Full Paper

Synthesis of Monomeric and Dimeric Acridine Compounds as Potential Therapeutics in Alzheimer and Prion Diseases

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Starting from substituted 9-chloroacridines, a series of quinacrine and spacered dimeric acridine compounds was prepared. Their ability to interrupt the protein association of prion- and Alzheimer-specific proteins and Ab peptides was explored using a fast screening system based on FACS analysis. The bis-acridines displayed a higher activity than the corresponding monomers. Among these derivatives, best results were obtained with the 2,4-dimethoxy-6-nitro compound **7h** for Aβ-peptides and the 2-methoxy-6-nitro compound **7f** for PrP.

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Introduction

Alzheimer's disease (AD) and prion diseases like the Creutzfeld-Jakob-Disease (CJD) or Kuru in humans and bovine spongiform encephalopathy (BSE) in cattle are most prominent examples of neurodegenerative disorders. They are mainly characterized by depositions in the central nervous system. The peptides and proteins are deposited as fibrils with enriched β-sheets and have a high tendency to associate and aggregate. In AD, the fibrils contain Aβ peptides, which are peptides of 39-43 amino acids. These Aβ peptides are released from the amyloid precursor protein (APP) by the action of β- and γ-secretase. The prion protein PrP^{c} consists of 209 amino acids and is expressed mainly in neurons and follicular dendritic cells. It can be metabolized by proteinase K but undergoes a conformational transformation during the process of establishing a prion disease into the Scrapie form PrP^{sc}, which is resistant against cleavage by proteases.

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Different approaches to inhibit the deposition of amyloid proteins are in the focus of scientific research. As for AD, by inhibition of β- and γ-secretases the production of Aβ [1] is significantly lowered. However, these proteases also act on other substrates *e.g.*, NOTCH1 in the case of γ-secretase [2]. Thus, other detrimental effects are also possible by inhibiting them. In addition, the deposition of proteins can be prevented by interrupting the association process of the monomers to form oligomers and fibrils by the addition of β-sheet breakers [3]. Following this theory, quinacrine (Fig. 1, **A**) and related compounds were investigated and shown to give *in vitro* promising results against prion diseases [4–7].

Furthermore, Zahn *et al*. identified the binding side of quinacrine at the C-terminal helix of PrP [8]. Consequently, dimeric acridine compounds (Fig. 1, **B**) were synthesized and they exhibited a ten-fold higher activity than the respective monomeric quinacrines [9]. The best results were obtained using 1,8-diamino-3,6-dioxaoctane and 1,4-bis-(3-aminopropyl)piperazine spacers between the acridine units. Additional QSAR studies suggest the importance of these spacers and the acridine moiety. So far, however, only few data are available to establish possible effects for the substituents of the acridine heterocycle.

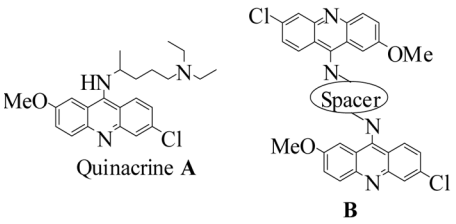


Figure 1. Structures of quinacrine **A** and dimeric acridine **B**.

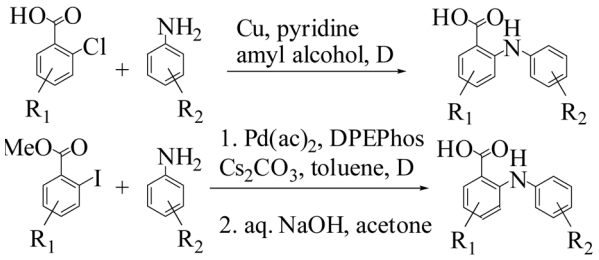
In this study, we synthesized several quinacrine and spacered bis-compounds with various different substituted acridines. An *in-vitro* assay based on FACS analysis was used for examining the ability of the substances to inhibit the association process of amyloid proteins and peptides. Using this method, we extended the screening of acridine derivatives to Alzheimer's disease-specific Aβ-peptides.

Results and discussion

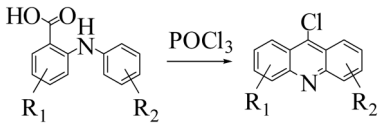
For the synthesis of substituted 9-chloroacridines, a synthetic route starting with the synthesis of the corresponding anthranilic acids by applying either Ullmann–Jourdan reaction or by using a modified Buchwald–Hartwig amination was established (Scheme 1) [10].

Starting materials for the copper-catalyzed Ullmann–Jourdan reaction [11] were substituted 2-chlorobenzoic acids and the corresponding aniline derivatives. The use of 3% copper bronze and 15% pyridine in amyl alcohol were the most suitable conditions and yielded the anthranilic acids in moderate yields. However, the scope of the reaction is limited to electron-rich anilines and electron-deficient benzoic acids, otherwise yields decreased or no reaction took place at all (*e.g.,* for fluorinated aniline derivatives). A more reliable and robust synthesis of anthranilic acids was found by using a palladium-catalyzed Buchwald–Hartwig amination starting from methyl 2-iodobenzoates and anilines using $Pd(ac)_2$, DPEPhos and Cs_2CO_3 as the base. The products were isolated in high yields and subsequent hydrolysis gave the corresponding acids. These anthranilic acids could be transformed into the corresponding 9-chloroacridines easily on reaction with $POCl_3$ (Scheme 2). According to this procedure, the synthesis of two novel compounds was performed (Table 1).

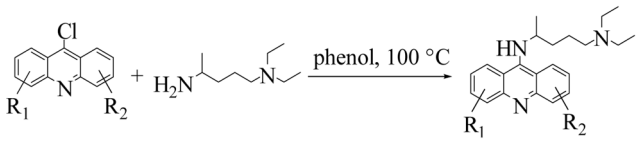
Starting from the 9-chloroacridines, the synthesis of several quinacrine and spacered bis-acridines was performed according to established procedures [9]. The reactions were carried out in phenol, which acts as catalyst for the accumulation of the product by formation of 9-



Scheme 1. Synthetic routes to *N*-phenylanthranilic acids.



Scheme 2. Ring-closure procedure.



Scheme 3. Synthesis of quinacrine compounds.

phenoxyacridine. The quinacrine compounds **4a–4i** (Table 2) were obtained by conversion of the 9-chloroacridines with an excess of 2-amino-5-diethylaminopentane (Scheme 3).

The synthesis of the dimeric acridine compounds was achieved in a quite similar way (Scheme 4). These reaction afforded the bis-acridine derivatives **5a–5e** from 1,8-diaminooctane, whereas compounds **6a–6i** were obtained using 1,8-diamino-3,6-dioxaoctane, and compounds **7a–7r** could be accessed from 1,4-bis-(3-aminopropyl)piperazine (Table 3).

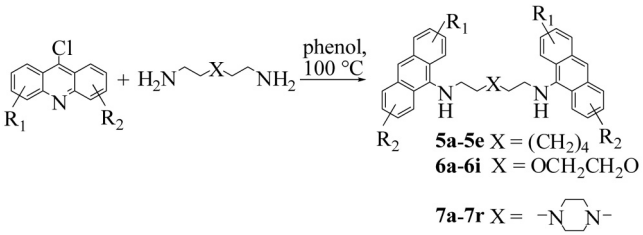
Several of these compounds, especially those carrying a piperazine spacer, displayed only poor solubility in most organic solvents. Thus, purification of these substances was tedious resulting in lowered yields. The NMR spectra of the compounds had to be recorded in DMSO-d_6 at higher temperatures applying prolonged recording time. Nevertheless, for several carbons in the ^{13}C-NMR spectra significant line broadening was observed. An unambiguous proof-of-structure was obtained by a single-crystal X-ray analysis. An ORTEP plot for compound **7o** is depicted in Fig. 2.

The quinacrine and bis-acridines were investigated for their ability to inhibit the addition of monomeric Ab-peptide or prion proteins to fibrils. The screening of the substances was performed by an *in-vitro* assay using FACS analysis [12, 13]. In order to compare the results from the FACS analysis with data from the well-established ScN2a

Table 1. Inhibition of Ab-peptide and prion-proteins at 0.1, 1.0, and 4.0 μM.

Compound	% of control Ab proteins (μM)			% of control PrPsc (μM)		
	0.1	1.0	4.0	0.1	1.0	4.0
Quinacrine						
4a	92	77	54	98	82	76
4b	>100	97	95	>100	98	98
4c	>100	98	91	>100	99	>100
4d	98	85	67	88	88	89
4e	99	90	73	95	96	94
4f	87	41	16	>100	81	52
4g	96	92	52	>100	>100	>100
4h	95	34	24	92	95	58
4i	63	22	11	>100	76	68
1,8-Diaminooctane						
5a	87	54	34	62	52	43
5b	64	6	4	>100	41	23
5c	>100	61	32	66	58	50
5d	97	87	74	97	89	87
5e	93	71	72	60	>100	86
1,8-Diamino-3,6-dioxooctane						
6a	85	56	14	70	48	35
6b	88	80	56	96	84	76
6c	87	50	8	64	43	36
6d	82	74	38	>100	98	92
6e	90	81	64	>100	96	94
6f	80	50	12	>100	73	89
6g	87	12	3	74	88	68
1,4-Bis-(3-aminopropyl)						
7a	48	2	6	86	46	28
7b	>100	93	58	92	68	37
7c	85	7	0,3	72	25	14
7d	80	51	4	61	56	49
7e	>100	53	12	96	79	77
7f	58	10	5	50	16	5
7g	52	24	11	87	63	60
7h	80	6	0,6	51	32	21
7i	20	9	4	59	29	26
7j	83	50	19	93	62	35
7k	87	74	12	79	72	57
7l	77	12	10	96	54	49
7m	81	48	38	65	81	47
7n	69	65	4	>100	>100	81
7o	61	7	6	>100	81	46
7p	73	26	3	93	85	36
7q	68	8	3	90	77	43
7r	98	51	8	83	88	58

cell-based assay, the 6-chloro-2-methoxy derivatives **4a**–**7a** were used as standards. Analysis of the data revealed a dose-dependent inhibition of the association process for prion proteins as well as for the Alzheimer-specific Ab-peptides. In general, the monomeric quinacrine derivatives were less active than the spacered bis-acridines. The best results for AD-specific Ab-peptides were observed with the 2-nitro-5-thiomethyl derivative **4i**. For the dimeric compounds, activity was shown to depend on



Scheme 4. Synthesis of bis-acridines

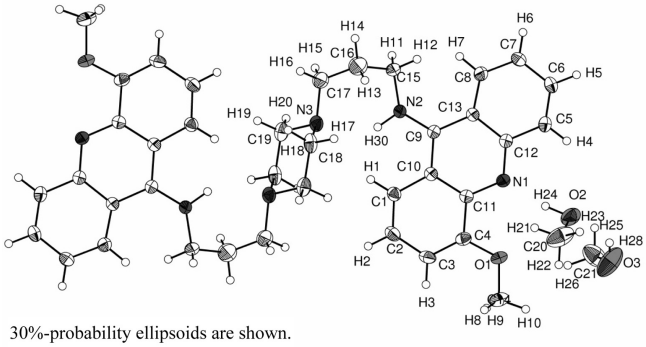


Figure 2. ORTEP diagram of compound **7o**.

the used spacer. For the 2-methoxy-6-chloro derivatives the 1,8-diamino-3,6-dioxaoctane spacer exhibited a higher activity than the 1,8-diaminooctane analogue. An even higher inhibitory effect was observed for the 1,4-bis-(3-aminopropyl)piperazine compound **7a**. In order to evaluate relationships between the substituents and the activity, a broad variety of derivatives was prepared and screened. In summary, the attachment of a methoxy group proved to be beneficial, whereas the Cl substituent seems to be redundant. Also, the addition of fluor substituents is unfavorable. However, an improved inhibitory effect was observed when a nitro group was introduced into the molecule additionally to the methoxy substituents. Therefore, the best compounds in this study were the 2,4-dimethoxy-6-nitro compound **7h** for AD-specific Ab-peptides and the 2-methoxy-6-nitro compound **7f** for PrP. The low cytotoxicity of these compounds associated with the inhibitory effect makes them interesting as starting point to develop new lead compounds, since the potential of 9-aminoacridines related to quinacrine has been demonstrated quite recently [14] and the safety and efficacy of quinacrine in human prion disease has been investigated [15] in some detail. As far as their mode-of-action is concerned, one might reason that the identification of chemical chaperones binding to the PrP structure and stabilizing it is one efficient strategy for antiprion drug discovery. However, some compounds have been shown to possess antiprion activities with low affinities

to PrP [16] indicating a mechanism involving additional modulation factors.

