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Short communication

Synthesis of pathogen inactivating nucleic acid intercalators

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Abstract

A series of antiviral compounds consisting of an intercalating acridine derived part, a spacer region and a reactive EDTA-derived conjugate was synthesized in an easy sequence starting from 1,ω-alkyldiamines. As shown in model screenings, in the presence of ascorbic acid the Fe-complexes of these compounds reduced the phage-titer of MS2-phages by several logarithmic decades.

Keywords: Intercalators; Antiviral agent; Pathogen inactivation; Acridines

1. Introduction

Largely in response to the AIDS epidemic, the amount of research directed towards the discovery of antiviral agents has grown dramatically over the last years. Of special interest have been the detection, the destruction or inactivation of viruses, bacteria and other pathogens in extracorporal fluids as blood and plasma. Whereas for the detection and classification of bacteria a number of well established methods has been developed and a repertoire of suitable antibiotics is readily available, the inactivation of viruses as well as of other pathogens remains difficult.

This is especially critical in the field of blood transfusion medicine; progress seems necessary in the development of techniques for disinfecting donated blood. Such an approach would offer the major advantage of removing or inactivating all pathogenic microorganisms from donor blood, even those for which the blood currently is not—or cannot be—tested.

Various groups are working on inactivation techniques based on compounds that interact with DNA or RNA of microorganisms and then bind inextricably with it. As a result, the microorganisms are no longer able to proliferate and perish.

There are several generally recognized ways in which molecules can bind reversibly to DNA or RNA. Whereas cationic small molecules composed of several repeated aromatic units with an annular topology similar to that of DNA bind in the minor groove in AT-rich regions, the recognition sequences of regulatory proteins primarily interact in the major groove usually in GC-rich regions [1,2]. Finally, in a third way, small molecules may bind to DNA by intercalation between the base pairs, a mode of reversible binding that is now understood to be the preferred binding mode of virtually any flat polyaromatic ligand of sufficiently large surface area and suitable steric properties [3]. The driving forces for intercalating are primarily stacking interactions [4–6] between the ligand chromophore and the base pairs.

A concept for the development of pathogen inactivating agents might introduce a molecular entity containing an acridine-derived intercalator [7] that binds to the nucleic acid of pathogens and of a conjugate that destroys the nucleic acids subsequently (Fig. 1).

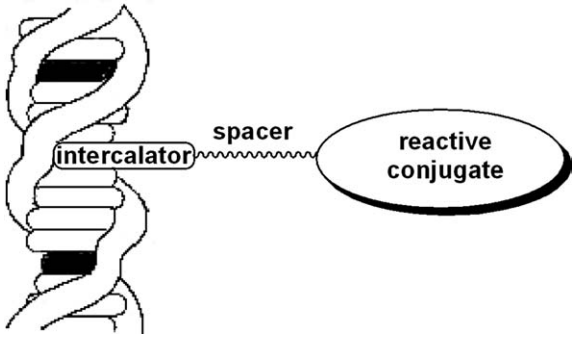

Fig. 1. Principal structure of the pathogen inactivating compounds.

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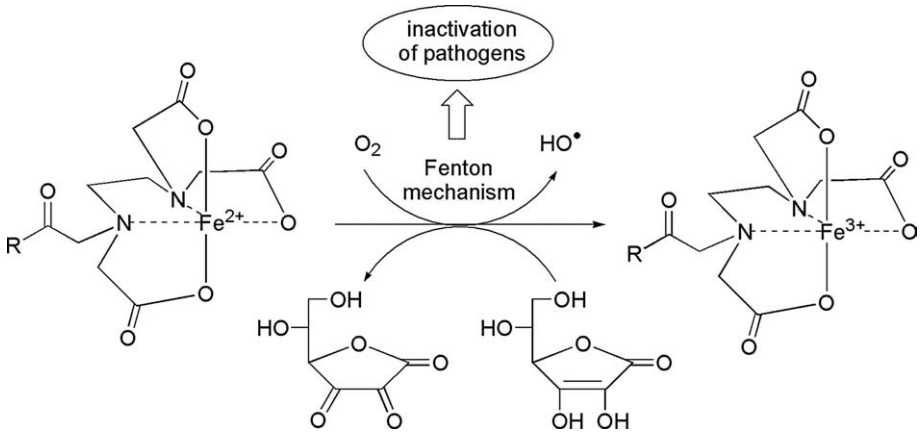


Fig. 2. Suggested Fenton mechanism for the damaging of DNA or RNA.

In our approach, the conjugate consists of a metal–chelate complex wherein the metal can change between at least two levels of oxidation. These compounds preferentially show an acridine [8–10] as the intercalator possessing in addition a spacer group to an EDTA Fe(II) chelate acting as the conjugate. Damage to the DNA should be accomplished by producing OH radicals by a Fe(II) catalyzed *Fenton* mechanism (Fig. 2) [11–13].

Indeed, a variety of products [11–13] may result from free radical attack [14–20] on DNA, among these the formation of thymine glycols (from thymine), 4,6-diamino-5-formamidopyrimidine (from adenine), 8-hydroxy-guanine (from guanine) and also strand breaks may occur. Addition of a reducing agent such as ascorbic acid leads to a cycle which increases the damage to the biological molecules.

2. Chemistry

As far as the synthesis (Scheme 1) of this spacer is concerned, a variety of 1,ω-diamines was mono-protected by the reaction with *tert*.butyl-dicarbonate in dry dioxane to afford the corresponding 1-amino-x-*tert*.butyloxycarbonyl-aminoalkanes **1** [20], **2** [21], **3** [22], **4** [23], **5** [24], **6** [25], **7** [26], **8** [27], **9** [26], **10** [28]. Thus, usually two equivalents of the diamine were allowed to react with one equivalent of *tert*.butyl-di-carbonate to result in approx. 40% yields of the corresponding products. These moderate yields could be improved, however, by using a 5–6 molar excess [29] of the amine.

These 1-amino-x-*tert*.butyloxycarbonylamino-alkanes **1–10** were allowed to react with 9-chloro-acridine [30,31] in the presence of phenol [32,33] to result in the formation of the corresponding *tert*.butyl *N*-[x-(9-acridinyl-amino)alkyl] carbamates **11–20**. Deprotection of these compounds by aq. hydrochloric acid for 10 h at 30 °C gave the corresponding dihydrochlorides **21–30**. Reaction of these amines with EDTA-triethylester (**31**) [34] [that was conveniently prepared even on a larger preparative scale from the corresponding tetra-ethylester **32** by selective enzymatic mono-deesterification using pig liver esterase (PLE)] using the mixed-anhydride method (isobutyl chloroformate/*N*-methylmorpholine *N*-oxide (NMM)) furnished the corresponding triethylesters **33–42**. Saponification of the esters was performed by their treatment with aq. sodium hydroxide to afford the target compounds **43–52**.

The target compounds were treated with an 2–5 molar excess of Fe^{3+}, lyophilized and incubated with the phages in Tris-buffer in the presence of sodium ascorbate [13].

3. Results

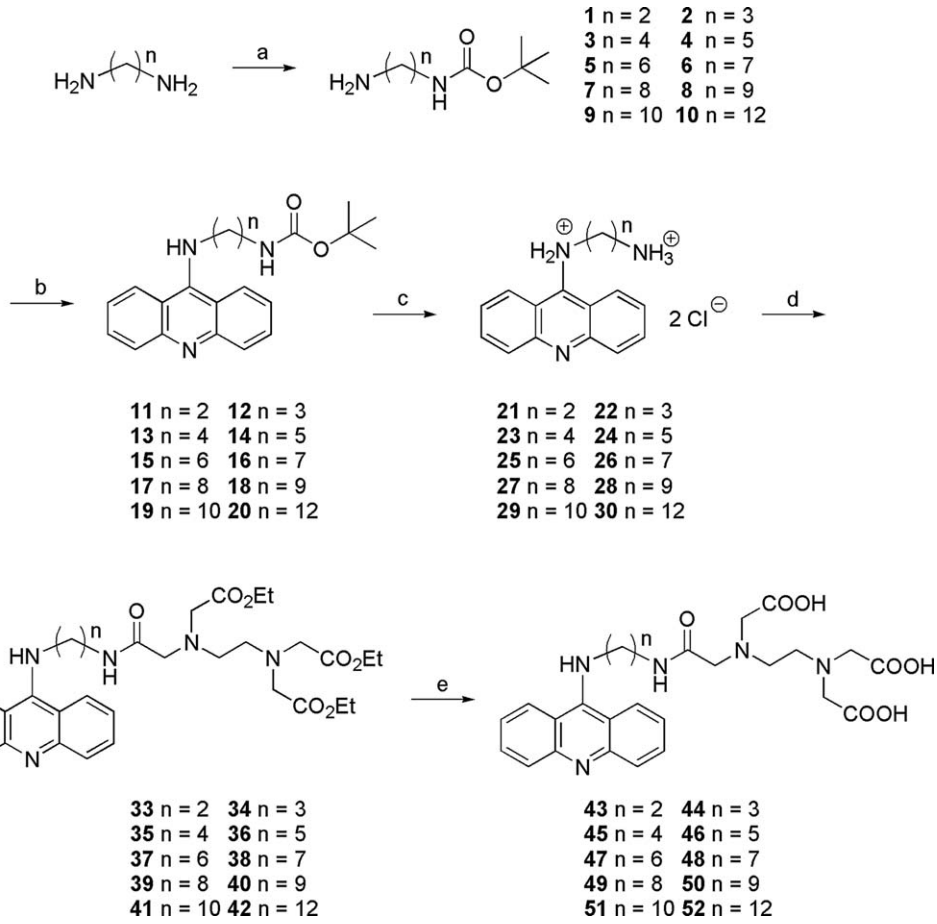
For biological screening the well established system containing MS2 bacteriophages (genus of the family leviviridae; uncoated, containing ssRNA) was used; these viruses contain the short version of the genome and have a separate gene for cell lysis [35].

As shown in Fig. 3 the length of the spacer exhibits significant effects on the reduction of the phage-titer. Best results were obtained for a spacer length of $n = 6$ giving rise to a reduction of the phage-titer of MS2 phages by > logarithmic decades.

As shown for compound **47** ($n = 6$) the inactivation of this virus depends both on the concentration and temperature (Fig. 4), the time of incubation (Fig. 5) as well as on the concentration of ascorbate (Fig. 6). Increased activity with increased concentration of ascorbate as well as the observation that no activity is associated with these compounds in the lack of ascorbate allows a triggering of the activity by the addition of ascorbic acid. No significant antipathogenic activity, however, was found upon incubating the MS2 phages with acridine, Fe(III)-loaded EDTA in the presence of ascorbate.

4. Conclusions

In this study we have investigated the antipathogenic activity of a reactive system constisting of an acridine-derived



Scheme 1. (a) $(Boc)_2O$; (b) 9-chloro-acridine/phenol; (c) 10% aq. HCl; (d) EDTA triethylester (**31**), *N*-methyl-morpholine, isobutylchloroformate; (e) aq. NaOH

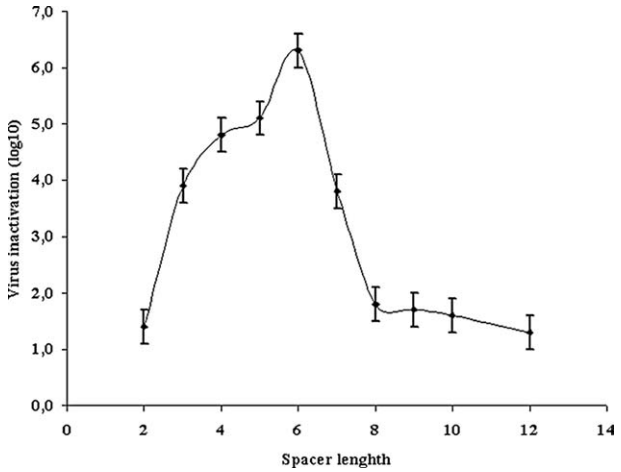


Fig. 3. Inactivation of phage MS2 as a function of spacer length (20 °C, 5 mmol Na-ascorbate, 101 μmol of compound **43–52** (Fe^{3+} loaded).

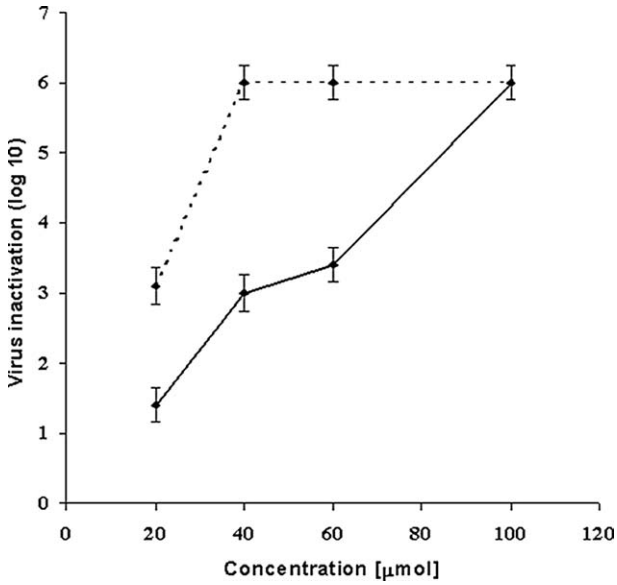


Fig. 4. Inactivation of MS2 phages as a function of concentration/temperature (**47**, incubation time 4 h; 5 mmol Na ascorbate; 25 °C, 37 °C).

intercalator, a spacer unit and an EDTA derived reactive part. Among these derivatives, compound **47** proved to be the compound showing the highest antipathogenic activity. Although these experiments showed the length of the spacer being crucial, presently no rationale can be given for this effect. The inactivation of the virus depends strongly on the presence of ascorbate obviously to trigger the catalytic *Fenton*-cycle. Further chemical modification of these compounds and their biological evaluation is underway and these results will be described in due course.

