Supporting Information

Synthesis, In vitro Cytotoxicity, and Structure–activity Relationship (SAR) studies of Multidentate Oxidovanadium(IV) Complexes as Anticancer Agents

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Table S1. Crystallographic data and structural refinement details for compound **1** and compound **2**.

	1	**2**
Empirical formula	$C_{12}H_{10}N_2O_6V$	$C_{14}H_{10}N_2O_6V$
Formula weight	329.16	353.18
Temperature, K	173(2)	173(2)
Wavelength, Å	Mo *Kα* (0.71073)	Mo *Kα* (0.71073)
Crystal system	Monoclinic	Triclinic
Space group	*P* 2_1/n	*P* ī
Unit cell dimensions		
a, Å	12.532(1)	7.615 (1)
b, Å	7.554(1)	9.752(1)
c, Å	14.088 (1)	9.767(1)
α, °		89.827(6)
β, °	96.707(4)	74.344(7)
γ, °		81.007(6)
V, $Å^3$	1324.47(2)	689.26(9)
Z	4	2
D (calculated), g/cm^3	1.651	1.702
Abs. coeff., mm^{-1}	0.779	0.755
F(000)	668	358
Crystal size, mm	0.20×0.18×0.10	0.15×0.15×0.10
θ range for data collection, °	3.08 ~ 27.00	2.97 ~ 27.00
Reflections collected / unique / R_{int}	5817/28460.0458	4840/2962/0.0280
Data / restraints / parameters	2846 / 3 / 198	2962 / 3 / 216
GOF on F^2	1.073	1.053
Final R indices R_1, ωR_2 [$I > 2\sigma(I)$]	0.0561, 0.1097	0.0351, 0.0845
R indices R_1, ωR_2 [all data]	0.0820, 0.1197	0.0417, 0.0889
Largest diff. peak and hole, e. $Å^{-3}$	0.366/-0.451	0.434/-0.341

Table S2. Crystallographic data and structural refinement details for compound **3** and compound **4**.

	3	**4**
Empirical formula	$C_{14}H_{17}N_3O_7V$	$C_{28}H_{29}N_5O_9V$
Formula weight	390.25	630.50
Temperature, K	173(2)	173(2)
Wavelength, Å	Mo *Kα* (0.71073)	Mo *Kα* (0.71073)
Crystal system	Monoclinic	Monoclinic
Space group	*P* 2_1/c	*P* 2_1/c
Unit cell dimensions		
a, Å	9.024(1)	7.156(1)
b, Å	15.584(1)	19.676(2)
c, Å	11.820(1)	19.862(2)
α, °		
β, °	100.912(3)	95.826(7)
γ, °		
V, Å^3	1632.26(9)	2781.9(3)
Z	4	4
D (calculated), g/cm^3	1.588	1.505
Abs. coeff., mm^{-1}	0.651	0.421
F(000)	804	1308
Crystal size, mm	0.18×0.15×0.08	0.20×0.10×0.10
θ range for data collection, °	3.15 ~ 27.00	2.92 ~ 26.00
Reflections collected / unique / R_{int}	6328/3469/0.0501	12451/5452/0.0584
Data / restraints / parameters	3469/6/238	5452/12/412
GOF on F^2	1.050	1.037
Final R indices R_1, ωR_2 [$I > 2\sigma(I)$]	0.0499, 0.1062	0.0584, 0.1049
R indices R_1, ωR_2 [all data]	0.0658, 0.1152	0.0888, 0.1171
Largest diff. peak and hole, e. Å^{-3}	0.378/-0.360	0.307/-0.464

Table S3. Crystallographic data and structural refinement details for compound **5**.

	5
Empirical formula	$C_{18}H_{21}N_3O_{10}V$
Formula weight	490.32
Temperature, K	173(2)
Wavelength, Å	Mo *Kα* (0.71073)
Crystal system	Monoclinic
Space group	*P* 2_1/c
Unit cell dimensions	
a, Å	8.162(1)
b, Å	23.355(1)
c, Å	11.045(1)
α, °	
β, °	106.358(4)
γ, °	
V, Å^3	2020.36(2)
Z	4
D (calculated), g/cm^3	1.612
Abs. coeff., mm^{-1}	0.555
F(000)	1012
Crystal size, mm	0.20×0.20×0.20
θ range for data collection, °	2.90 ~ 26.00
Reflections collected / unique / R_{int}	8402/3960/0.0352
Data / restraints / parameters	3960/9/309
GOF on F^2	1.048
Final R indices R_1, ωR_2 [$I > 2\sigma(I)$]	0.0404, 0.0847
R indices R_1, ωR_2 [all data]	0.0532, 0.0899
Largest diff. peak and hole, e. Å^{-3}	0.301/-0.433

Table S4. Selected bond distances (Å) and angles (º) for compound **1** [VO(ox)(bpy)(H_2O)] and compound **2** [VO(ox)(phen)(H_2O)].

1			
V(1)–O(5)	1.581(2)	V(1)–O(1w)	2.034(2)
V(1)–O(1)	1.996(2)	V(1)–N(1)	2.129(3)
V(1)–O(2)	1.999(2)	V(1)–N(2)	2.283(3)
O(5)–V(1)–O(1)	101.8(1)	O(2)–V(1)–N(1)	160.9(1)
O(5)–V(1)–O(2)	105.7(1)	O(1w)–V(1)–N(1)	95.9(1)
O(1)–V(1)–O(2)	80.8(1)	O(5)–V(1)–N(2)	164.5(1)
O(5)–V(1)–O(1w)	98.0(1)	O(1)–V(1)–N(2)	84.2(1)
O(1)–V(1)–O(1w)	159.1(1)	O(2)–V(1)–N(2)	89.3(1)
O(2)–V(1)–O(1w)	87.4(1)	O(1w)–V(1)–N(2)	78.4(1)
O(5)–V(1)–N(1)	92.5(1)	N(1)–V(1)–N(2)	73.0(1)
O(1)–V(1)–N(1)	90.0(1)		
2			
V(1)–O(5)	1.591(2)	V(1)–O(1w)	2.030(2)
V(1)–O(1)	2.002(1)	V(1)–N(1)	2.319(2)
V(1)–O(2)	1.994(1)	V(1)–N(2)	2.121(2)
O(5)–V(1)–O(1)	101.2(1)	O(2)–V(1)–N(1)	87.2(1)
O(5)–V(1)–O(2)	105.3(1)	O(1w)–V(1)–N(1)	80.2(1)
O(1)–V(1)–O(2)	81.0(1)	O(5)–V(1)–N(2)	93.8(1)
O(5)–V(1)–O(1w)	99.4(1)	O(1)–V(1)–N(2)	92.6(1)
O(1)–V(1)–O(1w)	158.6(1)	O(2)–V(1)–N(2)	160.7(1)
O(2)–V(1)–O(1w)	88.3(1)	O(1w)–V(1)–N(2)	91.5(1)
O(5)–V(1)–N(1)	167.4(1)	N(1)–V(1)–N(2)	73.7(1)
O(1)–V(1)–N(1)	80.9(1)		

Table S5. Selected bond distances (Å) and angles (º) for compound **3** [VO(ida)(bpy)]·2H_2O and compound **4** (phen)[VO(ida)(phen)]·4H_2O.

