Electronic Supplementary Information

Design and synthesis of a new class of 2,4-thiazolidinedione based macrocycles suitable for Fe^{3+}sensing

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Contents

Experimental

General

Melting points were recorded on a Köfler block and are uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AV-300 (300 MHz) spectrometer. Mass spectrum was acquired on a Waters Xevo G2QTof HRMS spectrometer. Analytical samples were dried *in vacuo* at room temperature. Microanalytical data were recorded on a Perkin-Elmer 2400 Series II C, H, N analyzer. Column chromatography was performed on silica gel (100-200 mesh) using petroleum ether (60-80°C) and petroleum ether-ethyl acetate mixtures as eluents. TLC was done with silica gel G. X-ray crystallographic studies were done by using a Bruker APEX II single crystal X-ray diffractometer. Bis-(2-formylphenoxy)alkanes used (**4a** [alkane = butane] and **4b** [alkane = pentane]) were prepared by a known method previously developed by us.[1] The UV-vis absorption and fluorescence spectra were taken with a UV-2450 spectrophotometer (Shimadzu, Japan) and a PerkinElmer LS-55 spectrofluorimeter (PerkinElmer, USA), respectively.

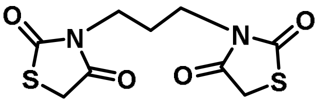
Synthesis of 2,4-thiazolidinedione

An aqueous solution of chloroacetic acid (50 mmol) and thiourea (55 mmol) was stirred for 15 minutes when a white precipitate separated out accompanied by considerable cooling. Concentrated HCl (50 mL) was added and the mixture was refluxed with stirring for 8h and then cooled to obtain 2,4-thiazolidinedione as a white precipitate which was filtered out, dried and crystallised from ethanol, Yield: 85%, M.p.126-127 °C (Lit.[2] 125-126°C).

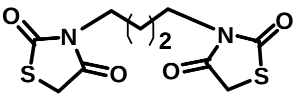
General procedure for synthesis of 4.

Two compounds of the series **4** have been synthesized by following a recently reported method for alkylation of 2,4-thiazolidinedione.[3] A solution 2,4-thiazolidinedione (20 mmol) and KOH (25 mmol) in ethanol (12 mL)was refluxed for 30 min and then cooled to 0 °C. The precipitate of the potassium salt of 2,4-thiazolidinedione was filtered and washed with cold ethanol. The solid thus obtained was taken in DMF (10 mL) with α,ω-dibromoalkane (8mmol) and refluxed for 3h. The reaction mixture was then cooled; water was added to it and extracted with ethyl acetate (3 x 20 mL). The combined organic layer was collected, dried over anhydrous Na_2SO_4 and the solvent was distilled off. The resulting crude material was subjected to column chromatography over silica gel to obtain the pure product (**4**). The synthesized compounds, **4a** and **4b**,were characterized from their ^{1}H NMR spectral data.

3,3'-(Propane-1,3-diyl)bis(thiazolidine-2,4-dione)(4a): Colourless needles, m.p. 94-95 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.83 (2H, br. s, N-CH_2-$C\underline{H}_2$-CH_2-N), 3.61 (2H, s, S-$C\underline{H}_2$-C=O), 4.01(4H, br. s, N-$C\underline{H}_2$-CH_2-$C\underline{H}_2$-N).



3,3'-(Butane-1,4-diyl)bis(thiazolidine-2,4-dione)(4b): Colourless needles, m.p. 104-105°C, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.61 (4H, br. s, -N-CH_2-$C\underline{H}_2$-$C\underline{H}_2$-CH_2-N-), 3.63 (2H, s, S-$C\underline{H}_2$-C=O), 3.95 (4H, br. s, N-$C\underline{H}_2$-CH_2-CH_2-$C\underline{H}_2$-N).

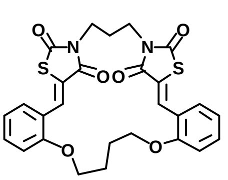


General procedure for synthesis of macrocyclic compounds (3a-c)

A mixture of *bis*-(2,4-thiazolidinedion-1-yl)alkane (**4a**/**4b**, 0.5 mmol) and bis-(2-formylphenoxy)alkane[1] (**5a**/**5b**, 0.5 mmol) was taken in toluene and catalytic amount of piperidine (10 drops) was added to it. The solution was diluted by addition of toluene to make the total volume 300-320 mL. The mixture was then refluxed with stirring for 50 h. After completion of the reaction as indicated by TLC, the reaction mixture was cooled and the solvent was distilled off. The crude mixture thus obtained was subjected to column chromatography to separate the desired product (**3a-c**) from the reaction mixture.

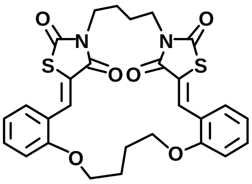
Spectral data of 3a-c

Compound 3a: Colorless crystalline solid, m. p. 268-269 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.16 (4H, br. s, O-CH_2-$C\underline{H}_2$-$C\underline{H}_2$-CH_2-O), 2.46-2.50 (2H, m, N-CH_2-$C\underline{H}_2$-CH_2-N), 3.74 (4H, t, J = 6.0 Hz, N-$C\underline{H}_2$-CH_2-$C\underline{H}_2$-N), 4.12 (4H, br. s, O-$C\underline{H}_2$-CH_2-CH_2-$C\underline{H}_2$-O), 6.93 (2H, br. d, J = 8.2 Hz, Ar-H), 7.04 (2H, br. t, J = 7.5 Hz, Ar-H), 7.39 (2H, br. t, J = 7.6 Hz, Ar-H), 7.47 (2H, br. d, J = 7.5 Hz, Ar-H), 8.38 (2H, s, =CH-); ^{13}C NMR (75MHz, $CDCl_3$): δ 23.3, 27.0, 37.5, 68.0, 111.8, 120.8, 121.7, 123.0, 128.7, 129.3, 132.0, 158.2, 165.9, 168.8; Elemental analysis (%) for

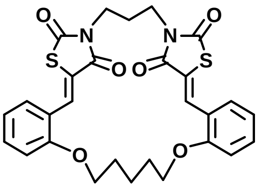


$C_{27}H_{24}N_2O_6S_2$, calculated C, 60.43; H, 4.51; N, 5.22, found C, 60.33; H, 4.23; N, 5.09; HRMS calcd for $C_{27}H_{25}N_2O_6S_2$ $(M+H)^+$: 537.1154, found: 537.1617.

