Photoswitchable Macrocycles Incorporating Acridane Moieties

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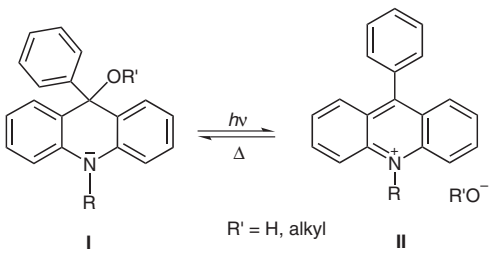
Abstract: Novel crown ethers incorporating one to three 9-phenylacridinium units were synthesized in moderate yields. The acridinium units within the macrocycles were converted into the photoactive *N*-methyl-9-methoxy-9-phenyl-9,10-dihydroacridine (*N*-methyl-9-methoxy-9-phenylacridane) units.

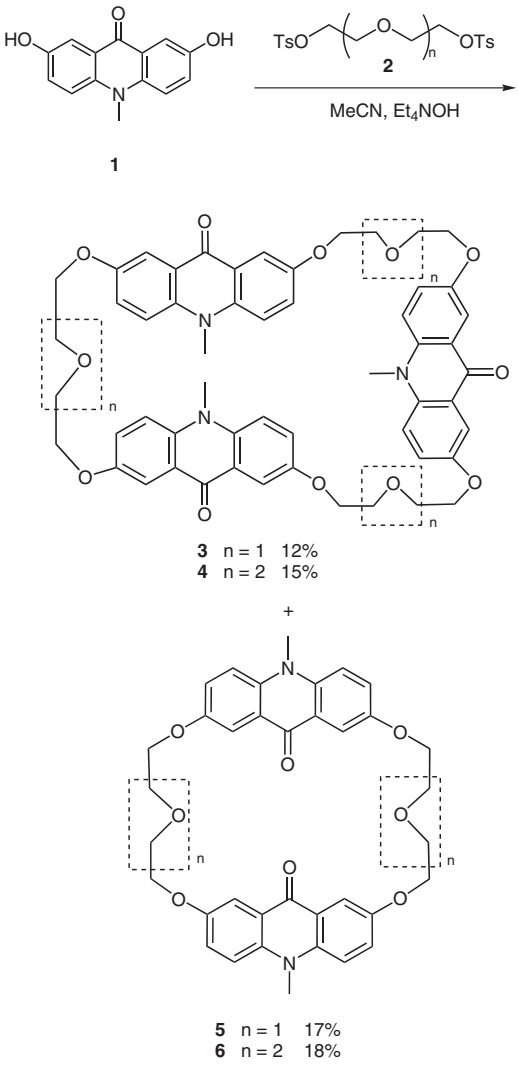
Key words: macrocycles, crown compounds, acridinium, acridane, heterocycles

Acridine and its derivatives are well-known DNA-intercalating compounds. Molecular recognition of nucleotides by cyclic receptors containing acridine subunits has been reported.[1] Macrocyclic receptors containing positively charged aromatic subunits, such as acridinium ions, linked by one or two bridges may bind to planar aromatic substrates by intercalation. We were interested in macrocyclic receptors bearing photoswitchable subunits because it would be useful to switch on and off the binding properties by means of an outside stimulus and thereby control the interaction between host and guest. These photoswitchable subunits should undergo drastic change in their shape and electronic properties, which should alter the binding properties of the macrocycle. We decided to synthesize macrocycles containing acridinium subunits of the type **II** and the corresponding acridane derivatives **I**, respectively. 9-Phenyl-9-hydroxyacridane **I** (Scheme 1) is known to convert into the corresponding acridinium hydroxide in the excited singlet state. The rate of the thermal back reaction depends strongly on the solvent properties.[2,3]

In this paper we describe, for the first time, the preparation of macrocycles incorporating the switchable acridane subunit. The synthon **1** was used to prepare crown ethers containing the 9-acridinone subunit incorporated along its longest diameter (Scheme 2). The reactions were carried out under highly dilute conditions in order to favor macrocycle formation.[4]



Scheme 1



Scheme 2

Surprisingly, macrocycles containing two and three acridinone moieties were obtained. A macrocycle **8**, incorporating two different recognition sites – the catechol and the acridinone units – could be obtained by the reaction of **1** with **7** (Scheme 3). The lateral incorporation of the acridinone moiety was possible using the synthon **9** (Scheme 4).

Unfortunately, it was not possible to incorporate two acridinone units in a crown of the type **10** because only the 12-

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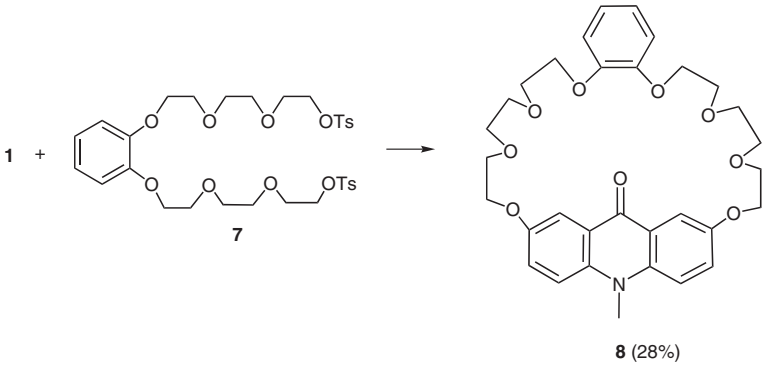
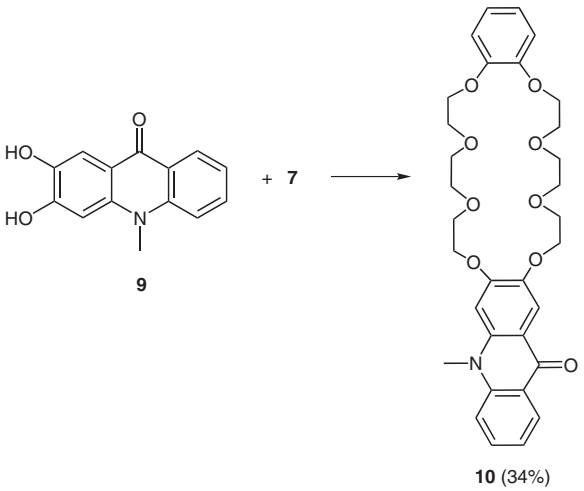
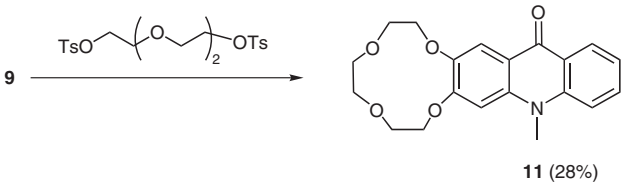


Scheme 3



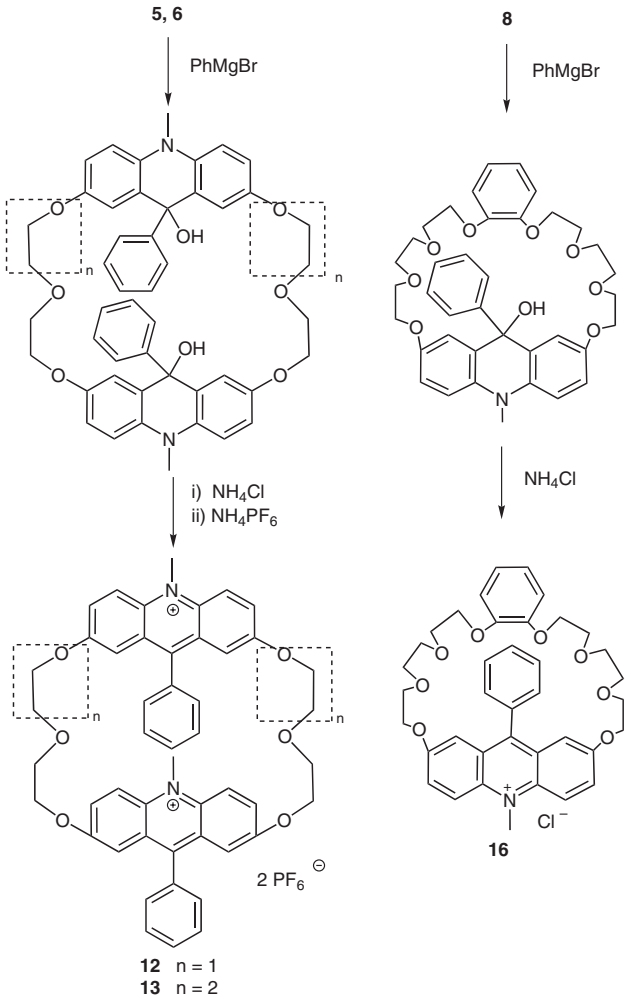
Scheme 4



Scheme 5

crown-4 (**11**), was formed in the reaction of **9** with tetraethylene glycol bistosylate (Scheme 5).

The obtained macrocycles were further functionalized by their conversion into 9-phenyl-9,10-dihydroacridines (acridanes) through reaction with phenylmagnesium bromide. The primarily formed acridanes could not be isolated because they were transformed into the corresponding acridinium salts during purification by chromatography (Scheme 6). However, the macrocycles containing the acridinium unit were subsequently transformed into the corresponding macrocycles with 9-methoxyacridane units by reaction with methanol in the presence of a base (Scheme 7 and Scheme 8). The small crown **11** could also be converted into the corresponding acridinium derivative (Scheme 9).