Experimental

General

Melting points are uncorrected (Leica hot stage microscope, Leica Microsystems, Germany), nmR spectra were recorded using the Varian spectrometers Gemini 200, Gemini 2000 or Unity 500 (Varian, USA; *d* given in ppm, *J* in Hz, internal Me_4Si or internal CCl_3F), IR spectra (film or KBr pellet) on a Perkin-Elmer FT-IR spectrometer Spectrum 1000 (Perkin-Elmer, USA), MS spectra were taken on a Intectra GmbH AMD 402 (electron impact, 70 eV; Intectra GmbH, Harpsted, Germany)) or on a Finnigan MAT TSQ 7000 (Thermo Electron Corporation, Bremen, Germany; electrospray, voltage 4.5 kV, sheath gas nitrogen) instrument. TLC was performed on silica gel (Merck 5554 – Merck, Darmstadt, Germany; detection by UV absorption). The solvents were dried according to usual procedures.

Crystal data of 7o

Crystals of **7o** were obtained by slow evaporation from a methanolic solution. $C_{40}H_{44}NO_2$, M = 612.80, monoclinic, space group $P2_{1/n}$, a = 8.5505 (19) Å, b = 21.083 (3) Å, c = 11.274 (3) Å, α = 90.00°, β = 93.73 (3)°, γ = 90.00°, V = 2028.1 (7) Å^3, Dx = 1.213 g/cm^3, and Z = 4. A single crystal was used for X-ray diffraction data collection on an IPDS Stadi IV employing graphite monochromated MoKα radiation. 14351 reflections measured, 3399 unique, 2357 reflections with $I>2\sigma_I$. R[F2>2r(F2)] = 0.0781, wR(F2) = 0.2059, GoF = 1.072. The structure was solved by direct method using the SHELX-97 program. Hydrogens were solved by mixed modes. Lists of atomic coordinates, anisotropic thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystal Crystallographic Data Centre, UK. CCDC No. 687482.

Chemistry

General procedure for the synthesis of monomeric acridine compounds GP1

A mixture of 9-chloroacridine (3.6 mmol) in phenol (5 g) was heated to 100°C for 15 min. Then, 2-amino-5-diethylaminopentane (0.6 g, 3.8 mmol) was added and stirring continued for 30 min. After cooling to 25°C, the mixture was chromatographed (SiO_2, gradient ethyl acetate, ethyl acetate / methanol / ammonium hydroxide, 80:20:1)

*N^4-(6-Chloro-2-methoxy-9-acridinyl)-N^1,N^1-diethyl-1,4-pentanediamine **4a***

Compound **4a** (0.9 g, 63%) was obtained from 6,9-dichloro-2-methoxyacridine (1.0 g, 3.6 mmol) and 2-amino-5-diethylaminopentane (0.30 g, 1.85 mmol) following GP1 as a yellow oil. IR (film) ν: 3318*br*, 2968*s*, 1633*s*, 1606*m*, 1563*s*, 1520*m*, 1470*s*, 1435*s*, 1383*m*, 1233*s*, 1071*m* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.92 (*t*, 6H, *J* = 7.0 Hz, CH_3), 1.24 (*d*, 3H, *J* = 6.2 Hz, CH_3 (1′)), 1.50–1.70 (*m*, 4H, CH_2(3′,4′)), 2.34 (*t*, 2H, *J* = 7.0 Hz, CH_2(5′)), 2.41 (*q*, 4H, *J* = 7.0 Hz, NCH_2), 3.94 (*s*, 3H, OCH_3), 3.95–4.04 (*m*, 1H, CH(2′)), 4.39 (*d*, 1H, *J* = 10.4 Hz, NH), 7.19 (*d*, 1H, *J* = 2.5 Hz, H-C(1)), 7.30 (*dd*, 1H, *J* = 9.1, 2.1 Hz, H-C(7)), 7.40 (*dd*, 1H, *J* = 9.5, 2.5 Hz, H-C(3)), 7.97 (*d*, 1H, *J* = 9.1 Hz, H-C(8)), 7.98 (*d*, 1H, *J* = 9.5 Hz, H-C(4)), 8.06 (*d*, 1H, *J* = 2.1 Hz, H-C(5)) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 11.6, 22.3, 24.2, 37.0, 46.9, 52.8, 55.5, 55.9, 99.3, 117.2, 119.2, 123.7, 124.4, 124.8, 128.3, 131.5, 134.5, 146.8, 148.1, 149.0, 156.0 ppm; UV-VIS (methanol) λ_{max} (log ε): 287 nm (4.72); MS (ESI, MeOH) *m*/*z*: 400.3 $[M + H]^+$ (100%).

*N^4-9-Acridinyl-N^1,N^1-diethyl-1,4-pentanediamine **4b** [17]*

Compound **4b** (1.0 g, 65%) was obtained from 9-chloroacridine (1.0 g, 4.7 mmol) and 2-amino-5-diethylaminopentane (0.80 g, 5.00 mmol) following GP1 as a yellow oil. IR (film) ν: 3300*br*, 3060*m*, 2968*s*, 2808*m*, 1615*s*, 1558*s*, 1520*s*, 1488*s*, 1422*s*, 1366*m*, 1259*s*, 1213*w*, 1133*m*, 1022*w* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.93 (*t*, 6H, *J* = 7.0 Hz, CH_3), 1.30 (d, 3H, *J* = 6.2 Hz, CH_3(1′)), 1.55–1.75 (*m*, 4H, CH_2(3′,4′)), 2.35 (*t*, 2H, *J* = 7.0 Hz, CH_2(5′)), 2.42 (*q*, 4H, *J* = 7.0 Hz, NCH_2), 4.10–4.20 (*m*, 1H, CH (2′)), 4.78 (*br s*, 1H, NH), 7.38 (*ddd*, 2H, *J* = 8.7, 6.7, 1.2 Hz, H-C(2)), 7.67 (*ddd*, 2H, *J* = 8.7, 6.6, 1.2 Hz, H-C(3)), 8.06–8.11 (*m*, 4H, H-C(1,4)) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 11.5, 22.2, 23.9, 37.1, 46.8, 52.7, 56.1, 118.1, 122.6, 123.4, 129.8, 129.9, 149.5, 150.9 ppm; UV-VIS (methanol) λ_{max} (log ε): 280 nm (4.74); MS (ESI, MeOH) *m*/*z*: 168.8 $[M + 2H]^{2+}$ (100%), 336.4 $[M + H]^+$ (40%); HRMS for $C_{22}H_{29}N_3$ calcd.: 335.2361; found: 335.2362.

*N^4-(2-Methoxy-9-acridinyl)-N^1,N^1-diethyl-1,4-pentanediamine **4c***

Compound **4c** (0.9 g, 60%) was obtained from 9-chloro-2-methoxyacridine (1.0 g, 4.1 mmol) and 2-amino-5-diethylaminopentane (0.7 g, 4.5 mmol) following GP1 as a yellow oil. IR (film) ν: 3301*br*, 3061*m*, 2967*s*, 2870*m*, 2805*m*, 1922*w*, 1633*s*, 1562*s*, 1524*s*, 1487*s*, 1469*s*, 1434*s*, 1368*s*, 1337*m*, 1282*m*, 1266*m*, 1232*s*, 1130*m*, 1104*m*, 1032*s* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.93 (*t*, 6H, *J* = 7.0 Hz, CH_3), 1.25 (d, 3H, *J* = 6.2 Hz, CH_3(1′)), 1.53–1.73 (*m*, 4H, CH_2(3′, 4′)), 2.35 (*t*, 2H, *J* = 7.0 Hz, CH_2(5′)), 2.42 (*q*, 4H, *J* = 7.0 Hz, NCH_2), 3.94 (*s*, 3H, OCH_3), 3.99–4.07 (*m*, 1H, CH (2′)), 4.78 (*d*, 1H, *J* = 10.4 Hz, NH), 7.25 (*d*, 1H, *J* = 2.5 Hz, H-C(1)), 7.37–7.43 (*m*, 2H, $H_{arom.}$), 7.62 (*ddd*, 1H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 8.01–8.06 (*m*, 2H, $H_{arom.}$), 8.09 (*d*, 1H, *J* = 8.3 Hz, H-C(4)) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 11.5, 22.2, 23.9, 36.9, 46.8, 52.8, 55.5, 55.7, 99.4, 119.2, 119.3, 122.0, 124.1, 124.2, 128.8, 130.3, 131.6, 146.4, 147.9, 148.9, 155.9 ppm; UV-VIS (methanol) λ_{max} (log ε): 279 nm (4.75); MS (ESI, MeOH) *m*/*z*: 183.8 $[M + 2H]^{2+}$ (30%), 366.4 $[M + H]^+$ (100%); HRMS for $C_{23}H_{31}N_3O$ calcd.: 365.2467; found: 365.2466.

*N^4-(2-Trifluoromethoxy-9-acridinyl)-N^1,N^1-diethyl-1,4-pentanediamine **4d***

Compound **4d** (0.4 g, 57%) was obtained from 9-chloro-2-trifluoromethoxyacridine (0.50 g, 1.68 mmol) and 2-amino-5-diethylaminopentane (0.30 g, 1.85 mmol) following GP1 as a yellow oil. IR (film) ν: 3244*br*, 2969*s*, 1633*m*, 1603*m*, 1563*s*, 1494*s*, 1456*s*, 1384*m*, 1258*s*, 1219*s*, 1166*s* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.93 (*t*, 6H, *J* = 7.0 Hz, CH_3), 1.25 (*d*, 3H, *J* = 6.2 Hz, CH_3(1′)), 1.50–1.80 (*m*, 4H, CH_2(3′, 4′)), 2.37 (*t*, 2H, *J* = 7.0 Hz, CH_2(5′)), 2.42 (*q*, 4H, *J* = 7.0 Hz, NCH_2), 4.05–4.15 (*m*, 1H, CH(2′)), 4.80 (*d*, 1H, *J* = 10.4 Hz, NH), 7.43 (*ddd*, 1H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 7.53 (*dd*, 1H, *J* = 9.5, 2.5 Hz, H-C(3)), 7.70 (*ddd*, 1H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 7.92 (*d*, 1H, *J* = 2.5 Hz, H-C(1)), 8.02–8.14 (*m*, 3H, $H_{arom.}$) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 11.5, 22.3, 24.0, 37.0, 46.8, 52.7, 56.2, 113.6, 117.4, 118.3, 120.7 (q, $J_{C,F}$ = 263.2 Hz), 122.0, 124.3, 124.4, 130.0, 130.1, 132.1, 144.4, 147.7, 149.5, 150.9 ppm; ^{19}F-NMR (188 MHz, $CDCl_3$) δ: −58.5 (*s*, OCF_3) ppm; UV-

VIS (methanol) λ_{max} (log ε): 282 nm (4.67); MS (ESI, MeOH) *m/z*: 210.8 $[M + 2H]^{2+}$ (15%), 420.3 $[M + H]^+$ (100%); HRMS for $C_{23}H_{28}F_3N_3O$ calcd.: 335.2361; found: 335.2362.

