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This paper is dedicated to the memory of the late Dr. R. N. Castle

Anthraquinone and pyrene intercalators were conjugated to different positions of several polyaza-pyridinocyclophanes by various linkers to provide thirteen new polyazacyclophane-intercalator conjugates **1-13**. These resulting conjugates contain two or three constrained secondary nitrogen atoms on the ring, which may serve as nucleophilic, coordinating or hydrogen-bonding sites for combinatorial, RNA interaction and coordination studies.

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Introduction.

Highly specific RNA-protein interactions are essential for cells to undergo gene expression [1]. Selective disruption of one or more of the required processes in gene expression represents a new frontier in drug discovery. Antisense technology uses oligomeric materials to target single- or double-stranded segments of RNA based on the nucleotide sequence of the RNA. Materials of this nature have been termed informational drugs [2]. In the case of antisense targeting of ssRNA, the use of Watson-Crick base-pair hydrogen bonding rules allow rapid design of lead antisense agents [3]. Antisense targeting of dsRNA may proceed through Hoogsteen binding rules in the major groove. However, unlike targeting a specific sequence of single- or double-stranded RNA with informational materials, targeting non-canonical secondary and tertiary structures of RNA (motifs) with oligomeric or non-oligomeric materials for therapeutic applications suffers from a lack of binding rules. Furthermore, knowledge of precise RNA motif-protein binding that may allow rational drug design is rarely available [4]. In order to selectively disrupt RNA motif-protein interactions for therapeutic applications, chemicals must be designed and synthesized, which can effectively compete with the proteins for the active site in the RNA motif. Several general binding interactions have been established for non-oligomeric molecules binding to nucleic acids [5-9]. Electrostatic interaction between positively charged molecules and the negatively charged RNA phosphate backbone is an initial and major mode of recognition. Second general mode of non-oligomeric molecule binding is in the major or minor groove of the nucleic acid. This generally involves direct hydrogen binding and/or van der Waals interactions within a groove of the RNA, which provides some sequence selectivity [9]. Third important binding mode is intercalation in which molecules with planar conformations may insert between base pairs of double-stranded DNA or RNA. Most often-studied intercalators have polarizable, electron-deficient, fused heteroaromatic chromophores, which generally exhibit

little sequence specificity [9]. Although incorporation of intercalators onto oligonucleotide [10] and other structures [11] have been studied, the incorporation of intercalators into the macrocyclic compounds has few examples. Most studies on macrocyclic compounds [12] focused on the complexation property of the macrocyclic compounds [13], except one involved biological activity studies [14]. The combination of intercalators with polyazacyclophane structures, which were combinatorialized with RNA-binding functionality sets [15a], could increase the interaction between non-oligomeric molecules and DNA or RNA targets, therefore, benefit drug action studies and the drug discovery.

Our recent research has been focused on the use of solution-phase combinatorial chemistry to discovery non-oligomeric molecules (lead discovery) that would selectively bind to RNA motifs required in the life cycle of bacteria [15-23]. In earlier work, we have synthesized polyazacyclophanes possessing positive charges located in constrained macrocycles of various ring sizes (polyazacyclophanes) as well as positively charged functional groups emanating from the aliphatic ring nitrogen atoms. Libraries of the functionalized polyazacyclophanes were screened in several functional RNA and antibacterial assays, and interesting activities were observed from certain libraries [15,18-22]. In order to take this work further, we were interested in enhancing the binding affinity of polyazacyclophanes while maintaining their binding specificity. We considered that, if after specific binding of a charged polyazacyclophane to an RNA motif - intercalation from a conjugated intercalator could take place in an adjacent helical portion (stem) of the RNA, the binding affinity would be enhanced. In this manner, the specificity of polyazacyclophane binding with an RNA motif would primarily be derived from the specific ionic interactions of the polyazacyclophane and enhanced binding would result from non-sequence specific anchoring of the intercalator moiety in a stem of the RNA motif. The discovery of an effective RNA-binding polyazacyclophane would be approached through a solution phase, simultaneous addition of functionalities (SPSAF) combinatorial technology

previously reported by our laboratory [15-21]. We have selected the 4-position of the pyridine ring of the polyazapyridinophane and the secondary nitrogen atom of the aliphatic ring of the polyazacyclophane as sites to conjugate several types of intercalators.

