

Coumarin Based Dual Chemosensor for Co²⁺ and Cu²⁺ Ions and Volatile Acid Vapour Sensing, Validation from DFT Studies, Zebrafish Bioimaging

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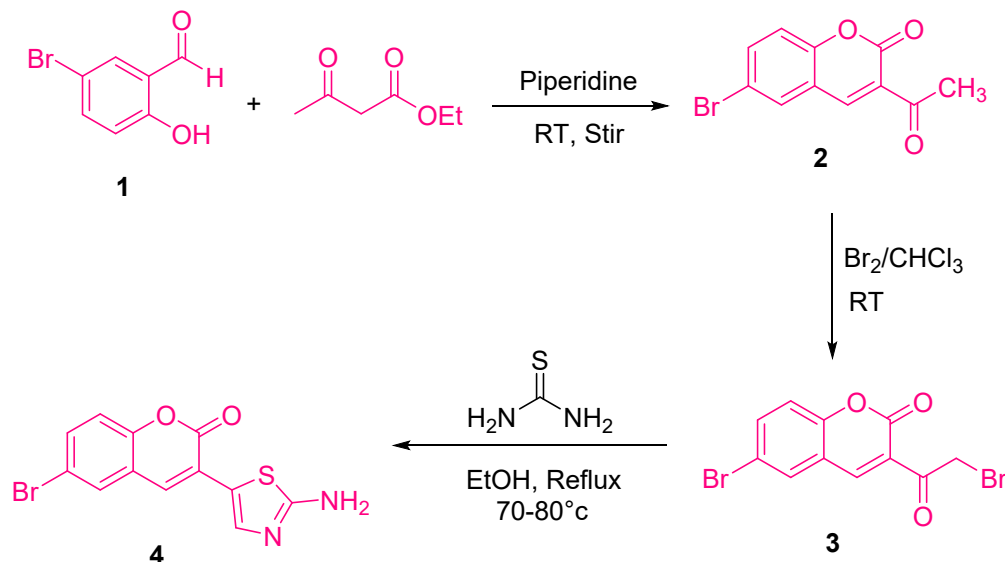
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Scheme 1. Synthetic strategy for coumarin thiazole amine (4).

Solvatochromic study:

To investigate the solvatochromic behavior of **TBCM**, various linear correlation techniques established by researchers such as Bilot–Kawski, Lippert–Mataga, Bakhshiev, and Kawski–Chamma–Viallet, were employed to assess the dipole moment values of the ground and singlet excited state by varying dielectric constant (ϵ) and refractive index (n). These methods involved linking spectroscopic characteristics with different solvent polarity functions. The equations that elucidate the relationship between solvatochromic shifts and solvent polarity functions are provided below.

Bilot–Kawski [1, 2] method to determine ground and excited state dipole moment

$$\bar{\nu}_a - \bar{\nu}_f = m_1 F_{B-K}(n, \epsilon) + \text{constant} \quad (1)$$

$$\bar{\nu}_a + \bar{\nu}_f = -m_2 \phi(n, \epsilon) + \text{constant} \quad (2)$$

$$\phi(n, \epsilon) = m_1 F_{B-K}(n, \epsilon) + 2g(n)$$

$$F_{B-K}(n, \epsilon) = \frac{2n^2 + 1}{n^2 + 2} \left[\frac{\epsilon - 1}{\epsilon + 2} - \frac{n^2 - 1}{n^2 + 2} \right] \text{ and } g(n) = \frac{3}{2} \left[\frac{n^4 - 1}{(n^2 + 2)^2} \right]$$

here, ν_a and ν_f represents the absorption and emission maxima in terms of wavenumber and the slopes

m_1 and m_2 can be calculated using

$$m_1 = \frac{2(\mu_e - \mu_g)^2}{hca^3} \quad \& \quad m_2 = \frac{2(\mu_e^2 - \mu_g^2)}{hca^3}$$

The constants h and c represent Planck's constant and the speed of light in a vacuum, respectively, with $h=6.626 \times 10^{-27}$ erg s and $c=2.998 \times 10^{10}$ cms⁻¹. The variable a designates the Onsager cavity radius, which reflects the radius of the spherical cavity in which the fluorophore molecule is placed

$a = \left[\frac{3M}{4\pi\rho N_A} \right]^{\frac{1}{3}}$). The variables μ_g and μ_e are the ground and excited state dipole moment and if they are parallel then the equations (3) and (4) are obtained

$$\mu_g = \frac{m_2 - m_1}{2} \left[\frac{hca^3}{2m_1} \right]^{\frac{1}{2}}$$

(3)

$$\mu_e = \frac{m_2 + m_1}{2} \left[\frac{hca^3}{2m_1} \right]^{\frac{1}{2}} \quad \text{also} \quad \mu_e = \mu_g \frac{m_2 + m_1}{m_2 - m_1} \quad \text{for } m_2 > m_1$$

(4)

If μ_g and μ_e are non-collinear vectors with an angular separation denoted as ϕ , the magnitude of ϕ can be determined by employing Equation (5).

$$\cos \phi = \frac{1}{2\mu_g\mu_e} \left[(\mu_g^2 + \mu_e^2) - \frac{m_1}{m_2} (\mu_g^2 - \mu_e^2) \right] \quad (5)$$

Lippert–Mataga [3], Bakhshiev [4], and Kawski–Chamma–Viallet [5, 6] method to estimate singlet excited state dipole moment

$$\bar{\nu}_a - \bar{\nu}_f = m_L - M F_{L-M}(n, \epsilon) + \text{constant} \quad (6)$$

$$\bar{\nu}_a - \bar{\nu}_f = m_B F_B(n, \epsilon) + \text{constant} \quad (7)$$

$$\frac{\bar{\nu}_a + \bar{\nu}_f}{2} = -m_{K-C-V} F_{K-C-V}(n, \varepsilon) + \text{constant}$$

(8)

$$F_{LM}(n, \varepsilon) = \frac{\varepsilon - 1}{2\varepsilon + 1} - \frac{n^2 - 1}{2n^2 + 1}$$

$$F_B(n, \varepsilon) = \frac{2n^2 + 1}{n^2 + 2} \left[\frac{\varepsilon - 1}{\varepsilon + 2} - \frac{n^2 - 1}{n^2 + 2} \right]$$

$$F_{KCV}(n, \varepsilon) = \frac{2n^2 + 1}{2(n^2 + 2)} \left(\frac{\varepsilon - 1}{\varepsilon + 2} - \frac{n^2 - 1}{n^2 + 2} \right) + \frac{3(n^4 - 1)}{2(n^2 + 2)^2}$$

where m_{L-M} , m_B , m_{K-C-V} are the slopes derived from the graphs $\bar{\nu}_a - \bar{\nu}_f$ vs. $F_{L-M}(n, \varepsilon)$,

$\bar{\nu}_a - \bar{\nu}_f$ vs. $F_B(n, \varepsilon)$, $\frac{\bar{\nu}_a + \bar{\nu}_f}{2}$ vs. $F_{K-C-V}(n, \varepsilon)$ and can be calculated by the following equations.

$$m_{LM} = \frac{2(\mu_e - \mu_g)^2}{hca^3} \quad \& \quad m_B = \frac{2(\mu_e - \mu_g)^2}{hca^3} \quad \& \quad m_{KCV} = \frac{2(\mu_e^2 - \mu_g^2)}{hca^3}$$

Table S1. The maximum absorption and emission data and spectral shift of **TBCM** in alcohols.