N^4-(2,4-Difluoro-9-acridinyl)-N^1,N^1-diethyl-1,4-pentanediamine ***4e***

Compound **4e** (0.57 g, 57%) was obtained from 9-chloro-2,4-difluoroacridine (1.0 g, 2.7 mmol) and 2-amino-5-diethylaminopentane (0.5 g, 3.1 mmol) following GP1 as a yellow oil. IR (film) ν: 3317*br*, 3042*m*, 2969*s*, 2871*m*, 2806*m*, 2360*w*, 1645*s*, 1567*s*, 1531s, 1486*s*, 1433*s*, 1383*m*, 1337*s*, 1280*s*, 1230*m*, 1126*s*, 1055*m* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.94 (*t*, 6H, *J* = 7.0 Hz, CH_3), 1.29 (d, 3H, *J* = 6.2 Hz, CH_3(1′)), 1.52–1.76 (*m*, 4H, CH_2(3′, 4′)), 2.37 (*t*, 2H, *J* = 7.0 Hz, CH_2(5′)), 2.42 (*q*, 4H, *J* = 7.0 Hz, NCH_2), 4.05–4.15 (*m*, 1H, CH(2′)), 4.74 (*d*, 1H, *J* = 10.4 Hz, NH), 7.23 (*ddd*, 1H, *J* = 10.4, 8.3, 2.5 Hz, H-C(3)), 7.44 (*ddd*, 1H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 7.50 (*ddd*, 1H, *J* = 10.4, 2.5, 1.6 Hz, H-C(1)), 7.69 (*ddd*, 1H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 8.05 (*d*, 1H, *J* = 8.7 Hz, $H_{arom.}$), 8.19 (*d*, 1H, *J* = 8.7 Hz, $H_{arom.}$) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 11.5, 22.3, 24.0, 37.0, 46.9, 52.7, 55.9, 101.4 (*dd*, $J_{C,F}$ = 23.0, 5.0 Hz), 105.3 (*dd*, $J_{C,F}$ = 30.7, 23.0 Hz), 118.6 (*d*, $J_{C,F}$ = 6.0 Hz), 118.8, 122.1, 124.8, 130.0, 130.7, 138.1 (*d*, $J_{C,F}$ = 13.0 Hz), 148.8, 150.4, 157.0 (*dd*, $J_{C,F}$ = 245.0, 12.0 Hz), 159.0(*dd*, $J_{C,F}$ = 260.5, 12.0 Hz) ppm; ^{19}F-NMR (188 MHz, $CDCl_3$) δ: −113.8 (*m*, F), −118.4 (*m*, F) ppm; UV-VIS (methanol) λ_{max} (log ε): 280 nm (4.73); MS (ESI, MeOH) *m/z*: 186.8 $[M + 2H]^{2+}$ (100%), 372.3 $[M + H]^+$ (90%); HRMS for $C_{22}H_{29}F_2N_3$ calcd.: 371.2173; found: 371.2173.

N^4-(5-Methoxy-3-nitro-9-acridinyl)-N^1,N^1-diethyl-1,4-pentanediamine ***4f***

Compound **4f** (0.9 g, 63%) was obtained from 9-chloro-5-methoxy-3-nitroacridine (1.0 g, 3.5 mmol) and 2-amino-5-diethylaminopentane (0.6 g, 3.8 mmol) following GP1 as an orange-colored oil. IR (film) ν: 3313*br*, 2968*s*, 2361*w*, 1673*m*, 1624*m*, 1568*s*, 1515*s*, 1463*s*, 1421*m*, 1345*s*, 1256*s*, 1137*m*, 1073*m* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.93 (*t*, 6H, *J* = 7.0 Hz, CH_3), 1.32 (*d*, 3H, *J* = 6.2 Hz, CH_3(1′)), 1.50–1.80 (*m*, 4H, CH_2(3′, 4′)), 2.36 (*t*, 2H, *J* = 7.0 Hz, CH_2(5′)), 2.42 (*q*, 4H, *J* = 7.0 Hz, NCH_2), 4.10–4.22 (*m*, 4H, OCH_3, CH(2′)), 5.06 (*d*, 1H, *J* = 9.9 Hz, NH), 7.04 (*d*, 1H, *J* = 7.5 Hz, H-C(6)), 7.40 (*dd*, 1H, *J* = 8.7, 7.5 Hz, H-C(7)), 7.62 (*d*, 1H, *J* = 8.7 Hz, H-C(8)), 8.06 (*dd*, 1H, *J* = 9.5, 2.5 Hz, H-C(2)), 8.20 (*d*, 1H, *J* = 9.5 Hz, H-C(1)), 9.18 (*d*, 1H, *J* = 2.5 Hz, H-C(4)) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 11.3, 22.2, 23.8, 37.0, 46.8, 52.6, 56.2, 56.3, 107.4, 113.8, 116.0, 119.7, 120.0, 125.1, 127.2, 127.5, 143.7, 147.0, 148.0, 150.9, 155.7 ppm; UV-VIS (methanol) λ_{max} (log ε): 297 nm (4.48); MS (ESI, MeOH) *m/z*: 411.6 $[M + H]^+$ (100%), 843.3 $[M_2 + Na]^+$ (15%); HRMS for $C_{23}H_{30}NO_3$ calcd.: 410.2318; found: 410.2319.

N^4-(4-Thiomethyl-9-acridinyl)-N^1,N^1-diethyl-1,4-pentanediamine ***4g***

Compound **4g** (1.0 g, 68%) was from obtained 9-chloro-4-thiomethylacridine **3a** (1.0 g, 3.9 mmol) and 2-amino-5-diethylaminopentane (0.7 g, 4.6 mmol) following GP1 as a yellow oil. IR (KBr) ν: 3057*m*, 2967*s*, 2869*m*, 2808*m*, 1671*w*, 1618*m*, 1599*s*, 1553*m*, 1487*s*, 1418*s*, 1381*s*, 1359*s*, 1256*m*, 1200*m*, 1124*s*, 1036*w* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.94 (*t*, 6H, *J* = 7.1 Hz, CH_3), 1.26 (*d*, 3H, *J* = 6.2 Hz, CH_3(1′)), 1.50–1.70 (*m*, 4H, CH_2(3′, 4′)), 2.35 (*t*, 2H, *J* = 7.1 Hz, CH_2(5′)), 2.43 (*q*, 4H, *J* = 7.1 Hz, NCH_2), 2.56 (*s*, 3H, SCH_3), 4.08–4.18 (*m*, 1H, CH(2′)), 4.72 (*br s*, 1H, NH), 7.28–7.34 (*m*, 2H, $H_{arom.}$), 7.30 (*dd*, 1H, *J* = 7.9, 7.5 Hz, $H_{arom.}$), 7.65 (*dd*, 1H, *J* = 7.9, 7.5 Hz, H_{arom}), 7.77–7.83 (*m*, 1H, $H_{arom.}$), 8.04 (*d*, 1H, *J* = 8.7 Hz, $H_{arom.}$), 8.17 (*d*, 1H, *J* = 8.7 Hz, $H_{arom.}$) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 11.3, 14.5, 22.1, 23.6, 36.9, 46.7, 52.6, 56.0, 117.6, 118.1, 118.5, 122.1, 122.3, 123.1, 123.8, 129.4, 130.4, 140.4, 146.6, 148.3, 150.9 ppm; UV-VIS (methanol) λ_{max} (log ε): 288 nm (4.72); MS (ESI, MeOH) *m/z*: 191.7 $[M + 2H]^{2+}$ (100%), 382.3 $[M + H]^+$ (80%); HRMS for $C_{23}H_{31}N_3S$ calcd.: 381.2239; found: 381.2238.

N^4-(3-Chloro-5-methoxy-9-acridinyl)-N^1,N^1-diethyl-1,4-pentanediamine ***4h*** *[18]*

Compound **4h** (1.0 g, 70%) was obtained from 3,9-dichloro-5-methoxyacridine (1.0 g, 3.6 mmol) and 2-amino-5-diethylaminopentane (0.6 g, 3.8 mmol) following GP1 as a yellow oil. IR (film) ν: 3288*br*, 2968*s*, 1669*m*, 1606*s*, 1564*s*, 1520*m*, 1456*s*, 1435*s*, 1388*s*, 1252*s*, 1132*m*, 1076*s* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.94 (*t*, 6H, *J* = 7.0 Hz, CH_3), 1.26 (*d*, 3H, *J* = 6.2 Hz, CH_3(1′)), 1.50-1.73 (*m*, 4H, CH_2(3′, 4′)), 2.37 (*t*, 2H, *J* = 7.0 Hz, CH_2(5′)), 2.46 (*q*, 4H, *J* = 7.0 Hz, NCH_2), 4.08 (*s*, 3H, OCH_3), 4.09–4.14 (*m*, 1H, CH(2′)), 4.80 (*br s*, 1H, NH), 6.96 (*d*, 1H, *J* = 7.5 Hz, $H_{arom.}$), 7.26–7.32 (*m*, 2H, $H_{arom.}$), 7.58 (*d*, 1H, *J* = 8.7 Hz, $H_{arom.}$), 8.00 (*d*, 1H, *J* = 9.1 Hz, $H_{arom.}$), 8.21 (*br s*, 1H, H-C(3)) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 11.1, 22.1, 23.5, 36.8, 46.6, 52.4, 56.1, 55.9, 106.9, 114.1, 116.6, 119.1, 123.5, 124.5, 124.7, 129.5, 135.4, 148.4, 151.0 ppm; UV-VIS (methanol) λ_{max} (log ε): 290 nm (4.76); MS (ESI, MeOH) *m/z*: 400.2 $[M + H]^+$ (100%); HRMS for $C_{23}H_{30}ClN_3O$ calcd.: 399.2077; found: 399.2079.

N^4-(2-Nitro-5-thiomethyl-9-acridinyl)-N^1,N^1-diethyl-1,4-pentanediamine ***4i***

Compound **4i** (0.12 g, 11%) was obtained from 9-chloro-2-nitro-5-thiomethylacridine **3b** (0.8 g, 2.6 mmol) and 2-amino-5-diethylaminopentane (0.5 g, 3.2 mmol) following GP1 as a red solid. M.p.: 93–95°C; IR (KBr) ν: 2967*s*, 2923*s*, 1617*s*, 1600*m*, 1572*s*, 1510*s*, 1493*s*, 1432*m*, 1310*s*, 1233*m*, 1204*w*, 1130*w*, 1076*w* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.93 (*t*, 6H, *J* = 7.0 Hz, CH_3), 1.40 (*d*, 3H, *J* = 6.2 Hz, CH_3(1′)), 1.54–1.84 (*m*, 4H, CH_2(3′, 4′)), 2.40 (*t*, 2H, *J* = 7.0 Hz, CH_2(5′)), 2.44 (*q*, 4H, *J* = 7.0 Hz, NCH_2), 2.55 (*s*, 3H, SCH_3), 4.26–4.36 (*m*, 1H, CH(2′)), 5.66 (*d*, 1H, *J* = 10.4 Hz, NH), 7.36–7.39 (*m*, 2H, H-C(6,7)), 7.75 (*dd*, 1H, *J* = 7.3, 2.4 Hz, H-C(8)), 8.13 (*d*, 1H, *J* = 9.2 Hz, H-C(4)), 8.31 (*dd*, 1H, *J* = 9.2, 2.4 Hz, H-C(3)), 9.15 (*d*, 1H, *J* = 2.4 Hz, H-C(1)) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 11.8, 14.6, 22.5, 24.3, 37.2, 46.9, 52.5, 56.5, 114.5, 116.0, 116.9, 117.5, 122.7, 124.1, 124.5, 131.5, 141.5, 142.5, 148.2, 150.1, 153.9 ppm; UV-VIS (methanol) λ_{max} (log ε): 268 nm (4.45); MS (ESI, MeOH) *m/z*: 427.2 $[M + H]^+$ (100%); HRMS for $C_{23}H_{30}NO_2S$ calcd.: 426.2089; found: 426.2088.

General procedure for the synthesis of dimeric acridine compounds GP2

A mixture of 9-chloroacridine (3.6 mmol) in phenol (5 g) was heated to 100°C for 15 min. Then, 1,4-bis-(3-aminopropyl)piperazine (0.28 g, 1.4 mmol) was added and stirring continued for 30 min. After cooling to 25°C, methanol (10 mL) was added and the resulting solution poured into diethyl ether under vigorous stirring. The product was collected by filtration and purified by column chromatography (SiO_2, dichloromethane / methanol / ammonium hydroxide, 80 : 20 : 1).

