

Electronic Supplementary Information

Oxidovanadium(V) complexes of aroylhydrazones incorporating heterocycles: Synthesis, characterization and study of DNA binding, photo-induced DNA cleavage and cytotoxic activities

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Table S1 Binding constant (K_b) values for the "CT-DNA-ligand" interactions.

Fig. S1 (A) Absorption spectral traces of the complexes **1** (a), **2** (b), **3** (c) and **4** (d) (25 μ M each) in 10 mM Tris-HCl buffer (pH 8.0) containing 1% DMF. The spectra were recorded up to 72 h at room temperature; and (B) ^1H NMR spectra of complex **1** in DMSO- d_6 in 0 h (a), after 72 h (b) and after heating (120°C) the solution (c).

Fig. S2 (a) The molecular structure of the second of the two independent molecules comprising the asymmetric unit of **2** showing the atom-labelling scheme and 70% displacement ellipsoids. Atoms are further designated with a suffix "a"; and (b) overlay diagram of the two independent molecules with the molecule containing the V1 atom shown in red. The molecules have been overlapped so that the V(=O) $_2$ units are superimposed.

Fig. S3 (a) The molecular structure of the second of the two independent molecules comprising the asymmetric unit of **4** showing the atom-labelling scheme and 70% displacement ellipsoids. Atoms are further designated with a suffix "a". The coordinated ethanol molecule is statistically disordered over two positions. The atoms comprising the second orientation of the disordered ethanol molecule are additionally labelled with a suffix "b" and are highlighted with dashed bonds; and (b) overlay diagram of the two independent molecules with the molecule containing the V1 atom shown in red; the inverted V2-containing molecule is shown for a better match. The molecules have been overlapped so that the V, O4 and N2 atoms are superimposed.

Fig. S4 A view of the unit cell contents for **1** in projection down the b -axis. The C–H...O [C2–H2...O3ⁱ = 2.57 Å, C2...O3ⁱ = 3.413(2) Å, angle at H2 = 147° for symmetry operation i: $x, \frac{1}{2}-y, -\frac{1}{2}+z$; and C4–H4...O3ⁱⁱ = 2.53 Å, C4...O3ⁱⁱ = 3.183(2) Å, angle at H4 = 126° for ii: $2-x, 1-y, -z$] and π ... π interactions [Cg(S1,C8-C11)...Cg(N1,C1-C5)ⁱⁱⁱ = 3.625(2) Å, angle of inclination = 4.96(19)° for iii: $1-x, -y, -z$] are shown as orange and purple dashed lines, respectively. The 2-thienyl ring is disordered over two co-planar conformations and the complementary Cg(S1b,C8b-C11b)...Cg(N1,C1-C5)ⁱⁱⁱ separation is 3.666(12) Å and the angle of inclination is 4.3(12)°.

Fig. S5 Crystal packing in **2**: (a) a view of the supramolecular chain comprising alternating V1- and V2-containing molecules sustained by N–H...O hydrogen bonding [N4–H1n...O2aⁱ = 2.406(19) Å, N4...O2aⁱ = 3.063(2) Å, with angle at H1n = 132.1(18)° for symmetry operation i: $1-x, 1-y, -z$; N4a–H3n...O3ⁱⁱ = 2.259(14) Å, N4a...O3ⁱⁱ = 3.033(2) Å, with angle at H3n = 148.6(19) for symmetry operation ii: $-x, 1-y, 1-z$], shown as orange dashed lines; and (b) a view of the unit cell contents in projection down the a -axis. The C–H...O [C4a–H4a3...O3aⁱⁱⁱ = 2.50 Å, C4a...O3aⁱⁱⁱ = 3.149(2) Å, angle at H4a3 = 126° for symmetry operation iii: $1-x, -y, -z$; C5a–H5a...O3aⁱ = 2.55 Å, C5a...O3aⁱ = 3.178(2) Å, angle at H5a = 124°; C10a–H10a...O2ⁱⁱ = 2.47 Å, C10a...O2ⁱⁱ = 3.283(2) Å, angle at H10a = 143°; and C15a–H15a...O3 = 2.57 Å, C15a...O3 = 3.235(2) Å, angle at H15a = 127°] interactions are shown as blue dashed lines.

Fig. S6 Crystal packing in **3**: (a) a view of the supramolecular layer in the ac -plane whereby the supramolecular chains are linked C–H... π (chelate) ring interactions [C4–H4... π (V,O1,N2,N3,C8)ⁱ = 2.68 Å, C4... π (V,O1,N2,N3,C8)ⁱ = 3.582(4) Å, with angle at

H4 = 164° for symmetry operation i: 1-x, 2-y, ½+z] shown as purple dashed lines, and (b) a view of the unit cell contents in projection down the *a*-axis showing the ...ABA... pattern of supramolecular layers stacked along the *b*-axis.