Scheme 6

Generally, it can be predicted that the steric constraint imposed by the acridinium substituent is large due to the flat structure of the acridinium moiety and the large twisting angle between the acridinium ring and the phenyl ring in the 9-position. In contrast, the phenyl group can be directed outwards of the macrocycle due to re-hybridization at the 9-position. Therefore, it may be expected that in the course of the photochemical reaction, the cavity of the macrocycle will become more blocked. Similar effects

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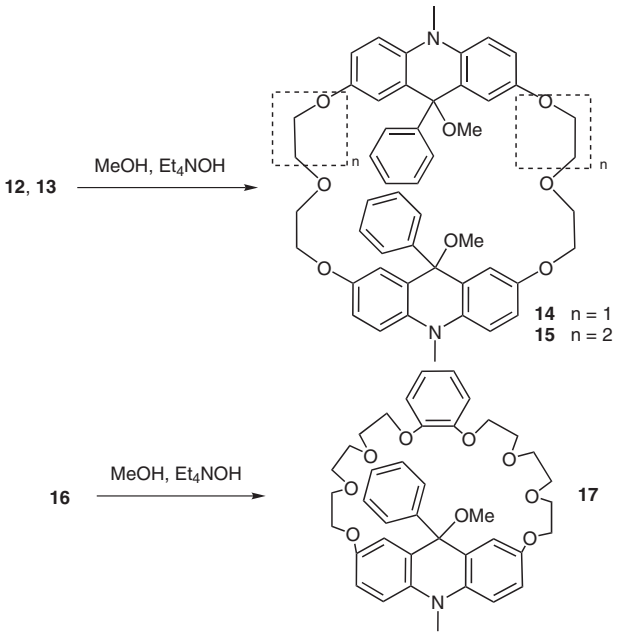
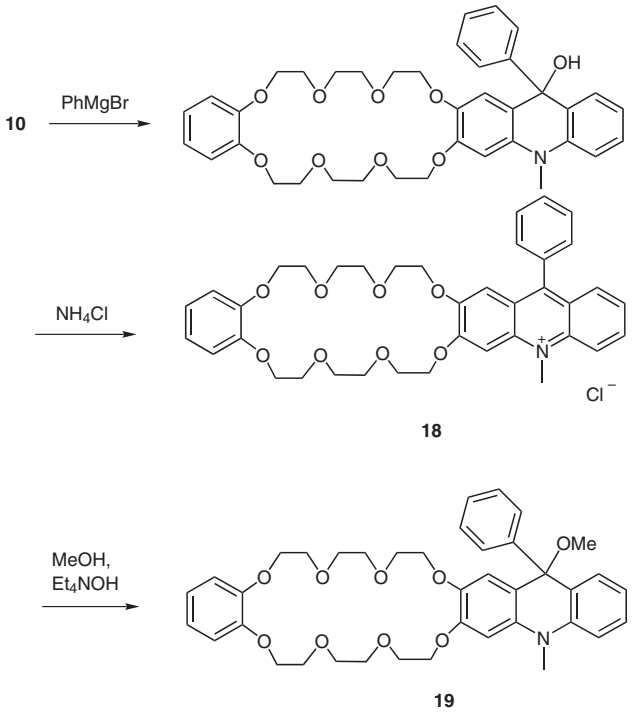


Scheme 7



Scheme 8

have recently been found in calixarenes.[5] Indeed, ^{1}H NMR spectra of the macrocycles **12** and **16** indicated the interaction of the acridinium units across space. The resonances of the acridinium protons at positions 4 and 5 of the acridinium units of the smaller ring **12**, are up-field shifted by 0.2 ppm compared with the same proton resonances of compound **13**. Furthermore, the rotational motion of the phenyl group is frozen at room temperature, resulting in a splitting of the proton resonances (Figure 1). The activation energy for the rotation of the phenyl group

Scheme 9

around the C9-phenyl axis, determined with the help of the coalescence temperature of NMR spectra recorded in DMSO-d_6 solution at different temperatures, is 18 kcal mol^{-1}. In contrast, the phenyl groups within the larger macrocycle **13** rotate freely at room temperature. The proton resonances of the catechol subunit of **16** are also split into two groups and up-field shifted by 0.6 and 0.2 ppm compared with the singlet of the same protons in the acridane compound **17**. We attribute this phenomenon to the π–π interaction of the acridinium moiety with the catechol unit. Molecular modeling (MM2) has shown that conformations of the macrocycle with distances between the two subunits of around 3 Å are possible (Figure 2). Accordingly, the proton resonances of the acridinium unit of **16** are also up-field shifted, compared with the model compound **21**, due to the interaction with the catechol unit. If the compound assumes the conformation depicted in Figure 2, then both the resonances of the methyl protons and of H3–H6 of the acridinium, may become up-field shifted. In contrast, the resonances of H1 and H8 are down-field shifted by 0.2 ppm due to their positions at the edge of the catechol moiety. All of the observed interactions between the subunits of the macrocycles **12** and **16** disappear in the corresponding macrocycles incorporating the acridane subunits.

All macrocycles with the acridane subunits underwent a photoreaction upon excitation with 313 nm light to form the corresponding acridinium-containing macrocycles, both in acetonitrile and alcoholic solutions. The thermal recovery of the acridane compound was slow in acetonitrile solution. The back reaction in alcoholic solution was accomplished within two hours and gave the acridane containing the alkoxy group of the alcohol used as solvent, e.g. the methoxy leaving group was replaced by the propoxy group in *n*-propanol solution. The individual photo- and thermal reactions could be followed by UV/Vis spectroscopy because the absorption maxima of the acridinium compounds is around 430 nm while that of the acridane is around 310 nm (see Figure 3 for an example). Because of the thermal back reaction, the photoreaction results in the formation of the acridinium compound until the equilibrium with the back reaction has become established.

We chose the macrocycles **18** and **19** to demonstrate that crown ethers incorporating acridinium and acridane units differ in their complexation behavior. We studied the ability of **18** and **19** to bind the guest **22** (Scheme 10). Pseu-

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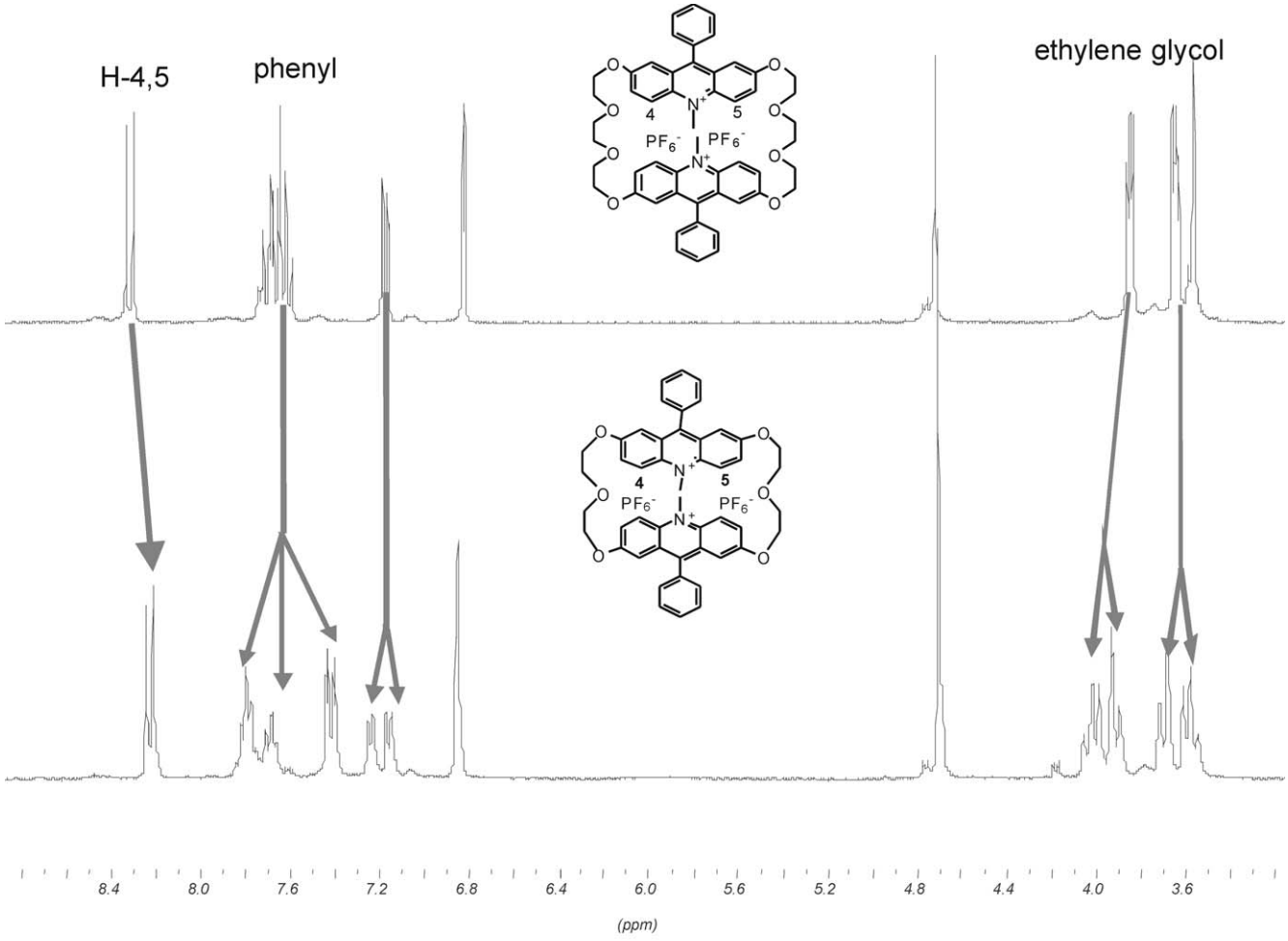
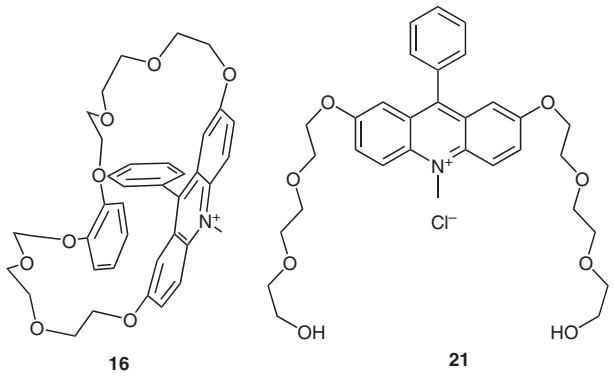


Figure 1 ^{1}H NMR spectra (CD_3CN) of macrocycles **12** and **13** showing the regions of the phenyl proton resonances and those of the ethyleneglycol spacers, which are split in the case of compound **12**.



