

Supporting information

Photophysics of 7-Mercapto-4-methylcoumarin and Derivatives: Complementary Fluorescence Behaviour to 7-Hydroxycoumarins

Anabel E. Lanterna, María González-Béjar, Mathieu Frenette and Juan C. Scaiano*

Corresponding author's email address: jscaiano@uottawa.ca (JCS)

Reagents

7-mercapto-4-methylcoumarin (>97%) is commercially available from Fluka and was recrystallized from hexanes/dichloromethane before use. Methylvinylketone (Aldrich) was purified by filtration over silica gel before use. All solvents were HPLC-grade or higher. Distilled, deionized (MilliQ purification systems) water was used. All other compounds were from Aldrich and used as received unless specified otherwise.

Instrumentation

Steady-state absorbance and fluorescence measurements were recorded on a CARY-50 spectrophotometer and a Photon Technology International (PTI) fluorimeter, respectively. Time-resolved fluorescence was acquired on a Photon Technology International (PTI) EasyLife LS Fluorescence Lifetime System.

Fluorescence Quantum Yield Measurements (Φ_F)

The fluorescence standard used was 7-methoxycoumarin-4-acetic acid in methanol ($\Phi_{STD}=0.18$, fluorescence $\lambda_{max}=378\text{nm}$).¹ Each fluorescence quantum yield was determined using at least 4 solutions at different concentrations for each chromophore ($\lambda_{exc} = 308 \text{ nm}$). The Φ_F were calculated using the following equation: (η = refractive index of the solvent; dF/dA = slope of the fitting curve, Fig. S3)

$$\Phi_F = \Phi_{STD} \frac{(dF/dA)}{(dF/dA)_{STD}} \left(\frac{\eta^2}{\eta_{STD}^2} \right)$$

Determination of the acid equilibrium constant (K_a) of C-SH

A saturated aqueous solution of C-SH was prepared and filtered through 0.45 μm PTFE filters (Whatman, Inc.). The filtered was diluted to achieve a maximum absorbance of ~ 0.2 above 320 nm. The pH was adjusted with HCl and NaOH and the final pH was read with an electrode pH meter. Absorption spectra were recorded at different pH and the absorption at 328 and 364 nm was plotted versus the pH values. The emission spectra were also recorded using 338 nm excitation wavelength (the approximate isosbestic point for the absorbance at all pH measured). All fluorescence spectra were corrected for scattering by subtracting the signal obtained from a dilute LUDOX® scattering solution in water.

Density Functional Theory Calculations

The Gaussian 09 software package was used to perform DFT calculations using the B3LYP functional. Geometry optimization and frequency calculations were done using the functional 6-311+g(d,p). No imaginary frequencies were found after optimization and the conformation with the lowest energy was chosen to represent the molecule. The bond distances reported in figure were obtained using the software GaussView.

Syntheses of C-SR derivatives

S-acetyl-7-mercapto-4-methylcoumarin (C-SAc)

In a 50mL round bottom flask equipped with a magnetic stir bar, 7-mercapto-4-methylcoumarin (201.2 mg, 1.047 mmol) was dissolved with 20 mL dichloromethane. Triethylamine (0.16 mL, 1.15 mmol) and acetic anhydride (0.11 mL, 1.15 mmol) were added sequentially with stirring. The reaction was stirred for 40 minutes before the reaction (+50 mL dichloromethane) was extracted with 10% HCl (50 mL) and 2x50 distilled water in a separatory funnel. The organic layer was dried over MgSO₄. After the solids were removed by filtration and the liquid evaporated, the resulting solid was recrystallized from petroleum ether and dichloromethane to afford 113mg (46% yield) of off-white solid. ¹H NMR (CDCl₃, 400 MHz): δ 7.63 (J=8 Hz, d, 1H, ArH), 7.42 (J=1.2Hz, d, 1H, ArH), 7.35-7.33 (J=8 Hz, q, 1H, ArH), 6.34 (J=1.1Hz q, 1H, =CH), 2.47 (s, 3H, CH₃), 2.45 (J=1.2Hz, d, 3H, CH₃). ¹³C NMR (CDCl₃, 120 MHz): δ 192.39, 160.11, 153.32, 151.68, 132.17, 129.75, 124.93, 122.44, 120.59 116.04, 30.44, 18.63. IR ν (cm⁻¹) 3058 (m), 1741 (s), 1692 (s), 1603 (m), 1400 (m), 1380 (m), 880 (m). m.p. 145-149 °C. MS (EI) m/z 234.04 (9.0), 192.02 (100.0), 164.03 (18.5), 135.02 (4.3), 102.05 (3.4), 68.98 (4.3), 51.02 (4.9), 43.02 (81.0), 39.02 (4.9). HRMS Calcd. for C₁₂H₁₀O₃S: 234.00351. Found: 234.0353.