Fig. S7 Crystal packing in **4**: (a) a view of the two-molecule aggregate whereby centrosymmetrically related V1-containing molecules are linked by ethanol-O-H...N hydrogen bonds, (b) equivalent dimer formed by the V2-containing molecule; second orientation of the disordered ethanol molecule and all non-participating hydrogen atoms removed for clarity [O6-H6o...N1ⁱ = 2.12 Å, O6...N1ⁱ = 2.873(3) Å, with angle at H6o = 149° for symmetry operation i: -x, 1-y, 1-z; O6a-H6oa...N1aⁱⁱ = 2.31 Å, O6a...N1aⁱⁱ = 2.95(2) Å, with angle at H6oa = 136° for symmetry operation ii: ½-x, ½-y, -z; for the second disordered conformation: O6b-H6ob...N1aⁱⁱ = 2.20 Å, O6b...N1aⁱⁱ = 2.99(2) Å, with angle at H6ob = 164°] shown as orange dashed lines, and (c) a view of the unit cell contents in projection down the *b*-axis showing the stacking of alternating layers of V1- and V2-containing molecules along the *a*-axis. The C-H...O [C8a-H8a...O2aⁱⁱⁱ = 2.57 Å, C8a...O2aⁱⁱⁱ = 3.398(4) Å, with angle at H8a = 149° for symmetry operation iii: ½-x, ½+y, ½-z] and π ... π [Cg(O3,C13-C16)...Cg(C1,C2,C7-C10)ⁱ = 3.702(2) Å, angle of inclination = 13.45(19)°; Cg(O3a,C13a-C16a)...Cg(C1a,C2a,C7a-C10a)ⁱⁱ = 3.641(2) Å, angle of inclination = 8.64(18)°] interactions are shown as blue and purple dashed lines, respectively.

Fig. S8 Electronic absorption spectra for **HL**¹ (a), **HL**² (b), **H₂L**³ (c) and **H₂L**⁴ (d) (25 µM each) upon the titration of CT-DNA (0 – 350 µM) in 10 mM Tris-HCl buffer (pH 8.0) containing 1% DMF. The inset shows the linear fit of [DNA]/(ε_a - ε_f) vs [DNA] from which the binding constant (K_b) was calculated using Eq. 1 (see main text).

Fig. S9. Fluorescence emission spectra of methyl green (MG) (2 µM) bound to CT-DNA (50 µM) in the presence of complex **1** (a), **2** (b), **3** (c) and **4** (d) (0–90 µM) in 10 mM Tris-HCl buffer (pH 8.0) containing 1% DMF. The arrow indicates the effect of increasing the concentration of the complex on the fluorescence emission of MG bound CT-DNA.

Fig. S10. Fluorescence emission spectra of ethidium bromide (EB) (2 µM) bound to CT-DNA (50 µM) in the presence of complex **1** (a), **2** (b), **3** (c) and **4** (d) (0–90 µM) in 10 mM Tris-HCl buffer (pH 8.0) containing 1% DMF. The arrow indicates the effect of increasing the concentration of the complex on the fluorescence emission of EB bound CT-DNA.

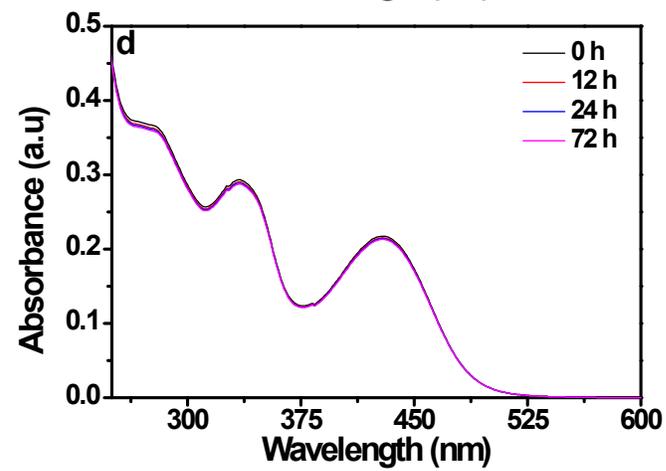
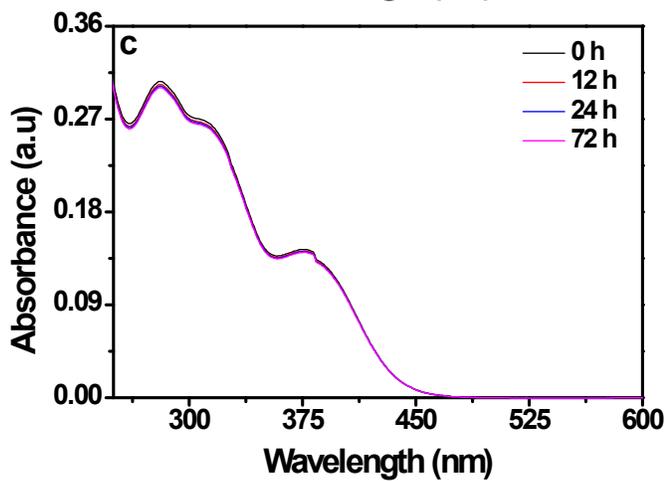
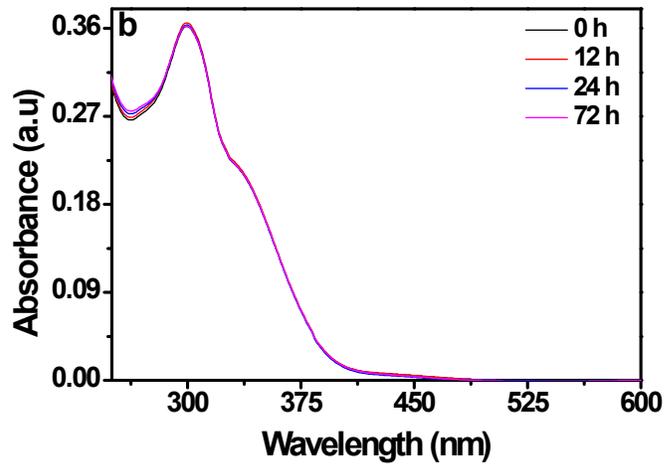
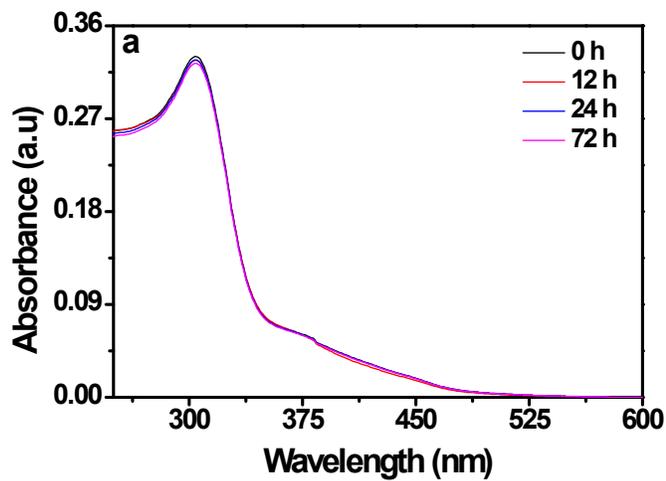
Fig. S11 Effect of DMF (1%) and ligands on the photo-induced cleavage of SC pUC19 DNA. 300 ng SC pUC19 DNA was photo-irradiated in absence and presence of 1% DMF and various ligands (100 µM) with UVA at 350 nm for 3 h. Lane 1, DNA only; Lane 2, DNA in presence of 1% DMF; Lane 3, DNA + **HL**¹; Lane 4, DNA + **HL**²; Lane 5, DNA + **H₂L**³; Lane 6, DNA + **H₂L**⁴.

