

# Synthesis of Dimeric Acridine Derived Nucleic Acid Intercalators

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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. Suitably mono-protected 1, $\omega$ -alkyldiamines gave upon reaction with 6,9-dichloro-2-methoxyacridine (**1**) followed by deprotection and reaction with EDTA dianhydride the target molecules. In the presence of ascorbate a reduction of the phage-titer of the MS2 phages by > 8 logarithmic decades was achieved.

**Key words:** Acridine, Antivirals, Intercalators, Fenton-Mechanism

## Introduction

Blood is a critical element of medical treatment. Every day, numerous units of blood are transfused for a variety of illnesses and conditions including accidents, burns, heart surgery, organ transplants, leukemia, cancer, sickle cell anemia, thalassemia, hemophilia, and others.

Although the blood supply is currently much safer than it has been in the past due to various efforts including increased testing and more stringent donor screening criteria, blood transfusions, unfortunately themselves can be a cause of illness. However, pathogens – viruses, bacteria, and parasites – are still transmitted from person-to-person through donated and transfused blood. The testing and donor screening that are used in blood collection facilities are only able to identify known pathogens. Additionally, new variants and strains of existing infectious agents continue to emerge, moving beyond the sensitivity of existing tests.

A second issue with testing is the presence of a "window period" in which an individual is infected, but the virus is not present in large enough quantities to be detected. However, these quantities are enough to infect a patient with blood. Although improved testing has decreased the window period *e.g.* for HIV from 20 days to 11 days, even at this level, however, tainted blood can slip through.

Quite recently, a new type of pathogen inactivating agents [1] (Fig. 1, type A) was introduced – consisting of an intercalator that binds to the nucleic acid of

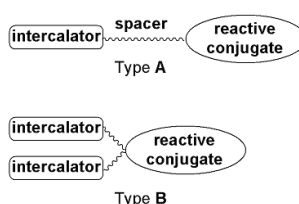
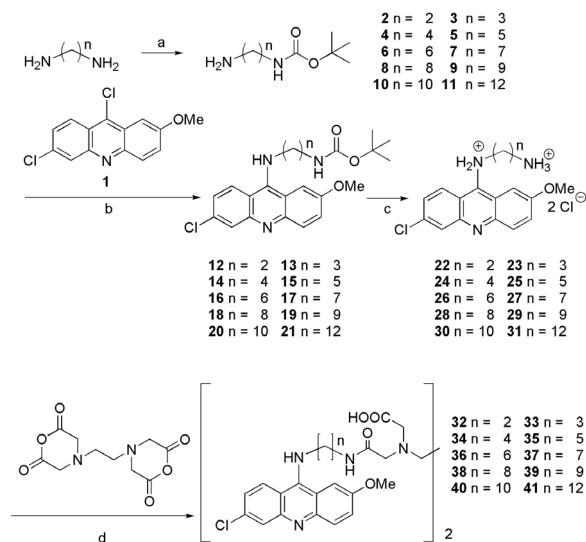


Fig. 1. Basic structures of the pathogen inactivating compounds.

pathogens combined with a conjugate that destroys the nucleic acid subsequently *via* a Fenton [2, 3] mechanism. The conjugate consisted of a metal-chelate complex wherein the metal can change between at least two levels of oxidation. These compounds preferentially showed an acridine as the intercalator possessing in addition a spacer group to an EDTA-Fe(II/III) chelate [4, 5] acting as the conjugate. Damage to the DNA was accomplished by producing OH radicals by a Fe(II) catalyzed Fenton mechanism [1, 6, 7]. Furthermore, the addition of a reducing agent such as ascorbate [8–11] leads to a cycle which increases the damage to the biological molecules.

## Results and Discussion

From preliminary modelling studies we concluded that an improved antipathogenic performance could be expected from compounds exhibiting a stronger ability to interact with DNA or RNA. Thus, from a better intercalating action of the compounds a higher degree of viral inactivation should be expected. Inspection of molecule models indicated that the length of the spacer between the aromatic rest and the chelator should be of some significance with respect to aspects



Scheme 1. a)  $(\text{Boc})_2\text{O}$ , dioxane; b) phenol; c) aq. HCl; d)  $\text{NEt}_3$ .

of binding and interaction. From these modelling studies we also concluded, that the use of substituted acridine moieties should be advantageous for an improved intercalation. Therefore, the synthesis of dimeric structures (Fig. 1, type **B**) was planned using 6-chloro-2-methoxy-acridines for the construction of the intercalating moiety.

As far as the synthesis (Scheme 1) of this spacer is concerned, a variety of 1, $\omega$ -diamines was mono-protected by the reaction with *tert*-butyl-dicarbonate in dry dioxane to afford the corresponding 1-amino-*x*-(*tert*-butyloxycarbonyl)amino-alkanes **2** [12], **3** [13], **4** [14], **5** [15], **6** [16], **7** [17], **8** [18], **9** [19], **10** [18], **11** [20]. Thus, usually two equivalents of the diamine were allowed to react with one equivalent of *tert*-butyl-dicarbonate to result in approx. 40% yields of the corresponding products. These moderate yields could be improved, however, by using a 5-6 molar excess of the amine.

These 1-amino-*x*-(*tert*-butyloxycarbonyl)amino-alkanes **2**–**11** were allowed to react with 6,9-dichloro-2-methoxyacridine (**1**) in the presence of phenol [21–24] to result in the formation of the corresponding *tert*-butyl N-[*x*-(9-acridinyl-amino)alkyl]-carbamates **12**–**21**. Deprotection of these compounds by aq. hydrochloric acid for 10 h at 30 °C gave the corresponding bishydrochlorides **22**–**31**. Reaction of these amines with EDTA dianhydride finally furnished the target compounds **32**–**40**.

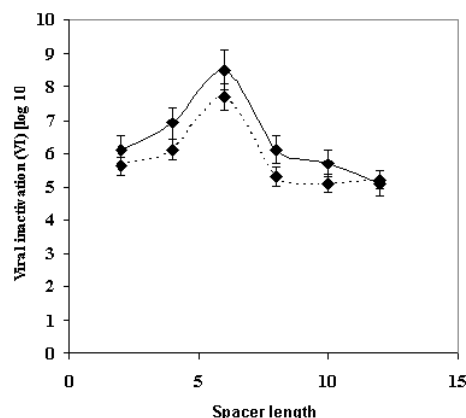


Fig. 2. Inactivation of phage MS2 as a function of spacer length (5 mmol Na-ascorbate, 101  $\mu\text{mol}$  of compounds, 3 equiv.  $\text{Fe}^{3+}$  loaded, incubation time 4 h) and of the temperature (–25 °C, –36 °C).

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.

In this preliminary screening, several of the target compounds were treated with an 2–5 molar excess of  $\text{Fe}^{3+}$ , lyophilized and incubated with the phages in Tris-buffer in the presence of sodium ascorbate. A reduction of the phagetiter of the MS2 phages by > 8 logarithmic decades was achieved.

From these experiments it can be assumed, that the inactivation of the virus depends both on the temperature, the time of incubation as well as on the concentration of the added ascorbate. 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.

Modifications in the structure of these compounds as well an extended biological screening are presently performed in our laboratories.

## Experimental Section

### General

The melting points are uncorrected (*Reichert* hot stage microscope), NMR spectra (internal  $\text{Me}_4\text{Si}$ ) were recorded using either a Bruker AM250 or a Varian XL300 instrument ( $\delta$  given in ppm, *J* in Hz), IR spectra (film or KBr pellet) on a Perkin-Elmer 298 instrument, MS spectra were taken either on a MAT311A or a Varian-112S instrument; for elemen-

tal analysis a Foss-Heraeus Vario EL instrument was used. TLC was performed on silica gel (Merck 5554, detection by dipping in a solution containing 10% sulfuric acid (400 ml), ammonium molybdate (20 g) and cerium(IV) sulfate (20 mg) followed by heating to 150 °C. All reactions were performed under dry argon.

*General procedure for the synthesis of 1-amino-x-(tert-butyl-oxy-carbonyl)amino-alkanes (GP1)*

To a suspension of the corresponding alkyl-1,x-diamine in dry dioxane (200 ml) at 0 °C within 5 h a solution of di-*tert*-butyl-dicarbonate (18.1 g, 83 mmol) in dry dioxane (200 ml) was slowly added. After stirring for an additional 6 h, the solvent was removed under reduced pressure and the residue extracted with ether (3 × 150 ml); the ether phase was discarded. To the combined extracts water (200 ml) was added, the pH-value of the aqueous phase adjusted to 3–4, the aq. layer was quickly separated and an aq. solution of Na<sub>2</sub>CO<sub>3</sub> (saturated, 100 ml) was added. The aq. phase was extracted with chloroform (3 × 150 ml), the combined extracts were dried (Na<sub>2</sub>SO<sub>4</sub>), and the solvent was removed under reduced pressure to afford the crude products that were used for the next steps without any further purification. Analytically pure samples, however, were obtained after chromatography (RP-18, methanol/water 9:1). Compounds **12–21**, **22–31** and **32–41** are members of homologous series and thus similar in their spectra; therefore, only representative values are given.