16 21

Figure 2

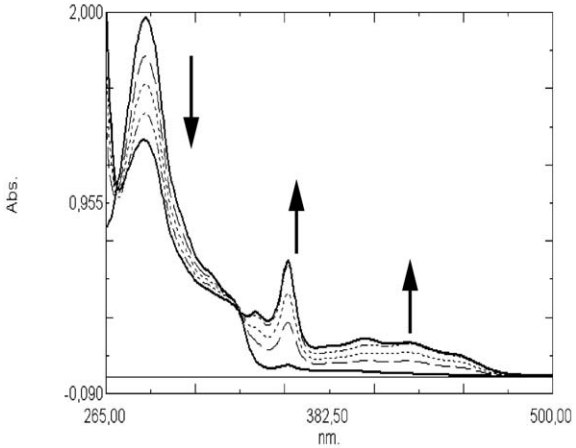


Figure 3 UV/Vis spectra of compound **19** in MeOH (7×10^{-5} M) recorded after consecutive irradiations (λ_{exc} = 313 nm) for 0, 3, 6, 12 and 30 min.

dorotaxanes based on 1,2-bis(pyridinium)ethane (**22**) as the axle and a dibenzo-24-crown-8 ether (DB24C8) as the wheel, have been previously reported.[6] The acridane-containing host **19** binds the guest **22**, and the complexation can easily be monitored with ^{1}H NMR spectroscopy because there is a slow exchange between free and complexed components on the NMR timescale. The appearance of two signal sets indicates complex formation. The binding constant could be determined by integration of suitable proton resonances of free and complexed components of the formed pseudorotaxanes. The association constant of **19/22** is 160 M^{-1} in deuterated nitromethane solution. The question arises as to whether

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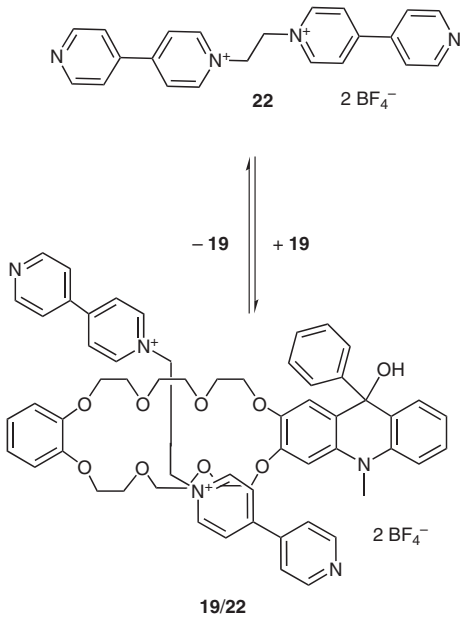

Scheme 10

the complexation of **22** by the host is influenced by replacing the acridane unit by the acridinium moiety. In fact, there is no complexation of **22** by the host **18** due to the repulsion of the positive charges present in both the host and the guest. The addition of **22** to **18** in acetonitrile or nitromethane solution did not cause any change in the ^{1}H NMR spectrum of **18**.

In summary, we have designed a series of new crown ethers that incorporate the acridane unit, which can be photochemically converted into the corresponding acridinium subunit. This transformation gives rise to drastic changes in the properties of the macrocycles such as electron-donor strength, shape and ability to bind. The latter was demonstrated with the different complexation properties of crown ethers incorporating acridinium and acridane units.

Column chromatography was performed on Merck silica gel 60 (0.040–0.063 mm, 230–400 mesh). ^{1}H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were recorded on a Bruker DPX 300 spectrometer, with chemical shifts (δ, ppm) referenced to TMS as an internal standard. The ^{1}H NMR spectra shown in Figure 1 were recorded on a Bruker AMX 600 (600 MHz) spectrometer. Atom-numbering for compounds is given in Figure 4 and Figure 5. ESI mass spectrometry was carried out on a triple quadrupole instrument (TSQ 700, Finnigan MAT, Bremen, Germany) equipped with an electrospray ion source (API-ESI) operating in the positive mode with a capillary temperature of 200 °C and a high voltage of 4.5 kV. The samples were dissolved in MeOH (concentration 10–50 pmol mL^{-1}). Nitrogen was used as sheath gas at a pressure of 3.4 bar. The spectra were composed of an average of 64 scans. UV/Vis spectra were recorded with a Shimadzu UV 2101 PC spectrometer. Melting points were determined using a Boetius (Rapido) apparatus and are uncorrected.

The activation energy of the rotation of the phenyl ring of compound **12** was estimated with the help of the equation $\Delta G = RT_c(22.96 + \ln T_c/\Delta\nu)$ with T_c, the coalescence temperature, 333 K and $\Delta\nu = \nu_A - \nu_B$, the difference of the proton resonances of the phenyl protons, measured in Hz.

Compound **22** was obtained according to the literature.[7]

2,7-Dihydroxy-10-methylacridin-9(10*H*)one (1)

We were not able to reproduce the synthetic route proposed in the literature,[8] therefore an independent synthesis was undertaken. A mixture of *p*-anisidine (1.5 g, 12.2 mmol) and 2-bromo-5-methoxybenzoic acid (2.0 g, 8.7 mmol) with anhydrous K_2CO_3 (1.7 g, 12.3 mmol) and copper (0.1 g) in anhydrous 1-pentanol (10 mL) was heated under reflux for 3 h. The solvent was evaporated under reduced pressure and the residue was dissolved in hot H_2O (200 mL) and then filtered through Celite. The Celite was washed with H_2O (500 mL) and the filtrate was acidified with concd HCl to pH 6. A colorless solid precipitated, which was isolated by filtration and washed with H_2O (2 × 50 mL). The solid was crystallized from $CHCl_3$ (40 mL) to give 5-methoxy-2-(4-methoxyphenylamino)benzoic acid.

Yield: 1.7 g (71%); mp 174–176 °C (Lit.[9] 162–165 °C).

^{1}H NMR ($CDCl_3$): δ = 3.79 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 6.90 (d, *J* = 8.3 Hz, 2 H), 6.98 (s, 2 H), 7.14 (d, *J* = 8.3 Hz, 2 H), 7.49 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 55.5 (OCH_3), 55.8 (OCH_3), 109.7 (C_q), 113.8 (CH), 114.7 (CH), 115.8 (CH), 124.5 (CH), 125.5 (CH), 133.9 (C_q), 145.1 (C_q), 150.5 (C_q), 156.5 (C_q), 173.1 (C_q).

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.74; H, 5.44; N, 5.10.

A mixture of 5-methoxy-2-(4-methoxyphenylamino)benzoic acid (1.7 g, 7.2 mmol) and polyphosphoric acid (10 g) was heated to 110 °C for 3 h. The solution was poured onto ice (400 mL) and the precipitate was filtered off and washed with H_2O (2 × 100 mL). The precipitate was dissolved in hot EtOH (1.5 L) and filtered. After 24 h the solution was concentrated to 150 mL and the resulting solid was recrystallized from EtOH to afford 2,7-dimethoxyacridin-9(10*H*)one.

Yield: 1.63 g (89%); mp 350–355 °C (Lit.[8] >300 °C).

^{1}H NMR (DMSO-d_6): δ = 3.86 (s, 6 H, OCH_3), 7.39 (dd, *J* = 3.0, 9.0 Hz, 2 H), 7.52 (d, *J* = 9.0 Hz, 2 H), 7.61 (d, *J* = 3.0 Hz, 2 H), 11.74 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 55.4 (OCH_3), 104.6 (CH), 119.3 (CH), 120.2 (C_q), 124.2 (CH), 135.5 (C_q), 153.9 (C_q), 175.5 (C_q).

Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.57; H, 5.13; N, 5.48. Found: C, 70.72; H, 5.30; N, 5.36.

HRMS (EI, 70 eV): *m/z* calcd for $C_{15}H_{13}NO_3$: 255.0895; found: 255.0899.

A solution of tetraethylammonium hydroxide (25% solution in MeOH, 11.07 g, 18.8 mmol) was added to a stirred suspension of 2,7-dimethoxyacridin-9(10*H*)one (1.2 g, 4.7 mmol) in MeCN (200 mL). Stirring was continued for 30 min until the mixture became clear. MeI (2.65 g, 18.8 mmol) was added and the reaction mixture was stirred for additional 24 h. The solvents were evaporated under reduced pressure and the remaining residue was dissolved in $CHCl_3$ (200 mL) then washed with H_2O (200 mL). The aqueous phase was extracted with $CHCl_3$ (2 × 200 mL) and the combined organic phases were dried ($MgSO_4$) and evaporated. The remaining solid was recrystallized from cyclohexane to afford 2,7-dimethoxy-10-methylacridin-9(10*H*)one.

Yield: 0.77 g (61%); R_f = 0.81 ($CHCl_3$–MeOH, 15:1); mp 170–172 °C (Lit.[8] 222.5 °C). The analytical data were in accord with literature values.

A suspension of 2,7-dimethoxy-10-methylacridin-9(10*H*)one (1.17 g, 4.3 mmol) in aq HBr (48%, 30 mL) was heated under reflux for

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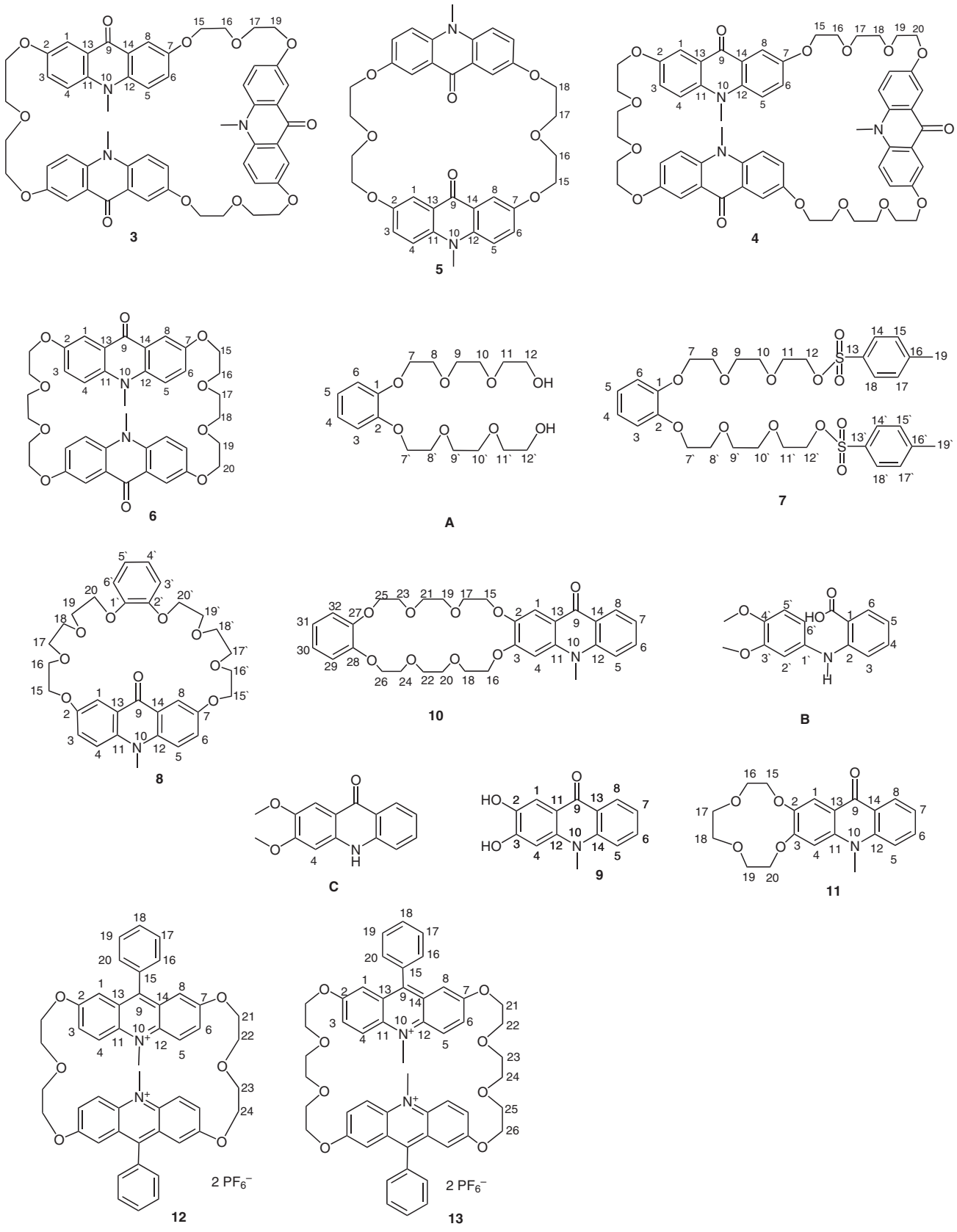

