Supporting Information

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Molecular Formula String Table

COMP	SMILE
2	O=C(NC1(C[C@H]2C3)C[C@H]3C[C@H](C2)C1)C4=CN(CCCCC)C5=C(C=C(NC6=CC=C([N+]([O-])=O)C7=N[Se]N=C67)C=C5)C4
3	O=C(NC12C[C@H]3C[C@H](C[C@@H](C3)C2)C1)C4=CN(CCCCC)C5=CC=C(NC(CCCCCN6C(C=CC=C7)=C7C(C)(C)/C6=C/C=C/C=C/C8=[N+](C)C(C=CC=C9)=C9C8(C)C)=O)C=C5C4=O.[I-]
4	O=C(NC12C[C@H]3C[C@H](C[C@@H](C3)C2)C1)C4=CN(CCCCC)C5=CC=C(NC(CCCCCN6C(C=CC=C7)=C7C(C)(C)/C6=C/C=C/C=C/C=C/C8=[N+](C)C(C=CC=C9)=C9C8(C)C)=O)C=C5C4=O.[I-]
5	O=C(NC12C[C@H]3C[C@H](C[C@@H](C3)C2)C1)C4=CN(CCCCC)C5=CC=C(NC(COC6=CC=C(C7=CC=C8N7[B-](F)(F)[N+]9=C(C%10=CC=CS%10)C=CC9=C8)C=C6)=O)C=C5C4=O
11	O=C(NC1(C[C@H]2C3)C[C@H]3C[C@H](C2)C1)C4=CC=CC=C4OCCNC5=CC=C([N+]([O-])=O)C6=NON=C65
12	O=C(NC1(C[C@H]2C3)C[C@H]3C[C@H](C2)C1)C4=CC=CC=C4OCCNC5=CC=C([N+]([O-])=O)C6=N[Se]N=C65

Table S1. Frontier orbital energies and HOMO–LUMO gaps of the phenyl (**13**) and cyclohexyl (**14**) derivatives, computed at the B3LYP-D3/6-31G** level of theory on the corresponding optimized geometries. Orbital energies are reported in hartree (Ha); gaps are given in both hartree and electronvolts (1 Ha = 27.2114 eV)

Compound	**HOMO (Ha)**	**LUMO (Ha)**	**$\Delta E_{HOMO–LUMO}$ (Ha)**	**$\Delta E_{HOMO–LUMO}$ (eV)**
13	−0.211791	−0.111297	0.100494	2.735
14	−0.216844	−0.101912	0.114932	3.127

Table S2. Molar extinction coefficients (ε) and Quantum Yield values.

Compound	**ε λ_{exc}**[a]			**QY**[b]	
	MeOH	**$CHCl_3$**	**PBS**	**MeOH**	**$CHCl_3$**
VM7	8400	8300	3900	0.82%	0.80%
2	7600	6500	2100	0.75%	1.04%

[a]Value measured in organic solvents ($CHCl_3$, DMSO, MeOH) and aqueous solution (PBS) at a concentration of 10^{-5} M, at the maximum excitation wavelength for each of the solvents. [b] Value measured in MeOH and $CHCl_3$ at a concentration providing Absorbance between 0.08 and 0.10 at the excitation wavelength.

