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Synthesis and X-ray crystallographic studies of novel proton-ionizable nitro- and halogen-substituted acridono-18-crown-6 chromo- and fluorogenic ionophores

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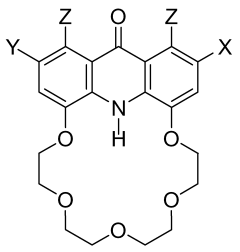
Dedicated to Professor Mihály Nógrádi on the occasion of his 70th birthday

Abstract—Starting from acridono-18-crown-6 ligand **1** (Fig. 1) seven new proton-ionizable chromogenic and fluorogenic ionophores **2**–**8** (Fig. 1) containing NO_2 group(s) and/or Br or Cl atom(s) in the aromatic rings were prepared by electrophilic substitution. The precursor macrocycle **1** was obtained by a modification of the reported procedure which made chromatography unnecessary in purification and gave higher yield. X-ray crystallographic studies of the complexes of acridono-18-crown-6 type ligands **1**, **2**, **3**, **6** and **8** show that the proton-ionizable units are in the acridone tautomeric form and that the ligands invariably bind a water molecule in their cavities by multipodal hydrogen bonding. In two cases (**6** and **8**) an additional DMF solvent molecule is also bound at the crown perimeter in the solid state.

1. Introduction

Crown ether type macrocycles containing proton-ionizable groups are of interest for many researchers, because at higher pH than their pK_a values they are mostly ionized to anions which increase the cation–crown complex stability with enhancement of selectivity, and avoid the need for a counter anion in cation transport through a liquid membrane or in solvent extraction.[1–6] Among a large number of proton-ionizable crown ethers that have been synthetized and studied,[1–13] from the point of view of our research the macrocycles containing a pyridone subcyclic unit (ligands **9** and **10** for example, see Fig. 2)[9–13] should be mentioned. The latter macrocycles were prepared by Bradshaw and co-workers.[9,10] In these ligands, the proton-ionizable subcyclic unit is part of the macroring and the water-insoluble macrocycle **10** proved to be an excellent carrier for potassium cation at source phase pH values higher than 12 in a H_2O (source phase)-CH_2Cl_2 (liquid membrane)-H_2O (receiving phase) system.[12,13] The transport of metal cations using ligand **10** is pH dependent so that transport can be turned on or off by adjusting the pH.[3,12,13] In the case of water soluble ligand **9** no transport occurred, because the crown ether distributed into the aqueous phase so that it was not available as a carrier.[12,13] Since the pK_a value for removal of a proton from the octyl-substituted ligand **10** is presumably close to that for pyridine-4(1*H*)-one (11.09 in water[14]) and water-soluble macrocycle **9** (10.98 in water[9]), respectively appreciable transport can only take place when most of the crown ether in question is ionized at the aqueous source phase-organic membrane interface.[12,13]



1: X = Y = Z = H
2: X = NO_2, Y = Z = H
3: X = Y = NO_2, Z = H
4: X = Br, Y = NO_2, Z = H
5: X = Y = Br, Z = H
6: X = Y = Br, Z = NO_2
7: X = Y = Cl, Z = H
8: X = Y = Cl, Z = NO_2

Figure 1. Schematics of acridono-18-crown-6 type ligands.

Keywords: acridones; proton-ionizable crown ethers; chromogenic ionophores; fluorogenic ionophores; multipodal hydrogen bonding; X-ray crystallography.

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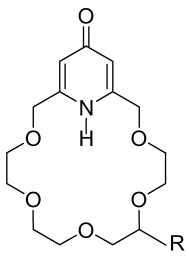


9: R = H
10: R = octyl

Figure 2. Schematics of pyridono-18-crown-6 type ligands.

Recently we reported the synthesis of fluorescent 18-crown-6 type ligand **1** (Fig. 1) containing acridone proton-ionizable subunit[15] where the proton-dissociative group is also part of the macroring. This water-insoluble ligand or its derivatives are good candidates for producing neutral complexes with cations, and functioning as carriers in different membrane systems or as extracting agents. The acridone tricyclic unit makes the 18-crown-6 framework rigid conferring high selectivity in the molecular recognition process.[16,17] Acridone derivatives have attractive coloration, crystallinity and strong fluorescence.[18–21] The aromatic rings of the acridone unit are prone to electrophilic substitution,[18,19] and by introducing appropriate substituents into the parent ligand **1** the acidity of the NH proton and its photophisycal behaviour can be favorably altered. This can open the door for creating new proton-ionizable chromogenic and fluorogenic host molecules. Such ligands, beside selective transport and extraction, are also potential photometric reagents for metal ion determination, since replacement of the proton of chromophore or fluorophore unit with a metal cation produces a change in color or fluorescence.

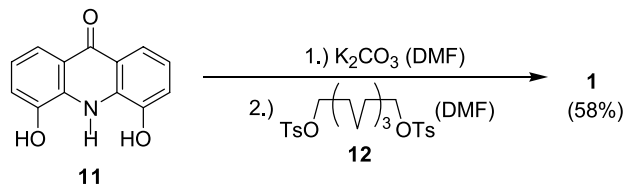
It should be mentioned that to our knowledge only one paper[22] reports the pK_a value of the parent acridone (acridine-9(10*H*)-one: 16.4 in DMSO which should be lower in water[23,24]). Since we were convinced that introducing electron withdrawing substituents into the aromatic rings of crown ether **1** would substantially increase the acidity of NH proton, we prepared ligands **2**–**8** (Fig. 1). Our supposition was right, because the first determined pK_a value for dinitro-substituted acridono-crown host **3** was 12.25 in MeOH[25] which can then be estimated[26] to be about 11.45 in water. The pK_a determination of the other acridono ligands and their studies for cation complexation, membrane transport and solvent extraction are underway and the results will be published in the future.