Solvents	λ_a (nm)	λ_f (nm)	ϑ_a (cm ⁻¹)	ϑ_f (cm ⁻¹)	$\vartheta_a - \vartheta_f$	$\vartheta_a + \vartheta_f$	$(\vartheta_a + \vartheta_f)/2$
Methanol	348	409	28735.63	24449.88	4285.75	53185.51	26592.75
Ethanol	349	403	28653.3	24813.9	3839.39	53467.19	26733.6
Propanol	350	403	28571.43	24813.9	3757.53	53385.32	26692.66
Butanol	350	403	28571.43	24813.9	3757.53	53385.32	26692.66
Pentanol	350	404	28571.43	24752.48	3818.95	53323.9	26661.95
Hexanol	351	406	28490.03	24630.54	3859.48	53120.57	26560.29
Heptanol	352	405	28409.09	24691.36	3717.73	53100.45	26550.22
Octanol	353	406	28328.61	24630.54	3698.07	52959.15	26479.58
Nonanol	352	404	28409.09	24752.48	3656.61	53161.57	26580.78
Decanol	353	405	28328.61	24691.36	3637.25	53019.97	26509.98

Table S2. The solvent polarity functions for various correlation methods with refractive index(n) and dielectric constant (ϵ).

Solvent	n	ϵ	$F(n, \epsilon)$	$\phi(n, \epsilon)$	F_{L-M}	F_B	F_{K-C-V}
Methanol	1.329	33.70	0.857478	1.305769	0.309015	0.857478	0.652885
Ethanol	1.361	24.30	0.811743	1.303191	0.288592	0.811743	0.651596
Propanol	1.385	20.60	0.78123	1.304843	0.2746	0.78123	0.652421
Butanol	1.399	17.40	0.749445	1.291732	0.263326	0.749445	0.645866
Pentanol	1.410	14.80	0.715799	1.27271	0.252415	0.715799	0.636355
Hexanol	1.418	13.00	0.686092	1.25361	0.243163	0.686092	0.626805
Heptanol	1.424	11.30	0.651766	1.227223	0.233144	0.651766	0.613611
Octanol	1.429	9.80	0.613759	1.195822	0.222223	0.613759	0.597911
Nonanol	1.434	9.00	0.588431	1.177089	0.214439	0.588431	0.588544
Decanol	1.437	8.00	0.552767	1.145378	0.204166	0.552767	0.572689

Table S3. The calculated slope, intercept, Onsager cavity radius, ground and excited state dipole moments for various correlation methods of TBCM in alcohols.

Methods		Slope	Intercept	Correlation Coefficient (R^2)	a_0 (Å)	μ_g (D)	μ_e (D)
Bilot-Kawski	m_1	720.9626	3240.9816	0.95008	11.23	12.9229	17.931
	m_2	4441.1005	47634.5741	0.92891			
Lippert-Mataga	m_{L-M}	2033.1265	3229.5466	0.91017			21.332
Bakhshiev	m_B	720.9626	3240.9816	0.95008			17.932
Kawski-Chamma-Viallet	m_{K-C-V}	4441.0895	23817.2958	0.92892			25.322
Gaussian 09					7.05	6.2066	26.4932