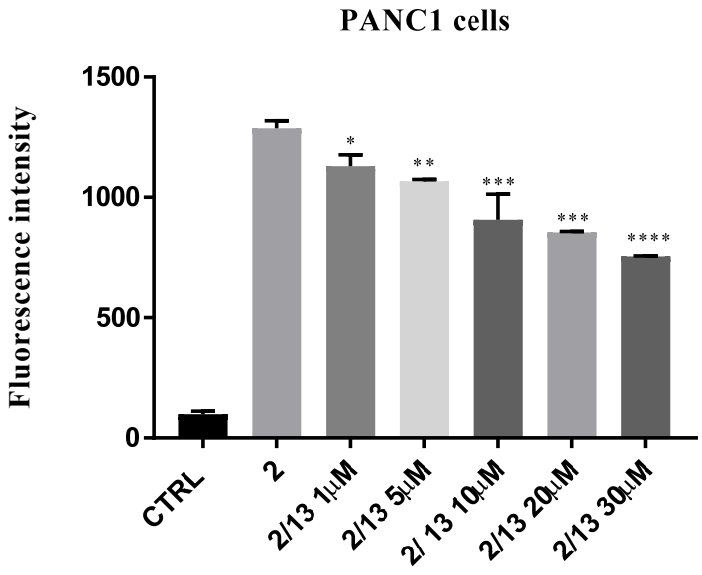
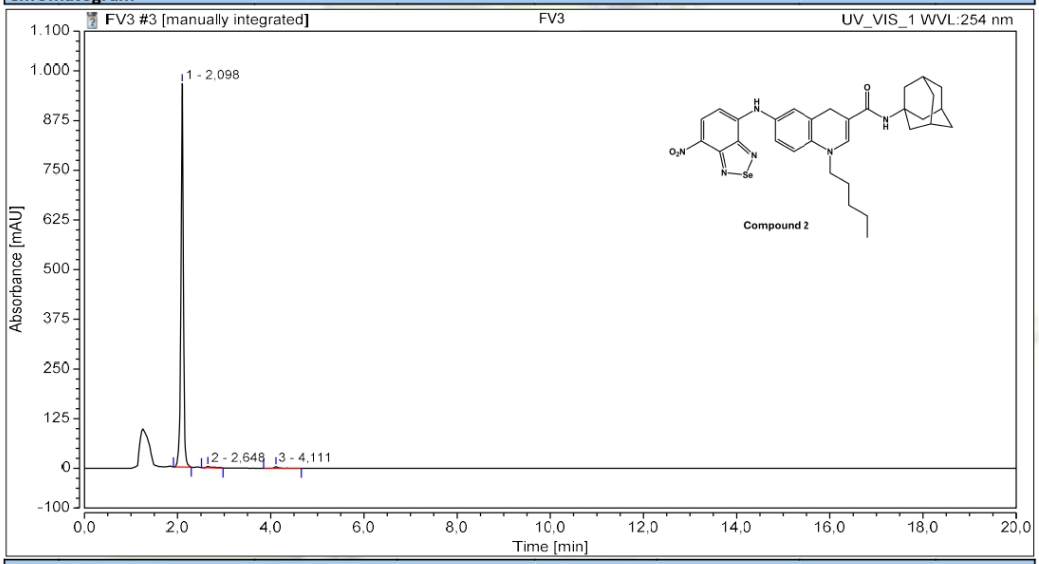


Figure S1. Flow-cytometry analysis with compound **2** at 10 μM alone and in the absence of the CB2R reference compound **13** (displacing agent) at different concentrations (1, 5, 10, 20, 30 μM) in the high CB2R level expressing cells PANC-1. CTRL represents cells without the fluorescent probe.

One-way ANOVA followed by Tukey post-hoc test was applied. Significance of symbols as follows: 2 symbols = $p < 0.005$; 3 symbols = $p < 0.001$; and 4 symbols = $p < 0.0001$. Legend for symbols as follows: * indicates vs **2** 10 μM.