*tert-Butyl N-(2-aminoethyl)carbamate (2)*

Following GP1 from 1,2-diaminoethane (10.0 g, 0.17 mol) **2** (6.3 g, 47.4%) was obtained as a viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.90 (br s, 1 H, NH), 3.15–3.11 (m, 2 H, CH<sub>2</sub>(2)), 2.77–2.74 (m, 2 H, CH<sub>2</sub>(1)), 1.41 (s, 9 H, *t*Bu). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 156.1 (CO), 79.1 (*t*Bu), 41.9 (CH<sub>2</sub>), 40.8 (CH<sub>2</sub>), 28.4 (*t*Bu). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 105 (7%) [(M-*i*butene)H]<sup>+</sup>, 161 (100%) [MH]<sup>+</sup>. – Analysis for C<sub>7</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub> (160.21): C 52.48, H 10.07, N 17.48; found C 52.37, H 10.23, N 17.58.

*tert-Butyl N-(3-aminopropyl)carbamate (3)*

Following GP1 from 1,3-diaminopropane (14.0 g, 0.19 mol) **3** (8.5 g, 52%) was obtained as a slightly yellowish viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.97 (br s, 1 H, NH), 3.17–3.12 (m, 2 H, CH<sub>2</sub>(3)), 2.71–2.68 (m, 2 H, CH<sub>2</sub>(1)), 1.58–1.51 (m, 2 H, CH<sub>2</sub>(2)), 1.38 (s, 9 H, *t*Bu). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 156.0 (CO), 79.0 (*t*Bu), 39.8 (CH<sub>2</sub>), 38.5 (CH<sub>2</sub>), 33.6 (CH<sub>2</sub>), 28.5 (*t*Bu). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 119 (8%) [(M-*i*butene)H]<sup>+</sup>, 175 (100%) [MH]<sup>+</sup>. – Analysis for C<sub>8</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub> (174.24): C 55.15, H 10.41, N 16.08; found C 55.01, H 10.27, N 15.88.

*tert-Butyl N-(4-aminobutyl)carbamate (4)*

Following GP1 from 1,4-diaminobutane (10.0 g, 113.0 mmol) **4** (4.2 g, 39%) was obtained as a viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.68 (br s, 1 H, NH), 3.08–3.06 (m, 2 H, CH<sub>2</sub>(4)), 2.68–2.65 (m, 2 H, CH<sub>2</sub>(1)), 1.50–1.42 (m, 4 H, 2 × CH<sub>2</sub>(2,3)), 1.39 (s, 9 H, *t*Bu). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 155.8 (CO), 78.9 (*t*Bu), 41.8 (CH<sub>2</sub>), 40.5 (CH<sub>2</sub>), 30.9 (CH<sub>2</sub>), 28.5 (*t*Bu), 27.6 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 133 (8%) [(M-*i*butene)H]<sup>+</sup>, 189 (100%) [MH]<sup>+</sup>. – Analysis for C<sub>9</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub> (188.27): C 57.42, H 10.71, N 14.88; found C 57.29, H 10.94, N 14.74.

*tert-Butyl N-(5-aminopentyl)carbamate (5)*

Following GP1 from 1,5-diaminopentane (15.3 g, 0.15 mol) **5** (6.0 g, 39.5%) was obtained as a slightly yellowish viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.53 (br s, 1 H, NH), 3.09–3.06 (m, 2 H, CH<sub>2</sub>(5)), 2.67–2.64 (m, 2 H, CH<sub>2</sub>(1)), 1.50–1.42 (m, 4 H, 2 × CH<sub>2</sub>(2,4)), 1.41 (s, 9 H, *t*Bu), 1.39–1.31 (m, 2 H, CH<sub>2</sub>(3)). – <sup>13</sup>C NMR (50.3 MHz, CDCl<sub>3</sub>): δ = 156.0 (CO), 79.1 (*t*Bu), 42.1 (CH<sub>2</sub>), 40.5 (CH<sub>2</sub>), 30.4 (CH<sub>2</sub>), 29.9 (CH<sub>2</sub>), 28.4 (*t*Bu), 24.1 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 203 (100%) [MH]<sup>+</sup>. – Analysis for C<sub>10</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub> (202.29): C 59.37, H 10.96, N 13.85; found C 59.22, H 10.64, N 13.97.

*tert-Butyl N-(6-aminohexyl)carbamate (6)*

Following GP1 from 1,6-diamino-hexane (19.0 g, 163 mmol) **6** (7.3 g, 40%) was obtained as a viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.62 (br s, 1 H, NH), 3.05–3.00 (m, 2 H, CH<sub>2</sub>(6)), 2.61–2.58 (m, 2 H, CH<sub>2</sub>(1)), 1.42–1.38 (m, 4 H, 2 × CH<sub>2</sub>(2,5)), 1.36 (s, 9 H, *t*Bu), 1.26–1.23 (m, 4 H, 2 × CH<sub>2</sub>(3,4)). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 155.8 (CO), 78.8 (*t*Bu), 42.1 (CH<sub>2</sub>), 40.5 (CH<sub>2</sub>), 33.7 (CH<sub>2</sub>), 30.0 (CH<sub>2</sub>), 28.4 (*t*Bu), 26.6 (CH<sub>2</sub>), 26.5 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 161 (8%) [(M-*i*butene)H]<sup>+</sup>, 217 (100%) [MH]<sup>+</sup>. – Analysis for C<sub>11</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub> (216.32): C 51.07, H 11.18, N 12.85; found C 50.85, H 11.46, N 12.67.

*tert-Butyl N-(7-aminoheptyl)carbamate (7)*

Following GP1 from 1,7-diamino-heptane (15.0 g, 115 mmol) **7** (5.9 g, 44%) was obtained as a viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.49 (br s, 1 H, NH), 3.10–3.05 (m, 2 H, CH<sub>2</sub>(7)), 2.67–2.63 (m, 2 H, CH<sub>2</sub>(1)), 1.46–1.42 (m, 4 H, 2 × CH<sub>2</sub>(2,6)), 1.42 (s, 9 H, *t*Bu), 1.33–1.27 (m, 6 H, 3 × CH<sub>2</sub>(3,4,5)). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 155.9 (CO), 78.9 (*t*Bu), 42.2 (CH<sub>2</sub>), 40.6 (CH<sub>2</sub>), 33.8 (CH<sub>2</sub>), 30.0 (CH<sub>2</sub>), 28.4 (*t*Bu), 29.1 (CH<sub>2</sub>), 26.8 (CH<sub>2</sub>), 26.8 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 131 (2%) [(M-Boc)H]<sup>+</sup>,

175 (11%) [(M-*i*-butene)H]<sup>+</sup>, 231 (100%) [MH]<sup>+</sup>. – Analysis for C<sub>12</sub>H<sub>26</sub>N<sub>2</sub>O<sub>2</sub> (230.35): C 62.57, H 11.38, N 12.16; found C 62.37, H 11.49, N 12.12.

*tert*-Butyl *N*-(8-aminooctyl)carbamate (**8**)

Following GP1 from 1,8-diaminooctane (15.7 g, 109 mmol) **8** (5.5 g, 41.3%) was obtained as a viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.53 (br s, 1 H, NH), 3.09–3.04 (m, 2 H, CH<sub>2</sub>(8)), 2.65–2.62 (m, 2 H, CH<sub>2</sub>(1)), 1.40–1.35 (m, 4 H, 2 × CH<sub>2</sub>(2,7)), 1.40 (s, 9 H, *t*Bu), 1.26 (br s, 8H, 4 × CH<sub>2</sub>(3–6)). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 155.9 (CO), 78.9 (*t*Bu), 42.3 (CH<sub>2</sub>), 40.7 (CH<sub>2</sub>), 33.9 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 29.5 (CH<sub>2</sub>), 29.3 (CH<sub>2</sub>), 28.5 (*t*Bu), 26.9 (CH<sub>2</sub>), 26.8 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 145 (4%) [(M-Boc)H]<sup>+</sup>, 189 (27%) [(M-*i*-butene)H]<sup>+</sup>, 245 (100%) [MH]<sup>+</sup>. – Analysis for C<sub>13</sub>H<sub>28</sub>N<sub>2</sub>O<sub>2</sub> (244.37): C 63.89, H 11.55, N 11.46; found C 63.81, H 11.80, N 11.26.