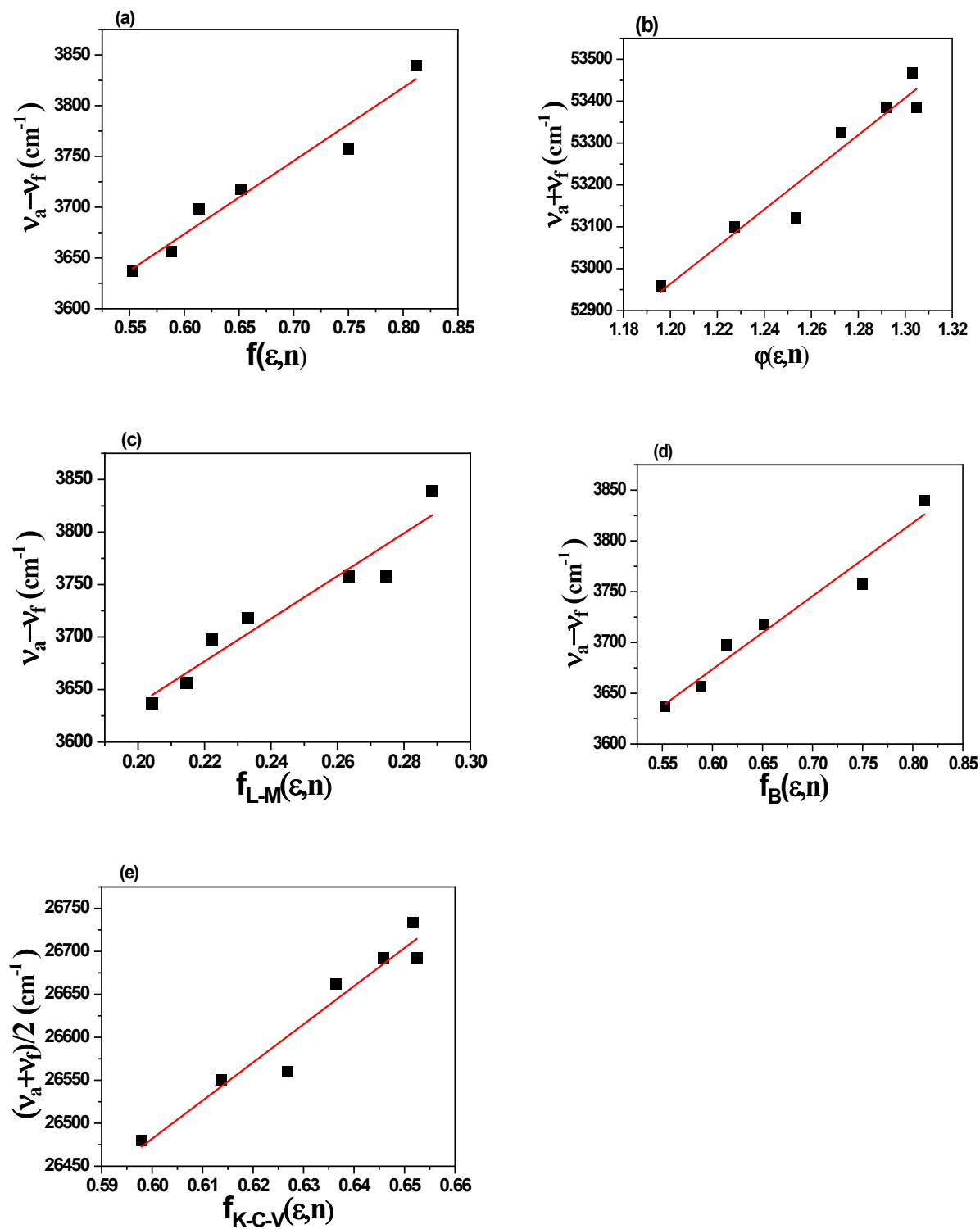


Figure S1. Linear correlation plots of TBCM for (a), (b) Bilot-Kawski, (c) Lippert-Mataga, (d) Bakhshiev, (e) Kawski-Chamma-Viallet methods in polar solvents.

Mulliken charges analysis

The electric charges present on individual atoms play a crucial role in determining various aspects of a molecule such as stability, molecular orbitals, polarizability, and other electronic properties [10]. The ground state and excited state Mulliken charges are computed using DFT and TDDFT with B3LYP/6311-G basis set. Detailed information regarding the ground state and excited state mulliken charges can be found in **Table S4**. A visual representation of the natural population analysis is presented in the form of a bar graph, as depicted in **Figure S2**. In the ground state, certain atoms with high electronegativity, such as C46, C53, O1, and O2, are identified as donors within the molecular framework. Approximately half of the carbon atoms exhibit a positive charge, contributing to the overall stability of the structure.

Table S4. The ground and excited state Mulliken charge of each atom of TBCM in alcohols.

	Atom	Ground state	Excited state
1	O	-0.32816	-0.39771
2	O	-0.4631	-0.53102
3	C	0.069565	0.007318
4	C	-0.07521	0.008213
5	H	0.176644	0.25056
6	N	-0.38838	-0.40998
7	N	-0.27465	-0.30205
8	N	-0.95993	-0.89443
9	N	-0.8041	-0.85867
10	S	0.523765	0.390355
11	C	-0.12081	-0.11822
12	H	0.144463	0.152877
13	C	-0.19507	-0.19037
14	H	0.142106	0.152049
15	C	-0.17571	-0.16625
16	H	0.144839	0.149119
17	C	-0.06508	-0.09139
18	H	0.170794	0.174142
19	C	0.011157	0.030525
20	C	-0.0559	-0.05555
21	H	0.194574	0.196772
22	C	-0.09947	-0.0459
23	C	-0.02754	-0.05616
24	H	0.170154	0.173194

25	C	-0.15759	-0.15546
26	H	0.155	0.158684
27	C	-0.12774	-0.12157
28	H	0.153886	0.160745
29	C	-0.15596	-0.15082
30	H	0.151775	0.161694
31	C	-0.06508	-0.05223
32	H	0.171869	0.186174
33	C	0.301058	0.363811
34	C	-0.19665	-0.24146
35	C	0.257587	0.355202
36	C	0.044762	0.045087
37	C	-0.06878	-0.08177
38	H	0.17188	0.20509
39	C	-0.18004	-0.14246
40	H	0.190508	0.195193
41	C	0.303097	0.275984
42	C	-0.19117	-0.18223
43	H	0.192842	0.206779
44	C	0.136903	0.077241
45	H	0.196114	0.177331
46	C	-0.54953	-0.45629
47	C	-0.04628	-0.15424
48	C	0.021256	-0.06807
49	H	0.199387	0.147874
50	C	-0.0665	-0.06301
51	C	-0.03348	-0.08621
52	H	0.186491	0.15742
53	C	-0.47045	-0.40443
54	C	-0.04969	-0.10542
55	H	0.181433	0.150505
56	C	-0.1294	-0.14958
57	H	0.195361	0.161166
58	C	0.227333	0.23928
59	C	0.44806	0.477176
60	C	-0.13236	-0.11043
61	H	0.148502	0.179371
62	C	-0.16048	-0.15684
63	H	0.147684	0.175826
64	C	-0.13721	-0.10102
65	H	0.18507	0.195948

66	C	0.236373	0.19543
67	C	-0.14187	-0.09934
68	H	0.191774	0.202673
69	C	-0.16065	-0.15661
70	H	0.150063	0.178503
71	C	-0.13879	-0.09975
72	H	0.187355	0.193857
73	C	0.238048	0.19206
74	C	-0.141	-0.09656
75	H	0.187577	0.203982
76	C	-0.15882	-0.15316
77	H	0.145143	0.183475
78	C	-0.13228	-0.10697
79	H	0.147934	0.183148
80	C	-0.16019	-0.15578
81	H	0.148366	0.176852
82	Br	0.236534	0.120694