HPLC chromatograms of representative final fluorescent compounds

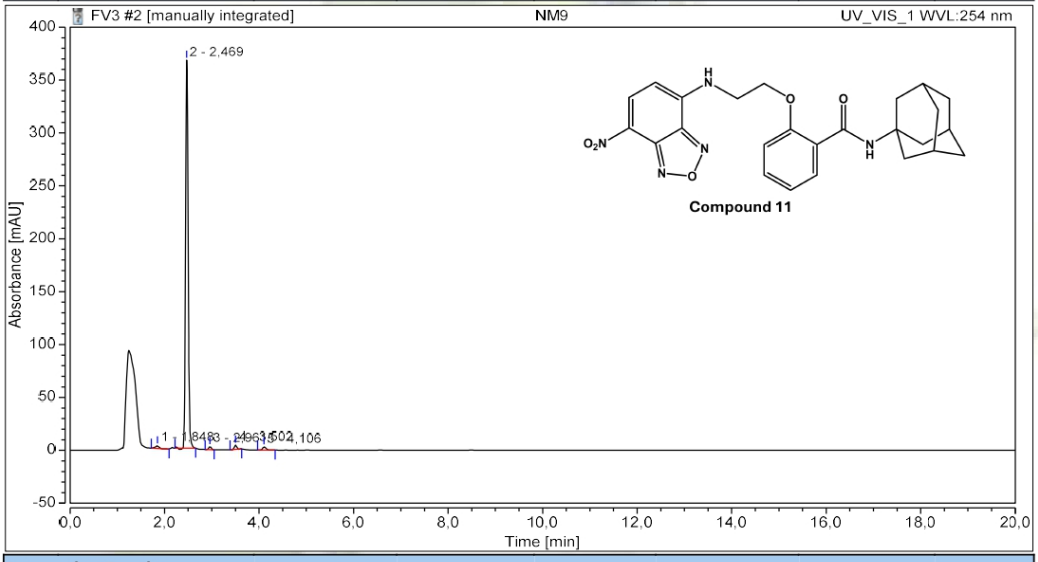
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		2,098	60,925	964,659	98,51	99,21	n.a.
2		2,648	0,583	3,669	0,94	0,38	n.a.
3		4,111	0,340	4,043	0,55	0,42	n.a.
Total:			**61,847**	**972,371**	**100,00**	**100,00**	

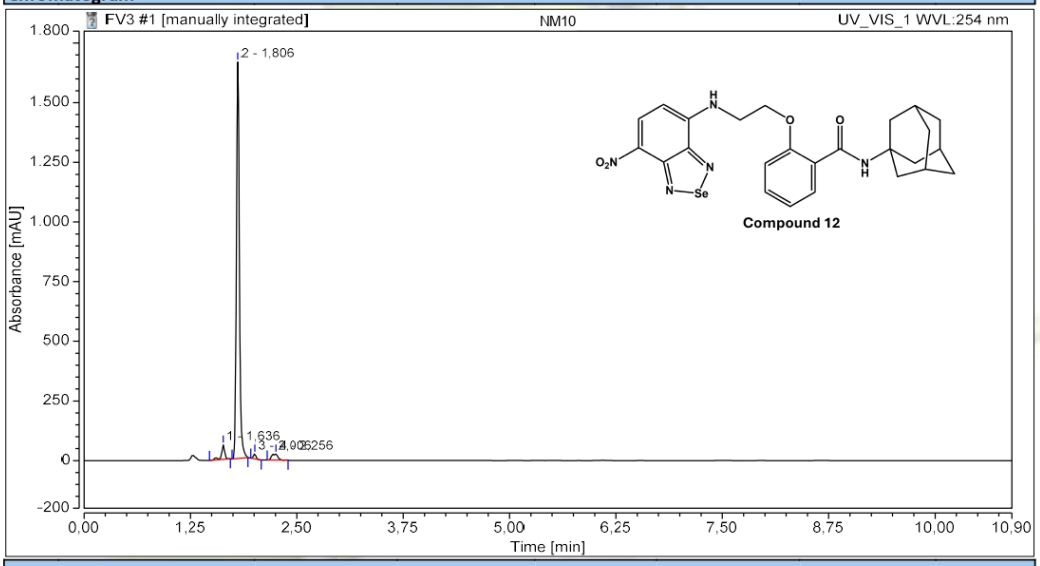
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		1,848	0,190	2,544	0,81	0,67	n.a.
2		2,469	22,632	366,693	96,43	96,67	n.a.
3		2,961	0,188	2,977	0,80	0,78	n.a.
4		3,502	0,206	3,974	0,88	1,05	n.a.
5		4,106	0,253	3,129	1,08	0,82	n.a.
Total:			**23,470**	**379,317**	**100,00**	**100,00**	

