12}][BF_4]_{10}Na\}^{6+}$; 1110 $\{[Cd_8(L^w)_{12}][BF_4]_9Na_2\}^{7+}$; 953 $\{[Cd_8(L^w)_{12}][BF_4]_8\}^{8+}$. For the purposes of solution spectroscopic titrations to measure binding constants, the complex was anion-exchanged to the nitrate salt $[Cd_8(L^w)_{12}](NO_3)_{16}$.

The 500 MHz ^1H NMR spectrum of $[Cd_8(L^w)_{12}](NO_3)_{16}$ (below) confirms the presence of two independent ligand environments, each with no internal symmetry, as required by the S_6 symmetric structure of the cage.[S1] This results in 48 independent ^1H signals.[S2] In particular, the presence of four pairs of doublets from diastereotopic CH_2 groups adjacent to the naphthyl units is clear from a COSY spectrum; these are labelled on the spectrum (A – D).

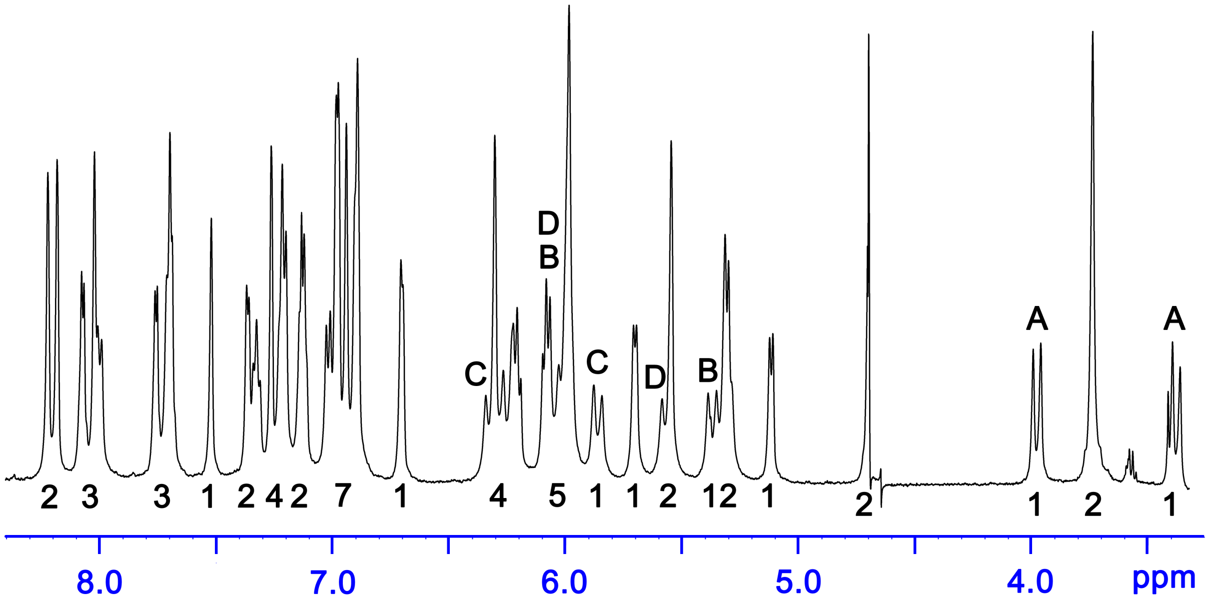


Fig. S1. 500 MHz ^1H NMR spectrum of $[Cd_8(L^w)_{12}](NO_3)_{16}$ in D_2O at 298K. Numbers under signals are the integral values.

In addition, the S_6 symmetric structure of the cage results in the presence of two (equivalent) *fac* tris-chelate Cd(II) centres, and six (equivalent) *mer* tris-chelate Cd(II) centres. This can be seen in the ^{113}Cd NMR spectrum of $[Cd_8(L^w)_{12}](NO_3)_{16}$ which shows two signals in an approximately 3:1 ratio.[S1]