Herein, we report the synthesis of a series of polyazapyridinocyclophane-intercalator conjugates **1-13** (Figure 1). These conjugates were synthesized through a series of appropriately protected polyazamacrocyclic compounds, which were obtained by cyclization methods developed in this work or our previous work. We have selected the well-studied intercalators, anthraquinone and pyrene, to attach to the polyazacyclophanes. Several types of linkers, ranging from two to

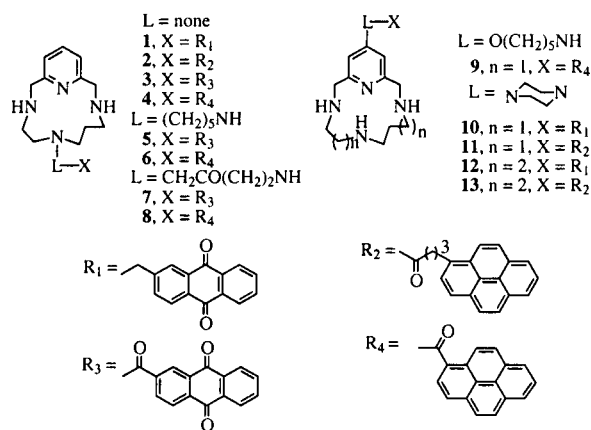


Figure 1. New Polyazacyclophane-Intercalator Conjugates

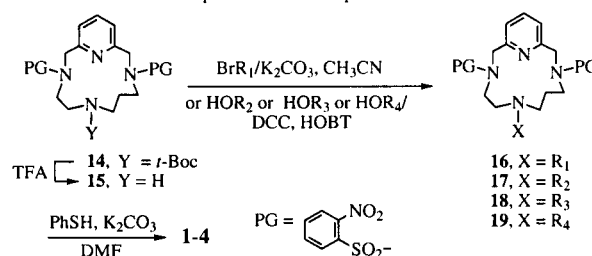
nine atoms, were utilized to attach the intercalator to the polyazacyclophanes. Thirteen and fifteen membered polyazapyridinophanes were employed. The final target polyazacyclophane-intercalator conjugates **1-13**, having two or three reactive nitrogen positions on the ring, would be utilized for combinatorial library generation, RNA interaction and coordination studies.

Results and Discussion.

Synthesis of novel compounds **1-4** is depicted in Scheme I. Orthogonally protected polyazapyridinocyclophane **14** was prepared according to our published procedure [16,17]. This compound has two different types of protecting groups on the ring. In our previous research, the 2-nitrobenzenesulfonyl protecting group (PG) was first removed by thiophenol leaving the *t*-Boc protecting group at the fixed position for the preparation of combinatorial libraries. Here, we wanted to introduce an intercalator into the bottom of this cyclophane compound. Therefore, we decided to selectively remove the *t*-Boc protecting group without affecting the 2-nitrobenzenesulfonyl groups on the ring. Selective deprotection of **14** with trifluoroacetic acid (TFA) provided compound **15** in 73% yield. Nucleophilic reaction of **15** with 2-(bromomethyl)anthraquinone in the

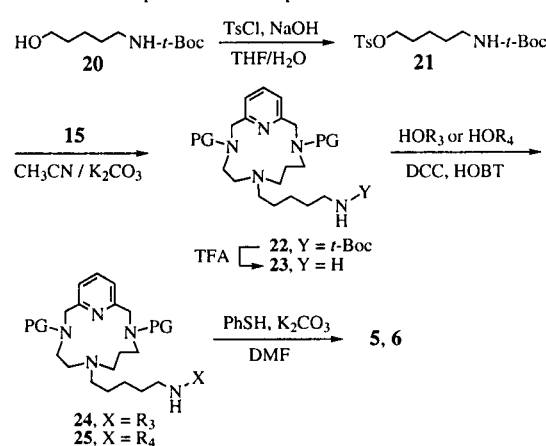
presence of anhydrous potassium carbonate gave compound **16**. Acylation of **15** with 1-pyrenebutyric acid (HOR_2), anthraquinone-2-carboxylic acid (HOR_3) and 1-pyrenecarboxylic acid (HOR_4) using dicyclohexylcarbodiimide (DCC) as coupling reagent in the presence of 1-hydroxybenzotriazole (HOBT) provided the corresponding amide derivatives **17-19** in 76-92% yields. 2-Nitrobenzenesulfonyl protected compounds **16-19** were treated with thiophenol in the presence of anhydrous potassium carbonate in DMF affording the desired intercalator-containing compounds **1-4** in 65-80% yields.