Figure 4

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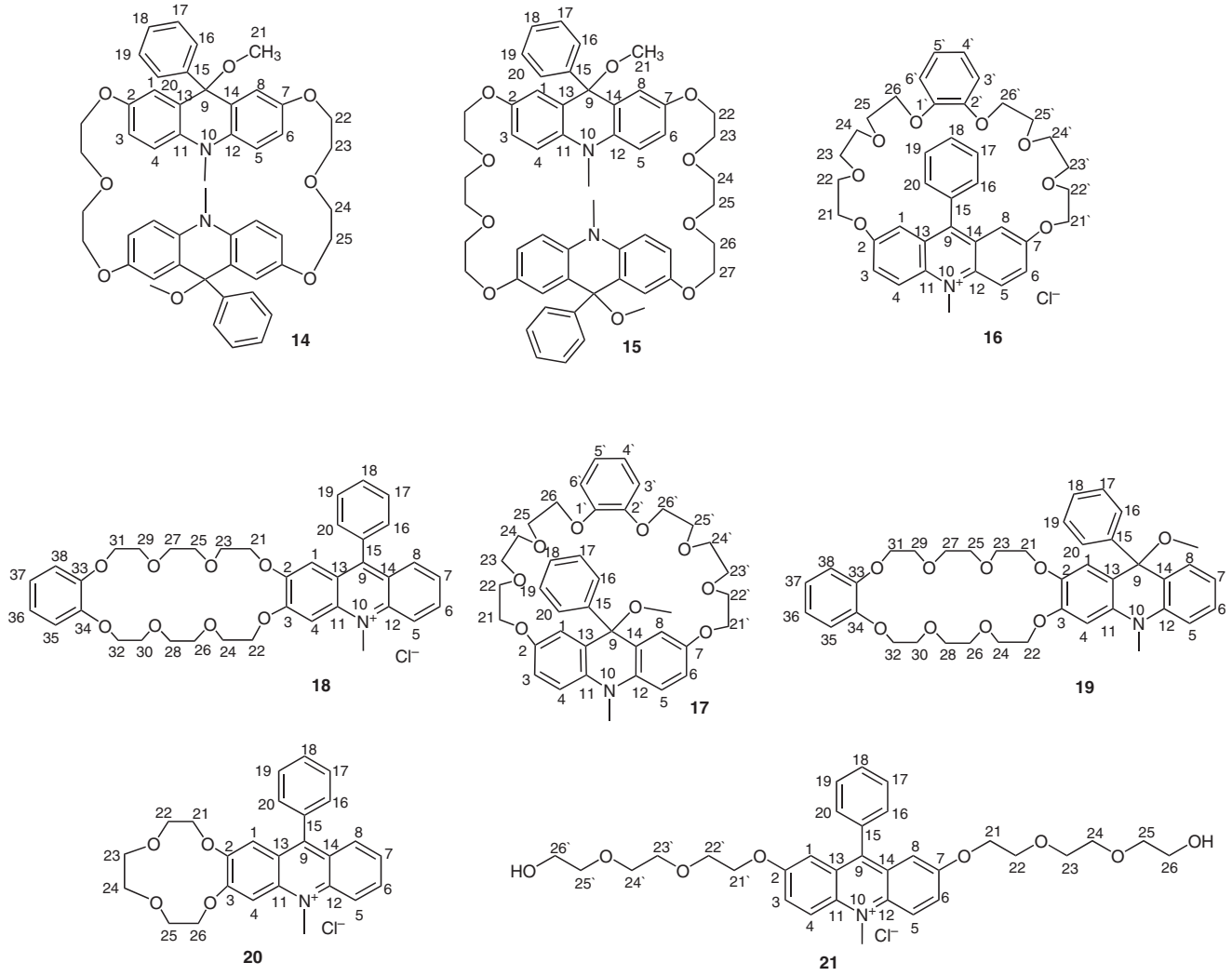

Figure 5

24 h. The solvent was removed in vacuo and the remaining solid was recrystallized from H_2O to afford **1**.

Yield: 1.0 g (98%); red powder; mp >360 °C (Lit.[8] >300 °C).

^{1}H NMR (CD_3OD): δ = 4.50 (s, 3 H, NCH_3), 7.81 (dd, *J* = 2.6, 9.4 Hz, 2 H), 7.99 (d, *J* = 2.6 Hz, 2 H), 8.26 (d, *J* = 9.4 Hz, 2 H).

^{13}C NMR (CD_3OD): δ = 35.3 (CH_3, NCH_3), 105.9 (CH), 118.8 (CH), 119.4 (C_q), 127.8 (CH), 136.9 (C_q), 154.3 (C_q), 169.5 (C_q).

Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.59; N, 5.80. Found: C, 69.94; H, 4.76; N, 5.72.

Compounds 3 and 5

To **1** (0.43 g, 1.3 mmol) in anhydrous MeCN (800 mL), tetraethylammonium hydroxide (20% solution in H_2O, 3.93 g, 5.3 mmol) was added. The mixture was heated under reflux for 30 min under an argon atmosphere. **2** (n = 1, 0.55 g, 1.3 mmol) in MeCN (40 mL) was added dropwise to the boiling solution over 12 h. After the addition was complete, the mixture was refluxed for 24 h. The reaction mixture was evaporated under reduced pressure and the residue was subjected to silica gel column chromatography ($CHCl_3$–MeOH, 15:1) to give **3** (R_f = 0.40) in the first yellow-colored fraction and **5** (R_f = 0.26).

3

Yield: 0.05 g (12%); R_f = 0.40 ($CHCl_3$–MeOH, 15:1); mp 215–220 °C.

^{1}H NMR (CD_3OD–$CDCl_3$, 6:1): δ = 4.00 (s, 9 H, NCH_3). 4.04 (m, 12 H, H-16,17), 4.28 (m, 12 H, H-15,19), 7.13 (d, *J* = 9.4 Hz, 4 H, H-4,5), 7.28 (dd, *J* = 9.4, 3.0 Hz, 4 H, H-3,6), 7.67 (d, *J* = 3.0 Hz, 6 H, H-1,8).

^{13}C NMR (CF_3CO_2D): δ = 36.8 (CH_3, NCH_3), 68.7 (C-15,19), 70.8 (C-16,17), 102.7 (C-1,8), 117.9 (C-11,12), 119.8 (C-4,5), 131.5 (C-3,6), 138.8 (C-13,14), 157.3 (C-2,7), 165.3 (C-9).

Anal. Calcd for $C_{54}H_{51}N_3O_{12}$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.79; H, 5.93; N, 4.19.

HRMS-ESI: *m*/*z* $[M + H]^+$ calcd for $C_{54}H_{52}N_3O_{12}$: 934.3546; found: 934.3552.

HRMS-ESI: *m*/*z* $[M + 2H]^{2+}$ calcd for $C_{54}H_{53}N_3O_{12}$: 467.6809; found: 467.6809.

5

Yield: 0.07 g (17%); R_f = 0.26 ($CHCl_3$–MeOH, 15:1); mp >320 °C.

^{1}H NMR (DMSO-d_6): δ = 3.76 (s, 6 H, NCH_3), 3.86 (br s, 8 H, H-16,17), 4.22 (br s, 8 H, H-15,18), 7.04 (dd, *J* = 9.4, 3.0 Hz, 4 H, H-3,6), 7.48 (d, *J* = 9.4 Hz, 4 H, H-4,5), 7.66 (d, *J* = 3.0 Hz, 4 H, H-1,8).

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^{13}C NMR (CF_3CO_2D): δ = 39.5 (CH_3, NCH_3), 69.3 (C-15,18), 71.7 (C-16,17), 98.0 (C-1,8), 115.9 (C-11,13), 120.0 (C-4,5), 144.2 (C-3,6), 150.7 (C-12,14), 151.3 (C-2,7), 163.2 (C-9).

Anal. Calcd for $C_{36}H_{34}N_2O_8$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.48; H, 6.03; N, 2.77.

HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{36}H_{35}N_2O_8$: 623.2388; found: 623.2388.

Compounds 4 and 6

To **1** (0.45 g, 1.4 mmol) in anhydrous MeCN (800 mL), tetraethylammonium hydroxide (20% solution in H_2O, 4.11 g, 5.6 mmol) was added. The mixture was heated under reflux for 30 min under an argon atmosphere. **2** (n = 2, 0.64 g, 1.4 mmol) in MeCN (40 mL) was added dropwise to the boiling solution over 9 h. After the addition was complete, the mixture was refluxed for 24 h. The reaction mixture was evaporated under reduced pressure and the residue was subjected to silica gel column chromatography ($CHCl_3$–MeOH, 15:1) to give **4** (R_f = 0.20) and **6** (R_f = 0.07).

4

Yield: 0.09 g (15%); mp >340 °C.

^{1}H NMR ($CDCl_3$): δ = 3.11 (s, 9 H, NCH_3), 3.70 (s, 12 H, H-17,18), 3.84 (m, 12 H, H-16,19), 4.03 (m, 12 H, H-15,20), 6.76 (d, *J* = 9.4 Hz, 6 H, H-4,5), 6.96 (dd, *J* = 3.0, 9.4 Hz, 6 H, H-3,6), 7.45 (d, *J* = 3.0 Hz, 6 H, H-1,8).

^{13}C NMR ($CDCl_3$): δ = 33.2 (CH_3, NCH_3), 67.3 (C-15,20), 69.6 (C-16,19), 70.8 (C-17,18), 106.0 (C-1,8), 116.2 (C-4,5), 121.4 (C-11,12), 124.2 (C-3,6), 136.2 (C-13,14), 152.8 (C-2,7), 175.8 (C-9).

Anal. Calcd for $C_{60}H_{63}N_3O_{15}$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.34; H, 6.00; N, 3.24.

HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{60}H_{64}N_3O_{15}$: 1066.4332; found: 1066.4353.

HRMS-ESI: *m/z* $[M + Na]^+$ calcd for $C_{60}H_{63}N_3O_{15}Na$: 1088.4151; found: 1088.4142.

