Fluorescent sensors for diamines†

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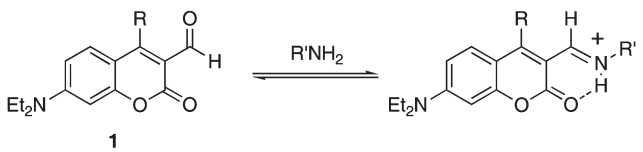
A series of seven diamine sensors was prepared using dimers of a quinolone aldehyde chromophore. Binding to six different diamine guests was explored by a combination of NMR, absorption and fluorescence spectroscopy. It was shown that the dimeric sensors bound the diamine guests by formation of a bis-iminium ion which produced large changes in the fluorescence of the quinolone core. Issues of selectivity between guests are discussed.

Introduction

Fluorescent sensors for intracellular analyte detection are rapidly becoming common biochemical tools. Sensors for cellular ions such as Ca^{+2} and Zn^{+2} are particularly well studied.[1] Sensors for the intracellular detection of organic analytes are less well developed due to the difficulty in obtaining selective and high affinity recognition of organic compounds in an aqueous environment.[2,3] We have been investigating a class of coumarin-containing fluorescent sensors for the specific sensing of amine-containing analytes (compound **1**, Scheme 1).[4] Compounds like **1** respond to the presence of amines by the formation of an iminium ion which, due to fortuitous hydrogen bonding, alters the fluorescent properties of the coumarin core. Importantly, this recognition and sensing method works well in an aqueous environment and gives a good fluorescent response to analyte binding. By attaching auxiliary recognition elements at the R group, selective sensors for amine containing analytes such as dopamine have been prepared.[5]

Zimmerman *et al*. have prepared receptors for diamines by incorporating trifluoromethyl ketones into a dendrimer.[6] As part of our program in amine sensing, we began a study in which dimeric versions of **1** could be used to bind diamines such as lysine.[7] During this study, we discovered that the coumarin core of **1** could be replaced by a quinolone group and that quinolone dimers such as **2** (Scheme 2) were quite synthetically accessible. Thus, a series of sensors could be prepared and the linking group (X) could be varied in order to achieve optimal binding properties. Herein, we report the synthesis and characterization of sensors such as **2** and their use in the fluorescent detection of diamines.



Scheme 1

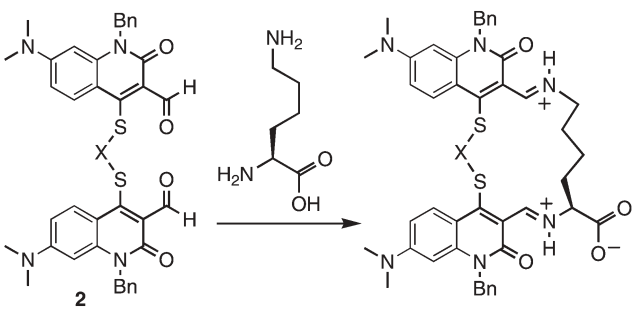
Experimental

Absorption and fluorescence experiments

Fluorescence spectra were recorded on a Shimadzu RF-5301 PC spectrofluorimeter at 37 °C. The excitation wavelength was 495 nm with excitation with emission slit widths of 5 nm each. Absorption spectra were recorded on a Cary 1E spectrophotometer at 37 °C. Solutions of each sensor were prepared at 10 μM in 50% MeOH–buffered water (50 mM HEPES, 240 mM NaCl, pH = 7.4 prior to dilution in MeOH). All guest solutions were prepared as above and contained 10 μM senor to prevent dilution. Binding isotherms were constructed by recording fluorescence intensity at 537 nm as a function of added analyte and fitting the data to a one-site model using Graphpad Prism software. A 1 : 1 binding model was assumed (verified by NMR) and the data fit this model well for all analytes tested. The fluorescence intensity at saturation (I_{sat}) was taken from the theoretical fit to the data.