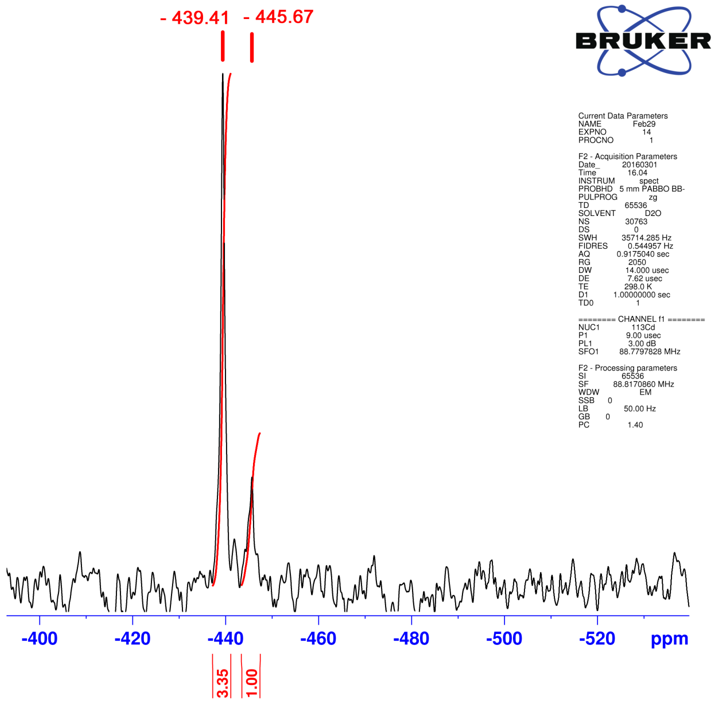


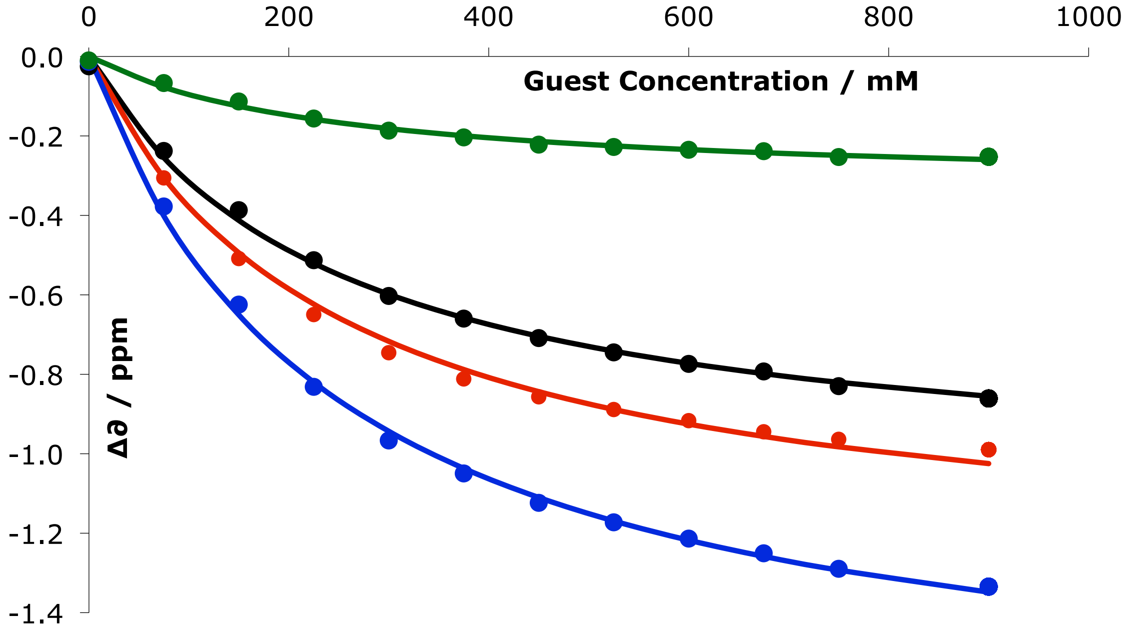
Fig. S2. ^{113}Cd NMR spectrum at 88.7 MHz of $[Cd_8(L^w)_{12}](NO_3)_{16}$ in D_2O at 298K (referenced to the lock signal)

NMR titrations with Co-H^o and Co-H^w

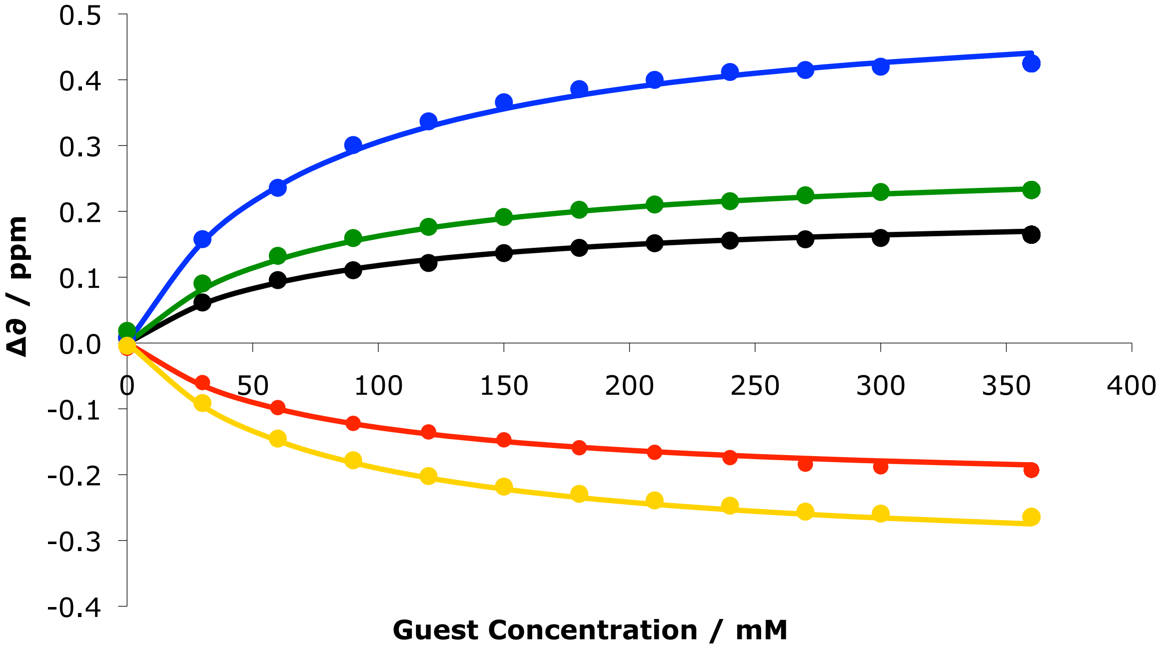
Cages **Co-H^o** and **Co-H^w** were prepared according to the previously published methods.[S1,S2] ^{1}H NMR titrations to measure binding constants of guests in cages **Co-H^o** and **Co-H^w** were performed according to the previously published method.[S3]