3			
V(1)–O(1)	1.990(2)	V(1)–N(1)	2.331(2)
V(1)–O(3)	1.995(2)	V(1)–N(2)	2.103(2)
V(1)–O(5)	1.601(2)	V(1)–N(3)	2.116(2)
O(5)–V(1)–O(1)	98.3(1)	O(3)–V(1)–N(3)	90.3(1)
O(5)–V(1)–O(3)	101.0(1)	N(2)–V(1)–N(3)	76.9 (1)
O(1)–V(1)–O(3)	92.6 (1)	O(5)–V(1)–N(1)	174.1(1)
O(5)–V(1)–N(2)	100.8(1)	O(1)–V(1)–N(1)	76.6 (1)
O(1)–V(1)–N(2)	92.8(1)	O(3)–V(1)–N(1)	76.4(1)
O(3)–V(1)–N(2)	156.6(1)	N(2)–V(1)–N(1)	82.7(1)
O(5)–V(1)–N(3)	101.6(1)	N(3)–V(1)–N(1)	83.9(1)
O(1)–V(1)–N(3)	159.0(1)		
4			
V(1)–O(1)	1.994(2)	V(1)–N(1)	2.341(2)
V(1)–O(3)	2.008(2)	V(1)–N(2)	2.113(2)
V(1)–O(5)	1.589(2)	V(1)–N(3)	2.129(2)
O(5)–V(1)–O(1)	101.5(1)	O(3)–V(1)–N(3)	92.7 (1)
O(5)–V(1)–O(3)	95.9 (1)	N(2)–V(1)–N(3)	78.0(1)
O(1)–V(1)–O(3)	94.5(1)	O(5)–V(1)–N(1)	170.6 (1)
O(5)–V(1)–N(2)	98.3 (1)	O(1)–V(1)–N(1)	77.1(1)
O(1)–V(1)–N(2)	89.1(1)	O(3)–V(1)–N(1)	75.0(1)
O(3)–V(1)–N(2)	164.3 (1)	N(2)–V(1)–N(1)	91.0(1)
O(5)–V(1)–N(3)	101.7 (1)	N(3)–V(1)–N(1)	81.5(1)
O(1)–V(1)–N(3)	154.8 (1)		

Table S6. Selected bond distances (Å) and angles (°) for compound **5** (Hphen)[VO(H_2O)(nta)]·2H_2O.

V(1)–O(1)	2.014(2)	V(1)–O(7)	1.601(2)
V(1)–O(3)	2.002(2)	V(1)–O(1)W	2.032(2)
V(1)–O(5)	2.012(2)	V(1)–N(1)	2.317(2)
O(7)–V(1)–O(3)	105.3(1)	O(5)–V(1)–O(1)W	165.5 (1)
O(7)–V(1)–O(5)	94.4(1)	O(1)–V(1)–O(1)W	86.6(1)
O(3)–V(1)–O(5)	90.7 (1)	O(7)–V(1)–N(1)	171.7 (1)
O(7)–V(1)–O(1)	103.8 (1)	O(3)–V(1)–N(1)	75.3(1)
O(3)–V(1)–O(1)	150.9(1)	O(5)–V(1)–N(1)	77.4(1)
O(5)–V(1)–O(1)	90.0(1)	O(1)–V(1)–N(1)	76.2(1)
O(7)–V(1)–O(1)W	100.1(1)	O(1)W–V(1)–N(1)	88.2(1)
O(3)–V(1)–O(1)W	86.5 (1)		

Table S7. Hydrogen bonds observed in compound **3** [VO(ida)(bpy)]·2H_2O.

D–H···A	*D–H (Å)*	*H···A (Å)*	*D···A (Å)*	*D–H···A(°)*
N1–H···O1w[a]	0.930	2.175	2.959	141.33
N1–H···O2w[b]	0.930	2.505	3.248	137.05
O2w–H···O4	0.852	1.917	2.755	167.32
O1w–H···O2	0.850	1.915	2.760	172.31
O2w–H···O2[c]	0.851	2.145	2.961	160.44
O1w–H···O2w[d]	0.850	2.067	2.797	143.56

Symmetry transformations: (a) $x + 1, y, z$; (b) $x, -y + ½, z - ½$; (c) $-x-1, y + ½, -z + ½$; (d) $x - 1, -y + ½, z - 1$.

Table S8. Hydrogen bonds observed in compound **4** (phen)[VO(ida)(phen)]·4H_2O.

D–H⋯A	*D–H (Å)*	*H⋯A (Å)*	*D⋯A (Å)*	*D–H⋯A(º)*
N1–H⋯N4[a]	0.930	2.280	3.095	145.91
N1–H⋯N5[b]	0.930	2.372	3.131	138.70
O1w–H⋯O2w[c]	0.855	1.949	2.790	167.37
O3w–H⋯O4w[d]	0.852	1.925	2.727	156.30
O3w–H⋯O4	0.849	1.980	2.818	169.06
O4w–H⋯O1w[e]	0.851	2.038	2.874	167.35
O2w–H⋯O2	0.852	1.972	2.816	170.58
O4w–H⋯O4	0.851	1.929	2.780	176.93
O1w–H⋯O2	0.852	1.928	2.775	172.15
O2w–H⋯O3w[f]	0.852	1.971	2.808	167.41

Symmetry transformations: (a) –x, y –½, –z + ½; (b) –x, y – ½, –z + ½; (c) x + 1, y, z; (d) x + 1, y, *z*; (e) *–x, y* + ½, *–z* + ½; (f) *–x, y* – ½, *–z* + ½.

Table S9. Hydrogen bonds observed in compound **5** (Hphen)[VO(H_2O)(nta)]·2H_2O.

D–H⋯A	*D–H (Å)*	*H⋯A (Å)*	*D⋯A (Å)*	*D–H⋯A(º)*
N2–H⋯O3w[a]	0.880	1.871	2.706	157.57
O1w⋯O4[b]	0.840	1.823	2.627	159.86
O1w–H⋯O2[c]	0.840	1.832	2.669	174.43
O2w–H⋯O6[d]	0.851	1.987	2.789	156.81
O2w–H⋯O5	0.843	1.957	2.786	167.35
O3w–H⋯O2w	0.851	1.957	2.789	165.65
O3w–H⋯O1	0.845	2.066	2.872	159.09

Symmetry transformations: (a) *–x* + 1, *y* + ½, *–z* + ½; (b) *x*, *-y* + 3/2, *z* – ½; (c) *x*, *-y* + 3/2, *z* + ½; (d) *–x* + 1, *-y* + 1, *-z* + 1.

Table S10. The comparison of anti-proliferation activity for compound **2**, the marketed platinum-based drugs and other vanadium(IV) on hepatoma cells.

	Hepatoma cell lines	IC_{50} (μM) 48h	Refs
Complex **2**	HepG2	29.07 ± 0.017	This work
	SMMC-7721	5.34 ± 0.034	This work
Cisplatin	HepG2	12.75 ± 0.80	63
	SMMC-7721	30.56± 0.80	63
	Hep3B	4.97 ± 0.86	64
	BEL-7404	11.1 ± 0.6	65
Oxaliplatin	HepG2	12.10 ± 5.03	66
	BEL-7404	24.7 ± 3.3	64
Carboplatin	BEL-7404	190.8 ± 17.8	65
$[V^{IV}O(satsc)(phen)]$	BEL-7402	55.16 ± 3.89	67
	HUH-7	47.93 ± 4.22	67
	HepG2	6.80 ± 0.76	67
$[V^{IV}O(3,5\text{-dibrsatsc})(phen)]$	BEL-7402	19.46 ± 2.14	67
	HUH-7	11.65 ± 1.85	67
	HepG2	1.68 ± 0.41	67
$[V^{IV}O(msatsc)(phen)]$	BEL-7402	30.80 ± 13.05	68
	HUH-7	2.87 ± 0.23	68
	HepG2	1.81 ± 0.38	68
$[V^{IV}O(4\text{-chlorosatsc})(phen)]$	BEL-7402	17.02 ± 3.69	68
	HUH-7	1.98 ± 0.72	68
	HepG2	1.33 ± 0.37	68

