BODIPY appended copper(II) complexes of curcumin showing mitochondria targeted remarkable photocytotoxicity in visible light

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Electronic Supplementary Information (ESI)

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Experimental Section

Materials and measurements:

All reagents and chemicals were from commercial sources (Polysales, India; TCI chemicals, India; Aldrich, USA) and used without any further purification unless stated. Solvents were purified by given procedures.[S1] Tetrabutylammonium perchlorate (TBAP) was obtained by reacting tetrabutylammonium bromide and perchloric acid.

The elemental analysis was performed using a Thermo Finnigan FLASH EA 1112 CHNS analyzer. The IR and UV/Vis spectra were recorded on Perkin Elmer Lambda 35 and Perkin Elmer spectrum one 55, respectively. Cyclic voltammograms were recorded at room temperature on an EG&G PAR model 253 VersaStat potentiostat/galvanostat with electrochemical analysis software 270 using a three electrode setup consisting of a glassy carbon working, platinum wire auxiliary and a saturated calomel reference electrode (SCE) in DMF using tetrabutylammonium perchlorate (TBAP) (0.1 M) as a supporting electrolyte. Electrospray ionization (ESI) mass spectral measurements were done using Agilent Q-TOF instrument. The NMR spectra were recorded with Bruker Avance 400 NMR spectrometer.

X-ray crystallographic procedures:

All geometric and intensity data were collected using an automated Bruker SMART APEX CCD diffractometer equipped with a fine focus 1.75 kW sealed tube Mo-K_α X-ray source (λ = 0.71073 Å) with increasing ω (width of 0.3° per frame) at a scan speed of 5 sec per frame. Intensity data were collected using ω-2θ scan mode and then corrected for the Lorentz–polarization as well as for absorption effects.[S2] The structures were solved and refined by WinGx suit of programs (Version 1.63.04a) with SHELXL-2013 method.[S3,S4] Initially all non-hydrogen positions were spotted in the difference Fourier maps, but during the final refinement, the hydrogen atoms (placed in geometrically ideal positions) were refined in the riding mode. Atomic positions for all the atoms, anisotropic thermal parameters for all the non-hydrogen atoms and isotropic thermal parameters for all the hydrogen atoms also accounted for the final refinement. The crystal structures were represented using Diamond software. Selected

crystallographic parameters, bond distances/angles, list of coordinates for the ligand L^2 are provided in Tables S2-S4.

Computational details:

The complexes **1** and **2** were optimized by using B3LYP/LanL2DZ functional by Density Functional Theory (DFT) method.[S5,S6] The initial coordinates for geometry of the ligand were adapted from the obtained crystal structure of L^2. All the jobs were run using Gaussian09 package.[S7] The coordinates of the optimized geometries of the complexes **1** and **2** are given in a list and HOMO and LUMO orbital diagrams are given in Fig. S9.

Synthetic procedures

Synthesis of Ligands (Scheme 1)

Synthesis of 4,4-difluoro-8-(4-chloromethylphenyl)-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene (A): The precursor species **A** was prepared using previous literature reports.[S8]

Synthesis of L^1: The precursor (1 g, 2.67 mmol, 1.0 eq.) was taken in a dry 100 ml round bottom flask in 50 ml CH_3CN. K_2CO_3 (739 mg, 5.35 mmol, 2.0 eq.) and KI (890 mg, 5.35 mmol, 2.0 eq.) dissolved in 10 ml of water were subsequently added to the mixture. Bis-(2-pyridylmethyl)amine (5.32 g, 26.7 mmol, 10.0 eq.) dissolved in 10 ml CH_3CN was added and the resulting solution was refluxed for 6 h. The solvent was evaporated under reduced pressure and resulting residue was dissolved in 50 ml dichloromethane. The organic layer was washed with water and brine solution, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give the crude product. It was then purified by silica gel column chromatography using EtOAc-MeOH as eluent (9:1) to afford an orange solid [L^1] (1.05 g, 1.96 mmol, 73% yield).

Characterization data: ^{1}H NMR (400 MHz, d_4-MeOD, TMS) δ: 8.47-8.46 (d, 2H), 7.86-7.82 (td, 2H), 7.71-7.69 (d, 2H), 7.66-7.64 (dd, 2H), 7.33 (d, 2H), 7.31-7.29 (dd, 2H), 6.05 (s, 2H), 3.82 (s, 4H), 3.80 (s, 2H), 2.49 (s, 6H), 1.36 (s,6H). ^{13}C NMR (d_4-MeOD) δ: 159.48, 155.68, 148.52, 143.56, 142.45, 140.41, 137.79, 134.24, 131.64, 130.32, 129.02, 128.37, 123.79, 123.26, 122.93, 121.26, 113.72, 59.58, 58.40, 29.91, 22.74, 13.62, 13.45. ^{11}B NMR (d_4-MeOD) δ: 0.96-0.45 (t);

^{19}F NMR (d_4-MeOD) δ: -147.03(m). ESI-MS (m/z in MeOH) calculated for $C_{32}H_{33}BF_2N_5$ $[M+H]^+$ 536.2797; found 536.2785.

Synthesis of L^2: L^1 (0.536 g, 1.0 mmol, 1.0 eq.) was taken in a 100 ml dry round bottom flask and dissolved in 50 ml of deoxygenated CH_2Cl_2 and N-iodo succinimide (NIS) (1.35 g, 6.0 mmol, 6.0 eq.) was added to it under N_2 atmosphere. It was then stirred at room temperature until full consumption of L^1 was found by thin layer chromatography (TLC). The reaction mixture was then washed with water, dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude product thus found, was then purified by silica gel column chromatography using EtOAc/MeOH as eluent (8:2) to afford a pink red solid [L^2] (0.62 g, 0.79 mmol, 78% yield).

Characterization data: ^{1}H NMR (400 MHz, d_6-DMSO, TMS) δ: 8.51-8.50 (d, 2H), 7.81-7.79 (td, 2H), 7.63-7.61 (d, 2H), 7.57-7.55 (d, 2H), 7.37-7.35 (d, 2H), 7.30-7.27 (dd, 2H), 3.77 (s, 6H), 2.50 (s, 6H), 1.27 (s, 6H). ^{11}B NMR (d_6-DMSO) δ: 0.77- 0.27 (t); ^{13}C NMR (d_6-DMSO) δ 156.88, 149.56, 137.87, 131.18, 128.67, 123.66, 100.47, 59.53, 57.86, 31.54, 17.54, 16.50. ^{19}F NMR (d_6-DMSO) δ: -146.64 (m). ESI-MS (m/z in MeOH) calculated for $C_{32}H_{31}BF_2I_2N_5$ $[M+H]^+$ 788.0729; found 788.0704.

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K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, GAUSSIAN 09 (Revision A.1), Gaussian, Inc., Wallingford, CT, 2009.

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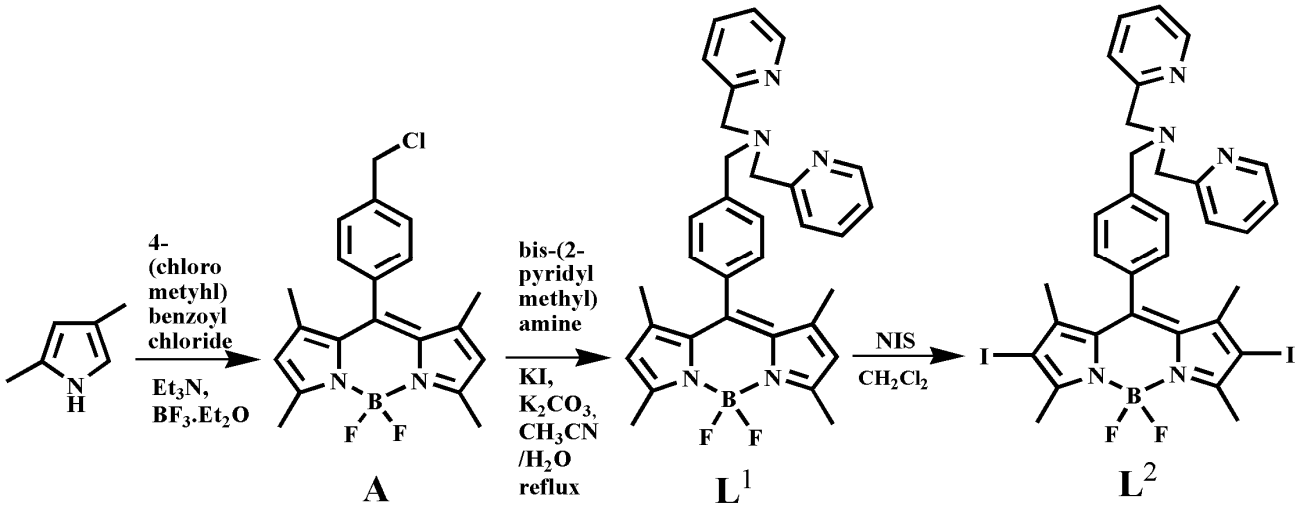
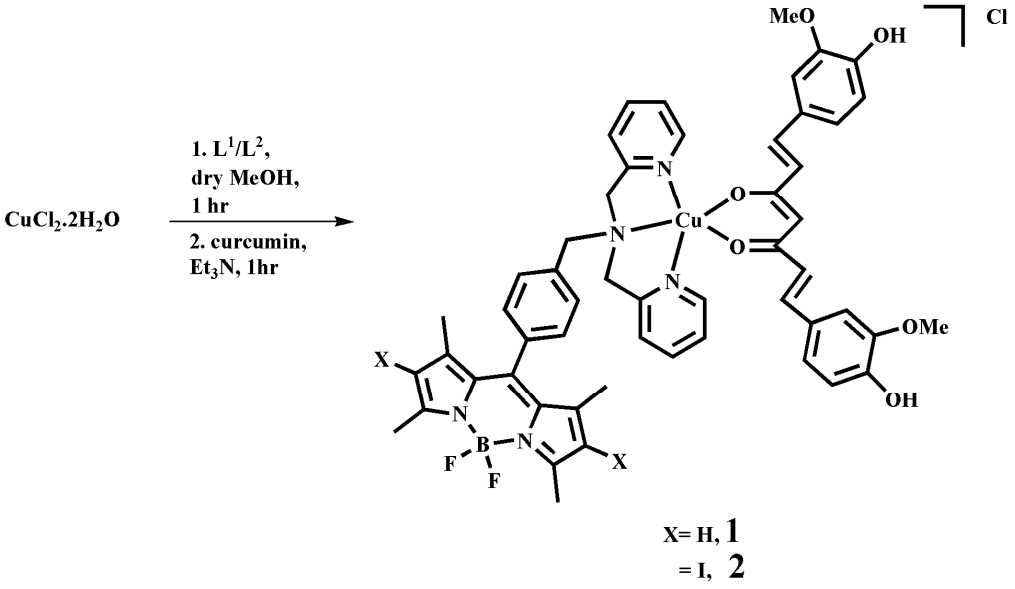
Schemes



Scheme S1. Synthesis of the BODIPY ligands.