Data from the NMR titrations is shown below. In all cases the concentration of host cage was 0.2 mM. For the fast exchange cases (1 – 4), the changes in chemical shift for at least four signals of the host, as guest is added, were plotted and fitted to a 1:1 host:guest binding model (all cases except **Co-H^w** / DMMP, *i.i.* cases 1 – 3) or a 1:2 host:guest binding model (**Co-H^w** / DMMP; case 4) to give the binding constants summarised in Table 1 of the main text. All measurements were performed three times (only one representative set of data is shown for each host/guest pair). For the slow exchange cases, where separate sets of signals could be resolved for free cage and cage/guest complexes, binding constants were determined by integration of the separate sets of signals.

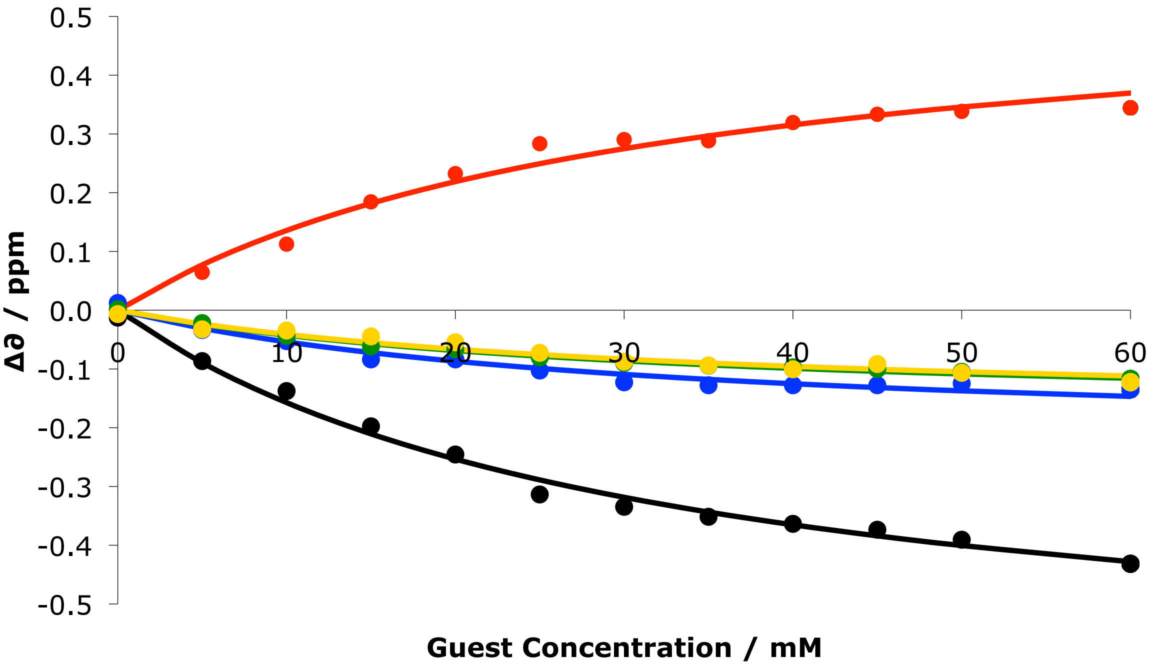
1. **Co-H^{o}** / DMMP in MeCN (fast exchange)



