

Synthesis and characterization of phosphorus-containing dendrimers bearing rhodamine derivatives as terminal groups

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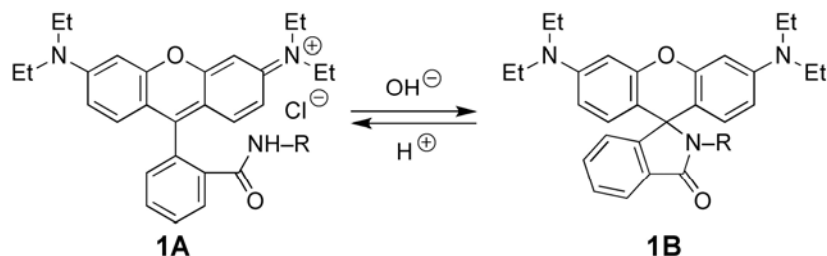
Abstract

The synthesis of two new derivatives of Rhodamine B functionalized by phenols is reported. For one rhodamine derivative, the equilibrium between the open form and the ring-closed (spirolactam) form is completely shifted toward the latter, whereas the constitution of the other rhodamine derivative precludes ring closure. The spirolactam derivative was grafted as terminal group to a first generation phosphorus-containing dendrimer. Attempts to open the spirolactam form by adding HCl failed and resulted only in protonation of the NEt₂ substituent of rhodamine.

Keywords: Dendrimers; rhodamine, chromophore, phosphorus, spirolactam

Introduction

Rhodamine derivatives pertain to one of the most largely used family of chromophores, owing to their photostability, high fluorescence intensity, and low cost compared to many other types of fluorophores. Beside the application as textile dyes, rhodamines are often used as sensitive labels or tracers for biological experiments, and as chemo-sensors for sensing ions.¹ This property is due to a pH-driven ring-opening / ring-closure (Scheme 1); the open form **1A** is colored and highly fluorescent, whereas the ring-closed form **1B** is colorless and non-fluorescent.²

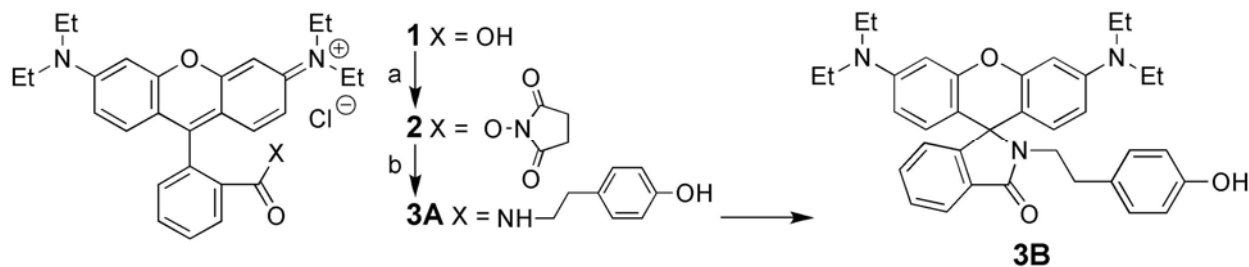


Scheme 1. pH-Driven equilibrium between open and closed (spirolactam) forms of rhodamines.

Frequently, grafting of a functionality as terminal groups of dendrimers enhances its properties. In the case of fluorescent groups, the presence of multiple fluorescent labels linked to dendrimers generally induces a brilliant fluorescence provided no quenching is caused by the close proximity of the fluorophores.³ We have shown that phosphorus-containing dendrimers are suitable for such purpose,⁴ also for obtaining brilliant two-photon absorption organic “nanodots”, as efficient as inorganic quantum dots.⁵ Grafting rhodamine derivatives as terminal groups of phosphorus-containing dendrimers may allow an enhancement of their sensing properties in biology (fluorescence in acidic conditions). Here we report the synthesis of new derivatives of Rhodamine B and their grafting as terminal groups of phosphorus-containing dendrimers.