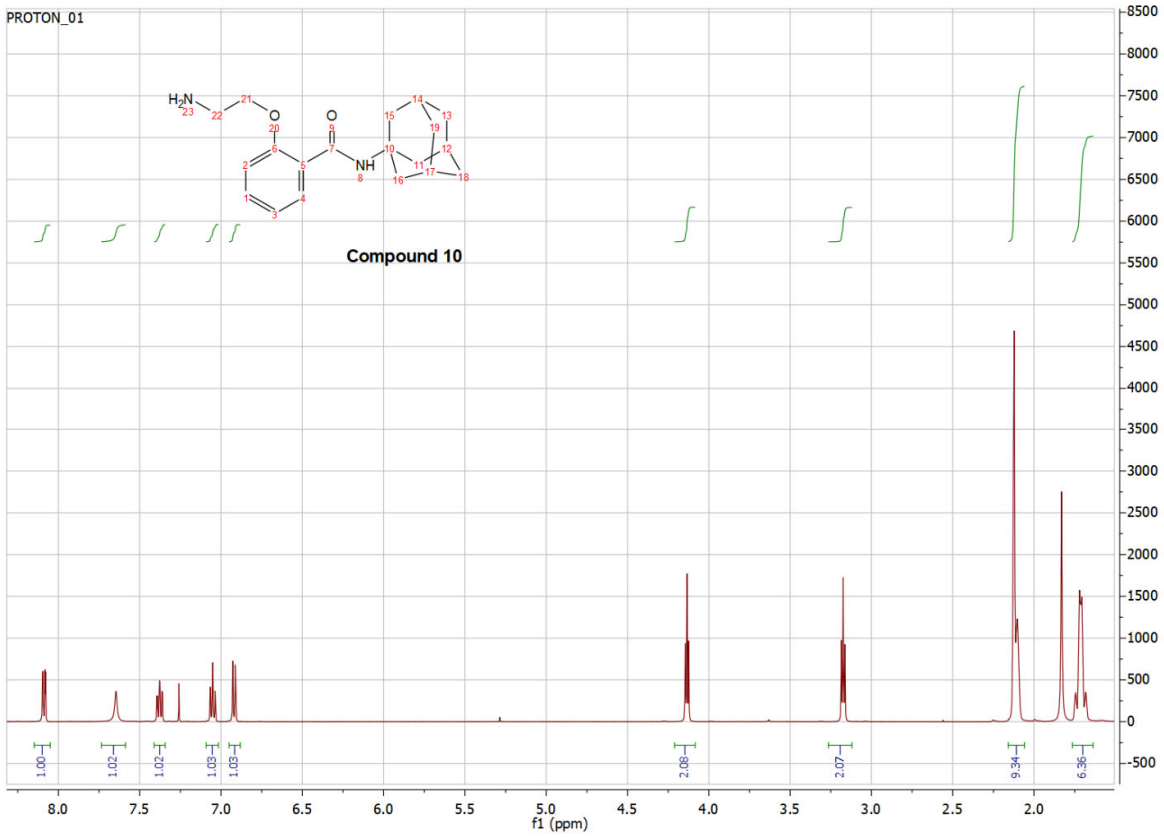
Chromatogram



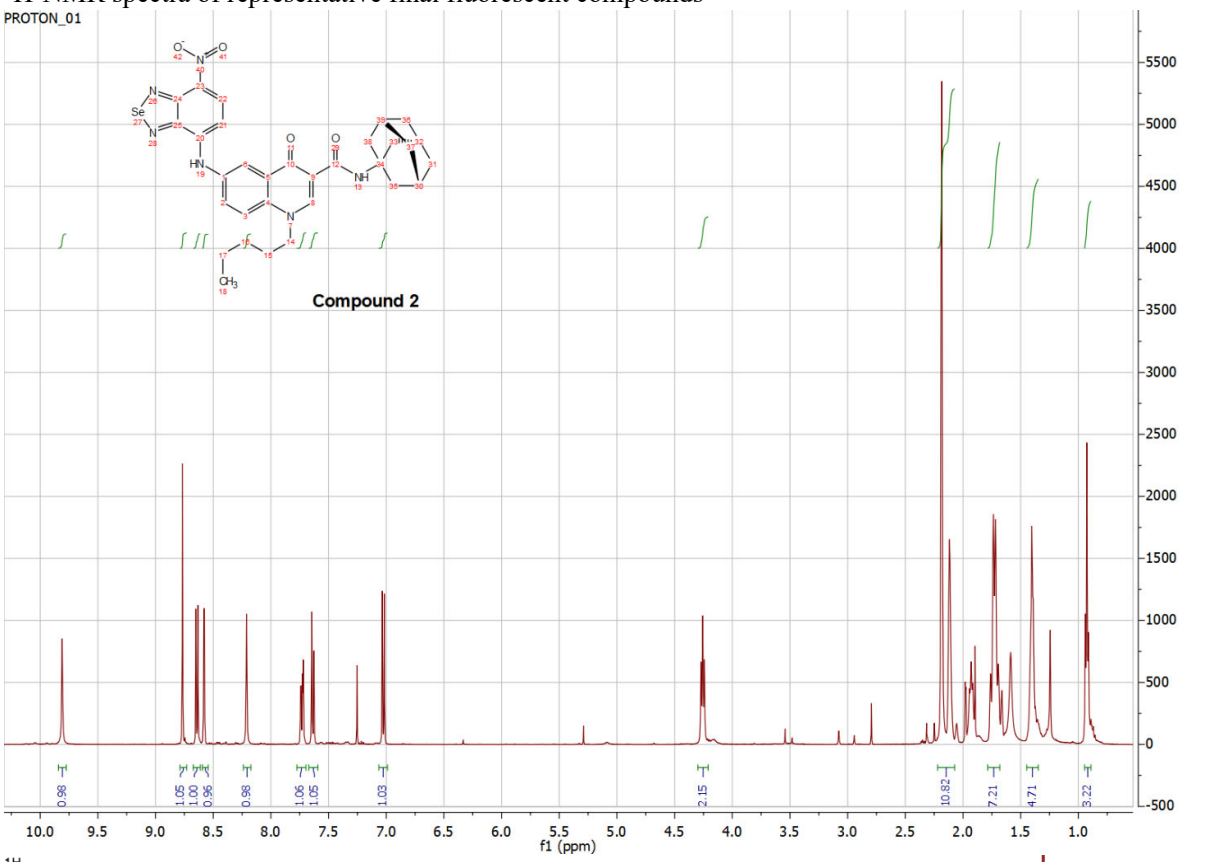
Integration Results

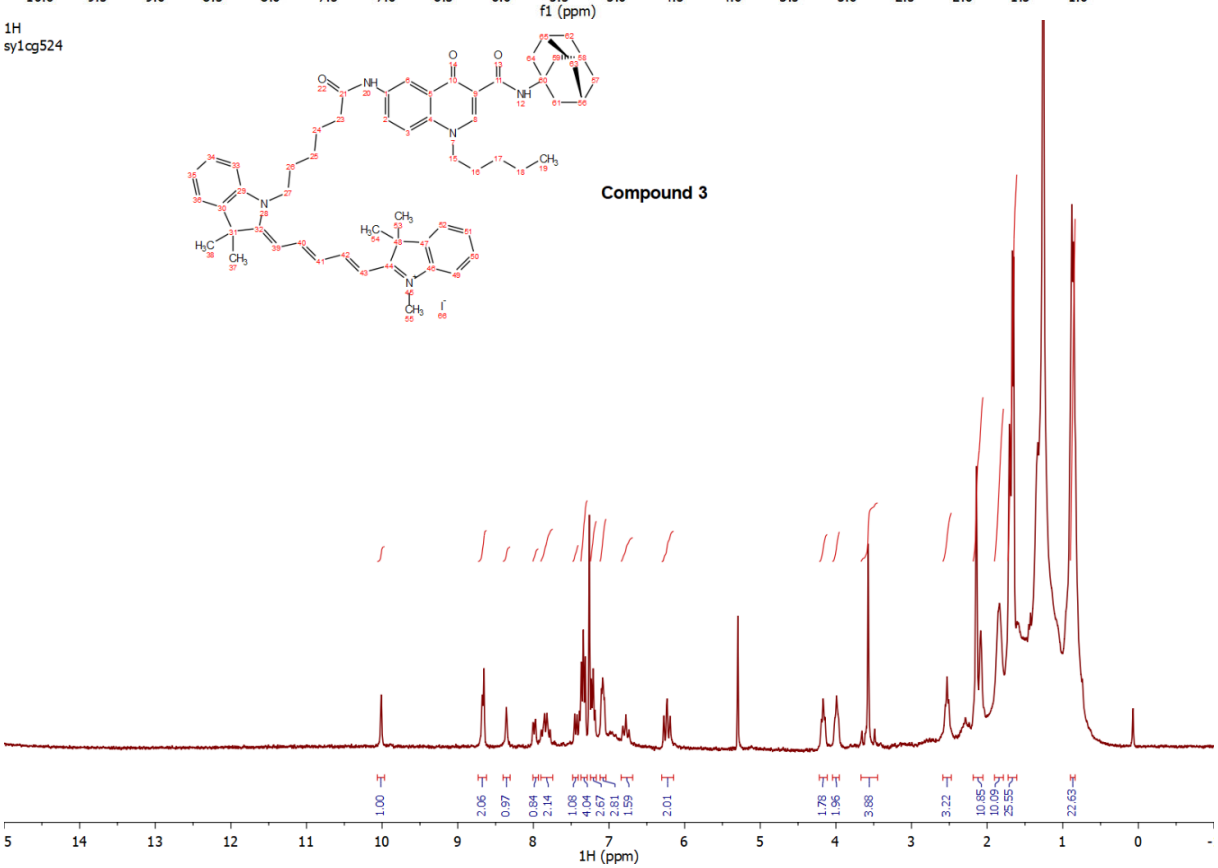
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		1,636	2,617	60,357	3,58	3,42	n.a.
2		1,806	67,780	1661,494	92,65	94,02	n.a.
3		2,006	0,674	20,003	0,92	1,13	n.a.
4		2,256	2,085	25,344	2,85	1,43	n.a.
Total:			**73,156**	**1767,198**	**100,00**	**100,00**	