*tert*-Butyl *N*-(9-aminononyl)carbamate (**9**)

Following GP1 from 1,9-diaminononane (15.0 g, 95 mmol) **9** (4.7 g, 38%) was obtained as an amorphous white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.52 (br s, 1 H, NH), 3.07–3.05 (m, 2 H, CH<sub>2</sub>(9)), 2.79–2.77 (m, 2 H, CH<sub>2</sub>(1)), 1.59–1.52 (m, 2 H, CH<sub>2</sub>(2)), 1.42–1.40 (m, 2 H, CH<sub>2</sub>(8)), 1.41 (s, 9 H, *t*Bu), 1.35–1.26 (br s, 10 H, 5 × CH<sub>2</sub>(3–7)). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 155.9 (CO), 80.0 (*t*Bu), 41.9 (CH<sub>2</sub>), 40.7 (CH<sub>2</sub>), 32.9 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.4 (CH<sub>2</sub>), 29.3 (CH<sub>2</sub>), 28.6 (*t*Bu), 26.9 (CH<sub>2</sub>), 26.8 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 159 (3%) [(M-Boc)H]<sup>+</sup>, 203 (11%) [(M-*i*-butene)H]<sup>+</sup>, 259 (100%) [MH]<sup>+</sup>. – Analysis for C<sub>14</sub>H<sub>30</sub>N<sub>2</sub>O<sub>2</sub> (258.40): C 65.07, H 11.70, N 10.84; found C 64.86, H 11.81, N 10.63.

*tert*-Butyl *N*-(10-aminodecyl)carbamate (**10**)

To a solution of 1,10-diaminodecane (15.0 g, 87 mmol) in dry dioxane (200 ml) at 0 °C a solution of di-*tert*-butyl-dicarbonate (9.5 g, 44 mmol) in dry dioxane (200 ml) was added during 5 h. Then the solvent was removed under reduced pressure and the residue was extracted with ether (3 × 150 ml). The ether was removed and **10** (6.7 g, 57%) was obtained as white amorphous solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.50 (br s, 1 H, NH), 3.09–3.04 (m, 2 H, CH<sub>2</sub>(10)), 2.66–2.63 (m, 2 H, CH<sub>2</sub>(1)), 1.41 (s, 9 H, *t*Bu), 1.40–1.36 (m, 4 H, 2 × CH<sub>2</sub>(2,9)), 1.26 (br s, 12 H, 6 × CH<sub>2</sub>(3–8)). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 155.8 (CO), 78.9 (*t*Bu), 42.3 (CH<sub>2</sub>), 40.6 (CH<sub>2</sub>), 33.9 (CH<sub>2</sub>), 30.1 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.5 (CH<sub>2</sub>), 29.5 (CH<sub>2</sub>), 29.3 (CH<sub>2</sub>), 28.5 (*t*Bu), 26.9 (CH<sub>2</sub>), 26.8 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 173 (5%) [(M-Boc)H]<sup>+</sup>, 217 (16%) [(M-*i*-butene)H]<sup>+</sup>, 273 (100%) [MH]<sup>+</sup>. – Analysis for

C<sub>15</sub>H<sub>32</sub>N<sub>2</sub>O<sub>2</sub> (272.43): C 66.13, H 11.84, N 10.28; found C 66.00, H 11.98, N 9.99.

*tert*-Butyl *N*-(12-aminododecyl)-carbamate (**11**)

Following the procedure given for the synthesis of **10** from 1,12-diamino-dodecane (17.0 g, 85 mmol) and di-*tert*-butyl-dicarbonate (9.3 g, 42.5 mmol) **11** (6.6 g, 52%) was obtained as a white amorphous solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.49 (br s, 1 H, NH), 3.08–3.06 (m, 2 H, CH<sub>2</sub>(12)), 2.67–2.63 (m, 2 H, CH<sub>2</sub>(1)), 1.42–1.37 (m, 4 H, 2 × CH<sub>2</sub>(2.11)), 1.41 (s, 9 H, *t*Bu), 1.29–1.24 (m, 16 H, 8 × CH<sub>2</sub>(3–10)). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 155.9 (CO), 78.9 (*t*Bu), 42.3 (CH<sub>2</sub>), 40.6 (CH<sub>2</sub>), 33.9 (CH<sub>2</sub>), 30.1 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.5 (CH<sub>2</sub>), 29.5 (CH<sub>2</sub>), 29.3 (CH<sub>2</sub>), 28.5 (*t*Bu), 26.9 (CH<sub>2</sub>), 26.8 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): *m/z* = 201 (19%) [(M-Boc)H]<sup>+</sup>, 245 (30%) [(M-*i*-butene)H]<sup>+</sup>, 301 (100%) [MH]<sup>+</sup>. – Analysis for C<sub>17</sub>H<sub>36</sub>N<sub>2</sub>O<sub>2</sub> (300.49): C 67.95, H 12.08, N 9.32; found C 67.68, H 12.32, N 9.31.

*tert*-Butyl *N*-{2-[9-(6-chloro-2-methoxyacridinyl)amino]-ethyl}-carbamate (**12**)

A mixture of 6,9-dichloro-2-methoxyacridine (**1**) (4.00 g, 14.4 mmol) and phenol (9 g, 95.6 mmol) was stirred at 90 °C for 30 min, then **2** (2.65 g, 16.6 mmol) was added and stirring continued for another 15 min. Chromatographic work up (silica gel, methanol/ethyl acetate 1:6) yielded **12** (1.11 g, 19%) as an amorphous orange-coloured solid. UV-vis (methanol): λ<sub>max</sub> (log ε) = 295 nm (4.67). – IR (KBr): ν = 3441s, 2978m, 1678s, 1630s, 1589s, 1367m, 1271s, 1248s, 1171s, 1090m, 1032m cm<sup>-1</sup>. – <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 8.06 (d, <sup>3</sup>J<sub>H,H</sub> = 9.44 Hz, 1 H, 8-H), 7.81 (d, <sup>4</sup>J<sub>H,H</sub> = 2.08 Hz, 1 H, 5-H), 7.77 (d, <sup>3</sup>J<sub>H,H</sub> = 9.23 Hz, 1 H, 4-H), 7.43 (d, <sup>4</sup>J<sub>H,H</sub> = 2.49 Hz, 1 H, 1-H), 7.18 (dd, <sup>3</sup>J<sub>H,H</sub> = 9.23 Hz, <sup>4</sup>J<sub>H,H</sub> = 2.49 Hz, 1 H, 3-H), 7.04 (dd, <sup>3</sup>J<sub>H,H</sub> = 9.44 Hz, <sup>4</sup>J<sub>H,H</sub> = 2.08 Hz, 1 H, 7-H), 6.13 (br s, 1 H, NH), 4.04–3.99 (m, 2 H, CH<sub>2</sub>(1')), 3.93 (s, 3 H, OCH<sub>3</sub>), 3.68–3.61 (m, 2 H, CH<sub>2</sub>(2')), 1.45 (s, 9 H, *t*Bu). – <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 157.7 (C=O), 155.9 (quart.), 153.3 (quart.), 142.5 (quart.), 138.3 (quart.), 138.1 (quart.), 126.3 (CH), 126.0 (CH), 124.0 (CH), 123.4 (CH), 121.2 (CH), 114.9 (quart.), 111.3 (quart.), 101.4 (CH), 80.1 (*t*Bu), 55.8 (OCH<sub>3</sub>), 51.2 (CH<sub>2</sub>(1')), 41.0 (CH<sub>2</sub>(2')), 28.4 (*t*Bu). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): 346 (16%) [(M-*i*-butene)H]<sup>+</sup>, 402 (100%) [M(<sup>35</sup>Cl)H]<sup>+</sup>, 404 (27%) [M(<sup>37</sup>Cl)H]<sup>+</sup>. – Analysis for C<sub>21</sub>H<sub>24</sub>ClN<sub>2</sub>O<sub>2</sub> (401.90): C 62.76, H 6.02, N 10.46; found C 62.35, H 6.17, N 10.22.

*tert*-Butyl *N*-{3-[9-(6-chloro-2-methoxyacridinyl)amino]-propyl}-carbamate (**13**)

Following the procedure given for **12** from **1** (3.0 g, 10.8 mmol), phenol (9.0 g, 95.6 mmol) and **3** (2.3 g,

13.2 mmol) **13** (3.59 g, 80%) was obtained as a yellow amorphous solid. UV-vis (methanol):  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 282 nm (4.72). – MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 360 (13%) [(M-*i*butene)H] $^+$ , 416 (100%) [M( $^{35}\text{Cl}$ )H] $^+$ , 418 (30%) [M( $^{37}\text{Cl}$ )H] $^+$ . – Analysis for  $\text{C}_{22}\text{H}_{26}\text{ClN}_2\text{O}_2$  (415.92): C 63.53, H 6.30, N 10.10; found C 63.26, H 6.55, N 10.3.

