New Journal of Chemistry

Supporting information for

Highly Selective Colorimetric and Fluorescent BODIPY Dyes for Sensing of Cysteine and/or Homocysteine

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1. **Experimental Section:**

Relative fluorescence quantum efficiencies of BODIPY derivatives were obtained by comparing the areas under the corrected emission spectrum of the test sample in various solvents with fluorescein (λ_{ex} = 480 nm) in 0.1 M NaOH aqueous solution (Φ = 0.90) as the standard or Cresy Violet perchlorate (λ_{ex} = 540 nm) in methanol as the standard (Φ = 0.54). Non-degassed, spectroscopic grade solvents and a 10 mm quartz cuvette were used. Dilute solutions (0.01<A<0.05) were used to minimize the reabsorption effects. Quantum yields were determined using the following equation:

$$\Phi_X = \Phi_S (I_X/I_S) (A_S/A_X) (n_X/n_S)^2$$

Where Φ_S stands for the reported quantum yield of the standard, I stands for the integrated emission spectra, A stands for the absorbance at the excitation wavelength and n stands for the refractive index of the solvent being used.

2. UV-vis and fluorescence spectroscopes

Table S1. Photophysical properties of BODIPYs **1-4** in methanol at room temperature.

BODIPY	λ_{abs} (nm),	λ_{em} (nm)	Φ^a	Stokes-shift (cm^{-1})
1	504	530	0.75	973
2	508	531	0.95	852
3	495	555	0.10	2184
4	516	532	0.91	583

[a]the fluorescence quantum yields Φ were calculated using fluorescein (λ_{ex} = 480 nm) in 0.1 M NaOH aqueous solution (Φ = 0.90) as the standard.

Table S2. Photophysical properties of BODIPYs **1** and **3** with or without various amino acids in MeOH/HEPES (45 mM, pH = 7.2, v/v = 1/1) solution.

BODIPY	λ_{abs} (nm),	λ_{em} (nm)	Φ^a	Stokes-shift (nm)
1	501	530	0.61	19
1-Cys[b]	516	528	0.08	12
1-Hcy[b]	514	527	0.16	13
1-other all analytes[c]	516	528	0.08	12
3	491	545	0.09	54
3-Cys[d]	516	547	0.26	31
3-other all analytes[e]	491	545	0.09	54

[a]the fluorescence quantum yields Φ were calculated using fluorescein (λ_{ex} = 480 nm) in 0.1 M NaOH aqueous solution (Φ = 0.90) as the standard and were recorded 1h after adding amino acids; [b] 200 equiv Cys or Hcy was added; [c]Other all analytes (400 equiv, respectively): Ala, Arg, Asp, Glu, Gly, His, Leu, Lys, Met, Pro, Ser, Thr, Val, Iso, and GHS; [d]400 equiv Cys was added; [e]Other all analytes (400 equiv, respectively): Hcy, Ala, Arg, Asp, Glu, Gly, His, Leu, Lys, Met, Pro, Ser, Thr, Val, Iso, and GHS

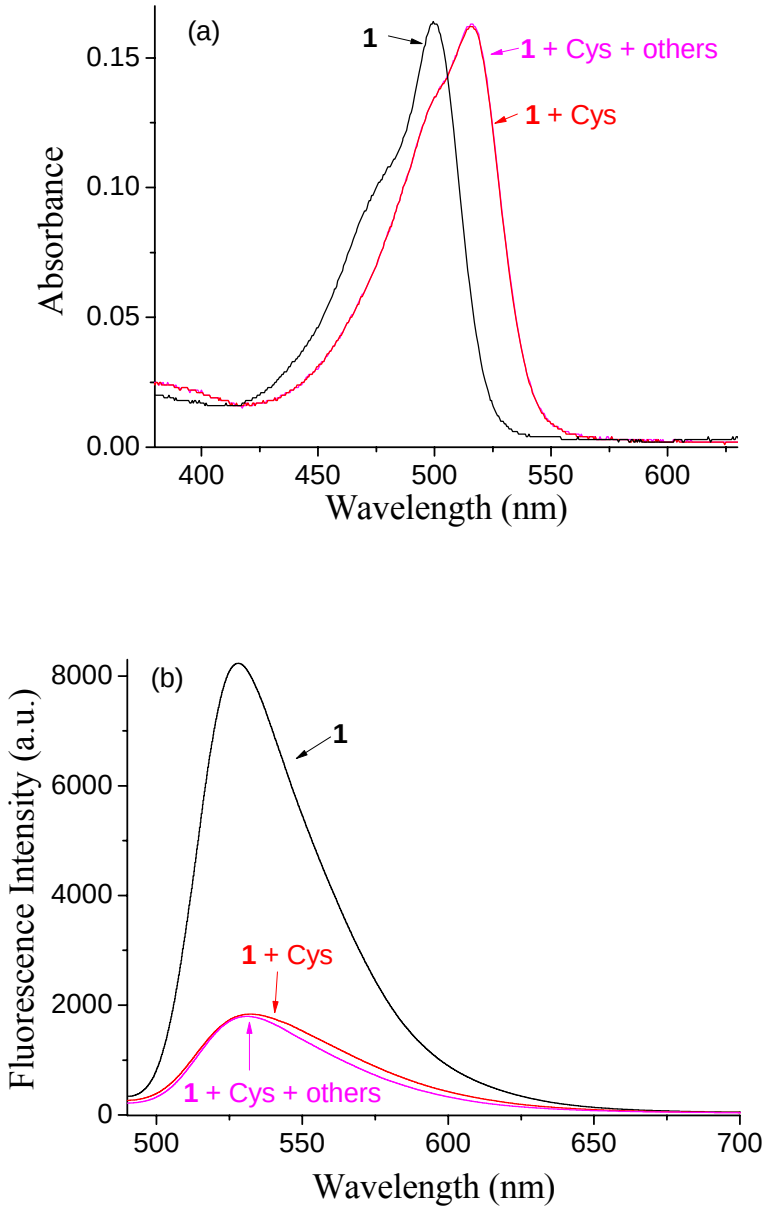


Figure S1. Absorption (a, 1×10^{-5} M) and fluorescence (b, 1×10^{-6} M, , $\lambda_{ex} = 480$ nm) spectra of BODIPY **1** in a MeOH/HEPES (45 mM, pH 7.2, 1:1, v/v) solution in the absence, or presence of 200 equiv of Cys or/and 400 equiv of other selected analytes (Ala, Arg, Asp, Glu, Gly, His, Leu, Lys, Met, Pro, Ser, Thr, Val, Iso, and GHS).