Scheme I
Preparation of Compounds **1-4**

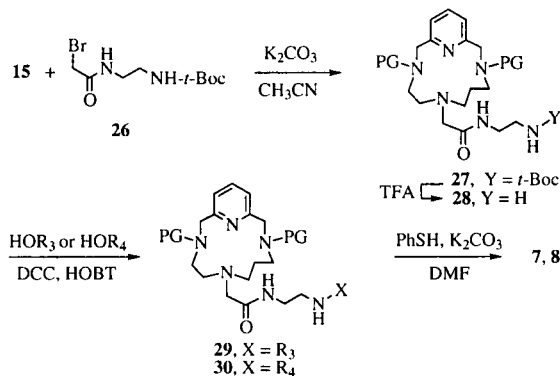


It has been demonstrated in the DNA-cleaving molecules that the linker moiety between the reactive group and the carrier is an important factor to the efficiency of DNA interaction and cleavage [24]. In our case, suitable linkers must position the intercalator for effective interactions. Thus, we designed and synthesized polyazacyclophanes **5-8** having different linkers between the intercalators and the carrier polyazacyclophane (Schemes II and III). 5-*t*-Boc-amino-1-pentanol (**20**), prepared from the corresponding amino alcohol according to the published procedure [18], was treated with tosyl chloride and sodium hydroxide to provide tosylate compound **21**. Alkylation of macrocyclic compound **15** with tosylate **21** in the presence of potassium carbonate afforded the orthogonally protected compound **22**. After

Scheme II
Preparation of Compounds **5** and **6**



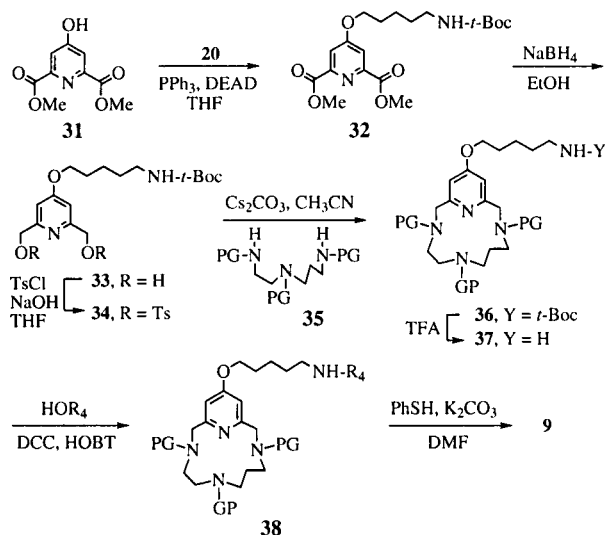
Scheme III
Preparation of Compounds 7 and 8



selectively removing the *t*-Boc protecting group at the end of the linker, the resulted primary amine of **23** was further reacted with anthraquinone-2-carboxylic acid and 1-pyrene-carboxylic acid under the same conditions described above for **17-19** providing compounds **24** and **25** in good yields. Removing 2-nitrobenzenesulfonyl protecting groups by thiophenol under the conditions described above afforded intercalator-substituted polyazacyclophanes **5** and **6**. Compounds **7** and **8** (Scheme III), having different linkers than compounds **5** and **6**, were synthesized in high yields as described above by the alkylation of **15** with the *t*-Boc-protected bromo compound **26** [25], selective deprotection with TFA, acylation of the corresponding intercalator carboxylic acids and final deprotection with thiophenol.

We then decided to synthesize compound **9** with an intercalator attached to the *para* position of the pyridine subunit of the polyazamacrocyclic structure. Scheme IV outlines the cyclization and attachment of the intercalator. Bradshaw and co-workers [26] reported the synthesis of