S-4-nitrophenyl-7-mercapto-4-methylcoumarin (C-SPhNO₂)

KOH pellets (777.0 mg, 13.85 mmol) were crushed in a mortar and pestle and then dissolved in DMSO (25mL) in a 50mL round bottom flask equipped with a stir bar. The reaction mixture was cooled over ice water and purged with argon. 7-mercapto-4-methylcoumarin (537.5 mg, 2.796 mmol) was added to the flask and purging was continued. 1-Fluoro-4-nitrobenzene (310 μ L, 2.922 mmol) was added drop-wise to the stirring solution. The reaction was allowed to proceed for 15 min and then was brought to room temperature. After an additional 1.75 h of stirring, ether (100 mL) was added to the reaction and then extracted with 3x100 mL distilled water in a separatory funnel. A yellow/green solid formed at the bottom of the ether layer and was filtered off using a Buchner funnel. The solid was then dissolved in dichloromethane, dried over MgSO₄, filtered off and brought to dryness under reduced pressure to afford 386.4mg (44% yield) of product. ¹H NMR (CDCl₃, 400 MHz): δ 8.17-8.15 (m, 2H, ArH), 7.63 (J=8.4Hz, d,

1H, ArH), 7.41-7.38 (m, 3H, ArH), 7.33 (J=3.3Hz, q, 1H, ArH), 6.33 (J=3.2Hz, d, 1H, =CH), 2.46 (J=1.2Hz, d, 3H, CH₃). ¹³C NMR (CDCl₃, 120 MHz): δ 159.94, 153.95, 151.60, 144.62, 137.27, 129.59, 127.69, 125.69, 124.45, 120.32, 115.79, 18.67. IR ν (cm⁻¹) 3091 (w), 1718 (s), 1505 (s), 1394 (m), 1336 (s), 1316 (m), 848 (m). m.p. 191-196 °C. MS (EI) m/z 313.04 (100.0), 285.04 (19.2), 161.99 (19.4), 142.99 (17.1), 111.99 (7.0), 72.04 (24.9), 30.99 (24.9). HRMS Calcd. for C₁₆H₁₁NO₄S: 313.0409. Found: 313.0402.

S-4-aminophenyl-7-mercapto-4-methylcoumarin (C-SPhNH₂)

Tin powder (657.8 mg, 5.541 mmol) and C-SPhNO₂ (134.0 mg, 0.4729 mmol) were added to a 50 mL round bottom flask equipped with a stir bar. Four portions of concentration HCl (3mL each, 12mL total) were added sequentially. After the vigorous reaction subsided, the round bottom flask was equipped with a reflux condenser and the solution was refluxed in a water bath. During refluxing, ethanol (3 mL) was added to help dissolved the nitro compound. After 1h of refluxing, the reaction flask was cooled and 20% w/v NaOH was added until the tin hydroxide was dissolved. Product was extracted from ethyl acetate (100 mL) and washed with 20% w/v NaOH (100 mL) and then twice with distilled water (100 mL each, 200 mL total). The organic layer was then dried over MgSO₄, filtered off and brought to dryness under reduced pressure to afford 47.9 mg (40% yield) of product. ¹H NMR (CDCl₃, 400 MHz): δ 7.40 (J=8.4Hz, d, 1H, ArH), 7.35-7.32 (m, 2H, ArH), 7.02 (J=3.5Hz, q, 1H, ArH), 6.84 (J=2Hz, d, 1H, ArH), 6.75-6.71 (m, 2H, NH₂), 6.16 (J=1.2Hz, d, 1H, =CH), 2.37 (J=1.2Hz, d, 3H, CH₃). ν (cm⁻¹) 3359 (m), 3451 (m), 1700 (s), 1595 (s), 1386 (m), 826 (m). m.p. 190-197°C. MS (EI) m/z 283.07 (100), 255.07 (5.2), 223.09 (5.0), 161.99 (13.2), 142.99 (11.0), 124.02 (13.08), 111.99 (5.6), 77.04 (7.2), 57.07 (7.6), 28.01 (37.1). HRMS Calcd. for C₁₆H₁₃NO₂S: 283.0667. Found: 283.0664.