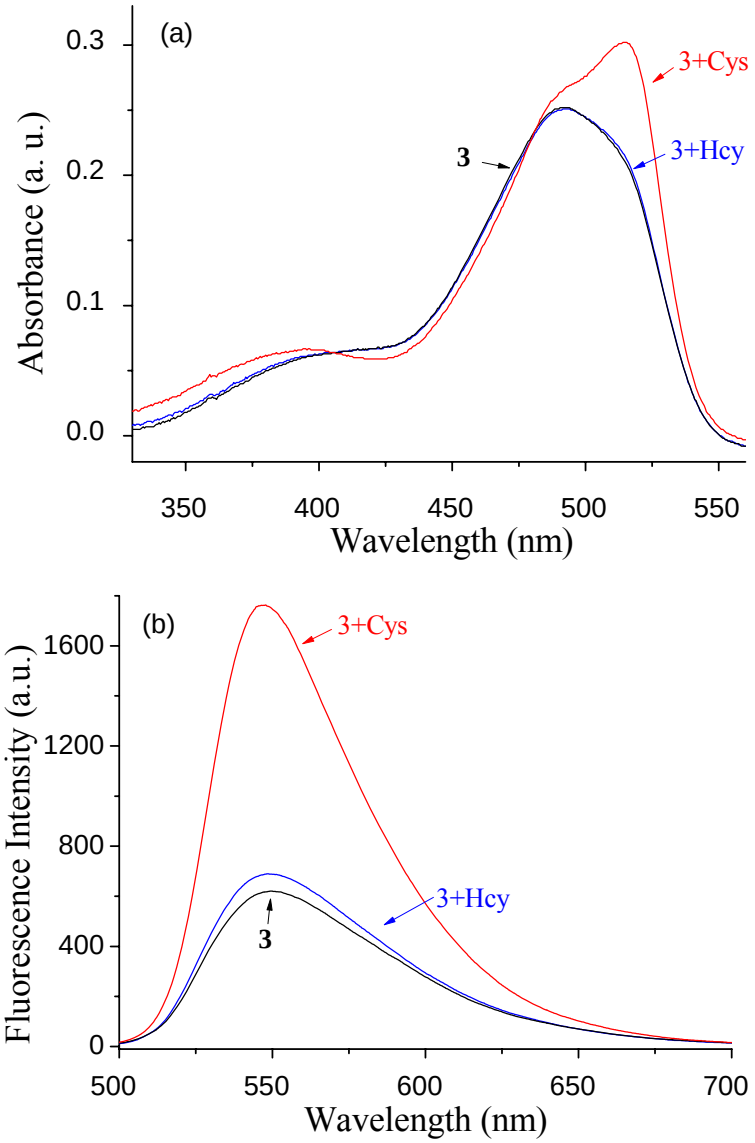


Figure S2. Absorption (a, 1×10^{-5} M) and emission (b, 1×10^{-6} M, $\lambda_{ex} = 480$ nm) spectra of BODIPY **3** with or without 200 equiv of Cys or Hcy in a MeOH/HEPES (45 mm, pH 7.2, 1:1, v/v) solution.

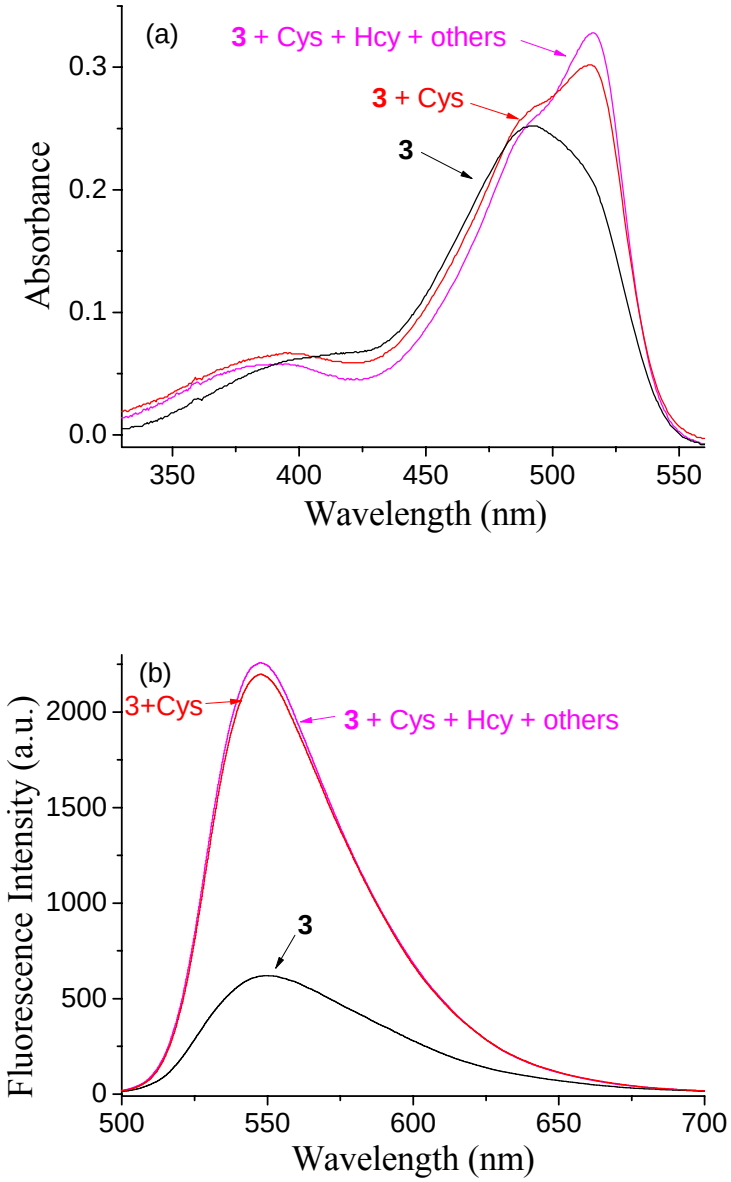


Figure S3. Absorption (a, 1×10^{-5} M) and fluorescence (b, 1×10^{-6} M, , $\lambda_{ex} = 480$ nm) spectra of BODIPY **3** in a MeOH/HEPES (45 mM, pH 7.2, 1:1, v/v) solution in the absence, or presence of 200 equiv of Cys or/and 400 equiv of other selected analytes containing 200 equiv of Hcy.

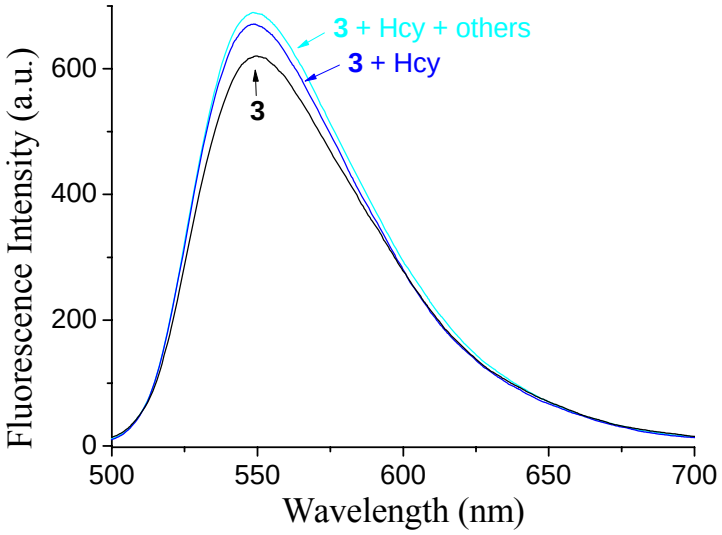


Figure S4. Fluorescence spectra of BODIPY **3** (1×10^{-6} M) in a MeOH/HEPES (45 mM, pH 7.2, 1:1, v/v) solution in the absence, or presence of 200 equiv of Hcy or/and 400 equiv of other selected analytes.