Compound 3b: Colorless crystalline solid, m.p. 276-277 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.71 (4H, br. s, N-CH$_2$-C$\underline{H}_2$-C$\underline{H}_2$-CH$_2$-N), 2.07 (4H, br. s, O-CH$_2$-C$\underline{H}_2$-C$\underline{H}_2$-CH$_2$-O), 3.81 (4H, br. s, N-C$\underline{H}_2$-CH$_2$-CH$_2$-C$\underline{H}_2$-N), 4.11 (4H, br. s, O-C$\underline{H}_2$-CH$_2$-CH$_2$-C$\underline{H}_2$-O), 6.96 (2H, d, J = 8.5 Hz, Ar-H), 7.05 (2H, t, J = 7.5Hz, Ar-H), 7.34-7.43 (4H, m, Ar-H), 8.31 (2H, s, =CH-); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.6, 26.2, 41.0, 68.1, 111.9, 120.9, 122.0, 123.2, 128.8, 130.2, 132.0, 157.8, 166.2, 168.7; Elemental analysis (%) for $C_{28}H_{26}N_2O_6S_2$, Calculated C, 61.08; H, 4.76; N, 5.09. Found C, 61.27; H, 4.51; N, 4.81, HRMS calcd for $C_{28}H_{26}N_2NaO_6S_2$ $(M+Na)^+$: 573.1130, found: 573.1931.

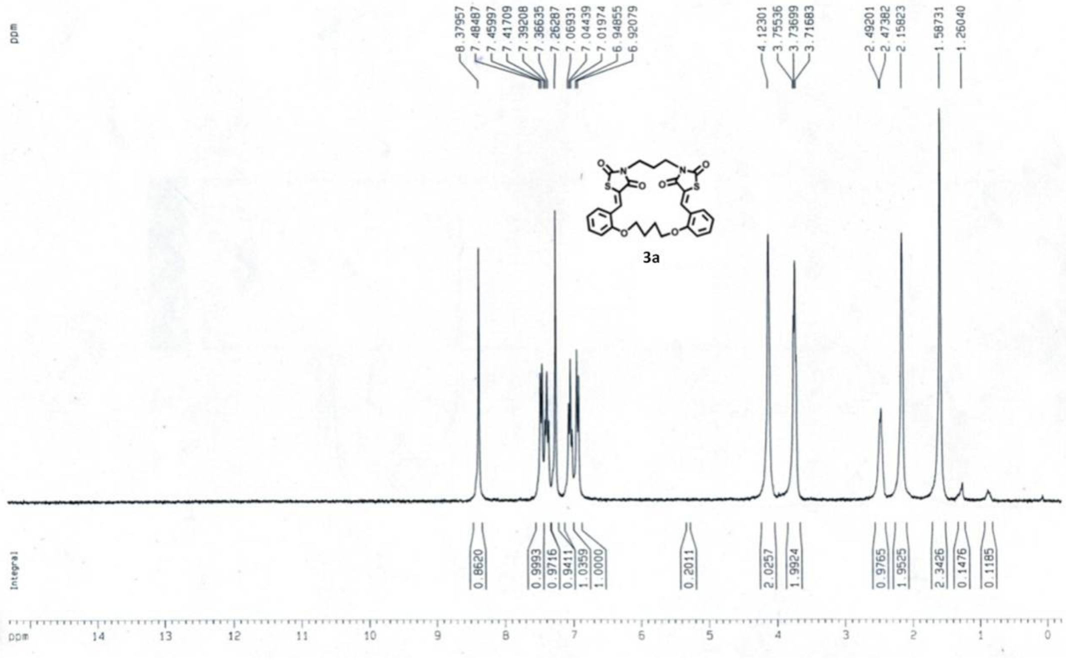


Compound 3c: Colorless crystalline solid, m.p. 280-281 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28-1.36 (2H, m, O-CH$_2$-CH$_2$-C$\underline{H}_2$-CH$_2$-CH$_2$-O), 1.72-1.74 (4H, m, O-CH$_2$-C$\underline{H}_2$-CH$_2$-C$\underline{H}_2$-CH$_2$-O), 2.35-2.43 (2H, m, N-CH$_2$-C$\underline{H}_2$-CH$_2$-N), 3.79 (4H, br. t, J = 5.2 Hz, N-C$\underline{H}_2$-CH$_2$-C$\underline{H}_2$-N), 4. 32 (4H, t, J = 5.6 Hz, O-C$\underline{H}_2$-CH$_2$-CH$_2$-CH$_2$-C$\underline{H}_2$-O), 6.95 (2H, d, J = 8.4 Hz, Ar-H), 7.01 (2H, t, J = 7.2 Hz, Ar-H), 7.33 (2H, t, J = 7.5 Hz, Ar-H), 7.42 (2H, d, J = 7.2 Hz, Ar-H) 8.21 (2H, s, =C$\underline{H}$-).; ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.8, 27.1, 29.2. 41.3, 66.8, 113.8, 121.6, 122.1, 123.8, 129.5, 129.9, 131.7, 157.7, 166.7, 168.8; Elemental analysis (%) for $C_{28}H_{26}N_2O_6S_2$, Calculated C, 61.08; H, 4.76; N, 5.09. Found C, 61.03; H, 4.57; N, 5.17; HRMS calcd for $C_{28}H_{26}N_2NaO_6S_2$ $(M+Na)^+$: 573.1130, found: 573.1343.