Fig. S12 Gel diagram depicting cleavage of SC pUC19 DNA by **1–4** in presence of various additives in 50 mM Tris-HCl buffer (pH 8.0) containing 1% DMF. SC pUC19 DNA (300 ng) in the presence of various additives was photo-irradiated at 350 nm for 3 h with **1–4** (100 µM). The additive concentrations were: sodium azide (0.5 mM), L-histidine (0.5 mM), KI (0.5 mM) and D-mannitol (0.5 mM). Lane 1, DNA + complex; Lane 2, DNA + complex + sodium azide; Lane 3, DNA + complex + L-histidine; Lane 4, DNA + complex + KI; Lane 5, DNA + complex + D-mannitol.

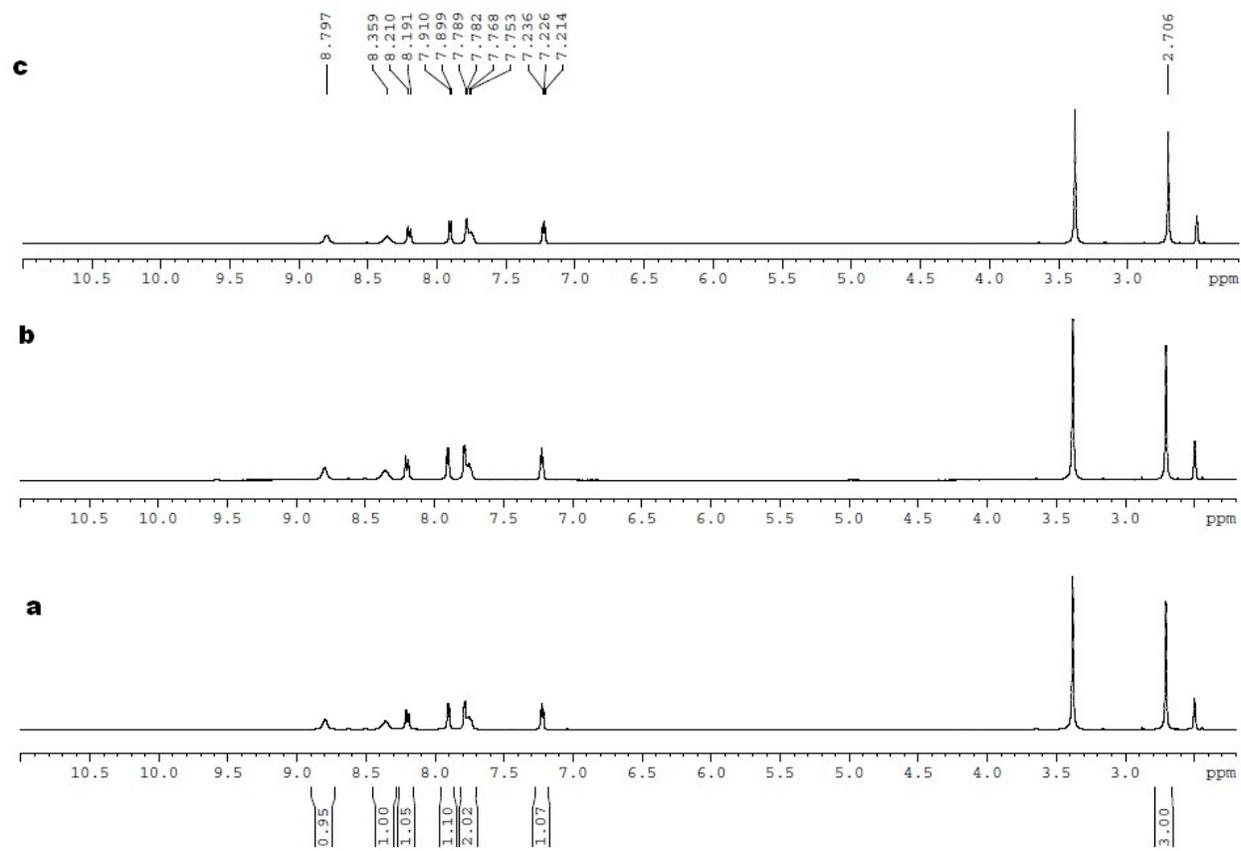
Table S1 Binding constant (K_b) values for the "CT-DNA-ligand" interactions.^a

Ligand	Binding constant (K_b) (M^{-1})
HL¹	7.42×10^3
HL²	3.88×10^3
H₂L³	2.91×10^4
H₂L⁴	2.48×10^3

^a The DNA binding constant was determined by the UV-vis spectral method.