6

Yield: 0.12 g (18%); mp >350 °C.

^{1}H NMR (CF_3CO_2D): δ = 3.48 (s, 8 H, H-17,18), 3.59 (br s, 8 H, H-16,19), 3.87 (br s, 8 H, H-15,20), 4.30 (s, 6 H, NCH_3), 6.78 (s, 4 H, H-1,8), 7.45 (d, *J* = 10.2 Hz, 4 H, H-3,6), 7.93 (d, *J* = 10.2 Hz, 4 H, H-4,5).

^{13}C NMR (CF_3CO_2D): δ = 39.4 (CH_3, NCH_3), 68.9 (C-15,20), 70.4 (C-16,19), 71.1 (C-17,18), 108.7 (C-1,8), 116.3 (C-4,5), 120.0 (C-11,12), 123.1 (C-3,6), 139.6 (C-13,14), 152.3 (C-2,7), 169.8 (C-9).

Anal. Calcd for $C_{40}H_{42}N_2O_{10}$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.28; H, 6.03; N, 3.27.

HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{40}H_{43}N_2O_{10}$: 711.2912; found: 711.2909.

1,2-Bis{2-[2-(2-tosyloxyethoxy)ethoxy]ethoxy}benzene (7)[10]

A mixture of catechol (3.10 g, 28 mmol), triethylene glycol monotosylate (17 g, 56 mmol) and anhydrous K_2CO_3 (10.11 g, 56 mmol) in acetone (300 mL) was heated under reflux for 30 h. The reaction mixture was evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2 (200 mL), washed with H_2O (200 mL) and the organic layer was dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography (EtOAc–MeOH, 8:2) to afford 1,2-bis{2-[2-(2-hydroxyethoxy)ethoxy]ethoxy}benzene (**A**, Figure 4).

Yield: 8.33 g (81%); colorless oil; R_f = 0.26 (EtOAc–MeOH, 8:2).

^{1}H NMR ($CDCl_3$): δ = 3.04 (br s, 2 H, OH), 3.61 (t, *J* = 4.1 Hz, 4 H, H-12,12′), 3.68 (m, 4 H, H-11,11′), 3.71 (m, 8 H, H-9,9′,10,10′), 3.89 (t, *J* = 4.53 Hz, 4 H, H-8,8′), 4.18 (t, *J* = 4.53 Hz, 4 H, H-7,7′), 6.92 (s, 4 H, H-3,4,5,6).

^{13}C NMR ($CDCl_3$): δ = 61.7 (C-9,9′), 68.7 (C-7,7′), 69.7 (C-8,8′), 70.4 (C-11,11′), 70.8 (C-10,10′), 72.7 (C-12,12′), 114.8 (C-4,5), 121.7 (C-3,6), 148.9 (C-1,2).

Anal. Calcd for $C_{18}H_{30}O_8$: C, 57.74; H, 8.07; Found: C, 57.39; H, 8.13.

A mixture of 1,2-bis-{2-[2-(2-hydroxyethoxy)ethoxy]ethoxy}benzene (6.4 g, 0.17 mol) and pyridine (6.7 g, 0.85 mol) in CH_2Cl_2 (150 mL) was stirred under cooling in an ice bath. To this solution *p*-toluenesulfonyl chloride (13.0 g, 0.68 mol) was added. The mixture was stirred for 2 h at 0 °C and for an additional 18 h at r.t., then the solution was washed with H_2O (200 mL) and extracted with CH_2Cl_2 (3 × 200 mL). The organic layer was separated, dried ($MgSO_4$) and evaporated. The residue (17.3 g) was purified by column chromatography (*n*-hexane–EtOAc, 3:7) to afford **7**.

Yield: 6.3 g (54%); colorless oil; R_f = 0.22 (*n*-hexane–EtOAc, 3:7).

^{1}H NMR ($CDCl_3$): δ = 2.43 (s, 6 H, H-19,19′), 3.68 (m, 8 H, H-9,9′,10,10′), 3.85 (m, 8 H, H-8,8′,11,11′), 4.15 (m, 8 H, H-7,7′,12,12′), 6.91 (m, 4 H, H-3,4,5,6), 7.32 (d, *J* = 7.9 Hz, 4 H, H-14,14′,18,18′), 7.78 (d, *J* = 8.3 Hz, 4 H, H-15,15′,17,17′).

^{13}C NMR ($CDCl_3$): δ = 21.6 (C-19,19′), 62.2 (C-9,9′), 68.8 (C-7,7′), 69.3 (C-8,8′), 69.8 (C-11,11′), 70.7 (C-10,10′), 70.8 (C-12,12′), 114.8 (C-3,6), 121.7 (C-4,5), 128.0 (C-15,15′,17,17′), 129.8 (C-14,14′,18,18′), 132.9 (C-16,16′), 144.8 (C-13,13′), 148.9 (C-1,2).

Anal. Calcd for $C_{32}H_{42}S_2O_{12}$: C, 56.29; H, 6.20; S, 9.39. Found: C, 56.47; H, 6.50; S, 9.17.

[2,7-(10-Methylacridin-9-one)]-(1′,2′-phenyl)-29-crown-8 (8)

Tetraethylammonium hydroxide (25% solution in MeOH, 4 g, 6.64 mmol) was added to a suspension of **1** (0.40 g, 1.66 mmol) in anhydrous MeCN (800 mL). The reaction mixture was heated under reflux for 30 min under an argon atmosphere then a solution of **7** (1.13 g, 1.66 mmol) in MeCN (40 mL) was added dropwise over 12 h. After the addition was complete, the mixture was refluxed for 24 h then the mixture was evaporated under reduced pressure. H_2O (200 mL) was added and the mixture was extracted with $CHCl_3$ (4 × 200 mL) then the combined organic phases were dried ($MgSO_4$) and evaporated. The residue was subjected to column chromatography (EtOAc–MeOH, 12:1) to give the pure product **8**.

Yield: 0.25 g (28%); R_f = 0.55 (EtOAc–MeOH, 12:1); mp 146–149 °C.

^{1}H NMR (CD_3OD): δ = 3.66 (m, 16 H, H-17,17′,18,18′,19,19′,20,20′), 3.81 (s, 3 H, NCH_3), 3.92 (t, *J* = 4.1 Hz, 4 H, H-16,16′), 4.41 (t, *J* = 4.1 Hz, 4 H, H-15,15′), 6.60 (m, 2 H, H-4′,5′), 6.75 (m, 2 H, H-3′,6′), 7.46 (dd, *J* = 3.0, 9.4 Hz, 2 H, H-3,6), 7.65 (d, *J* = 9.4 Hz, 2 H, H-4,5), 8.07 (d, *J* = 3.0 Hz, 2 H, H-1,8).

^{13}C NMR (CD_3OD): δ = 34.4 (CH_3, NCH_3), 69.0 (C-17,17′,18,18′), 69.5 (C-16,16′), 70.7 (C-19,19′), 71.5, (C-20,20′), 71.9 (C-15,15′), 109.2, (C-1,8), 116.1 (C-4′,5′), 118.3 (C-4,5), 122.5 (C-3′,6′), 122.9 (C-13,14), 126.5 (C-3,6), 138.6 (C-11,12), 150.0 (C-1′,2′), 155.2 (C-2,7), 178.5 (C-9).

Anal. Calcd for $C_{32}H_{37}NO_9 \cdot H_2O$: C, 64.31; H, 6.58; N, 2.34. Found: C, 64.62; H, 6.48; N, 2.34.

HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{32}H_{37}NO_9$: 580.2541; found: 580.2545.

HRMS-ESI: *m/z* $[M + Na]^+$ calcd for $C_{32}H_{37}NO_9Na$: 602.2361; found: 602.2358.

[2,3-(10-Methylacridin-9-one)]-(1′,2′-phenyl)-24-crown-8 (10)

Prepared from **9** following the procedure described for **8** above. After purification by column chromatography (EtOAc–MeOH, 6:1),

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the combined fractions containing the crown ether were evaporated. The residue was dissolved in $CHCl_3$ (40 mL) and poured into methyl *tert*-butyl ether (150 mL). The precipitate was filtered and the clear filtrate was evaporated to afford **10**.

Yield: 0.32 g (34%), yellow solid, R_f = 0.21 (EtOAc–MeOH, 6:1); mp 155–157 °C.

^{1}H NMR ($CDCl_3$): δ = 3.84 (s, 3 H, NCH_3), 3.87 (s, 8 H, H-19,20,21,22), 3.93 (m, 4 H, H-23,24), 3.95 (t, *J* = 4.5 Hz, 2 H, H-18), 4.03 (t, *J* = 4.5 Hz, 2 H, H-17), 4.14 (m, 4 H, H-25,26), 4.30 (m, 4 H, H-15,16), 6.86 (m, 5 H, H-4,29,30,31,32), 7.30 (t, *J* = 7.1 Hz, 1 H, H-7), 7.51 (d, *J* = 8.6 Hz, 1 H, H-5), 7.71 (dt, *J* = 8.6, 1.5 Hz, 1 H, H-6), 8.02 (s, 1 H, H-1), 8.55 (d, *J* = 7.1 Hz, 1 H, H-8).

^{13}C NMR ($CDCl_3$): δ = 30.4 (CH_3, NCH_3), 63.0, 63.2, 68.8, 69.2, 69.8, 70.5, 70.6, 72.8 (C-15,26), 108.9 (C-4), 114.6, (C-1), 116.1 (C-5), 122.2 (C-7), 122.7, (C-14), 124.7 (C-13), 127.9 (C-8), 129.8 (C-6), 130.9 (C-11,12), 137.0 (C-2), 148.9 (C-3), 153.3 (C-27,28), 176.6 (C-9).

Anal. Calcd for $C_{32}H_{37}NO_9$: C, 66.31; H, 6.43; N, 2.42. Found: C, 65.91; H, 6.55; N, 2.40.

HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{38}NO_9$: 580.2541; found: 580.2545.

HRMS-ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{37}NNaO_9$: 602.2361; found: 602.2358.

2,3-Dihydroxy-10-methylacridin-9(10*H*)-one (9)

A modified Ullmann reaction, which afforded a higher overall yield compared to the literature,[11] was used.

A mixture of 3,4-dimethoxyaniline (2.6 g, 17.0 mmol), 2-bromobenzoic acid (2.6 g, 13.0 mmol), anhydrous K_2CO_3 (2.5 g, 18.1 mmol) and copper (0.1 g) in anhydrous 1-pentanol (10 mL) was heated under reflux for 2 h. 1-Pentanol was removed in vacuo and the resulting mixture was treated with H_2O (200 mL) and heated to 80 °C. The hot mixture was filtered through Celite and washed with H_2O (500 mL). On acidification of the combined aqueous phases with concd HCl (pH 2), a colorless solid precipitated, which was filtered and washed with H_2O (2 × 50 mL). The solid was crystallized from $CHCl_3$ to give 2-(3,4-dimethoxyphenylamino)benzoic acid (**B**).