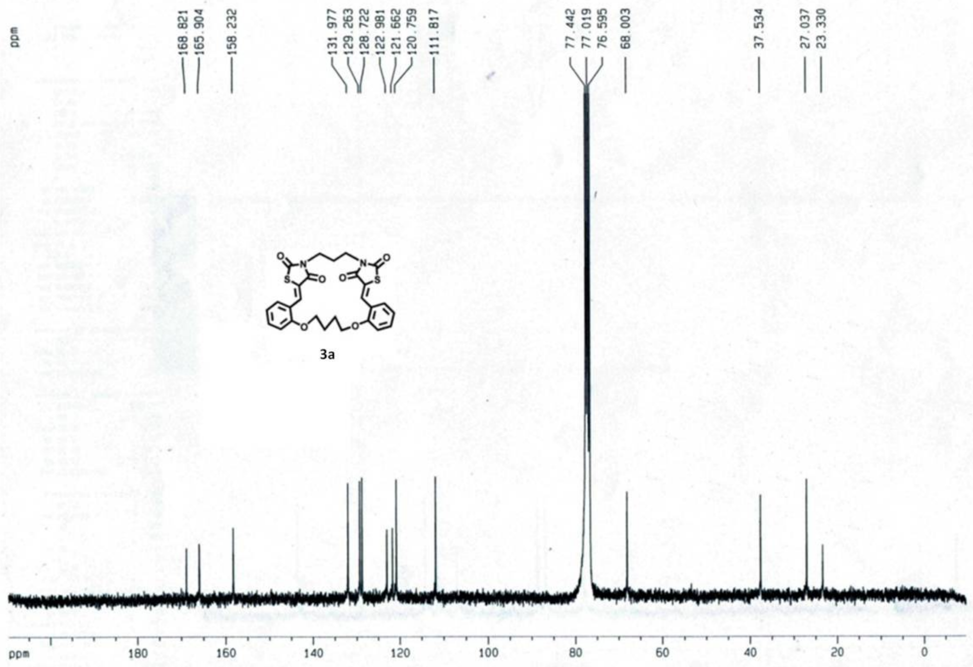


^{1}H and ^{13}C Spectra

^{1}H NMR Spectrum of 3a



^{13}C NMR Spectrum of 3a



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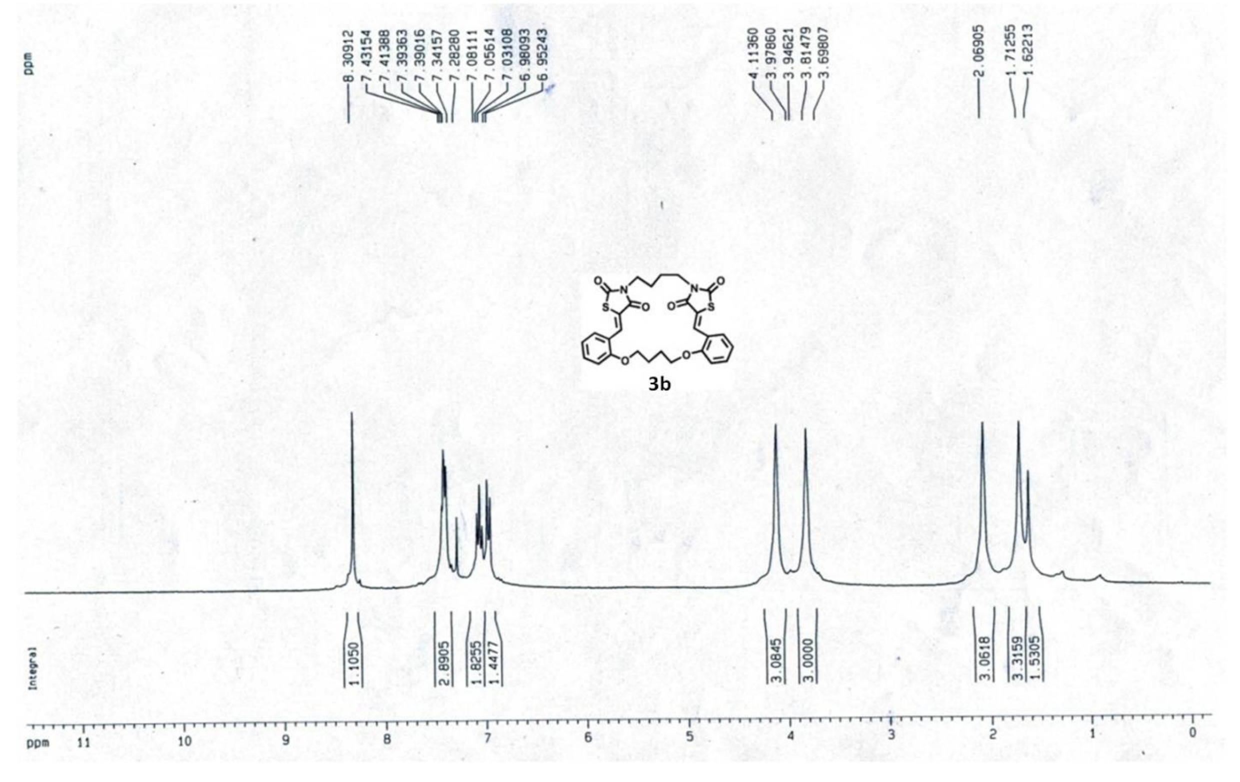
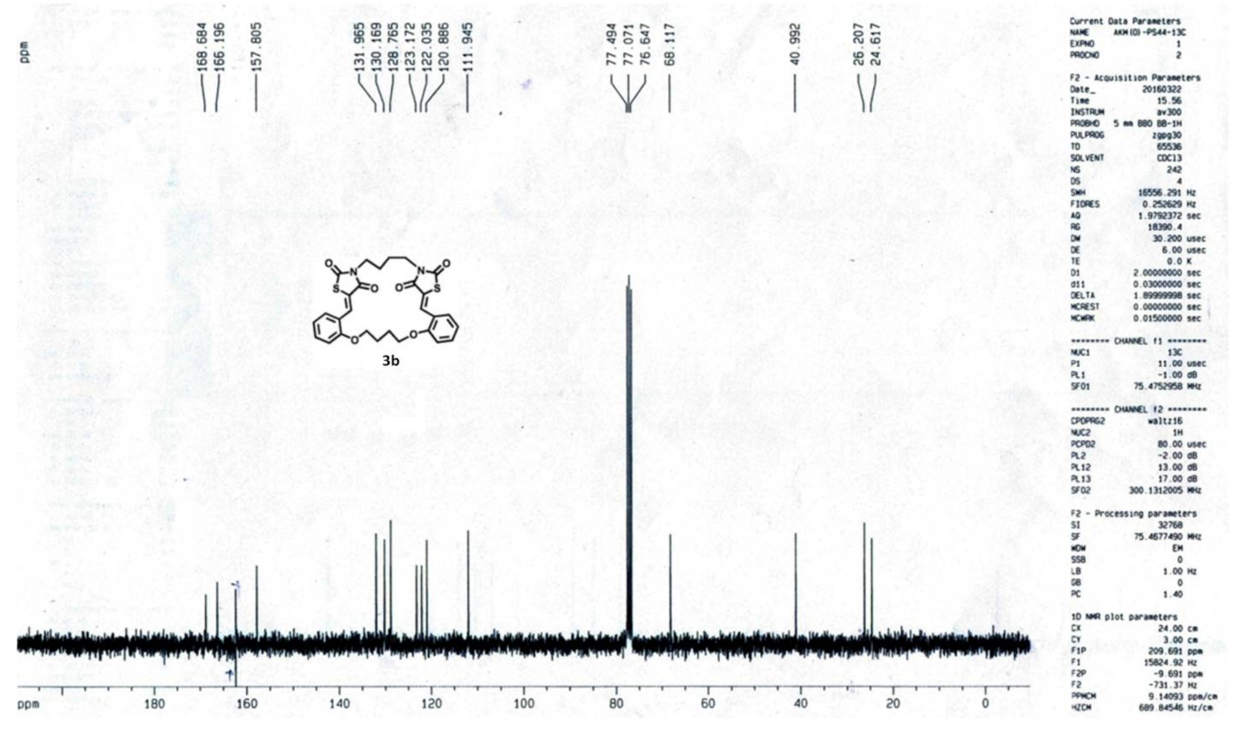