Scheme IV
Preparation of Compound 9

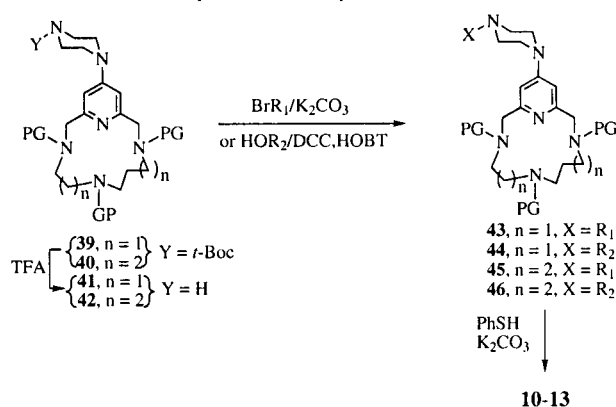


dimethyl 4-hydroxypyridine-2,6-dicarboxylate **31**, and its nucleophilic substitution reaction with a bromide compound. We synthesized the new ether compound **32** in 78% yield by directly connecting two hydroxyl compounds **31** and **20** under mild Mitsunobu reaction conditions at room temperature. The di-ester compound **32** was reduced to the corresponding hydroxymethyl compound **33** by sodium borohydride. Compound **33** was then reacted with tosyl chloride in the presence of sodium hydroxide providing ditosylate **34** in 96% yield. The orthogonally protected, new polyazamacrocyclic compound **36** was synthesized in 89% yield by the 1:1 cyclization of ditosylate **34** with tri-protected triamine **35** [18] in the presence of anhydrous cesium carbonate in DMF. After selectively removing the *t*-Boc group, the resulting primary amine on the linker of **37** was reacted with 1-pyrenecarboxylic acid (HOR_4) under the similar conditions described above to give compound **38** in a yield of 71%. Deprotection of compound **38** with thiophenol provided the desired polyazacyclophane-intercalator conjugate **9**.

Intercalator-containing compounds **10-13** with a piperazine linker on the pyridine subunit of the macrocyclic molecules were synthesized as outlined in Scheme V. Orthogonally protected compounds **39** and **40** were prepared in high yields based on our reported strategy [20]. Selective deprotection of **39** and **40** with TFA generated compounds **41** and **42** in 89% and 92% yields, respectively. Compounds **41** and **42** were reacted with 2-(bromo-methyl)anthraquinone and 1-pyrenebutyric acid, respectively, under alkylation and acylation conditions described above to give the corresponding macrocyclic compounds **43-46** in 72-97% yields. These compounds were then treated with thiophenol in the presence of potassium carbonate to remove the 2-nitrobenzenesulfonyl protecting groups on the rings affording the desired compounds **10-13** in 68-93% yields.

New Compounds **1-13**, **15-17**, **19**, **21-23**, **25**, **27-30**, **32-34**, **36**, **37**, **41-44** and **46** were all characterized by ^1H NMR, ^{13}C

Scheme V
Preparation of Compounds 10-13



NMR, high resolution (FAB) mass spectroscopic and elemental analyses. Intermediates **18**, **24**, **38** and **45** were characterized by ^1H NMR, ^{13}C NMR, high resolution (FAB) mass spectroscopy, and their corresponding derivatives were all confirmed by elemental analysis.

Series of combinatorial libraries have been produced from these new intercalator-conjugated polyazapyridino-cyclophane scaffolds and diverse functionalities [15a,18-20]. Some libraries exhibit antibacterial activity at MIC's of 2.5-10.0 μM and interrupt RNA-protein tat/TAR interaction at the MIC's of 4-20 μM . The detail biological results of these newly synthesized libraries will be reported in due course.

In conclusion, we have synthesized thirteen new polyazacyclophane-intercalator conjugates containing different intercalators attached to different positions of macrocyclic rings by a range of linkers through nineteen appropriately protected polyazamacrocyclic compounds. These conjugates have two or three secondary amine sites in 13- or 15-membered rings that are available for combinatorialization by solution-phase or solid support approaches. The overall strategy, including cyclization, selective deprotection, and attachment of the intercalator moieties, described in this work is an efficient process and should be applicable to related targets.

EXPERIMENTAL

Proton and carbon nuclear magnetic resonance (^1H and ^{13}C nmr) spectra were recorded at 199.975 MHz on a Varian Gemini 200 NMR spectrometer in deuteriochloroform unless otherwise indicated. Chemical shift values were expressed relative to the internal tetramethylsilane. High-resolution (FAB) positive ion mass spectra were recorded on a VG ZAB-VSE double focusing high-resolution mass spectrometer. Melting points were taken on a Thomas-Hoover apparatus and are uncorrected. Elemental analyses were performed by MHW laboratories, Phoenix, AZ. Compounds **14** [17], **20** [18], **26** [25], **31** [26], **35** [18], **39** and **40** [20] were prepared according to the reported procedures. Other materials and solvents were purchased from Aldrich Chemical Company without further purification.

General Procedure for the Preparation of Compounds **15**, **23**, **28**, **37**, **41** and **42** (Selective Deprotecting *t*-Boc) (Schemes I-V).