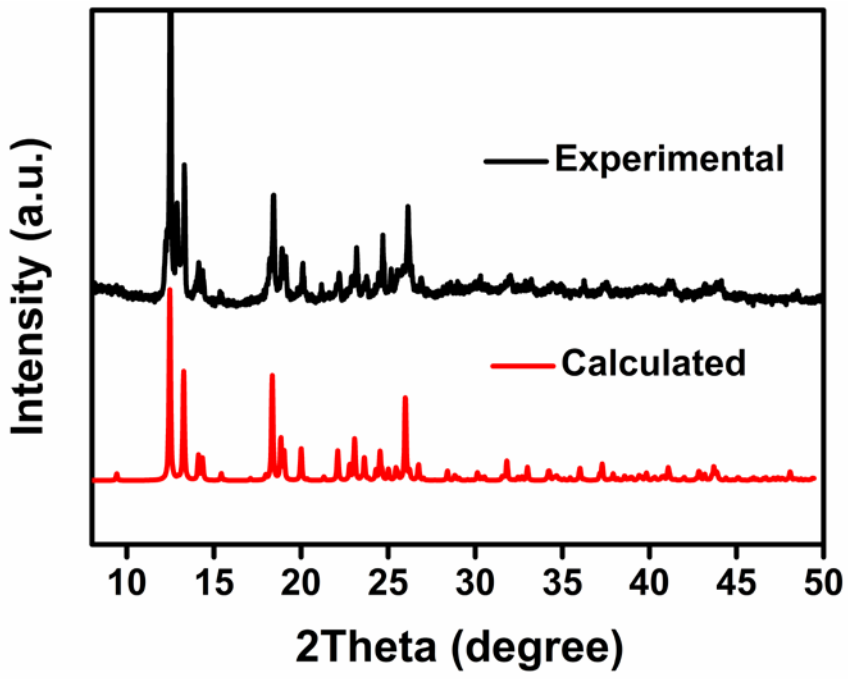

Figure S1. Calculated and experimental powder X-ray diffraction (PXRD) patterns of compound **1**.

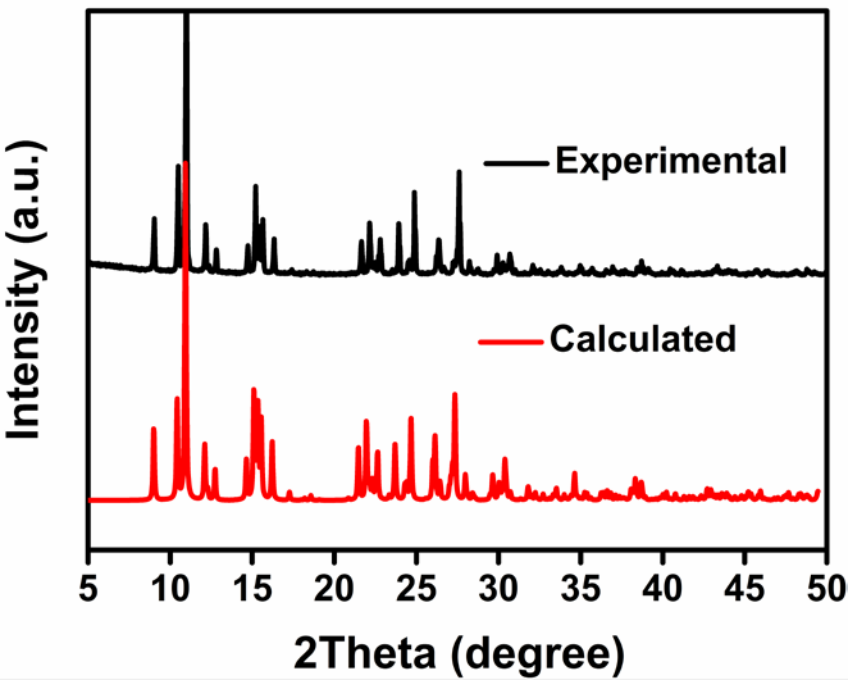

Figure S2. Calculated and experimental powder X-ray diffraction (PXRD) patterns of compound **2**.

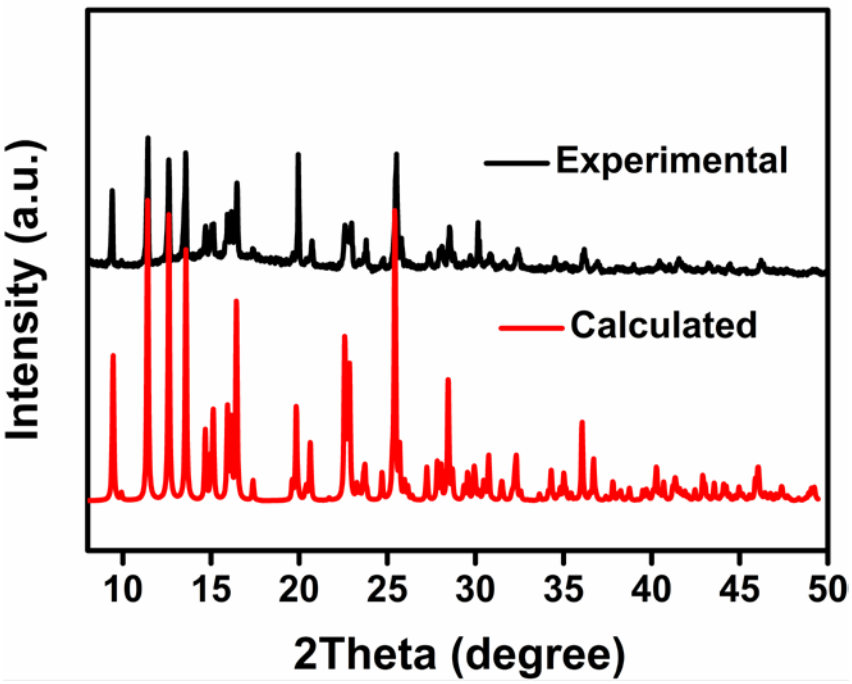

Figure S3. Calculated and experimental powder X-ray diffraction (PXRD) patterns of compound **3**.

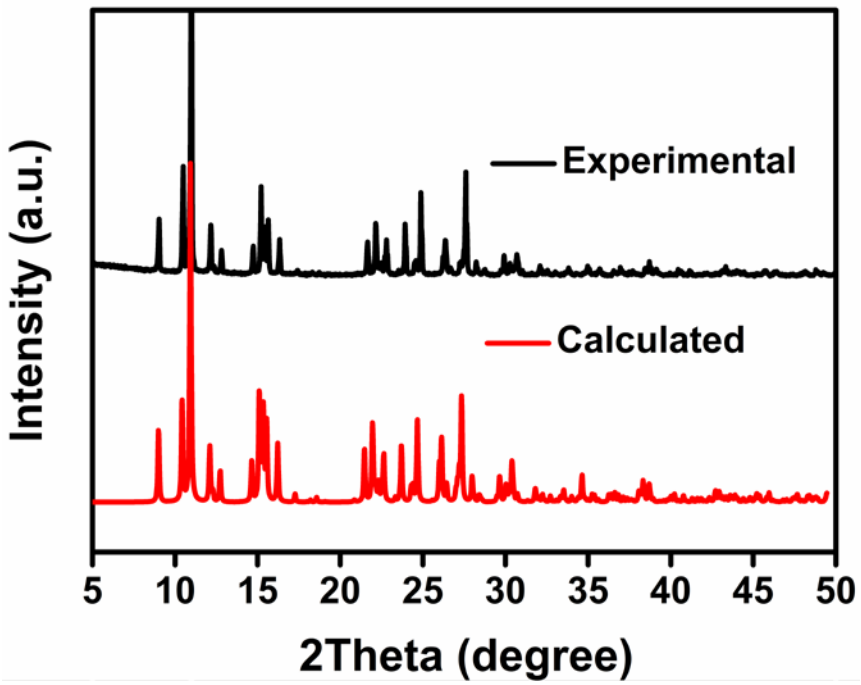

Figure S4. Calculated and experimental powder X-ray diffraction (PXRD) patterns of compound 4