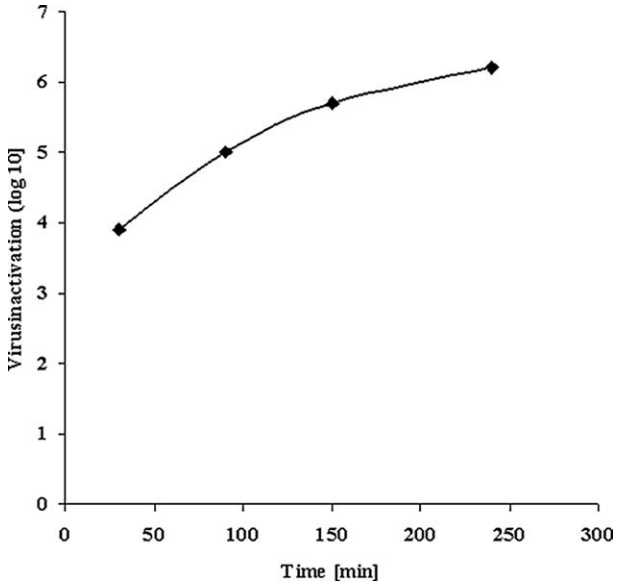


Fig. 5. Virusinactivation as a function of the incubation time (100 μmol **47**, Na ascorbate 100 μmol, 25 °C).

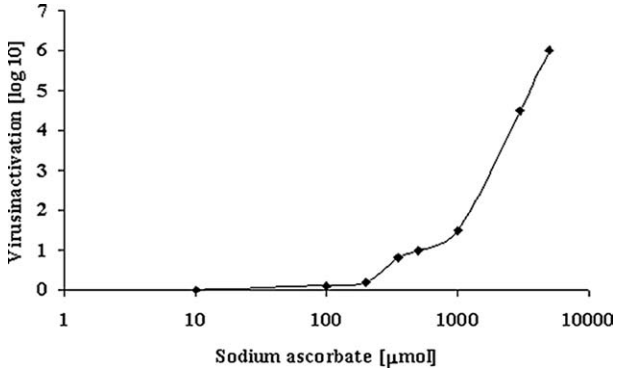


Fig. 6. Virusinactivation as a function of the ascorbate concentration (4 h, 25 °C, 50 μg/ml **47**).

5. Experimental

5.1. General

Melting points are uncorrected (*Leica* hot stage microscope), NMR spectra were recorded using the Varian spectrometers Gemini 200, Gemini 2000 or Unity 500 (δ given in ppm, *J* in Hz, internal Me_4Si), IR spectra (film or KBr pellet) on a Perkin-Elmer FT-IR spectrometer Spectrum 1000, MS spectra were taken on a Intectra GmbH AMD 402 (electron impact, 70 eV) or on a Finnigan MAT TSQ 7000 (electrospray, voltage 4.5 kV, sheath gas nitrogen) instrument; for elemental analysis a Foss-Heraeus Vario EL instrument was used; TLC was performed on silica gel (Merck 5554, detection by UV absorption or by treatment with a solution of 10% sulfuric acid, ammonium molybdate and cerium(IV)) sulfate followed by gentle heating. The solvents were dried according to usual procedures. Analyses indicated by the symbols of the elements were within ± 0.3% of the theoretical values.

5.1.1. General procedure for the synthesis of tert.butyl N-[x-(9-acridinylamino)alkyl]carbamates (GP1)

A mixture of 9-chloro-acridine (3.3 g, 15.5 mmol) and phenol (9.0 g, 95.6 mmol) was stirred at 90 °C for 30 min, then the corresponding 1-amino-x-*tert*.butyloxycarbonyl amino-alkane was added and the reaction mixture stirred for another 30 min at 105 °C. Then all the volatiles were removed under reduced pressure and the residue subjected to flash chromatography (silica gel, methanol/ethyl acetate 1:6).

5.1.2. General procedure for the synthesis of the N (1-(9-acridinyl)-1,x-alkanediamine dihydrochlorides (GP2)

The corresponding *tert*.butyl *N*-[x-(9-acridinylamino) alkyl]carbamate is stirred in methanol (200 ml) and aq. hydrochloric acid (10%, 20 ml) for 10 h at 30 °C. The solvents were removed under diminished pressure and the products were obtained. They were used without any further purification in the next step.

5.1.3. General procedure for the synthesis of ethyl 2-((2-{[x-(9-acridinylamino)alkyl]amino}-2-oxoethyl) {2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} acetates (GP3)

To an ice-cold solution of **31** (1.2 g, 2.67 mmol) and *N*-methyl-morpholine (1 ml) in DMF/ethyl acetate (1:1, 50 ml) isobutyl chloroformate (438 mg, 3.2 mmol) is slowly added via a syringe and the mixture is stirred at this temperature for 1 h. Then a solution of the corresponding *N* 1-(9-acridinyl)-1,2-alkanediamine dihydrochlorides in *N*-methyl-morpholine (2 ml) is added and stirring at room temperature is continued for 24 h. The solvents were removed under diminished pressure and the residue subjected to chromatography (silica gel, methanol/ethyl acetate 1:9) to afford the products.

5.1.4. General procedure for the synthesis of the 2-[{2-[(2-{[x-(9-acridinylamino)alkyl]amino}-2-oxo-ethyl) (carboxymethyl)amino]ethyl}(carboxymethyl) amino] acetic acids (GP4)

The corresponding ethyl 2-((2-{[x-(9-acridinylamino) alkyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxo-ethyl)amino]ethyl}amino) acetate and sodium hydroxide are dissolved in ethanol/water (5:1, 40 ml) and stirred at room temperature for 12 h; then the pH was carefully adjusted to 7. The solvents were removed under diminished pressure and the residue was carefully washed with ice-cold water (20 ml) and chloroform (150 ml) to obtain the products.

5.2. Bacteriophages and screening

The effect of the compounds on bacteriophages was tested on bacteriophages MS2 grown on its *E. coli* ATCC15597 host. Log-phase host bacteria for bacteriophage propagation were grown in tryptic soy broth (TSB, Sigma Chemicals) on an orbital shaker at room temperature until turbid. Before use, 100 μl of culture was inoculated into fresh TSB containing 0.0025% $CaCl_2$. The cultures were incubated in a 37 °C shaking water bath for 4 h until the log-phase was reached.

Fresh bacteriophages were cultured from freezer stocks. Log-phase host bacteria and phages were mixed at a multiplicity of infection of approximately 1 in 5 ml TSB. The culture was kept on ice for 15 min to facilitate adsorption of the phages to the host cells, then incubated overnight at 37 °C, the phage culture was filtered through a 0.2 μm cellulose acetate syringe filter to remove host bacteria and then stored at 4 °C. Typical yields were 1×10^{10} PFU/ml. Culturable counts of phage were performed by mixing 100 μl of phage suspension and 100 μl of host culture in 4 ml molten TSB top agar (containing 0.7% agar). The top agar was vortexed gently, then poured on TSB plates; the plates were incubated at 37 °C. Bacteriophages from freeze stocks were diluted into buffer (30 mM Tris, 150 mM KCl, pH 8.3) to a final population density of approximately 1×10^9 PFU/ml. Dilutions were prepared in phosphate-buffered saline solution. Initial as well post-exposure culturable counts were performed in triplicate. The counts were divided by the mean unexposed control counts to normalize the data and then log-transformed.

5.2.1. Tert.*butyl* N-*[2-(9-acridinylamino)ethyl]carbamate (**11**)*

Following GP1 from 9-chloro-acridine (3.3 g, 15.5 mmol), phenol (9 g, 95.6 mmol) and **1** (2.7 g, 17 mmol) **11** (4.5 g, 87%) was obtained as an amorphous, red solid. R_F (methanol/ethyl acetate 1:3) 0.62; UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.81); IR (KBr): ν = 2978m, 1687s, 1636m, 1561s, 1522s, 1261m, 1167m, 857w, 758m, 652w cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.16 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.98 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.53 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.24 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 5.50 (*br s*, 1 H, NH), 4.00–3.99 (*m*, 2 H, $CH_2(1')$), 3.61–3.60 (*m*, 2 H, $CH_2(2')$), 1.44 (*s*, 9 H, ^{t}Bu); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.8 (C=O), 152.8 (quart., C9), 146.6 (quart.), 130.8 (CH), 126.3 (CH), 123.7 (CH), 122.7 (CH), 115.1 (quart.), 80.3 (quart., ^{t}Bu), 52.2 ($CH_2(1')$), 41.0 ($CH_2(2')$), 28.4 (CH_3, ^{t}Bu); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 238 (4%) $[(M\text{-Boc})H]^+$, 282 (64%) $[(M\text{-}^i\text{butene})H]^+$, 338 (100%) $[MH]^+$; HRMS ($C_{20}H_{23}N_3O_2$): 337.17901; found: 337.17903; Anal. $C_{20}H_{23}N_3O_2$ (C, H, N).

5.2.2. Tert.*butyl* N-*[3-(9-acridinylamino)propyl] carbamate (**12**)*

Following GP1 from 9-chloro-acridine (3.5 g, 16.4 mmol), phenol (9.0 g, 95.6 mmol) and **2** (3.14 g, 18.0 mmol) **12** (5.5 g, 95.5%) was obtained as an amorphous solid. R_F (methanol/ethyl acetate 1:3) 0.60; UV-vis (methanol): λ_{max} (log ϵ) = 282 nm (4.77); IR (KBr): ν = 2976w, 2935w, 1683s, 1616m, 1564s, 1530s, 1393m, 1290m, 1263m, 1167m, 1141m, 758m, 647w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.19 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 8.02 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.62 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.32 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.87f (*br s*, 1 H, NH), 3.81–3.78 (*m*, 2 H, $CH_2(1')$), 3.38–3.36 (*m*, 2 H, $CH_2(3')$), 1.90–1.84 (*m*, 2 H, $CH_2(2')$), 1.47 (*s*, 9 H, ^{t}Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9 (C=O), 151.9 (quart., C9), 148.8 (quart.), 129.8 (CH), 128.9 (CH), 123.1 (CH), 122.9 (CH), 117.1 (quart.), 79.8 (quart., ^{t}Bu), 47.1 ($CH_2(1')$), 37.7 ($CH_2(3')$), 32.2 ($CH_2(2')$), 28.5 (CH_3, ^{t}Bu); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 252 (2%) $[(M\text{-Boc})H]^+$, 296 (8%) $[(M\text{-}^i\text{butene})H]^+$, 352 (100%) $[MH]^+$; HRMS ($C_{21}H_{25}N_3O_2$): 351.19466; found: 351.19467; Anal. $C_{21}H_{25}N_3O_2$ (C, H, N).

5.2.3. Tert.*butyl* N-*[4-(9-acridinylamino)butyl]carbamate (**13**)*

Following GP1 from 9-chloro-acridine (3.0 g, 14.0 mmol), phenol (8.0 g, 85.0 mmol) and **3** (2.8 g, 15.0 mmol) **13** (4.3 g, 84%) was obtained as an amorphous, orange-coloured solid; R_F (methanol/ethyl acetate 1:3) 0.61; UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.76); IR (KBr): ν = 2930w, 1688s, 1636m, 1590s, 1562s, 1520s, 1472m, 1391m, 1253s, 1170s, 858w, 756s, 651w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.10 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 8.00 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.55 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.28 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.69 (*br s*, 1 H, NH), 3.92–3.89 (*m*, 2 H, $CH_2(1')$), 3.24–3.14 (*m*, 2 H, $CH_2(4')$), 1.94–1.84 (*m*, 2 H, $CH_2(2')$), 1.71–1.63 (*m*, 2 H, $CH_2(3')$), 1.42 (*s*, 9 H, ^{t}Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1 (C=O), 153.1 (quart., C9), 145.8 (quart.), 131.1 (CH), 125.8 (CH), 123.6 (CH), 122.9 (CH), 115.2 (quart.), 79.3 (quart., ^{t}Bu), 49.8 ($CH_2(1')$), 40.1 ($CH_2(4')$), 28.5 (CH_2), 28.4 (CH_3, ^{t}Bu), 27.7 (CH_2); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 266 (1%) $[(M\text{-Boc})H]^+$, 310 (9%) $[(M\text{-}^i\text{butene})H]^+$, 366 (100%) $[MH]^+$; HRMS ($C_{22}H_{27}N_3O_2$): 365.2101; found: 365.2103; Anal. $C_{22}H_{27}N_3O_2$ (C, H, N).