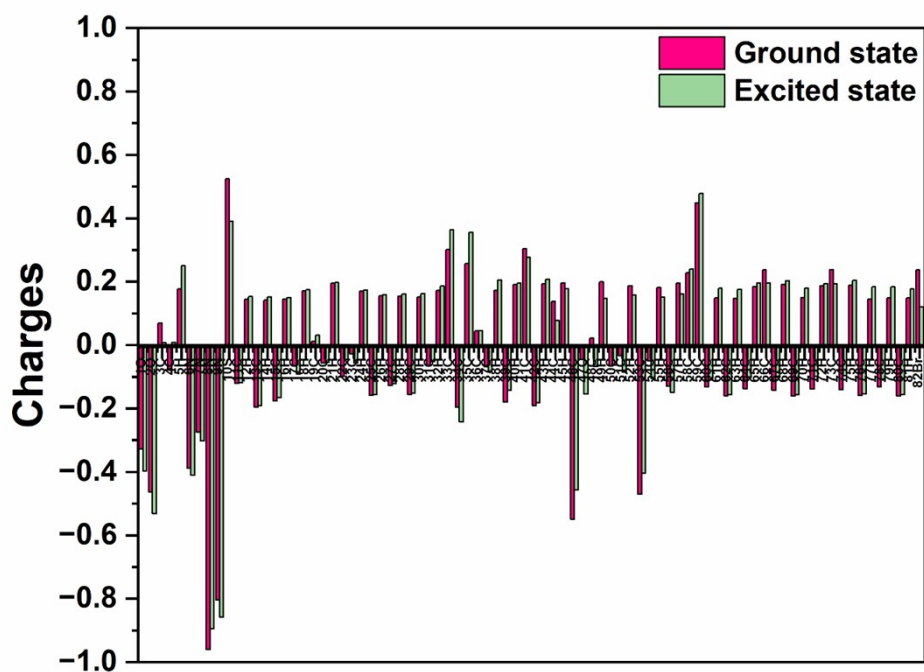


Figure S2. Bar graph showing Mulliken charges of each atom in both ground and excited state.

Tables S5. Second order Perturbation theory of Fock matrix element in NBO analysis of TBCM.

Donor(i)	Type	ED/e	Acceptor(j)	Type	ED/e	E(2)	E(i)-E(j)	F(i,j)
C 50 - C 58	π^*	0.44336	C 54 - C 56	π^*	0.29946	258.14	0.01	0.082
C 41 - C 42	π^*	0.39817	C 37 - C 39	π^*	0.29485	207.07	0.01	0.079
C 34 - C 35	π^*	0.32615	C 19 - C 20	π^*	0.37392	180.94	0.01	0.066
N 6 - C 33	π^*	0.37702	C 4 - C 36	π^*	0.40056	80.45	0.03	0.067
			C 34 - C 35	π^*	0.32615	52.35	0.03	0.058
C 3 - N 7	π^*	0.35203	C 44 - C 46	π^*	0.30398	98.98	0.02	0.073
O 1 - C 59	π^*	0.28820	C 47 - C 48	π^*	0.20835	52.98	0.03	0.076
Br 82	n_2	1.97641	C 53 - C 54	π^*	0.34598	3.20	0.81	0.046
S 10	n_2	1.62082	C 3 - N 7	π^*	0.35203	24.59	0.23	0.067
N 9	n_1	1.59928	N 6 - C 33	π^*	0.37702	41.79	0.28	0.097
N 8	n_1	1.72382	C 41 - C 42	π^*	0.39817	22.84	0.27	0.072
N 7	n_1	1.87644	C 3 - S 10	σ^*	0.12444	19.81	0.45	0.084
O 2	n_2	1.74075	O 1 - C 59	π^*	0.28820	36.35	0.31	0.096
O 1	n_2	1.82964	O 2 - C 59	σ^*	0.12369	38.54	0.51	0.127
C 71 - C 80	π	1.67852	C 73 - C 74	π^*	0.38935	21.27	0.27	0.069
C 54 - C 56	π	1.67231	C 50 - C 58	π^*	0.44336	22.94	0.27	0.072
C 3 - N 7	π	1.87954	C 44 - C 46	π^*	0.30398	16.02	0.34	0.069
C 4 - C 36	π	1.64428	C 41 - C 42	π^*	0.39817	20.03	0.27	0.066
C 11 - C 13	π	1.66409	C 19 - C 20	π^*	0.37392	20.41	0.28	0.068
C 15 - C 17	π	1.66485	C 11 - C 13	π^*	0.34311	21.14	0.27	0.068
C 19 - C 20	π	1.63926	C 11 - C 13	π^*	0.34311	21.27	0.27	0.068
C 22 - C 23	π	1.65209	C 29 - C 31	π^*	0.32149	20.73	0.28	0.068
C 25 - C 27	π	1.65482	C 22 - C 23	π^*	0.36834	21.60	0.28	0.069
C 29 - C 31	π	1.66393	C 22 - C 23	π^*	0.36834	20.16	0.28	0.067
C 34 - C 35	π	1.79433	N 6 - C 33	π^*	0.37702	14.29	0.27	0.058
C 37 - C 39	π	1.68771	C 41 - C 42	π^*	0.39817	21.63	0.27	0.070
C 41 - C 42	π	1.64171	C 4 - C 36	π^*	0.40056	22.17	0.28	0.072

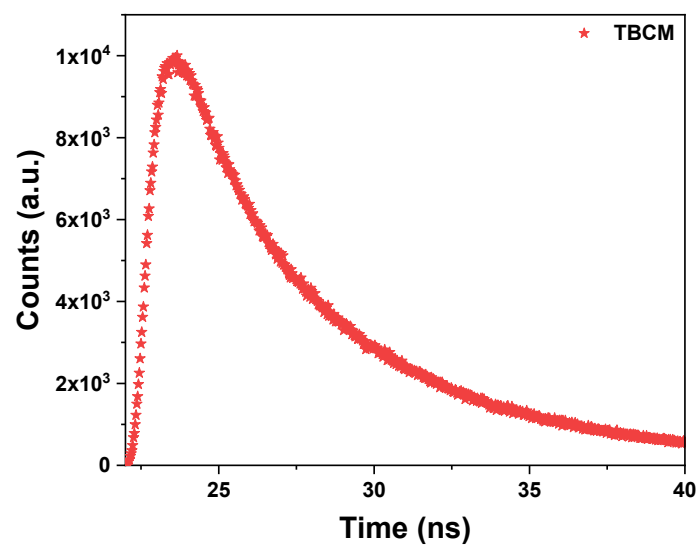


Figure S3. Life time studies of TBCM.

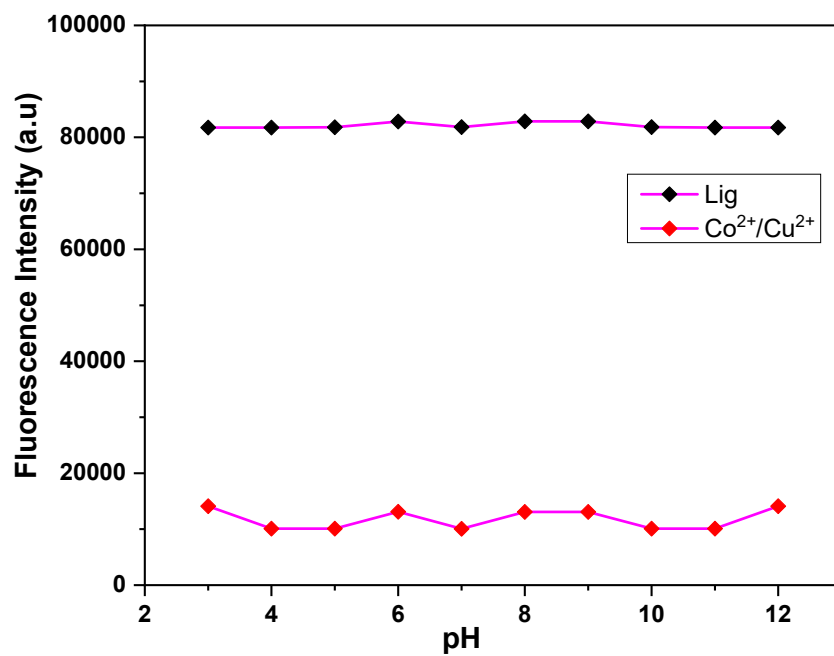


Figure S4. pH studies of **TBCM** with Cu²⁺/Co²⁺.