S-3-oxobutyl-7-mercapto-4-methylcoumarin (C-SMVK)

7-mercapto-4-methylcoumarin (400 mg, 2 mmol) was dissolved with 25 mL THF in a 50 mL round bottom flask equipped with a stir bar. The reaction mixture was cooled over ice water and purged under argon. K₂CO₃ (289.0 mg, 2.091 mmol) and methylvinylketone (185.5 μL, 2.226 mmol) were added sequentially with stirring. After 30 min, the solvent was removed under reduced pressure. The resulting solid was dissolved in dichloromethane (100 mL) and washed twice with distilled water (50 mL each, 100 mL total). The organic layer was then dried over MgSO₄, filtered off and brought to dryness under reduced pressure to afford 260 mg (48% yield) of product. ¹H NMR (CDCl₃, 400 MHz): δ 7.48 (J=8Hz, d, 1H, ArH), 7.18-7.15 (m, 2H, ArH), 6.23 (J=1.2Hz, q, 1H, =CH), 3.22 (J=7.2Hz, t, 2H, CH₂), 2.84 (J=7.2Hz, t, 2H, CH₂), 2.41 (J=1.2Hz d, 3H, CH₃), 2.19 (s, 3H, CH₃). ¹³C NMR (CDCl₃, 120 MHz): δ 205.78, 160.51, 153.88, 152.06, 142.34, 124.75, 123.18, 117.42, 114.45, 114.09, 42.41, 30.91, 30.09, 25.90, 18.56. IR ν (cm⁻¹) 3062 (w), 1712 (s), 1684 (m), 1605 (m), 1363 (m), 955 (m), 865 (m).

m.p. 112-113°C. MS (EI) m/z 262.06 (100), 219.05 (16.6), 192.02 (63.7), 161.99 (67.9), 149.99 (24.7), 142.99 (62.9), 111.99 (28.9), 68.98 (25.3), 50.00 (28.8), 31.00 (62.5). HRMS Calcd. for C₁₄H₁₄O₃S: 262.0664. Found: 262.0662.

Di-4-methylumbelliferyl-disulfide (C-SS-C)

Using a mortar and pestle, 7-mercapto-4-methylcoumarin (151.3 mg, 0.79 mmol), KMnO₄ (127.0 mg, 0.80 mmol) and neutral Al₂O₃ (88.8 mg, 0.87 mmol) were grinded together for 10 min. The product was extracted using a generous amount of dichloromethane and the resulting mother liquor was evaporated to dryness using a rotatory evaporator. The residual solid was recrystallized from ethanol and dichloromethane to afford 41.4 mg (28% yield) of pale yellow needles. ¹H NMR (CDCl₃, 400 MHz): δ 7.54 (J=1.2Hz, d, 1H, ArH), 7.44 (d, 1H, ArH), 7.38 (J=4Hz, q, 1H, ArH), 6.25 (d, 1H, =CH), 2.41 (J=8Hz, d, 3H, CH₃). ¹³C NMR (CDCl₃, 120 MHz): δ 160.14, 153.97, 151.80, 140.81, 125.25, 122.07, 119.05, 114.93, 114.36, 18.63. m.p. 234-245°C. MS (EI) m/z 382.03 (24.4), 318.10 (20.1), 290.05 (32.8), 191.01 (55.5), 163.02 (49.9), 91.1 (100.0), 77.04 (50.9), 68.98 (65.6). HRMS Calcd. for C₂₀H₁₄O₄S₂: 382.0334. Found: 382.0314.