5.2.4. Tert.*butyl* N-*[5-(9-acridinylamino)pentyl]carbamate (**14**)*

Following GP1 from 9-chloro-acridine (4.0 g, 18.7 mmol), phenol (10.0 g, 0.11 mol) and **4** (4.2 g, 20.6 mmol) **14** (5.7 g, 80.0%) was obtained as an amorphous, orange-coloured solid; R_F (methanol/ethyl acetate 1:3) 0.61; UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.73); IR (KBr): ν = 2979w, 1683s, 1634s, 1594s, 1533s, 1474w, 1366m, 1272m, 1171m, 756w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.93 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.38 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.14 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.75 (*br t*, $^3J_{H,H}$ = 5.40 Hz, 1 H, NH), 4.07–4.04 (*m*, 2 H, $CH_2(1')$), 3.18–3.13 (*m*, 2 H, $CH_2(5')$), 2.11–2.01 (*m*, 2 H, $CH_2(2')$), 1.67–1.51 (*m*, 4 H, 2 × $CH_2(3',4')$), 1.40 (*s*, 9 H, ^{t}Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2 (C=O), 156.0 (quart., C9), 140.2 (quart.), 133.2 (CH), 125.0 (CH), 122.8 (CH), 120.0 (CH), 112.5 (quart.), 79.1 (quart., ^{t}Bu), 48.5 ($CH_2(1')$), 40.2 ($CH_2(5')$), 30.0 (CH_2), 29.8 (CH_2), 28.5 (CH_3, ^{t}Bu), 24.2 (CH_2); MS

(ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 280 (2%) $[(M\text{-Boc})H]^+$, 324 (7%) $[(M\text{-}^i\text{butene})H]^+$, 380 (100%) $[MH]^+$; HRMS ($C_{23}H_{29}N_3O_2$): 379.22596; found: C 379.22599; Anal. $C_{23}H_{29}N_3O_2$ (C, H, N).

5.2.5. Tert.*butyl* N-*[6-(9-acridinylamino)hexyl] carbamate (**15**)*

Following GP1 from 9-chloro-acridine (3.0 g, 14.0 mmol), phenol (7.0 g, 74.4 mmol) and **5** (3.2 g, 15.0 mmol) **15** (5.0 g, 91%) was obtained as an orange-coloured amorphous solid; R_F (methanol/ethyl acetate 1:3) 0.63; UV-vis (methanol): λ_{max} (log ϵ) = 281 nm (4.63); IR (KBr): *ν* = 2932w, 1687s, 1634s, 1570s, 1533s, 1474s, 1391m, 1273m, 1252m, 1171s, 860w, 756m, 661w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 8.07 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.95 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.55 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.27 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.55 (*br s*, 1 H, NH), 3.86–3.82 (*m*, 2 H, $CH_2(1')$), 3.11–3.04 (*m*, 2 H, $CH_2(6')$), 1.87–1.78 (*m*, 2 H, $CH_2(2')$), 1.50–1.42 (*m*, 4 H, 2 × $CH_2(3',5')$), 1.41 (*s*, 9 H,^{t}Bu), 1.40–1.36 (*m*, 2 H, $CH_2(4')$); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 156.3 (C=O), 156.1 (quart., C9), 140.5 (quart.), 133.4 (CH), 125.1 (CH), 122.9 (CH), 120.2 (CH), 112.6 (quart.), 79.0 (quart., ^{t}Bu), 48.4 ($CH_2(1')$), 40.2 ($CH_2(6')$), 30.2 (CH_2), 29.9 (CH_2), 28.4 (CH_3, ^{t}Bu), 26.3 (CH_2), 26.2 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 294 (3%) $[(M\text{-Boc})H]^+$, 338 (7%) $[(M\text{-}^i\text{butene})H]^+$, 394 (100%) $[MH]^+$; HRMS ($C_{14\ H31}N_3O_2$): 393.24161; found: 393.24162; Anal. $C_{14}H_{31}N_3O_2$ (C, H, N).

5.2.6. Tert.*butyl* N-*[7-(9-acridinylamino)heptyl] carbamate (**16**)*

Following GP1 from 9-chloro-acridine (3.3 g, 15.4 mmol), phenol (9.0 g, 95.6 mmol) and **6** (3.9 g, 17.0 mmol) **16** (6.3 g, 83%) was obtained as an amorphous, orange-coloured solid; R_F (methanol/ethyl acetate 1:3) 0.64; UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.72); IR (KBr): *ν* = 2929w, 1691s, 1635m, 1563m, 1522m, 1473m, 1391m, 1272m, 1170m, 754m, 652w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 8.08 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.99 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.57 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.28 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.51 (*br s*, 1 H, NH), 3.87–3.83 (*m*, 2 H, $CH_2(1')$), 3.09–3.04 (*m*, 2 H, $CH_2(7')$), 1.86–1.79 (*m*, 2 H, $CH_2(2')$), 1.47–1.41 (*m*, 4 H, 2 × $CH_2(3',6')$), 1.41 (*s*, 9 H,^{t}Bu), 1.40–1.27 (*m*, 4 H, 2 × $CH_2(4',5')$); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 155.9 (C=O), 154.6 (quart., C9), 140.8 (quart.), 132.1 (CH), 124.2 (CH), 122.8 (CH), 117.0 (CH), 113.7 (quart.), 79.0 (quart., ^{t}Bu), 49.2 ($CH_2(1')$), 40.5 ($CH_2(7')$), 30.8 (CH_2), 30.0 (CH_2), 28.9 (CH_2), 28.5 (CH_3, ^{t}Bu), 26.8 (CH_2), 26.6 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 308 (7%) $[(M\text{-Boc})H]^+$, 352 (11%) $[(M\text{-}^i\text{butene})H]^+$, 408 (100%) $[MH]^+$; HRMS ($C_{25}H_{33}N_3O_2$): 407.25726; found: 407.25728; Anal. $C_{25}H_{33}N_3O_2$ (C, H, N).

5.2.7. Tert.*butyl* N-*[8-(9-acridinylamino)octyl]carbamate (**17**)*

Following GP1 from 9-chloro-acridine (1.4 g, 6.4 mmol), phenol (5.0 g, 53.1 mmol) and **7** (1.8 g, 7.36 mmol) **17** (2.2 g, 81.5%) was obtained as an amorphous, orange-coloured solid; R_F (methanol/ethyl acetate 1:3) 0.67; UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.76); IR (KBr): *ν* = 2931w, 1635s, 1594s, 1570s, 1537s, 1469s, 1257m, 1173m, 859w, 750m, 660w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 8.21 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.93 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.35–7.34 (*m*, 2 H, H-C(3,6)), 7.12 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.55 (*br s*, 1 H, NH), 4.08–4.04 (*m*, 2 H, $CH_2(1')$), 3.09–3.03 (*m*, 2 H, $CH_2(8')$), 2.07–1.99 (*m*, 2 H, $CH_2(2')$), 1.56–1.40 (*m*, 6 H, 3 × $CH_2(3',6',7')$), 1.41 (*s*, 9 H,^{t}Bu), 1.36–1.24 (*m*, 4 H, 2 × $CH_2(4',5')$); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 156.6 (C=O), 155.9 (quart., C9), 139.6 (quart.), 133.5 (CH), 125.2 (CH), 122.7 (CH), 119.3 (CH), 112.2 (quart.), 79.0 (quart., ^{t}Bu), 48.4 ($CH_2(1')$), 40.7 ($CH_2(8')$), 30.4 (CH_2), 30.1 (CH_2), 29.23 (CH_2), 29.18 (CH_2), 28.5 (CH_3, ^{t}Bu), 27.0 (CH_2), 26.8 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 322 (5%) $[(M\text{-Boc})H]^+$, 366 (10%) $[(M\text{-}^i\text{butene})H]^+$, 422 (100%) $[MH]^+$; HRMS ($C_{26}H_{35}N_3O_2$): 421.27291; found: 421.27294; Anal. $C_{26}H_{35}N_3O_2$ (C, H, N).

5.2.8. Tert.*butyl* N-*[9-(9-acridinylamino)nonyl] carbamate (**18**)*

Following GP1 from 9-chloro-acridine (2.33 g, 11.0 mmol), phenol (8.0 g, 85 mmol) and **8** (3.1 g, 12.0 mmol) **18** (4.4 g, 92%) was obtained as a red, amorphous solid; R_F (methanol/ethyl acetate 1:3) 0.69; UV-vis (methanol): λ_{max} (log ϵ) = 284 m (4.73); IR (KBr): *ν* = 2926w, 1687s, 1633m, 1561m, 1521m, 1471m, 1251s, 1169m, 756m, 651w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 8.12 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.98 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.49 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.22 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.51 (*br s*, 1 H, NH), 3.96–3.92 (*m*, 2 H, $CH_2(1'')$), 3.10–3.02 (*m*, 2 H, $CH_2(9')$), 1.94–1.85 (*m*, 2 H, $CH_2(2')$), 1.50–1.42 (*m*, 4 H, 2 × $CH_2(3',8')$), 1.42 (*s*, 9 H,^{t}Bu), 1.42–1.23 (*m*, 8 H, 4 × $CH_2(4',5',6',7')$; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 155.9 (C=O), 154.1 (quart., C9), 144.0 (quart.), 131.7 (CH), 124.0 (CH), 122.8 (CH), 114.1 (quart.), 79.0 (quart., ^{t}Bu), 49.6 ($CH_2(1')$), 40.6 ($CH_2(9')$), 31.0 (CH_2), 30.1 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 28.5 (CH_3, ^{t}Bu), 26.9 (CH_2), 26.7 (CH_2); MS (ESI, 4.1 V, 8 µl/min, N_2, methanol): *m/z* = 336 (7%) $[(M\text{-Boc})H]^+$, 380 (13%) $[(M\text{-}^i\text{butene})H]^+$, 436 (100%) $[MH]^+$; HRMS ($C_{27}H_{37}N_3O_2$): 435.28856; found: 435.28857; Anal. $C_{27}H_{37}N_3O_2$ (C, H, N).

5.2.9. Tert.*butyl* N-*[10-(9-acridinylamino)decyl] carbamate (**19**)*

According to GP1 from 9-chloro-acridine (3.0 g, 14 mmol), phenol (9.0 g, 95.6 mmol) and **9** (3.5 g, 13.0 mmol) followed by chromatography (silica gel,

methanol/ethylacetate 1:4 then methanol/ethyl acetate 1:6) **19** (3.6 g, 62%) was obtained as an orange-coloured, amorphous solid; R_F (methanol/ethyl acetate 1:3) 0.70; UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.93); IR (KBr): ν = 2927m, 1691s, 1615s, 1560s, 1520m, 1473m, 1391m, 1258m, 1172m, 857w, 757m, 650w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ =8.07 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 8.05 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.65 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.35 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 5.07 (*br s*, 1 H, NH) 4.50 (*br s*, 1 H, NH), 3.82–3.78 (*m*, 2 H, CH_2(1′)), 3.11–3.03 (*m*, 2 H, CH_2(10′)), 1.80–1.73 (*m*, 2 H, CH_2(2′)), 1.42–1.40 (*m*, 13 H, ^{t}Bu, 2 × CH_2(3′,9′)), 1.31–1.23 (*m*, 10 H, 5 × CH_2(4′,5′,6′,7′,8′); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9 (C=O), 151.2 (quart., C9), 149.3 (quart.), 129.7 (CH), 129.6 (*br*, CH), 122.9 (CH), 122.6 (CH), 116.6 (quart.), 79.0 (quart., ^{t}Bu), 51.0 (CH_2(1′)), 40.7 (CH_2(10′)), 31.9 (CH_2), 30.1 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.5 (CH_3, ^{t}Bu), 26.9 (CH_2), 26.8 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 350 (8%) $[(M\text{-Boc})H]^+$, 394 (11%) $[(M\text{-}^i\text{butene})H]^+$, 450 (100%) $[MH]^+$; HRMS ($C_{28}H_{39}N_3O_2$): 449.30421; found: 449.30423; Anal. $C_{28}H_{39}N_3O_2$ (C, H, N).

5.2.10. Tert.*butyl* N-*[12-(9-acridinylamino)dodecyl] carbamate (**20**)*

Following the procedure given for the synthesis of **19** from 9-chloro-acridine (2.4 g, 11.0 mmol), phenol (10.0 g, 0.11 mol) and **10** (3.6 g, 12.0 mmol) **20** (3.4 g, 65%) was obtained as a red, amorphous solid; R_F (methanol/ethyl acetate 1:3) 0.73; UV-vis (methanol): λ_{max} (log ϵ) = 282 nm (4.70); IR (KBr): ν = 2925m, 1694s, 1635s, 1589s, 1568s, 1532s, 1472s, 1390m, 1251m, 1170s, 860w, 754m, 661w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.18 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.94 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.41–7.37 (*m*, 2 H, H-C(3,6)), 7.14 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.49 (*br s*, 1 H, NH), 4.05–4.01 (*m*, 2 H, CH_2(1′)), 3.09–3.05 (*m*, 2 H, CH_2(12′)), 2.04–1.97 (*m*, 2 H, CH_2(2′)), 1.57–1.45 (*m*, 2 H, CH_2(11′)), 1.45–1.41 (*m*, 13 H, ^{t}Bu, 2 × CH_2(3′,10′)), 1.34–1.21 (*m*, 12 H, 6 × CH_2(4′,5′,6′,7′,8′,9′); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 156.6 (C=O), 141.0 (quart.), 133.0 (CH), 124.9 (CH), 122.8 (CH), 120.7 (CH), 112.9 (quart.), 79.0 (quart., ^{t}Bu), 48.9 (CH_2(1′)), 40.7 (CH_2(12′)), 30.6 (CH_2), 30.2 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 28.5 (CH_3, ^{t}Bu), 27.0 (CH_2), 26.9 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 378 (6%) $[(M\text{-Boc})H]^+$, 422 (10%) $[(M\text{-}^i\text{butene})H]^+$, 478 (100%) $[MH]^+$; HRMS ($C_{30}H_{43}N_3O_2$): 477.33551; found: 477.33553; Anal. $C_{30}H_{43}N_3O_2$ (C, H, N).

