Supporting Information Available

Novel Fluorescent pH Sensors Based on Intramolecular Hydrogen Bonding Ability of Naphthalimide

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Materials. All the solvents were of analytic grade. ^1H -NMR were measured on a Bruker AV-400 spectrometer with chemical shifts reported as ppm (in $\text{CDCl}_3/\text{DMSO}-d_6$, TMS as internal standard). Mass spectra were measured on a HP 1100 LC-MS spectrometer. Melting points were determined by an X-6 micro-melting point apparatus and are uncorrected. All pH measurements were made with a Sartorius basic pH-Meter PB-20. Fluorescence spectra were determined on a Hitachi F-4500, Absorption spectra were determined on a PGENERAL TU-1901 UV-VIS Spectrophotometer.

Experimental Procedures and Product Characterization

General procedure for the formation of 4a-4g

To a solution of 0.005mol of 2-[2-(2-hydroxy-ethylamino)-ethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione in 50 mL of chloroform was added dropwise substituted isothiocyanate (0.005 mol) over a period of 10 min. The reaction mixture was stirred for 1 h at room temperature. The solvent was removed under reduced pressure to give the crude thioureas. To a solution of crude thiourea (0.005 mol) in 50 ml of acetone was added methyl iodide (0.02 mol). The mixture was heated to reflux for 12 hrs. The solvent was removed under reduced pressure, and to the residue was added 50 ml of H_2O and 10 ml of concentrated aqueous ammonia. The precipitated product was filtered, washed with H_2O , and was purified by column chromatography on silica gel (methanol-chloroform, 1:20, v/v). The following new compounds were prepared.

2-[2-(2-Phenylimino-oxazolidin-3-yl)-ethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione(**4a**)

Yield 45%, m.p. = 161.1-162.5 $^{\circ}\text{C}$; IR (KBr) ν_{max} 1690, 1650, 1592, 1380 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.544 (d, $J = 7.2\text{Hz}$, 1H), 8.470(d, $J = 8\text{Hz}$, 1H), 8.334 (d, $J = 8.4\text{Hz}$, 1H), 7.621 (dd, $J = 7.2, 8.4\text{Hz}$, 1H), 7.128 (d, $J = 8\text{Hz}$, 1H), 6.875-6.836 (m, 2H), 6.676 (t, $J = 7.2\text{Hz}$, 1H), 6.343(d, $J = 7.6\text{Hz}$, 2H), 4.485 (t, $J = 5.6\text{Hz}$, 2H), 4.265 (t, $J = 7.6\text{Hz}$, 2H), 3.832 (t, $J = 5.6\text{Hz}$, 2H), 3.735 (t, $J = 7.6\text{Hz}$, 2H), 3.210-3.186 (m, 4H), 1.907-1.852 (m, 4H), 1.748-1.719 (m, 2H); HRMS (EI) calcd for $\text{C}_{28}\text{H}_{28}\text{N}_4\text{O}_3$ [M^+] 468.2161, found 468.2166.

2-[2-(2-(2-Methyl-phenyl)-imino-oxazolidin-3-yl)-ethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione(**4b**)

Yield 45%, m.p. = 160.7-160.7 $^{\circ}\text{C}$; IR (KBr) ν_{max} 1691, 1650, 1592, 1384 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.542 (d, $J = 7.8\text{Hz}$, 1H), 8.462 (d, $J = 8.4\text{Hz}$, 1H), 8.346 (d, $J = 7.8\text{Hz}$, 1H), 7.628 (dd, $J = 7.8, 7.8\text{Hz}$, 1H), 7.135 (d, $J = 8.4\text{Hz}$, 1H), 6.858 (d, $J = 7.2\text{Hz}$, 2H), 6.766 (t, $J = 7.2\text{Hz}$, 1H), 6.663 (t, $J = 7.2\text{Hz}$, 1H), 6.380 (t, $J = 7.2\text{Hz}$, 1H), 4.497 (t, $J = 5.6\text{Hz}$, 2H), 4.222 (t, $J = 8\text{Hz}$, 2H), 3.854 (t, $J = 5.6\text{Hz}$, 2H), 3.729 (t, $J = 8\text{Hz}$, 2H), 3.212-3.208 (m, 4H), 1.884-1.871 (m, 4H), 1.729-1.726 (m, 5H); HRMS (EI) calcd for $\text{C}_{29}\text{H}_{30}\text{N}_4\text{O}_3$ [M^+] 482.2318, found 482.2315.