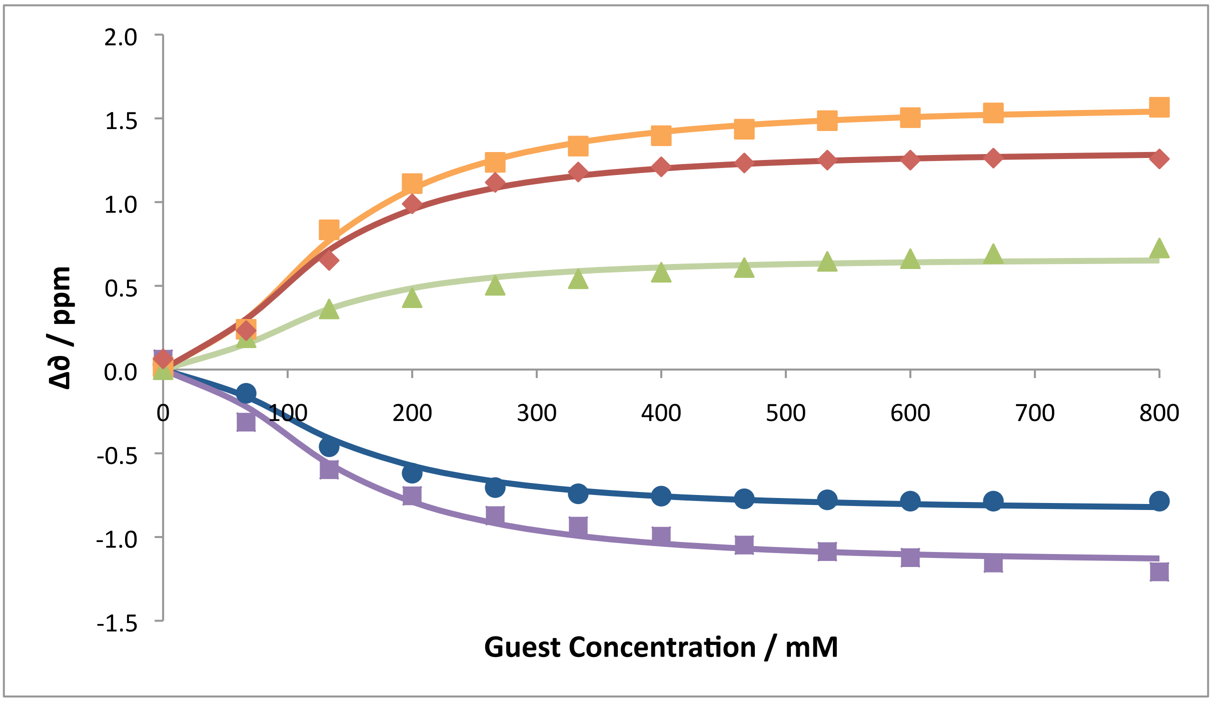
2. **Co-H^{o}** / DEMP in MeCN (fast exchange)



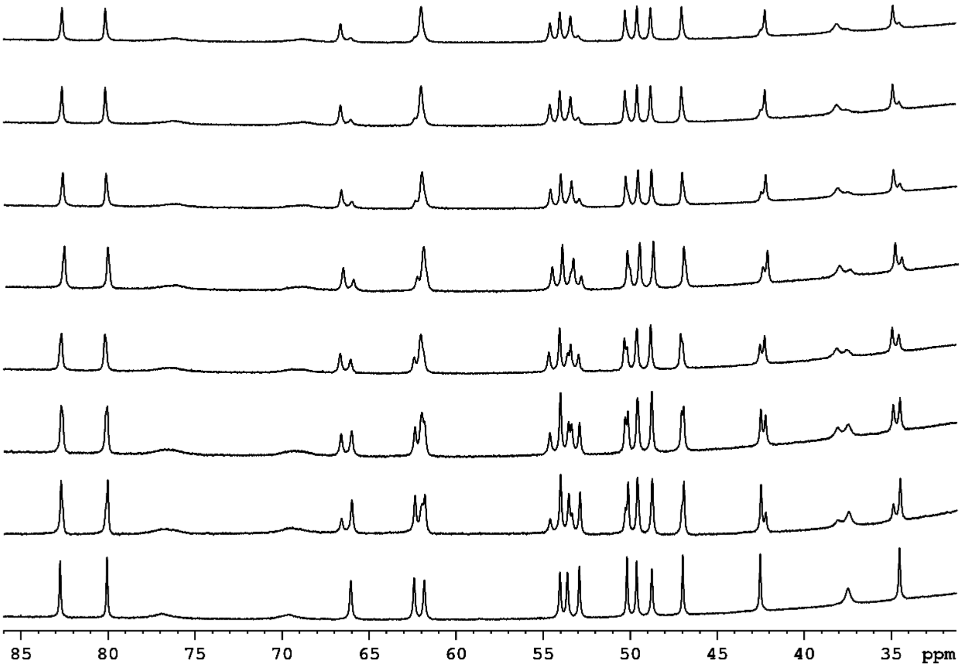
3. **Co-H^w** / DEMP in D_2O (fast exchange)