5.2.11. N *(1-(9-Acridinyl)-1,2-ethanediamine dihydrochloride (**21**)*

Following GP2 from **11** (4.5 g, 13.35 mmol) **21** (4.03 g, 97%) was obtained as an amorphous, yellow solid. UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.69); IR (KBr): ν = 1638s, 1588s, 1527s, 1469m, 1339m, 1270m, 1176w, 868w, 817w, 755m, 670w cm^{-1}; ^1H NMR (400 MHz, D_2O): δ = 8.10 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.79 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.52 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.40 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.27–4.24 (*m*, 2 H, CH_2(1′)), 3.41–3.38 (*m*, 2 H, CH_2(2′)); ^{13}C NMR (100 MHz, D_2O): δ = 156.0 (quart.), 139.3 (quart.), 135.4 (CH), 124.5 (CH), 124.0 (CH), 118.4 (CH), 112.1 (quart.), 45.5 (CH_2(1′)), 38.5 (CH_2(2′)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 238 (100%) $[MH]^+$.

5.2.12. N *(1-(9-Acridinyl)-1,3-propanediamine dihydrochloride (**22**)*

Following GP2 from **12** (5.5 g, 15.67 mmol) **22** (4.9 g, 96%) was obtained as an orange-coloured amorphous solid; UV-vis (methanol): λ_{max} (log ϵ) = 282 nm (4.75); IR (KBr): ν = 3071m, 3030m, 2992m, 1635s, 1592s, 1575s, 1532s, 1476s, 1336m, 1276m, 1172m, 852w, 801w, 756m, 662m cm^{-1}; ^1H NMR (400 MHz, D_2O): δ = 7.85–7.75 (*m*, 2 H, H-C(4,5)), 7.67–7.57 (*m*, 2 H, H-C(3,6)), 7.29–7.24 (*m*, 2 H, H-C(1,8)), 7.16–7.13 (*m*, 2 H, H-C(2,7)), 3.80–3.75 (*m*, 2 H, CH_2(1′)), 2.98–2.92 (*m*, 2 H, CH_2(3′)), 2.07–2.00 (*m*, 2 H, CH_2(2′)); ^{13}C NMR (100 MHz, D_2O): δ = 156.5 (quart.), 138.5 (quart.), 135.3 (CH), 124.4 (CH), 124.0 (CH), 118.0 (CH), 111.4 (quart.), 45.8 (CH_2(1′)), 37.0 (CH_2(3′)), 27.2 (CH_2(2′)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 252 (100%) $[MH]^+$.

5.2.13. N *(1-(9-Acridinyl)-1,4-butanediamine dihydrochloride (**23**)*

Following GP2 from **13** (4.3 g, 11.78 mmol) **23** (3.8 g, 95%) was obtained as a orange-coloured, amorphous solid; UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.76); IR (KBr): ν = 2928m, 1635s, 1592s, 1571m, 1535w, 1474m, 1346w, 1271w, 1174w, 859w, 802w, 755m, 663w cm^{-1}; ^1H NMR (400 MHz, D_2O): δ = 7.78 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H,2 × CH(4,5)), 7.61 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, 2 × CH(3,6)), 7.22 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H,2 × CH(2,7)), 7.16 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 3.68–3.65 (*m*, 2 H, CH_2(1′)), 2.91–2.87 (*m*, 2 H, CH_2(4′)), 1.75–1.66 (*m*, 2 H, CH_2(2′)), 1.64–1.56 (*m*, 2 H, CH_2(3′)); ^{13}C NMR (125 MHz, D_2O): δ = 156.2 (quart.), 138.3 (quart.), 135.3 (CH), 124.05 (CH), 124.03 (CH), 118.0 (CH), 111.2 (quart.), 46.2 (CH_2(1′)), 39.3 (CH_2(4′)), 26.4 (CH_2), 24.4 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 266 (100%) $[MH]^+$.

5.2.14. N *(1-(9-Acridinyl)-1,5-pentanediamine dihydrochloride (**24**)*

Following GP2 from **14** (5.7 g, 15.04 mmol) **24** (5.1 g, 96%) was obtained as an orange-coloured, amorphous solid; UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.78); IR (KBr): ν = 2928m, 1634s, 1592s, 1570m, 1532w, 1472m, 1340w, 1272w, 1171w, 859w, 754m, 661w cm^{-1}; ^1H NMR (400 MHz, D_2O): δ = 7.92 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H,

H-C(4,5)), 7.69 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.32–7.27 (*m*, 4 H, H-C(1,8), H-C(2,7)), 3.77–3.73 (*m*, 2 H, CH_2(1′)), 2.86–2.80 (*m*, 2 H, CH_2(5′)), 1.75–1.68 (*m*, 2 H, CH_2(2′)), 1.59–1.52 (*m*, 2 H, CH_2(4′)), 1.36–1.28 (*m*, 2 H, CH_2(3′)); ^{13}C NMR (125 MHz, D_2O): δ = 156.9 (quart.), 135.0 (CH), 123.6 (*br*, CH), 117.9 (CH), 48.4 (CH_2(1′)), 39.2 (CH_2(5′)), 28.5 (CH_2), 26.4 (CH_2), 23.0 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 280 (100%) $[MH]^+$.

5.2.15. N *(1-(9-Acridinyl)-1,6-hexanediamine dihydrochloride (**25**)*

Following GP2 from **15** (5.0 g, 12.72 mmol) **25** (4.5 g, 97%) was obtained as an amorphous, yellow solid; UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.52); IR (KBr): ν = 1634s, 1588s, 1538m, 1471s, 1335m, 1269w, 1221w, 872w, 757m, 678w cm^{-1}; ^{1}H NMR (400 MHz, D_2O): δ = 7.59 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.49 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.10 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 6.98 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 3.44–3.40 (*m*, 2 H, CH_2(1′)), 2.86–2.82 (*m*, 2 H, CH_2(6′)), 1.56–1.48 (*m*, 4 H, CH_2(2′,5′)), 1.28–1.23 (*m*, 4 H, CH_2(3′,4′)); ^{13}C NMR (100 MHz, D_2O): δ = 155.9 (quart.), 135.1 (CH), 123.8 (CH), 117.8 (CH), 48.6 (CH_2(1′)), 39.6 (CH_2(6′)), 29.1 (CH_2), 26.9 (CH_2), 25.7 (CH_2), 25.5 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 294 (100%) $[MH]^+$.

5.2.16. N *(1-(9-Acridinyl)-1,7-heptanediamine dihydrochloride (**26**)*

Following GP2 from **16** (6.3 g, 15.48 mmol) **26** (5.7 g, 97%) was obtained as a yellow, amorphous solid; UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.76); IR (KBr): ν = 2931m, 1634s, 1588s, 1567s, 1531s, 1473m, 1376w, 1335w, 1270w, 1176w, 879w, 748m, 669w cm^{-1}; ^{1}H NMR (400 MHz, D_2O): δ = 7.59 (*d*, $^3J_{H,H}$ = 8.51 Hz, 2 H, H-C(4,5)), 7.50 (t, $^3J_{H,H}$ = 7.26 Hz, 2 H, H-C(3,6)), 7.09 (*t*, $^3J_{H,H}$ = 7.57 Hz, 2 H, H-C(2,7)), 7.00 (*d*, $^3J_{H,H}$ = 8.51 Hz, 2 H, H-C(1,8)), 3.43–3.39 (*m*, 2 H, CH_2(1′)), 2.85–2.81 (*m*, 2 H, CH_2(7′)), 1.52–1.48 (*m*, 4 H, 2 × CH_2(2′,6′)), 1.20 (*br s*, 6 H, 3 × CH_2(3′,4′,5′)); ^{13}C NMR (100 MHz, D_2O): δ = 155.2 (quart.), 134.9 (CH), 123.8 (CH), 117.6 (CH), 48.4 (CH_2(1′)), 39.6 (CH_2(7′)), 29.1 (CH_2), 27.9 (CH_2), 26.8 (CH_2), 25.9 (CH_2), 25.7 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 308 (100%) $[MH]^+$.

5.2.17. N *(1-(9-Acridinyl)-1,8-octanediamine dihydrochloride (**27**)*

Following GP2 from **17** (2.2 g, 5.23 mmol) **27** (1.9 g, 93%) was obtained as a yellow, amorphous solid; UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.66); IR (KBr): ν = 1634s, 1588s, 1540s, 1470s, 1363m, 1337m, 1271m, 1190m, 1166m, 869w, 753s, 670w cm^{-1}; ^{1}H NMR (400 MHz, D_2O): δ = 7.77 (*m*, 2 H, H-C(4,5)), 7.61 (*t*, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.20 (*m*, 4 H, H-C(1,8), H-C(2,7)), 3.59 (*m*, 2 H, CH_2(1′)), 2.82–2.78 (*m*, 2 H, CH_2(8′)), 1.60–1.58 (*m*, 2 H, CH_2(2′)), 1.48–1.44 (*m*, 2 H, CH_2(7′)), 1.16 (*br s*, 8 H, 4 × CH_2(3′,4′,5′,6′)); ^{13}C NMR (100 MHz, D_2O): δ = 156.8 (quart.), 135.1 (CH), 123.7 (CH), 118.0 (CH), 48.8 (CH_2(1′)), 39.6 (CH_2(8′)), 29.1 (CH_2), 28.2 (CH_2), 28.2 (CH_2), 26.8 (CH_2), 25.9 (CH_2), 25.6 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 322 (100%) $[MH]^+$.

5.2.18. N *(1-(9-Acridinyl)-1,9-nonanediamine dihydrochloride (**28**)*

Following GP2 from **18** (4.4 g, 10.12 mmol) **28** (4.0 g, 97%) was obtained as a yellow, amorphous solid; UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.67); IR (KBr): ν = 2931m, 1634s, 1589s, 1568s, 1540m, 1478s, 1396m, 1362m, 1339m, 1274m, 1191m, 1168m, 858w, 759m, 657w cm^{-1}; ^{1}H NMR (400 MHz, D_2O): δ = 7.79 (*d*, $^3J_{H,H}$ = 8.92 Hz, 2 H, H-C(4,5)), 7.62 (t, $^3J_{H,H}$ = 7.26 Hz, 2 H, H-C(3,6)), 7.21 (*d*, $^3J_{H,H}$ = 8.51 Hz, 2 H, H-C(1,8)), 7.20 (*m*, 2 H, H-C(2,7)), 3.63–3.59 (*m*, 2 H, CH_2(1′)), 2.82–2.78 (*m*, 2 H, CH_2(9′)), 1.64–1.56 (*m*, 2 H, CH_2(2′)), 1.49–1.42 (*m*, 2 H, CH_2(8′)), 1.20–1.08 (m, 10 H, 5 × CH_2(3′,4′,5′,6′,7′)); ^{13}C NMR (100.6 MHz, D_2O): δ = 156.5 (quart.), 135.0 (CH), 117.9 (CH), 48.7 (CH_2(1′)), 39.6 (CH_2(9′)), 29.0 (CH_2), 28.5 (CH_2), 28.2 (CH_2), 28.2 (CH_2), 26.8 (CH_2), 26.0 (CH_2), 25.6 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 168 (18%) $[MH_2]^{2+}$, 336 (100%) $[MH]^+$.

5.2.19. N *(1-(9-Acridinyl)-1,10-decanediamine dihydrochloride (**29**)*

Following GP2 from **19** (3.6 g, 8.02 mmol) **29** (3.3 g, 98%) was obtained as an orange-coloured, amorphous solid; UV-vis (methanol): λ_{max} (log ϵ) = 281 nm (4.61); IR (KBr): ν = 2924m, 1634s, 1589s, 1531s, 1468s, 1339m, 1271m, 1190m, 1169w, 858w, 754m cm^{-1}; ^{1}H NMR (400 MHz, D_2O): δ = 7.60 (*m*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.60 (*m*, 2 H, H-C(3,6)), 7.19 (*m*, 4 H, H-C(1,8), H-C(2,7)), 3.59–3.55 (*m*, 2 H, CH_2(1′)), 2.83–2.79 (*m*, 2 H, CH_2(10′)), 1.59–1.56 (*m*, 2 H, CH_2(2′)), 1.48–1.42 (*m*, 2 H, CH_2(9′)), 1.08–1.16 (*m*, 12 H, 6 × CH_2(3′,4′,5′,6′,7′,8′)); ^{13}C NMR (100 MHz, CD_3OD): δ = 159.5 (quart.), 136.3 (CH), 129.7 (CH), 126.1 (CH), 119.5 (CH), 48.4 (CH_2(1′)), 40.8 (CH_2(11′)), 30.7 (CH_2), 30.5 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 30.2 (CH_2), 28.6 (CH_2), 27.9 (CH_2), 27.5 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 175 (45%) $[MH_2]^{2+}$, 350 (100%) $[MH]^+$.