Synthesis

Compound 5. Compound **4** (4.39 g, 19.4 mmol), bis-(2,4,6-trichlorophenyl) malonate (8.98 g, 19.4 mmol), and toluene (150 cm^3) were added to a flame-dried flask. A reflux condenser and drying tube were attached, and the mixture was refluxed for 20 h. The reaction mixture was cooled and filtered. The filtrate was washed with hexanes to yield the title compound as a tan powder (5.8 g, 100%). mp 284–286 °C,



Scheme 2

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decomp; ν_{max}(film)/cm^{-1} 1625, 1569, 1544, 1537, 1488, 1384 and 1354; δ_H/ppm (250 MHz, DMSO-d6) 11.0 (1 H, s), 7.65 (1 H, d, *J* 9.0), 7.19–7.28 (5 H, m), 6.59 (1 H, dd, *J* 2.0 and 9.0), 6.29 (1 H, d, *J* 1.9), 5.69 (1 H, s), 5.40 (2 H, s) and 2.86 (6 H, s); δ_C/ppm (62.5 MHz, DMSO-d6) 163.5, 161.9, 152.0, 140.8, 137.9, 128.4, 126.8, 126.7, 124.1, 107.1, 105.9, 96.2, 93.4, 43.9 and 39.6; *m*/*z* (FAB) 301.1529 (M + Li$^+$. $C_{18}H_{18}LiN_2O_2$ requires 301.1528).

Compound 6. $POCl_3$ (6.2 cm^3, 66.5 mmol) was added to DMF (13 cm^3, 168 mmol) at 0 °C in a dry flask equipped with a drying tube. The solution was stirred at 0 °C for 15 min then at ambient temperature for 3.5 h. DMF (250 cm^3) then compound **5** (13.8 g, 46.9 mmol) were added. The mixture was stirred at ambient temperature for 42 h. The resulting yellow suspension was poured onto H_2O (800 cm^3) and filtered. The filtrate was washed with MeOH (800 cm^3). The resulting yellow solid was 90% pure and was used in subsequent reactions. A portion of the material was purified *via* flash chromatography (Et_2O–CH_2Cl_2, 0 : 100 to 10 : 90) for characterization. mp 225°–226°; ν_{max}(film)/cm^{-1} 1682, 1637, 1611, 1583, 1558, 1514, 1496 and 1454; δ_H/ppm (300 MHz, $CDCl_3$; Me_4Si) 10.55 (1 H, s), 8.00 (1 H, d, *J* 9.4), 7.24–7.34 (5 H, m), 6.64 (1 H, dd, *J* 2.3 and 9.4), 6.20 (1 H, d, *J* 2.3), 5.49 (2 H, s) and 3.00 (6 H, s); δ_C/ppm (75 MHz, $CDCl_3$; Me_4Si) 189.5, 162.3, 153.8, 148.4, 142.3, 136.0, 134.2, 129.8, 128.9, 127.5, 126.8, 116.0, 109.6, 95.3, 46.2 and 40.1; *m*/*z* (FAB) 347.1144 (M + Li$^+$. $C_{19}H_{17}ClLiN_2O_2$ requires 347.1139).

General procedure for preparation of dimers 2a–g. Compound **6** (2.2 equiv.), dithiol (1 equiv.), K_2CO_3 (4 equiv.), and DMF (0.015 M in dithiol) were combined in a flame-dried, N_2-filled flask. The reaction mixture was stirred at ambient temperature overnight, then worked up according to the procedures below.