Scheme S2. Synthesis of the complexes (8-{[bis(2-pyridylmetyhl)amino]metyhlphenyl}-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene){(1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dionato}copper(II) chloride (**1**) and (8-{[bis(2-pyridylmetyhl)amino]metyhlphenyl}-4,4-difluoro-1,3,5,7-tetramethyl-2,6-diiodo-4-bora-3a,4a-diaza-s-indacene){(1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dionato}copper(II) chloride (**2**).

Tables

Table S1 Selected physicochemical data of the complexes and ligands

Entry	λ_{abs}/nm (ε/dm^3 mol^{-1} cm^{-1})[a]	λ_{em} /nm (λ_{exc} /nm)[a] [φ][b]	E_f / V (ΔE_p / mV) [c]	IR (cm^{-1}) ($\upsilon_{C=O}$, $\upsilon_{C=C}$)
L^1	500(24580)	510(465) [0.55]	-1.12 (133)	--
L^2	534(22370)	565(510) [0.01]	-0.84 (103)	--
1	501(20750), 435(18650)	512(465) [0.12]	-1.11 (107)	1600, 1496
2	535(17350), 432(18600)	510(430) [0.01]	-0.95	1606, 1505

[a] In (1:1) DMSO-phosphate buffer (pH= 7.4). [b] Fluorescence quantum yield values in DMSO using fluorescein in 0.1M NaOH as standard (φ = 0.79). [c] Cathodic peaks of cyclic voltammograms in DMF-0.1M TBAP, $E_f = 0.5(E_{pa} + E_{pc})$, $\Delta Ep = (E_{pa} - E_{pc})$, where E_{pa} and E_{pc} are the anodic and the cathodic peak potentials, respectively. The potentials are vs. SCE. Scan rate = 100 mV s^{-1}.

Table S2 Selected crystallographic data

Entry	L^2
Empirical formula	$C_{32}H_{30}BF_2I_2N_5$
Fw / g M^{-1}	787.22
Crystal system	Orthorhombic
Space group	$P2_1\ 2_1\ 2_1$
a / Å	10.3823(8)
b / Å	10.3886(8)
c / Å	29.879(2)
α / °	90
β / °	90
γ / °	90
U / $Å^3$	3222.7(4)
Z	4
$2\theta_{max}$ / °	52
T, K	298(2)
h,k,l max	12,12,36
ρ_{calcd} / g cm^{-3}	1.933
λ / Å (Mo-K_α)	0.71073
μ / mm^{-1}	1.993
Data / restraints / parameters	6306 / 0 / 379
F(000)	1544
Goodness-of-fit	0.938
R (F_o) [a], I > 2σ(I) [wR (F_o)]	0.0458 [0.1190]
R (all data)[wR (all data)]	0.0783[0.1190]

[a] $R = \Sigma \mid F_o \mid - \mid F_c \mid / \mid F_o \mid$. [b] $wR = \{R [w (F_o^2 - F_c^2)_2] / R [w (F_o)^2]\}^{1/2}$, $w = [\sigma^2 (F_o)^2 + (AP)^2 + BP]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$

Table S3 Selected bond distances (Å) and angels (^{o}) for L^{2}

B(1)-F(1)	1.379(11)
B(1)-F(2)	1.378(11)
B(1)-N(1)	1.555(10)
B(1)-N(2)	1.543(11)
C(1)-N(1)	1.346(9)
C(4)-N(1)	1.399(9)
C(6)-N(2)	1.399(9)
C(9)-N(2)	1.312(10)
C(2)-I(1)	2.055(7)
C(8)-I(2)	2.076(7)
C(20)-N(3)	1.465(9)
C(21)-N(3)	1.457(10)
C(27)-N(3)	1.455(9)
C(22)-N(4)	1.327(11)
C(26)-N(4)	1.344(17)
C(28)-N(5)	1.390(12)
C(32)-N(5)	1.376(15)
F(1)-B(1)-F(2)	110.5(7)
N(1)-B(1)-N(2)	107.3(6)
B(1)-N(1)-C(4)	125.3(6)
B(1)-N(2)-C(6)	125.1(6)
C(4)-C(5)-C(14)	118.5(6)
C(6)-C(5)-C(14)	119.9(6)
C(17)-C(20)-N(3)	111.4(6)
C(20)-N(3)-C(21)	110.9(6)
C(20)-N(3)-C(27)	111.7(5)
C(22)-C(21)-N(3)	111.0(6)
C(28)-C(27)-N(3)	113.1(6)

Figures

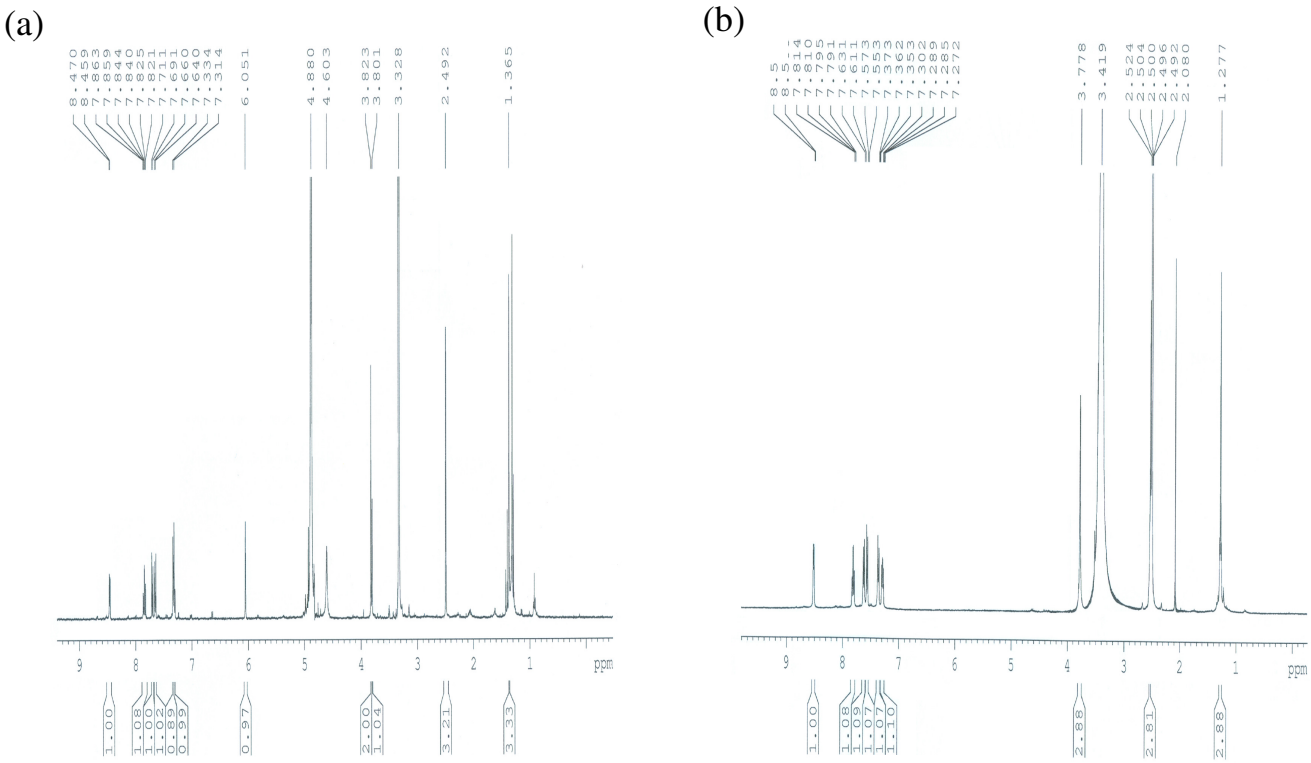


Fig. S1. ^{1}H NMR spectra of (a) L^{1} (in d_4-MeOD) and (b) L^{2} (in d_6-DMSO).

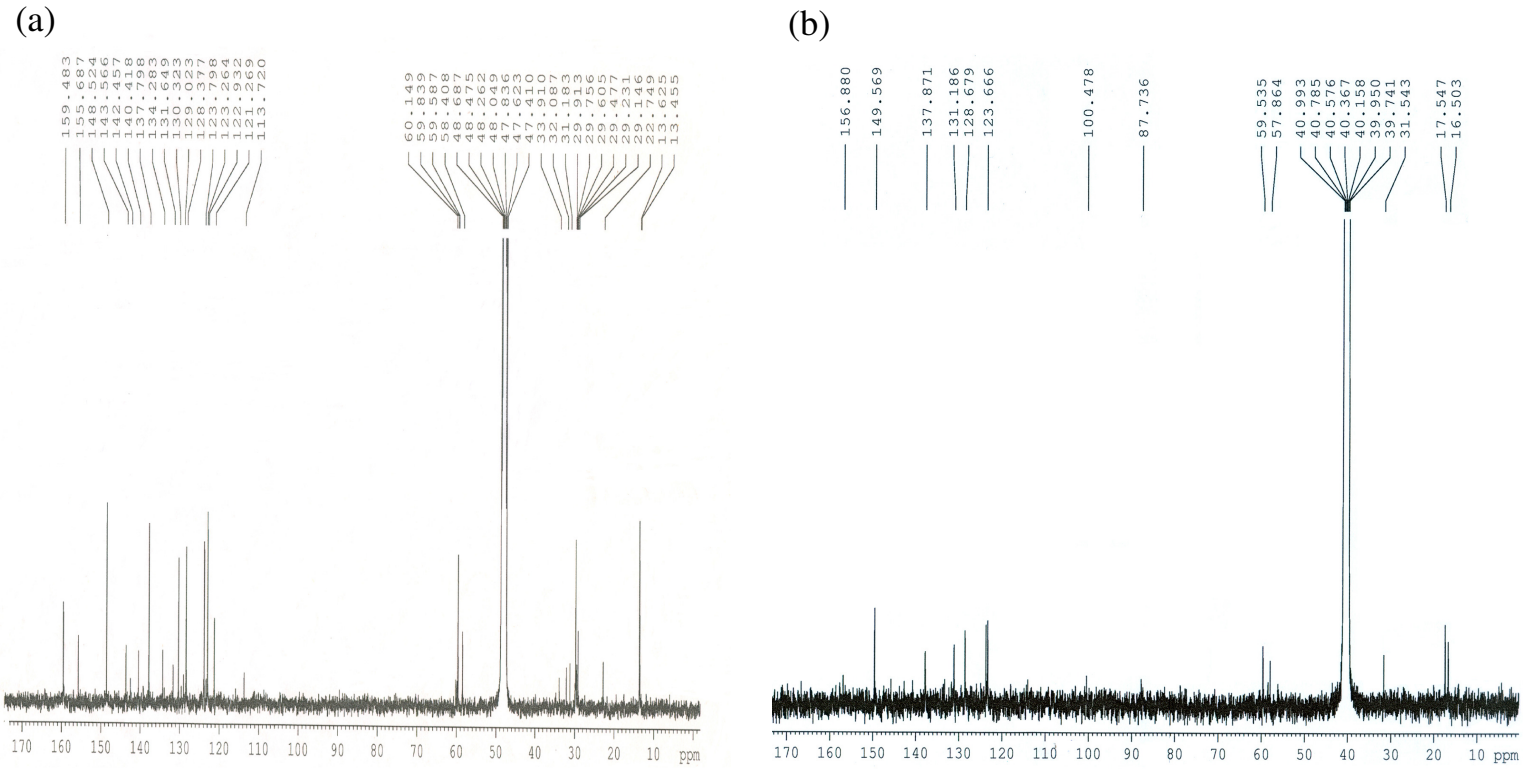


Fig. S2. ^{13}C NMR spectra of (a) L^1 (in d_4-MeOD) and (b) L^2 (in d_6-DMSO).