2-[2-(2-(2-Fluoro-phenyl)-imino-oxazolidin-3-yl)-ethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione(**4c**)

Yield 50%, m.p. = 184.4-185.9 $^{\circ}\text{C}$; IR (KBr) ν_{max} 1687, 1668, 1590, 1382 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.544 (d, $J = 7.2\text{Hz}$, 1H), 8.459 (d, $J = 7.8\text{Hz}$, 1H), 8.319 (d, $J = 8.8\text{Hz}$, 1H), 7.616 (dd, $J = 7.2, 8.8\text{Hz}$, 1H), 7.115 (d, $J = 7.8\text{Hz}$, 1H), 6.506-6.462 (m, 2H), 6.267-6.232 (m, 2H), 4.482 (t, $J = 5.6\text{Hz}$, 2H), 4.286 (t, $J = 7.6\text{Hz}$, 2H), 3.825 (t, $J = 5.6\text{Hz}$, 2H), 3.748 (t, $J = 7.6\text{Hz}$, 2H), 3.192-3.186 (m, 4H), 1.883-1.870 (m, 4H), 1.735-1.723 (m, 2H); HRMS (EI) calcd for $\text{C}_{28}\text{H}_{27}\text{N}_4\text{O}_3\text{F}$ [M^+] 486.2067, found 486.2077.

2-[2-(2-(4-Fluoro-phenyl)-imino-oxazolidin-3-yl)-ethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione(**4d**)

Yield 55%, m.p. = 208.7-208.7 $^{\circ}\text{C}$; IR (KBr) ν_{max} 1691, 1670, 1602, 1384 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.556 (d, $J = 7.2\text{Hz}$, 1H), 8.480 (d, $J = 8.4\text{Hz}$, 1H), 8.362 (d, $J = 8.4\text{Hz}$, 1H), 7.639 (dd, $J = 7.2, 8.4\text{Hz}$, 1H), 7.146 (d, $J = 8.4\text{Hz}$, 1H), 6.751-6.563 (m, 3H), 6.119-6.074 (m, 1H), 4.486 (t, $J = 5.6\text{Hz}$, 2H), 4.270 (t, $J = 7.8\text{Hz}$, 2H), 3.862 (t, $J = 5.6\text{Hz}$, 2H), 3.767 (t, $J = 7.8\text{Hz}$, 2H), 3.217-3.204 (m, 4H), 1.902-1.862 (m, 4H), 1.736-1.725 (m, 2H); HRMS (EI)

calcd for $C_{28}H_{27}N_4O_3F$ [M^+] 486.2067, found 486.2063.

2-[2-(2-(4-Nitro-phenyl)-imino-oxazolidin-3-yl)-ethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione(**4e**)

Yield 30%. m.p. = 220.0-220.6 °C; IR (KBr) ν_{max} 1693, 1652, 1563, 1315 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 8.426 (d, J = 7.8 Hz, 1H), 8.321 (d, J = 8 Hz, 1H), 8.202 (d, J = 8.8 Hz, 1H), 7.703 (dd, J = 7.8, 8.8 Hz, 1H), 7.452 (d, J = 8.8 Hz, 2H), 7.175 (d, J = 8 Hz, 1H), 6.146 (d, J = 8.8 Hz, 2H), 4.425-4.350 (m, 4H), 3.830-3.789 (m, 4H), 3.041-3.036 (m, 4H), 1.764-1.760 (m, 4H), 1.630-1.628 (m, 2H); HRMS (EI) calcd for $C_{28}H_{27}N_5O_5$ [M^+] 513.2012, found 513.2022.

2-[2-(2-Methylimino-oxazolidin-3-yl)-ethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione(**4f**)

Yield 65%. m.p. = 144.3-145.2 °C; IR (KBr) ν_{max} 1691, 1650, 1589, 1388 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 8.544 (d, J = 7.2 Hz, 1H), 8.483 (d, J = 8 Hz, 1H), 8.375 (d, J = 7.8 Hz, 1H), 7.662 (dd, J = 7.2, 8 Hz, 1H), 7.165 (d, J = 8 Hz, 1H), 4.399 (t, J = 5.6 Hz, 2H), 4.206 (t, J = 7.6 Hz, 2H), 3.619-3.566 (m, 4H), 3.222-3.210 (m, 4H), 2.515 (s, 3H), 1.896-1.856 (m, 4H), 1.730-1.720 (m, 2H); HRMS (EI) calcd for $C_{23}H_{26}N_4O_3$ [M^+] 406.2005, found 406.2009.

2-[2-(2-Naphyllimino-oxazolidin-3-yl)-ethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione(**4g**)

Yield 35%. m.p. = 177.6-178.3 °C; IR (KBr) ν_{max} 1691, 1652, 1589, 1384 cm^{-1} ; 1H NMR (400 MHz, DMSO- d_6) δ 8.470 (d, J = 7.2 Hz, 1H), 8.397-8.320 (m, 2H), 7.741 (t, J = 7.8 Hz, 1H), 7.587 (d, J = 7.8 Hz, 1H), 7.506 (d, J = 8 Hz, 1H), 7.259-7.174 (m, 3H), 7.021 (t, J = 7.8 Hz, 1H), 6.649 (t, J = 6.8 Hz, 1H), 6.474 (d, J = 7.2 Hz, 1H), 4.403 (t, J = 5.6 Hz, 2H), 3.894 (t, J = 7.6 Hz, 2H), 3.894 (t, J = 5.6 Hz, 2H), 3.775 (t, J = 7.6 Hz, 2H), 3.190-3.170 (m, 4H), 1.824-1.816 (m, 4H), 1.670-1.664 (m, 2H); HRMS (EI) calcd for $C_{32}H_{30}N_4O_3$ [M^+] 518.2318 found 518.2315.