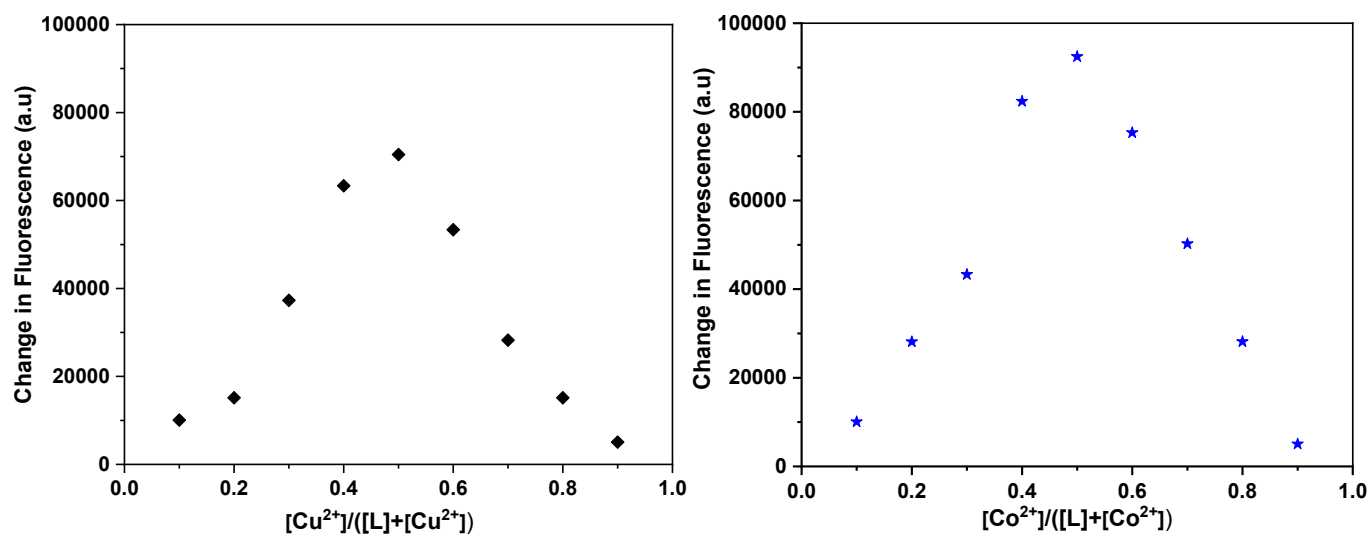


Figure S5. Job's plot of **TBCM** with metal ions.

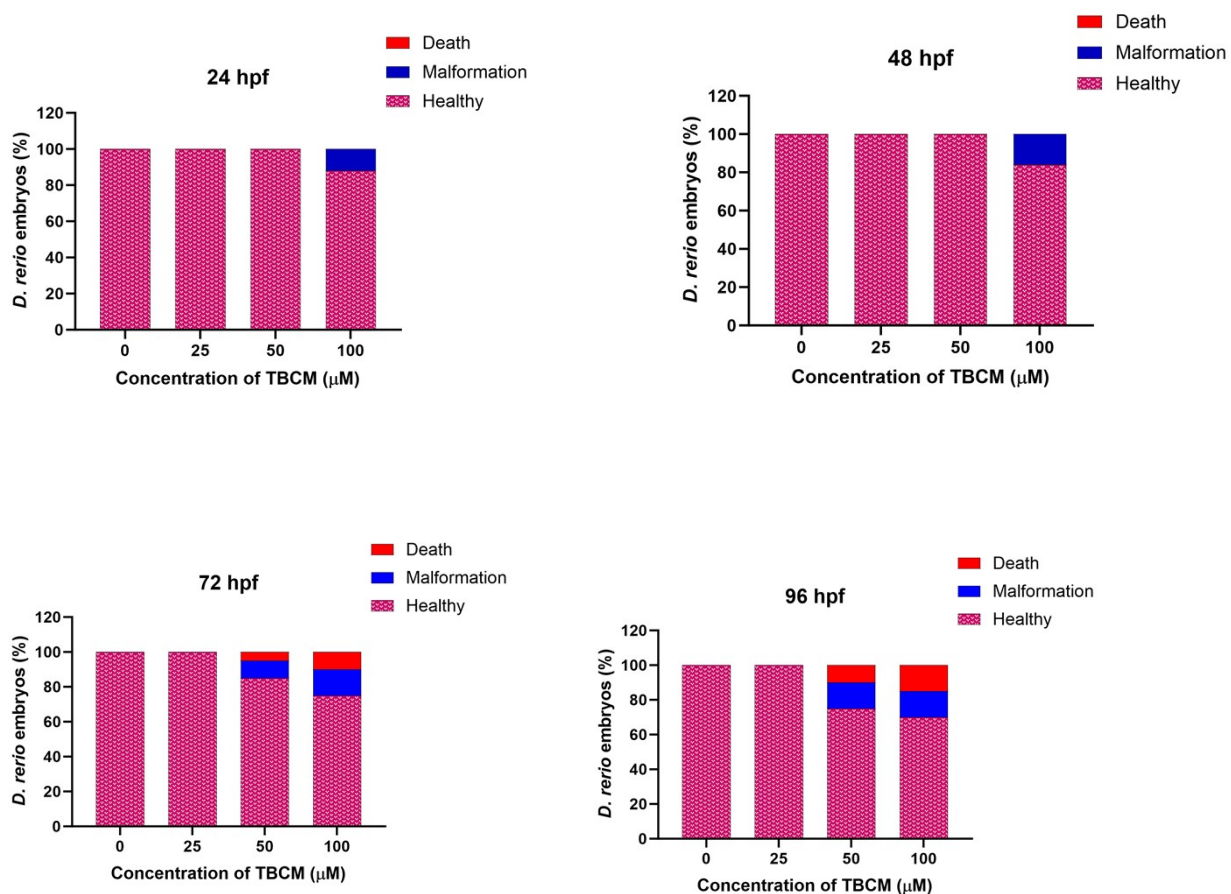


Figure S6. Dose-dependent toxic effect (developmental defects and death) of TBCM on *D. rerio* embryos for 24, 48, 72, and 96 hpf.