5.2.20. N *(1-(9-Acridinyl)-1,12-dodecanediamine dihydrochloride (**30**)*

Following GP2 from **20** (3.4 g, 7.13 mmol) **30** (3.1 g, 97%) was obtained as a yellow, amorphous solid; UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.71); IR (KBr): ν = 2924m, 1633s, 1592s, 1569s, 1534m, 1469s, 1339w, 1271m, 1191m, 1170w, 857w, 758m cm^{-1}; ^{1}H NMR (400 MHz, D_2O): δ = 7.68 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.55 (*t*, $^3J_{H,H}$ = 7.68 Hz, 2 H, H-C(3,6)), 7.14 (*d*, $^3J_{H,H}$ = 8.51 Hz, 2 H, H-C(1,8)), 7.14 (*m*, 2 H, H-C(2,7)),

3.52–3.48 (*m*, 2 H, CH_2(1′)), 2.81–2.78 (*m*, 2 H, CH_2(12′)), 1.53–1.43 (*m*, 4 H, 2 × CH_2(2′,11′)), 1.14–0.98 (*m*, 16 H, 8 × CH_2(3′,4′,5′,6′,7′,8′,9′,10′)); ^{13}C NMR (100 MHz, D_2O): δ = 156.0 (quart.), 135.1 (CH), 118.1 (CH), 48.5 (CH_2(1′)), 39.7 (CH_2(12′)), 29.1 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 28.9 (CH_2), 28.5 (CH_2), 28.4 (CH_2), 27.0 (CH_2), 26.1 (CH_2), 25.9 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 189 (39%) $[MH_2]^{2+}$, 378 (100%) $[MH]^+$.

*5.2.21. Ethylenediaminetetraacetic acid triethyl ester (**31**)*

To a solution of EDTA (15.0 g, 51.3 mmol) in ethanol (600 ml) conc. sulfuric acid (10 ml) was added and the mixture was heated under reflux for 6 h. After cooling to room temperature the reaction mixture was neutralized by the careful addition of $NaHCO_3$ and the solvents were removed under reduced pressure. The residue was suspended in water (200 ml) and extracted with chloroform (2 × 150 ml). The combined organic phases were dried (Na_2SO_4), the solvent was evaporated and EDTA-tetraethyl ester **32** (14.5 g, 70%) was obtained [mp 30–32 °C (lit.: 34 °C [36], 32 °C [37]); IR (KBr): *v* = 2982s, 2940m, 1736s, 1614w, 1447m, 1421m, 1368s, 1348s, 1190s, 1030s, 862w, 749m cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.12 (*q*, $^3J_{H,H}$ = 7.10 Hz, 8 H,4 × CH_2(2)), 3.56 (*s*, 8 H,4 × CH_2(3)), 2.87 (*s*, 4 H,2 × CH_2(4)), 1.23 (*t*, $^3J_{H,H}$ = 7.10 Hz, 12 H, 4 × CH_3(1)); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.3 (CO), 60.4 (C-2), 55.2 (C-3), 52.3 (C-4), 14.2 (C-1); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 405 (19%) $[MH]^+$, 427 (100%) $[MNa]^+$]. To an emulsion of **32** (20 g, 49.0 mmol) in water (1500 ml) containing Na_2HPO_4 (39.2 g, 276 mmol) and KH_2PO_4 (1.16 g, 8.5 mmol) at 27 °C PLE (BioChemica, 2.5 ml (3500 units)) were added and the mixture was stirred for 8 h. After extraction with hexane (2 × 50 ml, discarded) the aq. layer was extracted with dichloromethane (5 × 100 ml) and the combined organic phases were dried ($MgSO_4$), and the solvent was evaporated to yield **31** (14.5 g, 78%) as a viscous oil [38]. IR (KBr): *v* = 2983m, 2938m, 1738s, 1634m, 1378s, 1199s, 1097s, 1028m, 865w, 734w, 588w cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.15 (*m*, $^3J_{H,H}$ = 7.10 Hz, 6 H, 3 × CH_2), 3.53 (*s*, 4 H, 2 × CH_2), 3.47 (*s*, 2 H, CH_2), 3.45 (*s*, 2 H, CH_2), 2.84 (*s*, 4 H, CH_2), 1.24 (*t*, $^3J_{H,H}$ = 7.10 Hz, 9 H, 3 × CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.0 (CO), 170.9 (CO), 170.6 (CO), 70.0 (C-7), 60.8 (C-6), 57.0 (C-5), 56.1 (C-4), 54.6 (C-3), 52.5 (C-1), 51.7 (C-2), 14.1 (C-8,9); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 377 (39%) $[MH]^+$, 399 (100%) $[MNa]^+$, 415 (28%) $[MK]^+$, 791 (93%) $[M_2K]^+$; HRMS ($C_{16}H_{29}N_2O_8$): 376.14857; found: 376.14859.

*5.2.21. Ethyl 2-((2-{[2-(9-acridinylamino)ethyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} acetate (**33**)*

Following GP3 from **31** (1.2 g, 2.67 mmol), isobutyl chloroformate (438 mg, 3.2 mmol) and **21** (830 mg, 2.67 mmol) **33** (600 mg, 36%) was obtained as a syrup; R_F (methanol/ethyl acetate 1:6.4) 0.63; UV-vis (methanol): λ_{max} (log ϵ) = 281 nm (4.70); IR (KBr): *v* = 3314m, 2981w, 1737s, 1669s, 1560w, 1522s, 1474w, 1430w, 1382w, 1342w, 1261m, 1198s, 1141m, 1028m, 759m, 651w, 1170w, 857w, 758m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.85 (*t*, $^3J_{H,H}$ = 6.64 Hz, 1 H, NH), 8.23 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 8.05 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.62 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.31 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.08–4.01 (*m*, 8 H, 3 × CH_2(Et), CH_2(1′)), 3.77–3.72 (*m*, 2 H, CH_2(2′)), 3.39 (*s*, 4 H, 2 × CH_2(5″)), 3.33 (*s*, 2 H, CH_2(4″)), 3.21 (*s*, 2 H, CH_2(3″)), 2.67 (*s*, 4 H, 2 × CH_2(1″,2″)), 1.22–1.16 (*m*, 9 H, 3 × CH_3(Et)); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.0 (C=O), 170.7 (C=O), 170.6 (C=O), 152.4 (quart.), 147.5 (quart.), 130.0 (CH), 126.8 (CH), 123.5 (CH), 122.0 (CH), 115.0 (quart.), 60.3 (CH_2(Et)), 60.2 (CH_2(Et)), 57.9 (CH_2(4″)), 56.0 (CH_2(3″)), 55.0 (CH_2(5″)), 53.6 (CH_2(1″)), 52.2 (CH_2(2″)), 50.1 (CH_2(1′)), 39.7 (CH_2(2′)), 13.7 (CH_3(Et)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 596 (100%) $[MH]^+$, 618 (7%) $[MNa]^+$; HRMS ($C_{31}H_{41}N_5O_7$): 595.30060; found: 595.30061; Anal. $C_{31}H_{41}N_5O_7$ (C, H, N).

*5.2.22. Ethyl 2-((2-{[3-(9-acridinylamino)propyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} amino) acetate (**34**)*

Following GP3 from **31** (930 mg, 2.47 mmol), isobutyl chloroformate (337 mg, 2.47 mmol) and **22** (670 mg, 2.96 mmol) **34** (845 mg, 47%) was obtained as a syrup; R_F (methanol/ethyl acetate 1:6.4) 0.53; UV-vis (methanol): λ_{max} (log ϵ) = 282 nm (4.72); IR (KBr): *v* = 3262m, 2981w, 1738s, 1635m, 1590m, 1538m, 1471m, 1372w, 1273w, 1196s, 1028m, 754w, 661w cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.96–8.91 (*m*, 1 H, NH), 8.49 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 8.28 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.72 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.37 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.18–4.10 (*m*, 6 H, 3 × CH_2(Et)), 4.07–4.04 (*m*, 2 H, CH_2(1′)), 3.63–3.56 (*m*, 2 H, CH_2(3′)), 3.52 (*s*, 4 H, 2 × CH_2(5″)), 3.45 (*s*, 2 H, CH_2(4″)), 3.43 (*s*, 2 H, CH_2(3″)), 2.81 (*s*, 4 H, 2 × CH_2(1″,2″)), 2.16–2.11 (*m*, 2 H, CH_2(2′)), 1.27–1.22 (*m*, 9 H, 3 × CH_3(Et)); ^{13}C NMR (125 MHz, $CDCl_3$): δ =173.3 (C=O), 171.1 (C=O), 171.0 (C=O), 156.9 (quart.), 140.6 (quart.), 133.9 (CH), 123.8 (CH), 123.6 (CH), 121.0 (CH), 60.8 (CH_2(Et)), 60.7 (CH_2(Et)), 58.3 (CH_2(4″)), 55.8 (CH_2(3″)), 54.7 (CH_2(5″)), 53.0 (CH_2(1″)), 52.3 (CH_2(2″)), 45.0 (CH_2(1′)), 36.1 (CH_2(3′)), 30.6 (CH_2(2′)), 14.3 (CH_3(Et)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 610 (100%) $[MH]^+$, 632 (2%) $[MNa]^+$; HRMS $C_{32}H_{43}N_5O_7$: 609.31625; found: 609.31627; Anal. $C_{32}H_{43}N_5O_7$ (C, H, N).

*5.2.23. Ethyl 2-((2-{[4-(9-acridinylamino)butyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} amino) acetate (**35**)*

Following GP3 from **23** (900 mg, 2.66 mmol), **31** (1.2 g, 3.19 mmol) and isobutyl chloroformate (435 mg, 3.19 mmol)

35 (720 mg, 43%) was obtained as a viscous oil; R_F (methanol/ethyl acetate 1:6.4) 0.50; UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.65); IR (KBr): ν = 3280s, 2981w, 2920w, 1736s, 1657m, 1562m, 1473m, 1272w, 1195s, 1027m, 758w, 661w cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.16 (*t*, $^3J_{H,H}$ = 6.42 Hz, 1 H, NH), 8.11 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.98 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(1,8)), 7.57 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.28 (*t*, $^3J_{H,H}$ = 7.56 Hz, 2 H, H-C(2,7)), 4.11–4.04 (*m*, 6 H, 3 × CH_2(Et)), 3.86–3.83 (*m*, 2 H, CH_2(1′)), 3.47 (*s*, 4 H, 2 × CH_2(5″)), 3.36 (*s*, 2 H, CH_2(4″)), 3.34–3.30 (*m*, 2 H, CH_2(4′)), 3.26 (*s*, 2 H, CH_2(3″)), 2.79–2.72 (*m*, 4 H, 2 × CH_2(1″,2″)), 1.86–1.81 (*m*, 2 H, CH_2(2′)), 1.71–1.67 (*m*, 2 H, CH_2(3′)), 1.21–1.16 (*m*, 9 H, 3 × CH_3(Et)); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.6 (C=O), 171.3 (C=O), 171.0 (C=O), 152.1 (quart.), 147.9 (quart.), 130.2 (CH), 128.0 (CH), 123.2 (CH), 122.8 (CH), 116.0 (quart.), 60.7 (CH_2(Et)), 60.6 (CH_2(Et)), 58.7 (CH_2(4″)), 56.0 (CH_2(3″)), 54.7 (CH_2(5″)), 53.0 (CH_2(1″)), 52.2 (CH_2(2″)), 50.2 (CH_2(1′)), 38.5 (CH_2(4′)), 28.6 (CH_2), 27.1 (CH_2), 14.1 (CH_3(Et)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 624 (100%) $[MH]^+$, 646 (7%) $[MNa]^+$; HRMS ($C_{33}H_{45}N_5O_7$): 623.33190: found: 623.33193; Anal. $C_{33}H_{45}N_5O_7$ (C, H, N).

*5.2.24. Ethyl 2-((2-{[5-(9-acridinylamino)pentyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} amino) acetate (**36**)*

Following GP3 from **24** (1.0 g, 2.84 mmol), **31** (1.26 g, 3.36 mmol) and isobutyl chloroformate (458 mg, 3.36 mmol) **36** (950 mg, 52%) was obtained as a viscous oil; R_F (methanol/ethyl acetate 1:6.4) 0.46; UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.73); IR (KBr): ν = 3324m, 2981w, 2935w, 2860w, 1738s, 1660s, 1616w, 1560m, 1522s, 1474m, 1372w, 1260m, 1196s, 1028m, 859w, 761m, 651w cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.01 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 8.06–8.03 (*m*, 1 H, NH), 8.02 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(1,8)), 7.62 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.32 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(2,7)), 4.10–4.04 (*m*, 6 H, 3 × CH_2(Et)), 3.81–3.78 (*m*, 2 H, CH_2(1′)), 3.46 (*s*, 4 H, 2 × CH_2(5″)), 3.35 (*s*, 2 H, CH_2(4″)), 3.26 (*s*, 2 H, CH_2(3″)), 3.28–3.24 (*m*, 2 H, CH_2(5′)), 2.78–2.71 (*m*, 4 H, 2 × CH_2(1″,2″)), 1.84–1.78 (*m*, 2 H, CH_2(2′)), 1.58–1.53 (*m*, 2 H, CH_2(4′)), 1.49–1.45 (*m*, 2 H, CH_2(3′)), 1.20–1.16 (*m*, 9 H, 3 × CH_3(Et)); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2 (C=O), 171.1 (C=O), 170.8 (C=O), 151.2 (quart.), 149.2 (quart.), 129.6 (CH), 129.5 (CH), 122.8 (CH), 122.7 (CH), 116.5 (quart.), 60.7 (CH_2(Et)), 60.6 (CH_2(Et)), 58.7 (CH_2(4″)), 56.0 (CH_2(3)), 54.8 (CH_2(5″)), 53.0 (CH_2(1″)), 52.3 (CH_2(2″)), 50.9 (CH_2(1′)), 38.7 (CH_2(5′)), 31.2 (CH_2), 29.5 (CH_2), 24.2 (CH_2), 14.3 (CH_3(Et)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 638 (100%) $[MH]^+$, 660 (5%) $[MNa]^+$; HRMS ($C_{34\ H47}N_5O_7$): 637.34755; found: 637.34758; Anal. $C_{34}\ H_{47}N_5O_7$ (C, H, N).