Procedure for the formation of **4h**

To a solution of 0.005 mol of 2-[2-aminoethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione in 50 mL of chloroform was added dropwise substituted isothiocyanate (0.005 mol) over a period of 10 min. The reaction mixture was stirred for 1 h at room temperature. The solvent was removed under reduced pressure to give crude thioureas. The thiourea (0.005 mol) was dissolved in 20 ml 1,2-ethyldibromide. The mixture was heated to reflux for 12 hrs. The solvent was removed under reduced pressure, and to the residue was added 50 ml of H_2O and 10 ml of concentrated aqueous ammonia. The precipitated product was filtered, washed with H_2O , and was purified by column chromatography on silica gel (methanol-chloroform, 1:20).

2-[2-(2-Phenylimino-thiazolidin-3-yl)-ethyl]-6-piperidin-1-yl-benzo[de]isoquinoline-1,3-dione

Yield 55%. m.p. = 189.9-190.5 °C; IR (KBr) ν_{max} 1695, 1652, 1589, 1378 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 8.586 (d, J = 7.2 Hz, 1H), 8.509 (d, J = 8 Hz, 1H), 8.389 (d, J = 8.8 Hz, 1H), 7.677 (dd, J = 7.2, 8.8 Hz, 1H), 7.450 (d, J = 8 Hz, 1H), 7.302-7.102 (m, 5H), 4.489 (t, J = 6.0 Hz, 2H), 4.042 (t, J = 7.2 Hz, 2H), 3.655 (t, J = 6.0 Hz, 2H), 3.249-3.234 (m, 6H), 1.895-1.885 (m, 4H), 1.729-1.723 (m, 2H); HRMS (EI) calcd for $C_{28}H_{28}N_4O_2S$ [M^+] 484.1933, found 484.1931.

Spectroscopy data

a)

b)

c)

Fig.1 (a) Fluorescence characteristics of **4a** at 295 K in phosphate buffers of differing pH. (b) Fluorescence characteristics of **4b** at 295 K in phosphate buffers of differing pH. (c) pH Dependence of 4a-b ($I/I_{\max}$) at 295 K in phosphate buffers of differing pH (4a: exc = 413 nm; 4b: exc = 420 nm). The pH dependence of fluorescence intensity can be analyzed with below equation giving the pK_a value.

$$\log[(I_{\max} - I)/(I - I_{\min})] = \text{pH} - \text{pK}'_a$$

Table 1. Parameters of the absorption and fluorescence spectra of **4a-g** (All compounds were characterized at 295 K in phosphate buffers (ethanol : buffers=1:4) of differing pH.)

	4a	4b	4c	4d	4e	4f	4g
Absa	436	431	434	428	442	422	391
Aa	0.117	0.126	0.083	0.114	0.120	0.267	0.106
Abs b	422	425	431	425	439	422	391
Ab	0.110	0.129	0.073	0.111	0.126	0.263	0.107
Flua	547	550	551	515	535	557	528
Fa	0.00133	0.00126	0.00253	0.0281	0.00875	0.00656	0.00388
Flub	536	537	535	515	535	556	530
F b	0.0064	0.038	0.00267	0.0375	0.00984	0.000776	0.0054
pK _a	6.68	6.40	-	-	-	-	-

^a. The data was measured at pH 4.60. ^b The data was measured at pH_{10.34}.

a)

b)

Fig.2 (a) Fluorescence characteristics of **4h** under different pH values. (b) pH Dependence of **4a**, **4h** ($I/I_{\max}$) at 295 K in phosphate buffers of differing pH (**4a**: exc = 413 nm; **4h**: exc = 417 nm) Readings were made using a Perkin-Elmer LS50B fluorimeter in fluorescence mode).

Table 2 Parameters of the absorption and fluorescence spectra of **4h** (All compounds were characterized at 295 K in phosphate buffers (ethanol : buffers=1:4) of differing pH.

	4h
Abs (pH=4.60) [nm]	428
A	0.122
Abs (pH=10.34) [nm]	439
A	0.121
Flu (pH=4.60) [nm]	529
F (pH=4.60)	0.0073
Flu (pH=10.34) [nm]	535
F (pH=10.34)	0.234
pKa	7.53