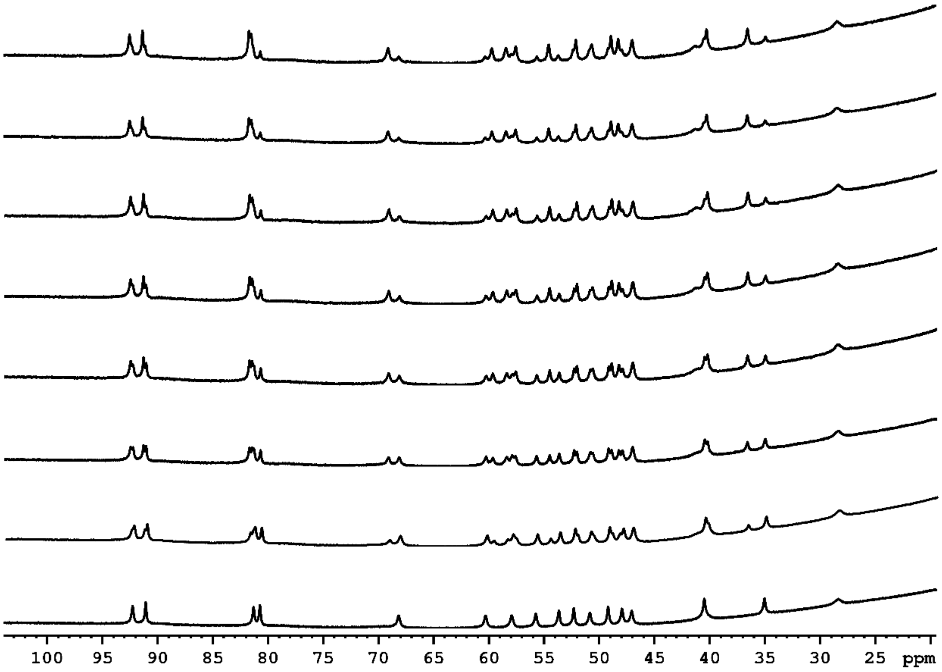
4. **Co-H^w** / DMMP in D_2O (fast exchange; this fits to a 1:2 host:guest model, see main text)



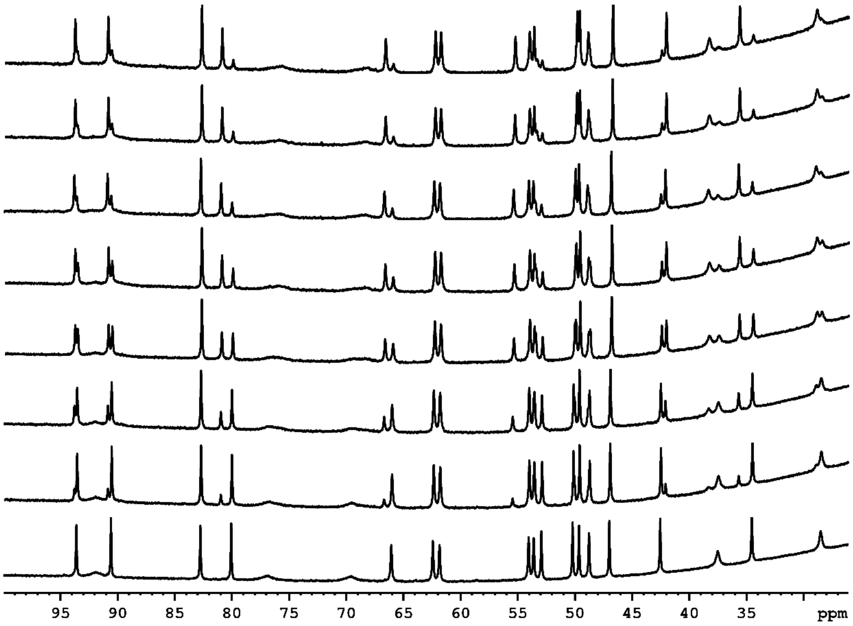
5. **Co-H°** / DEEP in MeCN (slow exchange). The bottom spectrum is free **Co-H°**; as DEEP is added the appearance of new signals for **Co-H°**/DEEP complex is clear.



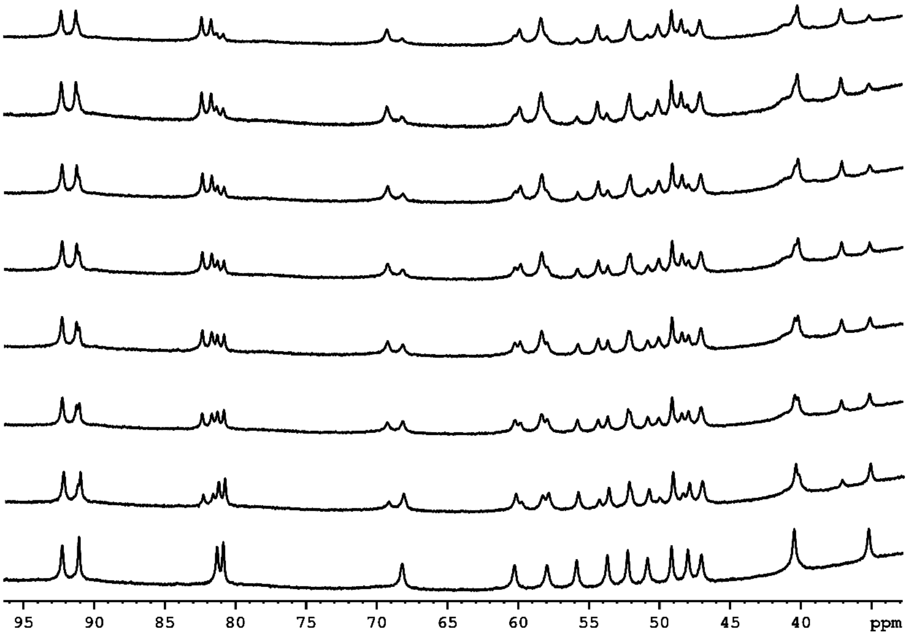
6. **Co-H^w** / DEEP in D_2O (slow exchange). The bottom spectrum is free **Co-H^w**; as DEEP is added the appearance of new signals for **Co-H^w**/DEEP complex is clear.