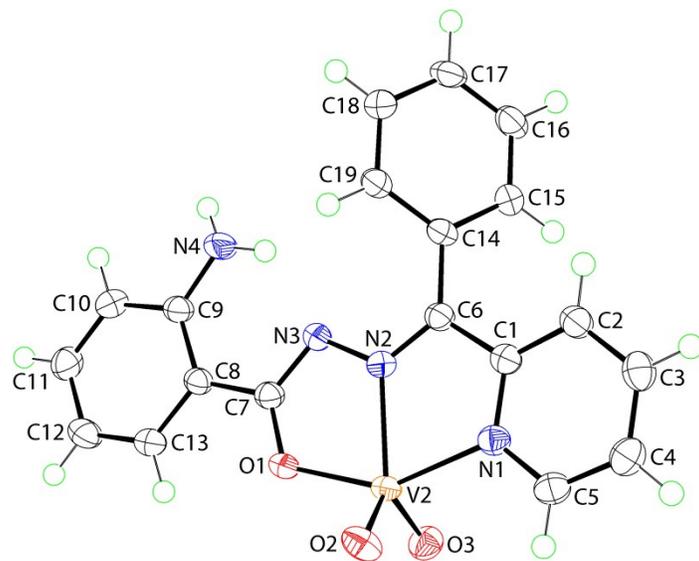


(A)

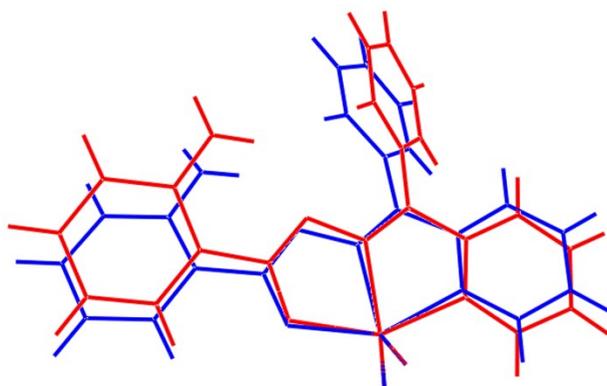


(B)

Fig. S1

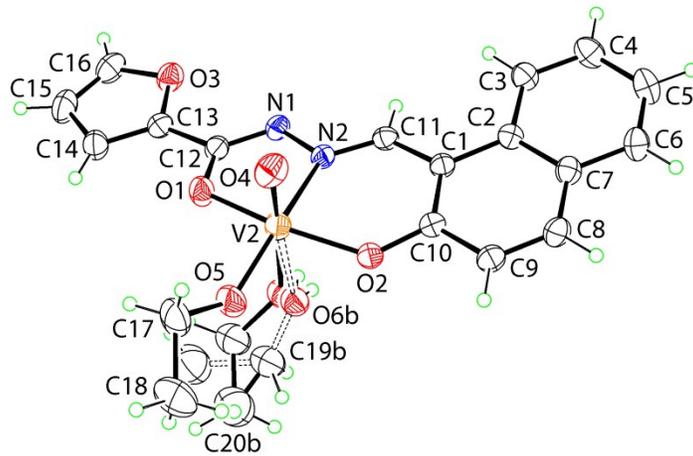


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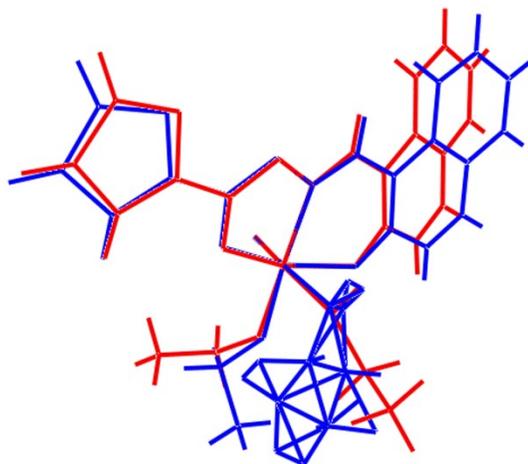


(b)

Fig. S2



(a)



(b)