It is noteworthy to mention here that to our knowledge no electrophilic substitution of 4,5-dimethoxyacridine-9(10*H*)-one a known compound[15,27,28] structurally related to the proton-ionizable unit of acridono-crown ether **1** has been reported, although the former has an interest in medicinal chemistry.[28]

This paper therefore reports the preparation of seven novel ligands **2**–**8** and the X-ray crystallographic studies of crown ethers **1**, **2**, **3**, **6** and **8**. A simplified procedure giving an improved yield of the parent acridono-18-crown-6 macrocycle **1** is also presented here.

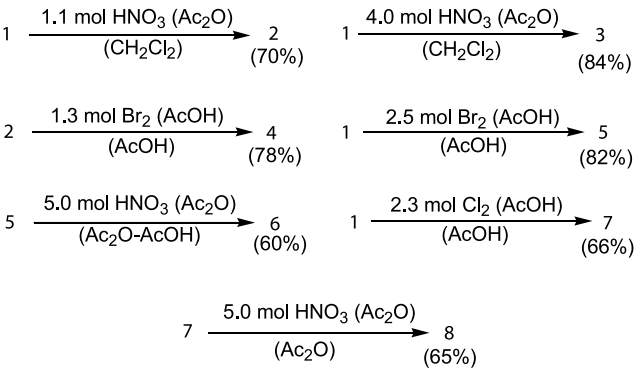
2. Results and discussion

The precursor acridono-crown ether **1** needed for the preparation of novel macrocycles **2**–**8** (Fig. 1) was obtained by the modification of one of the three procedures we reported earlier[15] (see also Scheme 1 and Experimental Section 3). In the preparation of ligand **1** more solvent (DMF) was used, a longer reaction time was applied, and after the reaction was complete (TLC analysis), the solvent was removed at a lower temperature than reported.[15] According to its ^{1}H NMR spectrum and TLC analysis, the crude product obtained this way was pure enough to make chromatography unnecessary, and it could be purified simply by crystallization from EtOH giving a higher yield than reported.[15]



Scheme 1. Preparation of the precursor acridono-18-crown-6 ligand **1** from 4,5-dihydroxyacridine-9(10*H*)-one (**11**) and tetraethylene glycol di-*p*-toluenesulfonate (**12**).

Nitroacridono-18-crown-6 ligand **2** was obtained from macrocycle **1** using a small excess of fuming nitric acid mixed with a large excess of acetic anhydride in CH_2Cl_2 (see Scheme 2). When 4 mol of fuming nitric acid were used for 1 mol of ligand **1**, with otherwise similar conditions, dinitroacridono-18-crown-6 ether **3** was obtained in a good yield. Nitroacridono-crown ether **2** was treated with a small excess of bromine in acetic acid to give the mono-brominated nitroacridono ligand **4**. The ^{1}H NMR spectrum of crown ether **4** clearly proved the positions of the bromine atom and the nitro group, even the coupling constants (J=2 Hz) between the protons in *meta* positions could easily be determined. Bromination and chlorination of the parent acridono-crown ether **1** using a little more than 2 mol of halogen in acetic acid furnished the dibromo- and dichloro-substituted acridono-18-crown-6 ligands **5** and **7**, respectively. Their structures were proved both by NMR spectroscopy and by the X-ray crystallographic analyses of their dinitro-derivatives **6** and **8**, respectively (see later). Dibromo- and dichloro-substituted acridono-crown ethers **5** and **7** were treated with 5 mol of fuming nitric acid in acetic



Scheme 2. Preparation of new proton-ionizable nitro- and halogen-substituted-acridono-18-crown-6 ligands **2**–**8**.

anhydride–acetic acid mixture to give dihalogeno–dinitroacridono ligands **6** and **8**, respectively. The X-ray crystallographic analyses showed the two nitro groups to be at positions 18 and 22 of the crown ethers (see later). The elemental (combustion) analyses showed that all the new ligands (**2**–**8**) contained 1 mol of water, and in the cases of crown ethers **2**, **3**, **6** and **8** X-ray analyses proved that this water molecule is complexed firmly by these macrocycles. When the ^{1}H NMR spectra were taken in $CDCl_3$ as in the cases of ligands **2** and **7** broad singlets with the correct intensities at 3.27 and 2.54, respectively, also confirmed a molecule of complexed water. Unfortunately ligands **3**, **4**, **5**, **6** and **8** are scarcely soluble in $CDCl_3$ and their NMR spectra were taken in DMSO-d_6. In the latter cases the broad singlets of complexed water had no proper intensities, because they were enlarged by the water content of the solvent, and we have therefore omitted them from the reported ^{1}H NMR data.