Results and Discussion

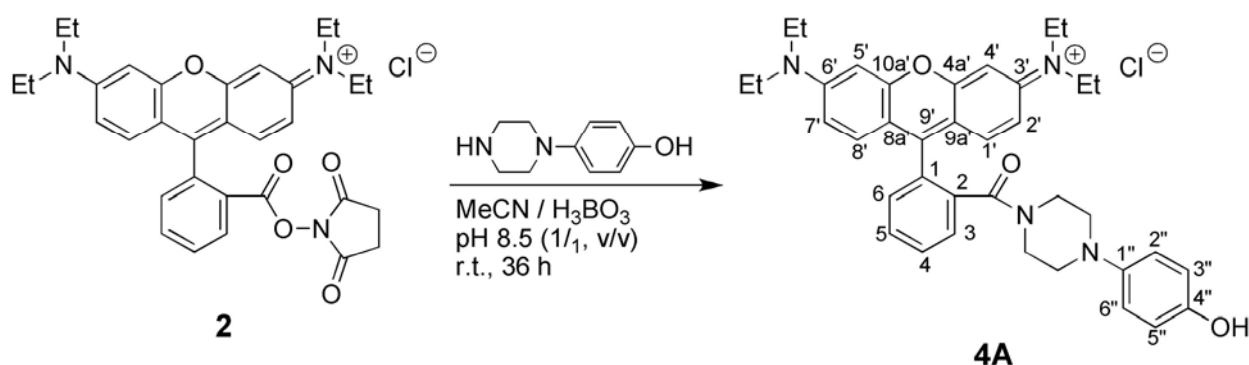
The phosphorus-containing dendrimers we synthesized contain P(S)Cl₂ or aldehyde groups as terminal groups. Since the P(S)Cl₂ group readily reacts with phenols Rhodamine B should be first functionalized to provide a phenol group, and the carboxylic acid group could serve for this purpose. As a linker for grafting various functionalities on P(S)Cl₂ groups we have used tyramine,⁶ which appears to be suitable here too. The reaction of the tyramine NH₂ function with the carboxylic acid group of Rhodamine B was attempted by two different ways. First, we tried the direct coupling using a classical peptidic coupling strategy based on the activation with hydroxybenzotriazole (HOBt) and dicyclohexylcarbodiimide (DCC); however, this attempt failed to afford the expected product. Then, we tried an indirect method (two steps) derived from the protocol for grafting of Rhodamine B to glycine.⁷ The first step was the esterification of the carboxylic acid group in Rhodamine B **1** with *N*-hydroxysuccinimide (NHS) in the presence of DCC. The resulting ester **2** was characterized by ¹³C NMR, displaying the CO signal at δ 160.74, while Rhodamine B **1** displays the CO signal at δ 167.7. The reaction of ester **2** with tyramine in acetonitrile and borate buffer formed compound **3**, which was isolated as a white powder upon column chromatography (Scheme 2).



Scheme 2. Reagents and conditions: a. NHS, DCC, MeCN 45 °C, 1h, then r.t., 20 h; b. MeCN/H₃BO₃ buffer pH 8.5 (1:1, v/v), r.t., 36 h.

Unexpectedly, compound **3** is colorless and non-fluorescent. Thus, the structure of **3** cannot be the open form **3A** but the spirolactam form **3B**; this was confirmed by the ^{13}C NMR signal at δ 65.13 assigned to the spiro-carbon.

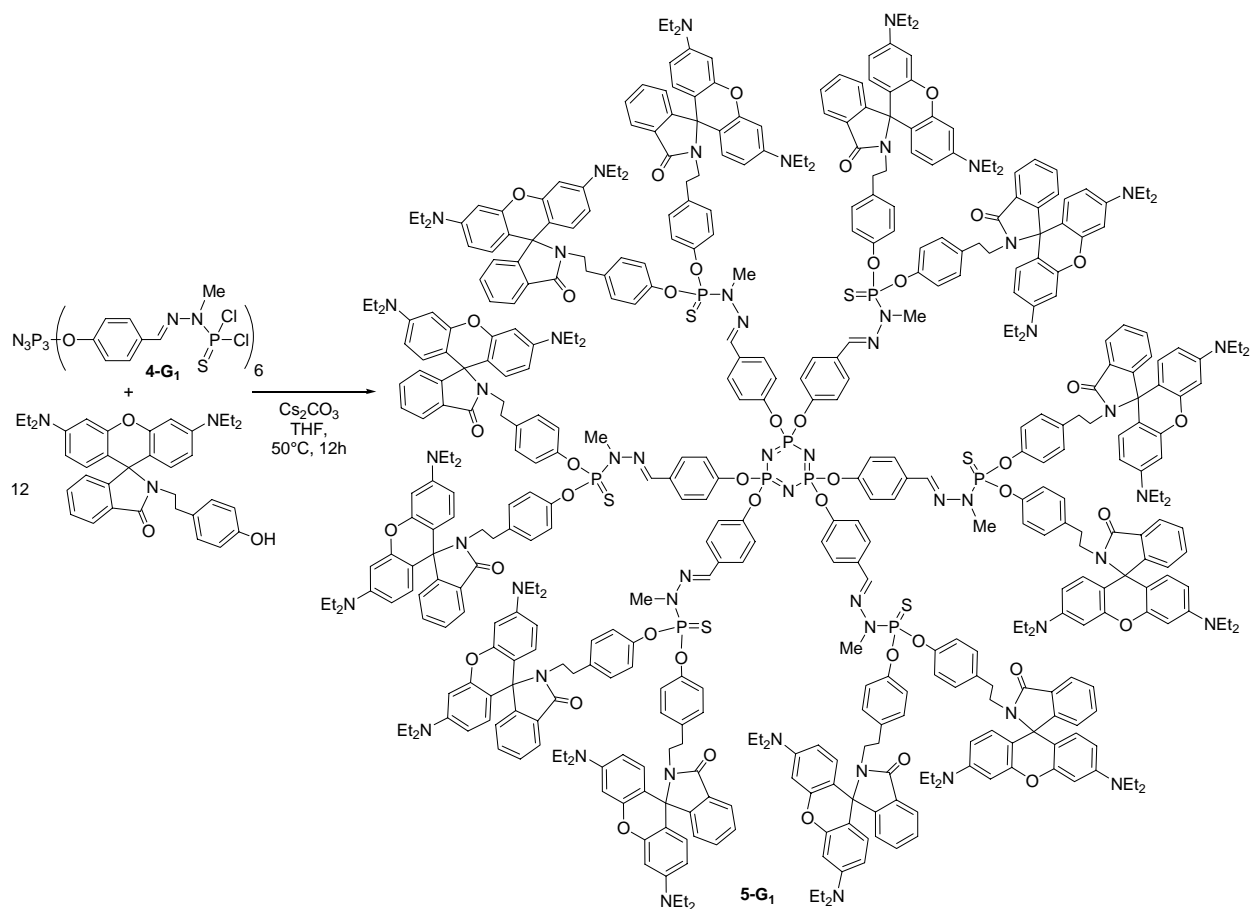
This result was unexpected but may be interesting for practical synthesis. THF and chloroform are good solvents for dendrimers and for spirolactam **3B**. An open form is anticipated to be insoluble in such solvents and permanently fluorescent. Therefore, the synthesis of a phenol derivative of Rhodamine B was devised that is prevented from ring closure: 4-hydroxyphenyl-piperazine was chosen for this purpose. The peptide coupling strategy used previously was successfully applied to afford compound **4**, which is dark purple in color and fluorescent as anticipated (Scheme 3). The open form **4A** was confirmed by the absence of a ^{13}C NMR signal at about δ 65 (spiro carbon) and by the signal at δ 167.87 (N–C=O).