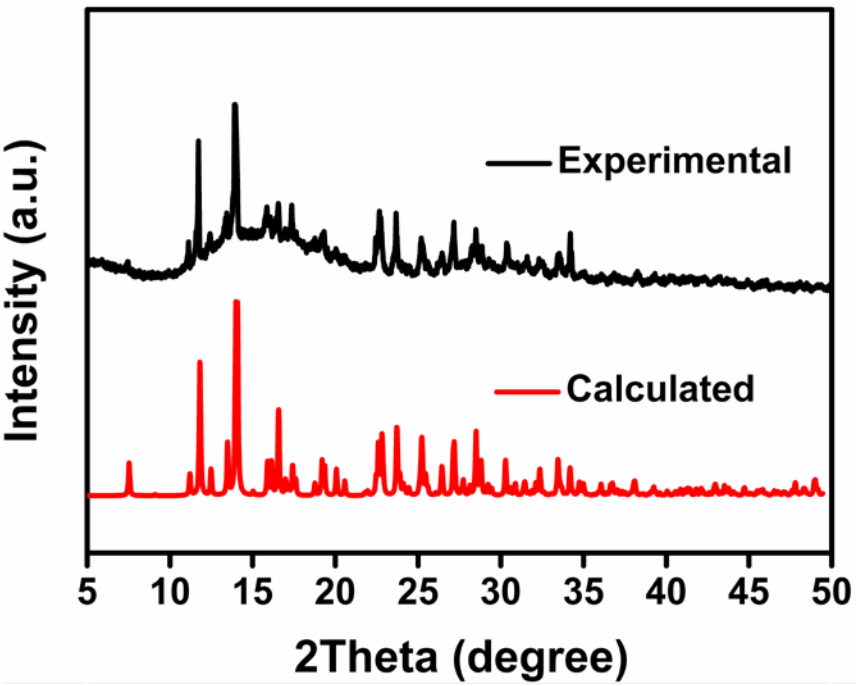

Figure S5. Calculated and experimental powder X-ray diffraction (PXRD) patterns of compound **5**.

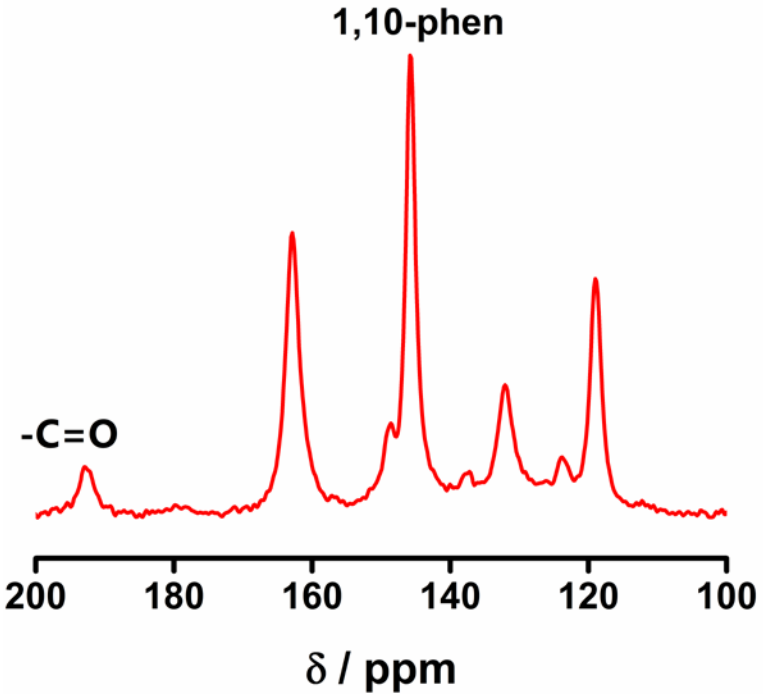

Figure S6. Solid state ^{13}C NMR spectrum of compound **2**.

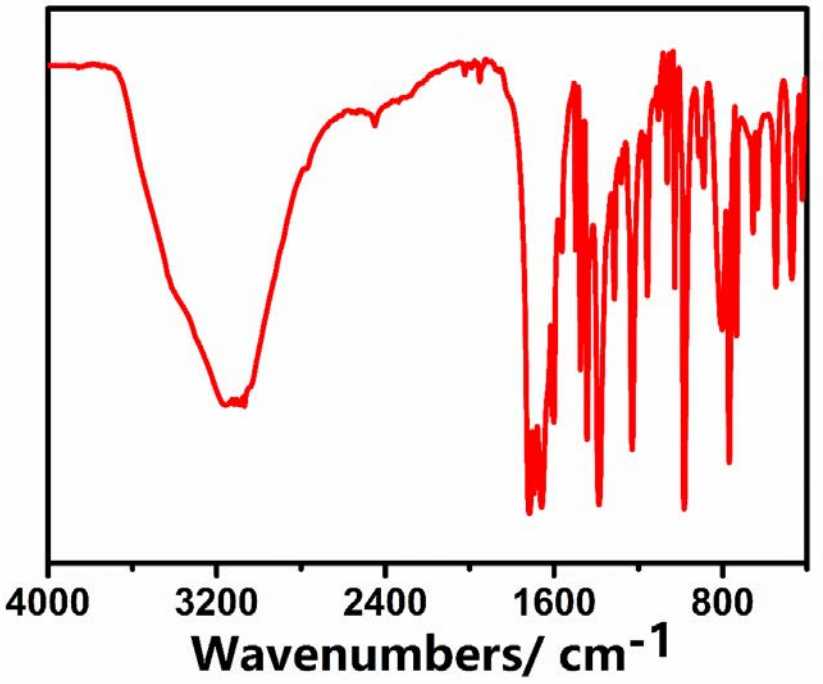

Figure S7. The FT-IR spectrum of vanadyl compound **1**.

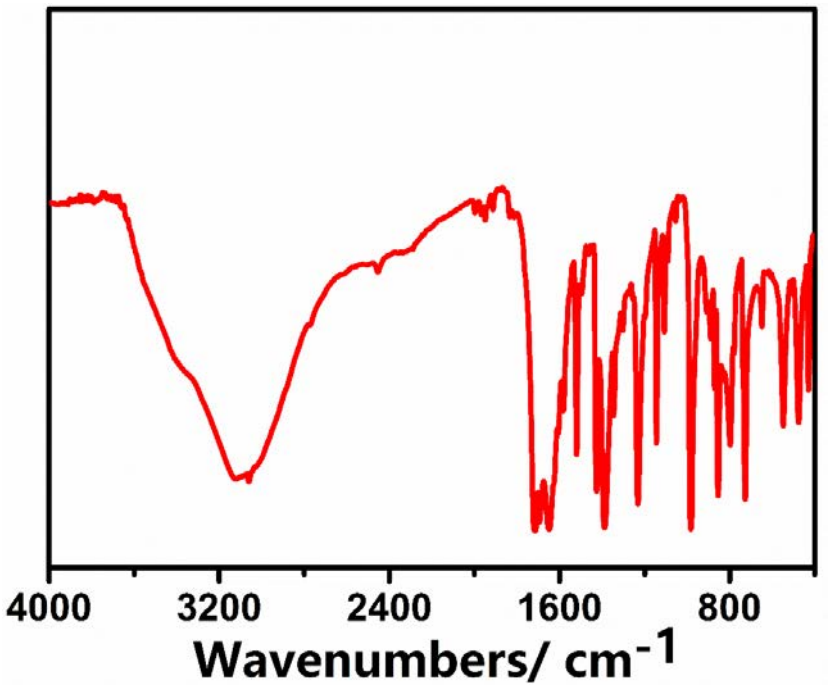

Figure S8. The FT-IR spectrum of vanadyl compound **2**.