*5.2.28. Ethyl 2-((2-{[6-(9-acridinylamino)hexyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} amino) acetate (**37**)*

Following GP3 from **25** (811 mg, 2.06 mmol), **31** (930 mg, 2.47 mmol) and isobutyl chloroformate (337 mg, 2.47 mmol) **37** (600 mg, 45%) was obtained as a viscous oil. R_F (methanol/ethyl acetate 1:6.4) 0.47; UV-vis (methanol): λ_{max}(log ϵ) = 281 nm (4.55); IR (KBr): ν = 3325m, 2981w, 2934w, 2857w, 1738s, 1667s, 1561m, 1522m, 1428m, 1383w, 1344m, 1261m, 1199s, 1028m, 860w, 762w, 652w cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.97 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(1,8)), 7.58 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.28 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(2,7)), 4.12–4.06 (*m*, 6 H, 3 × CH_2(Et)), 3.79–3.76 (*m*, 2 H, CH_2(1′)), 3.46 (*s*, 4 H, 2 × CH_2(5″)), 3.35 (*s*, 2 H, CH_2(4″)), 3.23 (*s*, 2 H, CH_2(3″)), 3.22–3.17 (*m*, 2 H, CH_2(6′)), 2.74 (*m*, 4 H, 2 × CH_2(1″,2″)), 1.79–1.73 (*m*, 2 H, CH_2(2′)), 1.53–1.41 (*m*, 4 H, 2 × CH_2(3′,5′)), 1.37–1.31 (*m*, 2 H, CH_2(4′)), 1.24–1.1.7 (*m*, 9 H, 3 × CH_3(Et)); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.3 (C=O), 171.1 (C=O), 170.9 (C=O), 151.8 (quart.), 149.0 (quart.), 130.1 (CH), 128.5 (CH), 122.9 (CH), 122.8 (CH), 116.1 (quart.), 60.6 (CH_2(Et)), 60.5 (CH_2(Et)), 58.7 (CH_2(4″)), 55.9 (CH_2(3″)), 54.8 (CH_2(5″)), 52.9 (CH_2(1″)), 52.2 (CH_2(2″)), 50.4 (CH_2(1′)), 38.7 (CH_2(6′)), 31.4 (CH_2), 29.4 (CH_2), 26.4 (CH_2), 26.3 (CH_2), 14.1 (CH_3(Et)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 652 (100%) $[MH]^+$; HRMS ($C_{35}H_{49}N_5O_7$): 651.36320; found: 651.36322; Anal. $C_{35}H_{49}N_5O_7$ (C, H, N).

*5.2.25. Ethyl 2-((2-{[7-(9-acridinylamino)heptyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} amino) acetate (**38**)*

Following GP3 from **26** (665 mg, 1.75 mmol), **31** (788 mg, 2.09 mmol) and isobutyl chloroformate (287 mg, 2.09 mmol) **38** (490 mg, 42%) was obtained as a viscous oil. R_F (methanol/ethyl acetate 1:6.4) 0.53; UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.66); IR (KBr): ν = 3335s, 2932w, 2857w, 1738s, 1667s, 1560s, 1521m, 1473m, 1383m, 1344m, 1260s, 1197s, 1028m, 858m, 761w, 651w cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 8.00 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.90 (*t*, $^3J_{H,H}$ = 5.81 Hz, 1 H, NH), 7.61 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.30 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.12–4.04 (*m*, 6 H, 3 × CH_2(Et)), 3.77–3.74 (*m*, 2 H, CH_2(1′)), 3.46 (*s*, 4 H, 2 × CH_2(5″)), 3.35 (*s*, 2 H, CH_2(4″)), 3.23 (*s*, 2 H, CH_2(3″)), 3.22–3.16 (*m*, 2 H, CH_2(7′)), 2.79–2.70 (*m*, 4 H, 2 × CH_2(1″,2″)), 1.77–1.71 (*m*, 2 H, CH_2(2′)), 1.48–1.43 (*m*, 2 H, CH_2(6′)), 1.42–1.33 (*m*, 2 H, CH_2(3′)), 1.30–1.28 (*m*, 4 H, 2 × CH_2(4′,5′)), 1.21–1.16 (*m*, 9 H, 3 × CH_3(Et)); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0 (C=O), 170.9 (C=O), 170.7 (C=O), 151.3 (quart.), 148.9 (quart.), 129.7 (CH), 129.0 (CH), 122.8 (CH), 122.7 (CH), 116.4 (quart.), 60.6 (CH_2(Et)), 60.5 (CH_2(Et)), 58.7 (CH_2(4″)), 55.9 (CH_2(3″)),

54.8 (CH_2(5″)), 52.9 (CH_2(1″)), 52.2 (CH_2(2″)), 50.8 (CH_2(1′)), 39.0 (CH_2(7′)), 31.6 (CH_2), 29.5 (CH_2), 28.9 (CH_2), 26.8 (CH_2), 26.7 (CH_2), 14.2 (CH_3(Et)); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 666 (100%) $[MH]^+$, 688 (5%) $[MNa]^+$; HRMS ($C_{36}H_{51}N_5O_7$): 665.37885; found: 665.37887; Anal. $C_{36}H_{51}N_5O_7$ (C, H, N).

*5.2.26. Ethyl 2-((2-{[8-(9-acridinylamino)octyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} amino) acetate (**39**)*

Following GP3 from **27** (1.2 g, 3.04 mmol), **31** (1.35 g, 3.6 mmol) and isobutyl chloroformate (492 mg, 3.6 mmol) **39** (865 mg, 42%) was obtained as a viscous oil. R_F (methanol/ethyl acetate 1:6.4) 0.60; UV-vis (methanol): λ_{max} (log ϵ) = 281 nm (4.73); IR (KBr): *v* = 3328s, 2930m, 2855m, 1739s, 1661s, 1560s, 1521m, 1474m, 1370m, 1344m, 1260s, 1195s, 1028s, 858m, 761m, 652w cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.01 (d, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.95 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(1,8)), 7.87 (*m*, 1 H, NH), 7.54 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.23 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(2,7)), 4.07–4.02 (*m*, 6 H, 3 × CH_2(Et)), 3.70–3.67 (*m*, 2 H, CH_2(1′)), 3.42 (*s*, 4 H, 2 × CH_2(5″)), 3.31 (*s*, 2 H, CH_2(4″)), 3.19 (*s*, 2 H, CH_2(3″)), 3.16–3.12 (*m*, 2 H, CH_2(8′)), 2.74–2.66 (*m*, 4 H, 2 × CH_2(1″,2″)), 1.68–1.62 (*m*, 2 H, CH_2(2′)), 1.41–1.39 (*m*, 2 H, CH_2(7′)), 1.31–1.28 (*m*, 2 H, CH_2(3′)), 1.21–1.18 (*m*, 6 H, 3 × CH_2(4′,5′,6′)), 1.16–1.12 (*m*, 9 H, 3 × CH_3(Et)); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.1 (C=O), 171.0 (C=O), 170.8 (C=O), 151.3 (quart.), 148.9 (quart.), 129.6 (CH), 128.8 (CH), 122.7 (CH), 122.6 (CH), 116.3 (quart.), 60.5 (CH_2(Et)), 60.3 (CH_2(Et)), 58.5 (CH_2(4″)), 55.7 (CH_2(3″)), 54.7 (CH_2(5″)), 52.7 (CH_2(1″)), 52.0 (CH_2(2″)), 50.6 (CH_2(1′)), 38.8 (CH_2(8′)), 31.4 (CH_2), 29.4 (CH_2), 28.9 (CH_2), 28.8 (CH_2), 26.5 (CH_2), 14.0 (CH_3(Et)); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 340 (8%) $[MH_2]^{2+}$, 680 (100%) $[MH]^+$, 703 (9%) $[MNa]^+$; HRMS ($C_{37}H_{53}N_5O_7$): 679.39450; found: 679.39452; Anal. $C_{37}H_{53}N_5O_7$ (C, H, N).

*5.2.27. Ethyl 2-((2-{[9-(9-acridinylamino)nonyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} amino) acetate (**40**)*

Following GP3 from **28** (1.2 g, 2.94 mmol), **31** (1.36 g, 3.52 mmol) and isobutyl chloroformate (482 mg, 3.52 mmol) **40** (790 mg, 39%) was obtained as a viscous oil. R_F (methanol/ethyl acetate 1:6.4) 0.63; UV-vis (methanol): λ_{max} (log ϵ) = 281 nm (4.69); IR (KBr): *v* = 3323m, 2928m, 2854m, 1738s, 1667s, 1561m, 1521m, 1384m, 1261s, 1196m, 1027m, 759m cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.08 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 8.03 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(1,8)), 7.91–7.87 (*m*, 1 H, NH), 7.62 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.32 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(2,7)), 4.12 (*q*, $^3J_{H,H}$ = 7.33 Hz, 2 H, CH_2(Et)), 4.11 (*q*, $^3J_{H,H}$ = 7.33 Hz, 4 H, 2 × CH_2(Et)), 3.80–3.77 (*m*, 2 H, CH_2(1′)), 3.49 (*s*, 4 H, 2 × CH_2(5″)), 3.38 (*s*, 2 H, CH_2(4″)), 3.25 (*s*, 2 H, CH_2(3″)), 3.23–3.19 (*m*, 2 H, CH_2(9′)), 2.81–2.73 (*m*, 4 H, 2 × CH_2(1″,2″)), 1.79–1.73 (*m*, 2 H, CH_2(2′)), 1.48–1.45 (*m*, 2 H, CH_2(8′)), 1.44–1.39 (*m*, 2 H, CH_2(3′)), 1.33–1.26 (*m*, 8 H, 4 × CH_2(4′,5′,6′,7′), 1.22 (*t*, $^3J_{H,H}$ = 7.33 Hz, 9 H, 3 × CH_3(Et)); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.3 (C=O), 171.2 (C=O), 171.0 (C=O), 151.6 (quart.), 149.0 (quart.), 129.9 (CH), 129.1 (CH), 122.9 (CH), 122.7 (CH), 116.4 (quart.), 60.7 (CH_2(Et)), 60.5 (CH_2(Et)), 58.7 (CH_2(4″)), 56.0 (CH_2(3″)), 54.9 (CH_2(5″)), 53.0 (CH_2(1″)), 52.3 (CH_2(2″)), 50.8 (CH_2(1′)), 39.1 (CH_2(9′)), 31.7 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 26.83 (CH_2), 26.78 (CH_2), 14.2 (CH_3(Et)); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 347 (9%) $[MH_2]^{2+}$, 694 (100%) $[MH]^+$, 716 (7%) $[MNa]^+$; HRMS ($C_{38}H_{55}N_5O_7$): 693.41015; found: 693.41016; Anal. $C_{38}H_{55}N_5O_7$ (C, H, N).

*5.2.28. Ethyl 2-((2-{[10-(9-acridinylamino)decyl]amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino]ethyl} amino) acetate (**41**)*

Following GP3 from **29** (900 mg, 2.13 mmol), **31** (961 mg, 2.56 mmol) and isobutyl chloroformate (350 mg, 2.56 mmol) **41** (605 mg, 40%) was obtained as a viscous oil. R_F (methanol/ethyl acetate 1:6.4) 0.64; UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.69); IR (KBr): *v* = 2928m, 2854m, 1740s, 1670s, 1560w, 1521m, 1474m, 1370m, 1260s, 1195m, 1029m, 858m, 760w, 651w cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(4,5)), 7.90 (*d*, $^3J_{H,H}$ = 8.72 Hz, 2 H, H-C(1,8)), 7.87–7.82 (*m*, 1 H, NH), 7.50 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(3,6)), 7.20 (*dd*, $^3J_{H,H}$ = 8.72 Hz, $^3J_{H,H}$ = 7.47 Hz, 2 H, H-C(2,7)), 4.04 (*q*, $^3J_{H,H}$ = 7.05 Hz, 6 H, 3 × CH_2(Et)), 3.71–3.68 (*m*, 2 H, CH_2(1′)), 3.42 (*s*, 4 H, 2 × CH_2(5″)), 3.31 (*s*, 2 H, CH_2(4″)), 3.18 (*s*, 2 H, CH_2(3″)), 3.17–3.12 (*m*, 2 H, CH_2(10′)), 2.72–2.65 (*m*, 4 H, 2 × CH_2(1″,2″)), 1.70–1.63 (*m*, 2 H, CH_2(2′)), 1.42–1.37 (*m*, 2 H, CH_2(9′)), 1.34–1.27 (*m*, 2 H, CH_2(3′)), 1.20–1.12 (*m*, 10 H, 5 × CH_2(4′,5′,6′,7′,8′), 1.14 (*t*, $^3J_{H,H}$ = 7.05 Hz, 9 H,2 × CH_3(Et)); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9 (C=O), 170.7 (C=O), 170.6 (C=O), 151.5 (quart.), 148.0 (quart.), 129.7 (CH), 128.0 (CH), 122.8 (CH), 122.4 (CH), 115.9 (quart.), 60.4 (CH_2(Et)), 60.3 (CH_2(Et)), 58.5 (CH_2(4″)), 55.8 (CH_2(3″)), 54.7 (CH_2(5″)), 52.8 (CH_2(1″)), 52.1 (CH_2(2″)), 50.4 (CH_2(1′)), 39.0 (CH_2(10′)), 31.4 (CH_2), 29.5 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.08 (CH_2), 26.06 (CH_2), 26.7 (CH_2), 14.1 (CH_3(Et)); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 708 (100%) $[MH]^+$, 730 (7%) $[MNa]^+$; HRMS ($C_{39}H_{57}N_5O_7$): 707.42580; found: 707.42583; Anal. $C_{39}H_{57}N_5O_7$ (C, H, N).