^{13}C NMR Spectrum of 3b



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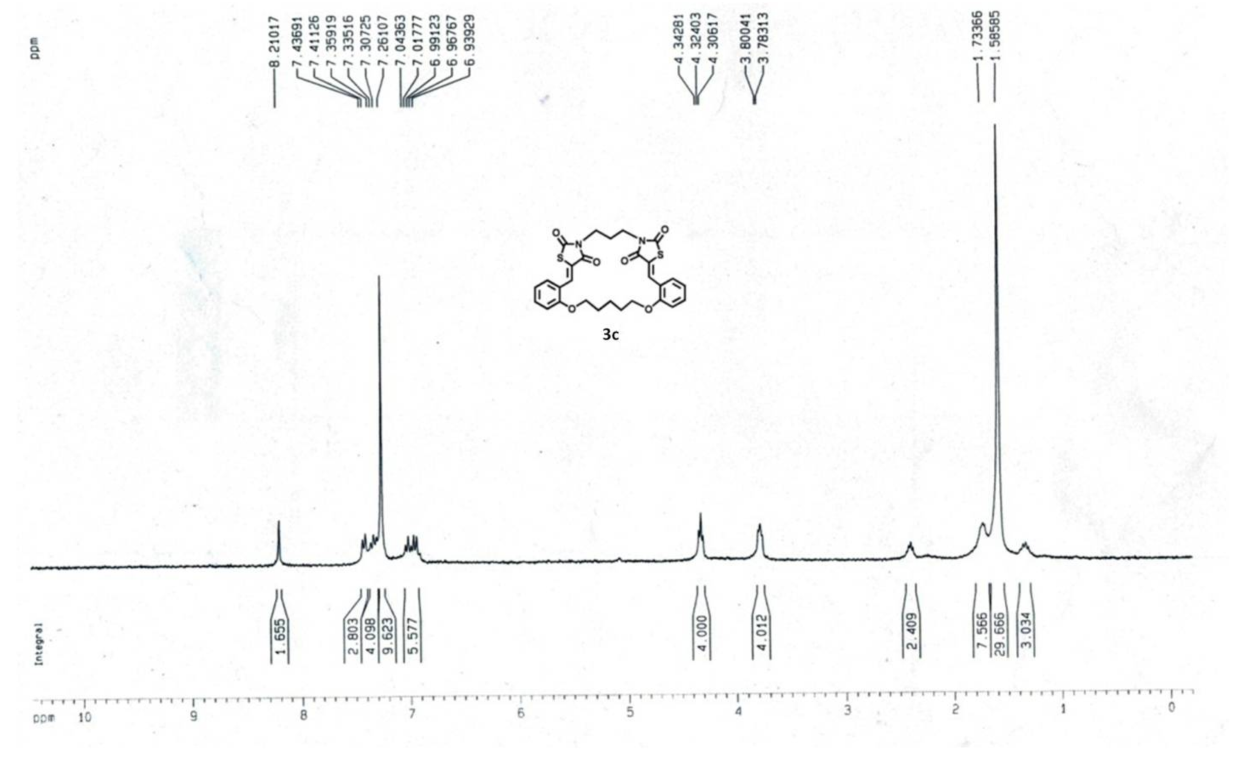
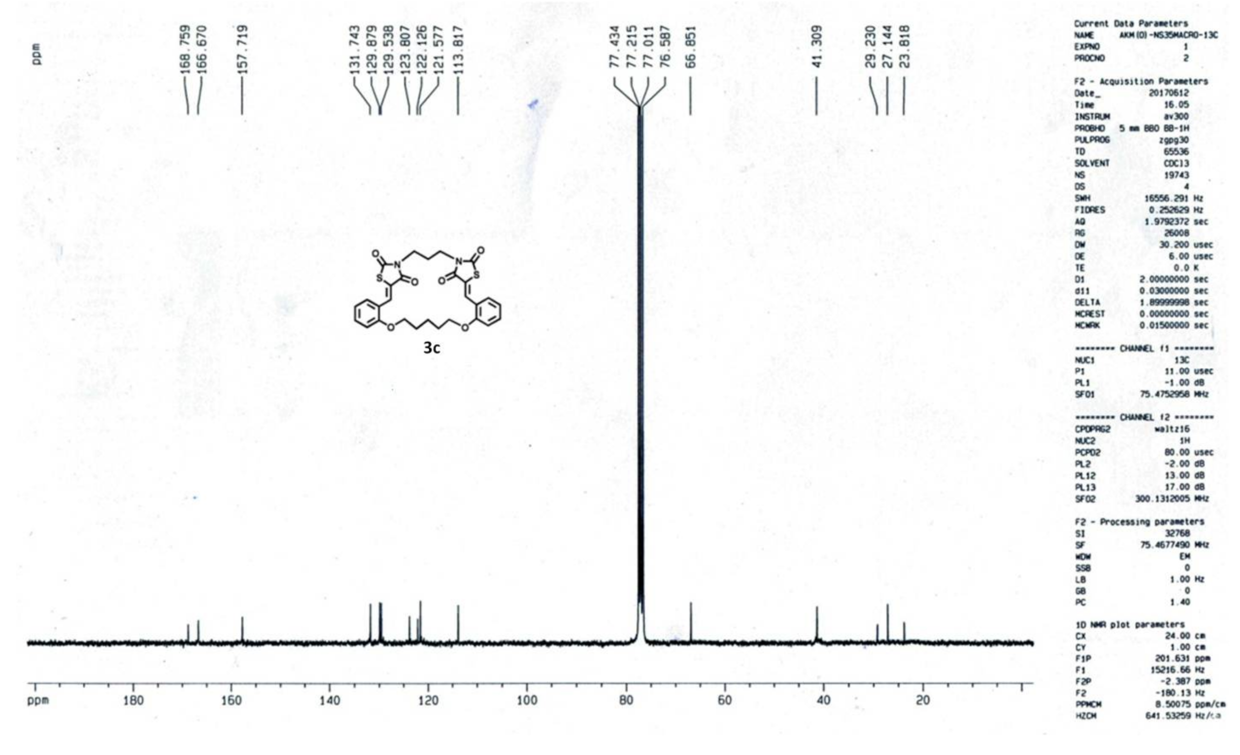