7. **Co-H°** / DIMP in MeCN (slow exchange). The bottom spectrum is free **Co-H°**; as DIMP is added the appearance of new signals for **Co-H°**/DIMP complex is clear.



8. **Co-H^w** / DIMP in D_2O (slow exchange). The bottom spectrum is free **Co-H^w**; as DIMP is added the appearance of new signals for **Co-H^w**/DIMP complex is clear.

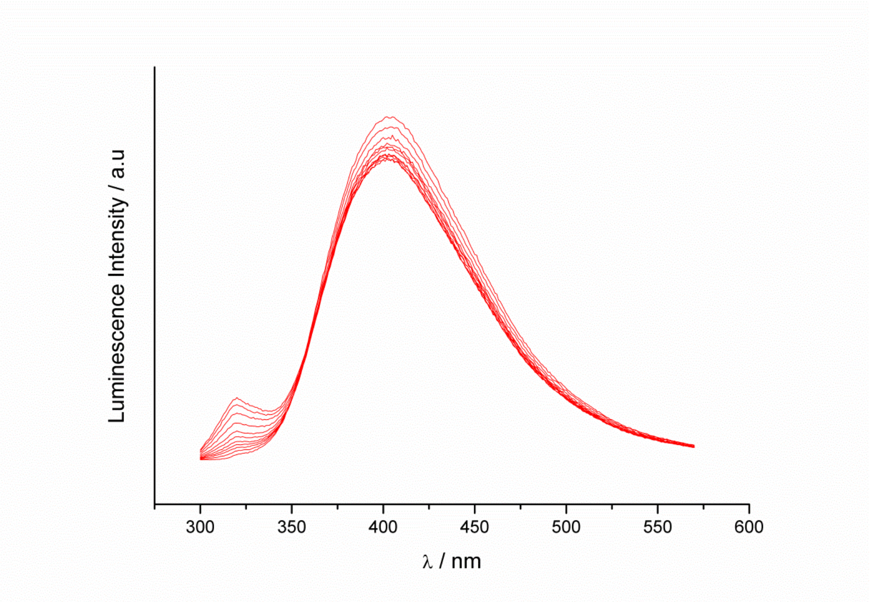


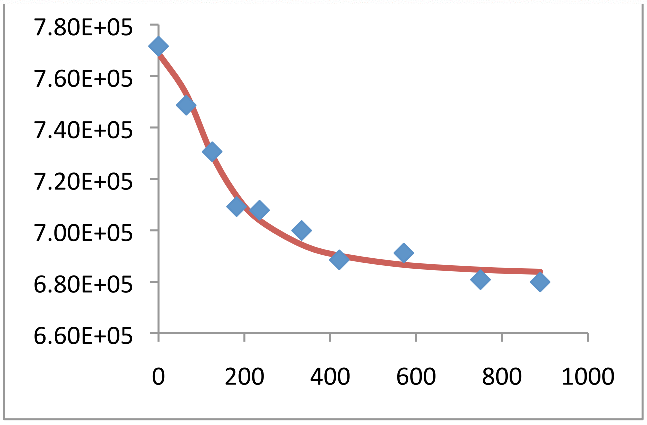
Fluorescence titrations with $[Cd_8(L^w)_{12}](NO_3)_{16}$

The fluorescence titrations were carried out by preparing a stock solution of $[Cd_8(L^w)_{12}](NO_3)_{16}$ (0.01 mM) in de-ionised water. Guest solutions (typically 200 mM) were made up using stock host solution. 1500 µL of host solution was added to a fluorescence cuvette with increasing amounts of guest solution then added, leaving 15 minutes after each addition of the guest solution to equilibrate. Fluorescence spectra were recorded on a Horiba-Jobin Yvon Fluoromax-4 spectrophotometer, with excitation at 300 nm and emission spectra recorded between 310 nm and 570 nm.

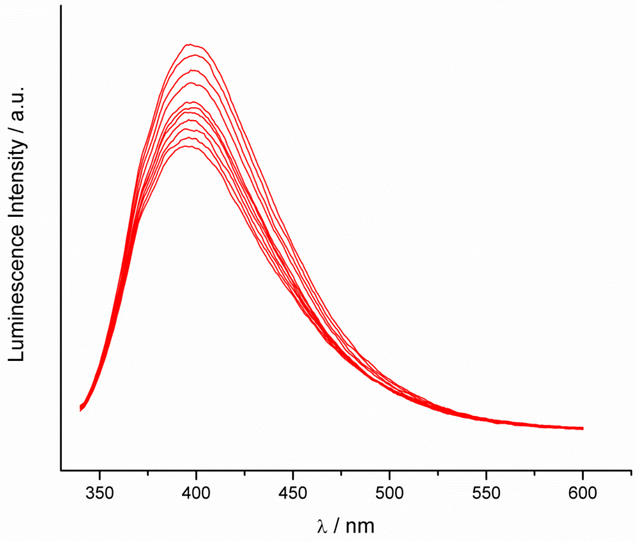
Measurements for the **Cd-H^{w}** / DIMP system are shown in the main text (Fig. 5). The others are shown here: in all cases binding of the phosphonate guest results in partial quenching of luminescence from the host.