It is noteworthy to mention that both the ^{1}H NMR spectrum taken in $CDCl_3$ and the combustion analysis showed only half mole of bound water for ligand 1,[15] but when this macrocycle was crystallized over days from EtOH in an open glass ampoule, the single crystal so obtained complexed 1 mol of water as all of the others (**2**, **3**, **6** and **8**) according to X-ray analysis. The X-ray crystal structures substantiate that this conserved water plays an important role. It always donates two H bridges to the same O atoms as well as accepting a H-bond from the acridone N atom. The solid state organization of these complexes is in some respect similar to that observed for a related *N*-methyl-acridono-23-crown-6 trihydrate crystal.[29] Obviously, these

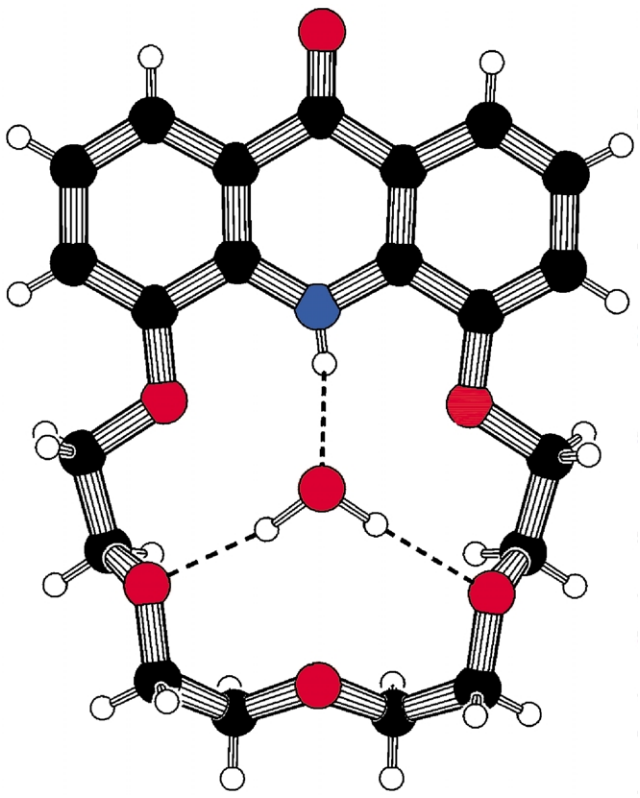


Figure 3. Molecular structure in the **1**·H_2O crystal, H-bridges are shown in broken lines.

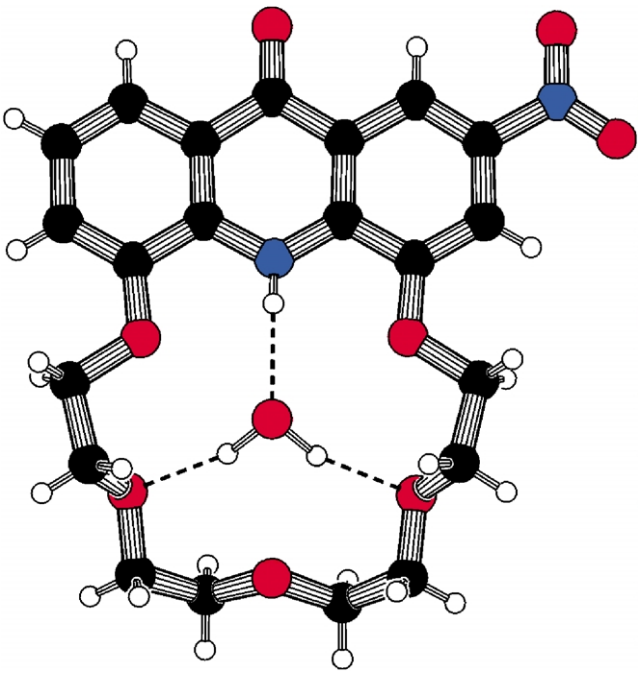


Figure 4. Molecular structure in the **2**·H_2O crystal, H-bridges are shown in broken lines.

crystal structures are primarily influenced by the H-bonding activity of the –NH group, which is in turn tuned by the substitution pattern of the acridone unit. Mean values of (e.g.) the intraring N–C bonds (1.373(8)Å calculated for five values) and the C=O bonds (1.226(6)Å for five values) do not indicate large substituent effects, but there does appear to be the expected modest correlation between these dimensions. Figures 3–7 indicate the basic structure forming crown ether units of these complex crystals. Analysis of hydrogen bridges show that water binds in a fairly uniform way in these crystals as far as H-bonding geometry goes (Table 1).

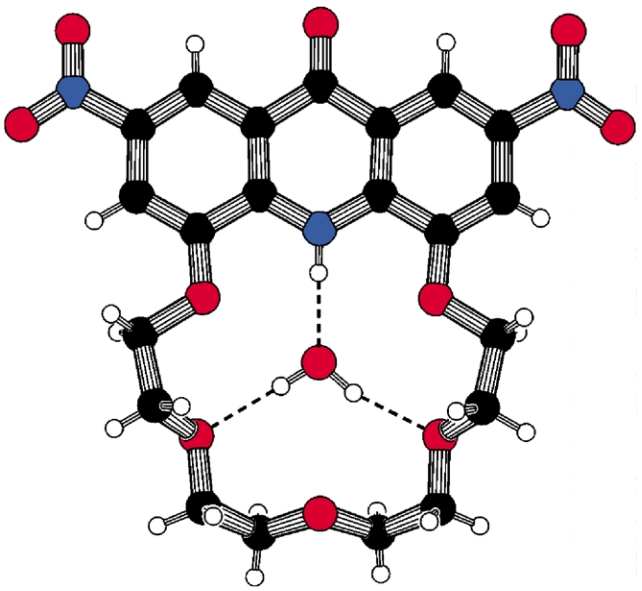


Figure 5. Molecular structure in the **3**·H_2O crystal, H-bridges are shown in broken lines.