3. Copies of ^{1}H NMR, ^{13}C NMR and High resolution mass spectra for all new compounds

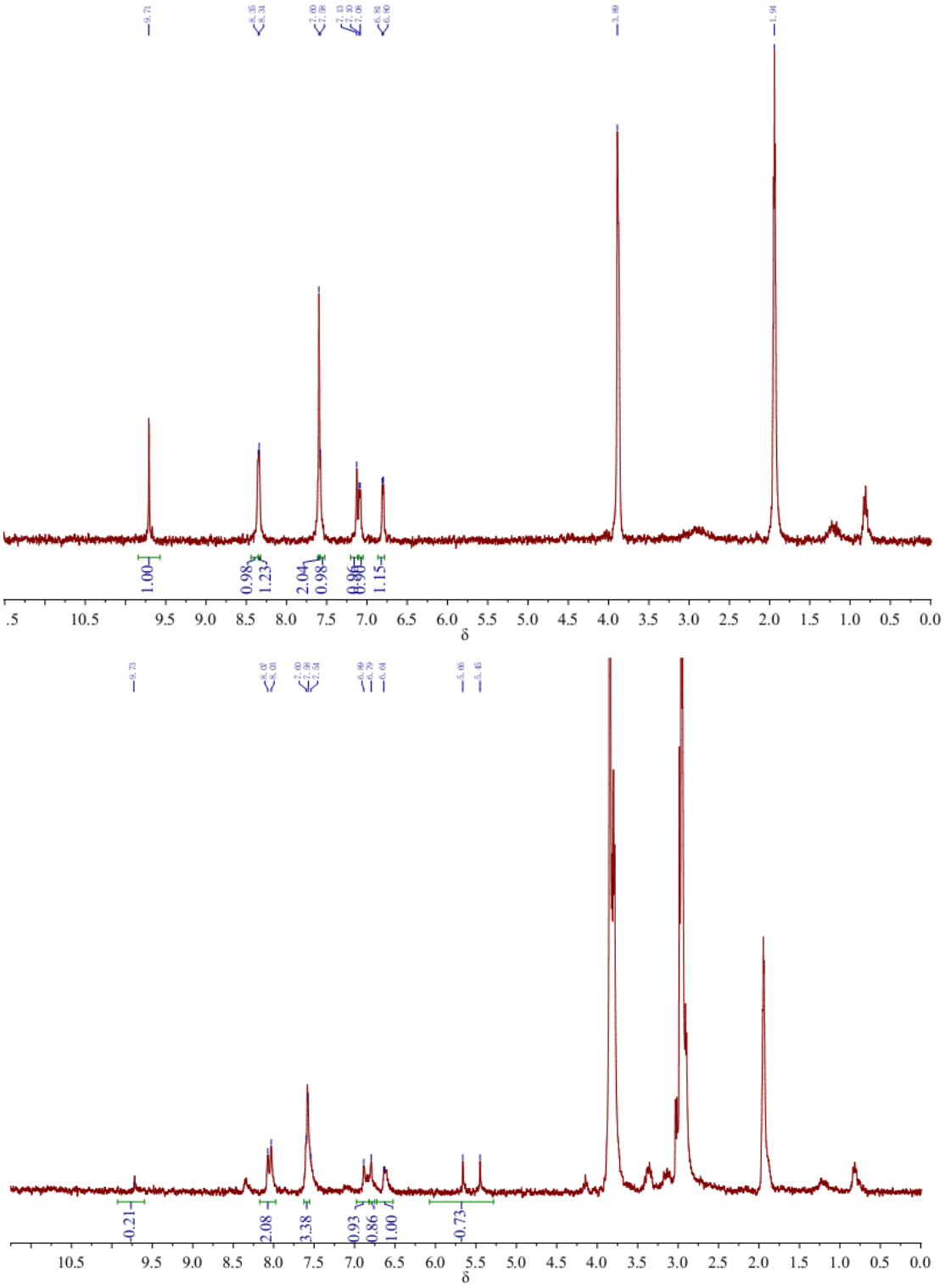


Figure S5. ^{1}H-NMR spectra of BODIPY **1** (3 mM, CD_3CN:D_2O=7:3) in the absence (top), or presence of 10 equiv of Cys (bottom, spectrum was recorded after addition of Cys for 1h).

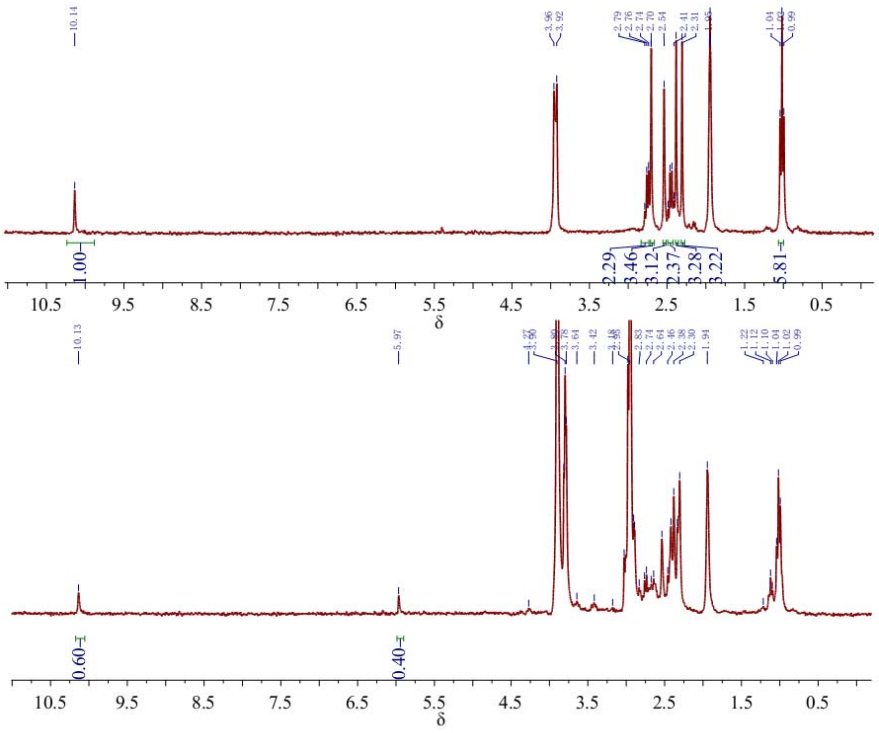
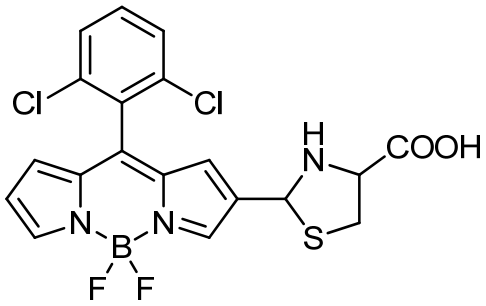


Figure S6. ^{1}H-NMR spectra of BODIPY **3** (3mM, CD_3CN:D_2O=7:3) in the absence (top), or presence of 10 equiv of Cys (bottom, spectrum was recorded after addition of Cys for 1h).