^{13}C NMR Spectrum of 3c



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P1                    11.00 usec
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SFO1            75.4752958 MHz

======== CHANNEL f2 ========
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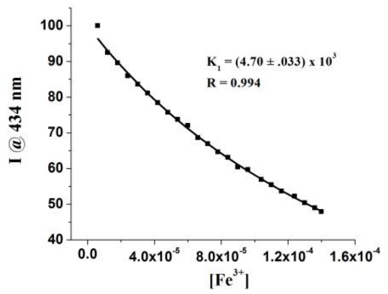
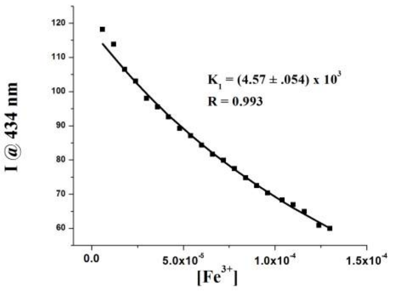
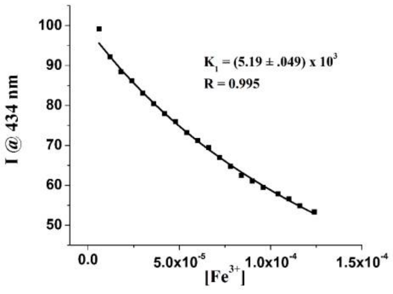
Non-linear fit to determine the binding constant of 3a-c with Fe^{3+}



3a

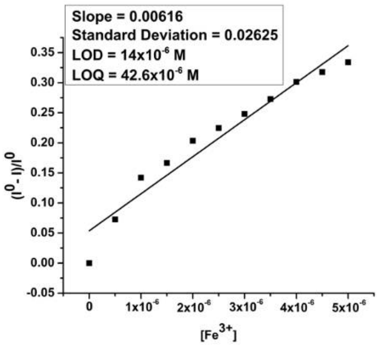


3b

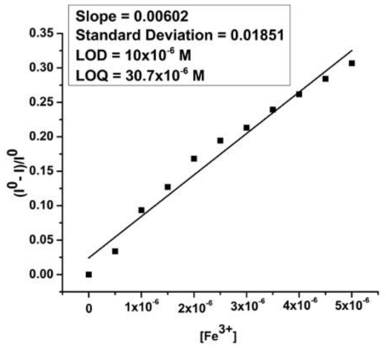


3c

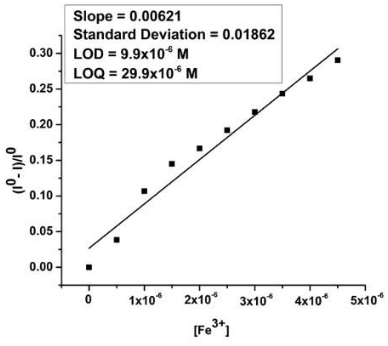
Determination of LOD and LOQ of Fe^{3+} ions from fluorescence titration data 3a-c