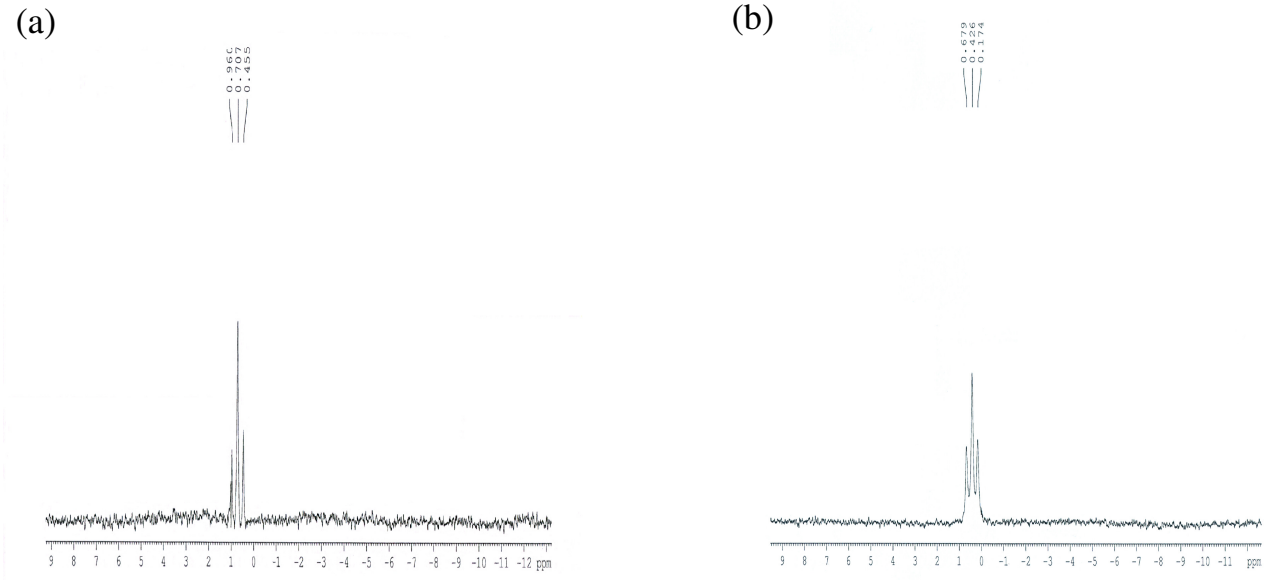


Fig S3. ^{11}B spectra of (a) L^1 (in d_4-MeOD) and (b) L^2 (in d_6-DMSO).

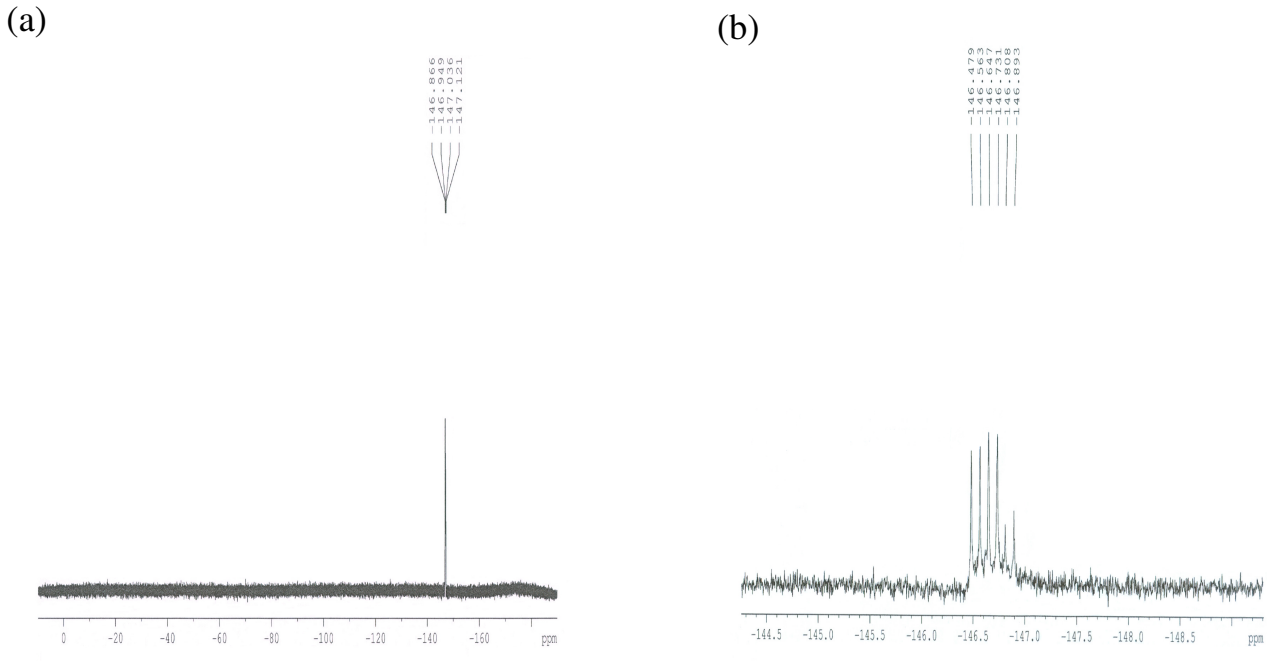
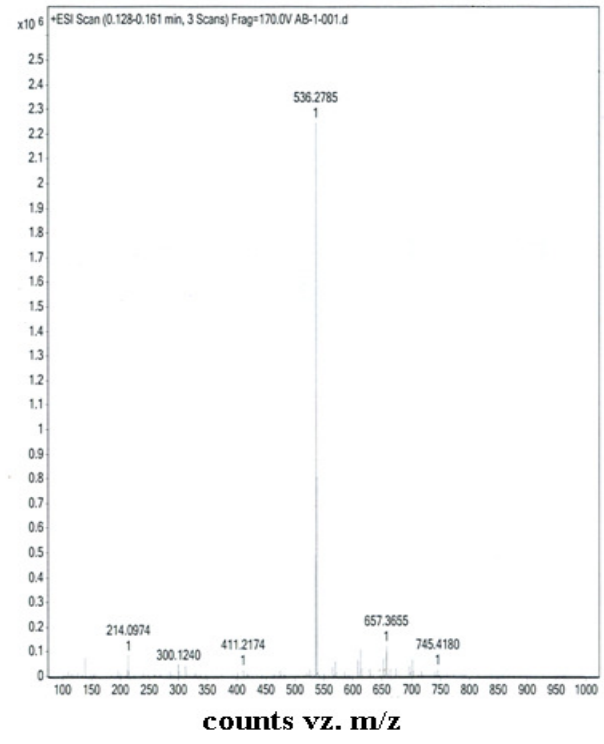


Fig. S4 ^{19}F spectra of (a) L^1 (in d_4-MeOD) and (b) L^2 (in d_6-DMSO).

(a)



(b)

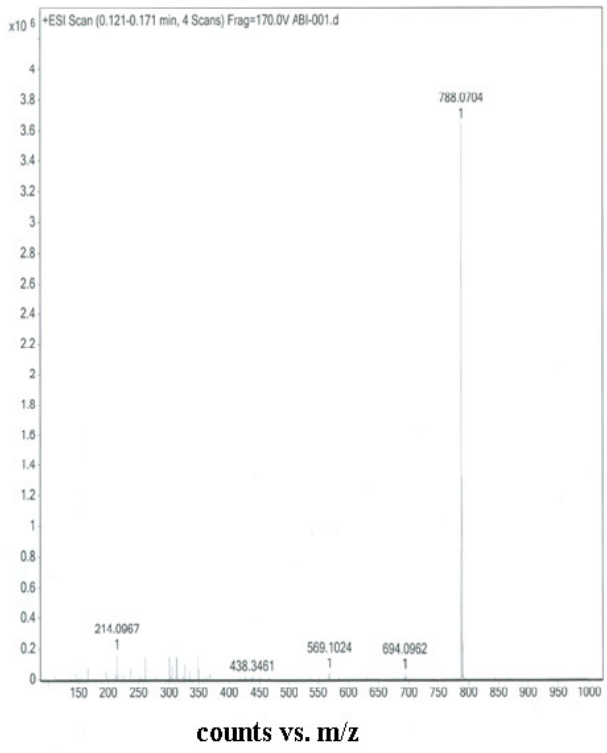


Fig. S5. Mass spectra of (a) L^1 and (b) L^2 (in MeOH).