5a

Calcd. **C19H15BCl2F2N3O2S** $[M+H]^+$ 468.0323

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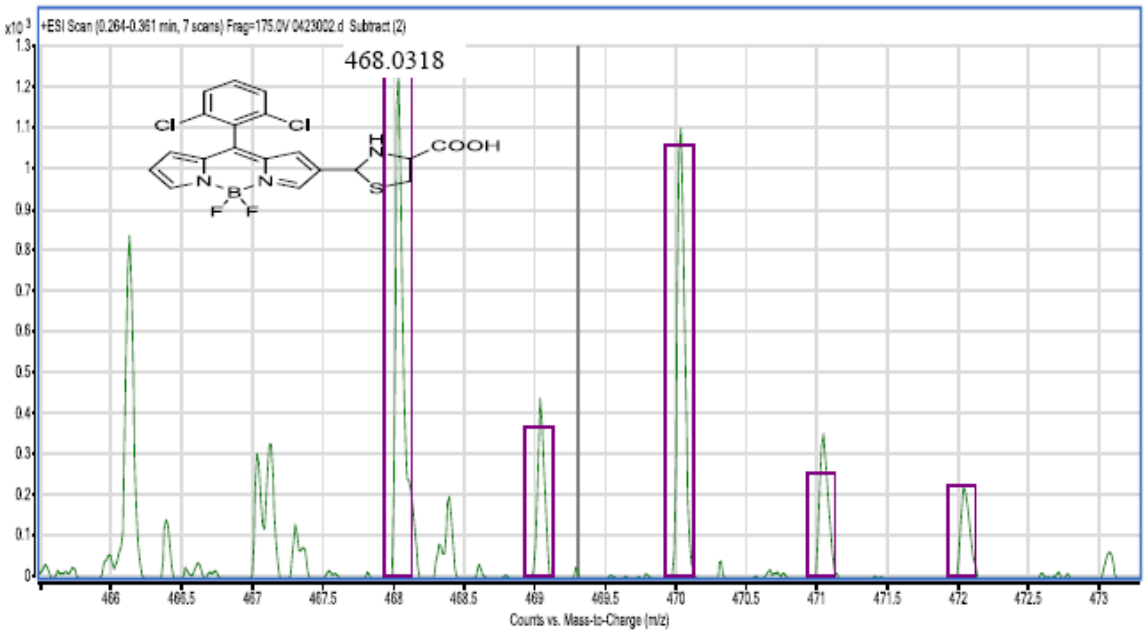
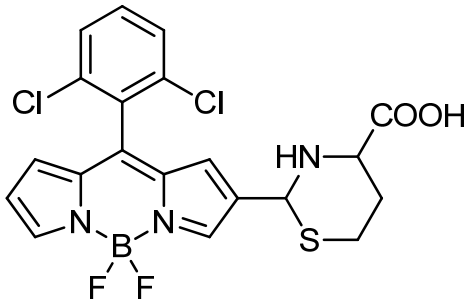
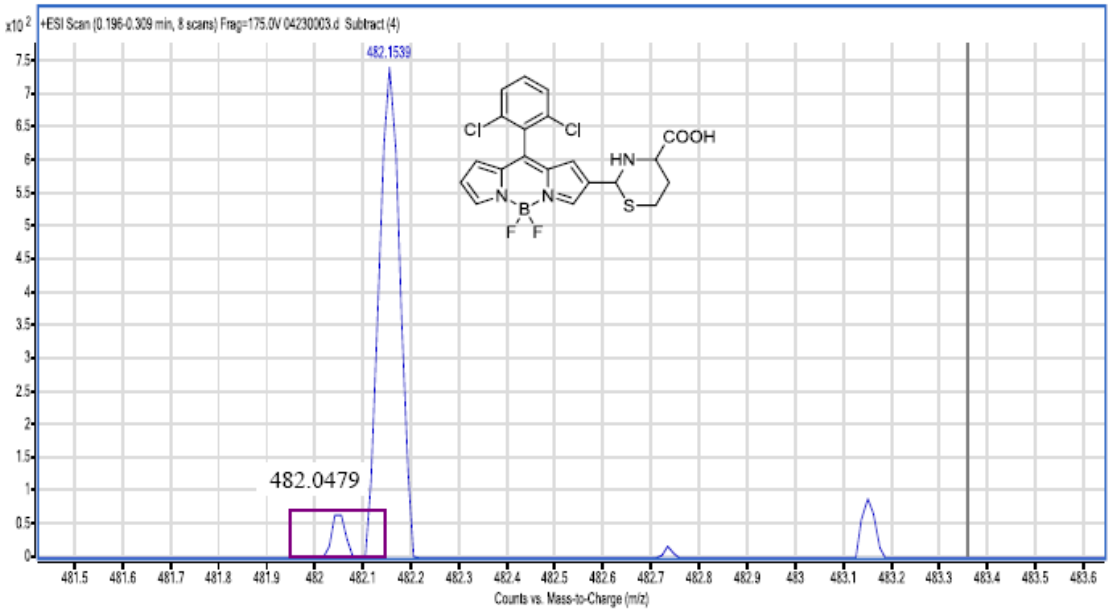