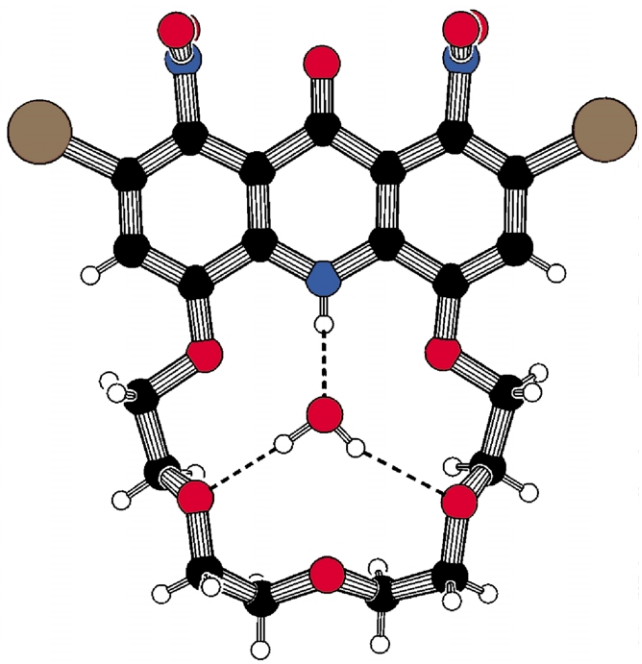


Figure 6. Molecular structure of **6**·H_2O from the **6**·H_2O·DMF crystal, H-bridges are shown in broken lines.

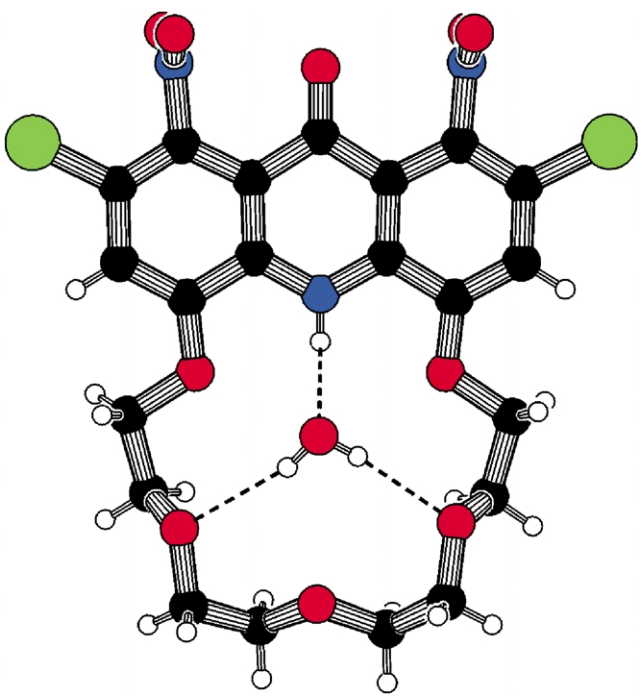


Figure 7. Molecular structure of **8**·H_2O from the **8**·H_2O·DMF crystal, H-bridges are shown in broken lines.

The molecular structures otherwise show usual bonding discrepancy in the distal positioned ethylenedioxy moieties opposing the acridone unit, as is usual for larger crown rings.

Table 1. Hydrogen bridge geometry to water molecules in the crown rings in **1**, **2**, **3**, **6** and **8** sorted by type. Meaningful standard deviations are only given for bridgehead distances

Compound	D–H···A	D–H (Å)	H···A (Å)	D···A (Å)	D–H···A (°)
1	N26–H26···Ow	0.85	2.44	3.158(3)	144
2		0.85	2.03	2.862(2)	167
3		0.88	1.84	2.703(1)	169
6		0.86	2.23	2.928(4)	138
8		0.86	2.21	2.911(3)	139
1	Ow–H1w···O5	1.14	1.97	3.064(3)	159
2		1.14	1.93	3.021(3)	159
3		0.89	1.98	2.857(2)	166
6		0.87	2.31	3.144(4)	160
8		0.80	2.17	2.971(3)	174
1	Ow-H2w···O11	1.06	2.06	3.108(3)	169
2		1.07	1.96	3.001(2)	163
3		0.92	1.93	2.833(1)	165
6		0.96	2.02	2.967(4)	170
8		0.83	2.31	3.120(3)	165

3. Experimental

3.1. General

Infrared spectra were obtained on a Zeiss Specord IR 75 spectrometer. ^1H (500 MHz) and ^{13}C (125 MHz) NMR spectra were taken on a Bruker DRX-500 Avance spectrometer. Elemental analyses were performed in the Microanalytical Laboratory of the Department of Organic Chemistry, L. Eötvös University, Budapest, Hungary. Melting points were taken on a Boetius micro melting point apparatus and were uncorrected. Starting materials were purchased from Aldrich Chemical Company unless otherwise noted. Silica gel 60 F_{254} (Merck) and aluminium oxide 60 F_{254} neutral type E (Merck) plates were used for TLC. Aluminium oxide (neutral, activated, Brockman I) and silica gel 60 (70–230 mesh, Merck) were used for column chromatography. Solvents were dried and purified according to well established[30] methods. Evaporations were carried out under reduced pressure unless otherwise stated.