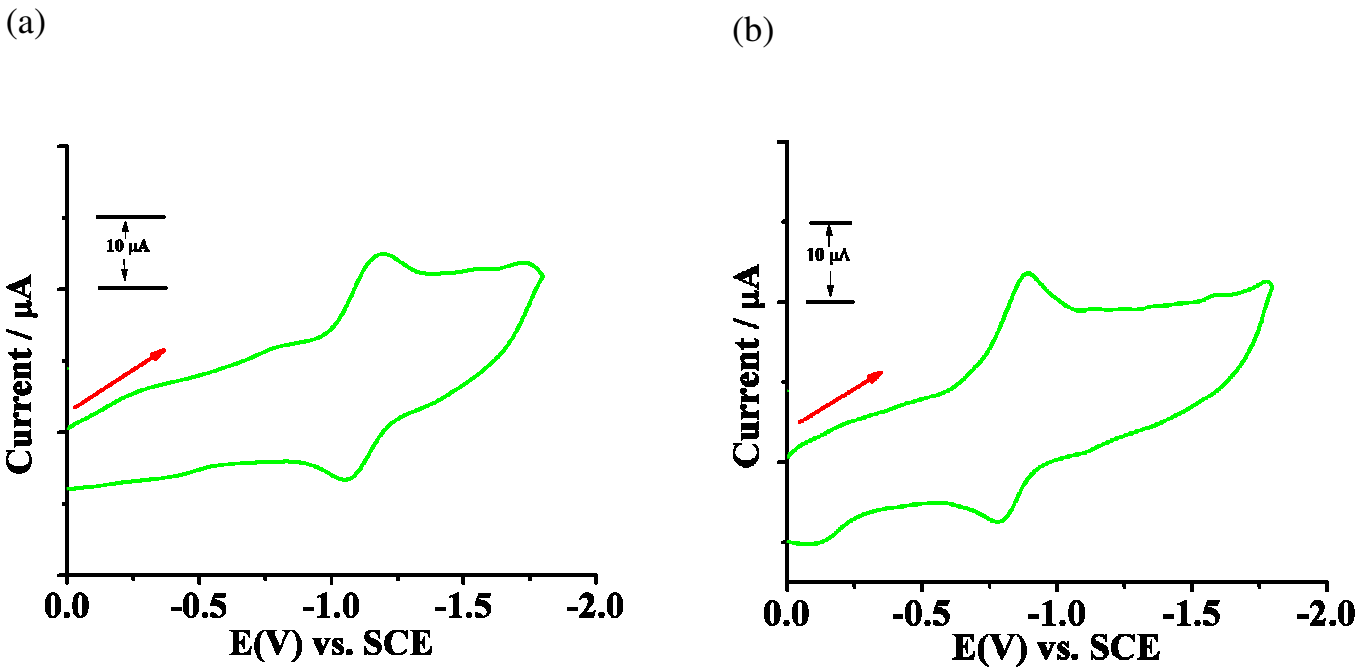
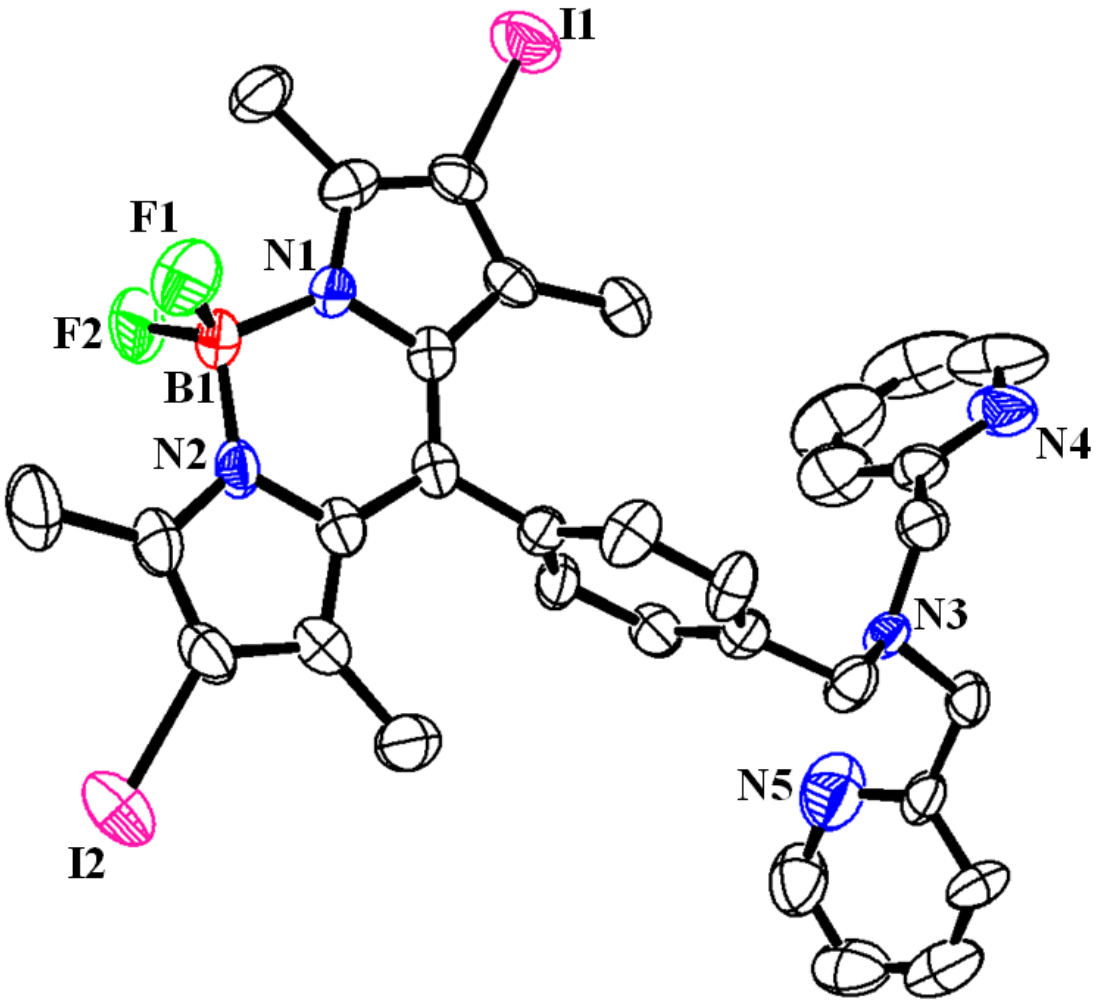


Fig. S6. Cyclic voltammograms of (a) L^1 and (b) L^2 in 0.1M TBAP-DMF using 1.0 mmol concentration at a scan rate of 100 mV sec^{-1}.

(a)



(b)

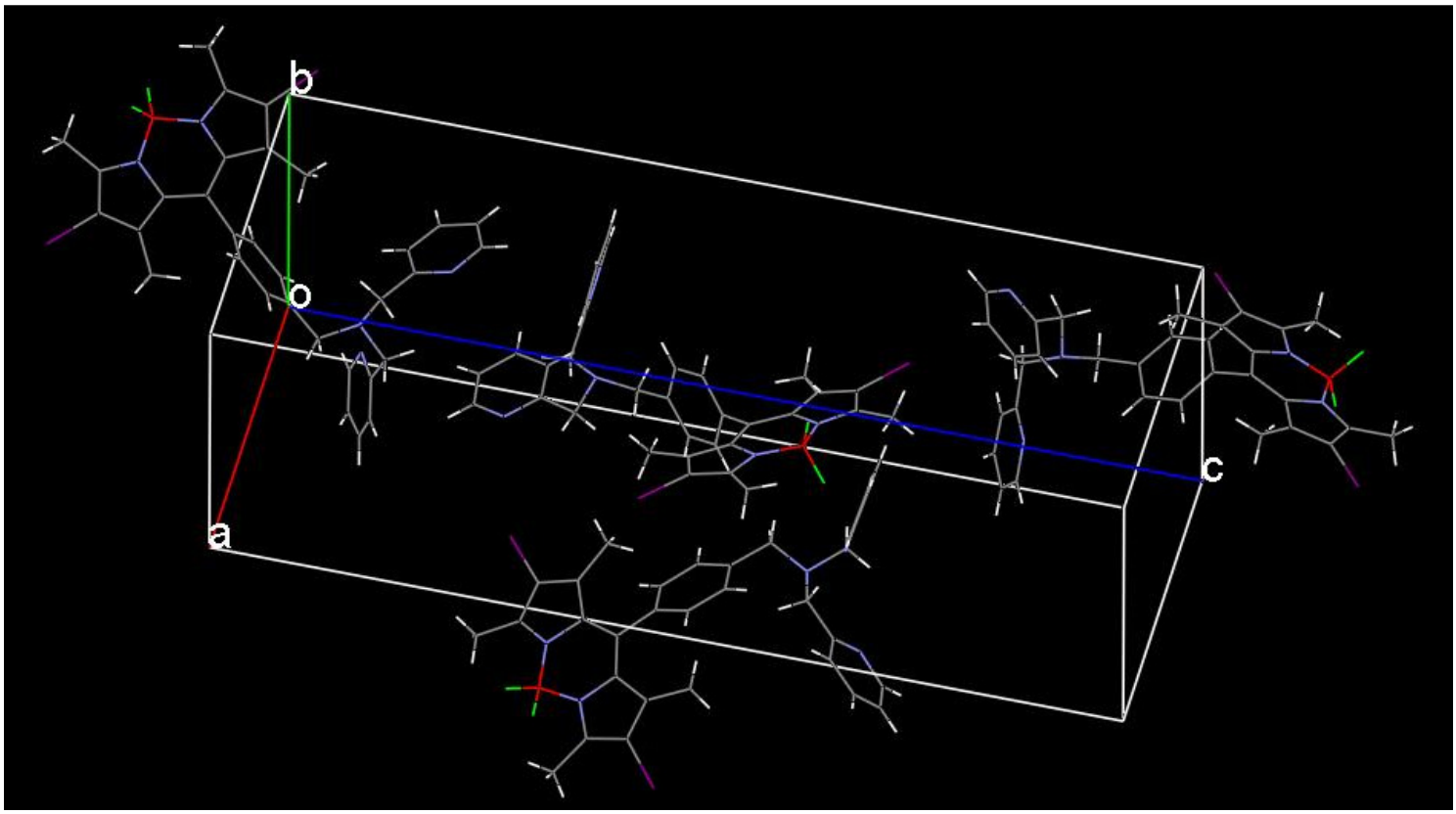


Fig. S7 **(a)** ORTEP view of the crystal structure of L^2 showing labeling scheme for hetero atoms and thermal ellipsoids at 50% probability level. Hydrogen atoms are not shown for clarity. [Colour codes: black – carbon, blue – nitrogen, red – boron, green – fluorine, purple – iodine]. **(b)** Unit cell packing diagram of the crystal structure of L^2. [Colour codes: black – carbon, white - hydrogen, blue – nitrogen, red- boron, green – fluorine, purple – iodine]