Fig. S3

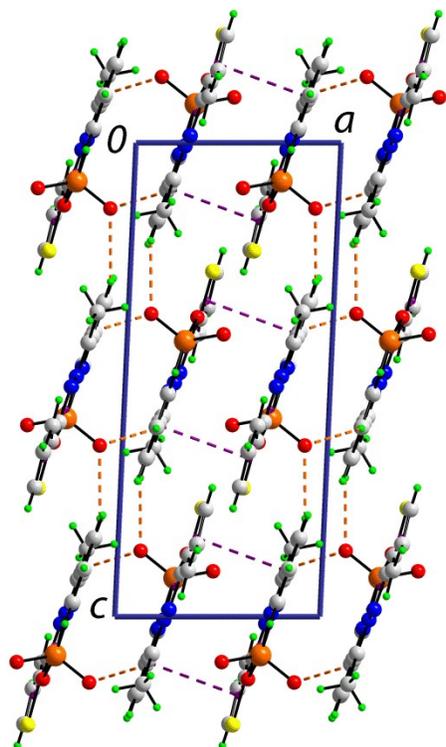
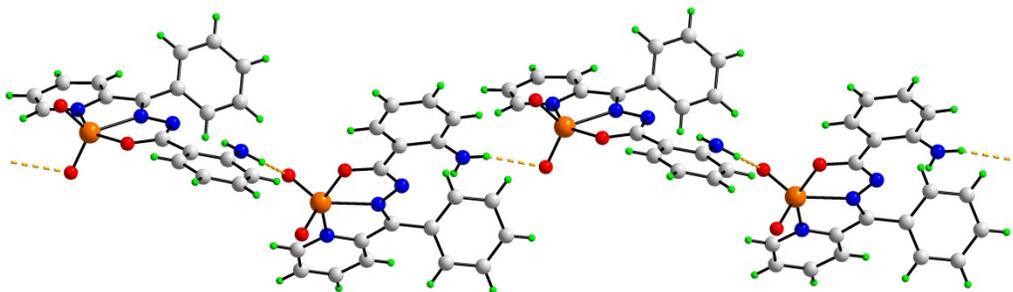
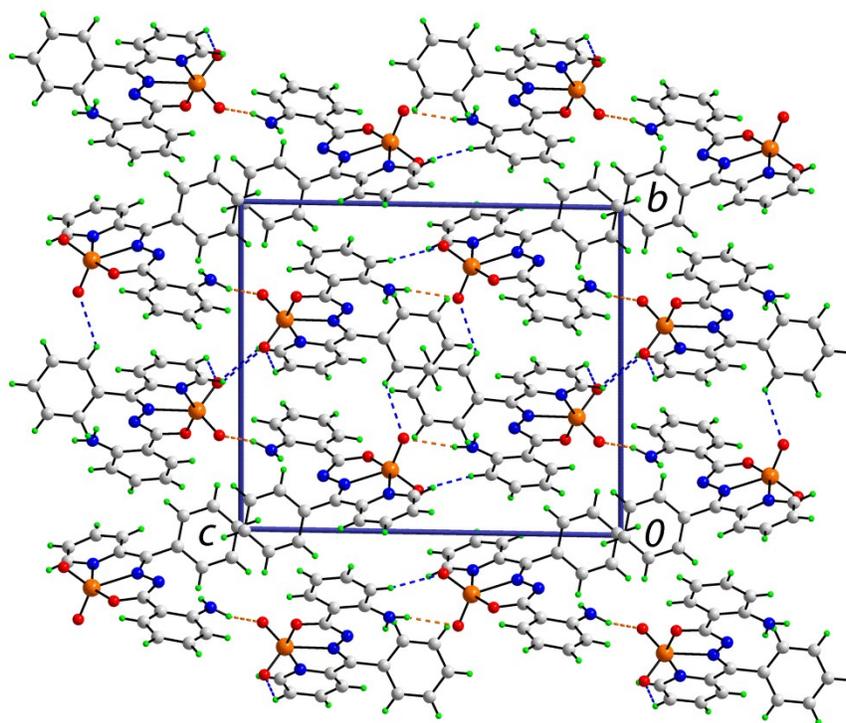


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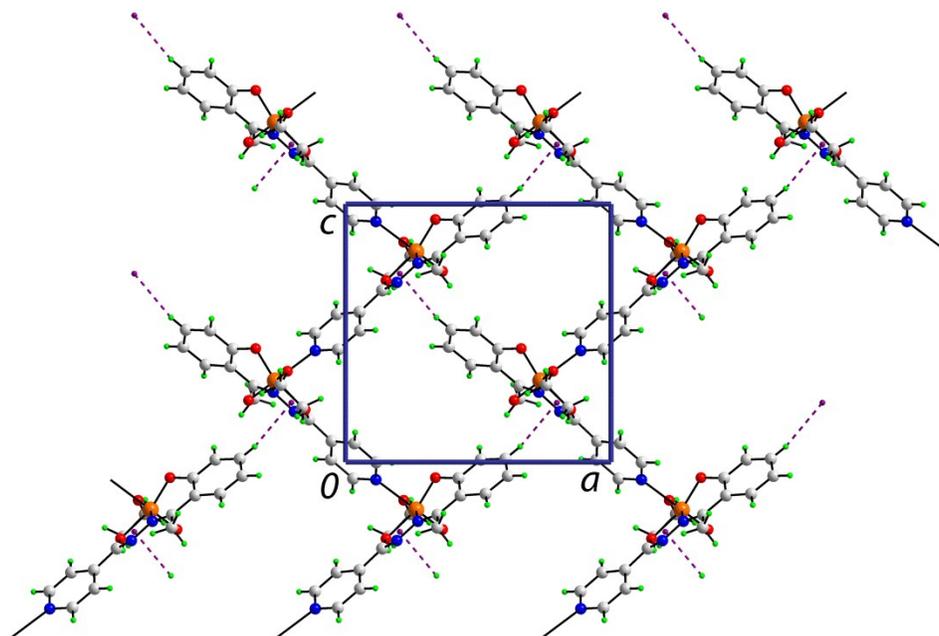