3a



3b



3c

Binding constants of some reported Fe^{3+} sensors

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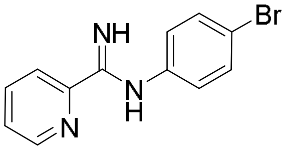
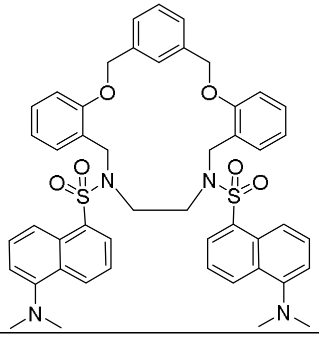
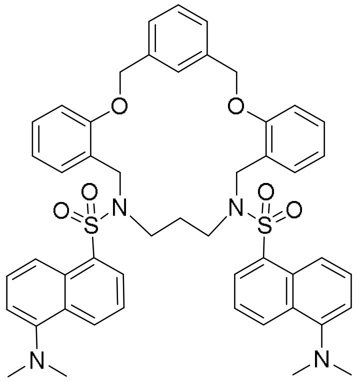
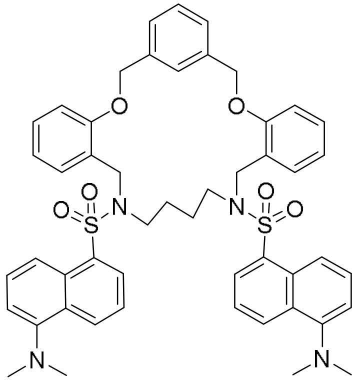
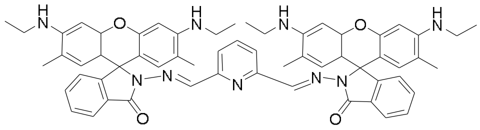
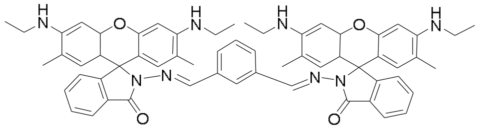
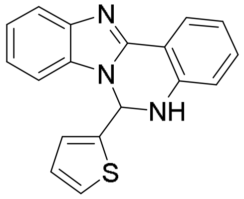
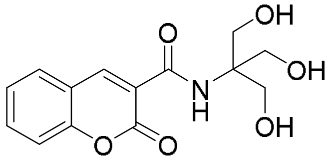
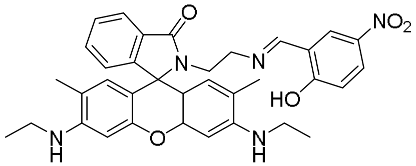
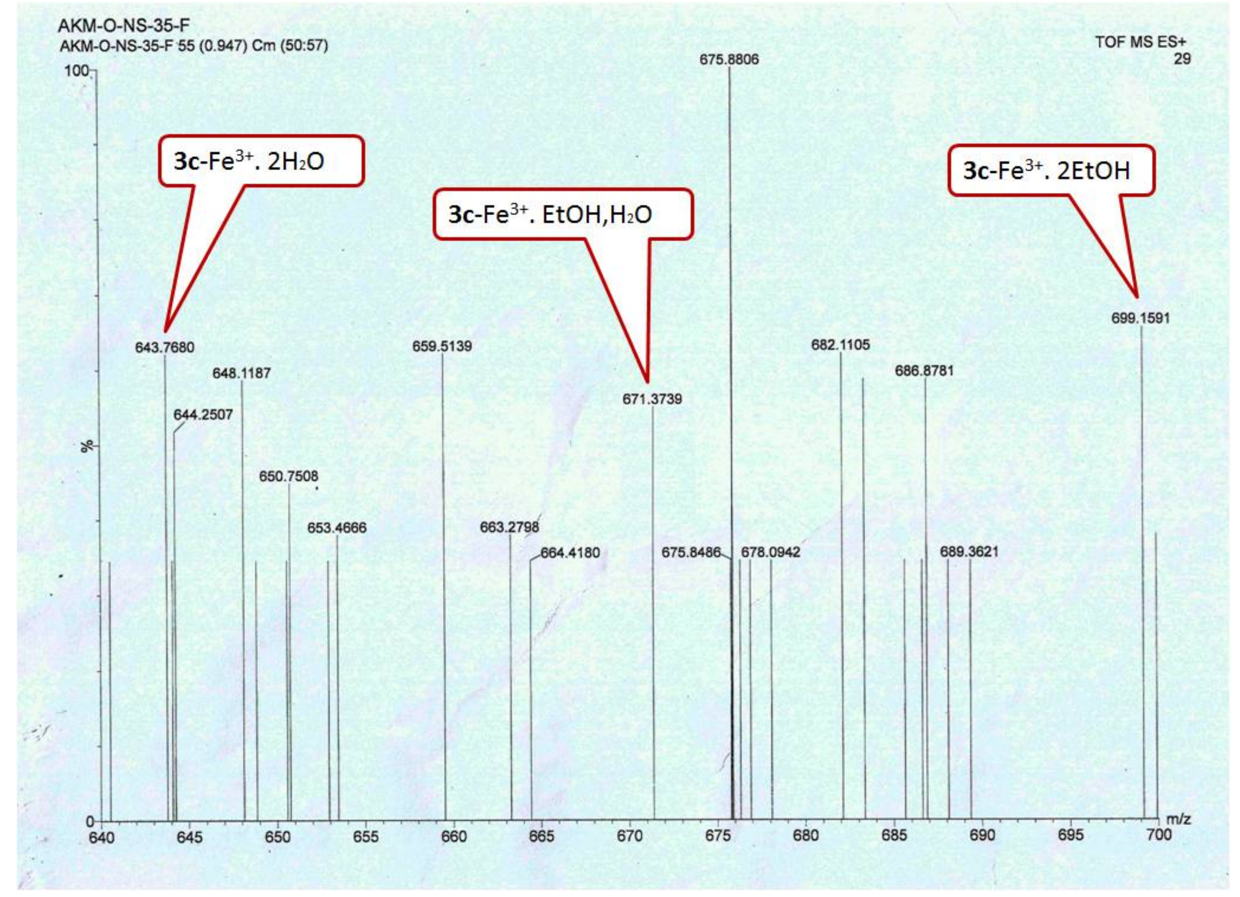
1		0.6×10^{-6} M, 1.9×10^{-6} M	5.00×10^{3} M^{-1}	J. Nandre, S. Patil, P. Patil, S. Sahoo, C. Redshaw, P. Mahulikar and U. Patil, *J Fluoresc*, 2014, **24**,1563
2		No Data, No Data	1.92×10^{3} M^{-1}	Y. Dai, K. Xua, C. Wang, X. Liu and P. Wang, *Supramolecular Chem.*, 2017, **29**, 315

3		9.11×10^{-5} M, No Data	2.41×10^{3} M^{-1}	Y. Dai, K. Xua, C. Wang, X. Liu and P. Wang, *Supramolecular Chem.*, 2017, **29**, 315
4		No Data, No Data	1.70×10^{3} M^{-1}	Y. Dai, K. Xua, C. Wang, X. Liu and P. Wang, *Supramolecular Chem.*, 2017, **29**, 315
5		No Data, No Data	7.50×10^{3} M^{-1}	A. J. Weerasinghe, C.Schmiesing, S.Varaganti, G. Ramakrishna, and E. Sinn, *J. Phys. Chem. B* 2010, **114**, 9413
6		No Data, No Data	5.10×10^{3} M^{-1}	A. J. Weerasinghe, C.Schmiesing, S.Varaganti, G. Ramakrishna, and E. Sinn, *J. Phys. Chem. B* 2010, **114**, 9413
7		2.0×10^{-6} M, 3.5×10^{-6} M	2.10×10^{2} $M^{-1/2}$	S. Sen,S. Sarkar,B. Chattopadhyay,A. Moirangthem, A. Basu, K. Dhara and P. Chattopadhyay, *Analyst*, 2012, **137**, 3335
8		No Data, No Data	5.70×10^{2} M^{-1}	J. Yao, W. Dou, W. Qin, W. Liu, *Inorg. Chem. Commun.*, 2009, **12**, 116

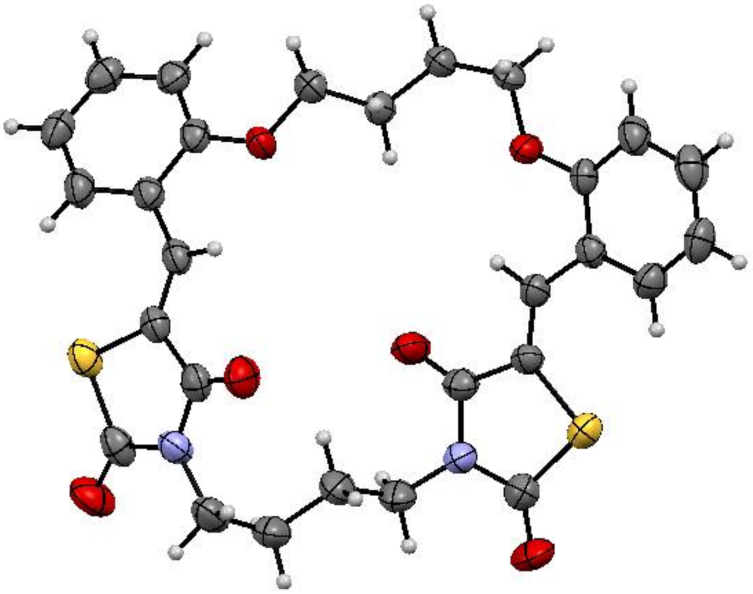
9		0.1×10^{-6} M, No data	No data	M. H. Lee, T.V.Giap, S. H. Kim, Y. H. Lee, C Kang and J. S. Kim, *Chem. Commun.*, 2010, **46**, 1407
10	Our compound **3c**	9.9 ×10^{-6} M, 29.9 ×10^{-6} M	8.11×10^{3} M^{-1}	This work