Compound 2a. The crude reaction mixture was poured into H_2O (200 cm^3) and filtered. The filtrate was washed into a flask with CH_2Cl_2 (100 cm^3), dried over Na_2SO_4, and the solvent was removed *in vacuo*. The yellow solid was purified *via* flash chromatography (THF–hex, 20 : 80 to 50 : 50), and the product was isolated as a yellow solid (47.6 mg, 76%). An analytically pure sample was obtained by recrystallization from toluene. mp 121 °C; ν_{max}(film)/cm^{-1} 2924, 1695, 1597, 1498, 1391 and 1170; δ_H/ppm (300 MHz, $CDCl_3$, Me_4Si) 10.54 (2 H, s), 8.28 (2 H, d, *J* 9.3), 7.33–7.23 (10 H, m), 7.06 (4 H, s), 6.60 (2 H, dd, *J* 2.2 and 9.3), 6.21 (2 H, d, *J* 2.1), 5.50 (4 H, s), 4.13 (4 H, s) and 2.99 (12 H, s); δ_C/ppm (75 MHz $CDCl_3$; Me_4Si) 190.5, 162.3, 153.6, 153.4, 142.0, 136.3, 131.0, 129.1, 128.8, 127.3, 126.8, 120.6, 112.5, 109.1, 95.7, 46.1, 41.9 and 40.1; *m*/*z* (FAB) 785.2807 (M + Li$^+$. $C_{46}H_{42}N_4O_4S_2Li$ requires 785.2795).

Compound 2b. The crude reaction mixture was poured into H_2O (200 cm^3) and filtered. The filtrate was washed into a flask with CH_2Cl_2 (100 cm^3), dried over Na_2SO_4, and the solvent was removed *in vacuo*. The yellow solid was purified *via* flash chromatography (THF–hex, 20 : 80 to 50 : 50), and the product was isolated as a yellow solid (45.6 mg, 57%). An analytically pure sample was obtained by recrystallization from toluene. mp 92 °C; ν_{max}(film)/cm^{-1} 2924, 1695, 1597, 1497, 1390 and 1170; δ_H/ppm (300 MHz, $CDCl_3$, Me_4Si) 10.55 (2H, s), 8.27 (2H, d, *J* 9.3 Hz), 7.33–7.23 (10H, m), 7.04 (4H, m), 6.62 (2H, dd, *J* 2.3, 9.4 Hz), 6.21 (2H, d, *J* 2.3 Hz), 5.50 (4H, s), 4.09 (4H, s) and 2.98 (12H, s); δ_C/ppm (75 MHz $CDCl_3$; Me_4Si) 190.5, 162.3, 153.6, 153.4, 142.1, 137.3, 136.4, 131.1, 129.7, 128.8, 128.6, 128.2, 127.3, 126.8, 120.7, 112.6, 109.2, 95.7, 46.2, 42.0 and 40.1; *m*/*z* (FAB) 785.2795 (M + Li$^+$. $C_{46}H_{42}N_4O_4S_2Li$ requires 785.2795).

Compound 2c. The crude reaction mixture was poured into H_2O (200 cm^3) and filtered. The filtrate was washed into a flask with CH_2Cl_2 (100 cm^3), dried over Na_2SO_4, and the solvent was removed *in vacuo*. The yellow solid was purified *via* flash chromatography (THF–hex, 20 : 80 to 50 : 50), and the product was isolated as a yellow solid (31.4 mg, 45%). An analytically pure sample was obtained by recrystallization from toluene. mp 109 °C; ν_{max}(film)/cm^{-1} 2924, 1633, 1597, 1498, 1391 and 1170; δ_H/ppm (300 MHz, $CDCl_3$, Me_4Si) 10.46 (2 H, s), 8.26 (2H, d, *J* 9.2), 7.33–7.24 (10 H, m), 7.07 (4 H, s), 6.58 (2 H, dd, *J* 2.3 and 9.4), 6.19 (2 H, d, *J* 2.3), 5.51 (4 H, s), 4.33 (4 H, s) and 2.97 (12 H, s); δ_C/ppm (75 MHz $CDCl_3$; Me_4Si) 190.4, 162.3, 153.6, 153.1, 142.0, 136.6, 135.5, 130.9, 128.8, 128.0, 127.3, 126.7, 120.5, 112.3, 109.2, 95.7, 46.0, 40.0 and 39.4; *m*/*z* (FAB) 785.2807 (M + Li$^+$. $C_{46}H_{42}N_4O_4S_2Li$ requires 785.2795).