S-methyl-7-mercapto-4-methylcoumarin (C-SMe)

In dry, distilled tetrahydrofuran, 7-mercapto-4-methylcoumarin (1g, 5.2 mmol) and 1.2 eq. of imidazole (0.425 g) were stirred at room temperature in a capped round bottom flask. Methyl Iodide (~1.2 eq., 0.4 mL) was added dropwise to the solution via syringe. After the reaction appeared complete by TLC, the solution was rotovapped and the residue was purified by column silica gel chromatography to afford 0.9 g (84% yield) of pale yellow powder. ¹H NMR (CDCl₃, 400 MHz): δ 7.47 (J=8.4Hz, d, 1H, ArH), 7.15-7.11 (m, 2H, ArH), 6.21 (J=0.4Hz, q, 1H, =CH), 2.53 (s, 3H, CH₃), 2.41-2.41 (J=1.2Hz, d, 3H, CH₃). ¹³C NMR (CDCl₃, 120 MHz): δ 160.67, 154.00, 152.21, 144.74, 124.43, 121.75, 116.70, 113.64, 112.62, 18.57, 14.95. IR ν (cm⁻¹) 3055 (w), 1742 (s), 1601 (s), 1387 (m) 858 (s). m.p. 125-128°C. MS (EI) m/z 202.04 (100), 178.05 (52.3), 163.02 (53.2), 134.02 (67.9), 102.05 (5.1), 89.02 (6.8), 77.04 (8.6), 51.02 (9.7), 31.00 (7.1). HRMS Calcd. for C₁₁H₁₀O₂S: 206.0402. Found: 206.0390.

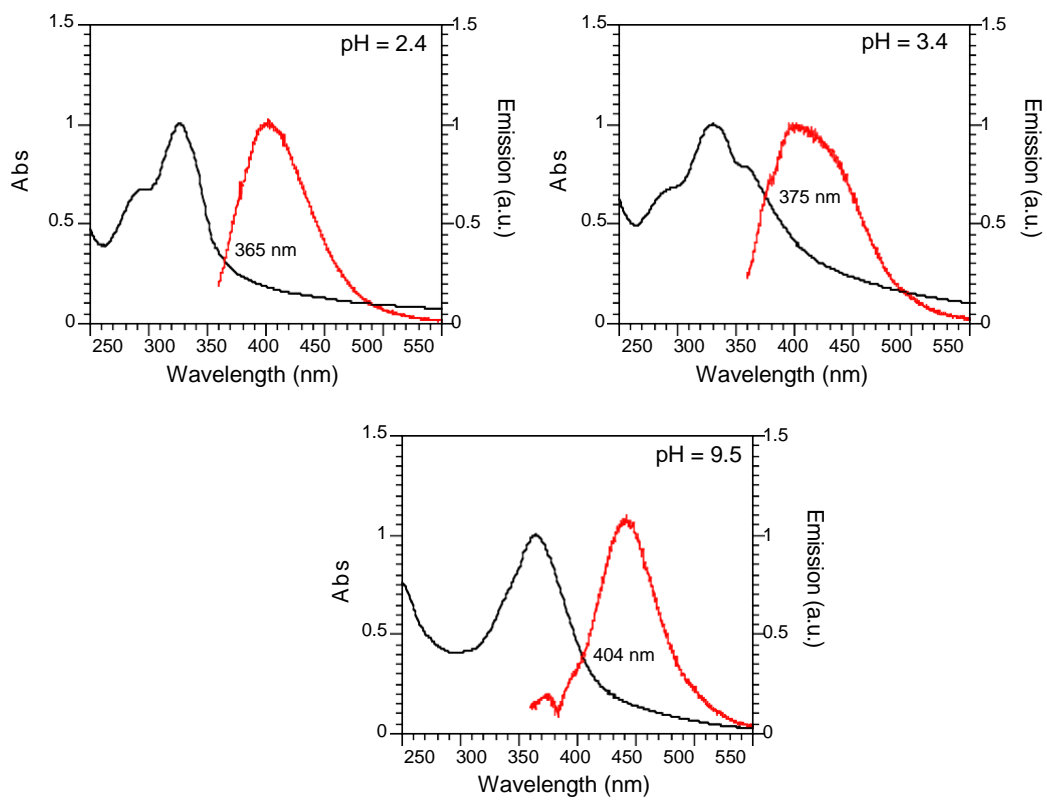


Figure S1. Normalized absorption (black) and emission (red) spectra of C-SH in different pH conditions. Notice in Neutral (pH ~ 3.4) conditions both species coexist.