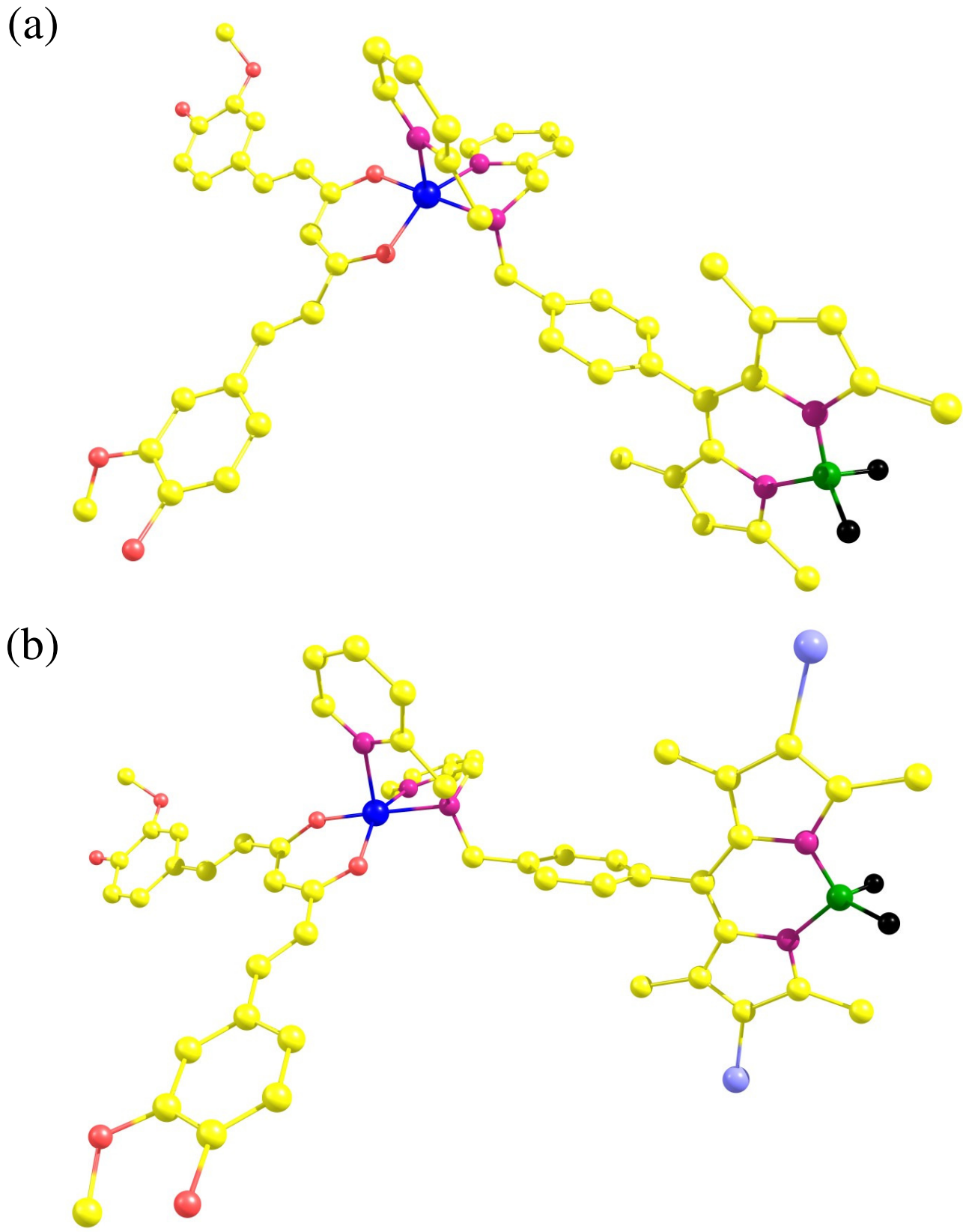
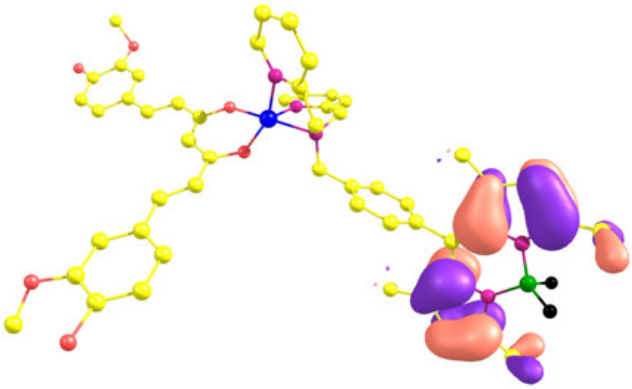
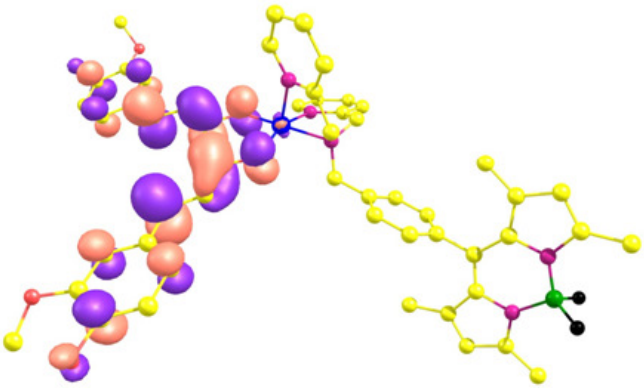


Fig. S8 Energy minimized structures of complexes (a) **1** and (b) **2.**

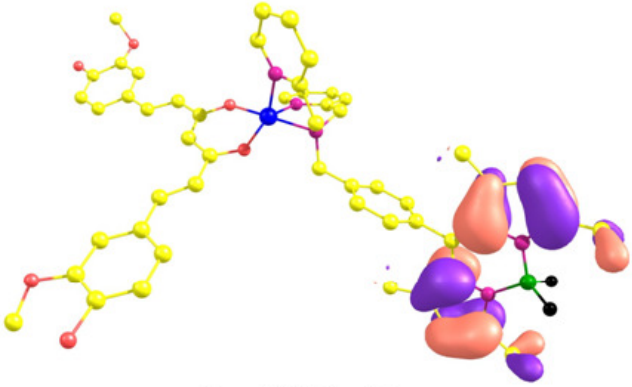
(a)



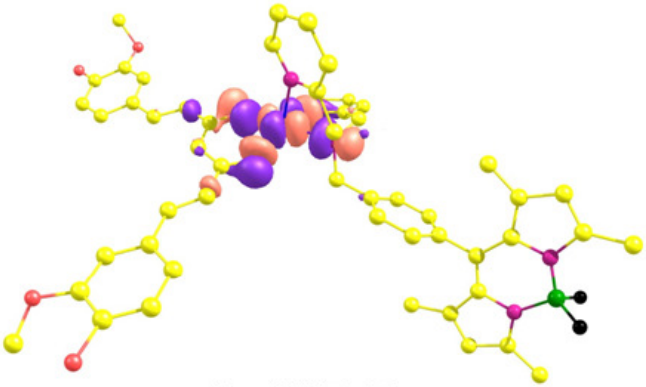
α - HOMO



α - LUMO



β - HOMO



β - LUMO

(b)

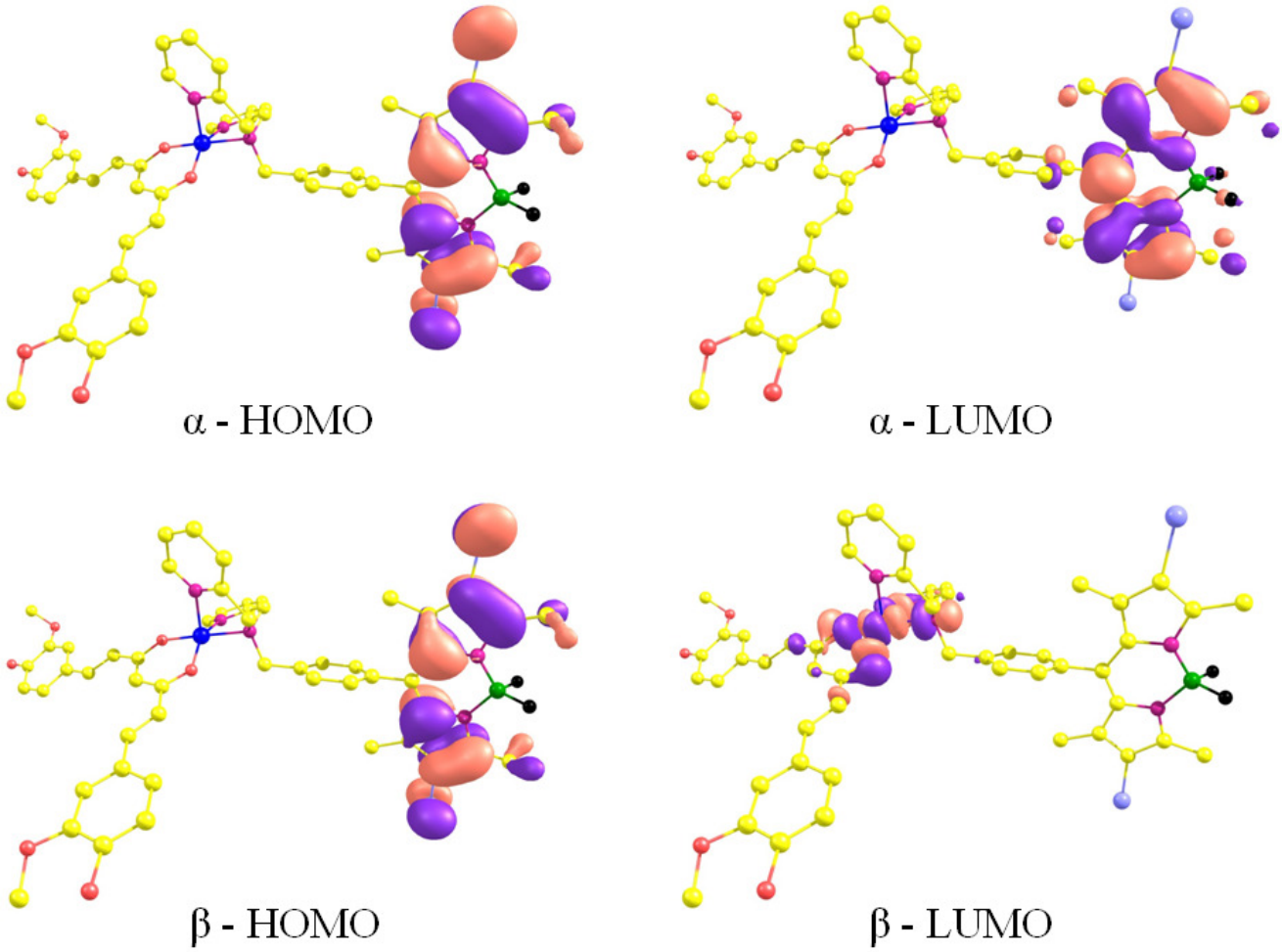
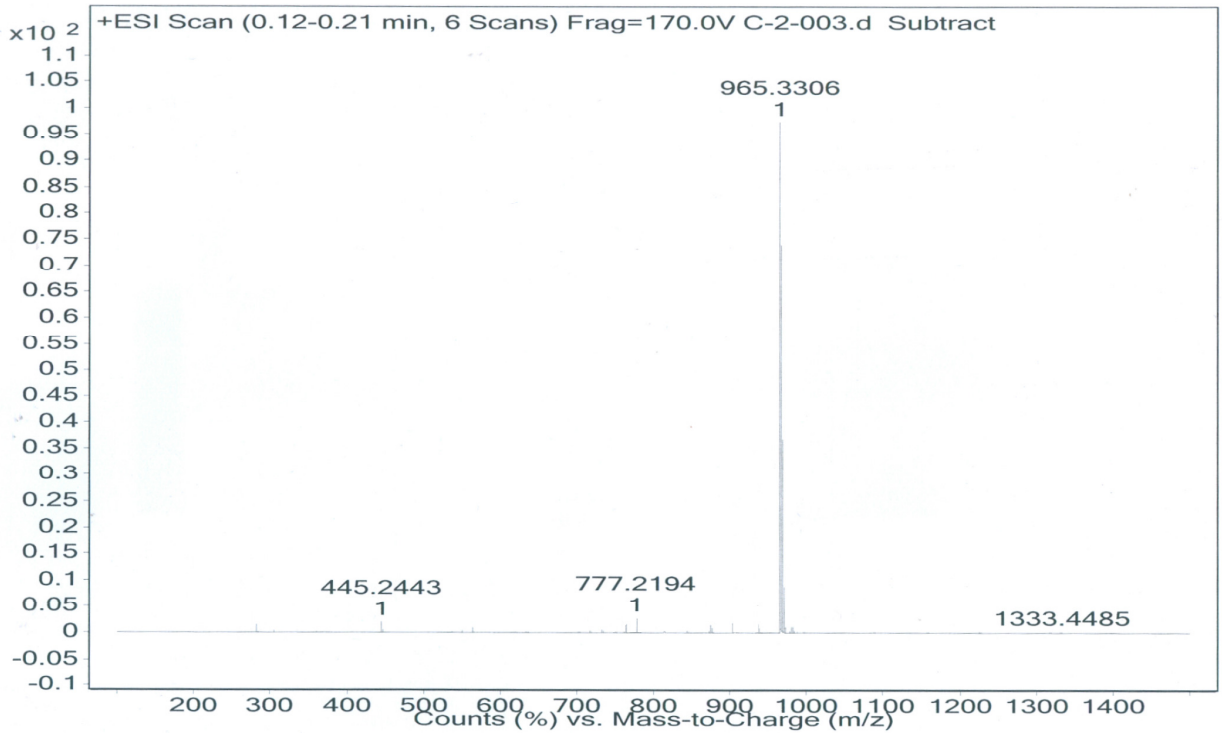