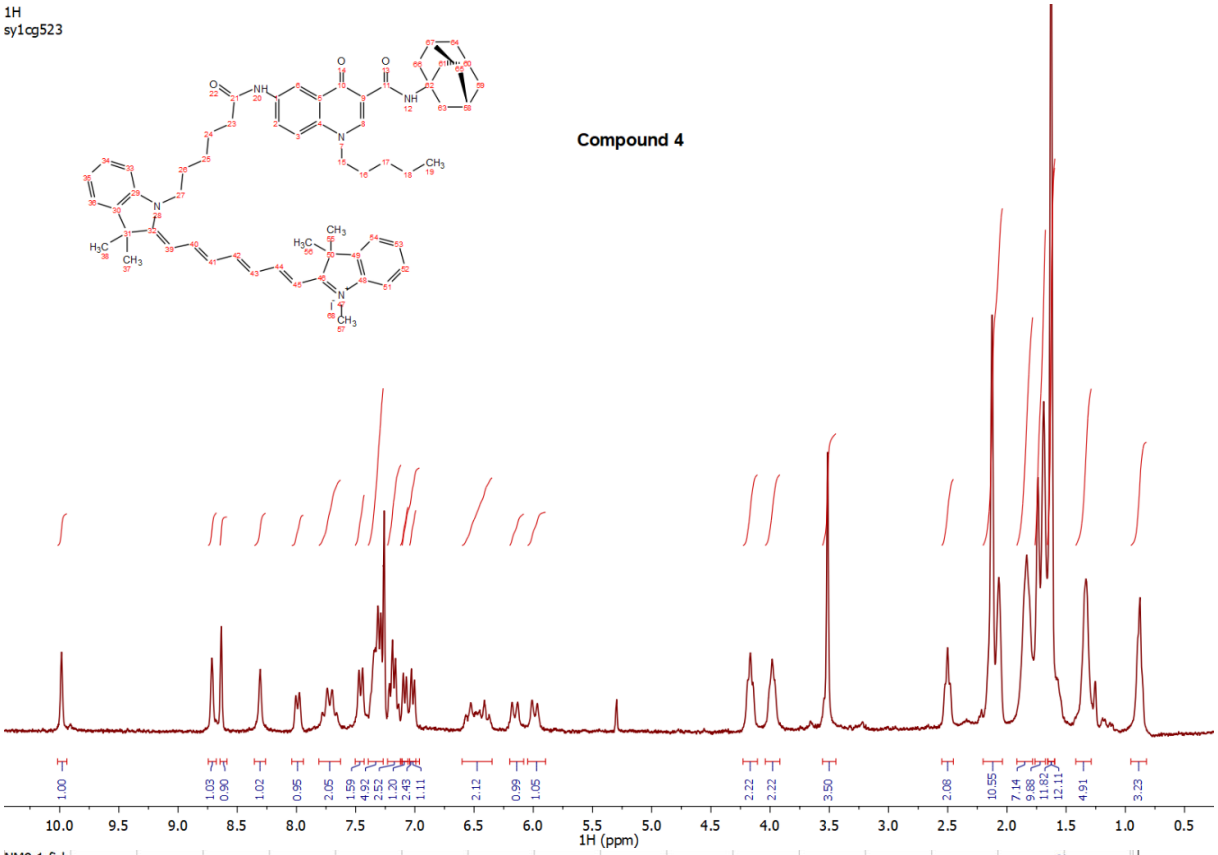
[1]H-NMR spectra of the key ammine

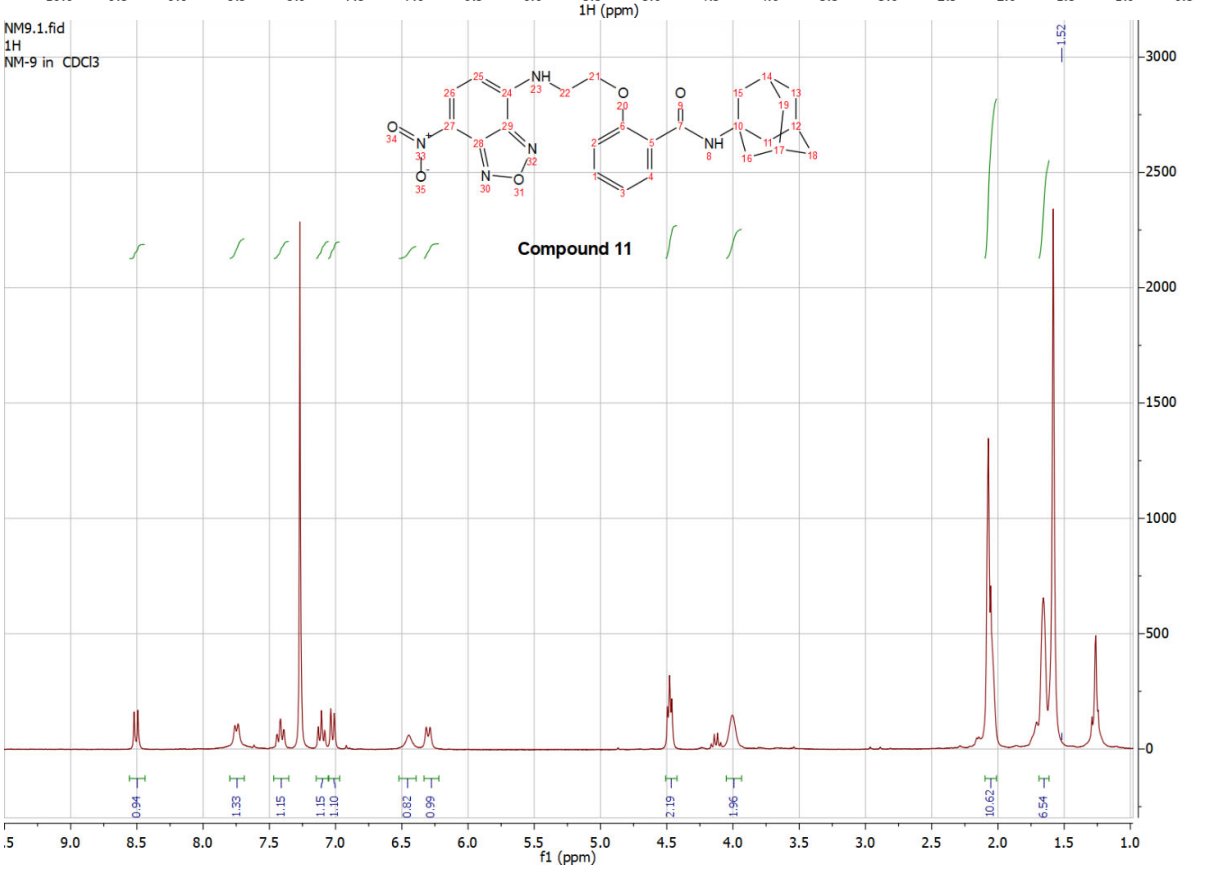