Experimental Section

General procedure for the synthesis 3-acetyl-6-bromo-2H-chromen-2-one (2)

An equivalent amount of 5-bromosalicylaldehyde (1.0 mmol, 0.20 g), (1) and ethylacetoacetate (1.0 mmol, 0.13 mL), was taken in a dry RB flask, few drops of piperidine was added to this mixture with continuous stirring for 30 min at room temperature. The solid separated was filtered and washed with ethanol until the yellow colour vanishes out completely.

General procedure for the preparation of 6-bromo-3-(2-bromoacetyl)-2H-chromen-2-one (3)

To a dry RB flask, a solution of bromine in chloroform was added with constant stirring containing solution of 3-acetyl-6-bromo-2H-chromen-2-one (1.0 mmol, 0.265 g), (**2**) in chloroform. Later, the mixture was heated under reflux for 1 h and cooled. After completion of the reaction as monitored by TLC, the solid separated was filtered, washed with chloroform and recrystallized from ethanol-chloroform mixture (3:1).

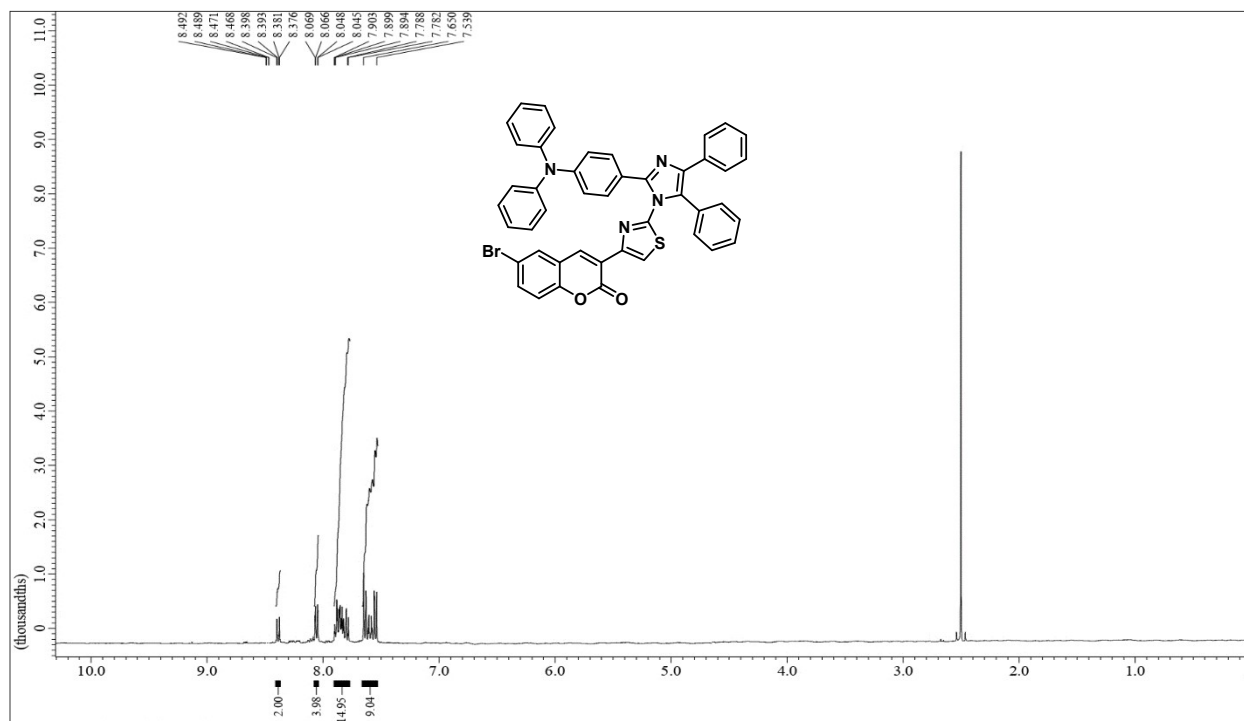
General procedure for the preparation of 3-(2-aminothiazol-5-yl)-6-bromo-2H-chromen-2-one (4)

In a dry RB flask, one equivalent of 6-bromo-3-(2-bromoacetyl)-2H-chromen-2-one (1.0 mmol, 0.343 g), (**3**) was taken in ethanol and was added an equimolar amount of thiourea (1.0 mmol, 0.076 g) with vigorous stirring and refluxed at 70 °C. After 20 min the addition of thiourea, the reaction mixture turned to an intense orange-yellow color and further precipitation of yellow solid was observed. Later evaporation of the solvent to 50% of its initial volume, the mixture was cooled, the solid formed was filtered out and washed with cold ethanol. The yellow solid was then dissolved in hot solution of 10% ammonium acetate (100 mL) in water, stirred for 30 min and then allowed to cool to room temperature. The corresponding solid **4** was filtered, washed with water and recrystallized from ethanol.