Scheme 3

Using cesium carbonate as a base, Rhodamine derivatives **3B** and **4A** were grafted as terminal groups on the first generation dendrimer **5-G₁**.⁷ Monitoring the reaction of compound **3B** by ^{31}P NMR showed the disappearance of the P(S)Cl₂ signal at δ 62.5 and the appearance of a signal at δ 68.5 corresponding to mono-substitution [P(S)Cl(OAr)]; disappearance of the latter signal and the appearance of a new signal at δ 62.7 indicated full substitution (dendrimer **5-G₁**) (Scheme 4). ^{31}P NMR is a very sensitive tool for the characterization of phosphorus-containing dendrimers,^{8,9} mass spectrometry, including MALDI-Tof, is not useful for proving the purity of the phosphorhydrazone-containing dendrimers.¹⁰

Dendrimer **5-G₁** is not fluorescent, indicating that the closed rhodamine form is retained upon grafting to dendrimers. In an attempt to open the spiro-form (cf. Scheme 1), an equivalent amount (1 H⁺ per terminal group) of aqueous HCl (0.1 N) was added to the solution of dendrimer **5-G₁** in THF; a pink color developed after 1.5 h. ^{31}P and ^1H NMR showed that the overall structure of the dendrimer was not changed by the addition of HCl. The ^{13}C NMR signal of the spiro carbon was still present indicating that most of the rhodamine moieties were not opened. Additional HCl did not open all spiro forms, the closed form prevailing in the equilibrium as confirmed by the very low fluorescence intensity of **5-G₁**-HCl compared to Rhodamine B (Figure 1) even in DMSO, which should favor the open form as polar solvents do in general.¹¹



Scheme 4

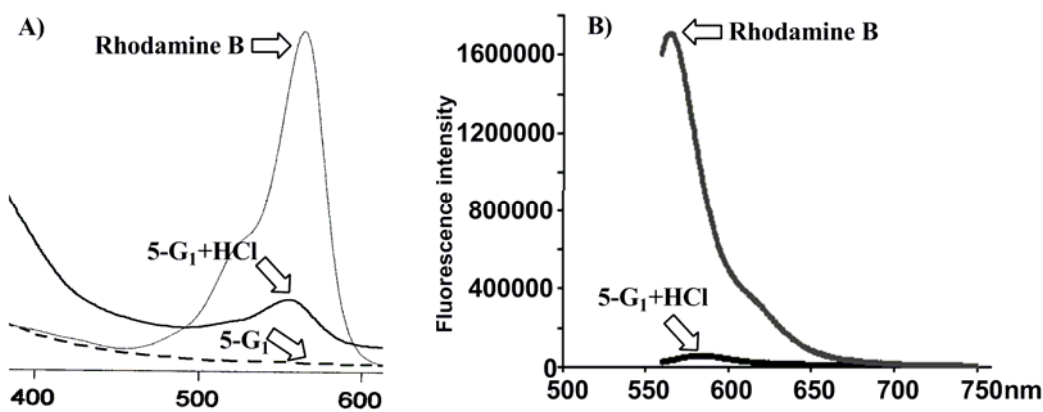


Figure 1. A) Vis spectra of Rhodamine B, dendrimer **5-G₁**, and dendrimer **5-G₁.HCl** (enhanced scale). B) Fluorescence spectra of Rhodamine B (ethanol) and dendrimer **5-G₁.HCl** (DMSO) after irradiation at 562 nm. The spectra were normalized for the same Optical Density at 562 nm.

Comparison of the ¹H and ¹³C NMR spectra of **5-G₁** before and after addition of HCl reveals several differences (Figure 2; data from compounds **2**, **3B**, and **4A** are also included). After

addition of HCl some signals are displayed like in the open form (e.g., 4',5'-H), others like in the spiro form (e.g., 1-C and 3',6'-C), or in between both forms (e.g., 8a',9a'-C and 4',5'-C).