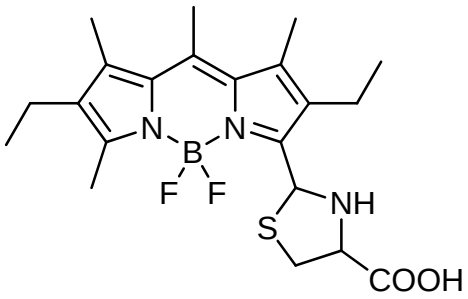


5b

Calcd. **C20H17BCl2F2N3O2S** $[M+H]^+$ 482.0480

Found: 482.0479

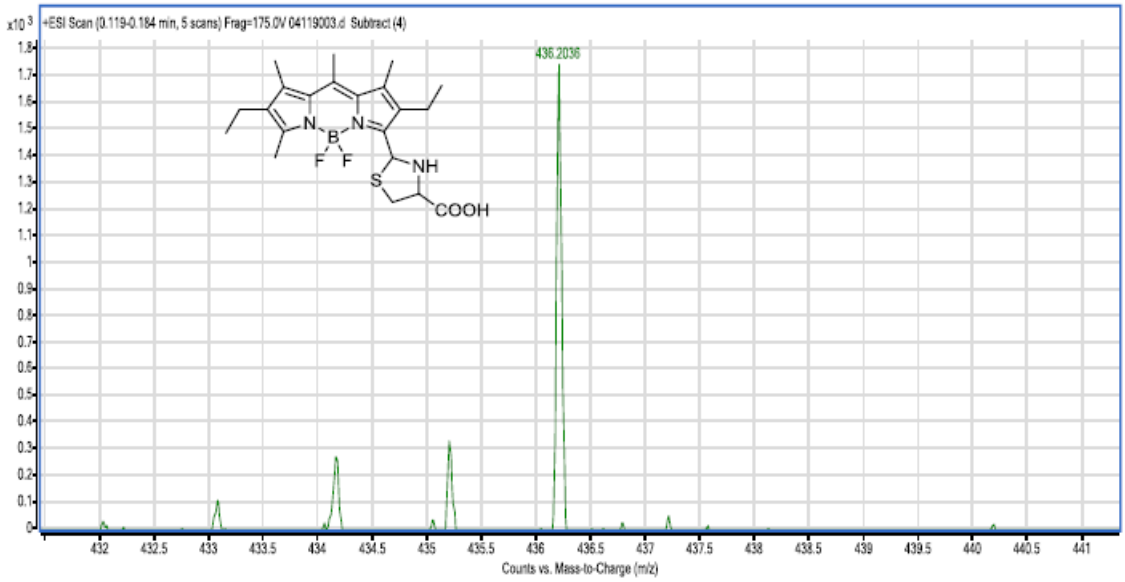




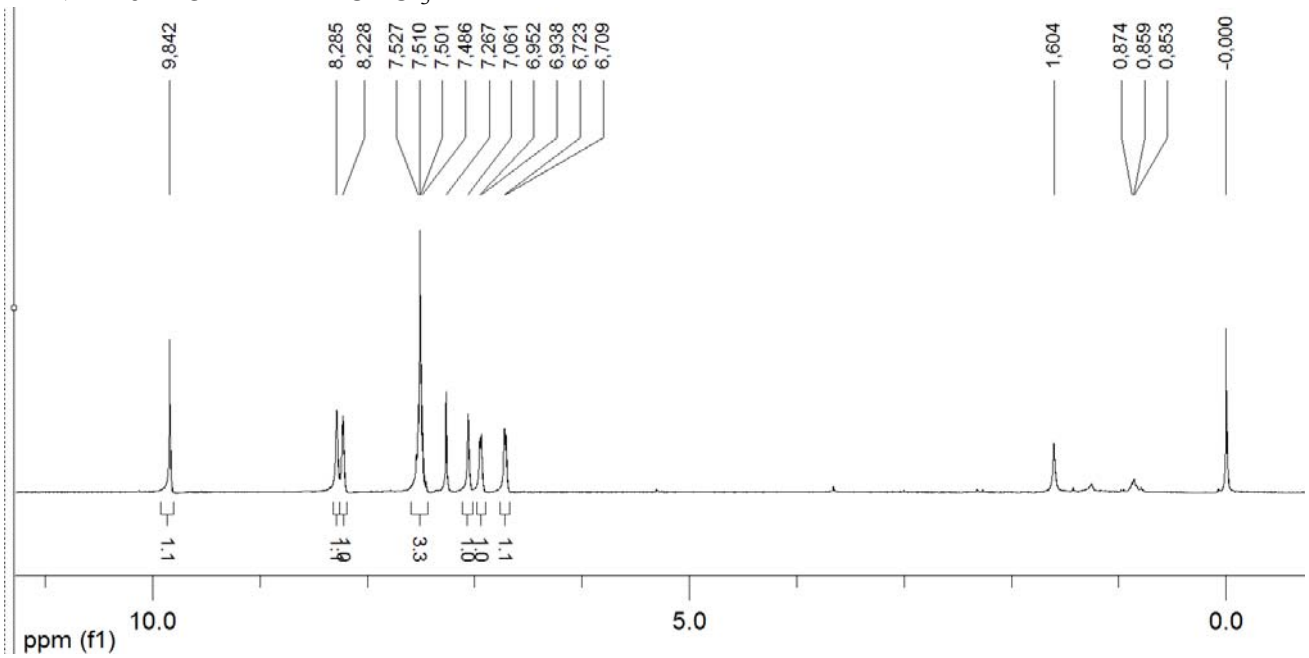
6

Calcd. **C21H29BF2N3O2S** $[M+H]^+$ 436.2042

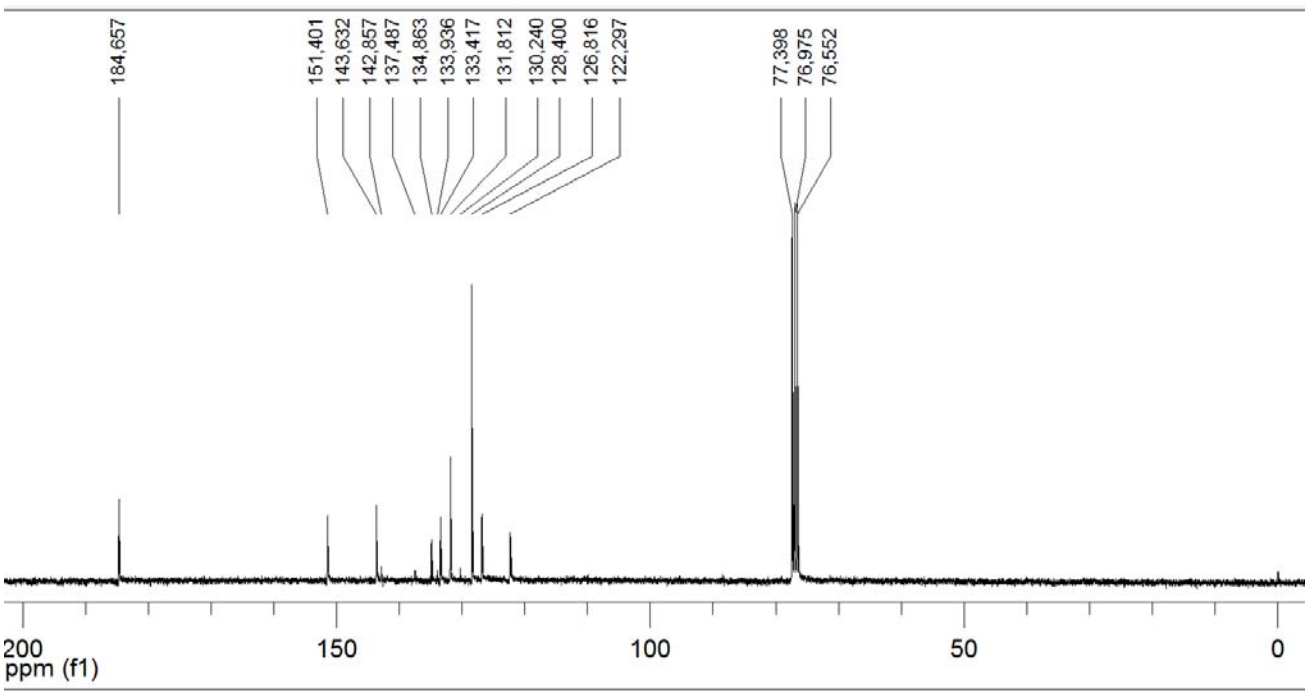
Found: 436.2036



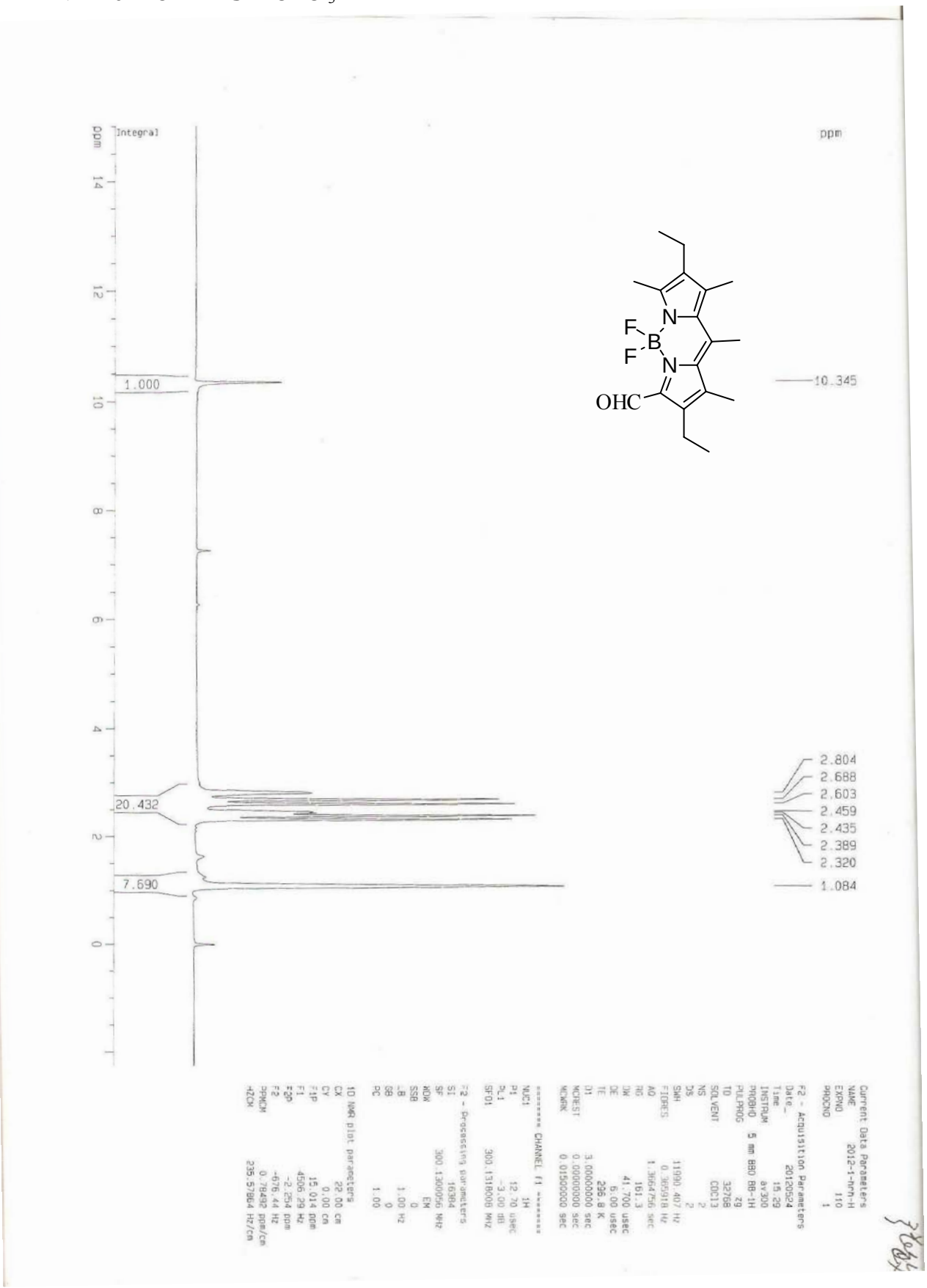
^{1}H NMR of BODIPY **1** in $CDCl_3$



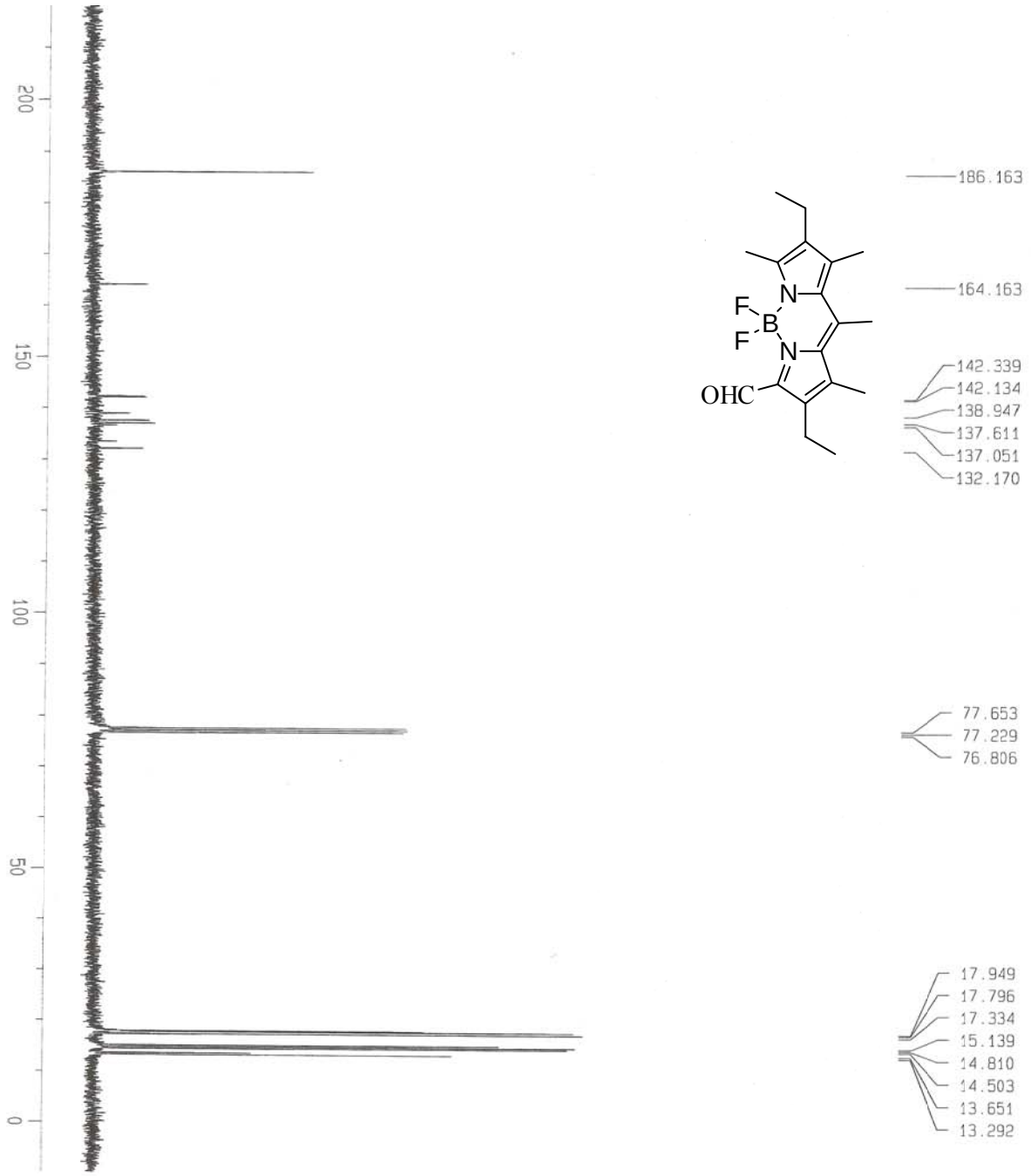
^{13}C NMR of BODIPY **1** in $CDCl_3$



^{1}H NMR of BODIPY **3** in $CDCl_3$



^{13}C NMR of BODIPY **3** in $CDCl_3$



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CY 0.00 cm
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F2P -9.838 ppm
F2 -742.48 Hz
PPMCM 10.91131 ppm/cm
HZCM 823.45197 Hz/cm

4. DFT calculation

The ground state geometry was optimized by using DFT method at b3lyp/6-31G (d) level. The same method was used for vibrational analysis to verify that the optimized structures correspond to local minima on the energy surface. TD-DFT computations were used to obtain the vertical excitation energies and oscillator strengths at the optimized ground state equilibrium geometries under the b3lyp/6-311G (2d,p) theoretical level. The TDDFT of all the molecules in Methanol were using the Self-Consistent Reaction Field (SCRF) method and th Polarizable Continuum Model (PCM). All of the calculations were carried out by the methods implemented in Gaussian 09 package.

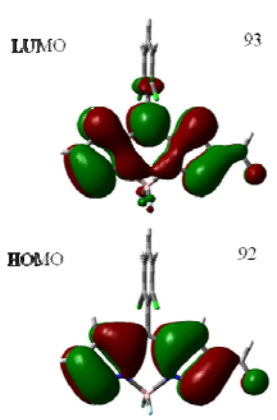