N,N-Bis-(6-chloro-2-methoxy-9-acridinyl)-1,8-octanediamine ***5a*** *[9]*

Compound **5a** (0.8 g, 80%) was obtained from 6,9-dichloro-2-methoxyacridine (1.0 g, 3.6 mmol) and 1,8-octanediamine (0.23 g, 1.60 mmol) following GP2 as a yellow solid. M.p.: 165°C (lit: 166.5–167.5°C [19]); IR (KBr) ν: 2929*s*, 1631*s*, 1563*s*, 1525*s*, 1437*s*, 1258*s*, 1234*m*, 1077*w* cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 1.05-1.21 (*m*, 8H, CH_2(3′, 4′, 5′, 6′)), 1.55–1.64 (*m*, 4H, CH_2(2′, 7′)), 3.60–3.70 (*m*, 4H, CH_2(1′, 8′)), 3.87 (*s*, 6H, OCH_3), 6.90 (*br s*, 2H, NH), 7.28 (*dd*, 2H, *J* = 9.1, 2.1 Hz, H-C(7)), 7.37 (*dd*, 2H, *J* = 9.5, 2.5 Hz, H-C(3)), 7.57 (*d*, 2H, *J* = 2.5 Hz, H-C(1)), 7.75–7.84 (*m*, 4H, H-C(5, 8)), 8.26 (*d*, 2H, *J* = 9.5 Hz, H-C(4)) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 26.0, 28.5, 30.4, 49.3, 55.5, 100.8, 114.4, 117.0, 122.3, 123.9, 126.4, 133.4, 147.7, 150.4, 154.9 ppm; UV-VIS (methanol) λ_{max} (log ε): 299 nm (4.94); MS (ESI, MeOH + TFA) *m*/*z*: 314.4 $[M + 2H]^{2+}$ (100%), 627.6 $[M + H]^+$ (40%).

N,N-Bis-9-acridinyl-1,8-octanediamine ***5b***

Compound **5b** (1.0 g, 82%) was obtained from 9-chloroacridine (1.0 g, 4.7 mmol) and 1,8-octanediamine (0.30 g, 2.10 mmol) following GP2 as a yellow solid. M.p.: 195°C (lit: 197–200°C [20], 165°C [21]); IR (KBr) ν: 3055*m*, 2930*s*, 2855*s*, 1614*s*, 1558*s*, 1520*s*, 1506*s*, 1468*s*, 1448*m*, 1426*s*, 1397*w*, 1371*m*, 1339*s*, 1288*w*, 1265*m*, 1222*w*, 1136*m*, 1122*m*, 1024*w* cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.25–1.30 (*m*, 4H, CH_2(4′, 5′)), 1.33–1.40 (m, 4H, CH_2(3′, 6′)), 1.67–1.77 (*m*, 4H, CH_2(2′, 7′)), 3.78 (*t*, 4H, *J* = 7.3 Hz, CH_2(1′, 8′)), 7.33 (*ddd*, 4H, *J* = 8.7, 6.4, 0.9 Hz, H-C(2)), 7.63 (*ddd*, 4H, *J* = 8.7, 6.4, 0.9 Hz, H-C(3)), 8.03–8.10 (*m*, 8H, H-C(1,4)) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$ + CD_3OD) δ: 26.4, 28.8, 31.1, 50.2, 115.7, 122.5, 122.7, 127.5, 130.1, 148.2, 152.0 ppm; UV-VIS [22] (methanol) λ_{max} (log ε): 282 nm (5.32); MS (ESI, MeOH) *m*/*z*: 250.3 $[M + 2H]^{2+}$ (100%), 499.4 $[M + H]^+$ (20%); HRMS for $C_{34}H_{34}N$ calcd.: 498.2783; found: 498.2784.

N,N-Bis-(2-methoxy-9-acridinyl)-1,8-octanediamine ***5c***

Compound **5c** (0.9 g, 92%) was obtained from 9-chloro-2-methoxyacridine (1.0 g, 4.1 mmol) and 1,8-octanediamine (0.26 g, 1.80 mmol) following GP2 as a yellow solid. M.p.: 190°C (lit: 186–187.5°C [23]); IR (KBr) ν: 3252*m*, 2962*s*, 2919*s*, 2822*s*, 1734*w*, 1633*s*, 1613*s*, 1555*s*, 1513*s*, 1459*s*, 1435*s*, 1386*m*, 1357*s*, 1341*s*, 1312*s*, 1272*m*, 1256*m*, 1229*m*, 1211*m*, 1176*m*, 1132*s*, 1085*m*, 1057*m*, 1028*s*, 1019*m* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.20–1.28 (*m*, 4H, CH_2(4′, 5′)), 1.30–1.40 (m, 4H, CH_2(3′, 6′)), 1.62–1.72 (*m*, 4H, CH_2(2′, 7′)), 3.60–3.70 (*m*, 4H, CH_2(1′, 8′)), 3.94 (*s*, 6H, OCH_3), 4.71 (*br s*, 2H, *NH*), 7.26 (*d*, 2H, *J* = 2.9 Hz, H-C(1)), 7.35–7.42 (*m*, 4H, $H_{arom.}$), 7.62 (*ddd*, 2H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 8.00–8.10 (*m*, 6H, $H_{arom.}$) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 26.8, 29.2, 31.8, 50.6, 55.5, 117.8, 118.0, 121.9, 123.6, 123.9, 128.1, 128.7, 129.8, 131.5, 146.2, 147.9, 149.4, 155.6 ppm; UV-VIS (methanol) λ_{max} (log ε): 278 nm (5.09); MS (ESI, MeOH) *m*/*z*: 280.3 $[M + 2H]^{2+}$ (100%), 559.4 $[M + H]^+$ (30%); HRMS for $C_{36}H_{38}NO_2$ calcd.: 558.2995; found: 558.2996.

N,N-Bis-(2-trifluoromethoxy-9-acridinyl)-1,8-octanediamine ***5d***

Compound **5d** (0.5 g, 50%) was obtained from 9-chloro-2-trifluoromethoxyacridine (1.0 g, 3.4 mmol) and 1,8-octanediamine (0.23 g, 1.60 mmol) following GP2 as a yellow oil. IR (film) ν: 3063*w*, 2931*m*, 2857*w*, 1618*w*, 1591*m*, 1565*s*, 1506*s*, 1475*s*, 1431*m*, 1357*m*, 1258*s*, 1218*s*, 1163*s*, 1024*w* cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.27–1.32 (*m*, 4H, CH_2(4′, 5′)), 1.34–1.41 (m, 4H, CH_2(3′, 6′)), 1.67–1.77 (*m*, 4H, CH_2(2′, 7′)), 3.70–3.80 (*m*, 4H, CH_2(1′, 8′)), 5.00 (*br s*, 2H, *NH*), 7.39 (*ddd*, 1H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 7.51 (*dd*, 1H, *J* = 9.5, 2.5 Hz, H-C(3)), 7.67 (*ddd*, 1H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 7.92 (*d*, 1H, *J* = 2.5 Hz, H-C(1)), 8.01–8.12 (*m*, 3H, $H_{arom.}$) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 26.6, 29.0, 31.6, 50.7, 113.9, 115.8, 116.7, 119.8, 120.7 (q, $J_{C,F}$ = 257.8 Hz), 121.8, 124.0, 124.5, 129.6, 130.3, 144.1, 147.8, 149.4, 151.3, 155.6 ppm; ^{19}F-NMR (188 MHz, $CDCl_3$) δ: -58.5 (*s*, OCF_3) ppm; UV-VIS (methanol) λ_{max} (log ε): 282 nm (5.42); MS (ESI, MeOH) *m*/*z*: 334.2 $[M + 2H]^{2+}$ (20%), 667.4 $[M + H]^+$ (100%); HRMS for $C_{36}H_{32}F_6NO_2$ calcd.: 666.2429; found: 666.2430.

N,N-Bis-(2,4-difluoro-9-acridinyl)-1,8-diaminooctane ***5e***

Compound **5e** (0.42 g, 37%) was obtained from 9-chloro-2-trifluoromethoxyacridine (1.0 g, 4.0 mmol) and 1,8-diaminooctane (0.27 g, 1.80 mmol) following GP2 as a yellow oil. IR (KBr) ν: 3050*m*, 2934*s*, 2853*m*, 1647*m*, 1605*m*, 1592*m*, 1570*m*, 1537*s*, 1511*s*, 1476*s*, 1458*s*, 1437*s*, 1395*m*, 1356*m*, 1282*s*, 1244*s*, 1124*s*, 1070*w*, 1000*m* cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.42–1.53 (*m*, 8H, CH_2(3′, 4′, 5′, 6′)), 1.95–2.04 (*m*, 4H, CH_2(2′, 7′)), 4.12–4.18 (*m*, 4H, CH_2(1′, 8′)), 5.00 (*br s*, 2H, *NH*), 7.59 (*ddd*, 2H, *J* = 8.7, 6.2, 1.3 Hz, H-C(6)), 7.81 (*ddd*, 2H, *J* = 11.2, 8.3, 2.5 Hz, H-C(3)), 7.98 (*ddd*, 2H, *J* = 8.7, 6.2, 1.3 Hz, H-C(7)), 8.02 (*dd*, 2H, *J* = 8.7, 2.5 Hz, H-C(1)), 8.14–8.25 (*m*, 2H, H-C(5)), 8.02 (*d*, 2H, *J* = 8.3, H-C(8)) ppm; ^{13}C-NMR (100 MHz, CD_3OD) δ: 27.7, 30.1, 30.4, 50.6, 111.1, 119.9, 122.7 (*d*, $J_{C,F}$ = 18.9 Hz), 125.3 (*d*, $J_{C,F}$ = 29.2 Hz), 136.8, 153.5 (*dd*, $J_{C,F}$ = 254.0, 12.7 Hz), 159.0 ppm; ^{19}F-NMR (188 MHz, $CDCl_3$) δ: −115.1 (*br s*, F), −125.4 (*m*, F) ppm; UV-VIS (methanol) λ_{max} (log ε): 279 nm (5.05); MS (ESI, MeOH) *m*/*z*: 571.4 $[M + H]^+$ (100%); HRMS for $C_{32}H_{28}F_2NO_2$ calcd.: 570.2407; found: 570.2407.

N,N-Bis-(6-chloro-2-methoxy-9-acridinyl)-1,8-diamino-3,6-dioxaoctane ***6a*** *[9]*

Compound **6a** (0.8 g, 80%) was obtained from 6,9-dichloro-2-methoxyacridine (1.0 g, 3.6 mmol) and 1,8-diamino-3,6-dioxaoctane (0.23 g, 1.60 mmol) following GP2 as a yellow solid. M.p.: 170°C; IR (KBr) ν: 2924*s*, 1629*s*, 1560*s*, 1465*s*, 1230*m*, 1130*m*, 1030*m* cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 3.48 (*s*, 4H, CH_2(4′, 5′)), 3.64 (*t*, 4H, *J* = 4.5 Hz, CH_2(2′, 7′)), 3.77–3.82 (*m*, 4H, CH_2(1′, 8′)), 3.85 (*s*, 6H, OCH_3), 7.23 (*dd*, 2H, *J* = 9.1, 2.1 Hz, H-C(7)), 7.32 (*dd*, 2H, *J* = 9.5, 2.5 Hz, H-C(3)), 7.54 (*d*, 2H, *J* = 2.5 Hz, H-C(1)), 7.65 (*d*, 2H, *J* = 9.1 Hz, H-C(8)), 7.70 (*d*, 2H, *J* = 2.1 Hz, H-C(5)), 8.26 (*d*, 2H, *J* = 9.5 Hz, H-C(4)) ppm; ^{13}C-NMR (125 MHz, 50°C, DMSO-d_6) δ: 49.0, 55.4, 69.5, 69.8, 101.2 , 114.8, 117.3, 122.5, 123.9, 125.0, 127.3, 129.0, 133.7, 144.4, 146.7, 150.7, 154.9 ppm; UV-VIS (methanol) λ_{max} (log ε): 283 nm (5.00); MS (ESI, MeOH + TFA) *m*/*z*: 316.5 $[M + 2H]^{2+}$ (100%), 631.5 $[M + H]^+$ (90%).