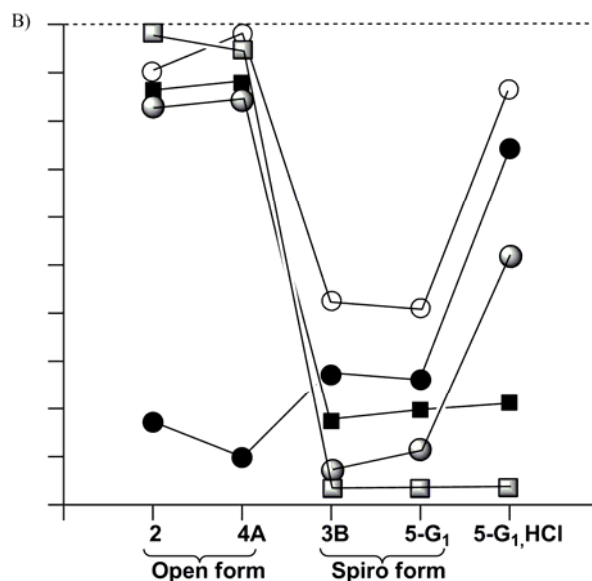


Figure 2. A) Numbering used for the NMR assignment of spirolactams. B) Chemical shifts of selected H and C atoms of xanthene moieties in **2**, **4a**, **3B**, **5G₁**, and **5G₁·HCl**: ○: 4',5'-H: ¹H NMR, scale δ 6–7; ●: 4',5'-C: ¹³C NMR, scale δ 95–105; ■: 3',6'-C: ¹³C NMR, scale δ 147–157; ●: 8a',9a'-C: ¹³C NMR, scale δ 105–115; ■: 1-C (= 9'-C): ¹³C NMR, scale δ 60–160).

Addition of HCl affected the ¹³C NMR chemical shifts of the xanthene ring, as well as the NCH₂CH₃ signal (**5-G₁**: δ 44.04; **5-G₁·HCl**: δ 47.36). This is taken as evidence that the NEt₂ groups were protonated, and that protonation opens only a few spirolactam rings, as indicated also by UV-Visible and fluorescence spectra (Figure 1). A gradient enhanced hydrogen-nitrogen multiple quantum coherence NMR experiment (¹H-¹⁵N HMBC) served to prove protonation at NEt₂. In this experiment, dendrimer **5-G₁** afforded four ¹⁵N NMR signals as expected (Figure 3). By comparison with a previous experiment,¹² the signals at δ -52 and δ -249 are attributed to the CH=N and N-Me groups of the dendrimer skeleton, respectively. ¹H/¹⁵N correlation allows to assign the signals at δ -226 and δ -304 to N-C=O and NEt₂ groups of Rhodamine, respectively. **5-G₁·HCl** is less soluble than **5-G₁**, and the same type of experiment required a longer time (48 h). A single new signal was observed at δ -328, compatible with Et₂NH⁺. However, this signal is less intense than the signal at δ -304 (neutral NEt₂) (Figure 3), and the ¹H NMR spectrum recorded after the experiment displays a more intensive signal at δ 1.1 for CH₃ of the NEt₂ groups beside the signal at δ 1.3 (CH₃ of Et₂NH⁺), indicating that protonation is reversible. The ¹H-¹⁵N HMBC experiments confirm that protonation occurs mainly at the NEt₂ groups.

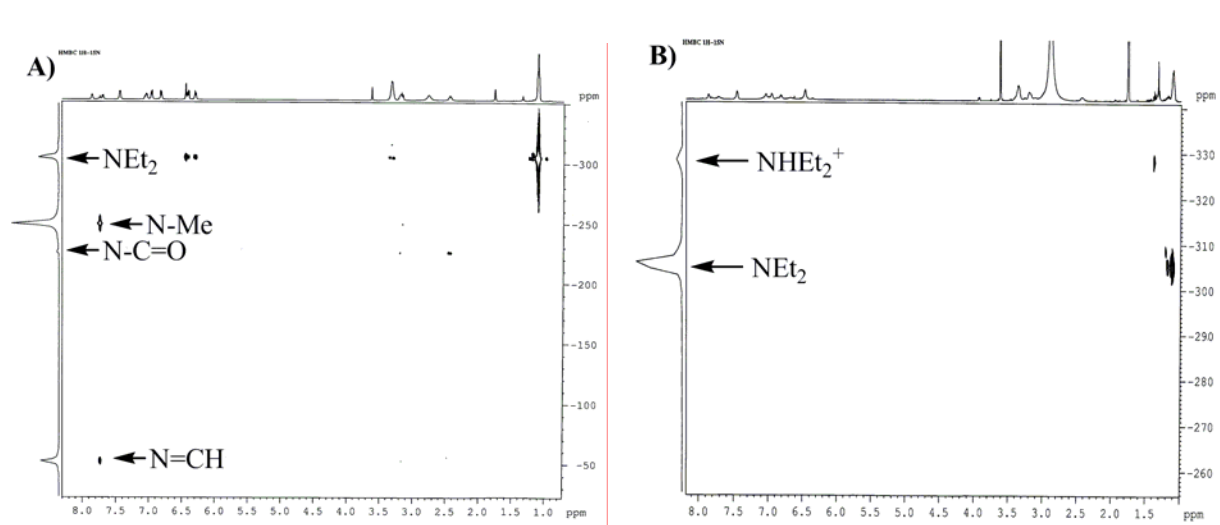


Figure 3. ^1H - ^{15}N HBMBC experiments. A) **5-G₁**. B) **5-G₁·HCl** (focus on the NEt_2 signal).