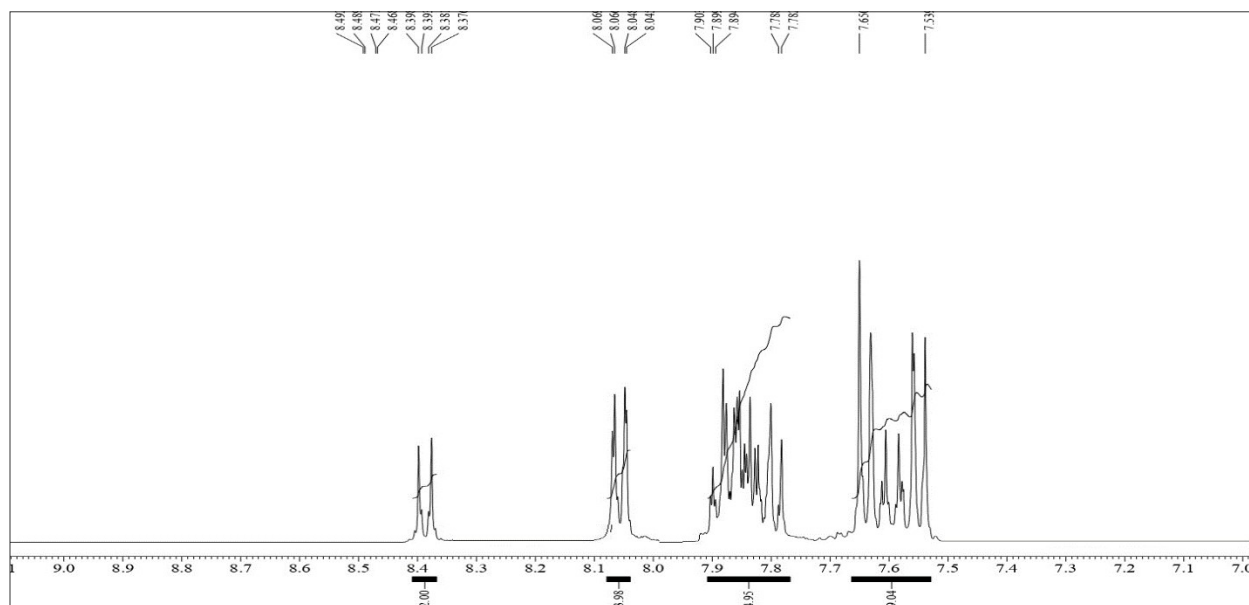
General procedure for the synthesis of chemosensor 6-bromo-3-(2-(2-(4-(diphenylamino)phenyl)-4,5-diphenyl-1H-imidazol-1-yl)thiazol-4-yl)-2H-chromen-2-one (TBCM)

Mixture of 1,2-diphenylethane-1,2-dione (1.0 mmol, 0.210g), 4-(diphenylamino)benzaldehyde (1.0 mmol, 0.27 g), 3-(2-aminothiazol-5-yl)-6-bromo-2H-

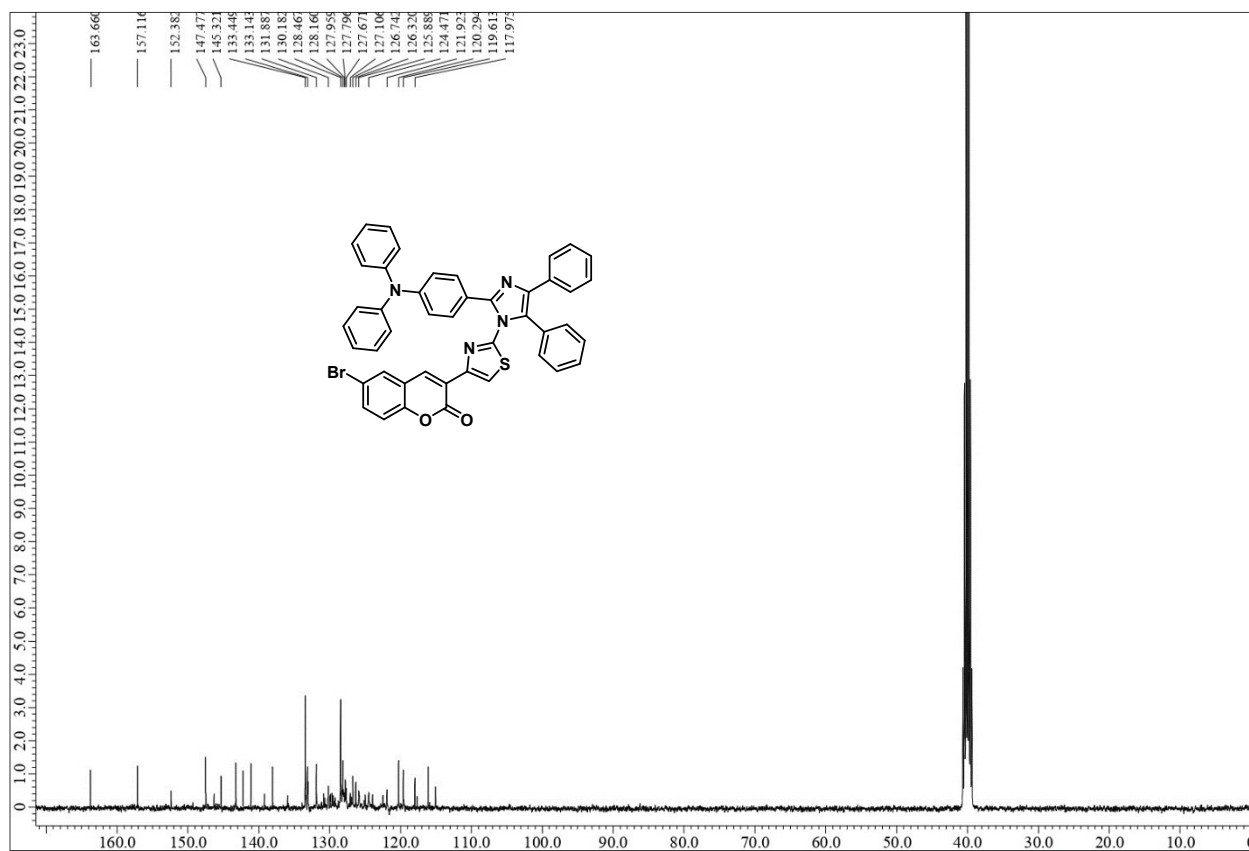
chromen-2-one (1.0 mmol, 0.32 g) and ammonium acetate (1.0 mmol, 0.077g) were taken in an equimolar concentration and dissolved in ethanol (~ 20mL). The reaction mixture was ultrasonicated (~ 20 min) and refluxed for about 6 h. After completion of the reaction as monitored by TLC, the resultant mixture was cooled to room temperature and poured to crushed ice. The obtained crude product was purified through column chromatography to get the desired compound. Pale yellowish solid (Yield: 90%); **¹H NMR** (400 MHz, DMSO-*d*₆) δ (ppm): δ 8.39 (dd, *J* = 6.8, 2.0 Hz, 2H), 8.06 (dd, *J* = 8.3, 1.3 Hz, 4H), 7.90-7.78 (m, 14H), 7.59 (d, *J* = 44.5 Hz, 9H). **¹³C NMR** (100 MHz, DMSO-*d*₆) δ (ppm): 163.7 (C=O of coumarin), 157.1 (thiazole carbon), 152.4 (C-O), 147.5, 146.3, 145.3, 143.2 (Imidazole carbon bonded to TPA), 141.1, 139.2, 138.0, 136.0, 133.4, 133.3, 133.1, 131.9, 130.9, 130.7, 130.2, 129.9, 129.7, 129.5, 129.2, 128.5, 128.2, 128.0, 127.8, 127.7, 127.1, 126.7, 126.3, 125.9, 125.2, 125.0, 124.5, 123.9, 122.5, 121.9, 120.3, 119.6 (C-Br), 118.0. **MS** *m/z*: 768 (M⁺), 770 (M+2). Elem. Anal. Calcd for C₄₅H₂₉ClN₄O₂S (%): Calcd. C, 74.52; H, 4.03; N, 7.73; Found: C, 74.55; H, 4.08; N, 7.79.