Compound 2d. The solvent from the crude reaction mixture was removed *in vacuo*. The resulting yellow solid was dissolved in H_2O (10 cm^3) and $CHCl_3$ (30 cm^3) and extracted with $CHCl_3$ (5 × 30 cm^3). The combined organic extracts were dried over $MgSO_4$. The solvent was removed *in vacuo*, and the yellow solid was purified *via* flash chromatography (THF–hexanes, 20 : 80 to 100 : 0), and the product was isolated as a yellow solid (91 mg, 91%). mp 224–226 °C, decomp; ν_{max}(film)/cm^{-1} 2927, 1694, 1598, 1503, 1390, 1364, 1164 and 1169; δ_H/ppm (300 MHz, $CDCl_3$; Me_4Si) 10.48 (2 H, s), 7.96 (2 H, d, *J* 9.4), 7.25–7.32 (10 H, m), 6.99–7.12 (4 H, m), 6.52 (2 H, dd, *J* 2.4 and 9.4), 6.23 (2 H, d, *J* 2.4), 5.55 (4 H, s) and 2.97 (12 H, s); δ_C/ppm (75 MHz, $CDCl_3$; Me_4Si) 190.1, 161.7, 153.5, 150.6, 142.5, 138.0, 136.3, 131.5, 129.9, 128.8, 128.8, 127.4, 127.2, 126.8, 121.2, 110.9, 109.4, 95.7, 46.4 and 40.0; *m*/*z* (FAB) 357.2516 (M + Li$^+$. $C_{44}H_{38}LiN_4O_4S_2$ requires 357.2495).

Compound 2e. The crude reaction mixture was poured onto H_2O (20 cm^3) and extracted with CH_2Cl_2 (5 × 30 cm^3). The combined organic extracts were dried on $MgSO_4$, and the solvent was removed *in vacuo*. The resulting red–brown solid was purified *via* flash chromatography (EtOAc–CH_2Cl_2, 0 : 100 to 20 : 80), and the product was isolated as a yellow solid (65.1 mg, 43%). mp 263–264 °C, decomp; ν_{max}(film)/cm^{-1} 2924, 1694, 1598, 1495, 1483, 1434, 1389, 1363 and 1171; δ_H/ppm (250 MHz, $CDCl_3$; Me_4Si) 10.53 (2 H, s), 8.10 (2 H, d, *J* 9.4), 7.22–7.30 (10 H, m), 6.95–7.05 (4 H, m), 6.55 (4 H, dd, *J* 2.2 and 9.4), 6.24 (2 H, d, *J* 2.2), 5.55 (4 H, s) and 2.96 (12 H, s); δ_C/ppm (75 MHz, $CDCl_3$; Me_4Si) 190.0, 161.6, 153.6, 151.7, 142.5, 136.3, 131.2, 130.4, 128.8, 127.7, 127.4, 126.9, 121.4,

111.4, 109.5, 95.7, 46.4 and 40.7; *m/z* (FAB) 357.2514 (M + Li^+. $C_{44}H_{38}LiN_4O_4S_2$ requires 357.2495).

Compound 2f. The crude reaction mixture was diluted with H_2O (30 cm^3) and extracted with CH_2Cl_2 (2 × 40 cm^3). The combined organic extracts were dried on Na_2SO_4, and the solvent was removed *in vacuo*. The resulting red–brown solid was purified *via* flash chromatography (EtOAc–CH_2Cl_2, 1 : 3 to 1 : 1), and the product was isolated as a yellow solid (53 mg, 72%). mp 226 °C; ν_{max}(film)/cm^{-1} 2924, 1684, 1596, 1497, 1390 and 1170; δ_H/ppm (500 MHz, $CDCl_3$, Me_4Si), 10.53 (2 H, s), 8.29 (2 H, d, *J* 9.4), 7.27 (12 H, m), 6.63 (2 H, dd, *J* 2.1 and 9.4), 6.20 (2 H, d, *J* 2.0), 5.49 (4 H, s),3.10 (4 H, t, *J* 6.9), 2.98 (12 H, s), 1.54(4 H, m) and 1.46 (2 H, m); δ_C/ppm (125 MHz $CDCl_3$; Me_4Si) 191.1, 163.2, 155.1, 154.5, 142.8, 137.1, 131.6, 129.6, 128.1, 127.6, 120.9, 113.3, 110.1, 96.5, 47.0, 40.9, 37.7 and 31.0; *m/z* (FAB) 723.2669 (M + Li^+. $C_{41}H_{40}N_4O_4S_2Li$ requires 723.2651).