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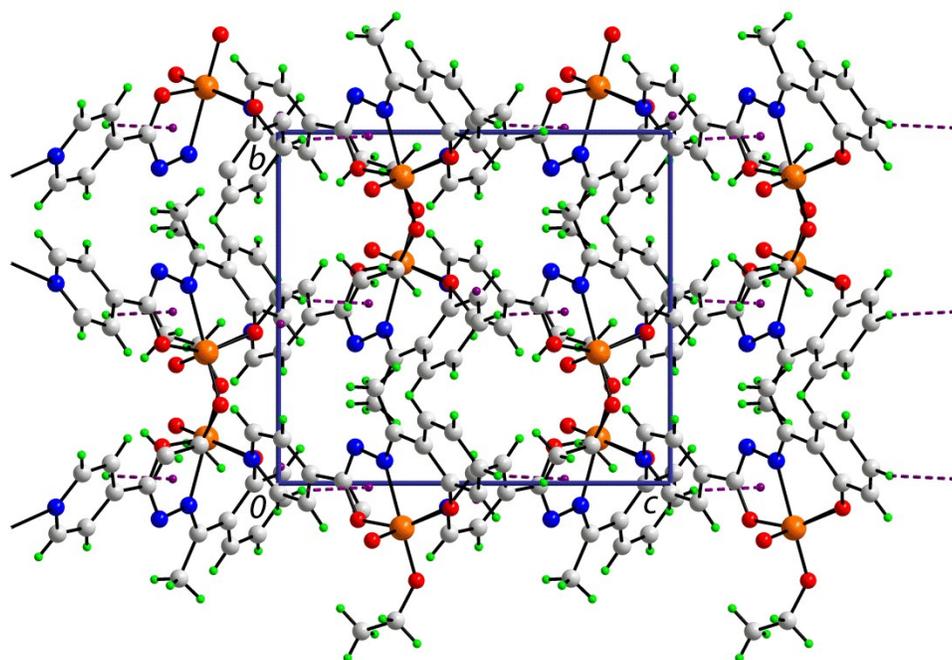


(b)

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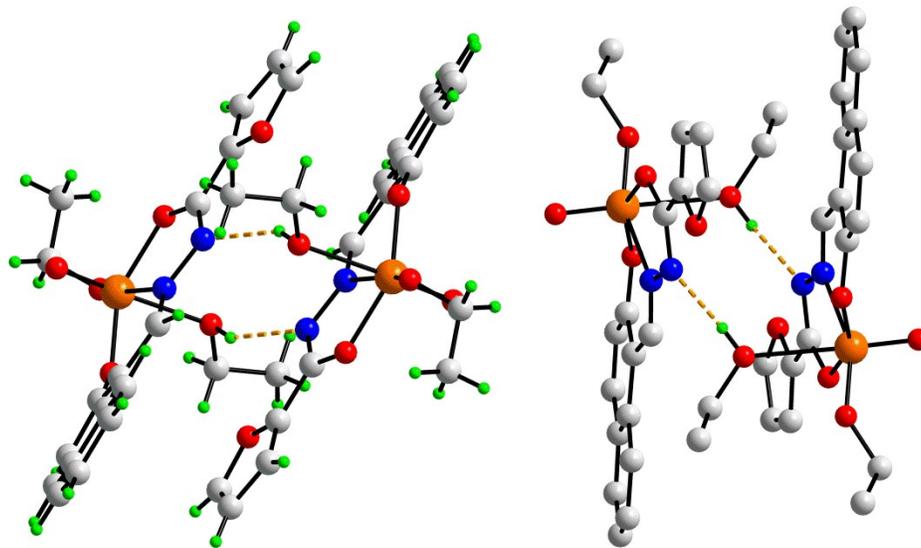


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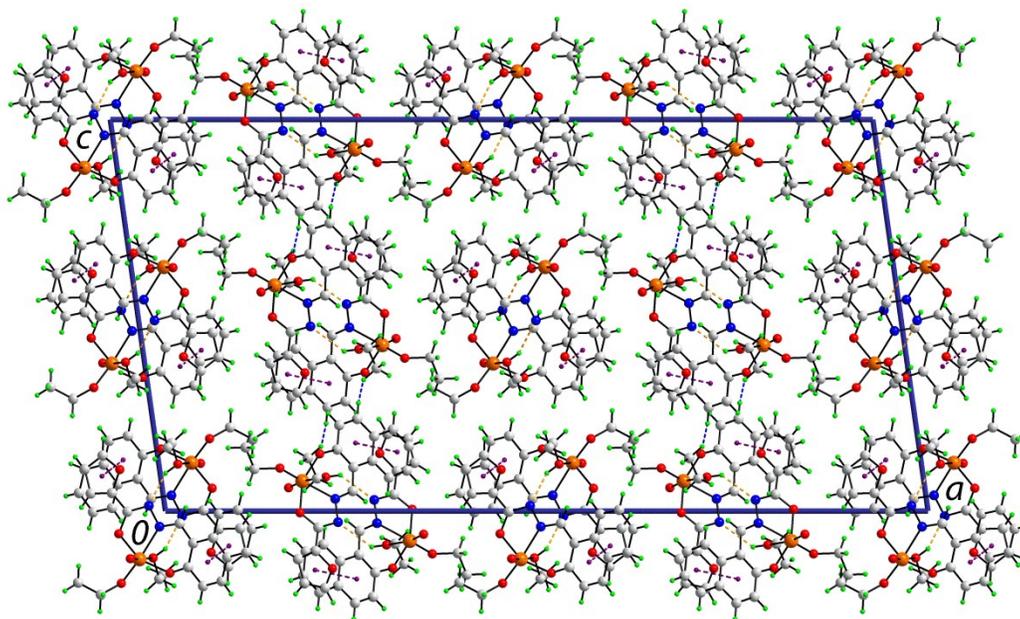
(b)

Fig. S6



(a)

(b)



(c)