*5.2.29. Ethyl 2-((2-{[12-(9-acridinylamino)dodecyl] amino}-2-oxoethyl){2-[di-(2-ethoxy-2-oxoethyl)amino] ethyl}amino) acetate (**42**)*

Following GP3 from **30** (930 mg, 2.06 mmol), **31** (930 mg, 2.47 mmol) and isobutyl chloroformate (337 mg, 2.47 mmol) **42** (730 mg, 48%) was obtained as a viscous oil. R_F (methanol/ethyl acetate 1:6.4) 0.66; UV-vis (methanol):

λ_{max} (log ϵ) = 281 nm (4.74); IR (KBr): ν = 2927m, 2854w, 1739s, 1667s, 1561m, 1522w, 1474w, 1373w, 1260s, 1196m, 1029m, 858m, 761w, 651w cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.08 (*d*, $^3J_{H,H}$ = 8.74 Hz, 2 H, H-C(4,5)), 8.04 (*d*, $^3J_{H,H}$ = 8.74 Hz, 2 H, H-C(1,8)), 7.90–7.85 (*m*, 1 H, NH), 7.64 (*dd*, $^3J_{H,H}$ = 8.74 Hz, $^3J_{H,H}$ = 7.49 Hz, 2 H, H-C(3,6)), 7.34 (*dd*, $^3J_{H,H}$ = 8.74 Hz, $^3J_{H,H}$ = 7.49 Hz, 2 H, H-C(2,7)), 4.16–4.10 (*m*, 2 H, CH_2(Et)), 3.81–3.78 (*m*, 2 H, CH_2(1′)), 3.50 (*s*, 4 H, CH_2(5″)), 3.39 (*s*, 2 H, CH_2(4″)), 3.26 (*s*, 2 H, CH_2(3″)), 3.24–3.19 (*m*, 2 H, CH_2(12′)), 2.82–2.74 (*m*, 4 H, 2 × CH_2(1″,2″)), 1.78–1.74 (*m*, 2 H, CH_2(2′)), 1.50–1.45 (*m*, 2 H, CH_2(11′)), 1.44–1.39 (*m*, 2 H, CH_2(3′)), 1.32–1.22 (*m*, 14 H, 7 × CH_2(4′,5′,6′,7′,8′,9′,10′), 1.25–1.21 (*m*, 9 H, 3 × CH_3(Et)); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 171.3 (C=O), 171.1 (C=O), 171.0 (C=O), 151.4 (quart.), 129.8 (CH), 123.0 (CH), 122.7 (CH), 116.6 (quart.), 60.7 (CH_2(Et)), 60.6 (CH_2(Et)), 58.8 (CH_2(4″)), 56.0 (CH_2(3″)), 54.9 (CH_2(5″)), 53.0 (CH_2(1″)), 52.3 (CH_2(2″)), 51.0 (CH_2(1′)), 39.2 (CH_2(12′)), 31.8 (CH_2), 29.7 (CH_2), 29.52 (CH_2), 29.46 (CH_2), 29.45 (CH_2), 29.3 (CH_2), 27.0 (CH_2), 26.9 (CH_2), 14.2 (CH_3(Et)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 368 (2%) $[MH_2]^{2+}$, 736 (100%) $[MH]^+$, 758 (6%) $[MNa]^+$; HRMS ($C_{41}H_{61}N_5O_7$): 735.45710; found: 735.45711; Anal. $C_{41}H_{61}N_5O_7$ (C, H, N).

*5.2.30. 2-[{2-[(2-{[2-(9-Acridinylamino)ethyl]amino}-2-oxoethyl)(carboxymethyl)-amino]ethyl}(carboxymethyl) amino] acetic acid (**43**)*

Following GP4 from **33** (180 mg, 0.302 mmol) **43** (129 mg, 84%) was obtained as an amorphous orange-red solid. UV-vis (methanol): λ_{max} (log ϵ) = 282 nm (4.66); IR (KBr): ν = 3854s, 2832m, 1590s, 1474w, 1407s, 1337m, 1261w, 1172w, 1123w, 1024w cm^{-1}; ^1H NMR (500 MHz, D_2O): δ = 7.53 (*d*, $^3J_{H,H}$ = 8.68 Hz, 2 H, H-C(4,5)), 7.42 (*dd*, $^3J_{H,H}$ = 8.68 Hz, $^3J_{H,H}$ = 7.37 Hz, 2 H, H-C(3,6)), 7.11 (*d*, $^3J_{H,H}$ = 8.55 Hz, 2 H, H-C(1,8)), 7.04 (*dd*, $^3J_{H,H}$ = 8.68 Hz, $^3J_{H,H}$ = 7.37 Hz, 2 H, H-C(2,7)), 3.59–3.54 (*m*, 2 H, CH_2(1′)), 3.33–3.28 (*m*, 2 H, CH_2(2′)), 3.01 (*s*, 4 H, 2 × CH_2(5″)), 2.91 (*s*, 2 H, CH_2(4″)), 2.83 (*s*, 2 H, CH_2(3″)), 2.46–2.41 (*m*, 2 H, CH_2(1″)), 2.37–2.31 (*m*, 2 H, CH_2(2″)); ^{13}C NMR (125 MHz, D_2O): δ = 178.8 (C=O), 175.1 (C=O), 154.1 (quart.), 142.1 (quart.), 133.1 (CH), 123.6 (CH), 123.3 (CH), 121.5 (CH), 112.6 (quart.), 58.5 (CH_2(3″)), 58.3 (CH_2(5″)), 57.8 (CH_2(4″)), 51.9 (CH_2(1″)), 51.7 (CH_2(2″)), 48.7 (CH_2(1′)), 39.1 (CH_2(2′)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 510 (100%) $[M - H]^-$; HRMS ($C_{25}H_{29}N_5O_7$): 511.20670; found: 511.20671.

*5.2.31. 2-[{2-[(2-{[3-(9-Acridinylamino)propyl]amino}-2-oxoethyl)(carboxymethyl)-amino]ethyl}(carboxymethyl) amino]acetic acid (**44**)*

Following GP4 from **34** (740 mg, 1.2 mmol) **44** (548 mg, 86%) was obtained as an amorphous, orange-coloured solid. UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.63); IR (KBr): ν = 3423s, 1591s, 1474m, 1409s, 1337m, 1261m, 1171w, 1123m cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 8.46 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.82–7.80 (*m*, 4 H, H-C(1,8), H-C(3,6)), 7.48–7.43 (*m*, 2 H, H-C(2,7)), 4.11–4.07 (*m*, 2 H, CH_2(1′)), 3.39–3.36 (*m*, 2 H, CH_2(3′)), 3.19 (*s*, 4 H, 2 × CH_2(5″)), 3.12 (*s*, 2 H, CH_2(4″)), 3.05 (*s*, 2 H, CH_2(3″)), 2.70–2.52 (*m*, 4 H, 2 × CH_2(1″,2″)), 2.15–2.08 (*m*, 2 H, CH_2(2′)); ^{13}C NMR (125 MHz, D_2O): δ = 179.0 (C=O), 174.1 (C=O), 154.6 (quart.), 140.7 (quart.), 133.6 (CH), 123.7 (CH), 123.3 (CH), 120.2 (CH), 111.8 (quart.), 58.8 (CH_2(3″)), 58.4 (CH_2(5″)), 58.2 (CH_2(4″)), 52.1 (CH_2(1″)), 51.9 (CH_2(2″)), 45.9 (CH_2(1′)), 36.2 (CH_2(3′)), 28.9 (CH_2(2′)); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 524 (100%) $[M - H]^-$; HRMS ($C_{26}H_{31}N_5O_7$): 525.22235; found: 525.22237.

*5.2.32. 2-[{2-[(2-{[4-(9-Acridinylamino)butyl]amino}-2-oxoethyl)(carboxymethyl)-amino]ethyl}(carboxymethyl)amino]acetic acid (**45**)*

Following GP4 from **35** (136 mg, 022 mmol) **45** (100 mg, 87%) was obtained as an orange-coloured, amorphous solid. UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.60); IR (KBr): ν = 3424s, 2927m, 2853m, 1636s, 1589s, 1471m, 1404m, 1336m, 1272m, 1191w, 1170w, 1121w cm^{-1}; ^1H NMR (500 MHz, D_2O): δ = 7.52 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.43 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 6.88 Hz, 2 H, H-C(3,6)), 7.04 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, CH(1,8)), 7.02 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 6.88 Hz, 2 H, H-C(2,7)), 3.36–3.33 (*m*, 2 H, CH_2(1′)), 3.17 (*s*, 4 H, 2 × CH_2(5″)), 3.11–3.07 (*m*, 2 H, CH_2(4′)), 3.08 (*s*, 2 H, CH_2(4″)), 3.01 (*s*, 2 H, CH_2(3″)), 2.69–2.63 (*m*, 2 H, CH_2(1″)), 2.60–2.55 (*m*, 2 H, CH_2(2″)), 1.50–1.46 (*m*, 2 H, CH_2(2′)), 1.43–1.39 (*m*, 2 H, CH_2(3′)); ^{13}C NMR (125 MHz, D_2O): δ = 178.9 (C=O), 173.9 (C=O), 154.6 (quart.), 140.3 (quart.), 133.8 (CH), 123.9 (CH), 123.3 (CH), 119.7 (CH), 111.7 (quart.), 58.7 (CH_2(3″)), 58.3 (CH_2(5″)), 58.1 (CH_2(4″)), 52.0 (CH_2(1″)), 51.7 (CH_2(2″)), 48.0 (CH_2(1′)), 38.4 (CH_2(4′)), 25.5 (CH_2), 25.7 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 538 (100%) $[M - H]^-$; HRMS ($C_{27}H_{33}N_5O_7$): 539.58022; found: 539.58023.

*5.2.33. 2-[{2-[(2-{[5-(9-Acridinylamino)pentyl]amino}-2-oxoethyl)(carboxymethyl)- amino]ethyl}(carboxymethyl)amino] acetic acid (**46**)*

Following GP4 from **36** (440 mg, 0.69 mmol) **46** (320 mg, 84%) was obtained as an orange-coloured, amorphous solid. UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.53); IR (KBr): ν = 3425s, 2935m, 1591s, 1473w, 1407m, 1337w, 1261w, 1171w, 1123w cm^{-1}; ^1H NMR (500 MHz, D_2O): δ = 7.28 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.24 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 6.87 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(2,7)), 6.76 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(1,8)), 3.33–3.26 (*m*, 4 H, 2 × CH_2(1′,3″)), 3.13 (*s*, 2 H, CH_2(4″)), 3.10–3.02 (*m*, 2 H, CH_2(5′)), 3.05 (*s*, 4 H, CH_2(5″)), 2.81–2.72 (*m*, 2 H, CH_2(1″)), 2.69–2.63 (*m*, 2 H, CH_2(2″)), 1.39–1.29 (*m*, 4 H, 2 × CH_2(2′,4′)), 1.14–1.06 (*m*, 2 H, CH_2(3′)); ^{13}C NMR (125 MHz, D_2O): δ = 178.8 (C=O), 173.4 (C=O), 154.4 (quart.), 138.6 (quart.), 134.4 (CH), 123.7 (CH), 123.4 (CH),

118.3 (CH), 110.7 (quart.), 58.5 (CH_2(3″)), 58.3 (CH_2(5″)), 57.9 (CH_2(4″)), 52.2 (CH_2(1″)), 51.3 (CH_2(2″)), 48.0 (CH_2(1′)), 38.8 (CH_2(5′)), 28.6 (CH_2), 27.9 (CH_2), 23.2 (CH_2); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 552 (100%) $[M - H]^-$; HRMS ($C_{28}H_{35}N_5O_7$): 553.25365; found: 553.25367.