*tert*-Butyl *N*-{4-[9-(6-chloro-2-methoxyacridinyl)amino]-butyl}-carbamate (**14**)

Following the procedure given for **12** from **1** (3.0 g, 10.8 mmol), phenol (9.0 g, 95.6 mmol) and **4** (2.43 g, 12.9 mmol) **14** (2.53 g, 55%) was obtained as a yellow amorphous solid. MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 374 (9%) [(M-*i*butene)H] $^+$ , 430 (100%) [M( $^{35}\text{Cl}$ )H] $^+$ , 432 (32%) [M( $^{37}\text{Cl}$ )H] $^+$ . – Analysis for  $\text{C}_{23}\text{H}_{28}\text{ClN}_2\text{O}_2$  (429.95): C 64.25, H 6.56, N 9.77; found C 64.01, H 6.68, N 9.58.

*tert*-Butyl *N*-{5-[9-(6-chloro-2-methoxyacridinyl)amino]-pentyl}-carbamate (**15**)

Following the procedure given for **12** from **1** (3.2 g, 11.5 mmol), phenol (9.0 g, 95.6 mmol) and **5** (2.89 g, 14.3 mmol) **15** (4.34 g, 85%) was obtained as a yellow amorphous solid. UV-vis (methanol):  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 283 nm (4.75). – IR (KBr):  $\nu$  = 3432s, 2932s, 1689s, 1631s, 1562s, 1520s, 1466s, 1436m, 1391m, 1365m, 1238s, 1170s, 1033m. –  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.03 (d,  $^4J_{\text{H,H}}$  = 2.08 Hz, 1 H, 5-H), 8.00 (d,  $^3J_{\text{H,H}}$  = 9.34 Hz, 1 H, 8-H), 7.95 (d,  $^3J_{\text{H,H}}$  = 9.44 Hz, 1 H, 4-H), 7.36 (dd,  $^3J_{\text{H,H}}$  = 9.44 Hz,  $^4J_{\text{H,H}}$  = 2.59 Hz, 1 H, 3-H), 7.27 (dd,  $^3J_{\text{H,H}}$  = 9.34 Hz,  $^4J_{\text{H,H}}$  = 2.08 Hz, 1 H, 7-H), 7.20 (d,  $^4J_{\text{H,H}}$  = 2.59 Hz, 1 H, 1-H), 4.53 (br s, 1 H, NH), 3.94 (s, 3 H,  $\text{OCH}_3$ ), 3.71–3.65 (m, 2 H,  $\text{CH}_2(1')$ ), 3.14–3.07 (m, 2 H,  $\text{CH}_2(5')$ ), 1.81–1.73 (m, 2 H,  $\text{CH}_2(2')$ ), 1.53–1.43 (m, 4 H, 2  $\times$   $\text{CH}_2(3',4')$ ), 1.41 (s, 9 H, *t*Bu). –  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 155.91 (C=O), 155.88 (quart.), 149.8 (quart.), 147.6 (quart.), 145.9 (quart.), 134.9 (quart.), 130.7 (CH), 127.5 (CH), 124.5 (CH), 124.4 (CH), 124.1 (CH), 117.7 (quart.), 115.5 (quart.), 99.4 (CH), 79.2 (*t*Bu), 55.6 ( $\text{OCH}_3$ ), 50.5 ( $\text{CH}_2(1')$ ), 40.2 ( $\text{CH}_2(5')$ ), 31.3 ( $\text{CH}_2$ ), 30.0 ( $\text{CH}_2$ ), 28.5 (*t*Bu), 24.2 ( $\text{CH}_2$ ). – MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 388 (10%) [(M-*i*butene)H] $^+$ , 444 (100%) [M( $^{35}\text{Cl}$ )H] $^+$ , 446 (30%) [M( $^{37}\text{Cl}$ )H] $^+$ . – Analysis for  $\text{C}_{24}\text{H}_{30}\text{ClN}_2\text{O}_2$  (443.98): C 64.93, H 6.81, N 9.46; found C 64.85, H 7.02, N 9.29.

*tert*-Butyl *N*-{6-[9-(6-chloro-2-methoxyacridinyl)amino]-hexyl}-carbamate (**16**)

Following the procedure given for **12** from **1** (6.65 g, 23.9 mmol), phenol (18.0 g, 0.2 mol) and **6** (6.2 g,

28.7 mmol) **16** (5.63 g, 51%) was obtained as a yellow amorphous solid. MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 402 (7%) [(M-*i*butene)H] $^+$ , 458 (100%) [M( $^{35}\text{Cl}$ )H] $^+$ , 460 (37%) [M( $^{37}\text{Cl}$ )H] $^+$ . – Analysis for  $\text{C}_{25}\text{H}_{32}\text{ClN}_2\text{O}_2$  (458.01): C 65.56, H 7.04, N 9.18; found C 65.37, H 7.26, N 9.11.

*tert*-Butyl *N*-{7-[9-(6-chloro-2-methoxyacridinyl)amino]-heptyl}-carbamate (**17**)

Following the procedure given for **12** from **1** (3.16 g, 11.4 mmol), phenol (9.0 g, 95.6 mmol) and **7** (2.87 g, 12.5 mmol) **17** (2.98 g, 56%) was obtained as a yellow amorphous solid. MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 372 (6%) [(M-Boc)H] $^+$ , 416 (12%) [(M-*i*butene)H] $^+$ , 472 (100%) [M( $^{35}\text{Cl}$ )H] $^+$ , 474 (34%) [M( $^{37}\text{Cl}$ )H] $^+$ . – Analysis for  $\text{C}_{26}\text{H}_{34}\text{ClN}_2\text{O}_2$  (472.03): C 66.16, H 7.26, N 8.90; found C 66.01, H 7.39, N 8.78.

*tert*-Butyl *N*-{8-[9-(6-chloro-2-methoxyacridinyl)amino]-octyl}-carbamate (**18**)

Following the procedure given for **12** from **1** (4.7 g, 16.9 mmol), phenol (14.0 g, 0.15 mol) and **8** (4.6 g, 18.6 mmol) **18** (4.00 g, 49%) was obtained as a yellow amorphous solid. MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 386 (3%) [(M-Boc)H] $^+$ , 430 (7%) [(M-*i*butene)H] $^+$ , 486 (100%) [M( $^{35}\text{Cl}$ )H] $^+$ , 488 (38%) [M( $^{37}\text{Cl}$ )H] $^+$ . – Analysis for  $\text{C}_{27}\text{H}_{36}\text{ClN}_2\text{O}_2$  (486.06): C 66.72, H 7.47, N 8.65; found C 66.51, H 7.63, N 8.42.

*tert*-Butyl *N*-{9-[9-(6-chloro-2-methoxyacridinyl)amino]-nonyl}-carbamate (**19**)

Following the procedure given for **12** from **1** (2.5 g, 9.0 mmol), phenol (9.0 g, 95.6 mmol) and **9** (2.97 g, 11.5 mmol) **19** (2.16 g, 48%) was obtained as an amorphous yellow solid. MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 400 (7%) [(M-Boc)H] $^+$ , 444 (17%) [(M-*i*butene)H] $^+$ , 500 (100%) [M( $^{35}\text{Cl}$ )H] $^+$ , 502 (33%) [M( $^{37}\text{Cl}$ )H] $^+$ . – Analysis for  $\text{C}_{28}\text{H}_{38}\text{ClN}_2\text{O}_2$  (500.09): C 67.25, H 7.66, N 8.40; found C 67.02, H 7.86, N 8.25.

*tert*-Butyl *N*-{3-[10-(6-chloro-2-methoxyacridinyl)amino]-decyl}-carbamate (**20**)

Following the procedure given for **12** from **1** (2.7 g, 9.7 mmol), phenol (9.0 g, 95.6 mmol) and **10** (2.7 g, 9.9 mmol) **20** (3.04 g, 61%) was obtained as an amorphous yellow solid. MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 414 (7%) [(M-Boc)H] $^+$ , 458 (12%) [(M-*i*butene)H] $^+$ , 514 (100%) [M( $^{35}\text{Cl}$ )H] $^+$ , 516 (33%) [M( $^{37}\text{Cl}$ )H] $^+$ . – Analysis for  $\text{C}_{29}\text{H}_{40}\text{ClN}_2\text{O}_2$  (514.11): C 67.75, H 7.84, N 8.17; found C 67.51, H 7.99, N 8.12.