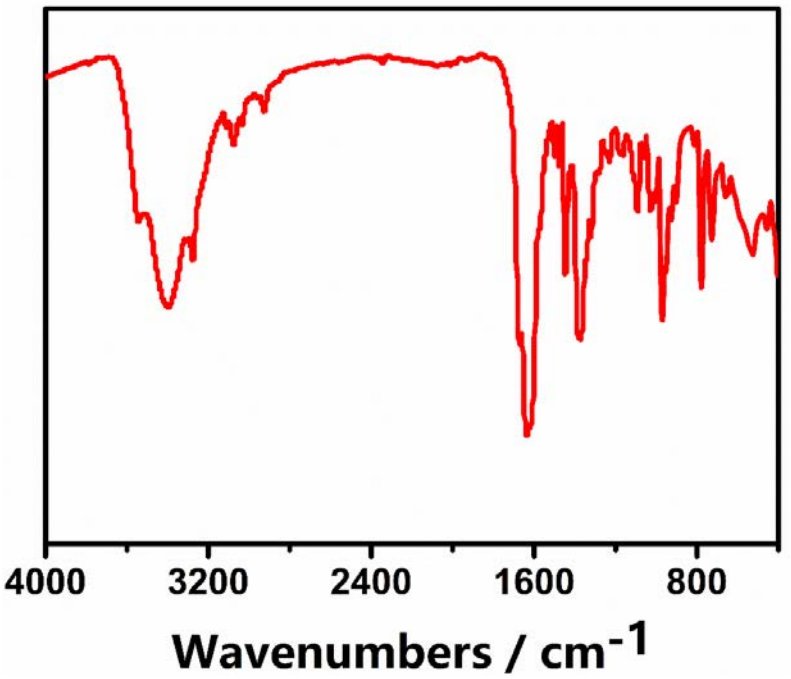

Figure S9. The FT-IR spectrum of vanadyl compound **3**.

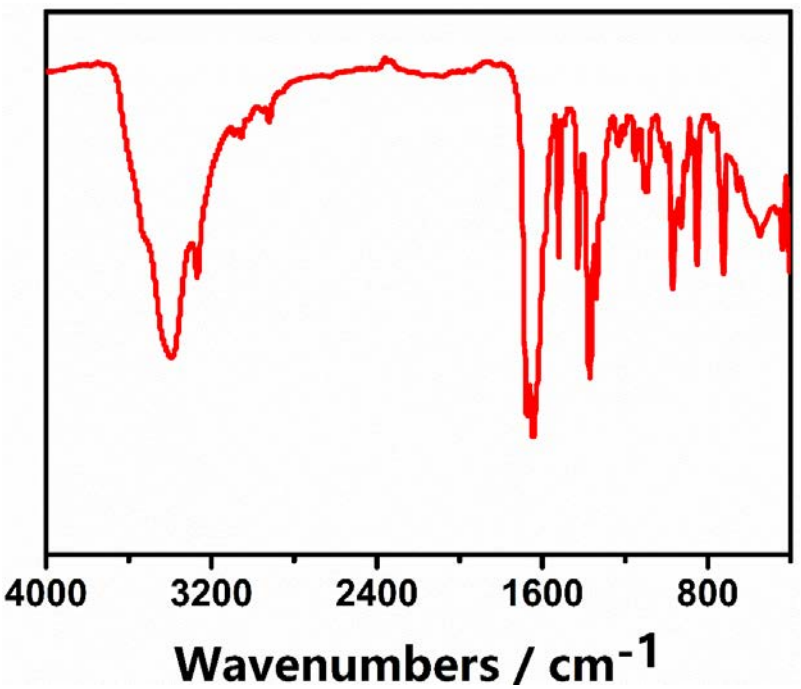

Figure S10. The FT-IR spectrum of vanadyl compound **4**.

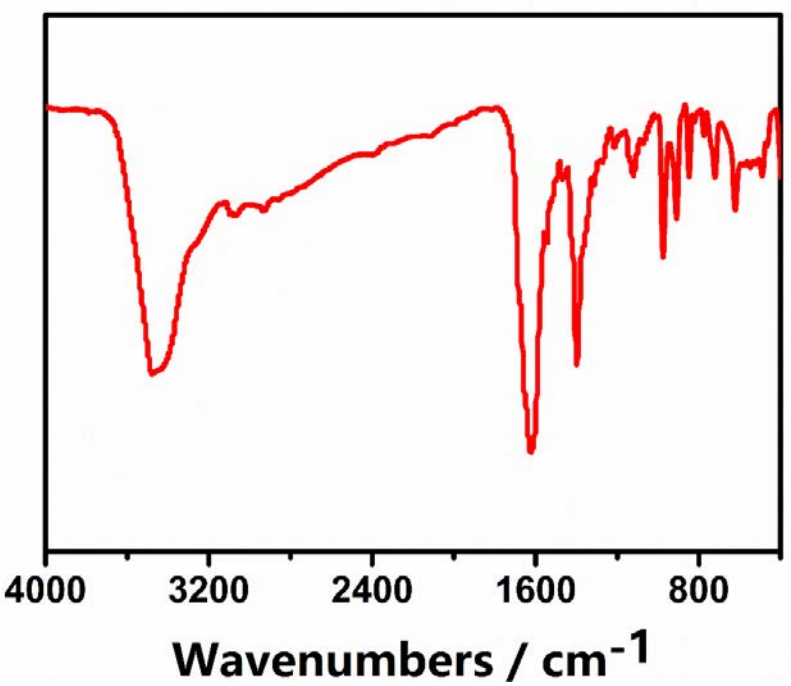

Figure S11. The FT-IR spectrum of vanadyl compound **5**.

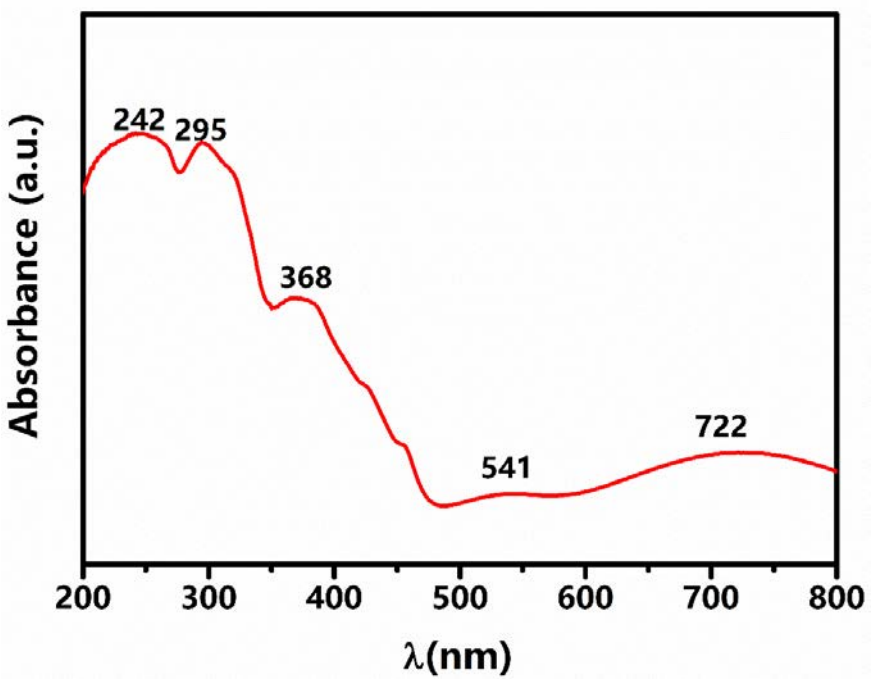

Figure S12. The solid diffuse UV-Vis spectrum of vanadyl compound **1**.

