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Rhodamine B Pentyl Ester and its Methyl, Ethyl, Propyl, and Butyl Homologues

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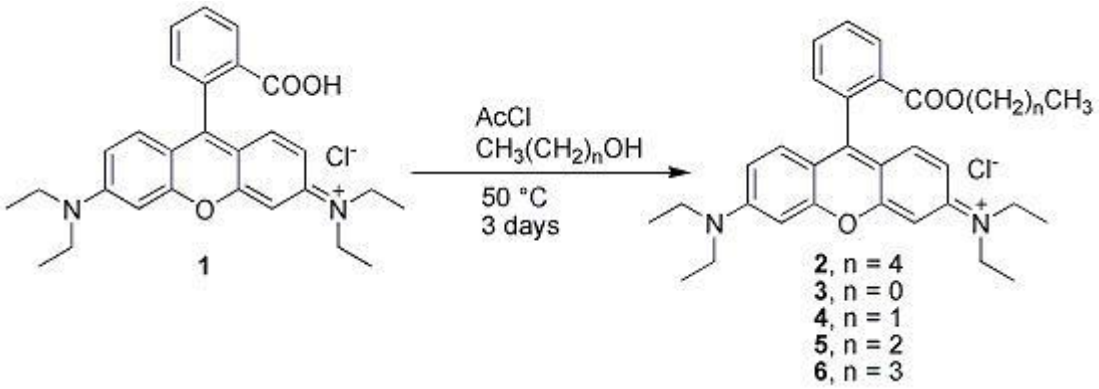

The rhodamines are a highly fluorescent class of compound used in many different fields of research, from the lasing medium in dye lasers to biological stains and markers for cellular drug resistance [1-3]. We are interested in the influence of lipophilicity on the transport of esters of rhodamine in multidrug resistance transporter assays. Herein we describe the synthesis of the novel compound rhodamine B pentyl ester (**2**), and deposit the spectral data of the known methyl (**3**), ethyl (**4**), propyl (**5**), and butyl (**6**) homologues [4]. Ester **2** was prepared by a slightly modified facile method [5] that utilizes anhydrous hydrogen chloride generated *in situ* by the addition of AcCl to a mixture of the rhodamine B free acid (**1**) and *n*-pentanol.

Rhodamine B pentyl ester (2)

N-[6-(Diethylamino)-9-[2-(pentyloxycarbonyl)phenyl]-3*H*-xanthen-3-ylidene]-*N*-ethylethanaminium chloride

Acetyl chloride (1.25 mL, 17.6 mmol) was added dropwise to a stirred mixture of rhodamine B (**1**, 100 mg, 0.21 mmol) and *n*-pentanol (25 mL), and the reaction was heated at 50°C under an atmosphere of argon. After 2 days the reaction was ~ 90% complete by TLC, and additional acetyl chloride (250 µL, 3.52 mmol) was added to drive the reaction to completion. After a further 24 h TLC indicated no remaining rhodamine B (**1**) and the solution was evaporated *in vacuo* (water bath temperature < 50 °C to avoid degradation of the product) to afford rhodamine B pentyl ester (**2**), which was contaminated with a small amount of *n*-pentanol. The molar ratio of rhodamine B pentyl ester (**2**):*n*-pentanol was ~ 3:1 by ^{1}H NMR. To separate the ester (**2**) from residual alcohol, the crude product was dissolved in water (100 mL) and washed with ethyl acetate (3 × 50 mL). Acetonitrile (35 mL) was added to the aqueous layer and this solution was lyophilised to afford the title compound (**2**), a hygroscopic amorphous solid (85%).

TLC R_f 0.41 (silica gel 60 F_{254} aluminum sheets, *n*-butanol:water:ethanol 9:2:1).

ES-MS, *m/z*: 513 $[M+H]^+$.