*tert*-Butyl *N*-{12-[9-(6-chloro-2-methoxyacridinyl)amino]-dodecyl}-carbamate (**21**)

Following the procedure given for **12** from **1** (5.56 g, 20.0 mmol), phenol (18.0 g, 0.2 mol) and **11** (7.2 g, 24.0 mmol) **21** (2.80 g, 26%) was obtained as a yellow amorphous solid. UV-vis (methanol):  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 283 nm (4.58). IR (KBr):  $\nu$  = 3367m, 2926s, 2853s, 2711m, 1688s, 1631s, 1562s, 1520s, 1467s, 1436s, 1392m, 1364s, 1273s, 1244s, 1171s, 1074m, 1032m  $\text{cm}^{-1}$ . –  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.98 (d,  $^4J_{\text{H,H}}$  = 2.08 Hz, 1 H, 5-H), 7.98 (d,  $^3J_{\text{H,H}}$  = 9.13 Hz, 1 H, 4-H), 7.87 (d,  $^3J_{\text{H,H}}$  = 9.34 Hz, 1 H, 8-H), 7.29–7.24 (m, 2 H, H-C(3,1)), 7.22 (dd,  $^3J_{\text{H,H}}$  = 9.34 Hz,  $^4J_{\text{H,H}}$  = 2.08 Hz, 1 H, 7-H), 4.49 (br s, 1 H, NH), 3.94 (s, 3 H,  $\text{OCH}_3$ ), 3.78–3.73 (m, 2 H,  $\text{CH}_2(1')$ ), 3.10–3.04 (m, 2 H,  $\text{CH}_2(12')$ ), 1.85–1.76 (m, 2 H,  $\text{CH}_2(2')$ ), 1.47–1.39 (m, 13 H, *t*Bu,  $2 \times \text{CH}_2(3',11')$ ), 1.35–1.19 (m, 14 H,  $5 \times \text{CH}_2(4'-10')$ ). –  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 155.8 (C=O), 155.7 (quart.), 150.9 (quart.), 140.1 (quart.), 136.0 (quart.), 124.8 (CH), 124.7 (CH), 124.1 (CH), 101.0 (CH), 79.0 (*t*Bu), 55.7 ( $\text{OCH}_3$ ), 50.2 ( $\text{CH}_2(1')$ ), 40.7 ( $\text{CH}_2(12')$ ), 31.5 ( $\text{CH}_2$ ), 30.1 ( $\text{CH}_2$ ), 29.57 ( $2 \times \text{CH}_2$ ), 29.54 ( $\text{CH}_2$ ), 29.52 ( $\text{CH}_2$ ), 29.37 ( $\text{CH}_2$ ), 29.32 ( $\text{CH}_2$ ), 28.5 (*t*Bu), 27.0 ( $\text{CH}_2$ ), 26.9 ( $\text{CH}_2$ ). – MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 442 (7%) [(M-Boc)H] $^+$ , 487 (15%) [(M-*i*-butene)H] $^+$ , 542 (100%) [ $\text{M}^{(35)\text{Cl}}\text{H}$ ] $^+$ , 544 (34%) [ $\text{M}^{(37)\text{Cl}}\text{H}$ ] $^+$ . – Analysis for  $\text{C}_{31}\text{H}_{44}\text{ClN}_2\text{O}_2$  (542.17): C 68.68, H 8.18, N 7.75; found C 68.55, H 8.29, N 7.53.

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,2-ethane-diamine bis(hydrochloride) (**22**)

A solution of **12** (1.06 g, 2.6 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) and trifluoroacetic acid (2 ml) was stirred for 16 h at room temperature. After evaporation of the solvents **22** (0.93 g, 94%) was obtained as a yellow amorphous solid. UV-vis (methanol):  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 292 nm (4.66). – IR (KBr):  $\nu$  = 3426s, 2967s, 1629s, 1590s, 1530m, 1500m, 1470m, 1446m, 1397w, 1373w, 1275m, 1249m, 1174m, 1094m, 1028w  $\text{cm}^{-1}$ . –  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  = 8.48 (d,  $^3J_{\text{H,H}}$  = 9.34 Hz, 1 H, 8-H), 7.96 (d,  $^4J_{\text{H,H}}$  = 2.49 Hz, 1 H, 1-H), 7.86 (d,  $^4J_{\text{H,H}}$  = 2.08 Hz, 1 H, 5-H), 7.79 (d,  $^3J_{\text{H,H}}$  = 9.34 Hz, 1 H, 4-H), 7.66 (dd,  $^3J_{\text{H,H}}$  = 9.34 Hz,  $^4J_{\text{H,H}}$  = 2.49 Hz, 1 H, 3-H), 7.53 (dd,  $^3J_{\text{H,H}}$  = 9.34 Hz,  $^4J_{\text{H,H}}$  = 2.08 Hz, 1 H, 7-H), 4.54–4.50 (m, 2 H,  $\text{CH}_2(1')$ ), 4.05 (s, 3 H,  $\text{OCH}_3$ ), 3.64–3.59 (m, 2 H,  $\text{CH}_2(2')$ ). –  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  = 157.6 (quart.), 157.5 (quart.), 141.9 (quart.), 140.7 (quart.), 135.4 (quart.), 128.8 (CH), 128.3 (CH), 125.6 (CH), 121.3 (CH), 118.4 (CH), 115.2 (quart.), 110.8 (quart.), 103.6 (CH), 57.2 ( $\text{OCH}_3$ ), 46.9 ( $\text{CH}_2(1')$ ), 39.7 ( $\text{CH}_2(2')$ ). – MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 302 (100%) [ $\text{M}^{(35)\text{Cl}}\text{H}$ ] $^+$ , 304 (30%) [ $\text{M}^{(37)\text{Cl}}\text{H}$ ] $^+$ .

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,3-propane-diamine bis(hydrochloride) (**23**)

A solution of **13** (3.39 g, 8.1 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) was stirred at room temperature for 16 h. After evaporation of the solvents **23** (3.07 g, 97%) was obtained as a yellow amorphous solid. MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 316 (100%) [ $\text{M}^{(35)\text{Cl}}\text{H}$ ] $^+$ , 318 (30%) [ $\text{M}^{(37)\text{Cl}}\text{H}$ ] $^+$ .

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,4-butane-diamine bis(hydrochloride) (**24**)

A solution of **14** (2.43 g, 5.7 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) was stirred at room temperature for 16 h. After evaporation of the solvents **24** (2.18 g, 96%) was obtained as a yellow amorphous solid. MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 330 (100%) [ $\text{M}^{(35)\text{Cl}}\text{H}$ ] $^+$ , 332 (32%) [ $\text{M}^{(37)\text{Cl}}\text{H}$ ] $^+$ .

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,5-pentane-diamine bis(hydrochloride) (**25**)

A solution of **15** (4.19 g, 9.4 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) was stirred at room temperature for 16 h. After evaporation of the solvents **25** (3.65 g, 93%) was obtained as a yellow amorphous solid. UV-vis (methanol):  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 294 nm (4.36). – IR (KBr):  $\nu$  = 3417s, 2965s, 2004w, 1627s, 1590s, 1567s, 1524m, 1497s, 1483s, 1420m, 1396m, 1358m, 1318m, 1292m, 1267m, 1245s, 1170m, 1120m, 1094m, 1029m  $\text{cm}^{-1}$ . –  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  = 7.67 (d,  $^3J_{\text{H,H}}$  = 9.34 Hz, 1 H, 8-H), 7.21 (dd,  $^3J_{\text{H,H}}$  = 9.34 Hz,  $^4J_{\text{H,H}}$  = 2.49 Hz, 1 H, 3-H), 7.10–7.02 (m, 3 H, H-C(1,4,7)), 6.90 (d,  $^4J_{\text{H,H}}$  = 2.08 Hz, 1 H, 5-H), 3.69 (s, 3 H,  $\text{OCH}_3$ ), 3.66–3.60 (m, 2 H,  $\text{CH}_2(1')$ ), 2.89–2.83 (m, 2 H,  $\text{CH}_2(5')$ ), 1.73–1.65 (m, 2 H,  $\text{CH}_2(2')$ ), 1.62–1.54 (m, 2 H,  $\text{CH}_2(4')$ ), 1.36–1.28 (m, 2 H,  $\text{CH}_2(3')$ ). –  $^{13}\text{C}$  NMR (100 MHz,  $\text{D}_2\text{O}$ ):  $\delta$  = 155.5 (quart.), 154.3 (quart.), 140.4 (quart.), 138.2 (quart.), 133.1 (quart.), 126.8 (CH), 124.3 (CH), 119.7 (CH), 116.7 (CH), 112.3 (quart.), 108.6 (quart.), 56.2 ( $\text{OCH}_3$ ), 48.5 ( $\text{CH}_2(1')$ ), 39.5 ( $\text{CH}_2(5')$ ), 29.1 ( $\text{CH}_2$ ), 26.7 ( $\text{CH}_2$ ), 23.3 ( $\text{CH}_2$ ). – MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 344 (100%) [ $\text{M}^{(35)\text{Cl}}\text{H}$ ] $^+$ , 346 (30%) [ $\text{M}^{(37)\text{Cl}}\text{H}$ ] $^+$ .

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,6-hexane-diamine bis(hydrochloride) (**26**)

A solution of **16** (6.50 g, 14.2 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) and trifluoroacetic acid (2 ml) was stirred at room temperature for 16 h. After evaporation of the solvents **26** (5.98 g, 98%) was obtained as an amorphous yellow solid. MS (ESI, 4.1 kV, 8  $\mu\text{l/min}$ ,  $\text{N}_2$ , methanol): 358 (100%) [ $\text{M}^{(35)\text{Cl}}\text{H}$ ] $^+$ , 360 (32%) [ $\text{M}^{(37)\text{Cl}}\text{H}$ ] $^+$ .