N,N-Bis -9-acridinyl-1,8-diamino-3,6-dioxaoctane ***6b***

Compound **6b** (0.4 g, 38%) was obtained from 9-chloroacridine (1.0 g, 4.7 mmol) and 1,8-diamino-3,6-dioxaoctane (0.31 g, 2.10 mmol) following GP2 as a yellow solid. M.p.: 154°C (lit: 150–153°C [24]); IR (KBr) ν: 3166*m*, 3058*m*, 2889*s*, 1625*s*, 1595*s*, 1561*s*, 1521*s*, 1488*s*, 1471*s*, 1418*m*, 1396*w*, 1350*s*, 1288*w*, 1256*s*, 1121*s*, 1090*m*, 1028*w* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.64–3.72 (*m*, 8H, CH_2(2′, 4′, 5′, 7′)), 3.87–3.95 (*m*, 4H, CH_2(1′, 8′)), 5.65 (*br s*, 2H, *NH*), 7.29 (*ddd*, 4H, *J* = 8.7, 6.4, 0.9 Hz, H-C(2)), 7.60 (*ddd*, 4H, *J* = 8.7, 6.4, 0.9 Hz, H-C(3)), 7.99–8.12 (*m*, 8H, H-C(1, 4)) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 50.4, 70.3, 70.6, 117.6, 122.8, 123.2, 128.1, 129.8, 150.5, 151.3 ppm; UV-VIS (methanol) λ_{max} (log ε): 277 nm (4.94); MS (ESI, MeOH) *m*/*z*: 252.3 $[M + 2H]^{2+}$ (15%), 503.3

$[M + H]^+$ (100%); HRMS for $C_{32}H_{30}NO_2$ calcd.: 502.2369; found: 502.2368.

N,N-Bis-(2-methoxy-9-acridinyl)-1,8-diamino-3,6-dioxaoctane ***6c***

Compound **6d** (0.8 g, 77%) was obtained from 9-chloro-2-methoxyacridine (1.0 g, 4.1 mmol) and 1,8-diamino-3,6-dioxaoctane (0.28 g, 1.90 mmol) following GP2 as a yellow solid. M.p.: 181–182°C; IR (KBr) ν: 3384*s*, 2991*m*, 2897*m*, 2869*m*, 1633*s*, 1561*s*, 1524*w*, 1488*s*, 1472*s*, 1456*m*, 1436*m*, 1421*s*, 1395*w*, 1370*w*, 1334*w*, 1320*w*, 1280*w*, 1257*w*, 1236*s*, 1150*w*, 1124*s*, 1114*s*, 1103*s*, 1032*s* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.60 (*t*, 4H, *J* = 4.5 Hz, CH_2(2′, 7′)), 3.68 (*s*, 4H, CH_2(4′, 5′)), 3.87–3.95 (*m*, 4H, CH_2(1′, 8′)), 3.90 (*s*, 6H, OCH_3), 5.25 (*br s*, 2H, *NH*), 7.30–7.40 (*m*, 6H, $H_{arom.}$), 7.59 (*ddd*, 2H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 7.99–8.14 (*m*, 6H, $H_{arom.}$) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 49.9, 55.5, 70.4, 70.6, 99.5, 119.0, 119.1, 122.0, 124.0, 128.7, 129.9, 131.6, 146.3, 147.9, 149.1, 155.9 ppm; UV-VIS (methanol) λ_{max} (log ε): 279 nm (4.96); MS (ESI, MeOH) *m*/*z*: 282.3 $[M + 2H]^{2+}$ (100%), 563.4 $[M + H]^+$ (99%); HRMS for $C_{34}H_{34}NO_4$ calcd.: 562.2580; found: 562.2580.

N,N-Bis-(2-trifluoromethoxy-9-acridinyl)-1,8-diamino-3,6-dioxaoctane ***6e***

Compound **6e** (0.36 g, 36%) was obtained from 9-chloro-2-trifluoromethoxyacridine (1.0 g, 3.4 mmol) and 1,8-diamino-3,6-dioxaoctane (0.22 g, 1.50 mmol) following GP2 as a yellow oil. IR (film) ν: 3386*m*, 2922*m*, 1631*s*, 1563*s*, 1522*s*, 1478*s*, 1431*s*, 1338*m*, 1259*s*, 1219*s*, 1162*s* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.62–3.80 (*m*, 8H, CH_2(2′, 4′, 5′, 7′)), 3.84–3.87 (*m*, 4H, CH_2(1′, 8′)), 5.50 (*br s*, 2H, *NH*), 7.34 (*ddd*, 2H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 7.51 (*dd*, 2H, *J* = 9.5, 2.5 Hz, H-C(3)), 7.64 (*ddd*, 2H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 7.95 (*d*, 2H, *J* = 2.5 Hz, H-C(1)), 8.02–8.14 (*m*, 6H, $H_{arom.}$) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 49.9, 70.3, 113.6, 117.1, 117.8, 120.6 (q, $J_{C,F}$ = 257.8 Hz) 122.1, 124.2, 124.5, 129.5, 130.2, 132.2, 144.4, 147.7, 149.6, 151.3 ppm; ^{19}F-NMR (188 MHz, $CDCl_3$) δ: −58.4 (*s*, OCF_3) ppm; UV-VIS (methanol) λ_{max} (log ε): 280 nm (5.00); MS (ESI, MeOH) *m*/*z*: 336.3 $[M + 2H]^{2+}$ (100%), 671.4 $[M + H]^+$ (45%); HRMS for $C_{34}H_{28}F_6NO_4$ calcd.: 670.2015; found: 670.2016.

N,N-Bis-(2,4-difluoro-9-acridinyl)-1,8-diamino-3,6-dioxaoctane ***6f***

Compound **6f** (0.36 g, 16%) was obtained from 9-chloro-2-trifluoromethoxyacridine (1.0 g, 4.0 mmol) and 1,8-diamino-3,6-dioxaoctane (0.27 g, 1.80 mmol) following GP2 as a yellow solid. M.p.: 115–116°C; IR (KBr) ν: 3056*m*, 2926*m*, 2873*m*, 1643*m*, 1604*w*, 1592*m*, 1565*s*, 1533*s*, 1514*s*, 1473*s*, 1433*s*, 1394*m*, 1334*m*, 1282*m*, 1240*m*, 1126*s*, 1514*s*, 1082*m*, 1031*w* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.69 (*t*, 4H, *J* = 4.5 Hz, CH_2(2′, 7′)), 3.73 (*s*, 4H, CH_2(4′, 5′)), 3.85–3.95 (*m*, 4H, CH_2(1′, 8′)), 5.45 (*br s*, 2H, *NH*), 7.18–7.25 (*m*, 2H, $H_{arom.}$), 7.36 (*ddd*, 2H, *J* = 8.3, 6.6, 0.9 Hz, $H_{arom.}$), 7.56 (*ddd*, 2H, *J* = 10.7, 2.1, 2.1 Hz, H-C(1)), 7.64 (*ddd*, 2H, *J* = 8.3, 6.6, 0.9 Hz, $H_{arom.}$), 8.05–8.20 (*m*, 4H, $H_{arom.}$) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 49.9, 70.3, 101.4, 105.3 (*dd*, $J_{C,F}$ = 31.0, 23.1 Hz), 118.3, 118.4, 122.3, 124.6, 130.1, 131.1, 137.7, 148.8, 150.4, 155.8, 158.1 ppm; ^{19}F-NMR (188 MHz, $CDCl_3$) δ: -113.7 (*m*, F), −118.2 (*m*, F) ppm; UV-VIS (methanol) λ_{max} (log ε): 278 nm (4.92); MS (ESI, MeOH) *m*/*z*: 575.5 $[M + H]^+$ (100%); HRMS for $C_{32}H_{28}F_2NO_2$ calcd.: 538.2180; found: 538.2182.

N,N-Bis-(4-thiomethyl-9-acridinyl)-1,8-diamino-3,6-dioxaoctane ***6g***

Compound **6g** (1.0 g, 80%) was obtained from 9-chloro-4-thiomethylacridine **3a** (1.2 g, 4.6 mmol) and 1,8-diamino-3,6-dioxaoctane (0.31 g, 2.10 mmol) following GP2 as a yellow solid. M.p.: 95–97°C; IR (KBr) ν: 2914*s*, 1622*s*, 1597*s*, 1565*s*, 1509*s*, 1457*s*, 1419*s*, 1336*m*, 1256*m*, 1123*s* cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.47 (*s*, 6H, SCH_3), 3.70 (*s*, 4H, CH_2(4′, 5′)), 3.74–3.80 (*m*, 4H, CH_2(2′, 7′)), 3.90–3.96 (*m*, 4H, CH_2(1′, 8′)), 7.16 (*dd*, 2H, *J* = 7.5, 7.1 Hz, $H_{arom.}$), 7.21–7.26 (*m*, 2H, $H_{arom.}$), 7.29 (*d*, 2H, *J* = 7.1 Hz, $H_{arom.}$), 7.53 (*ddd*, 2H, *J* = 7.5, 7.1, 1.3 Hz, $H_{arom.}$), 7.90–8.03 (*m*, 4H, $H_{arom.}$), 8.17 (*d*, 2H, *J* = 8.7 Hz, $H_{arom.}$) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 15.6, 50.0, 70.0, 70.2, 116.2, 116.8, 120.0, 122.9, 123.4, 130.4, 144.6, 146.1, 152.8, 154.9 ppm; UV-VIS (methanol) λ_{max} (log ε): 285 nm (4.88); MS (ESI, MeOH + TFA) *m*/*z*: 298.3 $[M + 2H]^{2+}$ (100%), 595.3 $[M + H]^+$ (75%); HRMS for $C_{34}H_{34}NO_2S_2$ calcd.: 594.2123; found: 594.2124.

N,N-Bis-(2-nitro-5-thiomethyl-9-acridinyl)-1,8-diamino-3,6-dioxaoctane ***6h***

Compound **6h** (0.26 g, 80%) was obtained from 9-chloro-2-nitro-5-thiomethylacridine **3b** (1.2 g, 3.9 mmol) and 1,8-diamino-3,6-dioxaoctane (0.23 g, 1.60 mmol) following GP2 as a red solid. M.p.: 205–207°C; IR (KBr) ν: 2921*s*, 1618*s*, 1598*s*, 1571*s*, 1515*s*, 1492*s*, 1435*m*, 1331*s*, 1309*s*, 1230*m*, 1130*m*, 1104*m* cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.43 (*s*, 6H, SCH_3), 3.55 (*s*, 4H, CH_2(4′, 5′)), 3.73 (*t*, 4H, *J* = 5.3 Hz, CH_2(2′, 7′)), 3.90–3.94 (*m*, 4H, CH_2(1′, 8′)), 7.25 (*dd*, 2H, *J* = 8.3, 7.5 Hz, H-C(7)), 7.33 (*d*, 2H, *J* = 7.5 Hz, H-C(6)), 7.77 (*d*, 2H, *J* = 9.2 Hz, H-C(4)), 7.98 (*d*, 2H, *J* = 8.3 Hz, H-C(8)), 8.14 (*dd*, 2H, *J* = 9.2, 2.4 Hz, H-C(3)), 9.26 (*d*, 2H, *J* = 2.4 Hz, H-C(1)) ppm; ^{13}C-NMR (125 MHz, 50°C, DMSO-d_6) δ: 13.4, 48.7, 69.2, 69.7, 114.7, 118.5, 122.0, 122.7, 123.7, 128.9, 130.0, 131.1, 139.6, 140.6, 146.8, 148.8, 154.1 ppm; UV-VIS (methanol) λ_{max} (log ε): 266 nm (4.53); MS (ESI, MeOH + TFA) *m*/*z*: 346.3 $[M + 2H]^{2+}$ (100%), 685.4 $[M + H]^+$ (100%); HRMS for $C_{34}H_{32}N_6O_6S_2$ calcd.: 684.1825; found: 684.1827.