Fig. S7

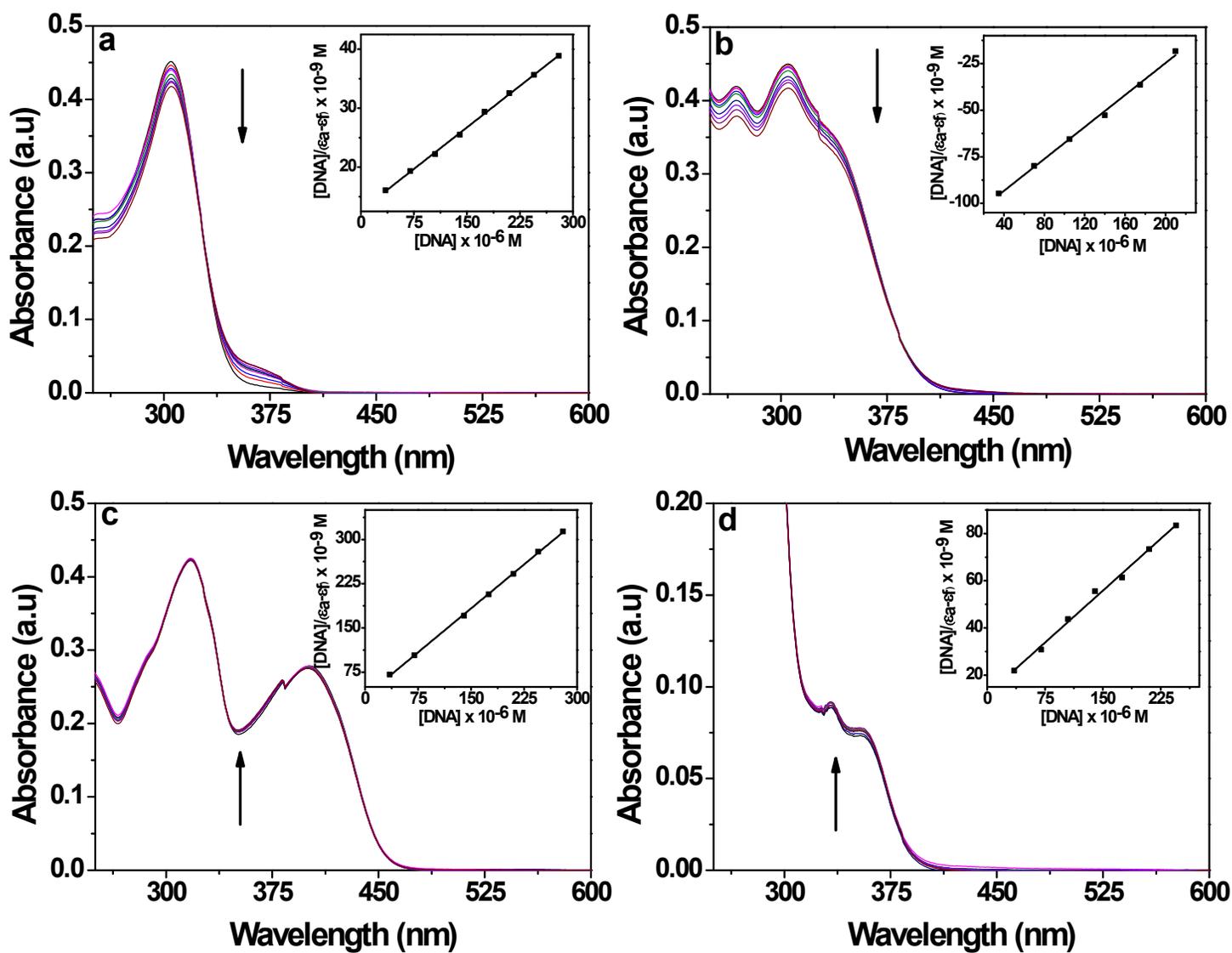


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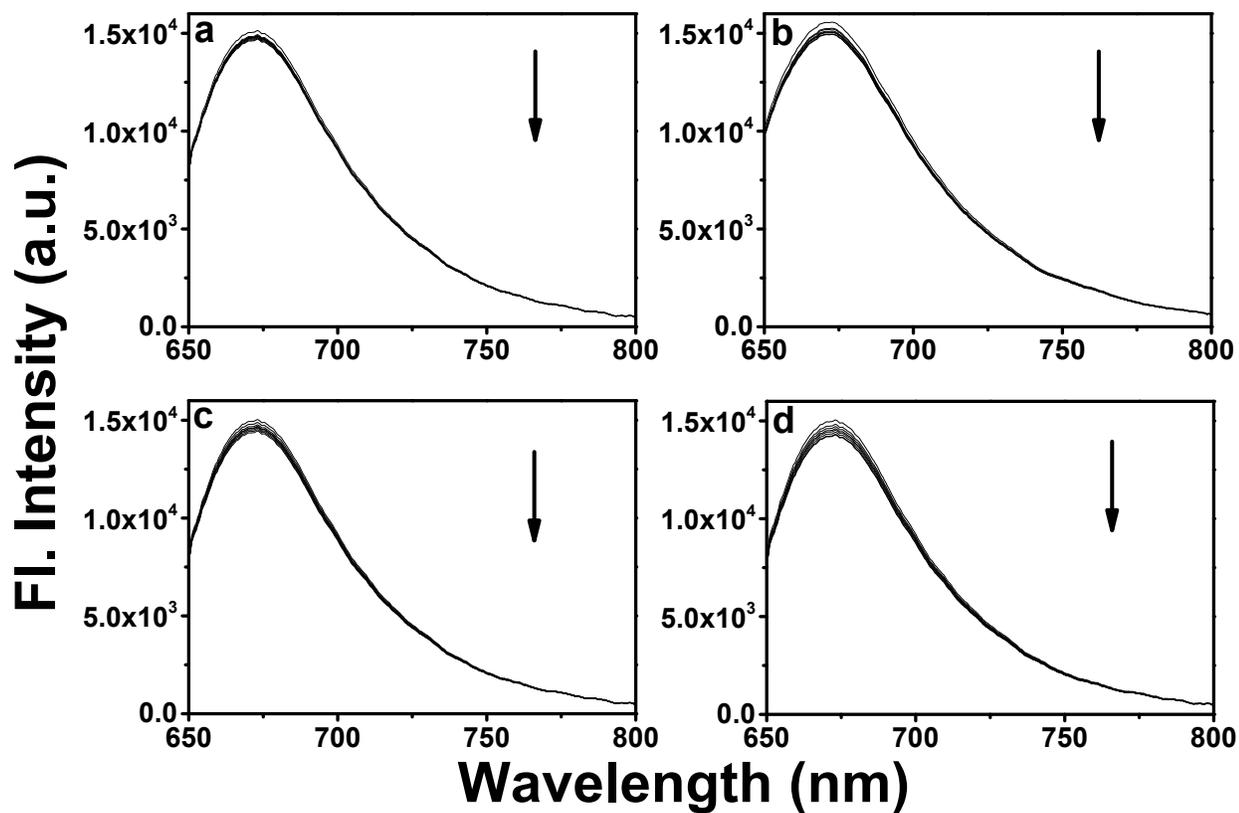