^{1}H NMR (500 MHz, d_6-DMSO) d 8.24 (1H, dd, *J* = 7.9 and 1.2 Hz), 7.91 (1H, dt, *J* = 7.5 and 1.3 Hz), 7.85 (1H, dt, *J* = 7.7 and 1.3 Hz), 7.51 (1H, dd, *J* = 7.5 and 1.1 Hz), 7.11 (2H, dd, *J* = 9.6 and 2.4 Hz), 7.02-6.99 (4H, m), 3.89 (2H, t, *J* = 6.2 Hz), 3.65 (8H, br q, *J* = 7.1 Hz), 1.20 (12H, br t, *J* = 7.0 Hz) overlapping with ~1.18-1.13 (2H, m), 1.06 (2H, sextet, *J* = 7.4 Hz), 0.88-0.82 (2H, m), 0.71 (3H, t, *J* = 7.4 Hz).

^{13}C NMR (100 MHz [6], d_6-DMSO) d 165.1, 157.6, 157.1, 155.1, 133.0, 132.7, 131.0, 130.9, 130.5, 130.4, 129.9, 114.6, 112.9, 95.9, 65.2, 45.3, 27.5, 27.4, 21.7, 13.6, 12.4.

UV-visible (H_2O): λ_{max} 559 nm.

HRMS calcd for $[M+H]^+$ 513.3117, found 513.3122.

The methyl (**3**), ethyl (**4**), propyl (**5**) and butyl (**6**) homologues of **2** were synthesized by the same method except that evaporation of the solution in vacuo afforded the ester (**3-6**) pure, without the need for partitioning between water and ethyl acetate. Previously these compounds were isolated as the bromide, iodide or perchlorate salts, and their spectra were recorded in $CDCl_3$ [4]. Herein we deposit the spectra of the chloride salts (**3-6**) recorded in d_6-DMSO.

Rhodamine B methyl ester (3)

***N*-[6-(Diethylamino)-9-[2-(methoxycarbonyl)phenyl]-3*H*-xanthen-3-ylidene]-*N*-ethylethanaminium chloride**
TLC R_f 0.35 (silica gel 60 F_{254} aluminum sheets, *n*-butanol:water:ethanol 9:2:1).

ES-MS, *m/z*: 457 $[M+H]^+$.

^{1}H NMR (500 MHz, d_6-DMSO) d 8.27 (1H, dd, *J* = 7.9 and 1.2 Hz), 7.92 (1H, dt, *J* = 7.6 and 1.3 Hz), 7.84 (1H, dt, *J* = 7.7 and 1.3 Hz), 7.51 (1H, dd, *J* = 7.5 and 1.1 Hz), 7.08 (2H, dd, *J* = 9.6 and 2.5 Hz), 6.99-6.97 (4H, m), 3.65 (8H, br q, *J* = 7.02 Hz), 3.60 (3H, s), 1.21 (12H, br t, *J* = 7.0 Hz).

^{13}C NMR (75 MHz, d_6-DMSO) d 165.0, 157.9, 157.1, 155.1, 133.4, 133.3, 130.8, 130.8, 130.5, 130.5, 129.2, 114.6, 112.8, 95.9, 52.5, 45.3, 12.5.

UV-visible (H_2O): λ_{max} 558 nm.

HRMS calcd for $[M+H]^+$ 457.2491, found 457.2481.

Rhodamine B ethyl ester (4)

***N*-[6-(Diethylamino)-9-[2-(ethoxycarbonyl)phenyl]-3*H*-xanthen-3-ylidene]-*N*-ethylethanaminium chloride**
TLC R_f 0.37 (silica gel 60 F_{254} aluminum sheets, *n*-butanol:water:ethanol 9:2:1).

ES-MS, *m/z*: 471 $[M+H]^+$.

^{1}H NMR (500 MHz, d_6-DMSO) d 8.25 (1H, dd, *J* = 7.9 and 1.1 Hz), 7.91 (1H, dt, *J* = 7.6 and 1.4 Hz),

7.84 (1H, dt, *J* = 7.7 and 1.2 Hz), 7.52 (1H, dd, *J* = 7.6 and 1.1 Hz), 7.09 (2H, dd, *J* = 9.6 and 2.5 Hz), 7.01-6.99 (4H, m), 3.98 (2H, q, *J* = 7.1 Hz), 3.65 (8H, br q, *J* = 7.0 Hz), 1.21 (12H, br t, *J* = 7.0 Hz), 0.90 (3H, t, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, d_6-DMSO) d 164.7, 157.7, 157.1, 155.1, 133.1, 133.0, 130.9, 130.7, 130.5, 130.4, 129.7, 114.6, 112.9, 95.9, 61.0, 45.4, 13.4, 12.4.