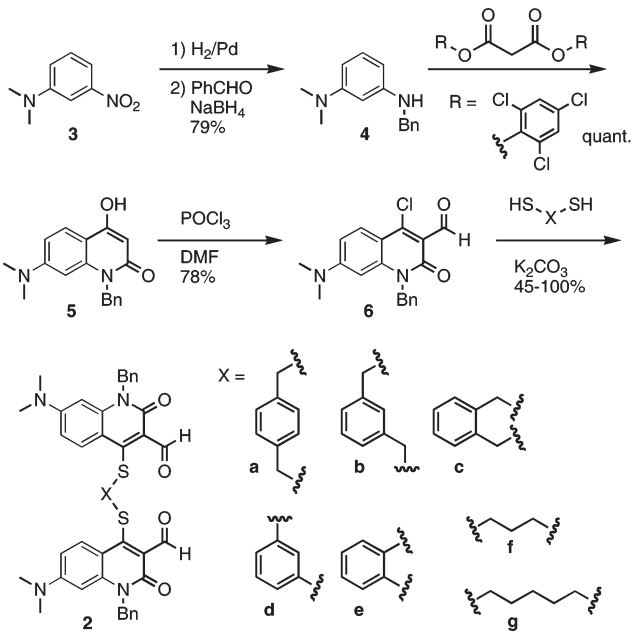
Compound 2g. The crude reaction mixture was diluted with CH_2Cl_2 (10 cm^3), filtered on a plug of cotton, and the solvent was removed *in vacuo* to yield a red–yellow solid (55 mg, 100%). mp 122 °C; ν_{max}(film)/cm^{-1} 2929, 2858, 1692, 1597, 1497, 1391 and 1170; δ_H/ppm (300 MHz, $CDCl_3$, Me_4Si) 10.59 (2 H, s), 8.34 (2 H, d, *J* 9.3), 7.26 (12 H, m), 6.65 (2 H, dd, *J* 2.3 and 9.3), 6.22 (2 H, d, *J* 2.2), 5.50 (4 H, s), 2.99 (12 H, m), 2.95 (4 H, t, *J* 7.1), 1.55 (4 H, p, *J* 6.8) and 1.46(2 H, m); δ_C/ppm (75 MHz $CDCl_3$; Me_4Si) 190.4, 162.3, 155.3, 153.7, 142.0, 136.4, 130.8, 130.8, 128.8, 127.4, 126.9, 120.3, 112.6, 109.1, 95.8, 46.3, 40.1, 38.2, 29.5 and 27.7; *m/z* (FAB) 751.2979 (M + Li^+. $C_{43}H_{44}N_4O_4S_2Li$ requires 751.2964).