Suitable single crystals for X-ray crystallographic studies were obtained from the almost saturated solutions of crown ethers in appropriate solvents (listed below for each ligand) which were allowed to stand at room temperature in glass ampoules. The following solvents were used: EtOH for ligand **1**, 1,2-dichloroethane for ligand **2**, and DMF for ligands **3**, **6**, and **8**.

3.1.1. 2,5,8,11,14-Pentaoxa-26-azatetracyclo[13.9.3.0.^{19,27}.0^{21,25}]heptacosa-1(24),15,17,19(27),21(25),22-hexaene-20(26*H*)-one (1, see Fig. 1 and Scheme 1). A mixture of acridonediol **11**[15] (4.54 g, 20 mmol), ditosylate **12**[31] (11.1 g, 22 mmol), finely powdered anhydrous K_2CO_3 (27.6 g, 0.2 mol) and dry DMF (450 ml) was stirred vigorously under Ar at room temperature (further on rt) for 10 min then at 50°C for 2 days. The solvent was removed at 40°C under reduced pressure and the residue was taken up in a mixture of water (0.5 l) and CH_2Cl_2 (1 l). The aqueous phase was extracted with CH_2Cl_2 (3×200 ml). The combined organic phase was dried over $MgSO_4$, filtered, and the solvent was removed. The crude product was purified by recrystallization from ethanol using charcoal to give **1**

semihydrate (4.62 g, 58%) which was identical in every respect to that prepared by the reported[15] procedure.

3.1.2. 17-Nitro-2,5,8,11,14-pentaoxa-26-azatetracyclo-[13.9.3.0.^{19,27}.0^{21,25}]heptacosa-1(24),15,17,19(27),21(25),22-hexaene-20(26*H*)-one (2, see Fig. 1 and Scheme 2). To a stirred solution of acridono-18-crown-6 ether (**1**) semihydrate (315 mg, 0.8 mmol) in dichloromethane (8 ml) was added under Ar at −20°C freshly prepared ice-cold solution of fuming nitric acid (54 mg, 0.86 mmol) and acetic anhydride (4.5 ml) dropwise. The mixture was stirred at −20°C for 1 h and then it was allowed to warm up to room temperature and stirring was continued for another half an hour. The volatile materials were removed under reduced pressure and the residue was triturated with ice-cold water. The yellow solid was filtered, washed three times with water, and air-dried. The crude product was recrystallized from 1,2-dichloroethane to give yellow needles of **2** (251 mg, 70%). Mp: 207–209°C; R_f=0.54 (silica gel TLC, 5% MeOH in CH_2Cl_2); IR (KBr) ν_{max} 3408, 1640, 1616, 1600, 1544, 1520, 1328, 1272, 1232, 1112, 1088, 960 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.27 (s, broad, 1 mol complexed H_2O, 2H), 3.72–3.77 (m, 4H), 3.78–3.83 (m, 4H), 4.01–4.06 (m, 4H), 4.31–4.36 (m, 4H), 7.11 (d, J=8 Hz, 1H), 7.23 (t, J=8 Hz, 1H), 7.67 (d, J=2 Hz, 1H), 7.97 (d, J=8 Hz, 1H), 8.92 (d, J=2 Hz, 1H), 10.07 (s, broad, NH, 1H); ^{13}C NMR ($CDCl_3$) δ 68.94, 69.11, 69.44, 70.44, 70.53, 71.48, 71.56, 73.18, 105.95, 113.64, 116.58, 118.72, 120.41, 122.82, 122.92, 131.17, 135.63, 141. 36, 147.40, 155.03, 177.28. Anal. calcd for: $C_{21}H_{22}N_2O_8{\cdot}H_2O$: C, 56.25; H, 5.39; N, 6.25. Found: C, 56.30; H, 5.35; N, 5.98.

3.1.3. 17,23-Dinitro-2,5,8,11,14-pentaoxa-26-azatetracyclo[13.9.3.0.^{19,27}.0^{21,25}]heptacosa-1(24),15,17,19(27),21(25),22-hexaene-20(26*H*)-one (3, see Fig. 1 and Scheme 2). To a stirred solution of acridono-18-crown-6 ether (**1**) semihydrate (320 mg, 0.83 mmol) in dichloromethane (12 ml) was added under Ar at 0°C freshly prepared ice-cold solution of fuming nitric acid (210 mg, 3.33 mmol) and acetic anhydride (2 ml) dropwise. The mixture was stirred at 0°C for 1 h and then it was allowed to warm up to room temperature and stirring was continued at this temperature for 2 h. The volatile materials were removed under reduced pressure and the residue was triturated with ice-cold water. The yellow solid was filtered, washed three times with water, and air-dried. The crude product was recrystallized from DMF to give yellow needles of **3** (320 mg, 84%). Mp: 247–249°C; R_f=0.62 (silica gel TLC, 5% MeOH in CH_2Cl_2); IR (KBr) ν_{max} 3472, 1632, 1620, 1604, 1544, 1516, 1336, 1276, 1216, 1088, 936 cm^{-1}; ^{1}H NMR (DMSO-d$_6$) δ 3.65–3.66 (m, 4H), 3.70–3.72 (m, 4H), 3.95–3.96 (m, 4H), 4.57–4.58 (m, 4H), 8.13 (d, J=2 Hz, 2H), 8.62 (d, J=2 Hz, 2H), 9.64 (s, broad, NH, 1H); ^{13}C NMR (DMSO-d$_6$) δ 68.00, 69.47, 70.10, 70.19, 107.73, 113.63, 134.33, 142.43, 147.25, 163.65, 175.05. Anal. calcd for: $C_{21}H_{21}N_3O_{10}{\cdot}H_2O$: C, 51.12; H, 4.70; N, 8.52. Found: C, 50.98; H, 4.85; N, 8.37.

