Electronic Supplementary Material (ESI) for Dalton Transactions.

Supporting information *for*

Structure and Thermodynamic Stability of Uranyl-Deferiprone Complexes and the Removal Efficacy of U(VI) at the Cellular Level

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S1. Potentiometric Titrations

All stock solutions were prepared using double-distilled water with a conductivity of 18.2 MΩ cm^{-1} after being boiled for two hours while being degassed with nitrogen overnight. 0.1M KCl solution was prepared by dissolving an appropriate amount of salt into the carbonate-free water, 0.1 M HCl and 0.1 M KOH stock solutions were obtained commercially and standardized with Borax and hydrogen phthalate, and the stock solutions for titration are protected under constant nitrogen flow. A prep-experiment was carried out to calibrate the glass electrode (Metrohm Microtrode) by measuring the variation of the electric potential during titrating 4.0 mL 0.1 M KOH into the 0.1 M KCl solution (containing 2 mL 0.1 M HCl). The *E*° and slope can be refined by the program GLEE,[1] and then the data in the Tiamo software is updated.

The potentiometric titration of DFP was carried out by dissolving DFP (13.9 mg, 0.01 mmol) in 25 mL 0.1 M KCl (contains 5% DMSO) to determine the protonation constants of DFP. Three parallel experiments were performed from pH 2.5 to 11. The ligand protonation constants, pK_{as}, are defined by eq 1-5 and analyzed using nonlinear least-squares program (hyperquad 2013).[2]

$$LH_{s-1}^{(n-s+1)-} + H^{+} \overset{K_s}{\Leftrightarrow} LH_{s}^{(n-s)-} \qquad [1]$$

$$K_{as} = \frac{\left[LH_{s-1}^{(n-s+1)-}\right]\left[H^{+}\right]}{\left[LH_{s}^{(n-s)-}\right]} = \frac{1}{K_s} \qquad [2]$$

$$\beta s = \frac{[LH_{s}^{(n-s)-}]}{[L^{n-}][H^{+}]^{s}} \qquad [3]$$

$$K_{as} = \frac{\beta s}{\beta s\text{ - }1} \qquad [4]$$

$$pK_{as} = \log\beta s - \log\beta s\text{ - }1 \qquad [5]$$

The cumulative formation constants of uranyl-DFP complex were measured by adding 10 μmol $UO_2(NO_3)_2 \cdot 6H_2O$ (5.02 mg) to a prepared solution containing 20 μmol DFP (from 200 μmol/mL solution) in 25 mL of 0.1 M KCl(containing 5% DMSO), then titrated from low to high pH (2.5-9.0).

Data were refined using the hyperquad 2013 software. The method of potentiometric titrations is consistent with previously described experiments. All titration experiments were performed with the Metrohm 905 apparatus, and the titration instruments were fully automated and controlled using Tiamo software. The nonlinear least-squares program was used to refine the titration data and the results are listed in **Table S1**. Three parallel experiments were performed for data consistency.

$$m\mathrm{M}^{2+} + l\mathrm{L}^{2-} + h\mathrm{H}^{+} = \mathrm{M}_m\mathrm{L}_l\mathrm{H}_h{}^{(2m-l+h)+}$$

$$\log\beta_{\mathrm{mlh}} = -\log\frac{[\mathrm{M}_m\mathrm{L}_l\mathrm{H}_h]^{2m-l+h}}{[\mathrm{M}]^m[\mathrm{L}]^l[\mathrm{H}]^h} \qquad [6]$$

Table S1: Protonation constants and metal chelate stability constants.

Protonation constants	DFP	Cumulative formation constants	DFP
pK_{a1}	9.73 ± 0.06	logβ_{111}	13.21 ± 0.24
pK_{a2}	3.70 ± 0.13	logβ_{110}	10.24 ± 0.13
		logβ_{120}	16.46 ± 0.38
		log$\beta_{12\text{-}1}$	7.47 ± 0.38
		pUO$_2$[a]	10.32 ± 0.17

[a]: pUO$_2$ = -log [UO$_2^{2+}$ free]; [UO$_2^{2+}$] = 10^{-4} M and [L] = 10^{-3} M

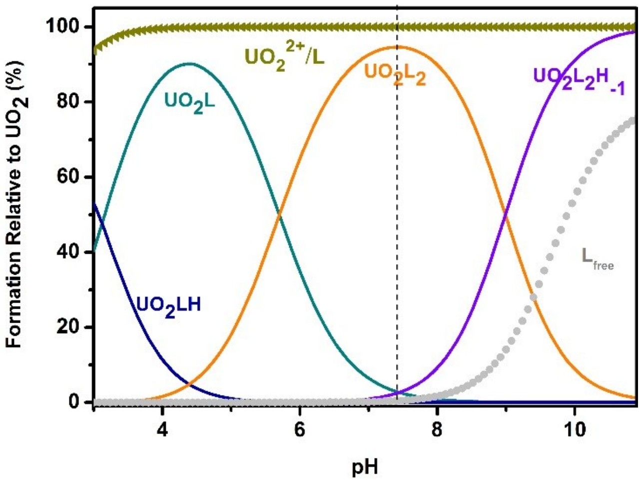

Figure S1: Species distribution of UO$_2^{2+}$/ L systems for solutions containing 1 X 10^{-4} M UO$_2^{2+}$ and 1 X 10^{-3} M ligands.

S2. The hydrogen-bond distances of compound 1.

Table S2: The hydrogen-bond distances of compound 1.