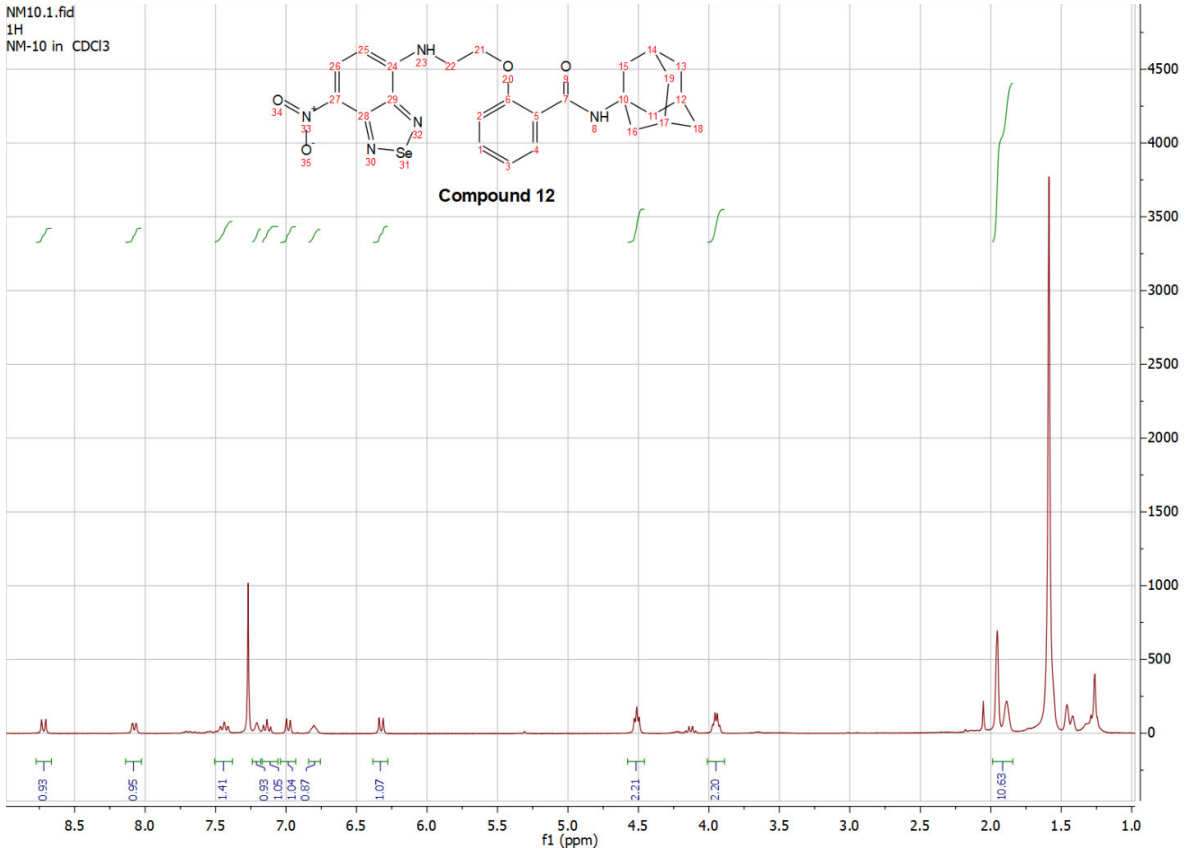
[1]H-NMR spectra of representative final fluorescent compounds






1H
sy1cg523
Compound 4
1H (ppm)


NM9.1.fid
1H
NM-9 in CDCl3
Compound 11
f1 (ppm)


NM10.1.fid
1H
NM-10 in CDCl3
Compound 12
f1 (ppm)