Compound 7. Compound **6** (200 mg, 0.587 mmol), NaSEt (74 mg, 0.880 mmol), and DMF (6 cm^3) were combined in a flame-dried, N_2-filled flask. The reaction mixture was stirred at ambient temperature for 28 h. CH_2Cl_2 was added, and the solution was washed with H_2O (4 × 30 cm^3) and brine (30 cm^3). The CH_2Cl_2 layer was dried on $MgSO_4$, and the solvent was removed *in vacuo*. The resulting yellow solid was purified *via* flash chromatography (Et_2O–CH_2Cl_2, 5 : 95 to 15 : 85), and the product was isolated as a yellow solid (86.7 mg, 40%). mp 163°–164°; ν_{max}(film)/cm^{-1} 1687, 1681, 1597, 1498, 1483, 1457, 1430 and 1391; δ_H/ppm (300 MHz, $CDCl_3$; Me_4Si) 10.63 (1 H, s), 8.36 (1 H, d, *J* 9.3), 7.25–7.30 (5 H, m), 6.62 (1 H, dd, *J* 2.3 and 9.3), 6.23 (1 H, d, *J* 2.1), 5.51 (2 H, s), 3.03 (2 H, q, *J* 7.4), 2.99 (6 H, s) and 1.25 (3 H, t, *J* 7.4); δ_C/ppm (75 MHz, $CDCl_3$; Me_4Si) 190.4, 162.0, 154.9, 153.5, 141.9, 136.3, 130.7, 128.7, 127.2, 126.8, 120.5, 112.5, 108.8, 95.6, 46.9, 40.0, 32.3 and 14.9; *m/z* (FAB) 373.1575 (M + Li^+. $C_{21}H_{22}LiN_2O_2S$ requires 373.1562).

Results and discussion

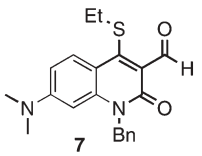
Synthesis

The synthesis of the series of diamine sensors is shown in Scheme 3. One of the drawbacks to the original coumarin sensors (*i.e.*, **1**, Scheme 1) was the limited functionality (R) that could be appended to the coumarin core. To expand the range of functionality available, the quinolone core (**6**, Scheme 3) was prepared in four steps from 3-nitro-dimethylaniline following close analogy to the coumarin series.[8] It was discovered that compound **6** could be treated with thiolates, which added in a Michael fashion, to produce thio-ethers having fluorescent properties which were similar to the original coumarins. To access diamine sensors, compound **6** was treated with several dithiols to produce a series of quinolone dimers **2a–g**. The linker connecting the quinolone cores (X) was varied in order to probe the effects of length and rigidity on the diamine binding properties.



Scheme 3

Spectroscopic analysis



The interactions of sensors **2a–g** were probed spectroscopically by UV–vis and fluorescence titration experiments. The series of sensors displayed poor water solubility properties compared to monomeric quinolones such as **7**; thus, spectroscopic analysis was carried out in a 1 : 1 methanol–buffer system. The absorption spectra showed trends similar to those observed with the coumarin analogs in which a large red shift in absorption maximum was observed upon addition of diamines to the sensors. As shown in Fig. 1(a), when sensor **2g** was titrated with diaminopropane, a 28 nm shift in absorbance was observed, consistent with a shift from aldehyde to iminium ion forms (*i.e.*, Scheme 2). The red shift in absorption has been attributed to the hydrogen bond between the formed iminium ion and the carbonyl group of the chromophore. In fluorescence mode, by exciting the chromophore at 495 nm, a large increase in fluorescence was observed