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,7-heptane-diamine bis(hydrochloride) (**27**)

A solution of **17** (3.11 g, 6.6 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) and trifluoroacetic acid (3 ml) was stirred at room temperature for 16 h. After evaporation of the solvents **27** (2.77 g, 95%) was obtained as a yellow amorphous solid. MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 372 (100%) [M(<sup>35</sup>Cl)H]<sup>+</sup>, 374 (31%) [M(<sup>37</sup>Cl)H]<sup>+</sup>.

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,8-octane-diamine bis(hydrochloride) (**28**)

A solution of **18** (3.90 g, 8.0 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) was stirred at room temperature for 16 h. After evaporation of the solvents **28** (3.52 g, 96%) was obtained as a yellow amorphous solid. MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 194 (30%) [M(<sup>35</sup>Cl)H<sub>2</sub>]<sup>2+</sup>, 195 (11%) [M(<sup>37</sup>Cl)H<sub>2</sub>]<sup>2+</sup>, 386 (100%) [M(<sup>35</sup>Cl)H]<sup>+</sup>, 388 (34%) [M(<sup>37</sup>Cl)H]<sup>+</sup>.

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,9-nonane-diamine bis(hydrochloride) (**29**)

A solution of **19** (1.91 g, 3.8 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) was stirred at room temperature for 16 h. After evaporation of the solvents **29** (1.71 g, 95%) was obtained as an amorphous yellow solid. MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 201 (38%) [M(<sup>35</sup>Cl)H<sub>2</sub>]<sup>2+</sup>, 202 (13%) [M(<sup>37</sup>Cl)H<sub>2</sub>]<sup>2+</sup>, 400 (100%) [M(<sup>35</sup>Cl)H]<sup>+</sup>, 402 (32%) [M(<sup>37</sup>Cl)H]<sup>+</sup>.

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,10-decane-diamine bis(hydrochloride) (**30**)

A solution of **20** (2.89 g, 5.6 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) and trifluoroacetic acid (2 ml) was stirred at room temperature for 16 h. After evaporation of the solvents **30** (2.68 g, 98%) was obtained as a yellow amorphous solid. MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 208 (73%) [M(<sup>35</sup>Cl)H<sub>2</sub>]<sup>2+</sup>, 209 (23%) [M(<sup>37</sup>Cl)H<sub>2</sub>]<sup>2+</sup>, 414 (100%) [M(<sup>35</sup>Cl)H]<sup>+</sup>, 416 (32%) [M(<sup>37</sup>Cl)H]<sup>+</sup>.

*N*<sup>1</sup>-[9-(6-Chloro-2-methoxyacridinyl)]-1,12-dodecane-diamine bis(hydrochloride) (**31**)

A solution of **21** (2.75 g, 5.1 mmol) in methanol (100 ml) containing aq. hydrochloric acid (10%, 10 ml) was stirred at room temperature for 16 h. After evaporation of the solvents **31** (2.53 g, 97%) was obtained as an amorphous yellow solid. UV-vis (methanol):  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 283 nm (4.58). – IR (KBr):  $\nu$  = 3367m, 2926s, 2853s, 2711m, 1688s, 1631s, 1562s, 1520s, 1467s, 1436s, 1392m, 1364s,

1273s, 1244s, 1171s, 1074m, 1032m. – <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  = 8.46 (d, <sup>3</sup>*J*<sub>H,H</sub> = 9.28 Hz, 1 H, 8-H), 7.83 (d, <sup>4</sup>*J*<sub>H,H</sub> = 2.44 Hz, 1 H, 1-H), 7.80 (d, <sup>4</sup>*J*<sub>H,H</sub> = 1.95 Hz, 1 H, 5-H), 7.76 (d, <sup>3</sup>*J*<sub>H,H</sub> = 9.28 Hz, 1 H, 4-H), 7.67 (dd, <sup>3</sup>*J*<sub>H,H</sub> = 9.28 Hz, <sup>4</sup>*J*<sub>H,H</sub> = 2.44 Hz, 1 H, 3-H), 7.50 (dd, <sup>3</sup>*J*<sub>H,H</sub> = 9.28 Hz, <sup>4</sup>*J*<sub>H,H</sub> = 1.95 Hz, 1 H, 7-H), 4.16–4.11 (m, 2 H, CH<sub>2</sub>(1')), 4.00 (s, 3 H, OCH<sub>3</sub>), 2.93–2.87 (m, 2 H, CH<sub>2</sub>(12')), 2.02–1.93 (m, 2 H, CH<sub>2</sub>(2')), 1.68–1.59 (m, 2 H, CH<sub>2</sub>(11')), 1.51–1.27 (m, 16H, 8  $\times$  CH<sub>2</sub>(3'–10')). – <sup>13</sup>C NMR (125 MHz, CD<sub>3</sub>OD):  $\delta$  = 158.2 (quart.), 158.0 (quart.), 155.7 (quart.), 141.8 (quart.), 141.5 (quart.), 135.8 (quart.), 129.2 (CH), 128.7 (CH), 125.0 (CH), 121.4 (CH), 118.4 (CH), 115.5 (quart.), 111.3 (quart.), 104.1, 79.0 (*t*Bu), 55.7 (OCH<sub>3</sub>), 50.2 (CH<sub>2</sub>(1')), 40.7 (CH<sub>2</sub>(12')), 31.5 (CH<sub>2</sub>), 30.1 (CH<sub>2</sub>), 29.57 (CH<sub>2</sub>), 29.54 (CH<sub>2</sub>), 29.52 (CH<sub>2</sub>), 29.37 (CH<sub>2</sub>), 29.32 (CH<sub>2</sub>), 28.5 (*t*Bu), 27.0 (CH<sub>2</sub>), 26.9 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 442 (7%) [(M-Boc)H]<sup>+</sup>, 487 (15%) [(M-*i*butene)H]<sup>+</sup>, 542 (100%) [M(<sup>35</sup>Cl)H]<sup>+</sup>, 544 (34%) [M(<sup>37</sup>Cl)H]<sup>+</sup>.

*2-((2-{[2-(9-{[6-Chloro-2-methoxyacridinyl]amino}ethyl)-amino]-2-oxoethyl}){2-[(2-{[2-(9-{[6-chloro-2-methoxyacridinyl]amino}ethyl)amino]-2-oxoethyl})(carboxymethyl)amino]ethyl}amino)acetic acid* (**32**)

A solution of **22** (500 mg, 1.34 mmol) in dry DMF (50 ml) containing triethylamine (3 ml) is stirred for 30 min at room temperature and EDTA dianhydride (154 mg, 0.60 mmol) is added and stirring is continued for another 15 h. After addition of acetone (10 ml) the precipitate is filtered off, washed with methanol (50 ml) and dried in vacuum to afford **32** (140 mg, 27%) as an orange amorphous solid. UV-vis (methanol):  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 296 nm (4.86). – IR (KBr):  $\nu$  = 3423s, 2936m, 1630s, 1588s, 1500m, 1475m, 1396m, 1249m, 1172m, 1090m, 1030w cm<sup>−1</sup>. – <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  = 8.44 (d, <sup>3</sup>*J*<sub>H,H</sub> = 9.34 Hz, 2 H, 2  $\times$  8-H), 7.69 (s, 2 H, 2  $\times$  1-H), 7.62 (d, <sup>3</sup>*J*<sub>H,H</sub> = 9.34 Hz, 2 H, 2  $\times$  4-H), 7.61 (s, 2 H, 2  $\times$  5-H), 7.54 (d, <sup>3</sup>*J*<sub>H,H</sub> = 9.34 Hz, 2 H, 2  $\times$  3-H), 7.38 (d, <sup>3</sup>*J*<sub>H,H</sub> = 9.34 Hz, 2 H, 2  $\times$  7-H), 4.27–4.23 (m, 4 H, 2  $\times$  CH<sub>2</sub>(1')), 3.98 (s, 6 H, 2  $\times$  OCH<sub>3</sub>), 3.78–3.74 (m, 4 H, 2  $\times$  CH<sub>2</sub>(2')), 3.67 (s, 4 H, 2  $\times$  CH<sub>2</sub>(2'')), 3.56 (s, 4 H, 2  $\times$  CH<sub>2</sub>(3'')), 3.09 (s, 4 H, 2  $\times$  CH<sub>2</sub>(1'')). – <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD):  $\delta$  = 173.3 (C=O), 173.1 (C=O), 158.1 (quart.), 141.8 (quart.), 128.6 (CH), 125.4 (CH), 121.3 (CH), 118.4 (CH), 111.3 (quart.), 58.3 (CH<sub>2</sub>(3'')), 57.4 (CH<sub>2</sub>(2'')), 57.0 (OCH<sub>3</sub>), 53.7 (CH<sub>2</sub>(1'')), 48.0 (CH<sub>2</sub>(1')), 40.7 (CH<sub>2</sub>(2')). – MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 431 (42%) [MH<sub>2</sub>]<sup>2+</sup>, 859 (79%) [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 861 (100%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 863 (23%) [M(<sup>37</sup>Cl)(<sup>37</sup>Cl)H]<sup>+</sup>. – Analysis for C<sub>42</sub>H<sub>44</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (859.75): C 58.68, H 5.16, N 8.25; found C 58.42, H 5.23, N 8.11.