N,N-Bis-(6-chloro-2-methoxy-9-acridinyl)-1,4-bis(3-aminopropyl)piperazine ***7a*** *[9], [25]*

Compound **7a** (0.5 g, 52%) was obtained 6,9-dichloro-2-methoxyacridine (1.0 g, 3.6 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.28 g, 1.4 mmol) following GP2 as a yellow solid. M.p.: 233–235°C (lit: 231–234°C [19]); IR (KBr) ν: 3284*s*, 2922*s*, 2819*s*, 1633*s*, 1606*m*, 1560*s*, 1516*s*, 1463*s*, 1442*m*, 1427*s*, 1375*w*, 1346*m*, 1307*w*, 1254*s*, 1238*s*, 1141*m*, 1071*w*, 1035*w*, 1002*w* cm^{-1}; ^{1}H-NMR (500 MHz, 80°C, DMSO-d_6) δ: 1.80–1.88 (*m*, 4H, CH_2(2′)), 2.23 (*s*, 8H, CH_2(pip.)), 2.34 (*t*, 4H, *J* = 6.9 Hz, CH_2(3′)), 3.75–3.82 (*m*, 4H, CH_2(1′)), 3.92 (*s*, 6H, OCH_3), 7.25 (*dd*, 2H, *J* = 9.1, 2.1 Hz, H-C(7)), 7.40 (*dd*, 2H, *J* = 9.5, 2.5 Hz, H-C(3)), 7.60 (*d*, 2H, *J* = 2.5 Hz, H-C(1)), 7.78–7.85 (*m*, 4H, H-C(5,8)), 8.31 (*d*, 2H, *J* = 9.5 Hz, H-C(4)) ppm; ^{13}C-NMR (125 MHz, 80°C, DMSO-d_6) δ: 27.2, 47.7, 52.3, 54.9, 55.4, 101.4, 114.4, 116.9, 122.1, 123.3, 124.0, 126.0, 129.3, 133.2, 147.3, 150.3, 154.8 ppm; UV-VIS (methanol) λ_{max} (log ε): 285 nm (4.23); MS (ESI, MeOH + TFA) *m*/*z*: 342.5 $[M + 2H]^{2+}$ (100%), 683.6 $[M + H]^+$ (40%).

N,N-Bis-9-acridinyl-1,4-bis-(3-aminopropyl)piperazine ***7b*** *[20], [26]*

Compound **7b** (0.84 g, 72%) was obtained from 9-chloroacridine (1.0 g, 4.7 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.42 g,

2.1 mmol) following GP2 as a yellow solid. M.p.: 250–251°C. IR (KBr) ν: 2935*m*, 2821*s*, 1616*s*, 1561*s*, 1519*s*, 1436*m*, 1396*m*, 1338*m*, 1310*w*, 1267*m*, 1139*m*, 1023*w* cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.00–2.05 (*m*, 4H, CH_2(2′)), 2.65–2.85 (*m*, 12H, CH_2(11,12)), 4.03–4.09. (*m*, 4H, CH_2(1′)), 7.32 (*ddd*, 4H, *J* = 8.7, 6.4, 0.9 Hz, H-C(2)), 7.66 (*ddd*, 4H, *J* = 8.7, 6.4, 0.9 Hz, H-C(3)), 8.05–8.12 (*m*, 4H, H-C(4)) 8.24 (*dd*, 4H, *J* = 8.7, 0.9 Hz, H-C(1)) ppm; ^{13}C-NMR (125 MHz, 45°C, DMSO-d_6) δ 27.2, 48.7, 52.6, 55.6, 112.4, 122.0, 123.5, 125.6, 131.2, 145.9, 152.1 ppm; UV-VIS (methanol) λ_{max} (log ε): 281 nm (4.93); MS (ESI, MeOH + TFA) *m*/*z*: 278.4 $[M + 2H]^{2+}$ (100%), 555.5 $[M + H]^+$ (18%); HRMS for $C_{36}H_{38}N_6$ calcd.: 554.3158; found: 554.3157.

N,N-Bis-(2-methoxy-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7c***

Compound **7c** (0.67 g, 61%) was obtained from 9-chloro-2-methoxyacridine (1.0 g, 4.1 mmol) and 1,4-bis-(3-aminopropyl)-piperazine (0.26 g, 1.8 mmol) following GP2 as a yellow solid. M.p.: 191–192°C; IR (KBr) ν: 2924*s*, 2815*s*, 1632*s*, 1561*s*, 1517*s*, 1488*s*, 1467*m*, 1426*s*, 1352*m*, 1308*w*, 1270*m*, 1233*s*, 1139*m*, 1034*m* cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 1.76–1.86 (*m*, 4H, CH_2(2′)), 2.18 (br *s*, 8H, CH_2(pip.)), 2.29 (*t*, 4H, *J* = 6.6 Hz, CH_2(3′)), 3.70–3.80 (*m*, 4H, CH_2(1′)), 3.90 (*s*, 6H, OCH_3), 6.73 (*br s*, 2H, *NH*), 7.30 (*ddd*, 2H, *J* = 7.8, 7.0, 1.2 Hz, $H_{arom.}$), 7.37 (*dd*, 2H, *J* = 8.7, 2.1 Hz, H-C(3)), 7.55–7.62 (*m*, 4H, $H_{arom.}$), 7.78–7.88 (*m*, 4H, $H_{arom.}$), 8.29 (*d*, 2H, *J* = 8.7 Hz, H-C(4)) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 27.5, 47.9, 52.6, 55.3, 55.5, 100.3, 116.4, 116.8, 120.0, 121.7, 122.2, 122.7, 123.3, 123.8, 128.5, 147.9, 150.0, 154.5 ppm; UV-VIS (methanol) λ_{max} (log ε): 289 nm (4.81); MS (ESI, MeOH + TFA) *m*/*z*: 308.4 $[M + 2H]^{2+}$ (100%), 615.6 $[M + H]^+$ (20%); HRMS for $C_{38}H_{32}N_6O_2$ calcd.: 614.3369; found: 614.3370.

N,N-Bis-(2-trifluoromethoxy-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7d***

Compound **7d** (0.14 g, 15%) was obtained from 9-chloro-2-trifluoromethoxyacridine (1.0 g, 3.4 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.30 g, 1.5 mmol) following GP2 as a yellow solid. M.p.: 200–201°C; IR (KBr) ν: 2925*m*, 2825*m*, 1618*m*, 1561*s*, 1517*s*, 1439*m*, 1356*m*, 1266*s*, 1218*s*, 1143*s*, 1004*w* cm^{-1}; ^{1}H-NMR (500 MHz, 80°C, DMSO-d_6) δ: 1.82–1.90 (*m*, 4H, CH_2(2′)), 2.27 (br *s*, 8H, CH_2(pip.)), 2.37 (*t*, 4H, *J* = 6.6 Hz, CH_2(3′)), 3.80–3.90 (*t*, 4H, CH_2(1′)), 7.25–7.32 (*m*, 2H, $H_{arom.}$), 7.50–7.90 (*m*, 8H, $H_{arom.}$), 8.20–8.30 (*m*, 4H, $H_{arom.}$) ppm; ^{13}C-NMR (125 MHz, 80°C, DMSO-d_6) δ: 27.2, 48.3, 52.3, 55.2, 115.3, 120.7 (q, $J_{C,F}$ = 263.2 Hz), 121.8, 123.2, 129.7, 142.2, 151.3 ppm; ^{19}F-NMR (188 MHz, DMSO-d_6) δ: −57.5 (*s*, OCF_3) ppm; UV-VIS (methanol) λ_{max} (log ε): 285 nm (4.77); MS (ESI, MeOH) *m*/*z*: 362.3 $[M + 2H]^{2+}$ (100%), 723.5 $[M + H]^+$ (30%), HRMS for $C_{38}H_{36}F_6N_6O_2$ calcd.: 722.2804; found: 722.2805.

N,N-Bis-(2,4-difluoro-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7e***

Compound **7e** (0.08 g, 7%) was obtained from 9-chloro-2,4-difluoroacridine (1.0 g, 4.0 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.36 g, 1.8 mmol) following GP2 as a yellow solid. M.p.: 220–221°C; IR (KBr) ν: 1626*s*, 1593*s*, 1540*m*, 1472*m*, 1329*m*, 1290*m*, 1199*w*, 1138*m*, 1006*w* cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 2.28–2.34 (*m*, 4H, CH_2(2′)), 3.25 (*t*, 4H, *J* = 6.6 Hz, CH_2(3′)), 3.47 (br *s*, 8H, CH_2(pip.)), 4.10–4.20 (*m*, 4H, CH_2(1′)), 7.49 (*ddd*, 2H, *J* = 8.7, 6.6, 0.9 Hz, H-C(6 oder 7)), 7.62 (*ddd*, 2H, *J* = 10.7, 8.7, 2.1 Hz, H-C(3)), 7.75 (*d*, 2H, *J* = 8.7 Hz, $H_{arom.}$), 7.83–7.91 (*m*, 4H, $H_{arom.}$), 8.23 (*d*, 2H, *J* = 8.7 Hz, $H_{arom.}$) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 23.9, 45.7, 49.1, 53.9, 109.9 (*ddd*, $J_{C,F}$ = 30.5, 21.2 Hz), 111.9, 113.4, 118.4, 124.6, 135.9, 136.2, 139.4, 151.6 (*dd*, $J_{C,F}$ = 253.3, 13.3 Hz), 156.8 (*dd*, $J_{C,F}$ = 254.0, 13.3 Hz), 157.4 ppm; ^{19}F-NMR (188 MHz, $CDCl_3$) δ: -115.7 (*m*, F), −119.6 (*m*, F) ppm; UV-VIS (methanol) λ_{max} (log ε): 284 nm (4.88); MS (ESI, MeOH) *m*/*z*: 314.3 $[M + 2H]^{2+}$ (70%), 627.5 $[M + H]^+$ (100%); HRMS for $C_{36}H_{36}F_2N_6$ calcd.: 590.2970; found: 590.2971.

N,N -Bis-(5-methoxy-3-nitro-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7f***

Compound **7f** (0.22 g, 17%) was obtained from 9-chloro-5-methoxy-3-nitro-acridine (1.2 g, 4.2 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.38 g, 1.9 mmol) following GP2 as a red solid. M.p.: 250°C (dec.); IR (KBr) ν: 2925*s*, 1626*s*, 1577*s*, 1542*s*, 1473*m*, 1350*s*, 1268*s*, 1101*s* cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 2.31–2.45 (*m*, 4H, CH_2(2′)), 3.40–3.60 (*m*, 12H, CH_2(3′, pip.)), 4.15 (s, 6H, OCH_3), 4.19–4.29 (*m*, 4H, CH_2(1′)), 7.55 (*dd*, 2H, *J* = 8.5, 7.9 Hz, H-C(7)), 7.60 (*d*, 2H, *J* = 7.9 Hz, H-C(1)), 8.15 (*dd*, 2H, *J* = 7.9, 2.4 Hz, H-C(2)), 8.18–8.34 (*m*, 2H, $H_{arom.}$), 8.84–9.00 (*m*, 2H, $H_{arom.}$), 9.20 (*d*, 2H, *J* = 2.4 Hz, H-C(4)) ppm; ^{13}C-NMR (125 MHz, 80°C, DMSO-d_6) δ: 29.0, 48.3, 53.0, 56.0, 56.4, 113.3, 114.5, 114.6, 117.0, 121.6, 121.9, 123.3, 128.2, 132.3, 140.3, 148.0, 150.0, 157.8 ppm; UV-VIS (methanol) λ_{max} (log ε): 289 nm (4.75); MS (ESI, MeOH) *m*/*z*: 353.3 $[M + 2H]^{2+}$ (100%), 700.5 $[M + H]^+$ (45%); HRMS for $C_{38}H_{40}N_8O_6$ calcd.: 704.3071; found: 704.3072.