Rhodamine derivative **4**, which cannot cyclize, was reacted with dendrimer **5-G₁**. The solubility of both compounds is different: dendrimer **5-G₁** was dissolved in THF and the rhodamine derivative **4** in acetonitrile. Upon mixing both reactant solutions the partly substituted dendrimer precipitates in the solvent mixture preventing the reaction to drive to completion.

Conclusions

We have synthesized two new rhodamine derivatives functionalized with a phenol, one for which the equilibrium is shifted toward the colorless and non-fluorescent spirolactam form **3B** and one which can be only in the open colored and fluorescent form **4A**. Due to problems of solubility, the salt **4** could not be grafted on a phosphorus-containing dendrimer, but the neutral rhodamine derivative **3B** was successfully grafted as terminal groups. A few papers have reported the synthesis of dendrimers labeled with rhodamine (rhodamine being linked to one or a few terminal functions^{13,14}) but to the best of our knowledge, **5-G₁** is the first example of a dendrimer bearing rhodamine moieties on all terminal groups. Addition of HCl did not damage the structure of the dendrimer, and does not open the spirolactam form of the rhodamine terminal groups (or only some of them). Protonation of the NEt_2 substituent of rhodamine takes place; this shows that the spirolactam form of the rhodamine derivative **3B** is particularly stable.

Experimental Section

General. All manipulations were carried out with standard high vacuum and dry-argon techniques. Filtrations were also carried out under argon. The solvents were dried (THF and

diethyl ether over sodium/benzophenone, pentane and dichloromethane over phosphorus pentoxide, acetonitrile over calcium hydride) and distilled prior to use. ^1H , ^{13}C , and ^{31}P NMR spectra were recorded with Bruker AC 200, AC 250, DPX 300 or AMX 400 spectrometers. References for NMR chemical shifts are 85% H_3PO_4 in water for ^{31}P , SiMe_4 for ^1H and ^{13}C , and CH_3NO_2 for ^{15}N NMR. ^{13}C NMR signals were assigned using J_{mod} , two dimensional HMBC, and HMQC, broad band or CW ^{31}P decoupling experiments when necessary, and were found consistent with previously reported data for the rhodamine derivatives.¹⁵ The numbering used for NMR assignments for open forms **2**, **4A** and for spiro lactam forms (**3B**, dendrimers **5-G₁** and **5-G₁·HCl**) is shown in Scheme 3 and Figure 2, respectively. Yields are not optimized.

***N*-[6-(Diethylamino)-9-[2-[(2,5-dioxopyrrolidin-1-yloxy)carbonyl]phenyl]-3*H*-xanthen-3-ylidene]-*N*-ethylethanaminium (2).** Applying the method previously described,⁷ a solution of dicyclohexylcarbodiimide (1.2 g, 5.8 mmol) in acetonitrile (50 mL) was added dropwise to a solution of Rhodamine B (**1**; 2.4 g, 5 mmol) and *N*-hydroxysuccinimide (0.6 g, 5.2 mmol) in acetonitrile (100 mL) at 45 °C. The resulting mixture was stirred at 45 °C for 1h, then at room temperature for 20 h. After filtration and evaporation to dryness, the crude product was purified by crystallization from absolute ethanol, to afford **2** as a dark purple powder (1.04 g, 29%). ^1H NMR (CDCl_3 , 300 MHz): δ 1.35 (t, $^3J = 6.6$ Hz, 12H, CH_3), 2.79 (s, 4H, CH_2CH_2), 3.66 (q, $^3J = 6.6$ Hz, 8H, NCH_2), 6.9 (br s, 4H, 2',4',5',7'-H), 7.10 (d, $^3J = 9.6$ Hz, 2H, 1',8'-H), 7.50 (d, $^3J = 7.2$ Hz, 1H, 6-H), 7.84 (dd, $^3J = 7.5$ Hz, 1H, 4-H), 8.00 (dd, $^3J = 7.2$ Hz, 1H, 5-H), 8.44 (d, $^3J = 7.8$ Hz, 1H, 3-H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 75.5 MHz): δ 12.73 (CH_3), 25.62 (CH_2CH_2), 46.29 (NCH_2), 96.77 (4',5'-C), 113.46 (8a',9a'-C), 114.47 (2',7'-C), 130.68 (2,6-C), 130.95 (1',8'-C), 131.13 (4-C), 131.79 (5-C), 134.54 (1-C), 134.94 (3-C), 155.66 (3',6'-C), 157.83 (9',4a',10a'-C), 160.74 (CO_2), 168.64 (NC=O).