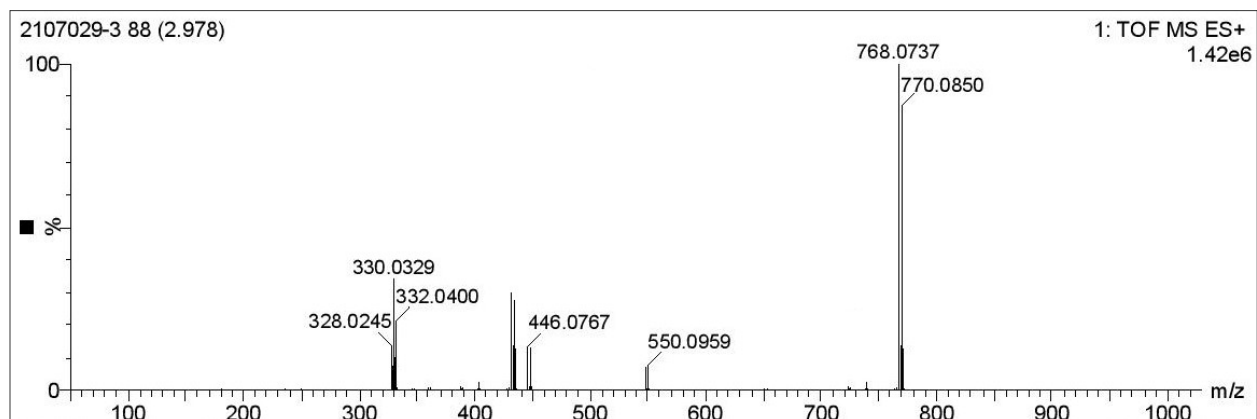
Spectrum No. 1 ^1H NMR spectrum of **TBCM** ($\text{DMSO-}d_6$, 400 MHz)



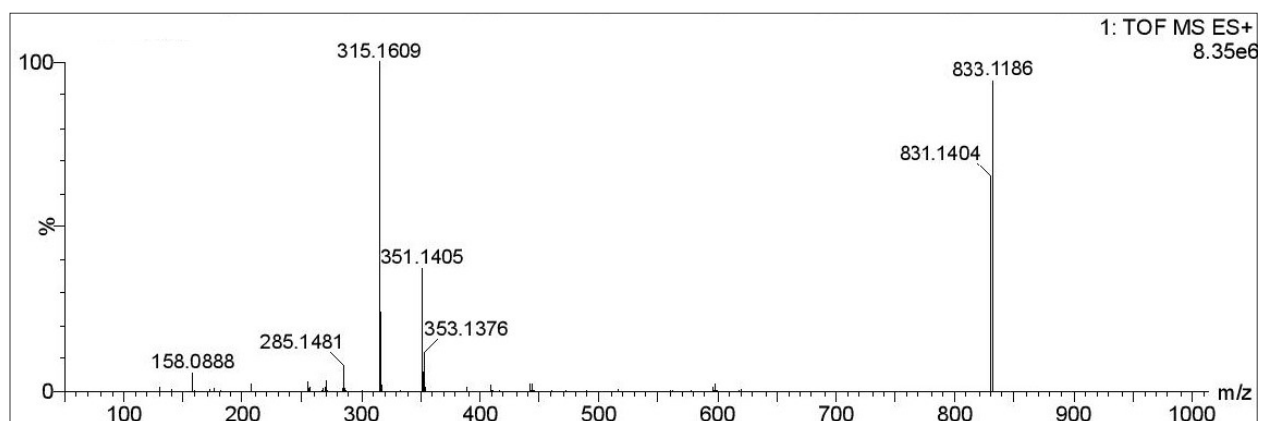
Spectrum No. 2 ^1H NMR spectrum expansion of **TBCM** ($\text{DMSO-}d_6$, 400 MHz)



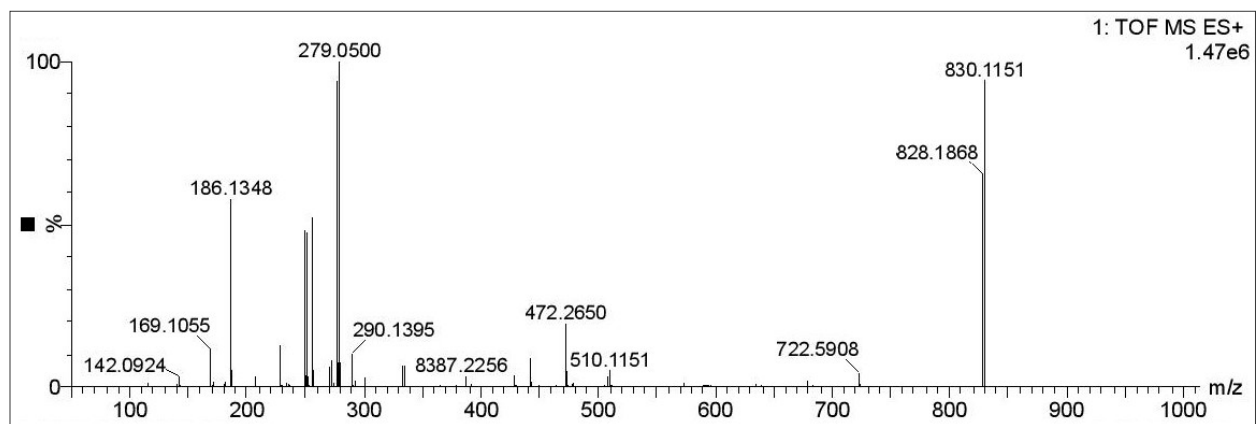
Spectrum No. 3 ^{13}C NMR spectrum of **TBCM** ($\text{DMSO-}d_6$, 100 MHz)



Spectrum No. 4 Mass spectrum of TBCM



Spectrum No. 5 Mass spectrum of [TBCM + Cu²⁺]



Spectrum No. 6 Mass spectrum of [TBCM + Co²⁺]

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