Fig. S9 HOMO - LUMO diagrams of complexes (a) **1** and (b) **2.** (Contour value = 0.03) [HOMO of complexes **1** and **2** localizes on BODIPY unit, while LUMO involves orbitals from metal coordinated curcumin moiety]

(a)



(b)

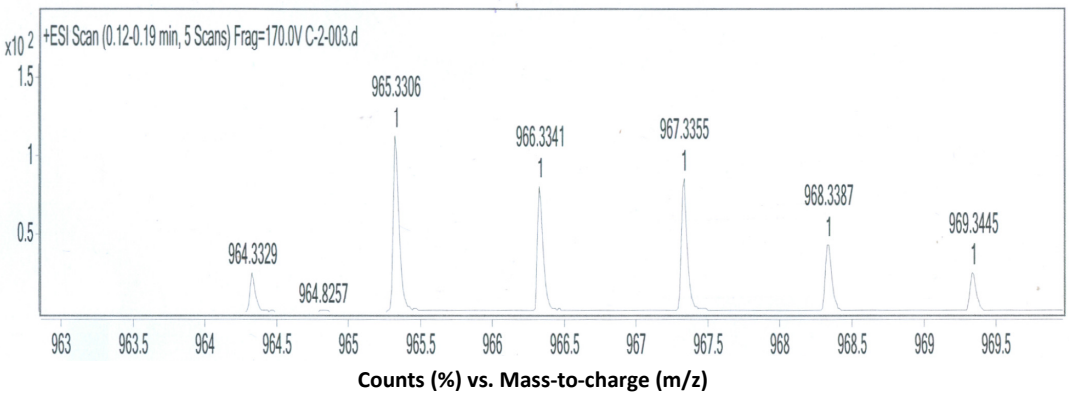
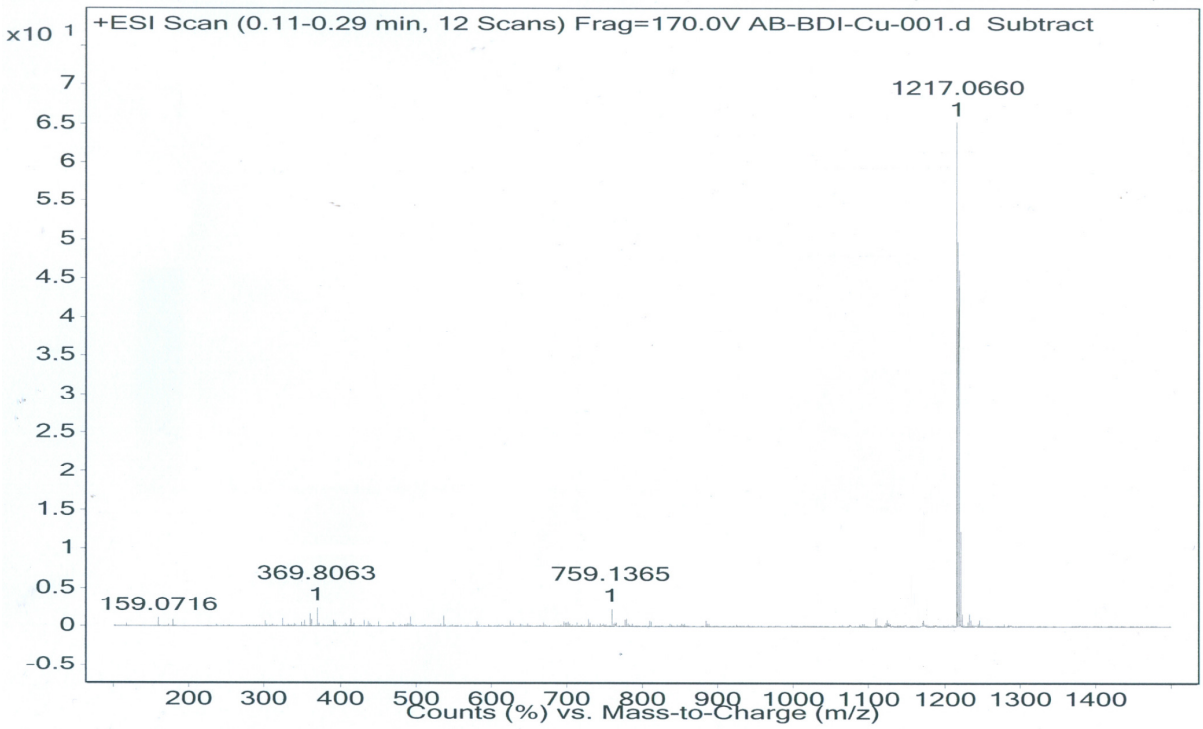


Fig. S10. ESI-MS spectrum of complex **1** in MeOH showing prominant peak of $[M\text{-}Cl]^+$ in (a) and the isotopic distribution of that peak in (b).

(a)



(b)

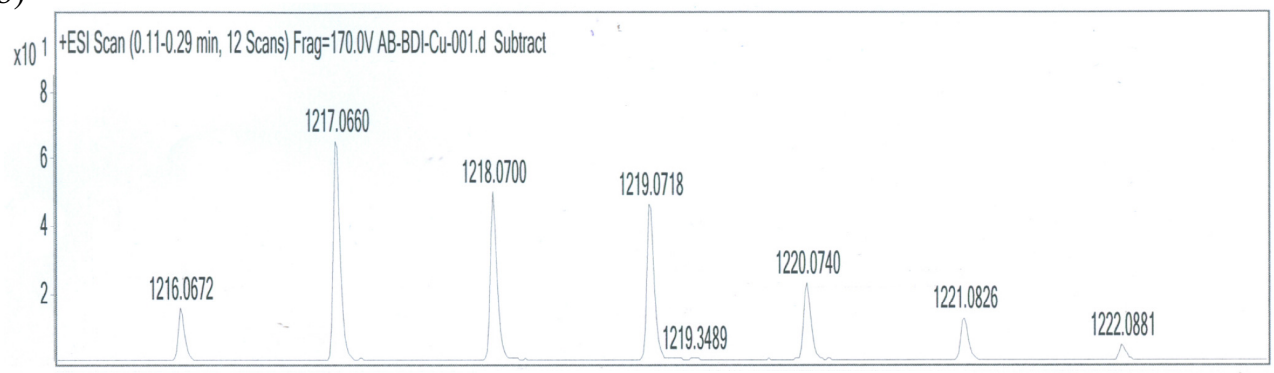


Fig. S11. ESI-MS spectrum of complex **2** in MeOH showing prominant peak of $[M\text{-}Cl]^+$ in (a) and the isotopic distribution of that peak in (b).

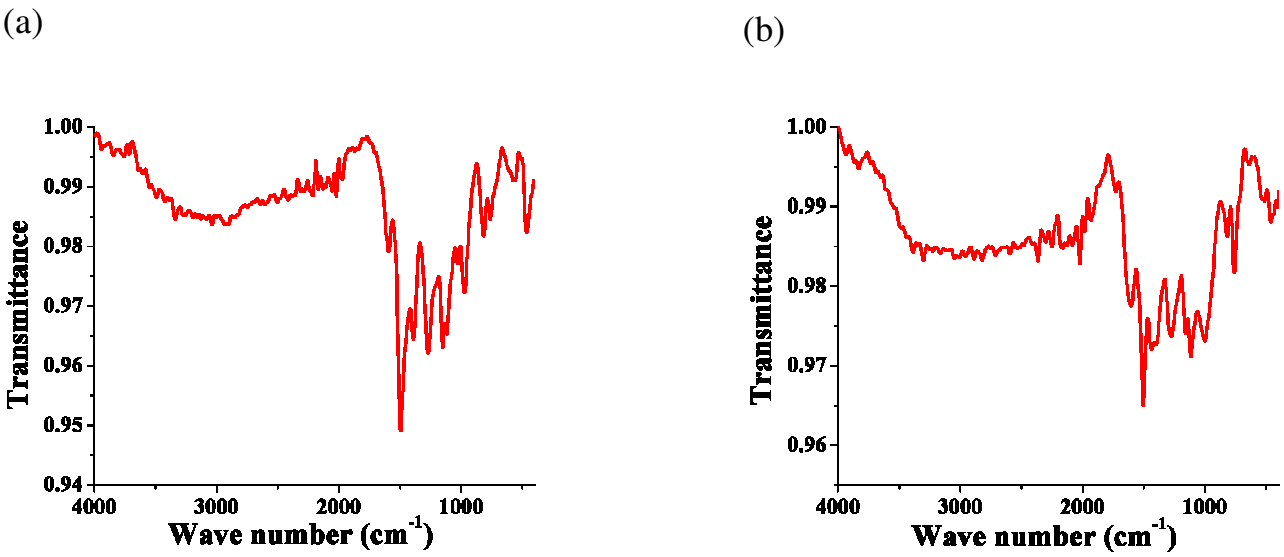


Fig. S12. IR spectra of the complexes (a) **1** and (b) **2**.