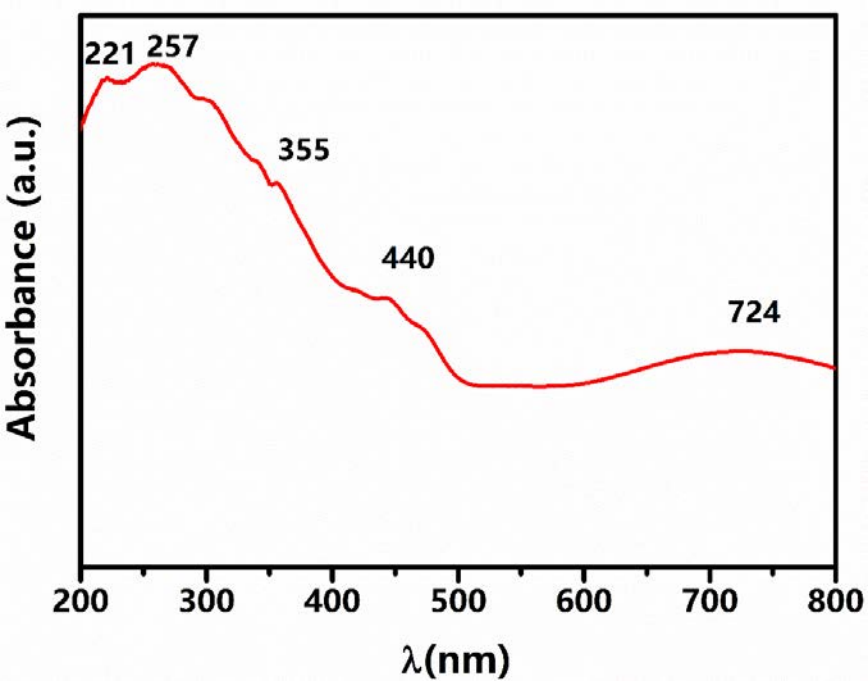

Figure S13. The solid diffuse UV-Vis spectrum of vanadyl compound **2**.

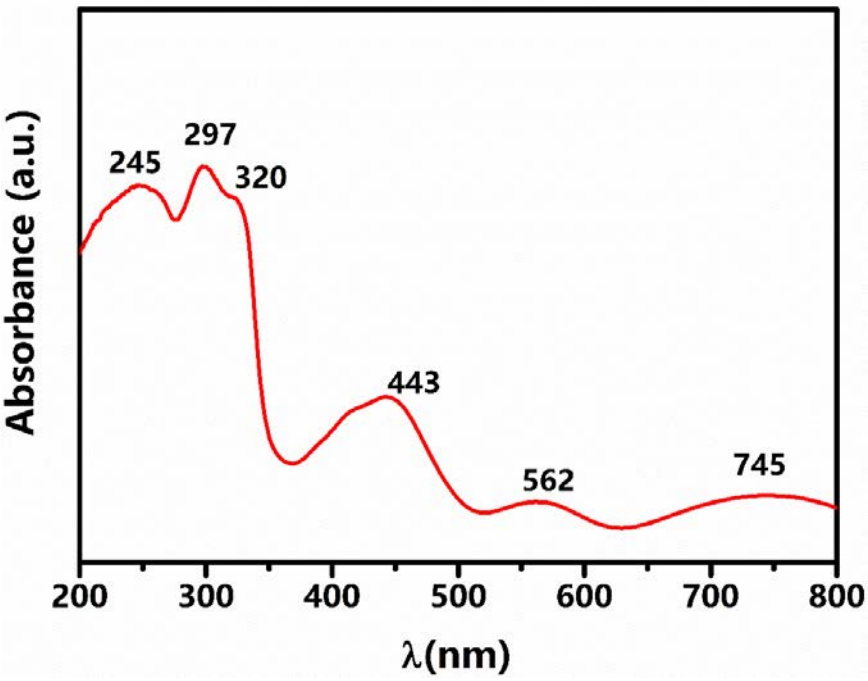

Figure S14. The solid diffuse UV-Vis spectrum of vanadyl compound **3**.

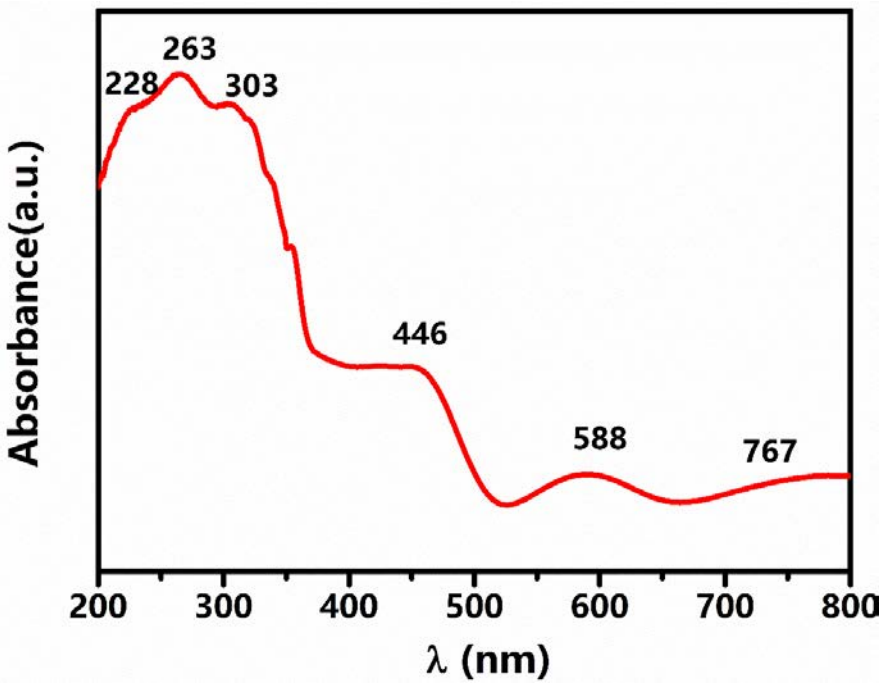

Figure S15. The solid diffuse UV-Vis spectrum of vanadyl compound **4**.

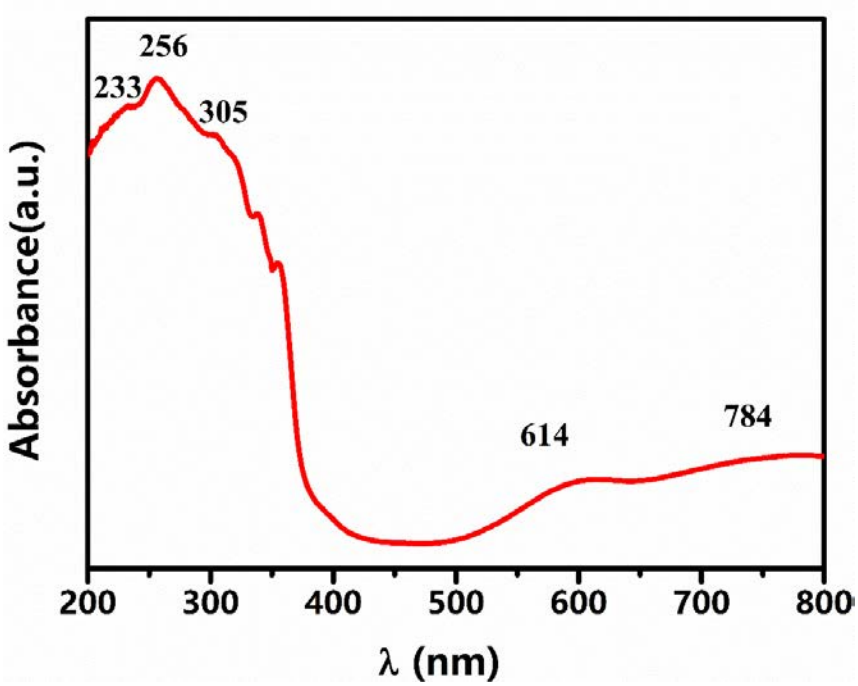

Figure S16. The solid diffuse UV-Vis spectrum of vanadyl compound **5**.