3.1.4. 17-Bromo-23-nitro-2,5,8,11,14-pentaoxa-26-azatetracyclo[13.9.3.0.^{19,27}.0^{21,25}]heptacosa-1(24),15,17,19(27),21(25),22-hexaene-20(26*H*)-one (4, see Fig. 1 and Scheme 2). To a stirred solution of nitroacridono-18-crown-6 ether (**2**) monohydrate (172 mg, 0.4 mmol) in glacial acetic acid (4 ml) was added under Ar in a cold water bath freshly prepared solution of bromine (80 mg, 0.5 mmol) in glacial acetic acid (2 ml) dropwise. The mixture was stirred in the cold water bath for 1 h and then it was allowed to warm up to rt and stirring was continued at this temperature for 2 h. The yellow precipitate was filtered off and dried under reduced pressure over KOH pellets. The crude product was recrystallized from DMF to give yellow needles of **4** (165 mg, 78%). Mp: 222–224°C; R_f=0.60 (silica gel TLC, 5% MeOH in CH_2Cl_2); IR (KBr) ν_{max} 3464, 1640, 1605, 1568, 1504, 1366, 1276, 1080, 940 cm^{-1}; ^{1}H NMR (DMSO-d$_6$) δ 3.65–3.69 (m, 4H), 3.70–3.74 (m, 4H), 3.92–3.94 (m, 2H), 3.95–3.97 (m, 2H), 4.42–4.45 (m, 2H), 4.52–4.55 (m, 2H), 7.61 (d, J=2 Hz, 1H), 7.90 (d, J=2 Hz, 1H), 8.02 (d, J=2 Hz, 1H), 8.60 (d, J=2 Hz, 1H) 9.24 (s, broad, NH, 1H). Anal. calcd for: $C_{21}H_{21}N_2O_8Br{\cdot}H_2O$: C, 47.83; H, 4.39; N, 5.31. Found: C, 47.73; H, 4.20; N, 5.02.

3.1.5. 17,23-Dibromo-2,5,8,11,14-pentaoxa-26-azatetracyclo[13.9.3.0.^{19,27}.0^{21,25}]heptacosa-1(24),15,17,19(27),21(25),22-hexaene-20(26*H*)-one (5, see Fig. 1 and Scheme 2). To a stirred solution of acridono-18-crown-6 ether (**1**) semihydrate (181 mg, 0.46 mmol) in glacial acetic acid (6 ml) was added under Ar in a cold water bath freshly prepared solution of bromine (184 mg, 1.15 mmol) in glacial acetic acid (2 ml) dropwise. The mixture was stirred in the cold water bath for 1 h and then it was allowed to warm up to rt and stirring was continued at this temperature for 2 h. The pale yellow precipitate was filtered off and dried under reduced pressure over KOH pellets. The crude product was recrystallized from DMF to give pale yellow crystals of **5** (212 mg, 82%). Mp: 249–251°C; R_f=0.65 (silica gel TLC, 5% MeOH in CH_2Cl_2); IR (KBr) ν_{max} 3416, 1624, 1608, 1592, 1524, 1488, 1376, 1264, 1112, 1080, 936 cm^{-1}; ^{1}H NMR (DMSO-d$_6$) δ 3.68–3.71 (m, 8H), 3.92–3.94 (m, 4H), 4.43–4.45 (m, 4H), 7.53 (d, J=2 Hz, 2H), 7.91 (d, J=2 Hz, 2H), 9.05 (s, broad, NH, 1H). Anal. calcd for: $C_{21}H_{21}Br_2NO_6{\cdot}H_2O$: C, 44.94; H, 4.13; N, 2.50. Found: C, 44.95; H, 4.04; N, 2.43.