2-((2-([3-(9-{6-Chloro-2-methoxyacridinyl}amino)propyl]-amino)-2-oxoethyl){2-([3-(9-{6-chloro-2-methoxyacridinyl}amino) propyl]amino)-2-oxoethyl}(carboxymethyl)amino)ethyl}amino) acetic acid (**33**)

Following the procedure for **32** from **23** (0.8 g, 2.06 mmol) and EDTA dianhydride (237 mg, 0.93 mmol) in dry DMF (35 ml) and triethylamine (3 ml) **33** (425 mg, 52%) was obtained as an amorphous orange solid. MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 445 (92%) [MH<sub>2</sub>]<sup>2+</sup>, 464 (71%) [MHK]<sup>2+</sup>, 471 (38%) [MNaK]<sup>2+</sup>, 887 (85%) [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 889 (100%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 891 (22%) [M(<sup>37</sup>Cl)(<sup>37</sup>Cl)H]<sup>+</sup>, 909 (10%) [MNa]<sup>+</sup>, 925 (20%) [MK]<sup>+</sup>. – Analysis for C<sub>44</sub>H<sub>48</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (887.83): C 59.53, H 5.45, N 7.99; found C 59.29, H 5.62, N 7.84.

2-((2-([4-(9-{6-Chloro-2-methoxyacridinyl}amino)butyl]-amino)-2-oxoethyl){2-([4-(9-{6-chloro-2-methoxyacridinyl}amino) butyl]amino)-2-oxoethyl}(carboxymethyl)amino)ethyl}amino) acetic acid (**34**)

Following the procedure for **32** from **24** (1.0 g, 2.5 mmol) and EDTA dianhydride (287 mg, 1.12 mmol) in dry DMF (60 ml) and triethylamine (5 ml) **34** (412 mg, 40%) was obtained as an orange amorphous solid. MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 459 (22%) [MH<sub>2</sub>]<sup>2+</sup>, 478 (78%) [MHK]<sup>2+</sup>, 486 (40%) [MNaK]<sup>2+</sup>, 915 (82%) [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 917 (100%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 919 (20%) [M(<sup>37</sup>Cl)(<sup>37</sup>Cl)H]<sup>+</sup>, 937 (10%) [MNa]<sup>+</sup>, 953 (30%) [MK]<sup>+</sup>. – Analysis for C<sub>46</sub>H<sub>52</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (915.88): C 60.33, H 5.72, N 12.23; found C 60.14, H 5.84, N 12.00.

2-((2-([5-(9-{6-Chloro-2-methoxyacridinyl}amino)pentyl]-amino)-2-oxoethyl){2-([5-(9-{6-chloro-2-methoxyacridinyl}amino) pentyl]amino)-2-oxoethyl}(carboxymethyl)amino)ethyl}amino) acetic acid (**35**)

Following the procedure for **32** from **25** (0.5 g, 1.2 mmol) and EDTA dianhydride (139 mg, 0.54 mmol) in dry DMF (50 ml) and triethylamine (5 ml) **35** (280 mg, 55%) was obtained as an amorphous orange solid. UV-vis (methanol):  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 298 nm (4.94). – IR (KBr):  $\nu$  = 3387s, 2934s, 1724w, 1631s, 1590s, 1501s, 1470m, 1396m, 1358m, 1273m, 1245s, 1170m, 1092m, 1029w cm<sup>-1</sup>. – <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  = 8.40 (d, <sup>3</sup>J<sub>H,H</sub> = 9.34 Hz, 2 H, 2  $\times$  8-H), 7.78 (d, <sup>4</sup>J<sub>H,H</sub> = 2.59 Hz, 2 H, 2  $\times$  1-H), 7.73 (d, <sup>4</sup>J<sub>H,H</sub> = 2.08 Hz, 2 H, 2  $\times$  5-H), 7.70 (d, <sup>3</sup>J<sub>H,H</sub> = 9.34 Hz, 2 H, 2  $\times$  4-H), 7.60 (dd, <sup>3</sup>J<sub>H,H</sub> = 9.34 Hz, <sup>4</sup>J<sub>H,H</sub> = 2.59 Hz, 2 H, 2  $\times$  3-H), 7.45 (dd, <sup>3</sup>J<sub>H,H</sub> = 9.34 Hz, <sup>4</sup>J<sub>H,H</sub> = 2.08 Hz, 2 H, 2  $\times$  7-H), 4.12–4.07 (m, 4 H, 2  $\times$  CH<sub>2</sub>(1')), 3.98 (s, 6 H, 2  $\times$  OCH<sub>3</sub>), 3.93 (s, 4 H, 2  $\times$  CH<sub>2</sub>(2')), 3.86 (s, 4 H, 2  $\times$  CH<sub>2</sub>(3')), 3.34 (s, 4 H, 2  $\times$  CH<sub>2</sub>(1'')), 3.30–3.26 (m, 4 H, 2  $\times$  CH<sub>2</sub>(5')), 2.05–1.97 (m, 4 H, 2  $\times$  CH<sub>2</sub>(2'')), 1.67–1.63 (m, 4 H, 2  $\times$  CH<sub>2</sub>(4')), 1.56–1.49 (m, 4 H, 2  $\times$  CH<sub>2</sub>(3')). –

<sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD):  $\delta$  = 172.4 (C=O), 170.1 (C=O), 157.8 (quart.), 141.8 (quart.), 128.5 (CH), 125.0 (CH), 121.4 (CH), 118.4 (CH), 58.2 (CH<sub>2</sub>(3')), 56.84 (OCH<sub>3</sub>), 56.80 (CH<sub>2</sub>(2')), 53.2 (CH<sub>2</sub>(1'')), 50.3 (CH<sub>2</sub>(1')), 40.0 (CH<sub>2</sub>(5')), 30.4 (CH<sub>2</sub>), 29.9 (CH<sub>2</sub>), 25.1 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 473 (32%) [MH<sub>2</sub>]<sup>2+</sup>, 492 (100%) [MHK]<sup>2+</sup>, 500 (34%) [MNaK]<sup>2+</sup>, 943 (42%) [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 945 (62%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 947 (16%) [M(<sup>37</sup>Cl)(<sup>37</sup>Cl)H]<sup>+</sup>, 965 (12%) [MNa]<sup>+</sup>, 981 (30%) [MK]<sup>+</sup>. – Analysis for C<sub>48</sub>H<sub>56</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (943.94): C 61.08, H 5.98, N 11.87; found C 59.95, H 6.14, N 11.65.

2-((2-([6-(9-{6-Chloro-2-methoxyacridinyl}amino)hexyl]-amino)-2-oxoethyl){2-([6-(9-{6-chloro-2-methoxyacridinyl}amino) hexyl]amino)-2-oxoethyl}(carboxymethyl)amino)ethyl}amino) acetic acid (**36**)

Following the procedure for **32** from **26** (1.5 g, 3.5 mmol) and EDTA dianhydride (405 mg, 1.58 mmol) in DMF (30 ml) and triethylamine (5 ml) **36** (980 mg, 64%) was obtained as an orange coloured amorphous solid. MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 487 (25%) [MH<sub>2</sub>]<sup>2+</sup>, 506 (56%) [MHK]<sup>2+</sup>, 514 (31%) [MNaK]<sup>2+</sup>, 971 (100%) [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 973 (90%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 975 (20%) [M(<sup>37</sup>Cl)(<sup>37</sup>Cl)H]<sup>+</sup>, 993 (10%) [MNa]<sup>+</sup>, 1009 (30%) [MK]<sup>+</sup>. – Analysis for C<sub>50</sub>H<sub>60</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (971.99): C 61.79, H 6.22, N 11.53; found C 61.54, H 6.39, N 11.42.