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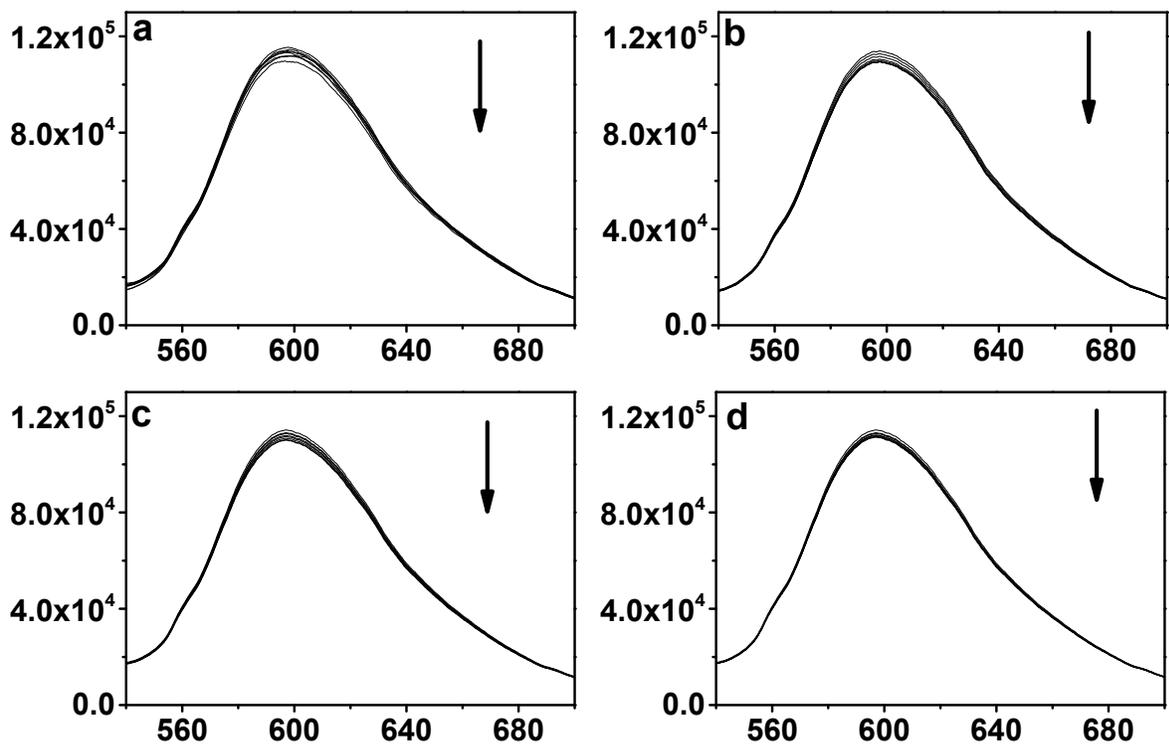


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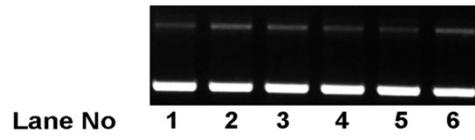


Fig. S11

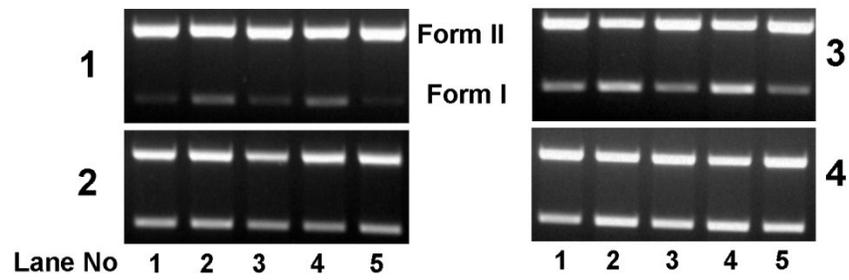


Fig. S12