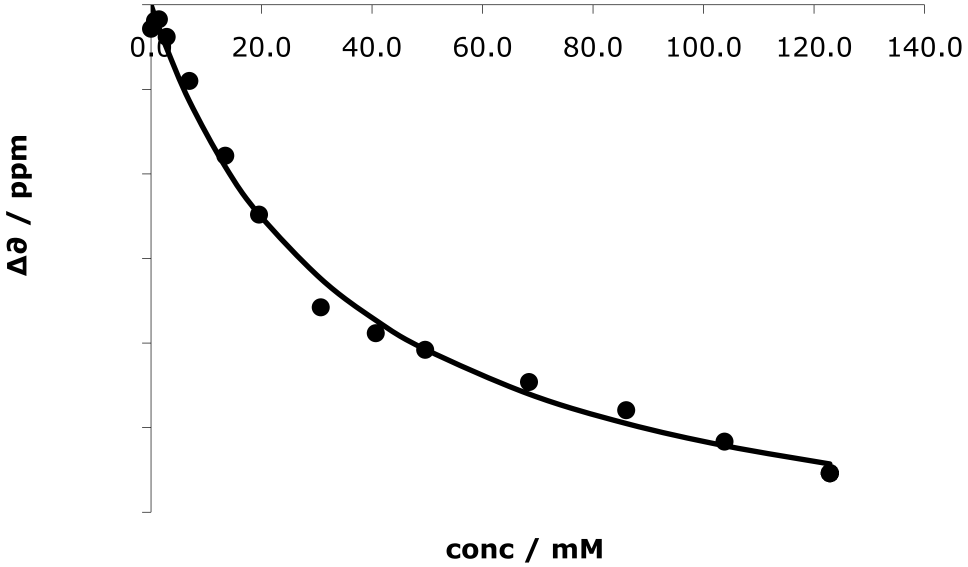
1. Cd-H^{w} / DMMP – fitted to a 1:2 host:guest model (see main text)