Figure S7. Frontier molecular orbitals (MO) of BODIPY **1** calculated with Time-dependent density functional theory (TDDFT) at the b3lyp/6-311G (2d,p) level (number of states: 20) using Gaussian 09.

Selected TDDFT paramete:

Excited State 1: Singlet-A 2.9435 eV 421.21 nm f = 0.5492 <S**2>=0.000

89 -> 93 -0.17021

92 -> 93 0.68566

92 <- 93 -0.10075

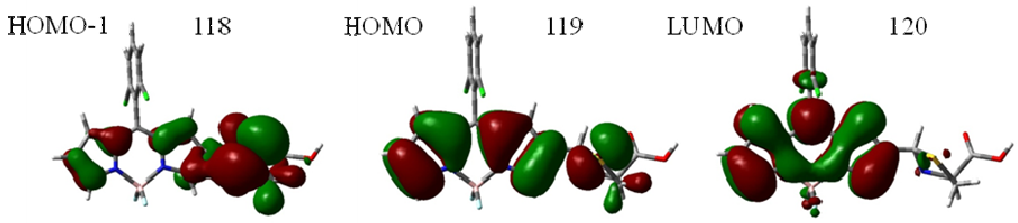

Figure S8. Frontier molecular orbitals (MO) of BODIPY **5a** calculated with Time-dependent density functional theory (TDDFT) at the b3lyp/6-311G (2d,p) level (number of states: 20) using Gaussian 09.

Selected TDDFT paramete:

Excited State 1: Singlet-A 2.6681 eV 464.70 nm f = 0.2787 <S**2>=0.000

118 ->120 0.38259

119 ->120 0.59010

Excited State 2: Singlet-A 2.9263 eV 423.69 nm f = 0.2783 <S**2>=0.000

115 ->120 0.12774

117 ->120 0.16171

118 ->120 0.57815

119 ->120 -0.35376

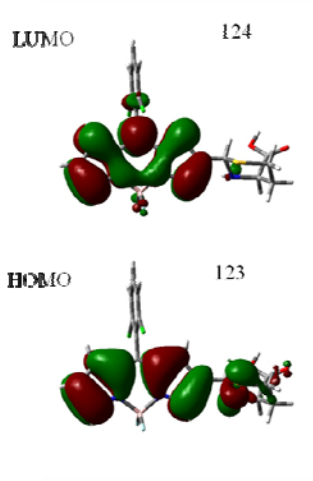

Figure S9. Frontier molecular orbitals (MO) of BODIPY **5b** calculated with Time-dependent density functional theory (TDDFT) at the b3lyp/6-311G (2d,p) level (number of states: 20) using Gaussian 09.

Selected TDDFT paramete:

Excited State 1: Singlet-A 2.6914 eV 460.66 nm f = 0.0461 <S**2>=0.000

122 ->124 0.66859

123 ->124 0.22784

Excited State 2: Singlet-A 2.8103 eV 441.18 nm f = 0.4114 <S**2>=0.000

119 ->124 0.13814

121 ->124 -0.27608

122 ->124 -0.21418

123 ->124 0.60134

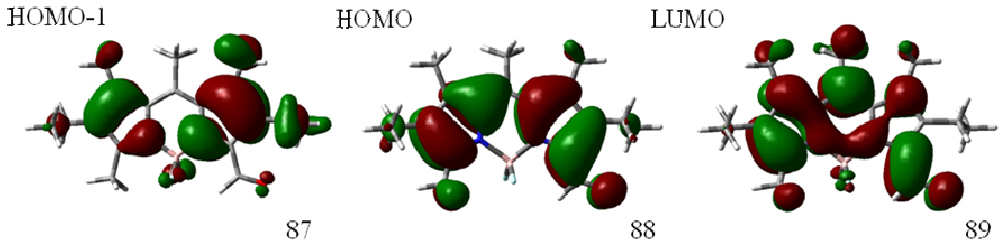

Figure S10. Frontier molecular orbitals (MO) of BODIPY **3** calculated with Time-dependent density functional theory (TDDFT) at the b3lyp/6-311G (2d,p) level (number of states: 20) using Gaussian 09.