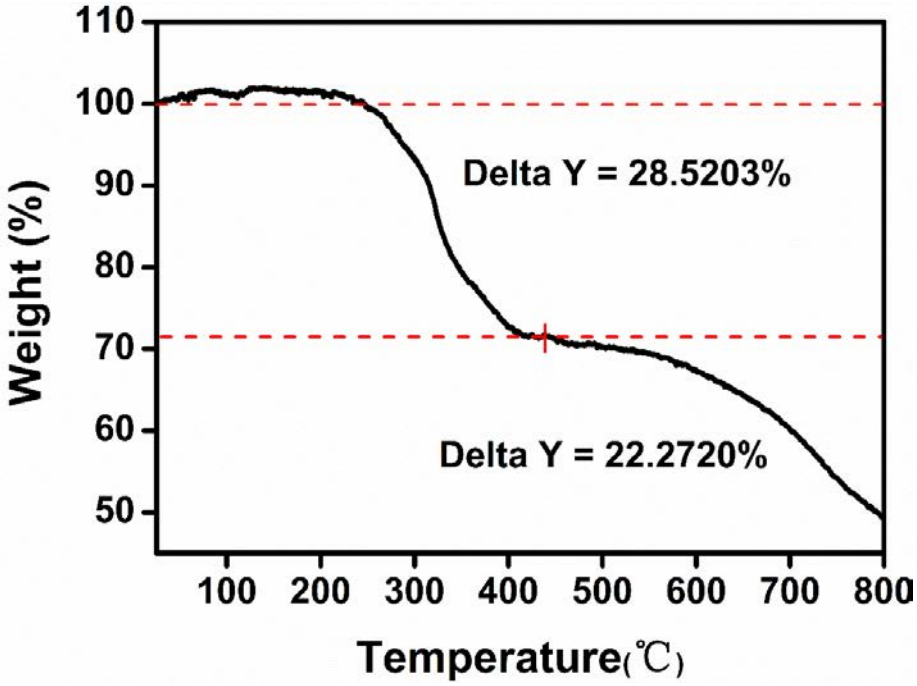

Figure S17. The thermal gravimetric analysis of compound **2**.

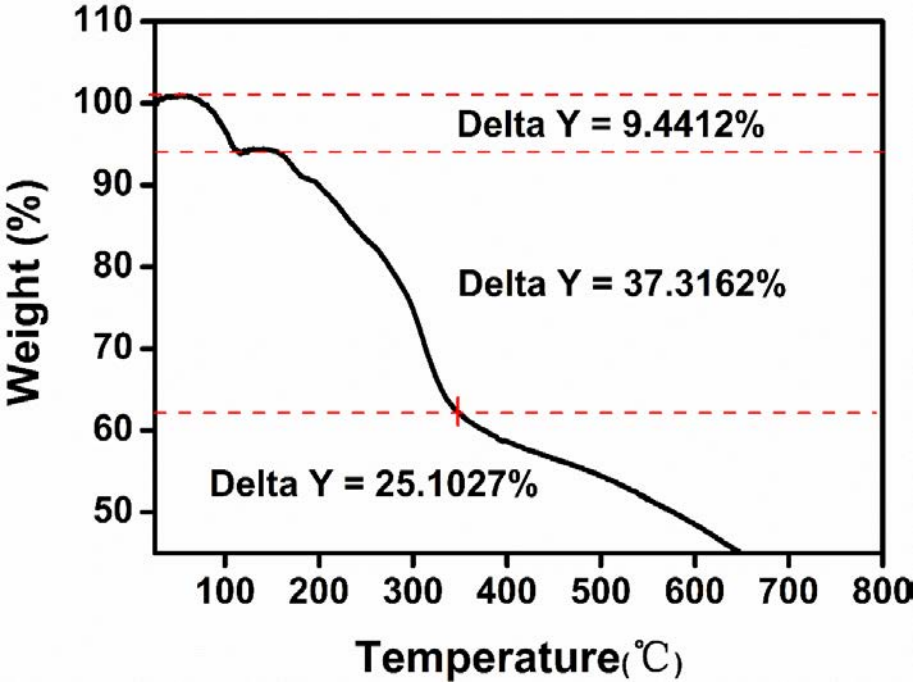

Figure S18. The thermal gravimetric analysis of compound **5**.

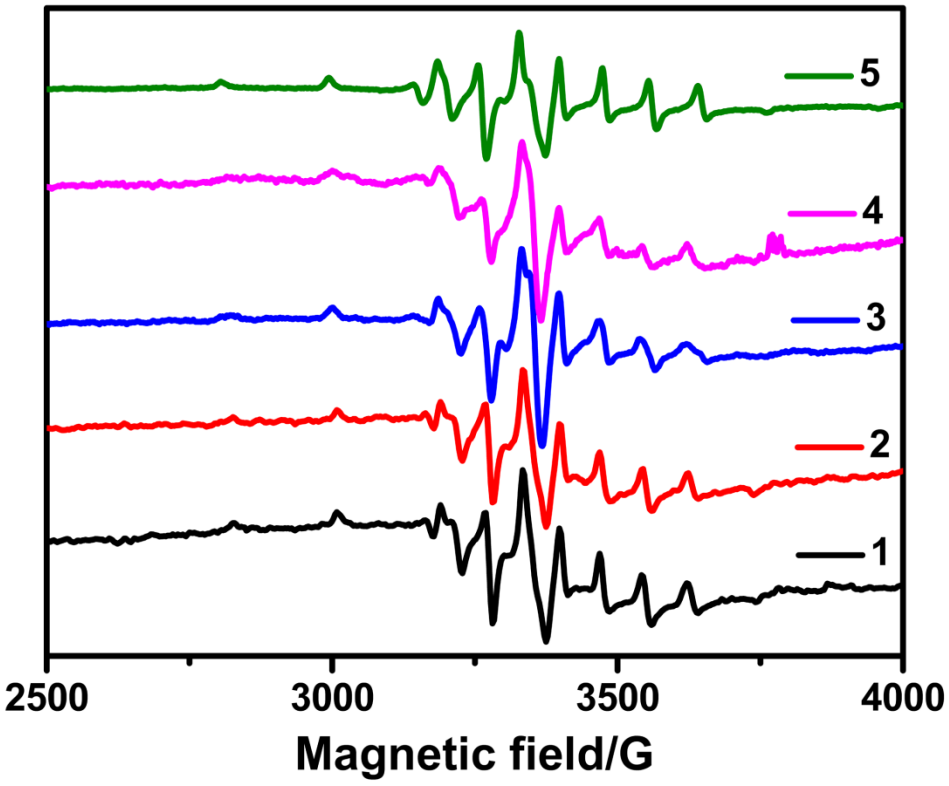

Figure S19. EPR spectra of compounds **1-5** in DMSO at 130 K (t = 0 h)