3.1.6. 17,23-Dibromo-18,22-dinitro-2,5,8,11,14-pentaoxa-26-azatetracyclo[13.9.3.0.^{19,27}.0^{21,25}]heptacosa-1(24),15,17,19(27),21(25),22-hexaene-20(26*H*)-one (6, see Fig. 1 and Scheme 2). To a stirred suspension of dibromoacridono-18-crown-6 ether (**5**) monohydrate (109 mg, 0.2 mmol) in 1:1 acetic anhydride–glacial acetic acid mixture (6 ml) was added under Ar in a cold water bath freshly prepared solution of fuming nitric acid (63 mg, 1 mmol) in acetic anhydride (4 ml) dropwise. After addition of the nitrating solution the reaction mixture became clear. The mixture was stirred in the cold water bath for 1 h and then it was allowed to warm up to rt and stirring was continued at this temperature for 24 h. The yellow precipitate was filtered off and dried under reduced pressure over KOH pellets. The crude product was recrystallized from DMF to give yellow crystals of **6** (78 mg, 60%). Mp: >360°C; R_f=0.32 (silica gel TLC, 3% MeOH in CH_2Cl_2); IR (KBr) ν_{max} 3392, 1640, 1628, 1616, 1548, 1536, 1528, 1488, 1364, 1272, 1124, 1080, 952 cm^{-1}; ^{1}H NMR (DMSO-d$_6$) δ 3.64–3.67 (m, 4H), 3.68–3.71 (m, 4H), 3.93–3.96 (m, 4H), 4.51–4.54 (m, 4H), 7.98 (s, 2H), 9.44 (s, broad, NH, 1H). Anal. calcd for: $C_{21}H_{19}Br_2N_3O_{10}{\cdot}H_2O$:

C, 38.73; H, 3.25; N, 6.45. Found: C, 38.99; H, 3.10; N, 6.43.

3.1.7. 17,23-Dichloro-2,5,8,11,14-pentaoxa-26-azatetracyclo[13.9.3.0.^{19,27}.0^{21,25}]heptacosa-1(24),15,17,19(27),21(25),22-hexaene-20(26*H*)-one (7, see Fig. 1 and Scheme 2). To a stirred solution of acridono-18-crown-6 ether (**1**) semihydrate (157 mg, 0.4 mmol) in glacial acetic acid (6 ml) was added under Ar in a cold water bath freshly prepared 8% (w/v) stock solution of chlorine in glacial acetic acid (0.8 ml, 0.9 mmol) in five portions during 2 h. The mixture was stirred in the cold water bath for 1 h and then it was allowed to warm up to rt and stirring was continued at this temperature for 2 h. The pale yellow precipitate was filtered off and dried under reduced pressure over KOH pellets. The crude product was recrystallized from $CHCl_3$–MeOH mixture to give pale yellow crystals of **7** (125 mg, 66%). Mp: 240–242°C; R_f=0.45 (silica gel TLC, 5% MeOH in CH_2Cl_2); IR (KBr) ν_{max} 3430, 1640, 1624, 1606, 1544, 1516, 1352, 1246, 1132, 1080, 850, 604 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.54 (s, broad, 1 mol complexed H_2O, 2H), 3.66 (s, 4H), 3.73 (s, 4H), 4.08 (s, 4H), 4.28 (s, 4H), 7.02 (d, J=2 Hz, 2H), 7.26 (d, J=2 Hz, 2H), 9.33 (s, broad, NH, 1H); ^{13}C NMR (DMSO-d_6) δ 69.28, 69.60, 70.72, 71.61, 113.60, 119.77, 123.01, 127.07, 131.10, 145.25, 174.61. Anal. calcd for: $C_{21}H_{21}Cl_2NO_6{\cdot}H_2O$: C, 53.40; H, 4.91; N, 2.97. Found: C, 53.21; H, 5.01; N, 2.73.

3.1.8. 17,23-Dichloro-18,22-dinitro-2,5,8,11,14-pentaoxa-26-azatetracyclo[13.9.3.0.^{19,27}.0^{21,25}]heptacosa-1(24),15,17,19(27),21(25),22-hexaene-20(26*H*)-one (8 see Fig. 1 and Scheme 2). To a stirred suspension of dichloroacridono-18-crown-6 ether (**7**) monohydrate (94 mg, 0.2 mmol) in acetic anhydride (8 ml) was added under Ar in a cold water bath a freshly prepared solution of fuming nitric acid (63 mg, 1 mmol) in acetic anhydride (4 ml) dropwise. After addition of the nitrating solution the reaction mixture became clear. The mixture was stirred in the cold water bath for 1 h and then it was allowed to warm up to room temperature and stirring was continued at this temperature for 24 h. The yellow precipitate was filtered off and dried under reduced pressure over KOH pellets. The crude product was recrystallized from DMF to give yellow crystals of **11** (73 mg, 65%). Mp: >360°C; R_f=0.37 (silica gel TLC, 25% EtOH in toluene); IR (KBr) ν_{max} 3384, 1640, 1632, 1616, 1548, 1536, 1528, 1488, 1456, 1368, 1272, 1120, 1096, 1084, 952, 824, 620 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.62–3.65 (m, 4H), 3.68–3.71 (m, 4H), 3.91–3.94 (m, 4H), 4.50–4.53 (m, 4H), 7.75 (s, 2H), 9.67 (s, broad, NH, 1H); ^{13}C NMR (DMSO-d_6) δ 68.12, 69.57, 70.31, 70.70, 112.85, 114.29, 119.52, 127.03, 129.90, 148.19, 176.11. Anal. calcd for: $C_{21}H_{19}Cl_2N_3O_{10}{\cdot}H_2O$: C, 44.86; H, 3.76; Cl, 12.61; N, 7.47. Found: C, 45.15; H, 3.65; Cl, 12.45; N, 7.60.