Yield: 2.96 g (80%); yellow crystals; mp 180–182 °C (Lit.[12] 180–181 °C).

^{1}H NMR ($CDCl_3$): δ = 3.91 (s, 3 H, CH_3), 3.88 (s, 3 H, CH_3), 6.71 (t, *J* = 8.28 Hz, 1 H, H-5), 6.80–6.90 (m, 3 H, H-2′,5′,6′), 7.00 (d, *J* = 8.6 Hz, 1 H, H-3), 7.30 (t, *J* = 8.6 Hz, 1 H, H-4), 8.02 (d, *J* = 8.3 Hz, 1 H, H-6), 9.16 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 56.1 (OCH_3), 56.0 (OCH_3), 109.4 (C-1′), 109.1, 111.7, 117.0 (C-2′,5′,6′), 113.7 (C-3), 116.4 (C-5), 132.5 (C-6), 133.2 (C-2), 135.3 (C-4), 146.5 (C-4′), 149.6 (C-3′), 150.3 (C-1), 173.3 (C_q, C=O).

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.93; H, 5.53; N, 5.13. Found: C, 66.19; H, 5.63; N, 5.37.

A mixture of 2-(3,4-dimethoxyphenylamino)benzoic acid (1.5 g, 5.49 mmol) and polyphosphoric acid (10 g) was heated at 110 °C for 2 h. The solution was poured onto ice and the precipitate was filtered off. The solid was crystallized from MeOH to give 2,3-dimethoxyacridin-9(10*H*)-one (**C**) as the phosphate.

Yield: 1.17 g (84%); mp 284–285 °C.

^{1}H NMR (DMSO-d_6): δ = 3.86 (s, 3 H, H-16). 3.92 (s, 3 H, H-15), 6.96 (s, 1 H, H-4), 7.22 (t, *J* = 7.1 Hz, 1 H, H-7), 7.49 (d, *J* = 8.3 Hz, 1 H, H-5), 7.57 (s, 1 H, H-1), 7.66 (t, *J* = 7.1 Hz, 1 H, H-6), 8.20 (d, *J* = 8.3 Hz, 1 H, H-8), 11.63 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 53.7 (CH_3), 53.9 (CH_3), 96.4 (C-4), 103.2 (C-1), 112.2 (C-5), 115.2 (C-7), 118.1 (C-12), 118.8 (C-8), 123.9 (C-13), 130.6 (C-11), 135.3 (C-14), 138.5 (C-6), 143.4 (C-2), 152.7 (C-3), 173.2 (C-9).

Anal. Calcd for $C_{15}H_{16}NO_7P$: C, 51.00; H, 4.56; N, 3.90; P, 8.77. Found: C, 50.91; H, 4.29; N, 3.92; P, 8.64.

To a suspension of 2,3-dimethoxyacridin-9(10*H*)one (0.8 g, 3.13 mmol) in MeCN (150 mL), tetraethylammonium hydroxide (20% solution in H_2O, 9.22 g, 12.5 mmol) was added. After stirring for 30 min at r.t., the suspension became a yellow-greenish fluorescent solution. To the solution MeI (1.77 g, 12.5 mmol) was added and stirring was continued for 24 h. The reaction mixture was evaporated under reduced pressure and the residue was dissolved in $CHCl_3$ (200 mL) and washed with H_2O (200 mL). The aqueous phase was extracted with $CHCl_3$ (3 × 200 mL) and the combined organic phases were dried ($MgSO_4$) and evaporated. The solid was crystallized from cyclohexane to afford 2,3-dimethoxy-10-methylacridin-9(10*H*)-one.

Yield: 0.62 g (74%); mp 192–195 °C (Lit.[11] 194–195 °C). The analytical data were in accord with literature values.[9]

A suspension of 2,3-dimethoxy-10-methylacridin-9(10*H*)one (1 g, 3.70 mmol) was heated under reflux in HBr (48%, 20 mL) for 20 h. The solvent was removed in vacuo and the resulting solid was crystallized from MeOH to give pure **9**.

Yield: 0.80 g (90%); red solid; R_f = 0.1 (EtOAc, 100%); mp 295–298 °C (Lit.[13] 222 °C).

^{1}H NMR (CD_3OD): δ = 4.07 (s, 3 H, NCH_3), 7.44 (s, 1 H, H-4), 7.79 (s, 1 H, H-1), 7.81 (dt, *J* = 8.3, 1.5 Hz, 1 H, H-7), 8.07 (d, *J* = 8.7 Hz, 1 H, H-5), 8.18 (dt, *J* = 8.3, 1.5 Hz, 1 H, H-6), 8.54 (d, *J* = 9.0 Hz, 1 H, H-8).

^{13}C NMR (CD_3OD): δ = 35.5 (NCH_3), 84.9 (C-4), 100.3 (C-1), 104.9 (C-7), 112.6 (C-5), 118.2 (C-11,13), 124.1 (C-12), 124.39 (C-8), 134.6 (C-14), 139.9 (C-6), 141.3 (C-2), 147.2 (C-3), 158.2 (C-9).

Anal. Calcd for $C_{14}H_{11}NO_3 \cdot H_2O$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.87; H, 4.48; N, 5.62.

2,3-(10-Methylacridine-9-one)crown-4 (11)

Compound **9** (0.5 g, 2.1 mmol) was dissolved in MeCN (800 mL) and treated with tetraethylammonium hydroxide (25% solution in MeOH, 4.8 g, 8.4 mmol). The solution was heated under reflux for 30 min then **2** (n = 2), dissolved in MeCN (40 mL) was added dropwise to the boiling solution over 8 h. The reaction was heated under reflux for an additional 24 h then the solvent was removed in vacuo. The remaining residue was purified by chromatography (EtOAc–MeOH, 5:1) and the yellowish fractions were collected. The solvent was removed from the combined fractions and the remaining residue was dissolved in $CHCl_3$ (40 mL). This solution was poured into methyl *tert*-butyl ether (150 mL) and the precipitate was filtered and dried to give **11**.

Yield: 0.21 g (28%); mp 73–75 °C.

^{1}H NMR (CD_3CN): δ = 3.61 (s, 4 H, H-17,18), 3.67 (t, *J* = 4.2 Hz, 2 H, H-19), 3.78 (s, 3 H, NCH_3), 3.79 (t, *J* = 4.1 Hz, 2 H, H-16), 4.14 (t, *J* = 4.1 Hz, 2 H, H-20), 4.25 (t, *J* = 4.1 Hz, 2 H, H-15), 7.07 (s, 1 H, H-4), 7.20 (dt, *J* = 7.9, 1.5 Hz, 1 H, H-7), 7.59 (d, *J* = 8.7 Hz, 1 H, H-5), 7.69 (dt, *J* = 1.5, 8.7 Hz, 1 H, H-6), 7.86 (s, 1 H, H-1), 8.30 (dd, *J* = 1.5, 7.9 Hz, 1 H, H-8).

^{13}C NMR ($CDCl_3$): δ = 35.4 (NCH_3), 63.7 (C-16), 64.5 (C-19), 67.8 (C-17,18), 70.4 (C-15), 72.3 (C-20), 102.6 (C-4), 115.5 (C-1), 115.9 (C-5), 122.0 (C-13,14), 122.4 (C-7), 127.0 (C-8), 131.2 (C-11,12), 137.0 (C-2), 139.9 (C-6), 146.8 (C-3), 176.0 (C-9).

Anal. Calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.35; H, 6.12; N, 3.82.

HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{22}NO_5$: 356.1492; found: 356.1498.

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HRMS-ESI: *m/z* [M + 2H]$^{2+}$ calcd for $C_{20}H_{22}NaNO_5$: 378.1312; found: 378.1318.

Di-2,7-(10-methyl-9-phenylacridinium)-28-crown-6 Dihexafluorophosphate (12)

A solution of **5** (0.4 g, 0.60 mmol) in THF (60 mL) was added dropwise over 2 h to a Grignard-compound prepared from bromobenzene (0.95 g, 6.1 mmol) and Mg (0.16 g, 6.1 mmol) in THF (10 mL). After the addition was complete, the mixture was refluxed for 16 h then the solvent was removed and the resulting oil was purified by column chromatography [MeOH–H_2O–aq NH_4Cl (7 M), 20:6:0.1]. The pooled fractions containing the product were combined and the solution was evaporated under reduced pressure. $CHCl_3$ (200 mL) was added, the solid was filtered off and the filtrate was evaporated. The resulting yellow residue was dissolved in H_2O and NH_4PF_6 was added to precipitate the product **12**, which was finally washed with H_2O (3 × 5 mL) and dried.

Yield: 0.49 g (80%); R_f = 0.1 [MeOH–H_2O–aq NH_4Cl (7 M), 20:6:0.1]; mp 308–315 °C.

^{1}H NMR (CD_3CN): δ = 3.57 (m, 8 H, H-22,24), 3.93 (m, 8 H, H-21,24), 4.70 (s, 6 H, NCH_3), 6.85 (d, *J* = 3.0 Hz, 4 H, H-1,8), 7.16 (d, *J* = 7.5 Hz, 2 H, H-16′,20′), 7.23 (d, *J* = 6.4 Hz, 2 H, H-16,20), 7.42 (dd, *J* = 9.8, 3.0 Hz, 4 H, H-3,6), 7.77 (m, 6 H, H-17,18,19), 8.23 (d, *J* = 9.8 Hz, 4 H, H-5,5).

^{13}C NMR (CD_3CN): δ = 40.8 (CH_3, NCH_3), 69.3 (C-21,24), 71.7 (C-22,23), 107.6 (C-1,8), 120.6 (C-4,5), 128.4 (C-13,14), 130.6 (C-16′,20′), 130.7 (C-16,20), 131.2 (C-18), 131.4 (C-17′,19′), 131.5 (C-17,19), 132.0 (C-3,6), 134.6 (C-9), 137.1 (C-11,12), 155.9 (C-2,7), 158.8 (C-15).

Anal. Calcd for $C_{48}H_{44}F_{12}N_2O_6P_2$: C, 55.71; H, 4.29; N, 2.71. Found: C, 55.41; H, 4.72; N, 2.99.

HRMS-ESI: *m/z* [M – $2PF_6$]$^{2+}$ calcd for $C_{48}H_{44}N_2O_6$: 372.1594; found: 372.1604.

Di-2,7-(10-methyl-9-phenylacridinium)-34-crown-8 Dihexafluorophosphate (13)

Prepared from **6** following the procedure described for **12** above.

Yield: 0.45 g (66%); mp 130–132 °C.