HRMS showing 3c-Fe^{3+}. 2EtOH (i), 3c-Fe^{3+}. 2H$_2$O (ii) and 3c-Fe^{3+}. EtOH,H$_2$O (iii) in protonated from.

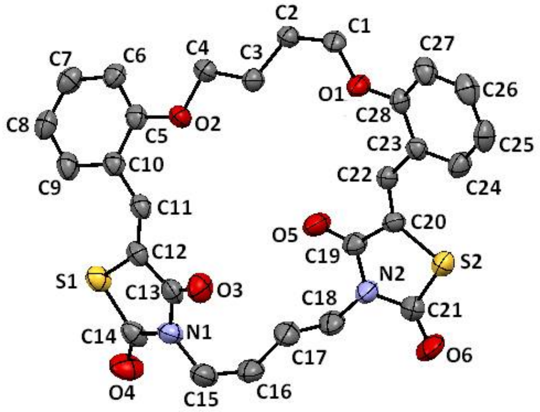


X-ray Data of 3b

Empirical formula	$C_{30}H_{29}N_4O_6S_2$
Formula weight	605.69
Temperature/K	296.0
Crystal system	Triclinic
Space group	P-1
a/Å, b/Å, c/Å	7.3581(6), 11.8774(10), 30.672(2)
α/°, β/°, γ/°	90.010(6), 90.016(6), 104.434(6)
Volume/Å^3	2595.9(4)
Z	4
ρ_{calc} mg/ mm^3	1.550
m/mm^{-1}	0.262
F(000)	1268
Theta range for data collection	0.66 to 32.94°
Index ranges	$-11 \le h \le 11$, $-18 \le k \le 17$, $-42 \le l \le 45$
Reflections collected	49077
Independent reflections	16336[R(int) = 0.1728]
Data/restraints/parameters	16336/0/685
Goodness-of-fit on F^2	0.831
Final R indexes [I>2σ (I)]	$R_1 = 0.0827$, $wR_2 = 0.1666$
Final R indexes [all data]	$R_1 = 0.2942$, $wR_2 = 0.2548$
Largest diff. peak/hole / e Å^{-3}	0.294/-0.303



Computational Methods. A GAUSSIAN 09 program package[4] was used for all calculations in this paper. For the DFT calculation Becke three parameters hybrid exchange[5] and the Lee–Yang–Parr correlation functionals[6] (**B3LYP**) were used as functionals. The DFT method was used to optimize the geometry of the molecule. For Fe^{3+} ion lanl2dz and for C N O S atoms 6-31+g (d,p) basis set was used. Hartree-fock method with STO-3G basis set was used also for calculation of MEP for the compound.



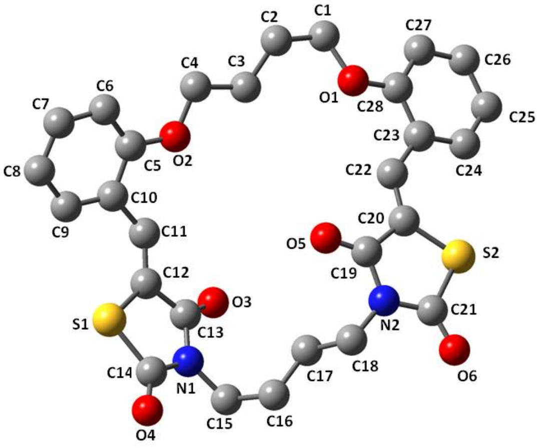
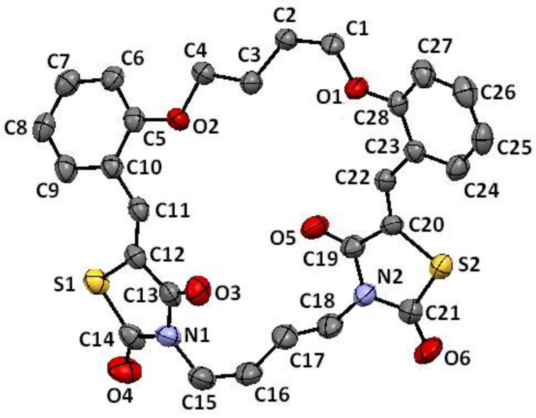


Table 1 Selected bond lengths

Bond	Bond length (Å)	
	X-Ray	DFT
C1-C2	1.490 (6)	1.493
C2-C3	1.514 (6)	1.512
C3-C4	1.504 (6)	1.504
C4-O2	1.433 (5)	1.433
O2-C5	1.366 (5)	1.367
C5-C10	1.414 (6)	1.416
C10-C11	1.451 (6)	1.453
C11-C12	1.344 (6)	1.345
C12-C13	1.471 (6)	1.470
C12-S1	1.755 (4)	1.755
C13-N1	1.391 (6)	1.389
C13-O3	1.211 (5)	1.211
C14-N1	1.378 (6)	1.379
C14-S1	1.777 (5)	1.777
C14-O4	1.197 (5)	1.199

N1-C15	1.473 (6)	1.470
C15-C16	1.509 (7)	1.511
C16-C17	1.516 (6)	1.519
C17-C18	1.514 (7)	1.514
C18-N2	1.450 (6)	1.455
N2-C19	1.390 (5)	1.389
N2-C21	1.373 (6)	1.372
C21-O6	1.211 (5)	1.212
C21-S2	1.766 (5)	1.765
S2-C20	1.753 (4)	1.754
C19-C20	1.464 (6)	1.467
C19-O5	1.209 (5)	1.207
C20-C22	1.330 (6)	1.330
C22-C23	1.443 (6)	1.443
C23-C28	1.411 (6)	1.412
C28-O1	1.367 (5)	1.371
O1-C1	1.437 (5)	1.437