3',6'-Bis(diethylamino)-2-(4-hydroxyphenethyl)spiro[isindoline-1,9'-xanthen]-3-one (3B). A solution of tyramine (210 mg, 1.5 mmol) in borate buffer at pH 8.5 (40 mL) was added to a solution of **2** (800 mg, 1.4 mmol) in acetonitrile (40 mL). The resulting mixture was stirred for 36 h at room temperature. Evaporation of acetonitrile induced precipitation in the borate buffer. The precipitate was filtered off and crystallized from ethanol containing water (1 %v). The product was further purified by column chromatography (silica; dichloromethane \rightarrow dichloromethane/ethanol 9/1, v/v) and isolated as a white powder **3B** (157 mg, 20%). ^1H NMR (CDCl_3 , 300 MHz): δ 1.18 (t, $^3J = 7.2$ Hz, 12H, CH_3), 2.39 (t, $^3J = 8.4$ Hz, 2H, CH_2Ar), 3.28 (t, $^3J = 8.4$ Hz, 2H, CH_2N), 3.35 (q, $^3J = 7.2$ Hz, 8H, CH_2N), 5.85 (s, 1H, OH), 6.27 (d, $^3J = 9.0$ Hz, 2H, 2',7'-H), 6.43 (s, 2H, 4',5'-H), 6.44 (d, $^3J = 11.0$ Hz, 2H, 1',8'-H), 6.73, 6.70 (AA', 2H, 3'',5''-H), 6.86, 6.83 (BB', 2H, 2'',6''-H), 7.14 (m, 1H, 7-H), 7.46 (m, 2H, 5,6-H), 7.94 (m, 1H, 4-H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 75.5 MHz): δ 12.59 (CH_3), 33.73 (ArCH_2), 42.37 (CH_2N), 44.37 (CH_2), 65.13 (1-C), 97.72 (4',5'-C), 105.71 (8a',9a'-C), 108.14 (2',7'-C), 115.15 (3'',5''-C), 122.78 (4-C), 123.80 (7-C), 128.07 (5-C), 129.00 (1',8'-C), 129.81 (2'',6''-C), 131.31 (3a-C), 131.63 (1''-C), 132.32 (6-C), 148.81 (3',6'-C), 153.29 (7a-C), 153.47 (4a',10a'-C), 154.27 (4''-C), 167.80

(3-C). MS-ESI: m/z 562.7 $[M+H]^+$, 584.7 $[M+Na]^+$. Anal. calcd. for $C_{36}H_{39}N_3O_3$ (561.71): C, 76.98; H, 7.00; N, 7.48. Found: C, 76.79; H, 7.23; N, 7.47.

***N*-[6-(Diethylamino)-9-[2-[4-(4-hydroxyphenyl)piperazine-1-carbonyl]phenyl]-3*H*-xanthen-3-ylidene]-*N*-ethylethanaminium chloride (4A).** A solution of compound **1** (100 mg, 0.17 mmol) in acetonitrile (5 mL) was added to a suspension of 4-hydroxyphenylpiperazine (30.3 mg, 0.17 mmol) in borate buffer at pH 8.5 (5 mL). The resulting mixture (suspension) was stirred for 12 h at room temperature. After evaporation of solvents, chloroform (10 mL) was added to the crude mixture and filtered. The solution was evaporated to dryness, and the crude product was purified by crystallization (twice) in absolute ethanol. Compound **4A** was isolated as a dark purple powder (12 mg, 11%). 1H NMR (CD_3OD , 300 MHz): δ 1.29 (t, $^3J_{HH} = 7.2$ Hz, 12H, $N-CH_2CH_3$), 2.45–2.80 (m, 4H, $C_6H_4NCH_2CH_2$), 3.54 (t, $^3J_{HH} = 4.5$ Hz, 4H, $C_6H_4NCH_2CH_2$), 3.68 (q, $^3J_{HH} = 7.2$ Hz, 8H, NCH_2CH_3), 6.69, 6.66 (AA', 2H, 3'',5''-H), 6.75, 6.72 (BB', 2H, 2'',6''-H), 6.98 (d, $^4J_{HH} = 2$ Hz, 2H, 4',5'-H), 7.08 (dd, $^3J_{HH} = 9.6$ Hz, $^4J_{HH} = 2$ Hz, 2H, 2',7'-H), 7.33 (d, $^3J_{HH} = 9.6$ Hz, 2H, 1',8'-H), 7.57 (dd, $^3J_{HH} = 8$ Hz, $^4J_{HH} = 1$ Hz, 1H, 6-H), 7.72 (dt, $^3J_{HH} = 8$ Hz, $^4J_{HH} = 1$ Hz, 1H, 4-H), 7.79 (m, 2H, 3,5-H). $^{13}C\{^1H\}$ NMR (CD_3OD , 75.5 MHz): δ 11.43 (NCH_2CH_3), 41.68, 45.25 (2s, $C_6H_4NCH_2CH_2$), 45.49 (NCH_2CH_3), 50.97, 51.40 (2s, $C_6H_4NCH_2CH_2$), 95.93 (4',5'-C), 113.49 (8a', 9a'-C), 114.04 (2',7'-C), 115.25 (3'',5''-C), 119.10 (2'',6''-C), 127.54 (6-C), 129.93 (4-C), 130.17 (5-C), 130.64 (2-C), 131.99 (1',8'-C), 135.40 (1-C), 135.46 (3-C), 144.10 (4''-C), 152.12 (1''-C), 155.62 (9'-C), 155.80 (3',6'-C), 157.88 (4a',10a'-C), 167.87 (NC=O). Anal. calcd. for $C_{38}H_{43}ClN_4O_3$ (639.23): C, 71.40; H, 6.78; N, 8.77. Found: C, 71.29; H, 6.65; N, 8.67.