*5.2.34. 2-[{2-[(2-{[6-(9-Acridinylamino)hexyl]amino}-2-oxoethyl)(carboxymethyl)- amino]ethyl}(carboxymethyl)amino] acetic acid (**47**)*

Following GP4 from **37** (620 mg, 0.95 mmol) **47** (448 mg, 83%) was obtained as an orange-coloured, amorphous solid. UV-vis (methanol): λ_{max} (log ϵ) = 283 nm (4.53); IR (KBr): *ν* = 3423s, 2934m, 1590s, 1408w, 1336m, 1260m, 1171w, 1122w cm^{-1}; ^{1}H NMR (500 MHz, D_2O): *δ* = 7.51 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.42 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.11 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(1,8)), 7.01 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, CH(2,7)), 3.29–3.24 (*m*, 2 H, CH_2(1′)), 3.09 (*s*, 4 H, 2 × CH_2(5″)), 3.07 (*s*, 2 H, CH_2(4″)), 3.06–3.02 (*m*, 2 H, CH_2(6′)), 3.02 (*s*, 2 H, CH_2(3″)), 2.60–2.53 (*m*, 4 H, CH_2(1″, 2″)), 1.45–1.37 (*m*, 2 H, CH_2(2′)), 1.35–1.31 (*m*, 2 H, CH_2(5′)), 1.15–1.09 (*m*, 4 H, 2 × CH_2(3′,4′)); ^{13}C NMR (125 MHz, D_2O): *δ* = 179.1 (C=O), 173.8 (C=O), 154.2 (quart.), 141.5 (quart.), 133.3 (CH), 123.8 (CH), 123.0 (CH), 120.7 (CH), 112.1 (quart.), 58.8 (CH_2(3″)), 58.4 (CH_2(5″)), 58.2 (CH_2(4″)), 52.0 (CH_2(1″)), 51.9 (CH_2(2″)), 48.4 (CH_2(1′)), 38.8 (CH_2(6′)), 29.1 (CH_2), 28.1 (CH_2), 25.5 (CH_2), 25.4 (CH_2); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 566 (100%) $[M - H]^-$; HRMS ($C_{29}H_{37}N_5O_7$): 567.26930; found: 567.26931.

*5.2.35. 2-[{2-[(2-{[7-(9-Acridinylamino)heptyl]amino}-2-oxoethyl)(carboxymethyl)- amino]ethyl}(carboxymethyl)amino] acetic acid (**48**)*

Following GP4 from **38** (250 mg, 0375 mmol) **48** (172 mg, 79%) was obtained as an orange-coloured, amorphous solid. UV-vis (methanol): λ_{max} (log ϵ) = 281 nm (4.68); IR (KBr): *ν* = 3425s, 2935w, 2856w, 1635s, 1592s, 1473w, 1407m, 1338w, 1272w, 1171w, 1123w cm^{-1}; ^{1}H NMR (500 MHz, D_2O): *δ* = 7.28 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.25 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 6.85 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(2,7)), 6.83 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(1,8)), 3,34 (*s*, 4 H, 2 × CH_2(5″)), 3.17 (*s*, 2 H, CH_2(4″)), 3.06 (s, 2 H, CH_2(3″)), 3.07–3.01 (*m*, 4 H, 2 × CH_2(1′,7′)), 2.88–2.80 (*s*, 2 H, CH_2(1″)), 2.74–2.68 (*s*, 2 H, CH_2(2″)), 1.35–1.22 (*m*, 4 H, 2 × CH_2(2′,6′)), 1.09–1.00 (*m*, 6H, 3xCH_2(3′,4′,5′)); ^{13}C NMR (125 MHz, D_2O): *δ* = 178.7 (C=O), 173.5 (C=O), 154.3 (quart.), 139.1 (quart.), 134.1 (CH), 123.6 (CH), 123.2 (CH), 118.8 (CH), 110.9 (quart.), 58.6 (CH_2(3″)), 58.3 (CH_2(5″)), 57.7 (CH_2(4″)), 52.2 (CH_2(1″)), 51.4 (CH_2(2″)), 48.1 (CH_2(1′)), 38.9 (CH_2(7′)), 28.8 (CH_2), 28.2 (CH_2), 27.7 (CH_2), 25.8 (CH_2), 25.6 (CH_2); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 580 (100%) $[M - H]^-$; HRMS ($C_{30}H_{39}N_5O_7$): 581.28495; found: 581.28497.

*5.2.36. 2-[{2-[(2-{[8-(9-Acridinylamino)octyl]amino}-2-oxoethyl)(carboxymethyl)- amino]ethyl}(carboxymethyl)amino] acetic acid (**49**)*

Following GP4 from **39** (134 mg, 0.197 mmol) **49** (99 mg, 85%) was obtained as an amorphous, orange-coloured solid. UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.57); IR (KBr): *ν* = 3425s, 2853m, 1589s, 1473m, 1407m, 1336w, 1260w, 1170w, 1122w cm^{-1}; ^{1}H NMR (500 MHz, D_2O): *δ* = 7.57 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.45 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.20 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(1,8)), 7.03 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(2,7)), 3.32–3.29 (*m*, 2 H, CH_2(1′)), 3.14 (*s*, 4 H, 2 × CH_2(5″)), 3.09 (*s*, 2 H, CH_2(4″)), 3.03 (*s*, 2 H, CH_2(3″)), 3.02–2.98 (*m*, 2 H, CH_2(8′)), 2.66–2.55 (*m*, 4 H, 2 × CH_2(1″,2″)), 1.43–1.37 (*m*, 2 H, CH_2(2′)), 1.30–1.23 (*m*, 2 H, CH_2(7′)), 1.07–0.98 (*m*, 8 H, 4 × CH_2(3′,4′,5′,6′)); ^{13}C NMR (125 MHz, D_2O): *δ* = 179.0 (C=O), 173.7 (C=O), 154.4 (quart.), 141.8 (quart.), 133.3 (CH), 123.8 (CH), 123.0 (CH), 121.0 (CH), 112.3 (quart.), 58.8 (CH_2(3″)), 58.3 (CH_2(5″)), 58.2 (CH_2(4″)), 52.0 (CH_2(1″)), 51.9 (CH_2(2″)), 48.5 (CH_2(1′)), 38.9 (CH_2(8′)), 29.1 (CH_2), 28.2 (CH_2), 28.0 (CH_2), 27.9 (CH_2), 25.8 (CH_2), 25.6 (CH_2); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 594 (100%) $[M - H]^-$; HRMS ($C_{31}H_{41}N_5O_7$): 595.30060; found: 595.30061.

*5.2.37. 2-[{2-[(2-{[9-(9-Acridinylamino)nonyl]amino}-2-oxoethyl)(carboxymethyl)- amino]ethyl}(carboxymethyl)amino] acetic acid (**50**)*

Following GP4 from **40** (730 mg, 1.05 mmol) **50** (564 mg, 88%) was obtained as a yellow, amorphous solid. UV-vis (methanol): λ_{max}(log ϵ) = 284 nm (4.55); IR (KBr): *ν* = 3442s, 1591s, 1408m, 1337w, 1124w cm^{-1}; ^{1}H NMR (500 MHz, D_2O): *δ* = 7.42 (*d*, $^3J_{H,H}$ = 8.68 Hz, 2 H, H-C(4,5)), 7.36 (*dd*, $^3J_{H,H}$ = 8.68 Hz, $^3J_{H,H}$ = 7.63 Hz, 2 H, H-C(3,6)), 7.04 (*d*, $^3J_{H,H}$ = 8.68 Hz, 2 H, H-C(1,8)), 6.92 (*dd*, $^3J_{H,H}$ = 8.68 Hz, $^3J_{H,H}$ = 7.63 Hz, 2 H, H-C(2,7)), 3.38 (*s*, 4 H, 2 × CH_2(5″)), 3.20–3.15 (*m*, 2 H, CH_2(1′)), 3.17 (*s*, 2 H, CH_2(4″)), 3.07 (*s*, 2 H, CH_2(3″)), 2.99–2.96 (*m*, 2 H, CH_2(9′)), 2.91–2.85 (*m*, 2 H, CH_2(1″)), 2.75–2.70 (*m*, 2 H, CH_2(2″)), 1.31–1.20 (*m*, 4 H, 2 × CH_2(2′,8′)), 0.98–0.85 (*m*, 10 H, 5 × CH_2(3′,4′,5′,6′,7′)); ^{13}C NMR (125 MHz, D_2O): *δ* = 178.6 (C=O), 173.2 (C=O), 154.9 (quart.), 139.5 (quart.), 134.2 (CH), 123.8 (CH), 123.3 (CH), 119.1 (CH), 111.3 (quart.), 58.5 (CH_2(3″)), 58.3 (CH_2(5″)), 57.6 (CH_2(4″)), 52.3 (CH_2(1″)), 51.0 (CH_2(2″)), 48.2 (CH_2(1′)), 39.1 (CH_2(9′)), 28.9 (CH_2), 28.4 (CH_2), 28.3 (CH_2), 28.2 (CH_2), 28.0 (CH_2), 26.1 (CH_2), 25.7 (CH_2); MS (ESI, 4.1 kV, 8 μl/min, N_2, methanol): *m/z* = 608 (100%) $[M - H]^-$; HRMS ($C_{32}H_{43}N_5O_7$): 609.31625; found: 609.31625.

*5.2.38. 2-[{2-[(2-{[10-(9-Acridinylamino)decyl]amino}-2-oxoethyl)(carboxymethyl)- amino]ethyl}(carboxymethyl)amino] acetic acid (**51**)*

Following GP4 from **41** (260 mg, 0.367 mmol) **51** (174 mg, 76%) was obtained as an amorphous, yellow solid. UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.66); IR (KBr):

ν = 3418s, 2924m, 2851s, 1644s, 1590s, 1473m, 1408m, 1337m, 1272w, 1172w, 1122w, 1024w cm^{-1}; ^1H NMR (500 MHz, D_2O): δ = 7.50 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.36 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(3,6)), 7.18 (*d*, $^3J_{H,H}$ = 8.48 Hz, 2 H, H-C(1,8)), 6.92 (*dd*, $^3J_{H,H}$ = 8.71 Hz, $^3J_{H,H}$ = 7.33 Hz, 2 H, H-C(2,7)), 3.29 (*s*, 4 H, 2 × CH_2(5″)), 3.23–3.20 (*m*, 2 H, CH_2(1′)), 3.13 (*s*, 2 H, CH_2(4″)), 3.04 (*s*, 2 H, CH_2(3″)), 2.95–2.92 (*m*, 2 H, CH_2(10′)), 2.80–2.74 (*m*, 2 H, CH_2(1″)), 2.68–2.63 (*m*, 2 H, CH_2(2″)), 1.31–1.28 (*m*, 2 H, CH_2(2′)), 1.21–1.16 (*m*, 2 H, CH_2(9′)), 0.89–0.87 (*m*, 4 H, 2 × CH_2(3′,8′)), 0.82–0.76 (*m*, 8 H, 4 × CH_2(4′,5′,6′,7′)); ^{13}C NMR (125 MHz, D_2O): δ = 178.7 (C=O), 173.2 (C=O), 154.6 (quart.), 140.8 (quart.), 133.6 (CH), 123.7 (CH), 123.1 (CH), 120.3 (CH), 112.0 (quart.), 58.6 (CH_2(3″)), 58.2 (CH_2(5″)), 57.9 (CH_2(4″)), 52.2 (CH_2(1″)), 51.3 (CH_2(2″)), 48.4 (CH_2(1′)), 39.1 (CH_2(10′)), 29.1 (CH_2), 28.60 (CH_2), 28.56 (CH_2), 28.40 (CH_2), 28.38 (CH_2), 28.2 (CH_2), 26.2 (CH_2), 25.9 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 622 (100%) [M – H]$^-$; HRMS ($C_{33}H_{45}N_5O_7$): 623.33190; found: 623.33192.

*5.2.39. 2-[{2-[(2-{[12-(9-Acridinylamino)dodecyl]amino}-2-oxoethyl)(carboxymethyl)- amino]ethyl}(carboxymethyl)amino] acetic acid (**52**)*

Following GP4 from **42** (400 mg, 0.54 mmol) **52** (286 mg, 81%) was obtained as an amorphous, yellow solid. UV-vis (methanol): λ_{max} (log ϵ) = 284 nm (4.35); IR (KBr): ν = 3424s, 2925m, 2852s, 1590s, 1471m, 1407s, 1337m, 1272m, 1191w, 1170w, 1122w, 1022w cm^{-1}; ^1H NMR (500 MHz, D_2O): δ = 7.62 (*d*, $^3J_{H,H}$ = 8.71 Hz, 2 H, H-C(4,5)), 7.40–7.34 (*m*, 4 H, H-C(1,8), H-C(3,6)), 6.95–6.89 (*m*, 2 H, H-C(2,7)), 3.35–3.29 (*m*, 2 H, CH_2(1′)), 3.26 (*s*, 4 H, 2 × CH_2(5″)), 3.11 (*s*, 2 H, CH_2(4″)), 3.04 (*s*, 2 H, CH_2(3″)), 2.92–2.87 (*m*, 2 H, CH_2(12′)), 2.78–2.68 (*s*, 2 H, CH_2(1″)), 2.64–2.59 (*s*, 2 H, CH_2(2″)), 1.40–1.33 (*m*, 2 H, CH_2(2′)), 1.18–1.10 (*m*, 2 H, CH_2(3′)), 0.93–0.61 (*m*, 16 H, 7 × CH_2 (4′- 11′)); ^{13}C NMR (125 MHz, D_2O): δ = 178.6 (C=O), 172.9 (C=O), 154.4 (quart.), 142.0 (quart.), 133.1 (CH), 123.7 (CH), 122.9 (CH), 121.5 (CH), 112.7 (quart.), 58.6 (CH_2(3″)), 58.1 (CH_2(5″)), 58.0 (CH_2(4″)), 52.2 (CH_2(1″)), 51.2 (CH_2(2″)), 48.6 (CH_2(1′)), 39.1 (CH_2(12′)), 29.6 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 28.8 (CH_2), 28.6 (CH_2), 26.5 (CH_2), 26.2 (CH_2); MS (ESI, 4.1 kV, 8 µl/min, N_2, methanol): *m/z* = 650 (100%) [M – H]$^-$; HRMS ($C_{35}H_{49}N_5O_7$): 651.36320; found: 651.36322.

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