Selected TDDFT paramete:

Excited State 1: Singlet-A 2.7186 eV 456.06 nm f = 0.5198 <S**2>=0.000

87 -> 89 -0.19827

88 -> 89 0.67968

Excited State 2: Singlet-A 3.0999 eV 399.96 nm f = 0.2050 <S**2>=0.000

85 -> 89 0.13580

87 -> 89 0.66059

88 -> 89 0.20155

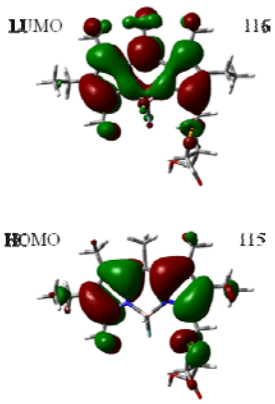

Figure S11. Frontier molecular orbitals (MO) of BODIPY **6** calculated with Time-dependent density functional theory (TDDFT) at the b3lyp/6-311G (2d,p) level (number of states: 20) using Gaussian 09.

Selected TDDFT paramete:

Excited State 1: Singlet-A 2.7295 eV 454.23 nm f = 0.4993 <S**2>=0.000

113 ->116 -0.13637

114 ->116 -0.15397

115 ->116 0.67799

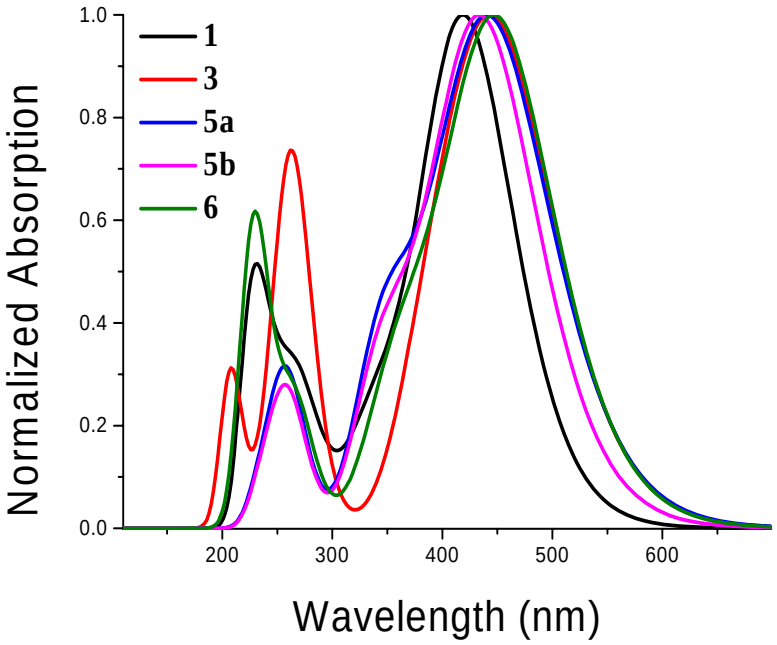

Figure S12. DFT calculated absorption spectra of **1**, **3, 5a, 5b** and **6** in Methanol.

DFT optimized coordinates for BODIPY 1, 3, 5a, 5b and 6.

Compound **1**

B	2.46534800	1.45569400	0.08911300
C	0.97526900	3.56055500	-0.20146200
C	-0.39393500	3.91611900	-0.25287300
C	-1.11378700	2.73739000	-0.16576300
C	-0.16832200	1.67722300	-0.06594000
C	-0.34641000	0.29631900	-0.00155900
C	0.75895300	-0.56999900	0.02171300
C	0.82992500	-1.97868400	0.01728700
C	2.18512100	-2.32091900	-0.01069400
C	2.90749200	-1.09881700	-0.01874900
F	2.99717800	1.72432100	1.33251000

F	3.33337300	1.77521200	-0.93074200
N	1.11099500	2.23564200	-0.08962500
N	2.06522900	-0.06667300	0.00236400
C	-1.72721000	-0.27460300	0.01817100
C	-2.40325900	-0.51437000	1.22757700
C	-2.40778100	-0.59894700	-1.16865200
C	-3.68983300	-1.05015100	1.25947200
C	-3.69453100	-1.13531100	-1.15761200
C	-4.33022100	-1.35858000	0.06155100
H	-4.17501600	-1.21959000	2.21405700
H	-4.18347900	-1.37179900	-2.09587800
H	-5.33244100	-1.77610300	0.07816000
H	-2.18808500	2.61599500	-0.18044600
H	-0.78148900	4.92088800	-0.34770300
H	1.84748700	4.19992800	-0.23870900
H	3.97932200	-0.95651200	-0.03585000
H	-0.01479900	-2.65459000	0.02242900
C	2.77211700	-3.65952600	-0.03516700
H	2.03500100	-4.49210700	-0.02115700
O	3.96956400	-3.88372200	-0.06815900
Cl	-1.63513000	-0.33048300	-2.71978800
Cl	-1.62368100	-0.13537500	2.75131200

Compound **3**

B	0.06083400	-1.40626800	0.16520900
C	2.58788300	-1.02500100	0.23831900

C	3.52940300	0.04452400	0.26723100
C	2.80750200	1.22376400	0.22207000
C	1.41417400	0.85815400	0.17961300
C	2.85503300	-2.49231800	0.24566000
C	5.01926800	-0.13406400	0.27586200
C	5.58294600	-0.38508500	-1.12760000
C	3.41819300	2.59186300	0.15870300
C	0.24694600	1.60686400	0.11191900
C	-1.01462200	0.96770900	-0.04756000
C	-2.32218400	1.50558300	-0.23515600
C	-3.19206600	0.41908300	-0.35807700
C	-2.40247200	-0.74053300	-0.23038800
C	0.29285900	3.10556200	0.20761000
C	-2.74390700	2.94289600	-0.31908300
C	-4.68048500	0.44004500	-0.55089000
C	-5.06278790	0.45493681	-2.03463930
C	-2.83895200	-2.14714700	-0.25835400
F	-0.09244300	-2.05923100	1.37274200
F	0.13356700	-2.31019700	-0.88031400
N	1.35468000	-0.53609200	0.18086400
N	-1.10578700	-0.40446500	-0.06429000
H	2.18692400	-2.99309200	0.95125600
H	3.89256200	-2.69670300	0.51620200
H	2.65428500	-2.91382900	-0.74426000
H	5.49704800	0.74711000	0.71602800
H	5.28230700	-0.97287500	0.93076600

H	5.13743000	-1.28226700	-1.56953900
H	6.66794600	-0.52064100	-1.10005600
H	5.35636300	0.45637300	-1.78971900
H	4.49233800	2.51429300	-0.02384800
H	3.28419400	3.14830300	1.09333400
H	2.98985300	3.19029900	-0.65028500
H	1.20951500	3.45079500	0.67787400
H	-0.54517700	3.47282900	0.80022100
H	0.22000700	3.56344000	-0.78632200
H	-3.78013800	3.00788700	-0.65725500
H	-2.13219000	3.51840800	-1.01950000
H	-2.69321100	3.44422500	0.65442000
H	-5.12980348	-0.42952729	-0.05896530
H	-5.09149450	1.33096041	-0.07001547
H	-4.66304321	1.35424286	-2.51050381
H	-6.14973860	0.45633363	-2.15769631
H	-4.65749823	-0.42112408	-2.55153171
H	-2.03860200	-2.90542800	-0.26207100
O	-4.01103700	-2.46377600	-0.28204300