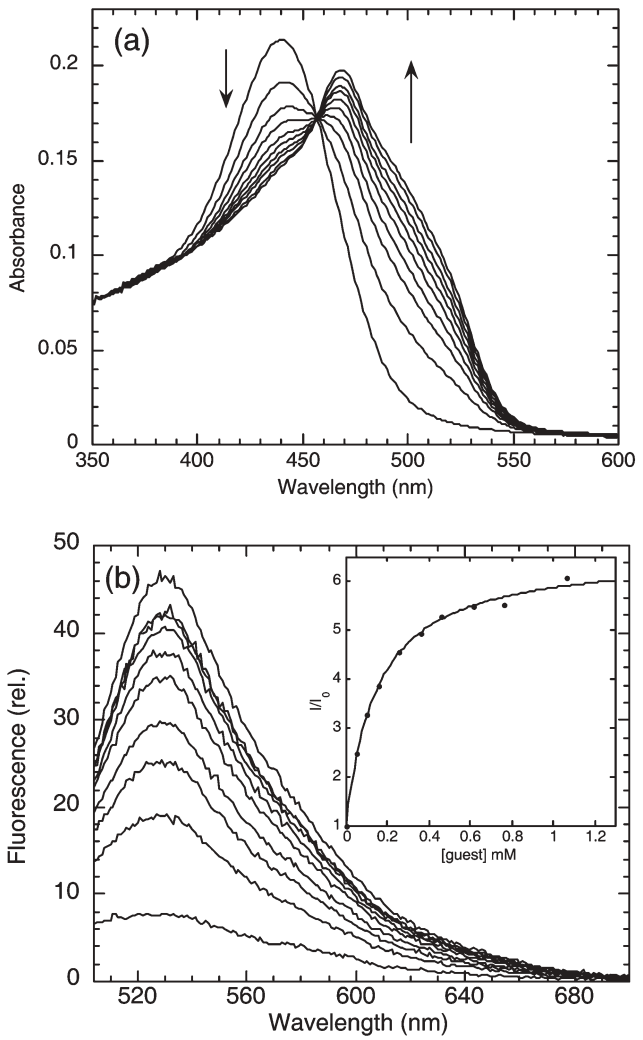
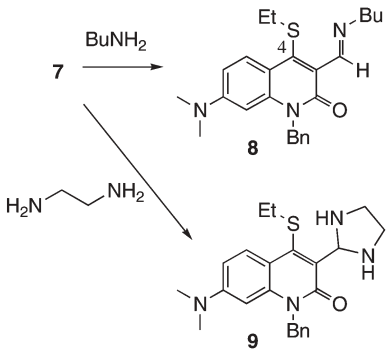


Fig. 1 (a) UV–vis and (b) fluorescence titrations of sensor **2g** with diaminopropane (10 μM sensor in 50% MeOH–buffered water [50 mM HEPES, 240 mM NaCl, pH = 7.4]). Curves in (a) correspond to the addition of 0.05, 0.1, 0.015, 0.26, 0.36, 0.46, 0.61, 0.76, 1.1 mM guest. Inset in (b) is the theoretical fit to the binding isotherm.

upon titration with the diamine (Fig. 1(b)). The fluorescence increase was fitted to a one-site binding isotherm which gave a binding constant of 6700 M^{-1} (inset in Fig. 1(b)) with a maximum fluorescence increase at saturation (I_{sat}/I_0) of 6.6-fold.



Scheme 4

Results of titrations with six different guests for each of the eight sensors are tabulated in Table 1.

NMR characterization

The mode of binding and stoichiometry were confirmed by NMR experiments. First, compound **7** was titrated with butylamine in MeOH-d_4 and clean conversion to the imine (**8** in Scheme 4) was observed. The use of pure methanol solvent for the NMR experiments was necessitated by the poor solubility of the sensor. In contrast to butylamine, ethylene diamine appeared to produce an aminal with the aldehyde (compound **9**). The dimeric sensors, however, behaved as expected (*i.e.*, Scheme 2). For example, addition of one equivalent of diaminopentane to a solution of sensor **2a** (1.4 mM in $CDCl_3$) gave complete conversion to the bis-imine with no sign of aminal formation. Similarly ethylene diamine also produced the bis-imine product by NMR. These experiments served to demonstrate the mode of binding in this potentially complicated system and furthermore confirmed the 1 : 1 stoichiometry of the interaction since one equivalent of diamine completely converted the sensor aldehydes to imines.[9]

Selectivities

The data shown in Table 1 provide a number of trends in relative affinity. In all cases, the diamines bound better than butylamine with the obvious exception of the monoaldehyde **7**. The extent of the difference varied from 2.5 fold for sensor **2a** to 160 fold for **2g**. This effect validated our assumptions about the utility of aldehyde dimers as diamine sensors. The

Table 1 Binding constants and maximum fluorescence enhancements for various amine guests binding to sensors **2a–g** and **7**