N,N-Bis-(2-methoxy-6-nitro-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7g***

Compound **7g** (0.22 g, 17%) was obtained from 9-chloro-2-methoxy-6-nitro-acridine (1.2 g, 4.2 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.38 g, 1.90 mmol) following GP2 as a red solid. M.p.: 262°C (dec.); IR (KBr) ν: 2925*s*, 2830*m*, 1634*s*, 1573*s*, 1540*s*, 1515*s*, 1482*m*, 1430*m*, 1342*s*, 1236*s*, 1139*m*, 1077*m*, 1030*m* cm^{-1}; ^{1}H-NMR (500 MHz, 80°C, DMSO-d_6) δ: 1.84–1.97 (*m*, 4H, CH_2(2′)), 2.25 (*br s*, 8H, CH_2(pip.)), 2.37 (*t*, 4H, *J* = 6.6 Hz, CH_2(3′)), 3.80–3.90 (*m*, 4H, CH_2(1′)), 3.96 (*s*, 6H, OCH_3), 7.42 (*dd*, 2H, *J* = 7.5, 2.5 Hz, H-C(3)), 7.66 (*d*, 2H, *J* = 2.5 Hz, H-C(1)), 7.86–7.98 (*m*, 4H, $H_{arom.}$), 8.51 (*d*, 2H, *J* = 9.1 Hz, H-C(4)), 8.60–8.70 (*m*, 2H, H_{arom}) ppm; ^{13}C-NMR (125 MHz, 45°C, DMSO-d_6) δ: 28.4, 47.8, 52.0, 55.4, 55.7, 101.1, 105.0, 113.3, 113.7, 114.0, 114.6, 119.4 124.5, 125.0, 125.9, 126.6, 150.0, 155.8 ppm; UV-VIS (methanol) λ_{max} (log ε): 287 nm (4.85); MS (ESI, MeOH) *m*/*z*: 353.3 $[M + 2H]^{2+}$ (100%), 700.5 $[M + H]^+$ (25%); HRMS for $C_{38}H_{40}N_8O_6$ calcd.: 704.3071; found: 704.3072.

N,N-Bis-(2,4-dimethoxy-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7h***

Compound **7h** (1.1 g, 65%) was obtained from 9-chloro-2,4-dimethoxy-acridine (1.5 g, 5.5 mmol) and 1,4-bis-(3-aminopropyl)-piperazine (0.50 g, 2.50 mmol) following GP2 as a yellow solid. M.p.: 224°C; IR (KBr) ν: 2934*s*, 1628*s*, 1570*m*, 1530*s*, 1466*s*, 1422*s*, 1343*m*, 1285*s*, 1209*m*, 1159*s*, 1056*w* cm^{-1}; ^{1}H-NMR(400 MHz, $CDCl_3$) δ: 1.92–2.00 (*m*, 4H, CH_2(2′)), 2.55–2.65 (*m*, 12H, CH_2(3′, pip.)), 3.73–3.83 (*m*, 4H, CH_2(1′)), 3.94 (*s*, 6H, OCH_3), 4.07 (*s*, 6H, OCH_3), 6.69 (*d*, 2H, *J* = 2.5 Hz, $H_{arom.}$), 6.95 (*d*, 2H, *J* = 2.5 Hz, $H_{arom.}$), 7.37 (*ddd*, 2H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 7.60 (*ddd*, 2H, *J* = 8.7, 6.6, 1.2 Hz, $H_{arom.}$), 8.16 (*d*, 2H, *J* = 8.7 Hz, $H_{arom.}$), 8.21 (*d*, 2H, *J* = 8.7 Hz, $H_{arom.}$) ppm; ^{13}C-NMR(100 MHz, $CDCl_3$) δ: 27.3, 50.0, 53.5, 55.5, 56.2, 57.4, 92.3, 101.2, 118.2, 118.3, 122.3, 123.8, 128.4, 130.15,

139.2, 146.6, 150.1, 155.5, 156.1 ppm; UV-VIS (methanol) λ_{max} (log ε): 286 nm (4.82); MS (*ESI*, MeOH) *m/z*: 339.0 $[M + 2H]^{2+}$ (25%), 675.7 $[M + H]^+$ (100%); HRMS for $C_{40}H_{46}N_6O_4$ calcd.: 674.3581; found: 674.3582.

N,N-Bis-(2,4-dimethoxy-6-nitro-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7i***

Compound **7i** (0.6 g, 42%) was obtained from 9-chloro-2,4-dimethoxy-6-nitro-acridine (1.3 g, 4.2 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.38 g, 1.90 mmol) following GP2 as a red solid. M.p.: 155°C; IR (KBr) ν: 2935*s*, 2832*s*, 1630*s*, 1615*s*, 1568*s*, 1519*s*, 1466*s*, 1432*s*, 1373*m*, 1341*s*, 1292*s*, 1209*s*, 1165*s*, 1148*s*, 1108*s*, 1048*m*, 1006*m* cm^{-1}; ^{1}HNMR (400 MHz, CD_3OD) δ: 2.42–2.52 (*m*, 4H, $CH_2(2')$), 3.30 (*br s*, 8H, CH_2(pip.)), 3.40 (*t*, 4H, *J* = 6.6 Hz, $CH_2(3')$), 3.98 (*s*, 6H, OCH_3), 4.14 (*s*, 6H, OCH_3), 4.24–4.33 (*m*, 4H, $CH_2(1')$), 7.14 (*d*, 2H, *J* = 2.5 Hz, $H_{arom.}$), 7.38 (*d*, 2H, *J* = 2.5 Hz, $H_{arom.}$), 8.16 (*dd*, 2H, *J* = 9.5, 2.5 Hz, H-C(7)) 8.64 (*d*, 2H, *J* = 9.5 Hz, H-C(8)), 9.00 (*d*, 2H, *J* = 2.5 Hz, H-C(5)) ppm; ^{13}C-NMR (125 MHz, 45°C, DMSO-d_6) δ: 29.6, 48.5, 53.3, 56.3, 56.7, 57.4, 92.8, 103.4, 114.8, 115.5, 119.6, 127.0, 127.4, 140.4, 145.6, 147.6, 155.7, 156.9, 157.4 ppm; UV-VIS (methanol) λ_{max} (log ε): 287 nm (4.85); MS (ESI, MeOH) *m/z*: 383.3 $[M + 2H]^{2+}$ (100%), 765.5 $[M + H]^+$ (20%); HRMS for $C_{40}H_{44}N_8O_8$ calcd.: 764.3282; found: 764.3284.

N,N-Bis-(3-fluoro-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7j***

Compound **7j** (0.74 g, 36%) was obtained from 9-chloro-3-fluoroacridine (2.0 g, 8.6 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.70 g, 3.50 mmol) following GP2 as a red solid. M.p.: 270°C (dec.); IR (KBr) ν: 3238*m*, 3045*m*, 2938*m*, 2823*m*, 2610*m*, 1639*s*, 1591*s*, 1540*s*, 1477*s*, 1362*m*, 1270*s*, 1189*m*, 1161*m*, 1142*m*, 1116*w*, 1098*w*, 1082*w* cm^{-1}; ^{1}H-NMR (500 MHz, 80°C, DMSO-d_6) δ: 1.92–2.02 (*m*, 4H, $CH_2(2')$), 2.38 (*br s*, 8H, CH_2(pip.)), 3.22–3.31 (*m*, 4H, $CH_2(3')$), 3.99–4.07 (*m*, 4H, $CH_2(1')$), 7.25 (*ddd*, 2H, *J* = 9.5, 7.5, 2.5 Hz, $H_{arom.}$), 7.37–7.44 (*m*, 2H, $H_{arom.}$), 7.50 (*dd*, 2H, *J* = 10.4, 2.5 Hz, H-C(4)), 7.75–7.82 (*m*, 4H, $H_{arom.}$), 8.41 (*d*, 2H, *J* = 8.5 Hz, $H_{arom.}$), 8.50 (*d*, 2H, *J* = 9.1, 6.1 Hz, H-C(1)) ppm; ^{13}C-NMR (125 MHz, 80°C, DMSO-d_6) δ: 27.5, 49.5, 52.2, 55.1, 105.3, 121.1, 122.0, 122.5, 124.2, 124.8, 127.7, 129.3, 129.8, 130.3, 151.2, 158.5 (*d*, $J_{C,F}$ = 250.9 Hz), 160.7 ppm; ^{19}F-NMR (188 MHz, DMSO-d_6) δ: −112.0 (*m*, F) ppm; UV-VIS (methanol) λ_{max} (log ε): 283 nm (4.99); MS (ESI, MeOH) *m/z*: 296.3 $[M + 2H]^{2+}$ (100%), 591.5 $[M + H]^+$ (30%); HRMS for $C_{36}H_{36}F_2N_6$ calcd.: 590.2970; found: 590.2970.

N,N-Bis-(1-fluoro-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7k***

Compound **7k** (0.71 g, 47%) was obtained from 9-chloro-1-fluoroacridine (1.5 g, 6.5 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.52 g, 2.60 mmol) following GP2 as a yellow solid. M.p.: 182°C; IR (KBr) ν: 3252*s*, 2919*s*, 2822*s*, 1633*m*, 1613*m*, 1555*s*, 1513*s*, 1461*s*, 1435*m*, 1386*m*, 1357*m*, 1341*m*, 1312*m*, 1272*w*, 1229*w*, 1210*w*, 1131*m*, 1028*w*, 1019*m* cm^{-1}; ^{1}H-NMR (500 MHz, 80°C, DMSO-d_6) δ: 1.74–1.84 (*m*, 4H, $CH_2(2')$), 2.22 (*s*, 8H, CH_2(pip.)), 2.32 (*t*, 4H, *J* = 6.7 Hz, $CH_2(3')$), 3.63–3.73 (*m*, 4H, $CH_2(1')$), 6.93 (*dd*, 2H, *J* = 12.8, 7.9 Hz, $H_{arom.}$), 7.23 (*dd*, 2H, *J* = 7.3, 7.3 Hz, $H_{arom.}$), 7.40–7.64 (*m*, 8H, $H_{arom.}$), 8.13 (*d*, 2H, *J* = 7.9 Hz, $H_{arom.}$) ppm; ^{13}C-NMR (125 MHz, 45°C, DMSO-d_6) δ: 23.1, 45.7, 47.7, 52.9, 55.4, 102.9, 109.2, 111.4, 112.9, 118.2, 123.7, 125.7, 135.1 135.7, 139.3, 141.6, 157.4, 165.1 (*d*, $J_{C,F}$ = 251.6 Hz) ppm; ^{19}F-NMR (188 MHz, 50°C, DMSO-d_6) δ: −101.8 (*m*, F) ppm; UV-VIS (methanol) λ_{max} (log ε): 282 nm (5.03); MS (ESI, MeOH) *m/z*: 296.3 $[M + 2H]^{2+}$ (100%), 591.5 $[M + H]^+$ (40%); HRMS for $C_{36}H_{36}F_2N_6$ calcd.: 590.2970; found: 590.2969.

N,N-Bis-(2-trifluoromethoxy-7-nitro-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7l***

Compound **7l** (0.07 g, 12%) was obtained from 9-chloro-2-trifluoromethoxy-7-nitroacridine (0.6 g, 1.8 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.14 g, 0.70 mmol) following GP2 as a red solid. M.p.: 221°C (dec.); IR (KBr) ν: 2944*m*, 2822*m*, 1618*m*, 1578*s*, 1524*s*, 1490*s*, 1450*m*, 1324*s*, 1253*s*, 1222*s*, 1205*s*, 1170*s*, 1102*m*, 1011*w* cm^{-1}; ^{1}H-NMR (400 MHz, 50°C, CD_3OD) δ: 2.03–2.13 (*m*, 4H, *J* = 6.6 Hz, $CH_2(2')$), 2.48 (br *s*, 8H, CH_2(pip.)), 2.50–2.60 (*m*, 4H, $CH_2(3')$), 4.02–4.12 (*m*, 4H, $CH_2(1')$), 7.63 (*dd*, 2H, *J* = 9.5, 2.5 Hz, H-C(3)), 7.75 (*d*, 2H, *J* = 9.5 Hz, $H_{arom.}$), 7.85 (*d*, 2H, *J* = 9.5 Hz, $H_{arom.}$), 8.20 (*d*, 2H, *J* = 2.5 Hz, H-C(1)), 8.33 (*dd*, 2H, *J* = 9.5, 2.5 Hz, H-C(6)), 9.27 (*d*, 2H, *J* = 2.5 Hz, H-C(8)) ppm; ^{13}C-NMR (125 MHz, 90°C, DMSO-d_6) δ: 28.9, 49.9, 53.5, 56.2, 114.0, 115.7, 121.1 (*q*, $J_{C,F}$ = 250.0 Hz), 123.1, 123.9, 125.4, 126.6, 141.2, 143.9, 149.8, 154.5 ppm; ^{19}F-NMR (188 MHz, DMSO-d_6) δ: −60.0 (*s*, OCF_3) ppm; UV-VIS (methanol) λ_{max} (log ε): 262 nm (4.65); MS (ESI, MeOH) *m/z*: 407.3 $[M + 2H]^{2+}$ (10%), 813.4 $[M + H]^+$ (100%); HRMS for $C_{36}H_{34}F_6N_8O_6$ calcd.: 812.2506; found: 812.2505.