Dendrimer 5-G₁. Cesium carbonate (114 mg, 0.351 mmol) was added to a solution of **3B** (100 mg, 0.18 mmol) and first generation dendrimer **4-G₁^{8b}** (26.6 mg, 14.5 μ mol) in THF (5 mL). The resulting mixture was stirred at 50 °C for 12 h. After filtration, the filtrate was evaporated to dryness. The crude product was dissolved in a minimum of dichloromethane. Upon pouring into an ice-cold mixture of pentane/diethylether (4/1, 300 mL) a precipitate was formed. This process was repeated twice to afford dendrimer **5-G₁** as a white powder (107 mg, 91%). $^{31}P\{^1H\}$ NMR (THF- d_8 , 121.5 MHz): $\delta = 8.53$ (s, N_3P_3), 62.69 (s, P=S). 1H NMR (THF- d_8 , 300 MHz): $\delta = 1.11$ (m, 144H, NCH_2CH_3), 2.43 (br s, 24H, $C_6H_4CH_2CH_2N$), 3.18 (br s, 42H, $C_6H_4CH_2CH_2N$, NCH_3), 3.32 (m, 96H, NCH_2CH_3), 6.28 (m, 24H, 2',7'-H), 6.33–6.50 (m, 48H, 1',4',5',8'-H), 6.80 (m, 24H, 3'',5''-H), 6.95 (m, 24H, 2'',6''-H), 7.04 (m, 24H, 7-H, c-H), 7.41 (m, 24H, 5,6-H), 7.60–7.75 (m, 18H, b-H, CH=N), 7.81 (br s, 12H, 4-H). $^{13}C\{^1H\}$ NMR (THF- d_8 , 75.5 MHz): $\delta = 12.01$ (s, NCH_2CH_3), 32.80 (br s, NCH_3), 33.92 ($C_6H_4CH_2CH_2N$), 41.84 ($C_6H_4CH_2CH_2N$), 44.04 (NCH_2CH_3), 64.34 (1-C), 97.59 (4',5'-C), 106.16 (8a',9a'-C), 107.96 (2',7'-C), 121.02 (2s, 3'',5'',c-C), 122.20 (4-C), 123.64 (7-C), 127.63 (5-C), 128.67 (2'',6'',b-C), 129.34 (1',8'-C), 131.68 (1'',a-C), 131.88 (3a,6-C), 136.56 (CH=N), 148.64 (d-C), 148.99 (3',6'-C), 153.45 (7a,4a',10a',4''-C), 166.50 (3-C). Anal. Calcd. for $C_{480}H_{504}N_{51}O_{42}P_9S_6$ (8130.61): C, 70.91; H, 6.25; N, 8.79. Found: C, 71.09; H, 6.36; N, 8.66.

Dendrimer 5-G₁·HCl. To a solution of dendrimer **5-G₁** (37 mg, 51.3 μ mol) in THF- d_8 (2 mL), was added 0.1 N HCl (713 μ l). The mixture was stirred at room temperature for 36 h, and

analyzed by NMR. $^{31}\text{P}\{^1\text{H}\}$ NMR (THF- d_8 , 121.5 MHz): δ 8.56 (s, N_3P_3), 62.64 (s, P=S). ^1H NMR (THF- d_8 , 300 MHz): δ = 1.33 (m, 144H, NCH_2CH_3), 2.38 (br s, 24H, $\text{C}_6\text{H}_4\text{CH}_2\text{CH}_2\text{N}$), 3.11 (br s, 42H, $\text{C}_6\text{H}_4\text{CH}_2\text{CH}_2\text{N}$, NCH_3), 3.38 (m, 96H, NCH_2CH_3), 6.48 (m, 24H, 2',7'-H), 6.61 (m, 24H, 1',8'-H), 6.73 (m, 24H, 3'',5''-H), 6.84 (m, 48H, 2'',6''-H, 4',5'-H), 6.92 (m, 24H, 7,c-H), 7.50 (m, 24H, 5,6-H), 7.62 (m, 12H, b-H), 7.75 (br s, 6H, $\text{CH}=\text{N}$), 7.80 (m, 12H, 4-H). $^{13}\text{C}\{^1\text{H}\}$ NMR (THF- d_8 , 75.5 MHz): δ 11.21 (NCH_2CH_3), 32.46 (br, NCH_3), 33.66 ($\text{C}_6\text{H}_4\text{CH}_2\text{CH}_2\text{N}$), 42.06 ($\text{C}_6\text{H}_4\text{CH}_2\text{CH}_2\text{N}$), 47.36 ($\text{N-CH}_2\text{-CH}_3$), 64.59 (1-C), 102.63 (4',5'-C), 110.40 (8a',9a'-C), 111.64 (2',7'-C), 120.97 (br, 3'',5'',c-C), 122.89 (4-C), 123.42 (7-C), 128.61 (5-C), 129.21 (2'',6'',b-C), 129.42 (1',8'-C), 130.71 (1'',a-C), 132.96 (3a,6-C), 136.06 ($\text{CH}=\text{N}$), 145.46 (3',6'-C), 149.01 (d-C), 152.87 (7a,4a',10a',4''-C), 167.85 (3-C).