	Butylamine		Diaminopropane		Diaminobutane		Diaminopentane		Ornithine		Lysine	
Sensor	K_a/M^{-1} [a]	I_{sat}/I_0 [b]	K_a/M^{-1}	I_{sat}/I_0	K_a/M^{-1}	I_{sat}/I_0	K_a/M^{-1}	I_{sat}/I_0	K_a/M^{-1}	I_{sat}/I_0	K_a (M^{-1})	I_{sat}/I_0
2a	160	12	590	8.3	640	16	470	17	580	14	410	15
2b	93	20	820	14	600	21	620	19	1000	22	540	29
2c	130	13	3300	6.5	520	10	480	10	840	12	780	14
2d	72	8.8	3400	16	1600	15	1200	15	3300	13	2100	4.7
2e	30	10	350	8.5	160	10	350	4.3	680	7.3	800	10
2f	31	26	2100	15	690	24	270	24	550	22	1500	24
2g	43	38	6700	6.6	1500	27	2200	18	2400	20	2800	27
7	76	32	—	—	—	—	—	—	—	—	129	41

[a] Error in K_a is ±20% based on duplicate titrations. [b] I_{sat}/I_0 is the maximum change in fluorescence derived from the theoretical fit to the binding isotherm.

interesting feature of the series of sensors was their relative selectivity for the various guests. The *a priori* expectation for the dialdehyde sensors was that all would bind to most diamines, however, shorter linkers would favor short chain diamines over long chain diamines and *vice versa*. Furthermore, guests which do not fit properly to a particular sensor would produce lower fluorescence response. This expectation is predicated on the observation that only a properly aligned hydrogen bond in the iminium ion state would produce an adduct with strongly shifted absorption characteristics compared to the unbound sensor.[4] Thus, a mismatch between the sensor and guest might result in poor hydrogen bonding and consequently poor fluorescence responses.

As seen in Table 1, the range of binding constants for the different length guests varied over approximately an order of magnitude from 160–6700 M^{-1}. Between the xylene linked sensors **2a–c**, very little selectivity was observed except for the preference for the smaller *ortho*-linked sensor to bind the smaller diamine. The *meta*-linked sensor (**2b**) demonstrated a small preference for ornithine which was coupled with a very large fluorescence increase (22 fold) for that guest.

Looking at the phenyl linked sensors **2d** and **2e**, it is interesting to note that the *meta*-phenyl linked sensor had overall higher affinity for all guests compared to the *ortho*-phenyl linked sensor. In fact, **2d** was selective between the amino acid guests with a preference for ornithine which was not observed for **2e**. Indeed, the maximum fluorescence change for **2d** was much larger for ornithine than for lysine which may indicate a better binding geometry for ornithine. Surprisingly, the most selective sensors of the group were the flexible sensors **2f** and **2g**. Excluding diaminopropane, the preferred guest in both cases was lysine. Although the selectivity was higher for **2f**, the overall binding constant was higher for **2g**. Indeed, in both cases the fluorescence increase was much smaller for diaminopropane than the other guests. Thus, the sensors could distinguish guests based not only on the binding constant, but also on the relative fluorescence change which was induced.

Conclusions

Sensors for diamines were readily prepared by dimerization of a quinolone aldehyde core. The aldehyde sensors bound the diamine guests by the formation of 1 : 1 bis-iminium ion adducts. Good binding constants and excellent fluorescence enhancements were observed in partly aqueous methanol. Furthermore, useful selectivities for different length guests were achieved by variation of the linker portion of the sensor.

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9 The NMR experiments revealed a secondary reaction in which amine guests can substitute the thiol group at C4 (*e.g.*, compound **10**). The existance of this species could be verified specroscopically. The amine adduct **10** (λ_{max} = 378 nm) was blue-shifted compared to the parent thioethyl quinolone **7** (λ_{max} = 441 nm) and grew in quite rapidly in the pure methanol experiment. In the methanol–buffer experiments, this blue-shifted band did not appear except at very high concentration of amine guest over long times. Presumably, in the neutral buffered conditions of the latter experiments, the amines were largely protonated and not nucleophilic. Thus, in the course of the fluorescence titrations reported in Table 1, the change in fluorescence was, in fact, only due to iminium ion formation.