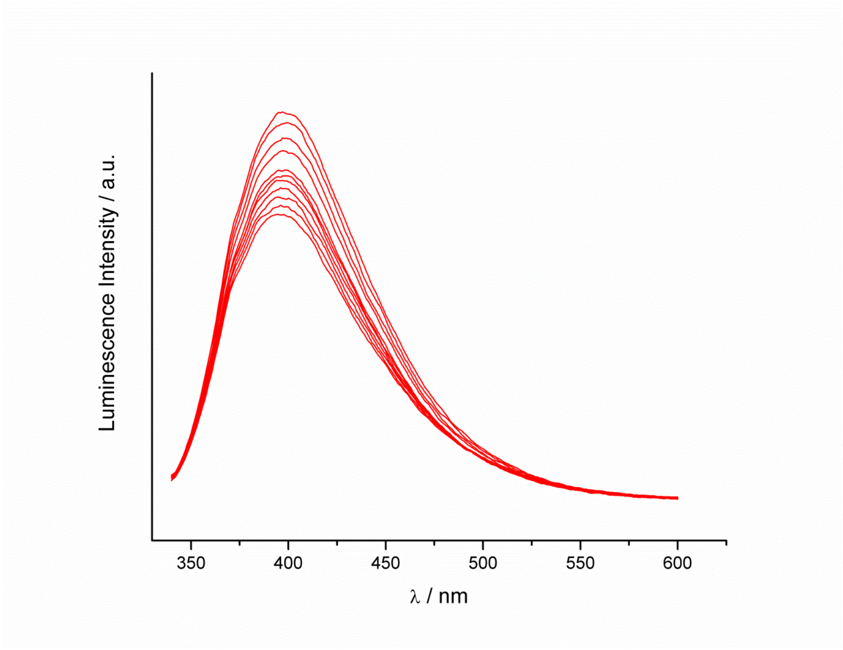


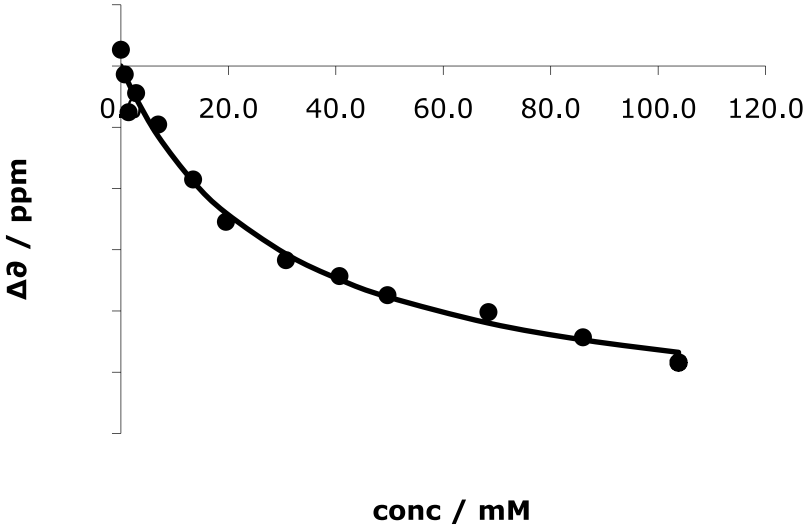
2. Cd-H^{w} / DEMP – fitted to a 1:1 host:guest model (see main text)





3. Cd-H^{w} / DEEP – fitted to a 1:1 host:guest model (see main text)





X-ray crystallography

Crystal data, data collection and refinement parameters are summarised in Table S1 below. Intensity data were collected on Bruker Apex-II or D8-Venture diffractometers at the University of Sheffield. In each case a crystal was removed from the mother liquor, coated with oil, and transferred rapidly to a stream of cold N_2 on the diffractometer to prevent any decomposition due to solvent loss. In all cases, after integration of the raw data, and before merging, an empirical absorption correction was applied (SADABS)[S4] based on comparison of multiple symmetry-equivalent measurements. The structures were solved by direct methods and refined by full-matrix least squares on weighted F^2 values for all reflections using the SHELX suite of programs.[S5] In all cases crystals exhibited the usual problems of this type of structure, *viz.* weak scattering due to a combination of poor crystallinity, solvation, and disorder of anions / solvent molecules. All three structures contained large solvent-accessible voids whose volume was *ca.* 40% of the total unit cell volume. These showed in the refinement to contain diffuse electron density which could not meaningfully be modelled, ascribed to severely disordered solvent molecules as well as those anions that could not be located. This diffuse electron density was removed from the refinements using the SQUEEZE function in PLATON (see CIFs for full details).[S6] The result is that, as usual for structures of this type, the R1 values are relatively high (11 – 15%) although the gross features of the cages and the bound guests are quite clear: accordingly we do not over-analyse structural minutiae. CCDC deposition numbers: 1458105 –1458107.

Complex	$[Co_8(L^o)_{12}](BF_4)_{16}$• $PO(OEt)_2Et$•0.5H_2O	$[Co_8(L^o)_{12}](BF_4)_{16}$• $PO(OPr^i)_2Me$	$[Co_8(L^w)_{12}](BF_4)_{16}$• $(PO(OMe)_2Me)_2$
Formula	C342 H280 B16 Co8 F64 N72 O3.5 P	C343 H281 B16 Co8 F64 N72 O3 P	C366 H330 B16 Co8 F64 N72 O30 P2
M	7345.73	7350.75	8139.34
T, K	100(2)	100(2)	100(2)
Crystal System	Monoclinic	Monoclinic	Monoclinic
Space Group	C2/c	C2/c	C2/c
a, Å	32.8826(6)	32.7148(10)	27.477(4)
b, Å	30.1786(6)	29.7919(8) Å	39.201(6)
c, Å	40.0732(8)	39.8554(11) Å	41.992(7)
β, °	96.4980(10)	96.733(2)	107.133(5)
V , Å^3	39511.2(13)	38576.6(19)	43224(12)
Z	4	4	4
ρ, g cm^{-3}	1.235	1.266	1.251
Crystal size, mm^3	0.4 x 0.3 x 0.3	0.2 x 0.1 x 0.1	0.2 x 0.1 x 0.1
Source	Cu-Kα	Mo-Kα	Mo-Kα
μ, mm^{-1}	3.362	0.431	0.399
Independent data / restraints / parameters	30236 / 2478 / 1681	43994 / 2142 / 1674	38209 / 2545 / 1779
Final *R*1, w*R*2	0.114, 0.378	0.134, 0.432	0.148, 0.497

S1 I. S. Tidmarsh, T. B. Faust, H. Adams, L. P. Harding, L Russo, W. Clegg and M. D. Ward, *J. Am. Chem. Soc.,* 2008, **130**, 15167.

S2 M. Whitehead, S. Turega, A. Stephenson, C. A. Hunter and M. D. Ward, *Chem. Sci.,* 2013, **4**, 2744.

S3 S. Turega, M. Whitehead, B. R. Hall, A. J. H. M. Meijer, C. A. Hunter and M. D. Ward, *Inorg. Chem.,* 2013, **52**, 1122.

S4 G. M. Sheldrick, SADABS: A program for absorption correction with the Siemens SMART system, University of Göttingen, Germany, 2008.

S5 G. M. Sheldrick, *Acta Crystallogr. Sect. A,* 2008, **64**, 112.

S6 A. Spek, *J. Appl. Cryst.,* 2003, **36**, 7; P. van der Sluis and A. L. Spek, *Acta Cryst. A,* 1990, **46**, 194.