N,N-Bis-(3-chloro-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7m***

Compound **7m** (0.66 g, 44%) was obtained from 3,9-dichloroacridine (1.5 g, 6.0 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.48 g, 2.40 mmol) following GP2 as a yellow solid. M.p.: 182°C (dec.); IR (KBr) ν: 3287*s*, 2925*m*, 2824*m*, 1607*s*, 1563*s*, 1521*s*, 1449*s*, 1383*w*, 1355*m*, 1343*m*, 1310*m*, 1252*m*, 1140*m*, 1080*m*, 1028*w* cm^{-1}; ^{1}H-NMR (400 MHz, 50°C, CD_3OD) δ: 2.42–2.52 (*m*, 4H, $CH_2(2')$), 3.50–3.59 (m, 12H, $CH_2(3'$, pip.)), 4.27–4.38 (*m*, 4H, $CH_2(1')$), 7.55 (*d* 2H, *J* = 8.7 Hz, $H_{arom.}$), 7.61 (*dd*, 2H, *J* = 7.9, 7.1 Hz, $H_{arom.}$), 7.79–7.85 (*m*, 4H, $H_{arom.}$), 7.99 (*dd*, 2H, *J* = 7.9, 7.1 Hz, $H_{arom.}$), 8.57 (*m*, 4H, $H_{arom.}$) ppm; UV-VIS (methanol) λ_{max} (log ε): 289 nm (4.54); MS (ESI, MeOH) *m/z*: 312.4 $[M + 2H]^{2+}$ (100%), 623.4 $[M + H]^+$ (40%); HRMS for $C_{36}H_{36}Cl_2N_6$ calcd.: 622.2379; found: 622.2379.

N,N-Bis-(2,3,4-trifluoro-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7n***

Compound **7n** (0.26 g, 17%) was obtained from 9-chloro-2,3,4-trifluoroacridine (1.5 g, 5.6 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.46 g, 2.30 mmol) following GP2 as a yellow solid. M.p.: 224°C; IR (KBr) ν: 2925*m*, 1629*s*, 1596*s*, 1544*m*, 1518*m*, 1481*m*, 1402*m*, 1300*m*, 1262*m*, 1150*m*, 1065*m* cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD) δ: 2.42–2.52 (*m*, 4H, $CH_2(2')$), 3.34 (*br s*, 4H, $CH_2(3')$), 3.58 (br *s*, 8H, CH_2(pip.)), 4.30–4.40 (*m*, 4H, $CH_2(1')$), 7.62–7.68 (*m*, 2H, $H_{arom.}$), 8.00–8.05 (*m*, 4H, $H_{arom.}$), 8.44–8.57 (*m*, 4H, $H_{arom.}$) ppm; ^{13}C-NMR (125 MHz, 80°C, DMSO-d_6) δ: 25.5 (*t*, $CH_2(2')$), 47.9 (*t*, $CH_2(1')$), 50.7 (*t*, CH_2(pip.)), 55.1 (*t*, $CH_2(3')$), 108.5, 110.1, 114.0, 117.1, 119.9, 126.0, 130.3, 131.1, 137.3, 141.7 (*dd*, $J_{C,F}$ = 254.0, 15.7 Hz), 147.0, 144.6 (*dd*, $J_{C,F}$ = 250.4, 12.0 Hz), 146.5 (*dd*, $J_{C,F}$ = 250.1, 10.7 Hz), 149.6, 159.5 ppm; ^{19}F-NMR (188 MHz, DMSO-d_6) δ: −139.4 (*m*, F), −150.6 (*m*, F), −151.8 (*m*, F) ppm; UV-VIS (methanol) λ_{max} (log ε): 283 nm (4.81); MS (ESI, MeOH) *m/z*: 332.3 $[M + 2H]^{2+}$ (20%), 663.4 $[M + H]^+$ (100%); HRMS for $C_{36}H_{32}F_6N_6$ calcd.: 662.2593; found: 662.2593.

N,N-Bis-(4-methoxy-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7o***

Compound **7o** (1.23 g, 82%) was obtained from 9-chloro-4-methoxyacridine (1.5 g, 6.2 mmol) and 1,4-bis-(3-aminopropyl)-piperazine (0.50 g, 2.50 mmol) following GP2 as a yellow solid. M.p.: 194°C; IR (KBr) ν: 3252*s*, 2914*s*, 2826*s*, 1614*m*, 1570*s*, 1524*s*, 1467*s*, 1431*s*, 1331*m*, 1312*m*, 1269*s*, 1249*s*, 1134*s*, 1083*s*, 1025*w* cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 1.80–1.88 (*m*, 4H, CH_2(2′)), 2.31 (*br s*, 8H, CH_2(pip.)), 2.38 (*t*, 4H, *J* = 6.7 Hz, CH_2(3′)), 3.81–3.86 (*m*, 4H, CH_2(1′)), 3.96 (*s*, 6H, OCH_3), 7.06 (*d*, 2H, *J* = 7.5 Hz, $H_{arom.}$), 7.18 (*dd*, 2H, *J* = 7.9 Hz, $H_{arom.}$), 7.27 (*dd*, 2H, *J* = 7.9 Hz, $H_{arom.}$), 7.80–7.88 (*m*, 4H, $H_{arom.}$), 8.28 (*d*, 2H, *J* = 8.7 Hz, $H_{arom.}$) ppm; ^{13}C-NMR (125 MHz, 80°C, DMSO-d_6) δ: 27.3, 48.8, 52.4, 55.5, 55.6, 108.1, 116.0, 116.7, 117.3, 120.9, 121.4, 124.3 125.7, 129.1, 138.7, 145.4, 151.3, 152.7 ppm; UV-VIS (methanol) λ_{max} (log ε): 284 nm (5.25); MS (ESI, MeOH) *m*/*z*: 308.4 $[M + 2H]^{2+}$ (100%), 615.5 $[M + H]^+$ (40%); HRMS for $C_{38}H_{42}N_6O_2$ calcd.: 614.3369; found: 614.3369.

N,N-Bis-(4-thiomethyl-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7p***

Compound **7p** (0.84 g, 62%) was obtained from 9-chloro-4-thiomethylacridine **3a** (1.2 g, 4.6 mmol) and 1,4-bis-(3-aminopropyl)-piperazine (0.42 g, 2.10 mmol) following GP2 as a yellow solid. M.p.: 177–178°C; IR (KBr) ν: 2921*s*, 2819*s*, 1618*s*, 1599*m*, 1557*m*, 1511*s*, 1456*m*, 1437*s*, 1336*m*, 1306*m*, 1257*m*, 1137*s* cm^{-1}; ^{1}H-NMR (400 MHz, 50°C, DMSO-d_6) δ: 1.80–1.94 (*m*, 4H, CH_2(2′)), 2.34 (s, 6H, SCH_3), 2.40–2.54 (*m*, 12H, CH_2(3′, pip.)), 3.81–3.90 (*m*, 4H, CH_2(1′)), 7.23–7.40 (*m*, 6H, $H_{arom.}$), 7.65 (*dd*, 2H, *J* = 7.9, 7.5 Hz, $H_{arom.}$), 7.89 (*d*, 2H, *J* = 7.9 Hz, $H_{arom.}$), 8.08 (*d*, 2H, *J* = 8.7 Hz, $H_{arom.}$), 8.35 (*d*, 2H, *J* = 8.7 Hz, $H_{arom.}$) ppm; ^{13}C-NMR (125 MHz, 90°C, DMSO-d_6) δ: 17.6, 26.3, 47.9, 51.7, 54.8, 114.9, 115.8, 119.2, 121.6, 122.0, 123.2, 123.6, 128.0, 129.4, 138.0, 145.2, 146.9, 151.8 ppm; UV-VIS (methanol) λ_{max} (log ε): 287 nm (4.00); MS (ESI, MeOH) *m*/*z*: 325.1 $[M + 2H]^{2+}$ (100%), 647.5 $[M + H]^+$ (20%); HRMS for $C_{38}H_{42}N_6S_2$ calcd.: 646.2912; found: 646.2910.

N,N-Bis-(3-chloro-5-methoxy-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7q***

Compound **7q** (1.0 g, 57%) was obtained from 3,9-dichloro-5-methoxyacridine (1.5 g, 6.1 mmol) and 1,4-bis-(3-aminopropyl)-piperazine (0.50 g, 2.50 mmol) following GP2 as a yellow solid. M.p.: 224–225°C; IR (KBr) ν: 2930*s*, 2826*s*, 1618*s*, 1564*s*, 1522*s*, 1458*s*, 1437*s*, 1348*m*, 1310*m*, 1250*s*, 1147*m*, 1084*s* cm^{-1}; ^{1}H-NMR (400 MHz, 45°C, $CDCl_3$) δ: 1.92–2.00 (*m*, 4H, CH_2(2′)), 2.66–2.74 (*m*, 12H, CH_2(3′, pip.)), 3.94–3.98 (*m*, 4H, CH_2(1′)), 4.08 (*s*, 6H, OCH_3), 6.97 (*d*, 2H, *J* = 7.5 Hz, $H_{arom.}$), 7.17–7.23 (*m*, 4H, $H_{arom.}$), 7.73 (*d*, 2H, *J* = 8.7 Hz, $H_{arom.}$), 8.11–8.16 (*m*, 4H, $H_{arom.}$); ^{13}C-NMR (125 MHz, 50°C, DMSO-d_6) δ: 27.2, 47.7, 52.3, 54.9, 56.3, 101.4, 114.4, 116.9, 122.1, 123.3, 124.0, 126.0, 129.3, 133.2, 147.3, 150.3, 154.8 ppm; UV-VIS (methanol) λ_{max} (log ε): 288 nm (4.64); MS (ESI, MeOH + TFA) *m*/*z*: 342.4 $[M + 2H]^{2+}$ (40%), 683.6 $[M + H]^+$ (100%); HRMS for $C_{38}H_{40}Cl_2N_6O_2$ calcd.: 682.2590; found: 682.2591.

N,N-Bis-(2-nitro-5-thiomethyl-9-acridinyl)-1,4-bis-(3-aminopropyl)piperazine ***7r***

Compound **7r** (0.5 g, 45%) was obtained from 9-chloro-2-nitro-5-thiomethylacridine **3b** (1.2 g, 3.9 mmol) and 1,4-bis-(3-aminopropyl)piperazine (0.30 g, 1.50 mmol) following GP2 as an orange-colored solid. M.p.: 246–248°C; IR (KBr) ν: 2923*s*, 1631*s*, 1598*s*, 1545*s*, 1521*s*, 1478*s*, 1437*s*, 1336*s*, 1240*m*, 11182*m*, 1137*m*, 1102*w* cm^{-1}; ^{1}H-NMR (400 MHz, 50°C, DMSO-d_6) δ: 2.40–2.44 (*m*, 4H, CH_2(2′)), 2.63 (*s*, 6H, SCH_3), 3.20–3.40 (*m*, 12H, CH_2(3′, pip.)), 4.22–4.28 (*m*, 4H, CH_2(1′)), 7.56 (*dd*, 2H, *J* = 8.3, 7.5 Hz, H-C(7)), 8.06 (*d*, 2H, *J* = 7.5 Hz, H-C(6)), 8.43–8.62 (*m*, 6H, $H_{arom.}$), 9.42 (*br s*, 2H, H-C(1)) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 17.6, 22.9, 46.7, 53.0, 56.0, 113.0, 119.2, 120.3, 121.2, 122.4, 123.0, 124.8, 125.7, 127.2, 136.1, 139.1, 141.2, 144.5 ppm; UV-VIS (methanol) λ_{max} (log ε): 283 nm (4.64); MS (ESI, MeOH + TFA) *m*/*z*: 369.3 $[M + 2H]^{2+}$ (25%), 737.4 $[M + H]^+$ (100%); HRMS for $C_{36}H_{40}N_8O_4S_2$ calcd.: 736.2614; found: 736.2615.

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