^{1}H NMR (CD_3CN): δ = 3.59 (br s, 8 H, H-23,24), 3.64 (m, 8 H, H-22,25), 3.84 (m, 8 H, H-21,26), 4.71 (s, 6 H, NCH_3), 6.82 (d, *J* = 2.6 Hz, 4 H, H-1,8), 7.16 (d, *J* = 6.8 Hz, 4 H, H-16,20), 7.65 (m, 10 H, H-3,6,17,18,19), 8.32 (d, *J* = 9.8 Hz, 4 H, H-5,5).

^{13}C NMR (CD_3CN): δ = 40.9 (CH_3, NCH_3), 70.2 (C-23,24), 70.3 (C-22,25), 72.1 (C-21,26), 107.5 (C-1,8), 121.4 (C-4,5), 128.8 (C-13,14), 130.9 (C-16,20), 131.2 (C-17,19), 131.9 (C-18), 132.1 (C-3,6), 134.5 (C-9), 137.6 (C-11,12), 156.4 (C-2,7), 158.7 (C-15).

Anal. Calcd for $C_{52}H_{52}F_{12}N_2O_8P_2$: C, 55.62; H, 4.67; N, 2.49. Found: C, 55.34; H, 4.91; N, 2.77.

HRMS-ESI: *m/z* [M – $2PF_6$]$^{2+}$ calcd for $C_{52}H_{52}N_2O_8$: 416.1856; found: 416.1586.

Preparation of Crown Ethers Containing the Acridane Unit: General Procedure

A mixture of the acridinium crown ether (0.3 mmol) in MeOH (40 mL) was stirred at r.t. and titrated with tetraethylammonium hydroxide (25% solution in MeOH) until the solution decolorized. When the addition was complete, the mixture was stirred at r.t. for 1 h, then the solution was evaporated under reduced pressure. The residue was dissolved in $CHCl_3$ and the solution was filtered. The filtrate was evaporated in vacuo to afford the acridane compounds in quantitative yield.

Di-2,7-(10-methyl-9-phenyl-9-methoxyacridane)-28-crown-6 (14)

Mp 157–160 °C.

^{1}H NMR ($CDCl_3$): δ = 3.00 (s, 6 H, OCH_3), 3.40 (s, 6 H, NCH_3), 3.72 (m, 8 H, H-23,24), 4.08 (m, 8 H, H-22,25), 7.44–7.01 (m, 12 H, H-1,2,4,5,6,8), 7.83 (m, 10 H, H-16,17,18,19,20).

^{13}C NMR ($CDCl_3$): δ = 33.4 (CH_3, NCH_3), 51.5 (CH_3, OCH_3), 68.7 (C-22,25), 70.5 (C-23,24), 79.8 (C-9), 113.0 (C-4,5), 115.8 (C-1,8), 116.8 (C-3,6), 125.7 (C-18), 127.6 (C-16,20), 127.8 (C-17,19), 135.7 (C-13,14), 141.8 (C-11,12), 144.2 (C-15), 152.9 (C-2,7).

Anal. Calcd for $C_{50}H_{50}N_2O_8$: C, 74.42; H, 6.25; N, 3.47. Found: C, 74.33; H, 6.46; N, 3.21.

HRMS-ESI: *m/z* [M + 2H]$^{2+}$ calcd for $C_{50}H_{50}N_2O_8$: 405.1856; found: 405.2833.

Bis-2,7-(10-methyl-9-phenyl-9-methoxyacridane)-51-crown-12 (15)

Mp 160–165 °C.

^{1}H NMR ($CDCl_3$): δ = 2.89 (s, 3 H, H-21), 2.94 (s, 3 H, H-21), 3.34 (s, 3 H, NCH_3), 3.38 (s, 3 H, NCH_3), 3.65 (m, 8 H, H-22,25), 3.77 (m, 8 H, H-23,26), 4.05 (m, 8 H, H-22,27), 7.24–6.96 (m, 12 H, H-1,3,4,5,6,8), 7.65 (m, 10 H, H-16,17,18,19,20).

^{13}C NMR ($CDCl_3$): δ = 33.5 (CH_3, NCH_3). 51.4 (CH_3, OCH_3), 67.9 (C-22,27), 69.6 (C-24,25), 70.8 (C-23,26), 90.1 (C-9), 112.9 (C-4,5), 114.1 (C-1,8), 115.7 (C-3,6), 124.8 (C-18), 125.6 (C-16,20), 127.8 (C-19,17), 127.9 (C-13,14), 135.8 (C-11,12), 138.5 (C-15), 152.6 (C-2,7).

Anal. Calcd for $C_{56}H_{66}N_2O_{10}$: C, 72.55; H, 7.18; N, 3.02. Found: C, 74.13; H, 6.76; N, 3.36.

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{56}H_{66}N_2O_{10}$: 927.4790; found: 927.4786.

[2,7-(10-Methyl-9-phenylacridinium)]-(1′,2′-phenyl)-29-crown-8 Chloride (16)

A solution of **8** (0.4 g, 0.69 mmol) in THF (60 mL) was added dropwise over 2 h to a Grignard-compound prepared from bromobenzene (1.1 g, 6.9 mmol) and Mg (0.16 g, 6.06 mmol) in THF (10 mL). After the addition was complete, the mixture was refluxed for 18 h then the solvent was removed and the resulting oil was purified by chromatography [MeOH–H_2O–aq NH_4Cl (7 M), 20:6:0.1]. The pooled fractions containing the product were evaporated under reduced pressure and $CHCl_3$ (200 mL) was added. Inorganic salts were filtered off and the filtrate was evaporated in vacuo to give **16**.

Yield: 0.22 g (46%); R_f = 0.5 [MeOH–H_2O–aq NH_4Cl (7 M), 20:6:0.1]; mp 78–80 °C.

^{1}H NMR ($CDCl_3$): δ = 3.52 (m, 12 H, H-23,23′,24,24′,25,25′), 3.81 (t, *J* = 4.1 Hz, 4 H, H-22,22′), 4.25 (t, *J* = 4.1 Hz, 4 H, H-21,21′), 4.98 (s, 3 H, NCH_3), 6.28 (m, 2 H, H-4′,5′), 6.70 (m, 2 H, H-3′,6′), 7.23 (d, *J* = 2.6 Hz, 2 H, H-1,8), 7.60 (d, *J* = 7.5 Hz, 2 H, H-16,20), 7.70 (m, 3 H, H-17,18,19), 7.91 (dd, *J* = 9.8, 2.6 Hz, 2 H, H-3,6), 8.68 (d, *J* = 9.8 Hz, 2 H, H-4,5).

^{13}C NMR ($CDCl_3$): δ = 40.6 (NCH_3), 68.3, 68.4, 69.2 (C-23,23′,24,24′,25,25′), 69.9 (C-22,22′), 70.6 (C-12,21′,26,26′), 107.3 (C-1,8), 114.4 (C-4′,5′), 120.6 (C-4,5), 121.6 (C-3′,6′), 128.7 (C-13,14), 128.9 (C-17,19), 129.9 (C-18), 130.1 (C-16,20), 131.3 (C-3,6), 133.9 (C-9), 136.2 (C-11,12), 148.0 (C-2,7), 157.3 (C-15).

Anal. Calcd for $C_{38}H_{42}ClNO_8$: C, 67.50; H, 6.26; N, 2.07. Found: C, 67.28; H, 6.39; N, 2.11.

HRMS-ESI: *m/z* [M –Cl]$^+$ calcd for $C_{38}H_{42}NO_8$: 640.2910; found: 640.2918.

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[2,3-(10-Methyl-9-phenylacridinium)]-(1′,2′-phenyl)-24-crown-8 Chloride (18)

Prepared from **10** following the procedure described for **16** above.

Yield: 0.25 g (54%); R_f = 0.2 [MeOH–H_2O–aq NH_4Cl (7 M), 20:6:0.1]; mp 70–72 °C.

^{1}H NMR ($CDCl_3$): δ = 3.75 (m, 8 H, H-25,26,27,28), 3.82 (m, 8 H, H-21,23,29,30), 3.88 (m, 2 H, H-24), 3.98 (m, 4 H, H-31,32), 4.92 (m, 2 H, H-22), 5.02 (br s, 3 H, NCH_3), 6.66 (m, 4 H, H-35,36,37,38), 6.69 (s, 1 H, H-1), 7.21 (m, 2 H, H-16,20), 7.59 (m, 4 H, H-7,17,18,19), 7.68 (d, *J* = 8.3 Hz, 1 H, H-8), 8.18 (m, 1 H, H-6), 8.23 (s, 1 H, H-4), 8.57 (d, *J* = 9.0 Hz, 1 H, H-5).

^{13}C NMR ($CDCl_3$): δ = 40.3 (CH_3, NCH_3), 68.9, 69.0, 69.1, 69.2, 69.5, 69.8, 69.9, 71.0, 71.1, 71.3, 71.5, 72.0 (C-21,22,23,24,25,26,27,28,29,30,31,32), 99.5 (C-1), 105.7 (C-4), 113.6 (C-36,37), 118.2 (C-5), 121.2 (C-35,38), 122.8 (C-13), 124.5 (C-14), 126.7 (C-6), 129.1 (C-8,16,17,19,20), 130.2 (C-18), 135.8 (C-7), 139.1 (C-12), 141.5 (C-11), 148.6 (C-2), 150.1 (C-3), 154.8 (C-33,34), 160.7 (C-15).

Anal. Calcd for $C_{38}H_{42}NO_8Cl$: C, 67.50; H, 6.26; N, 2.07; Cl, 5.24. Found: C, 67.64; H, 6.51; N, 2.21; Cl, 5.30.

HRMS-ESI: *m*/*z* [M – Cl]$^+$ calcd for $C_{38}H_{42}NO_8$: 640.2910; found: 640.2916.

UV/Vis (*n*-propanol): λ_{max} (ε) = 277 (44000), 397 nm (8500).

[2,7-(10-Methyl-9-phenyl-9-methoxyacridane)]-(1′,2′-phenyl)-29-crown-8 (17)

Obtained according to the general procedure, using toluene instead of $CHCl_3$.

Mp 68–73 °C.

^{1}H NMR ($CDCl_3$): δ = 3.05 (s, 3 H, OCH_3), 3.36 (s, 3 H, NCH_3), 3.65 (m, 8 H, H-23,23′,24,24′), 3.68 (m, 4 H, H-25,25′), 3.76 (t, *J* = 6.0 Hz, 4 H, H-22,22′), 4.10 (m, 8 H, H-21,21′,26,26′), 6.87 (s, 6 H, H-4,5,3′,4′,5′,6′), 7.02 (d, *J* = 1.5 Hz, 2 H, H-3,6), 7.10 (d, *J* = 7.1 Hz, 1 H, H-18), 7.23 (t, *J* = 7.5 Hz, 2 H, H-17,19), 7.25 (s, 2 H, H-1,8), 7.31 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 33.4 (CH_3, NCH_3), 51.3 (CH_3, OCH_3), 68.1, 68.9, 69.5, 69.7, 70.7 (CH_2), 100.8 (C_q), 112.9 (CH), 114.3 (CH), 115.8 (CH), 116.9 (CH), 121.3 (C_q), 124.6 (CH), 126.0 (CH), 126.4 (CH), 127.8 (CH), 135.1 (C_q), 136.1 (C_q), 148.8 (C_q), 152.0 (C_q).