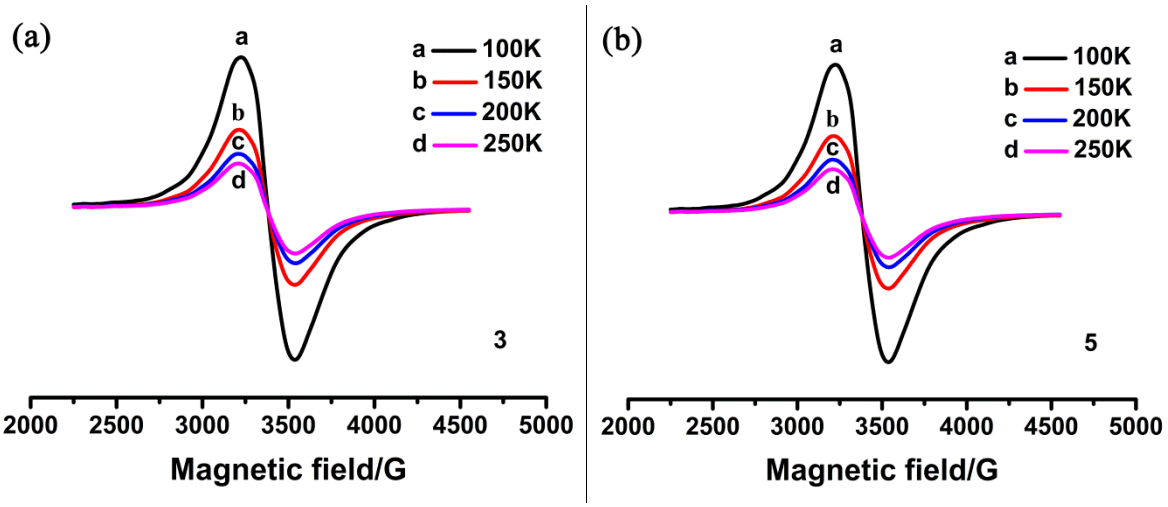

Figure S20. X-band EPR spectra in solid state of (a) compound **3**, (b) compound **5** at various temperatures.

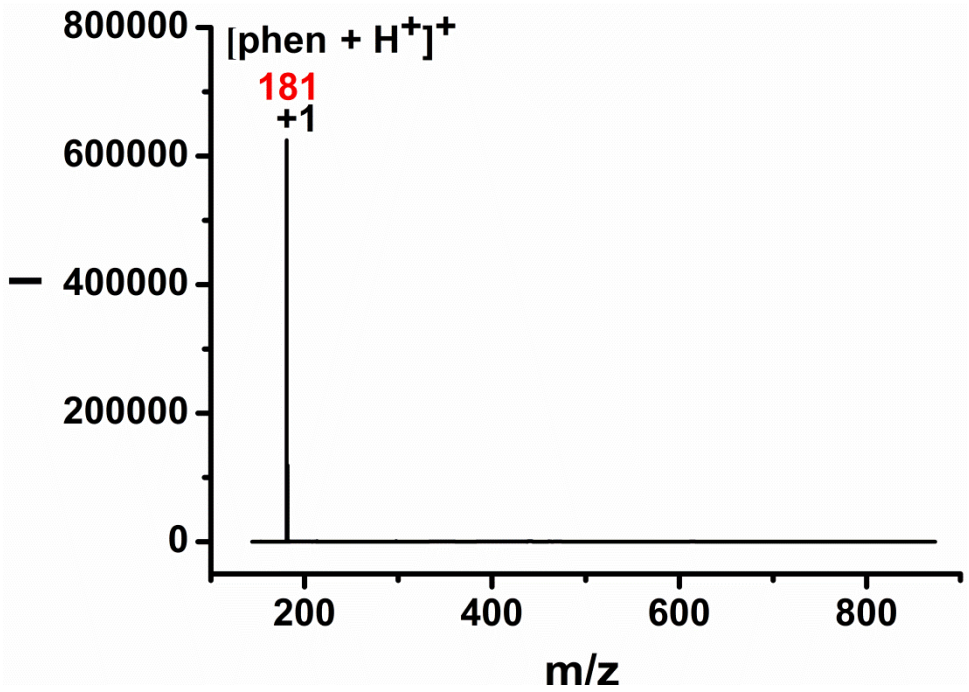

Figure S21. ESI-MS spectrum of compound **5** in positive ion mode.

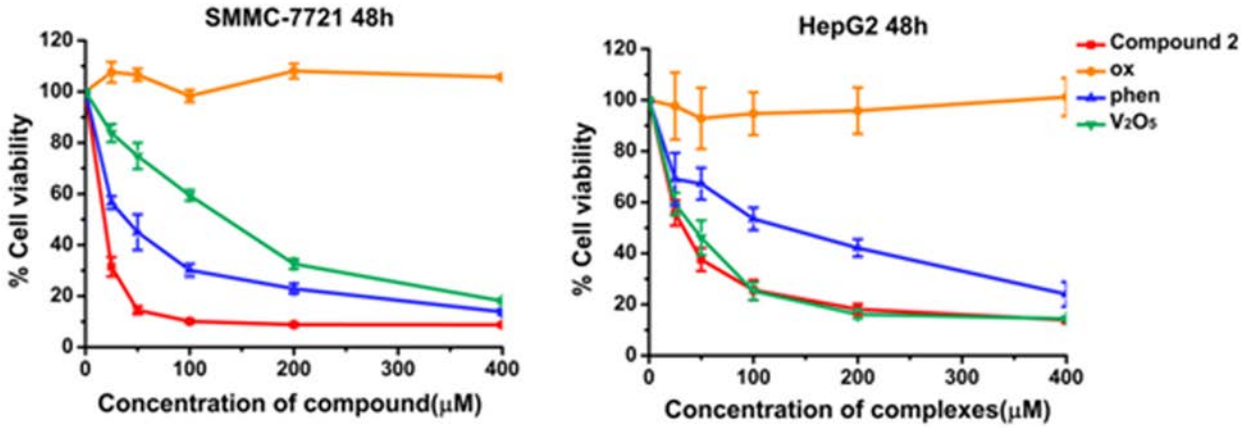

Figure S22. SMMC-7721 and HepG2 cells were incubated with various concentrations of compound **2**, and ligands for 48 h, respectively.

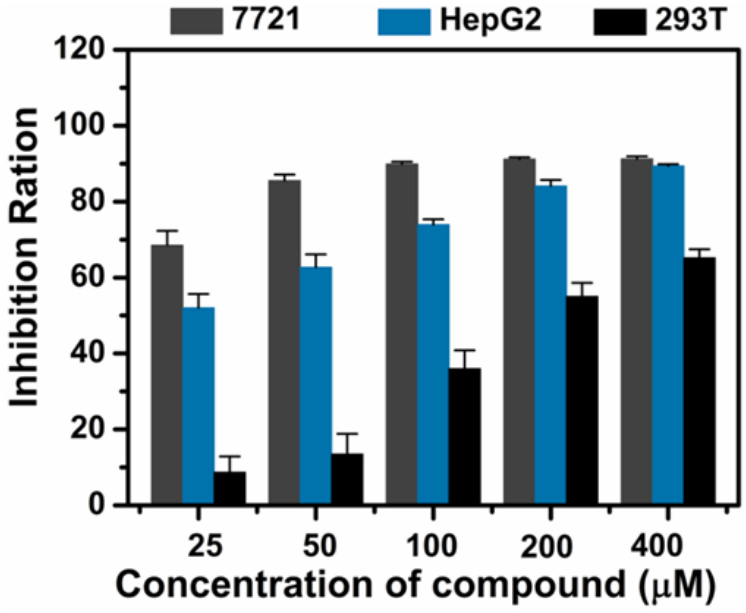

Figure S23. Inhibitory effect of compound **2** on SMMC-7721, HepG2 and 293T cells after 48 h (n = 3, error bar = S.D.).