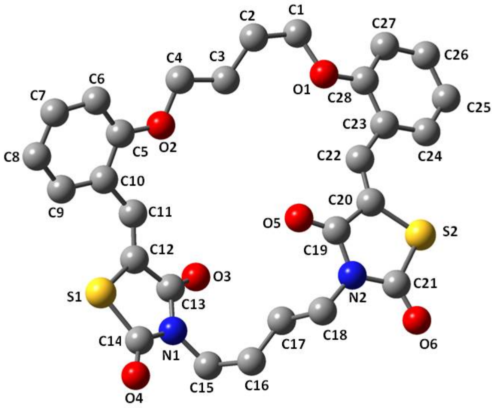
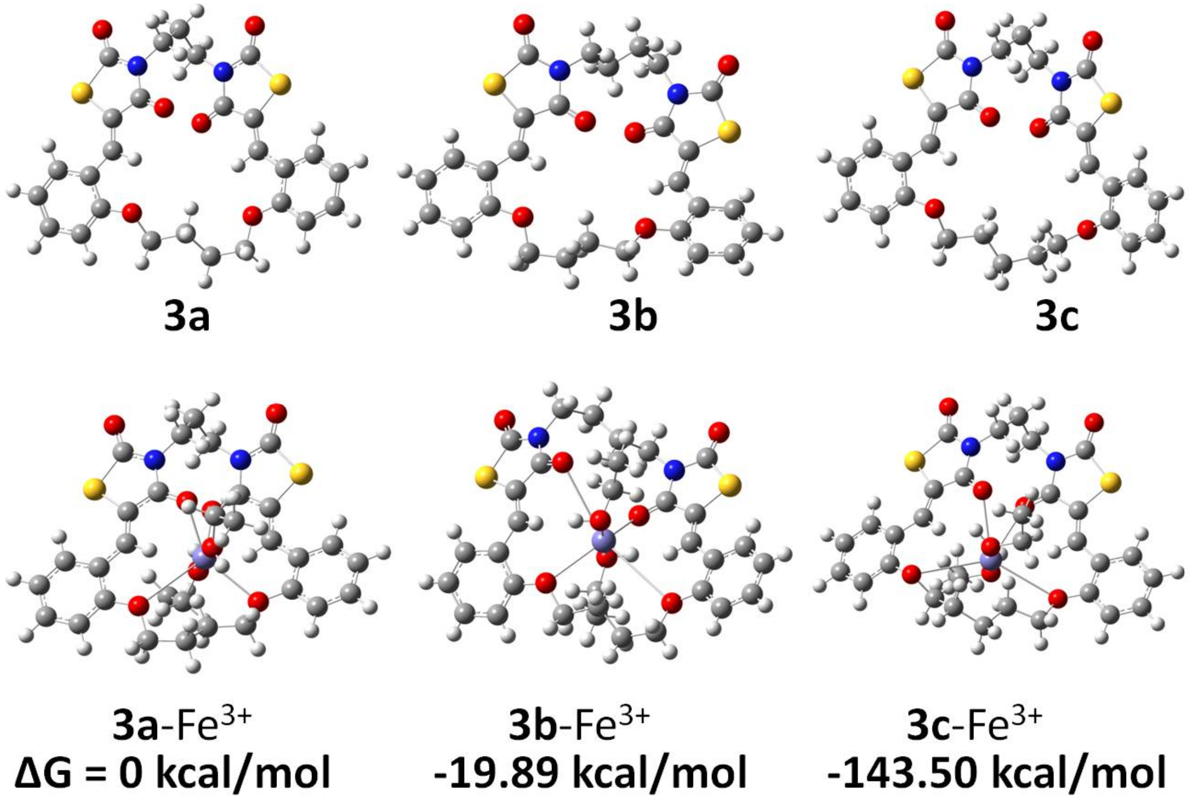


Table 2: Selected bond angles

Bond angle	Bond angle (degree)	
	x-ray	DFT
O1-C1- C2	106.8(3)	106.86
O1-C28-C23	115.4(4)	115.13
O1-C28-C27	122.8(4)	122.85
O2-C5-C6	123.8(4)	123.71
O2-C5-C10	115.1(4)	115.16
O2-C4-C3	107.9(4)	107.75
C1-C2-C3	114.3(4)	114.00
C20-S2-C21	91.7(2)	91.50
C20-C22-C23	132.2(4)	132.08

C22-C20-S2	130.5(4)	130.60
C22-C20-C19	119.4(4)	119.31
N2-C19-C20	111.3(4)	111.07
N2-C21-S2	110.9(3)	110.70
N2-C18-C17	111.5(4)	111.55
N1-C15-C16	113.1(4)	113.19
N1-C14-S1	110.1(3)	110.10
N1-C13-C12	110.2(4)	110.25
C11-C12-S1	128.1(4)	128.16
C11-C12-C13	121.3(4)	121.15
O6-C21-S2	124.0(4)	124.12
O6-C21-N2	125.1(5)	125.15
C28-O1-C1	118.6(3)	118.42
C28-C23-C22	118.3(4)	118.38
C19-C20-S2	110.0(3)	110.00
C19-N2-C18	121.8(4)	121.38
C6-C5-C10	121.2(4)	121.13
C12-S1-C14	91.5(2)	91.51
C12-C11-C10	128.9(4)	128.66
O4-C14-S1	124.0(4)	124.05
O4-C14-N1	125.9(5)	125.84
C21-N2-C19	115.9(4)	116.27
C21-N2-C18	122.3(4)	122.25
C5-O2-C4	118.0(3)	117.90
C5-C10-C11	118.4(4)	118.12
C15-C16-C17	113.6(4)	113.23
O5-C19-C20	126.7(4)	126.63
O5-C19-N2	122.0(4)	122.29
O3-C13-N1	123.1(5)	122.99
O3-C13-C12	126.7(5)	126.74
C24-C23-C22	125.4(4)	125.36
C24-C23-C28	116.3(4)	116.16
C18-C17-C16	115.9(4)	115.65
C5-O2-C4	118.0(3)	117.25
C14-N1-C15	120.1(4)	120.14
C14-N1-C13	116.9(4)	116.84
C13-N1-C15	122.9(4)	122.89
C13-C12-S1	110.3(3)	110.34
C27-C28-C23	121.8(4)	122.02
C9-C10-C11	124.1(4)	124.35
C9-C10-C5	117.5(4)	117.50

Optimized structure of 3a-c and their complex with Fe^{3+}



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