Compound **5a**

B	0.98341800	2.91751600	-0.24859200
C	3.54915700	3.24062000	-0.01003100
C	4.72597600	2.46567400	0.06673700
C	4.32851700	1.13587700	0.05375800
C	2.91116600	1.12622100	-0.02798700
C	1.99747400	0.06484900	-0.02996000

C	0.62124700	0.30506300	-0.05052200
C	-0.48497700	-0.58404200	-0.00769000
C	-1.63784600	0.18985200	-0.00752100
C	-1.20906100	1.54205900	-0.05358000
F	0.80414600	3.43226400	-1.51847500
F	0.64835800	3.83165700	0.72823800
N	2.47010200	2.44737400	-0.06732700
N	0.12382400	1.60925700	-0.08407400
C	2.50028200	-1.34155300	0.01391100
C	2.73039000	-2.00525200	1.23202700
C	2.76631700	-2.06339000	-1.16295100
C	3.20172800	-3.31644000	1.28172600
C	3.23787100	-3.37500600	-1.13511600
C	3.45392000	-3.99635000	0.09260400
H	3.36512600	-3.78970600	2.24333800
H	3.43001100	-3.89418400	-2.06727500
H	3.82085300	-5.01793500	0.12284000
H	4.95775800	0.25807100	0.10670600
H	5.73403700	2.85161900	0.12882900
H	3.43896400	4.31678300	-0.02687400
H	-1.81674500	2.43553500	-0.07717000
H	-0.42196500	-1.66364200	0.02575200
C	-3.05392600	-0.28101900	0.04164800
H	-3.09439700	-1.34855200	-0.20653900
N	-3.92205300	0.53526400	-0.82000300
H	-3.79869000	0.23721900	-1.78721000

S	-3.82336900	-0.11768300	1.75050300
C	-5.31298600	0.41023600	-0.41913000
H	-5.91200500	1.16742800	-0.94485300
C	-5.33499100	0.70011500	1.08869200
H	-5.28210000	1.77700900	1.26229500
H	-6.22367600	0.29497000	1.57408400
C	-5.92224800	-0.95109200	-0.78469300
O	-5.38975800	-1.77324800	-1.49739500
O	-7.16055800	-1.11573000	-0.26688400
H	-7.47575200	-1.98780900	-0.57274500
Cl	2.50458600	-1.31114400	-2.72543400
Cl	2.42213200	-1.17984000	2.74828200

Compound **5b**

B	1.21206000	2.92873100	-0.37048300
C	3.79503500	3.15609800	-0.21244300
C	4.94261800	2.33686500	-0.13177100
C	4.49239300	1.02632900	-0.07123600
C	3.07297600	1.07167600	-0.11305400
C	2.11840100	0.05208700	-0.03391100
C	0.75169000	0.35057800	-0.02015500
C	-0.38450500	-0.48847500	0.11190500
C	-1.50516800	0.33286500	0.11713900
C	-1.02620300	1.66195700	-0.01109800
F	1.01618300	3.36948400	-1.66567100
F	0.94784000	3.91548900	0.55507200

N	2.68454500	2.40730500	-0.20284300
N	0.30751900	1.67070100	-0.09928500
C	2.56372400	-1.37076700	0.06576900
C	2.79899500	-1.98422600	1.30903300
C	2.76738100	-2.15857400	-1.08068400
C	3.21485200	-3.31116400	1.41080600
C	3.18359600	-3.48664400	-1.00060200
C	3.40576800	-4.05746100	0.25040600
H	3.38411700	-3.74466100	2.39001700
H	3.32906300	-4.05752500	-1.91075100
H	3.73000500	-5.09139400	0.32142200
H	5.08699500	0.12653800	0.00679300
H	5.96653100	2.68367800	-0.11482400
H	3.72786800	4.23406600	-0.27642900
H	-1.59817900	2.57864200	-0.04596600
H	-0.36354400	-1.56611300	0.20334100
C	-2.94134900	-0.06406700	0.25803900
H	-3.03181800	-1.15062000	0.09789400
N	-3.76537100	0.71395000	-0.66865000
H	-3.36470500	0.62463700	-1.60077100
S	-3.46824500	0.25133700	2.01084100
C	-5.18426200	0.36093500	-0.70880100
C	-5.24558800	-0.16515000	1.79294300
H	-5.35630700	-1.24460000	1.64088100
H	-5.73053600	0.08590600	2.74098500
C	-5.87808800	0.61384900	0.63894700

H	-6.93092800	0.32815200	0.54490100
H	-5.82590700	1.68670000	0.84742100
H	-5.64515500	1.02828300	-1.45137400
C	-5.49010900	-1.05734600	-1.22931400
O	-6.45101900	-1.73088600	-0.93124800
O	-4.56803000	-1.47061500	-2.13698000
H	-4.86513400	-2.34773300	-2.44565100
Cl	2.56974600	-1.07364000	2.78954500
Cl	2.49470500	-1.47057300	-2.67094200

Compound **6**

B	-0.40162019	0.19201403	-0.11235067
C	-2.68704200	-0.82386889	-0.92770282
C	-3.97473529	-0.31783553	-1.22413159
C	-3.94481286	1.08793766	-1.13026172
C	-2.63587596	1.44440704	-0.81768369
C	-2.27576555	-2.30715627	-0.94050908
C	-5.20609211	-1.16753269	-1.58971704
C	-5.96277552	-1.55178111	-0.30519735
C	-5.13016071	2.04828797	-1.34422245
C	-2.06645785	2.72895369	-0.72241413
C	-0.66439962	2.79071528	-0.60086047
C	0.17449478	3.89976510	-0.68252256
C	1.49862721	3.41937729	-0.60645887
C	1.46559700	2.01242101	-0.44962970
C	-2.92959516	4.00307273	-0.78576028

C	-0.26123513	5.36919355	-0.83957102
C	2.77270730	4.28312505	-0.68162522
C	3.17733516	4.72777508	0.73645287
F	0.38290697	-0.84406092	-0.77672502
F	-0.39830208	-0.05481027	1.32710376
N	-1.89028075	0.20704228	-0.62256098
N	0.18579392	1.62586663	-0.38663314
H	-1.91971666	-2.57009171	-1.91462446
H	-3.12199902	-2.91443568	-0.69460330
H	-1.50028950	-2.46840634	-0.22151725
H	-5.85224963	-0.60401420	-2.23019933
H	-4.88870427	-2.05539445	-2.09535474
H	-5.31543145	-2.11473628	0.33418076
H	-6.81745422	-2.14382274	-0.55806776
H	-6.28084779	-0.66449623	0.20092736
H	-5.81830454	1.61694663	-2.04094199
H	-4.76980918	2.97943693	-1.72917901
H	-5.62596523	2.21626201	-0.41091464
H	-3.89694654	3.79955179	-0.37674116
H	-3.03143588	4.31492029	-1.80450251
H	-2.45944123	4.78059756	-0.22044073
H	0.48927722	5.90815850	-1.37936244
H	-0.38987279	5.80885004	0.12738602
H	-1.18603044	5.41130465	-1.37638639
H	3.56672636	3.71158726	-1.11557514
H	2.58293906	5.14593571	-1.28592768

H	2.38300169	5.29639793	1.17282577
H	4.05965754	5.33076668	0.68236323
H	3.37139544	3.86530431	1.33951457
C	2.69004986	1.08210904	-0.35558096
H	2.97081288	0.77463463	-1.34094405
N	3.88098740	1.72991695	0.28307230
H	4.71936424	1.28441671	-0.03161648
S	2.25181400	-0.27690803	0.71778068
C	3.78814349	1.45379984	1.72349095
H	2.92241404	1.91524336	2.15205456
C	3.66283202	-0.08314856	1.73324290
H	3.53142960	-0.49918720	2.71049378
H	4.52876943	-0.53414302	1.29392061
C	5.02576980	1.94620776	2.49568171
O	4.87249915	2.52239905	3.79575900
H	4.92898226	1.83155223	4.46040000
O	6.17130240	1.84131901	1.98389238