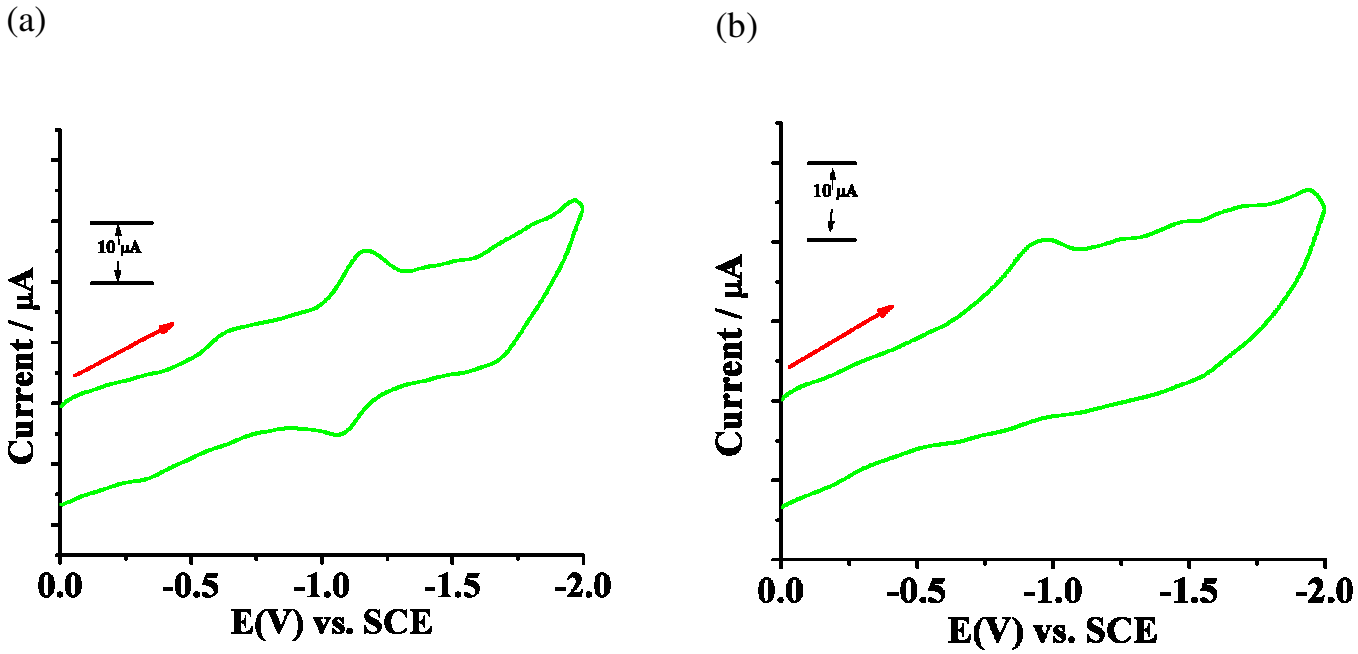


Fig. S13. Cyclic voltammograms of the complexes (a) **1** and (b) **2** in 0.1M TBAP-DMF using 1.0 mmol concentration at a scan rate of 100 mV sec^{-1}.

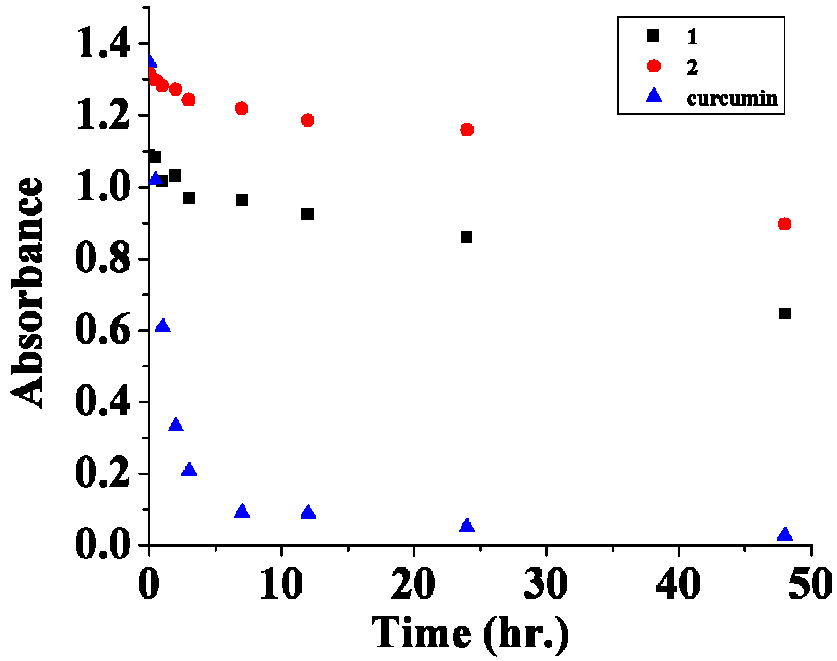


Fig. S14. Time dependent absorbance plot (434 nm) of curcumin and complexes **1** and **2** (concentration = 50 µM) in 1% DMSO DMEM-10% FBS buffer (pH = 7.4). The plot shows the instability of curcumin and its relative stability on binding to Cu(II).

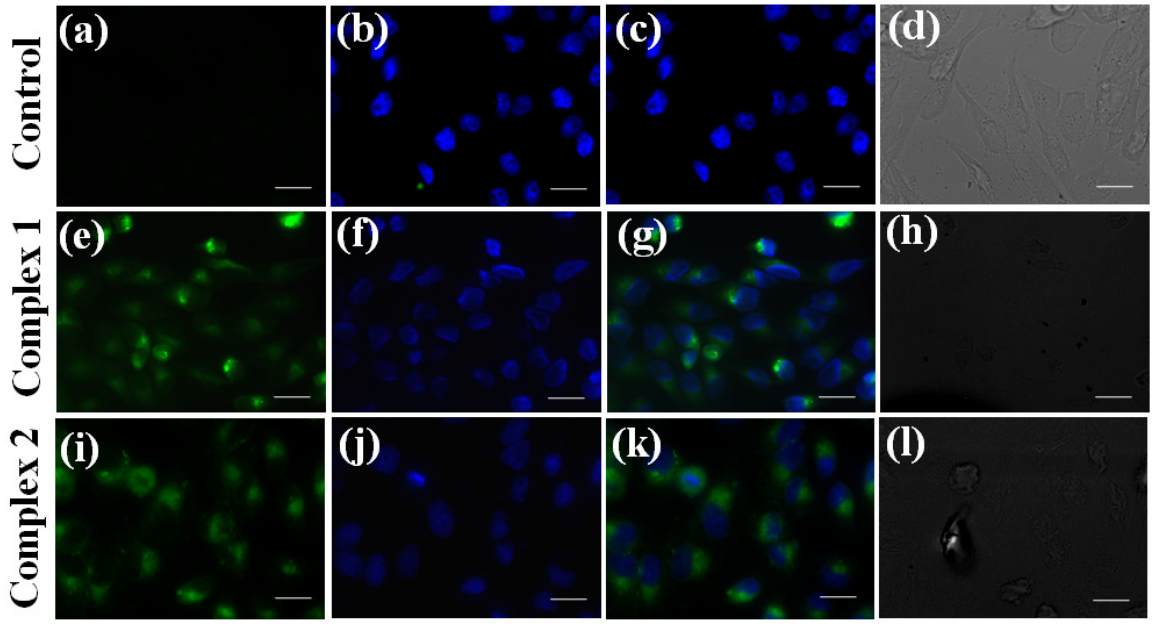


Fig. S15. Fluorescence microscopic images of the HeLa cells treated with complexes **1** and **2** (10 μM) and nuclear staining Hoechst 33342 dye (5 μg ml^{-1}) on 2 h incubation: panels (e, i) show the green emission of the complexes; panels (b, f, j) show the blue emission of the Hoechst dye; panels (c, g, k) are the merged images and panels (d, h, l) are the bright field images. Panel (a) is the control in absence of the complex or the Hoechst dye. Scale bar = 20 μm.

Table S4. List of coordinates for energy minimized structures:

Complex 1 coordinates –

29	1.724256000	-1.643481000	0.311856000	1	0.739904000	-1.963690000	6.315523000
7	1.349893000	-3.452490000	-0.534532000	6	2.223435000	-2.397880000	4.791644000
7	1.542232000	-1.966635000	2.516546000	1	2.990901000	-2.735906000	5.480050000
7	-0.394520000	-1.661396000	0.564121000	6	2.470897000	-2.387775000	3.408373000
6	2.251987000	-4.145601000	-1.273526000	1	3.421858000	-2.712221000	2.997091000
1	3.237548000	-3.699115000	-1.347318000	6	-0.981082000	-0.871148000	-0.597313000
6	1.910492000	-5.360618000	-1.886826000	1	-0.465922000	0.093839000	-0.581964000
1	2.648964000	-5.896943000	-2.472927000	1	-0.677007000	-1.396889000	-1.509782000
6	0.601722000	-5.855290000	-1.728063000	6	-9.507027000	-1.287308000	1.521215000
1	0.306924000	-6.789848000	-2.196551000	6	-8.437279000	-1.926208000	2.208717000
6	-0.324218000	-5.126716000	-0.957158000	6	-7.235074000	-1.621111000	1.553051000
1	-1.338271000	-5.488753000	-0.816031000	6	-7.584495000	-0.773135000	0.436709000
6	0.084024000	-3.921979000	-0.363006000	6	-6.810006000	-0.157925000	-0.571917000
6	-0.804815000	-3.103745000	0.557182000	6	-7.415760000	0.634531000	-1.568720000
1	-1.861575000	-3.215672000	0.284986000	6	-6.878159000	1.365063000	-2.696376000
1	-0.691920000	-3.493393000	1.576255000	6	-7.972628000	1.967989000	-3.331779000
6	-0.627581000	-1.009231000	1.892405000	6	-9.159578000	1.625663000	-2.623566000
1	-0.429865000	0.059679000	1.754031000	6	-10.968505000	-1.319802000	1.843250000
1	-1.668190000	-1.126843000	2.224332000	1	-11.353713000	-0.305053000	2.000168000
6	0.327854000	-1.539269000	2.954222000	1	-11.149651000	-1.916541000	2.741668000
6	0.002154000	-1.533085000	4.321978000	1	-11.539854000	-1.743917000	1.008469000
1	-0.976544000	-1.195482000	4.650754000	6	-5.879162000	-2.117759000	1.985611000
6	0.965935000	-1.964227000	5.253064000	1	-5.199294000	-1.291394000	2.227985000