UV-visible (H_2O): λ_{max} 559 nm.

HRMS calcd for $[M+H]^+$ 471.2648, found 471.2643.

Rhodamine B propyl ester (5)
***N*-[6-(Diethylamino)-9-[2-(propoxycarbonyl)phenyl]-3*H*-xanthen-3-ylidene]-*N*-ethylethanaminium chloride**

TLC R_f 0.39 (silica gel 60 F_{254} aluminum sheets, *n*-butanol:water:ethanol 9:2:1).

ES-MS, *m/z*: 485 $[M+H]^+$.

^{1}H NMR (500 MHz, d_6-DMSO) d 8.25 (1H, dd, *J* = 7.8 and 1.2 Hz), 7.91 (1H, dt, *J* = 7.6 and 1.3 Hz), 7.85 (1H, dt, *J* = 7.7 and 1.2 Hz), 7.52 (1H, dd, *J* = 7.5 and 1.0 Hz), 7.09 (2H, dd, *J* = 9.6 and 2.5 Hz), 7.02-6.99 (4H, m), 3.89 (2H, t, *J* = 6.4 Hz), 3.65 (8H, br q, *J* = 7.0 Hz), 1.29 (2H, sextet, *J* = 6.9 Hz), 1.20 (12H, br t, *J* = 7.0 Hz), 0.62 (3H, t, *J* = 7.4 Hz).

^{13}C NMR (75 MHz, d_6-DMSO) d 164.9, 157.7, 157.1, 155.1, 133.1, 132.9, 130.9, 130.8, 130.5, 130.4, 129.8, 114.6, 112.9, 95.9, 66.7, 45.4, 21.1, 12.4, 10.0.

UV-visible (H_2O): λ_{max} 559 nm.

HRMS calcd for $[M+H]^+$ 485.2804, found 485.2801.

Rhodamine B butyl ester (6)
***N*-[6-(Diethylamino)-9-[2-(butoxycarbonyl)phenyl]-3*H*-xanthen-3-ylidene]-*N*-ethylethanaminium chloride**

TLC R_f 0.40 (silica gel 60 F_{254} aluminum sheets, *n*-butanol:water:ethanol 9:2:1).

ES-MS, *m/z*: 499 $[M+H]^+$.

^{1}H NMR (500 MHz, d_6-DMSO) d 8.24 (1H, dd, *J* = 7.9 and 1.2 Hz), 7.91 (1H, dt, *J* = 7.5 and 1.4 Hz), 7.84 (1H, dt, *J* = 7.7 and 1.4 Hz), 7.51 (1H, dd, *J* = 7.6 and 1.1 Hz), 7.10 (2H, dd, *J* = 9.6 and 2.5 Hz), 7.02-7.00 (4H, m), 3.91 (2H, t, *J* = 6.2 Hz), 3.65 (8H, br q, *J* = 7.2 Hz), 1.21 (12H, br t, *J* = 7.0 Hz) overlapping with ~1.20-1.15 (2H, m), 0.94 (2H, sextet, *J* = 7.6 Hz), 0.68 (3H, t, *J* = 7.4 Hz).

^{13}C NMR (75 MHz, d_6-DMSO) d 165.0, 157.5, 157.1, 155.1, 133.0, 132.7, 130.9, 130.7, 130.4, 130.3, 129.8, 114.6, 112.8, 95.8, 64.9, 45.3, 29.8, 18.4, 13.4, 12.4.

UV-visible (H_2O): λ_{max} 559 nm.

HRMS calcd for $[M+H]^+$ 499.2961, found 499.2973.

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6. The ^{13}C NMR spectra of **3**-**6** were run at 75 MHz whereas the ^{13}C NMR spectrum of **2** was recorded at 100 MHz to enable resolution of the resonances which appeared at 27.46 and 27.43 ppm in the 100 MHz spectrum.