Hydrogen bonds distances (Å) for $[(UO_2)(H_2O)(C_7NO_2H_8)_2]\cdot 4H_2O$			
O5-C7	3.249	O3w- O4w	2.863
O5-C12	2.404	O4w-O6	2.767/3.327
O5-O4w	3.026	O4w-O4w	3.280
O3w-C6	3.417		

S3. Cytotoxicity of U(VI).

Table S3. Dosage-dependent cell growth rate of NRK cells treated with $UO_2(NO_3)_2\cdot 6H_2O$

concentration(μM)	Survival Rate（%）
6.2	96.7±4.3
12.4	90.9±0.09
24.8	71.2±1.3
49.6	68.5±1.9
89.2	63.3±1.8

S4. Cytotoxicity of U(VI) and chelating agents.

Table S4. Dosage-dependent cell growth rate of NRK-52E cells treated with $UO_2(NO_3)_2\cdot 6H_2O$, U[(VI), 12.4 μM] + DFP , U[(VI), 12.4 μM] + DTPA and DFP.

Concentration	UO_2+DFP Survival	UO_2+DTPA Survival	DFP Survival Rate

(μM)	Rate (%)	Rate (%)	(%)
20	81.3±1.4	84.4±1.4	93.8±3.5
40	80.0±1.2	83±1.5	90.1±3.1
80	68.8±1.3	82.1±2.1	72.1±2.5
160	47.9±1.5	79.8±2.4	42.4±1.3
320	24.8±0.2	76.6±1.4	29.8±6.3

S5. U(VI) uptake and release.

Table S5. Effects of DFP and DTPA on U(VI) uptake and release in NRK cells exposed to U(VI)

Group	Ligands Concentration(μM)	U (ng/10^6 Cells)
Control	0	109.0 ± 5.6
UO_2+DTPA	20	115.6 ± 31.3
UO_2+DFP1	40	77.8 ± 4.0
UO_2+DFP2	80	36.2 ± 7.3
UO_2+DFP3	320	24.2 ± 4.9

S6. Crystal structure of the uranyl-DFP complex reported by Keramidas *et al*.

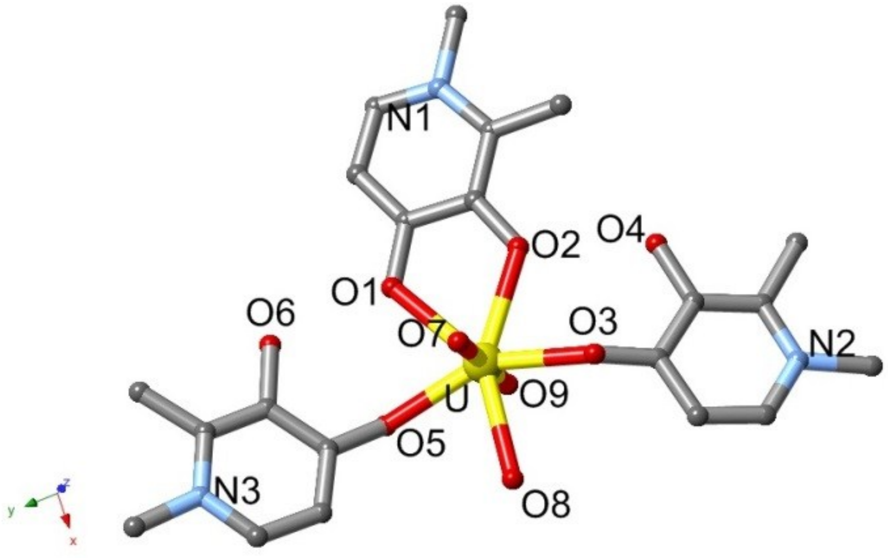

Figure S2: Ligand DFP and view of the crystal structure of it’s uranyl complex.

S7. FT-IR spectra of DFP, $UO_2(NO_3)_2·6H_2O$, and compound 1.

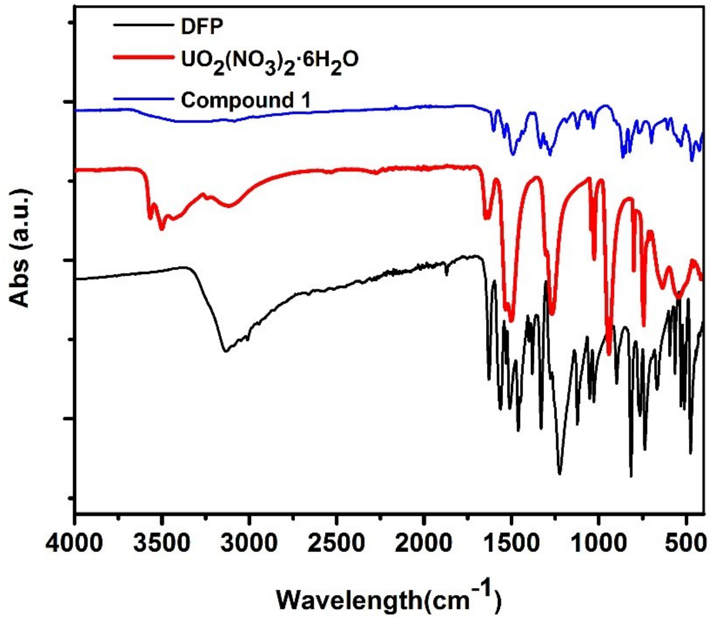

Figure S3: FT-IR spectra of DFP, $UO_2(NO_3)_2·6H_2O$, and compound 1. All spectra were normalized for peak position comparison.

Reference:

1 P. Gans, B. O'Suuivan, *Talanta*. 2000, **51**, 33-37.
2 P. Gans, A. Sabatini, A. Vacca, *Talanta*. 1996, **43**, 1739-1753.