1	-5.394740000	-2.717030000	1.204590000
1	-5.981133000	-2.745058000	2.877987000
6	-10.567858000	2.033700000	-2.923985000
1	-11.006685000	2.567756000	-2.072413000
1	-11.198187000	1.152982000	-3.097592000
1	-10.599744000	2.677643000	-3.807276000
6	-5.449019000	1.493994000	-3.157051000
1	-4.803418000	1.929238000	-2.384731000
1	-5.399510000	2.140972000	-4.039348000
1	-5.015378000	0.523983000	-3.429558000
6	-5.321807000	-0.345359000	-0.576595000
6	-4.731213000	-1.408585000	-1.289461000
1	-5.362714000	-2.094053000	-1.848444000
6	-3.335064000	-1.576923000	-1.292354000
1	-2.898810000	-2.384641000	-1.878567000
6	-2.492940000	-0.693574000	-0.580322000
6	-3.091603000	0.379674000	0.117542000
1	-2.466424000	1.099802000	0.642189000
6	-4.485921000	0.550657000	0.122955000
1	-4.928958000	1.385429000	0.659654000
7	-8.990435000	-0.598891000	0.462086000
7	-8.820967000	0.827813000	-1.570119000
5	-9.798624000	0.233577000	-0.545193000
9	-10.774181000	-0.599415000	-1.210079000
9	-10.509670000	1.290265000	0.138615000
1	-8.549516000	-2.542910000	3.089665000
1	-7.938008000	2.591755000	-4.214113000
8	1.728896000	0.313283000	0.381724000
8	3.620401000	-1.743705000	-0.086944000
6	2.792399000	1.102690000	0.280114000
6	4.473195000	-0.724699000	-0.146269000
6	4.104097000	0.626552000	0.045115000
1	4.896829000	1.360894000	0.004427000
6	2.486965000	2.533204000	0.437399000
1	1.435998000	2.725705000	0.641536000
6	5.855771000	-1.137703000	-0.427633000
1	5.984377000	-2.217842000	-0.435700000
6	3.372565000	3.567542000	0.346694000
1	4.417175000	3.341298000	0.133864000
6	6.913438000	-0.316701000	-0.692895000
1	6.748431000	0.760789000	-0.711700000
6	8.288950000	-0.725491000	-0.981973000
6	8.716585000	-2.077523000	-0.957203000
6	9.244503000	0.270699000	-1.300964000
1	8.034559000	-2.884601000	-0.709948000
1	8.948990000	1.316988000	-1.319563000
6	10.035131000	-2.441406000	-1.252490000
6	10.567606000	-0.076797000	-1.602701000
1	11.289004000	0.697836000	-1.858227000
6	10.971002000	-1.424975000	-1.596277000

6	3.084117000	4.994173000	0.506977000
6	4.151778000	5.915072000	0.371649000
6	1.792323000	5.506914000	0.791653000
1	5.158439000	5.569142000	0.151271000
1	0.942266000	4.839856000	0.896062000
6	3.974249000	7.298609000	0.522298000
6	1.599010000	6.882874000	0.946503000
1	0.606522000	7.269687000	1.174648000
6	2.677072000	7.785923000	0.829569000
8	2.520664000	9.158305000	1.024952000
1	1.607286000	9.399018000	1.283300000
8	12.265013000	-1.819722000	-1.932328000
1	12.826203000	-1.067288000	-2.211840000
8	5.118813000	8.083885000	0.444624000
8	10.318531000	-3.803903000	-1.276630000
6	5.097038000	9.354731000	-0.301593000
1	6.133736000	9.697027000	-0.291307000
1	4.769407000	9.182345000	-1.335568000
1	4.442553000	10.080570000	0.184341000
6	11.531866000	-4.311997000	-0.611386000
1	11.465260000	-5.397645000	-0.706681000
1	12.431292000	-3.933995000	-1.101013000
1	11.528832000	-4.028303000	0.449793000

Complex2 Coordinates -

29	3.134769000	-1.666565000	-0.261005000
7	2.728707000	-3.054522000	-1.690051000
7	2.990066000	-2.748022000	1.689603000
7	1.018988000	-1.773516000	0.012074000
6	3.609311000	-3.436993000	-2.648395000
1	4.596644000	-2.993556000	-2.580014000
6	3.245303000	-4.352387000	-3.647860000
1	3.966938000	-4.643129000	-4.403631000
6	1.936598000	-4.871929000	-3.646600000
1	1.624673000	-5.577343000	-4.411369000
6	1.033042000	-4.467785000	-2.645083000
1	0.019692000	-4.857393000	-2.619451000
6	1.463236000	-3.554938000	-1.669206000
6	0.601439000	-3.120592000	-0.496636000
1	-0.462378000	-3.133941000	-0.764092000
1	0.739239000	-3.845609000	0.314764000
6	0.815283000	-1.633545000	1.489416000
1	1.018659000	-0.585113000	1.734927000
1	-0.219846000	-1.860308000	1.779749000
6	1.786433000	-2.506532000	2.274408000
6	1.485600000	-2.990044000	3.559860000
1	0.514937000	-2.793794000	4.006141000
6	2.463711000	-3.724758000	4.256572000
1	2.256892000	-4.104644000	5.252956000
6	3.709927000	-3.963571000	3.646564000

1	4.487579000	-4.525035000	4.153686000
6	3.932415000	-3.459068000	2.353984000
1	4.873645000	-3.614168000	1.835584000
6	0.421317000	-0.623436000	-0.784375000
1	0.942104000	0.273661000	-0.436469000
1	0.709439000	-0.791649000	-1.828409000
6	-8.060885000	-1.637239000	1.321392000
6	-6.969212000	-2.443976000	1.769056000
6	-5.774690000	-1.963490000	1.202049000
6	-6.154515000	-0.832224000	0.388217000
6	-5.401618000	0.041759000	-0.430453000
6	-6.031529000	1.070522000	-1.163721000
6	-5.511928000	2.088312000	-2.050730000
6	-6.630457000	2.820990000	-2.485945000
6	-7.811073000	2.282193000	-1.883880000
6	-9.518868000	-1.757909000	1.631257000
1	-9.965205000	-0.770641000	1.783471000
1	-9.675541000	-2.371433000	2.521902000
1	-10.050523000	-2.222734000	0.790288000
6	-4.400954000	-2.537470000	1.422268000
1	-3.755224000	-1.837525000	1.967202000
1	-3.902699000	-2.772205000	0.474915000
1	-4.467708000	-3.458138000	2.009757000
6	-9.234284000	2.718442000	-2.023611000
1	-9.622781000	3.066974000	-1.058536000
1	-9.864867000	1.875707000	-2.329190000
1	-9.325224000	3.523374000	-2.756043000
6	-4.082752000	2.341238000	-2.449123000
1	-3.699756000	1.549023000	-3.104956000
1	-3.418075000	2.394382000	-1.580726000
1	-4.003392000	3.286467000	-2.994315000
6	-3.914710000	-0.131253000	-0.520193000
6	-3.340196000	-0.876217000	-1.569931000
1	-3.981937000	-1.321207000	-2.325776000
6	-1.945686000	-1.036744000	-1.649312000
1	-1.522393000	-1.588730000	-2.487329000
6	-1.089267000	-0.461280000	-0.683893000
6	-1.672597000	0.299800000	0.354337000
1	-1.036804000	0.789660000	1.089337000
6	-3.065702000	0.459259000	0.439355000
1	-3.496304000	1.052985000	1.241383000
7	-7.556767000	-0.677513000	0.494689000
7	-7.436275000	1.236340000	-1.094285000
5	-8.390173000	0.394299000	-0.229595000
9	-9.391236000	-0.235007000	-1.053675000
9	-9.059083000	1.238382000	0.730913000
53	-7.174144000	-4.092801000	3.065984000
53	-6.619936000	4.455554000	-3.815005000
8	3.155082000	0.140516000	0.492643000
8	5.021495000	-1.622048000	-0.707868000

6	4.226884000	0.904085000	0.674651000
6	5.881556000	-0.649230000	-0.418841000
6	5.529246000	0.542069000	0.256018000
1	6.327230000	1.242417000	0.461515000
6	3.940452000	2.175937000	1.356023000
1	2.884103000	2.313266000	1.576567000
6	7.253048000	-0.932982000	-0.864920000
1	7.376127000	-1.943443000	-1.248376000
6	4.850462000	3.125909000	1.719450000
1	5.902555000	2.952351000	1.494135000
6	8.305889000	-0.064250000	-0.863660000
1	8.144857000	0.953264000	-0.506839000
6	9.669727000	-0.340872000	-1.317465000
6	10.087843000	-1.613859000	-1.782366000
6	10.623146000	0.706837000	-1.293528000
1	9.406869000	-2.458190000	-1.816097000
1	10.334923000	1.692116000	-0.935017000
6	11.394749000	-1.846894000	-2.225207000
6	11.934680000	0.491260000	-1.735770000
1	12.654519000	1.308245000	-1.723409000
6	12.328152000	-0.771731000	-2.215867000
6	4.580861000	4.389363000	2.408523000
6	5.676356000	5.229771000	2.724941000
6	3.280649000	4.820121000	2.778043000
1	6.690709000	4.942779000	2.459602000
1	2.409872000	4.215056000	2.545553000
6	5.516908000	6.450963000	3.397014000
6	3.104837000	6.033707000	3.449483000
1	2.104661000	6.354983000	3.737827000
6	4.208752000	6.849315000	3.777575000
8	4.066288000	8.041738000	4.487043000
1	3.139209000	8.212837000	4.752009000
8	13.609073000	-1.018153000	-2.707447000
1	14.167996000	-0.213967000	-2.718340000
8	6.680745000	7.139981000	3.718617000
8	11.664718000	-3.112877000	-2.736133000
6	6.753693000	8.600085000	3.531086000
1	7.791777000	8.854154000	3.754327000
1	6.519363000	8.860998000	2.490315000
1	6.072265000	9.114800000	4.210856000
6	12.899418000	-3.816432000	-2.344522000
1	12.811686000	-4.803611000	-2.802727000
1	13.781039000	-3.292065000	-2.717705000
1	12.949888000	-3.913806000	-1.251617000