Anal. Calcd for $C_{40}H_{49}NO_9$: C, 69.85; H, 7.18; N, 2.04. Found: C, 69.55; H, 7.21; N, 2.37.

[2,3-(10-Methyl-9-phenyl-9-methoxyacridane)]-(1′,2′-phenyl)-24-crown-8 (19)

Obtained according to the general procedure using toluene instead of $CHCl_3$.

Mp 47–50 °C.

^{1}H NMR ($CDCl_3$): δ = 2.90 (s, 3 H, OCH_3), 3.45 (s, 3 H, NCH_3), 3.67 (s, 8 H, H-25,26,27,28), 3.81 (m, 2 H, H-24), 3.75 (m, 6 H, H-23,29,30), 4.04 (m, 6 H, H-21,31,32), 4.18 (m, 2 H, H-22), 6.66 (s, 1 H, H-4), 6.74 (s, 1 H, H-1), 6.84 (s, 6 H, H-5,7,35,36,37,38), 7.08 (t, *J* = 7.2 Hz, 2 H, H-17,19), 7.23 (m, 5 H, H-6,8,16,18,20).

^{13}C NMR ($CDCl_3$): δ = 33.7 (CH_3, NCH_3), 56.1 (CH_3, OCH_3), 68.8, 69.7, 69.9, 70.7, 70.8, 71.3 (C-21,22,23,24,25,26,27,28,29,30,31,32), 97.2 (C-9), 112.1 (C-4), 114.9 (C-36,37), 115.5 (C-8), 119.9 (C-5), 121.4 (C-7), 121.6 (C-35,38), 124.0 (C-13), 125.8 (C-14), 126.1 (C-18), 126.6 (C-16,20), 127.6 (C-17,19), 128.2 (C-6), 134.9 (C-11), 140.8 (C-12), 142.4 (C-2), 143.1 (C-15), 145.4 (C-3), 150.7 (C-33,34).

Anal. Calcd for $C_{40}H_{49}NO_9$: C, 69.85; H, 7.18; N, 2.04. Found: C, 69.90 H, 6.83; N, 2.09.

HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{40}H_{50}NO_9$: 688.3480; found: 688.3478.

HRMS-ESI: *m*/*z* [M + H + Na]$^{2+}$ calcd for $C_{40}H_{50}NNaO_9$: 355.6686; found: 355.6684.

UV/Vis (*n*-propanol): λ_{max} (ε) = 278 nm (29000).

2,3-(10-Methyl-9-phenylacridinium)crown-4 Chloride (20)

Obtained according to the general procedure used for the synthesis of compound **12** and isolated as the chloride.

Yield: 0.22 g (46%); mp 43–45 °C.

^{1}H NMR (CD_3CN): δ = 3.65 (m, 6 H, H-22,23,24), 3.94 (t, *J* = 4.1 Hz, 2 H, H-25), 4.15 (t, *J* = 4.6 Hz, 4 H, H-21), 4.63 (t, *J* = 4.5 Hz, 2 H, H-26), 4.71 (s, 3 H, NCH_3), 7.27 (s, 1 H, H-1), 7.48 (m, 2 H, H-16,20), 7.72 (m, 4 H, H-7,17,18,19), 7.79 (s, 1 H, H-4), 7.86 (dd, *J* = 8.7, 1.5 Hz, 1 H, H-8), 8.22 (dt, *J* = 9.0, 1.5 Hz, 1 H, H-6), 8.50 (d, *J* = 9.4 Hz, 1 H, H-5).

^{13}C NMR (CD_3CN): δ = 40.4 (NCH_3), 69.7 (C-25), 70.5 (C-22), 71.9 (C-23,24), 73.9 (C-26), 75.8 (C-21), 102.4 (C-4), 116.7 (C-1), 119.5 (C-5), 124.8 (C-13), 126.5 (C-14), 128.5 (C-7), 130.9 (C-17,18,19), 131.0 (C-8), 131.2 (C-16,20), 135.2 (C-12), 137.7 (C-6), 141.6 (C-11), 153.4 (C-2), 158.6 (C-3), 164.4 (C-15).

Anal. Calcd for $C_{26}H_{26}ClNO_4$: C, 69.10; H, 5.80; N, 3.10. Found: C, 68.83; H, 5.53; N, 2.99.

HRMS-ESI: *m*/*z* [M – Cl]$^+$ calcd for $C_{26}H_{26}NO_4$: 416.1856; found: 416.1861.

2,7-Bis{2-[2-(2-hydroxyethoxy)ethoxy]ethoxy}-10-methyl-9-phenylacridinium Chloride (21)

Compound **1** (1.9 g, 7.15 mmol) dissolved in anhydrous THF (120 mL) was added to a boiling solution of the Grignard-compound prepared from bromobenzene (2.23 g, 14.3 mmol) and Mg (0.38 g) in THF (30 mL). The reaction mixture was heated under reflux for 24 h then filtered and the filtrate was evaporated. The remaining residue was purified by column chromatography [MeOH–H_2O–aq NH_4Cl (7 M), 12:3:0.1] and the yellow fractions containing the product were combined and evaporated. The remaining solid was dissolved in MeCN, filtered and the solvent was removed in vacuo to give 2,7-dimethoxy-10-methyl-9-phenylacridinium chloride.

Yield: 1.4 g (55%); yellow solid; mp 182–185 °C.

^{1}H NMR (CD_3OD): δ = 4.00 (s, 6 H, OCH_3), 5.15 (s, 3 H, NCH_3), 7.29 (d, *J* = 3.0 Hz, 2 H), 7.79 (m, 2 H), 8.03 (m, 3 H), 8.20 (dd, *J* = 3.0, 9.8 Hz, 2 H), 8.88 (d, *J* = 9.8 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 38.8 (NCH_3), 55.9 (OCH_3), 105.3 (CH), 119.9 (CH), 127.8 (C_q), 129.5 (CH), 129.9 (CH), 130.6 (CH), 130.8 (CH), 134.0 (C_q), 136.7 (C_q), 129.0 (C_q), 157.6 (C_q).

Anal. Calcd for $C_{22}H_{20}ClNO_2$: C, 72.16; H, 5.46; N, 3.82. Found: C, 71.95; H, 5.87; N, 3.94.

HRMS-ESI: *m*/*z* [M – Cl]$^+$ calcd for $C_{22}H_{20}NO_2$: 330.1489; found: 330.1492.

2,7-Dimethoxy-10-methyl-9-phenylacridinium chloride (1 g, 3.0 mmol), dissolved in aq HBr (47%, 20 mL), was heated under reflux for 2 h. The solvent was removed in vacuo and the crude product was recrystallized from MeOH to give 2,7-dihydroxy-10-methyl-9-phenylacridinium bromide.

Yield: 1.06 g (92%); yellow-orange solid; mp 210–214 °C.

^{1}H NMR (CD_3OD): δ = 4.87 (s, 3 H, NCH_3), 7.06 (d, *J* = 2.6 Hz, 2 H), 7.50 (m, 2 H), 7.73 (m, 3 H), 7.88 (dd, *J* = 2.6, 9.8 Hz, 2 H), 8.60 (d, *J* = 9.8 Hz, 2 H).

^{13}C NMR (CD_3OD): δ = 38.1 (NCH_3), 107.6 (CH), 120.1 (CH), 128.4 (C_q), 129.0 (CH), 129.9 (CH), 129.0 (CH), 129.5 (CH), 129.6 (CH), 130.6 (CH), 134.7 (C_q), 135.9 (C_q), 153.9 (C_q), 156.6 (C_q).

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Anal. Calcd for $C_{20}H_{16}BrNO_2$: C, 62.84; H, 4.22; N, 3.66; Br, 20.90. Found: C, 62.49; H, 4.11; N, 3.23; Br, 21.05.

2,7-Dihydroxy-10-methyl-9-phenyl-acridinium bromide (0.55 g, 1.4 mmol), dissolved in MeCN (200 mL), was treated with tetramethylammonium hydroxide (25% in MeOH, 4.3 g, 7.28 mmol). The violet solution was heated under reflux for 1 h. After cooling, tris-ethyleneglycol-bis-tosylate (1.66 g, 5.46 mmol) was added and the reaction mixture was heated under reflux for 24 h. The solvent was removed in vacuo and the crude product was purified by column chromatography [MeOH–H_2O–aq NH_4Cl (7 M), 11:3:0.1]. After evaporation of the solvents, NH_4Cl was removed with water. The residue was taken up in CH_2Cl_2 (50 mL), then the solution was treated with H_2O (2 × 10 mL). The solution was dried and evaporated to give **21**.

Yield: 0.8 g (73%); R_f = 0.42 [MeOH–H_2O–aq NH_4Cl (7 M), 11:3:0.1]; mp 55–57 °C.

^{1}H NMR ($CDCl_3$): δ = 3.41 (s, 2 H, OH), 3.53 (t, *J* = 4.9 Hz, 4 H, H-26,26′), 3.62 (m, 12 H, H-23,23′,24,24′,25,25′), 3.78 (t, *J* = 4.9 Hz, 4 H, H-22,22′), 4.02 (t, *J* = 3.7 Hz, 4 H, H-21,21′), 5.16 (s, 3 H, N-CH_3), 6.91 (d, *J* = 2.6 Hz, 2 H, H-1,8), 7.35 (m, 2 H, H-16,20), 7.64 (m, 3 H, H-17,18,19), 7.98 (dd, *J* = 2.6, 9.8 Hz, 2 H, H-3,6), 8.82 (d, *J* = 9.8 Hz, 2 H, H-4,5).

^{13}C NMR (CD_3OD): δ = 40.1 (NCH_3), 61.2 (C-26,26′), 68.5 (C-21,21′), 69.6 (C-22,22′), 70.5 (C-23,23′), 70.8 (C-25,25′), 72.7 (C-24,24′), 105.9 (C-1,8), 121.1 (C-4,5), 128.4 (C-13,14), 129.0 (C-16,20), 130.4 (C-17,18,19), 134.4 (C-9), 137.2 (C-11,12), 155.4 (C-15), 157.6 (C-2,7).

Anal. Calcd for $C_{32}H_{40}ClNO_8$: C, 63.77; H, 6.64; N, 2.32; Cl, 5.90. Found: C, 63.49; H, 6.44; N, 2.61; Cl, 6.00.

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