2-((2-([7-(9-{6-Chloro-2-methoxyacridinyl}amino)heptyl]-amino)-2-oxoethyl){2-([7-(9-{6-chloro-2-methoxyacridinyl}amino) heptyl]amino)-2-oxoethyl}(carboxymethyl)amino)ethyl}amino) acetic acid (**37**)

Following the procedure for **32** from **27** (0.5 g, 1.13 mmol) and EDTA dianhydride (144 mg, 0.68 mmol) in DMF (10 ml) and triethylamine (3 ml) **37** (290 mg, 52%) was obtained as an amorphous orange solid. MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 501 (21%) [MH<sub>2</sub>]<sup>2+</sup>, 520 (87%) [MHK]<sup>2+</sup>, 528 (22%) [MNaK]<sup>2+</sup>, 1000 (100%) [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 1002 (83%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 1004 (22%) [M(<sup>37</sup>Cl)(<sup>37</sup>Cl)H]<sup>+</sup>, 1022 (9%) [MNa]<sup>+</sup>, 1038 (28%) [MK]<sup>+</sup>. – Analysis for C<sub>52</sub>H<sub>64</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (1000.64): C 62.46, H 6.45, N 11.21; found C 62.39, H 6.61, N 11.02.

2-((2-([8-(9-{6-Chloro-2-methoxyacridinyl}amino)octyl]-amino)-2-oxoethyl){2-([8-(9-{6-chloro-2-methoxyacridinyl}amino) octyl]amino)-2-oxoethyl}(carboxymethyl)amino)ethyl}amino) acetic acid (**38**)

Following the procedure for **32** from **28** (0.7 g, 1.53 mmol) and EDTA dianhydride (176 mg, 0.69 mmol) in DMF (35 ml) and triethylamine (3 ml) **38** (320 mg, 45%) was obtained as an amorphous orange coloured solid. MS (ESI, 4.1 kV, 8  $\mu$ l/min, N<sub>2</sub>, methanol): 515 (32%) [MH<sub>2</sub>]<sup>2+</sup>, 534 (100%) [MHK]<sup>2+</sup>, 1028 (25%) [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 1030 (9%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 1050 (7%) [MNa]<sup>+</sup>, 1066 (42%)



[MK]<sup>+</sup>. – Analysis for C<sub>54</sub>H<sub>68</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (1028.09): C 63.09, H 6.67, N 10.90; found C 62.94, H 6.81, N 10.77.

2-((2-([9-(9-{6-Chloro-2-methoxyacridinyl}amino)nonyl]amino)-2-oxoethyl){2-([9-(9-{6-chloro-2-methoxyacridinyl}amino)nonyl]amino)-2-oxoethyl}(carboxymethyl)amino)ethyl)amino) acetic acid (**39**)

Following the procedure for **32** from **29** (1.0 g, 2.1 mmol) and EDTA dianhydride (244 mg, 0.95 mmol) in DMF (50 ml) and triethylamine (5 ml) **39** (630 mg, 63%) was obtained as an amorphous orange coloured solid. MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): 534 (18%) [MHK]<sup>2+</sup>, 558 (100%) [MH<sub>2</sub><sup>+</sup>(NaCl)]<sup>2+</sup>, 1055 (15%) [MH]<sup>+</sup>, 1094 (7%) [MK]<sup>+</sup>, 1112 [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H<sup>+</sup>(NaCl)]<sup>+</sup>, 1114 [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H<sup>+</sup>(NaCl)]<sup>+</sup>, 1116 (9%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H<sup>+</sup>(NaCl)]<sup>+</sup>. – Analysis for C<sub>56</sub>H<sub>72</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (1056.15): C 63.69, H 6.87, N 10.61; found C 63.51, H 7.01, N 10.42.

2-((2-([10-(9-{6-Chloro-2-methoxyacridinyl}amino)decyl]amino)-2-oxoethyl){2-([10-(9-{6-chloro-2-methoxyacridinyl}amino)decyl]amino)-2-oxoethyl}(carboxymethyl)amino)ethyl)amino) acetic acid (**40**)

Following the procedure for **32** from **30** (1.5 g, 3.1 mmol) and EDTA dianhydride (384 mg, 1.5 mmol) in DMF (30 ml) and triethylamine (5 ml) **40** (1.20 g, 74%) was obtained as an amorphous orange coloured solid. MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): 543 (100%) [MH<sub>2</sub>]<sup>2+</sup>, 563 (33%) [MHK]<sup>2+</sup>, 570 (27%) [MNaK]<sup>2+</sup>, 1084 (50%) [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 1086 (98%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 1088 (20%) [M(<sup>37</sup>Cl)(<sup>37</sup>Cl)H]<sup>+</sup>, 1121 (10%) [MK]<sup>+</sup>. – Analysis for C<sub>58</sub>H<sub>76</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (1084.21): C 64.25, H 7.07, N 10.34; found C 64.01, H 7.23, N 10.21.

2-((2-([12-(9-{6-Chloro-2-methoxyacridinyl}amino)dodecyl]amino)-2-oxoethyl){2-([12-(9-{6-chloro-2-methoxyacridinyl}amino)dodecyl]amino)-2-oxoethyl}(carboxymethyl)amino)ethyl)amino) acetic acid (**41**)

Following the procedure for **32** from **31** (2.06 g, 4.0 mmol) and EDTA dianhydride (512 mg, 2.0 mmol)

in DMF (50 ml) and triethylamine (5 ml) **40** (1.04 g, 46%) was obtained as an amorphous orange coloured solid. UV-vis (methanol, 0.1% TFA): λ<sub>max</sub> (log ε) = 295 nm (4.92). – IR (KBr): ν = 3416s, 2926s, 2853s, 1742m, 1672m, 1628s, 1589s, 1563s, 1500m, 1467m, 1384m, 1361m, 1248s, 1171m, 1091m, 1031m cm<sup>-1</sup>. – <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ = 8.41 (d, <sup>3</sup>J<sub>H,H</sub> = 9.23 Hz, 2 H, 2 × 8-H), 7.79 (d, <sup>4</sup>J<sub>H,H</sub> = 2.59 Hz, 2 H, 2 × 1-H), 7.77 (d, <sup>4</sup>J<sub>H,H</sub> = 2.08 Hz, 2 H, 2 × 5-H), 7.74 (d, <sup>3</sup>J<sub>H,H</sub> = 9.23 Hz, 2 H, 2 × 4-H), 7.60 (dd, <sup>3</sup>J<sub>H,H</sub> = 9.23 Hz, <sup>4</sup>J<sub>H,H</sub> = 2.59 Hz, 2 H, 2 × 3-H), 7.44 (dd, <sup>3</sup>J<sub>H,H</sub> = 9.23 Hz, <sup>4</sup>J<sub>H,H</sub> = 2.08 Hz, 2 H, 2 × 7-H), 4.13–4.08 (m, 4 H, 2 × CH<sub>2</sub>(1')), 4.05 (s, 4 H, 2 × CH<sub>2</sub>(2')), 3.99 (s, 6 H, 2 × OCH<sub>3</sub>), 3.98 (s, 4 H, 2 × CH<sub>2</sub>(3')), 3.51 (s, 4 H, 2 × CH<sub>2</sub>(1'')), 3.25–3.20 (m, 4 H, 2 × CH<sub>2</sub>(12')), 2.01–1.93 (m, 4 H, 2 × CH<sub>2</sub>(2')), 1.56–1.22 (m, 36 H, 18 × CH<sub>2</sub>(3'-11')). – <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD): δ = 170.3 (C=O), 167.9 (C=O), 158.1 (quart.), 157.8 (quart.), 141.8 (quart.), 130.2 (quart.), 128.6 (CH), 125.0 (CH), 121.4 (CH), 118.5 (CH), 116.1 (CH), 111.3 (quart.), 57.6 (CH<sub>2</sub>(3')), 56.9 (OCH<sub>3</sub>), 56.0 (CH<sub>2</sub>(2')), 53.1 (CH<sub>2</sub>(1'')), 50.4 (CH<sub>2</sub>(1')), 40.8 (CH<sub>2</sub>(10')), 30.79 (CH<sub>2</sub>), 30.68 (CH<sub>2</sub>), 30.61 (CH<sub>2</sub>), 30.57 (CH<sub>2</sub>), 30.42 (CH<sub>2</sub>), 30.26 (CH<sub>2</sub>), 28.1 (CH<sub>2</sub>), 27.8 (CH<sub>2</sub>). – MS (ESI, 4.1 kV, 8 μl/min, N<sub>2</sub>, methanol): 381 (45%) [MH<sub>3</sub>]<sup>3+</sup>, 393 (24%) [MKH<sub>2</sub>]<sup>3+</sup>, 571 (100%) [MH<sub>2</sub>]<sup>2+</sup>, 590 (28%) [MHK]<sup>2+</sup>, 1140 (29%) [M(<sup>35</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 1142 (48%) [M(<sup>37</sup>Cl)(<sup>35</sup>Cl)H]<sup>+</sup>, 1144 (14%) [M(<sup>37</sup>Cl)(<sup>37</sup>Cl)H]<sup>+</sup>, 1177 (10%) [MK]<sup>+</sup>. – Analysis for C<sub>62</sub>H<sub>84</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> (1116.29): C 64.56, H 7.59, N 10.04; found C 64.37, H 7.69, N 9.86.

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