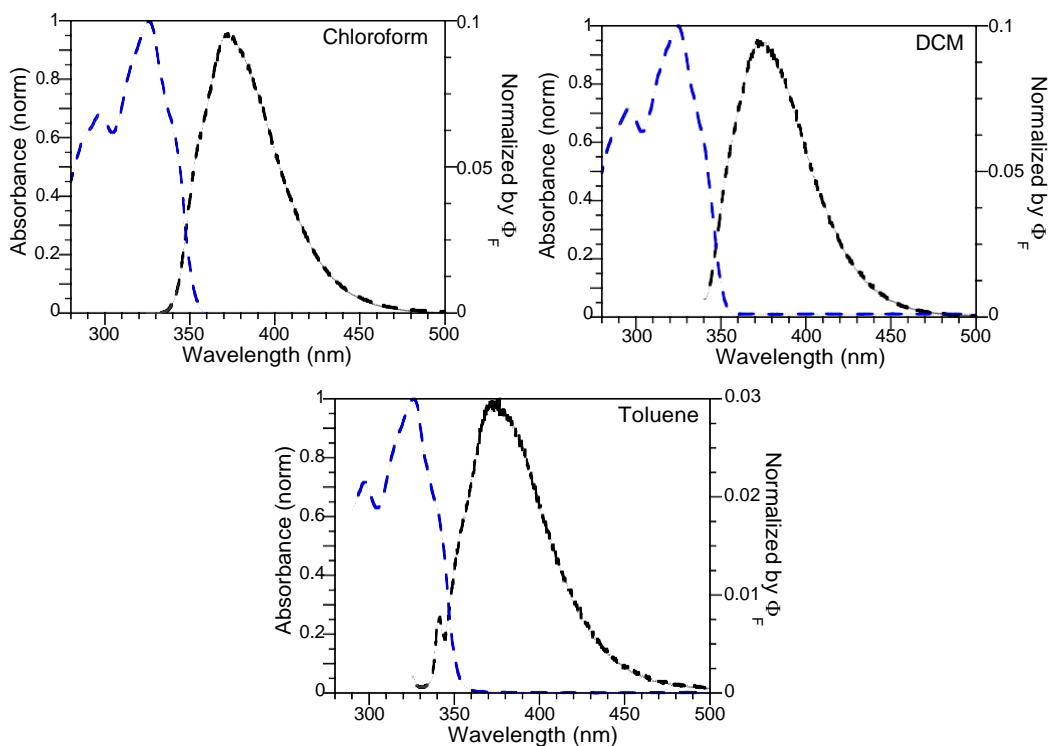


Figure S2. UV absorption (blue) and emission (black) spectra of C-SH in non-protic solvents: Chloroform, dichloromethane and toluene. The fluorescence spectra were normalized and scaled by Φ_F .

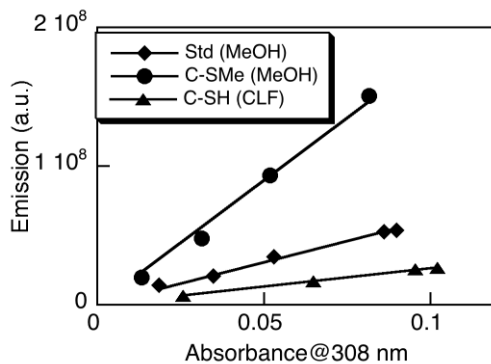


Figure S3. Plot showing some examples of the absorbance vs emission (area under the curve) upon excitation at 308 nm for different concentrations of C-SH in MeOH and C-SMe in chloroform as compared to the standard 7-methoxycoumarin-4-acetic acid in methanol.

References

- (1) R. Farinotti, P. Siard, J. Bourson, S. Kirkiacharian, B. Valeur, G. Mahuzier *Journal of Chromatography* **1983**, 269, 81.
- (2) E. Oliveros, S. H. Bossmann, S. Nonell, C. Marti, G. Heit, G. Troscher, A. Neuner, C. Martinez, A. M. Braun *New Journal of Chemistry* **1999**, 23, 85.
- (3) R. W. Redmond, J. N. Gamlin *Photochemistry and Photobiology* **1999**, 70, 391.
- (4) Y. Usui *Chemistry Letters* **1973**, 2, 743.