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References

1. Kim, H. N.; Lee, M. H.; Kim, H. J.; Kim, J. S.; Yoon, J. *Chem. Soc. Rev.* **2008**, *37*, 1465.
2. (a) Adamczyk, M.; Grote, J. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2327. (b) Huang, J.; Xu, Y.; Qian, X. *J. Org. Chem.* **2009**, *74*, 2167.
3. Some recent reviews about fluorescent dendrimers: (a) Adronov, A.; Fréchet, J. M. J. *Chem. Commun.* **2000**, 1701. (b) Burn, P. L.; Lo, S. C.; Samuel, I. D. W. *Adv. Mater.* **2007**, *19*, 1675. (c) Caminade, A. M.; Hameau, A.; Majoral, J. P. *Chem. Eur. J.* **2009**, *15*, 9270.
4. (a) Brauge, L.; Caminade, A. M.; Majoral, J. P.; Slomkowski, S.; Wolszczak, M. *Macromolecules* **2001**, *34*, 5599. (b) Leclaire, J.; Dagiral, R.; Fery-Forgues, S.; Coppel, Y.; Donnadiou, B.; Caminade, A. M.; Majoral, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 15762. (c) Brauge, L.; Vériot, G.; Franc, G.; Deloncle, R.; Caminade, A. M.; Majoral, J. P. *Tetrahedron* **2006**, *62*, 11891. (d) Franc, G.; Mazères, S.; Turrin, C. O.; Vendier, L.; Duhayon, C.; Caminade, A. M.; Majoral, J. P. *J. Org. Chem.* **2007**, *72*, 8707. (e) Martinez-Ferrero, E.; Franc, G.; Mazères, S.; Turrin, C. O.; Caminade, A. M.; Majoral, J. P.; Sanchez, C. *Chem. Eur. J.* **2008**, *14*, 7658. (f) Fuchs, S.; Pla-Quintana, A.; Mazères, S.; Caminade, A. M.; Majoral, J. P. *Org. Lett.* **2008**, *10*, 4751.
5. (a) Mongin, O.; Krishna, T. R.; Werts, M. H. V.; Caminade, A. M.; Majoral, J. P.; Blanchard-Desce, M. *Chem. Commun.* **2006**, 915. (b) Krishna, T. R.; Parent, M.; Werts, M. H. V.; Moreaux, L.; Gmouh, S.; Charpak, S.; Caminade, A. M.; Majoral, J. P.; Blanchard-Desce, M. *Angew. Chem. Int. Ed.* **2006**, *45*, 4645. (c) Mongin, O.; Pla-Quintana, A.;

- Terenziani, F.; Drouin, D.; Le Droumaguet, C.; Caminade, A. M.; Majoral, J. P.; Blanchard-Desce, M. *New J. Chem.* **2007**, *31*, 1354.
6. (a) Griffe, L.; Poupot, M.; Marchand, P.; Maraval, A.; Turrin, C. O.; Rolland, O.; Métivier, P.; Bacquet, G.; Fournié, J. J.; Caminade, A. M.; Poupot, R.; Majoral, J. P. *Angew. Chem. Int. Ed.* **2007**, *46*, 2523. (b) Rolland, O.; Griffe, L.; Poupot, M.; Maraval, A.; Ouali, A.; Coppel, Y.; Fournié, J. J.; Bacquet, G.; Turrin, C. O.; Caminade, A. M.; Majoral, J. P.; Poupot, R. *Chem. Eur. J.* **2008**, *14*, 4836. (c) Servin, P.; Laurent, R.; Romerosa, A.; Peruzzini, M.; Majoral, J. P.; Caminade, A. M. *Organometallics* **2008**, *27*, 2066.
7. Meng, Q.; Yu, M.; Zhang, H.; Ren, J.; Huang, D. *Dyes and Pigments* **2007**, *73*, 254.
8. (a) Launay, N.; Caminade, A. M.; Lahana, R.; Majoral, J. P. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1589. (b) Launay, N.; Caminade, A. M.; Majoral, J. P. *J. Organomet. Chem.* **1997**, *529*, 51.
9. (a) Brauge, L.; Magro, G.; Caminade, A. M.; Majoral, J. P. *J. Am. Chem. Soc.* **2001**, *123*, 6698; correction: *ibid. J. Am. Chem. Soc.* **2001**, *123*, 8446. (b) Maraval, V.; Caminade, A. M.; Majoral, J. P.; Blais, J. C. *Angew. Chem. Int. Ed.* **2003**, *42*, 1822. (c) Caminade, A. M.; Laurent, R.; Majoral, J. P. *Adv. Drug Deliv. Rev.* **2005**, *57*, 2130.
10. Blais, J. C.; Turrin, C. O.; Caminade, A. M.; Majoral, J. P. *Anal. Chem.* **2000**, *72*, 5097.
11. Nedelcev, T.; Racko, D.; Krupa, I. *Dyes and Pigments* **2008**, *76*, 550.
12. Deloncle, R.; Coppel, Y.; Rebut, C.; Majoral, J. P.; Caminade, A. M. *Mag. Res. Chem.* **2008**, *46*, 493.
13. Chang, T.; Rozkiewicz, D. I.; Ravoo, B. J.; Meijer, E. W.; Reinhoudt, D. N. *Nano Letters* **2007**, *7*, 978.
14. Dhanikula, R. S.; Argaw, A.; Bouchard J. F.; Hildgen, P. *Mol. Pharm.* **2008**, *5*, 105.
15. Ramos, S. S.; Vilhena, A. F.; Santos, L.; Almeida, P. *Magn. Res. Chem.* **2000**, *38*, 475.