3.2. X-Ray diffraction experiments of the complexes of 1, 2, 3, 6 and 8

Typical X-ray structure determination procedures were carried out, glue sealed crystals were mounted on a glass fiber. Raw intensity data, collected on Enraf–Nonius CAD4 diffractometers (graphite monochromator, either Cu Kα radiation, λ=1.54184 Å or Mo *K*α radiation, λ=0.710730 Å, T=293–295(2) K, $\omega/2\theta$ scans, typical completeness in θ=0.97–0.99, cell parameters by least-squares of the setting angles of 25 reflections, θ ranges given separately), were only corrected for Lorentz and for polarization and eventually for decay effects, initial structure models were always given by direct methods.[32] Structure models were completed/checked by difference electron density maps that also gave relevant non-trivial H atom positions (such as water, –NH etc.) and refined to completion by full-matrix least-squares refinement.[33] On F^2 by using anisotropic displacement parameters for all non-hydrogen atoms. Pertinent details: **1**·H_2O: $C_{21}H_{25}NO_7$, Fwt.: 403.42, monoclinic, space group $P2_1/c$, a=13.183(1) Å, b=11.325(1) Å, c=14.284(1) Å, α=90°, β=110.58(1)°, γ=90°, V=1996.5(3) Å^3, Z=4, D_x=1.342 mg/m^3. Cell parameters θ ranges: 25.14≤θ≤29.11°; Cu *K*α, 5.12≤θ≤75.59° range, 4425 reflections total, 4139 unique [R(int)=0.0071, $R(\sigma)$=0.0473]; 2074 reflections with $I>2\sigma(I)$. R_1=0.0464 and wR_2=0.1214 for 2074 [$I>2\sigma(I)$] and R_1=0.1034 and wR_2=0.1357 for 4139 intensity data.

Compound **2**·H_2O. $C_{21}H_{23.5}N_2O_{8.75}$, Fwt.: 443.92, triclinic, space group P-1, a=8.376(1) Å, b=10.331(1) Å, c=12.717(1) Å, α=98.09(1)°, β=107.42(1)°, γ=99.55(1)°, V=1013.99(18) Å^3, Z=2, D_x=1.454 mg/m^3. Cell parameters θ ranges: 15.07≤θ≤15.92°; Mo *K*α, 2.61≤θ≤29.97° range, 12552 reflections total, 5830 unique [R(int)=0.0169, $R(\sigma)$=0.0335]; 3105 reflections with $I>2\sigma(I)$. R_1=0.0551 and wR_2=0.1542 for 3105 [$I>2\sigma(I)$] and R_1=0.1018 and wR_2=0.1734 for 5830 intensity data.

Compound **3**·H_2O. $C_{21}H_{23}N_3O_{11}$, Fwt.: 493.42, monoclinic, space group $C2/c$, a=12.786(1) Å, b=25.289(1) Å, c=14.397(1) Å, α=90.00°, β=108.66(1)°, γ=90.00°, V=4410.5(5) Å^3, Z=8, D_x=1.486 mg/m^3. Cell parameters θ ranges: 18.94≤θ≤19.91°; Mo *K*α, 2.70≤θ≤31.97° range, 7934 reflections total, 7524 unique [R(int)=0.0078, $R(\sigma)$=0.0240]; 3772 reflections with $I>2\sigma(I)$. R_1=0.0454 and wR_2=0.1290 for 3772 [$I>2\sigma(I)$] and R_1=0.0974 and wR_2=0.1436 for 7524 intensity data.

Compound **6**·H_2O·DMF. $C_{24}H_{28}Br_2N_4O_{12}$, Fwt.: 724.32, triclinic, space group P-1, a=10.684(4) Å, b=12.161(6) Å, c=12.971(5) Å, α=98.31(3)°, β=113.40(3)°, γ=106.69(4)°, V=1416.0(10) Å^3, Z=2, D_x=1.699 mg/m^3. Cell parameters θ ranges: 16.94≤θ≤17.92°; Mo *K*α, 2.24≤θ≤29.98° range, 8788 reflections total, 8238 unique [R(int)=0.0102, $R(\sigma)$=0.0528]; 4691 reflections with $I>2\sigma(I)$. R_1=0.0426 and wR_2=0.1137 for 4691 [$I>2\sigma(I)$] and R_1=0.0926 and wR_2=0.1221 for 8238 intensity data.

Compound **8**·H_2O·DMF. $C_{24}H_{28}Cl_2N_4O_{12}$, Fwt.: 635.40, triclinic, space group P-1, a=10.686(1) Å, b=12.035(2) Å, c=12.989(2) Å, α=67.13(1)°, β=66.43(1)°, γ=73.68(1)°, V=1395.1(3) Å^3, Z=2, D_x=1.513 mg/m^3. Cell parameters θ ranges: 32.29≤θ≤39.33°; Cu *K*α, 4.03≤θ≤75.42° range, 6047 reflections total, 5671 unique [R(int)=0.0072, $R(\sigma)$=0.0117]; 4887 reflections with $I>2\sigma(I)$. R_1=0.0627 and wR_2=0.1795 for 4887 [$I>2\sigma(I)$] and R_1=0.0682 and wR_2=0.1852 for 5671 intensity data. CCDC-212209, CCDC–212210, CCDC–212211, CCDC-212212 and CCDC-212213 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge

via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336-033; or deposit@ccdc.cam.ac.uk).

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