A solution of *t*-Boc-protected compound **14** [17], **22**, **27**, **36**, **39** [20] or **40** [20] (2.0 mmoles) and 10 ml of trifluoroacetic acid (TFA) in 10 ml of methylene chloride was stirred at room temperature overnight. The solvent and excess TFA were evaporated, and the residue was dissolved in water. The solution was adjusted to pH = 10 with aqueous sodium hydroxide solution and extracted with chloroform. The combined organic phase was washed with 5% sodium bicarbonate aqueous solution and brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by flash chromatography on a silica gel column. Chromatographic eluents, product yields and spectral properties are listed below.

3,10-Bis(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo-[10.3.1]hexadeca-1(16),12,14-triene (**15**) (Scheme I).

Compound **15** was purified using methanol/30% aqueous ammonium hydroxide: 100/1 as an eluent and isolated as a white foam in a yield of 73%; ^1H nmr: (δ) 1.49-1.68 (m, 2H), 1.95-2.25 (br, 1H), 2.22 (t, 2H, J = 4.8 Hz), 2.34 (t, 2H, J = 5.4 Hz), 3.32-3.43 (m, 4H), 4.49 (s, 2H), 4.54 (s, 2H), 7.31 (d, 1H, J = 7.3 Hz), 7.44 (d, 1H, J = 8 Hz), 7.60-7.74 (m, 7H), 7.92-8.05 (m, 2H); ^{13}C nmr: (δ) 27.5, 44.8, 46.2, 47.2, 50.4, 55.2, 55.5, 122.7, 123.8, 124.3, 130.4, 131.2, 131.9, 132.4, 142.6, 133.8, 138.2, 148.3, 148.5, 156.0, 156.2; hrms (FAB): m/z 591.134 ($M + H$)⁺ ($\text{C}_{26}\text{H}_{27}\text{N}_6\text{O}_8\text{S}_2$ requires 591.133).

Anal. Calcd. for $\text{C}_{26}\text{H}_{26}\text{N}_6\text{O}_8\text{S}_2 \cdot \text{H}_2\text{O}$: C, 47.36; H, 4.64; N, 13.82. Found: C, 47.04; H, 4.50; N, 13.51.

General Procedure for the Preparation of Compounds **16**, **43** and **45** (Alkylation) (Schemes I and V).

A mixture of compound **15**, **41** or **42** (2.0 mmoles), 2-(bromomethyl)anthraquinone (0.78 g, 2.6 mmoles) and anhydrous potassium carbonate (5.0 g, 36.0 mmoles) in 30 ml of anhydrous dimethylformamide (containing 10 ml of acetonitrile for **43** and **45**) was stirred at room temperature overnight. The solvent was evaporated and the residue was dissolved in chloroform-water. The organic phase was separated, and the aqueous phase was extracted with chloroform. The combined organic phase was washed with brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by flash chromatography on a silica gel column. Chromatographic eluents, product yield and spectral properties are listed below.

6-(2-Anthraquinonemethyl)-3,10-bis(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**16**) (Scheme I).

Compound **16** was purified using methylene chloride as an eluent and isolated as a pale yellow foam in a yield of 76%; ^1H nmr: (δ) 1.20-1.45 (m, 2H), 2.01-2.25 (m, 4H), 3.10-3.42 (m, 4H), 3.45 (s, 2H), 4.51 (s, 4H), 7.40-8.10 (m, 18H); ^{13}C nmr: (δ) 25.9, 46.8, 47.4, 50.2, 50.8, 54.8, 59.6, 124.1, 124.3, 125.3, 126.8, 127.0, 127.4, 128.2, 129.0, 130.3, 130.5, 131.9, 132.5, 133.5, 133.8, 134.2, 138.7, 146.7, 148.3, 155.2, 155.8, 182.7, 183.0; hrms (FAB): m/z 811.185 ($M + H$)⁺ ($\text{C}_{39}\text{H}_{35}\text{N}_6\text{O}_{10}\text{S}_2$ requires 811.185).

Anal. Calcd. for $\text{C}_{39}\text{H}_{34}\text{N}_6\text{O}_{10}\text{S}_2$: C, 57.75; H, 4.23; N, 10.37. Found: C, 58.00; H, 4.45; N, 10.13.

General Procedure for the Preparation of Compounds **17-19**, **24**, **25**, **29**, **30**, **38**, **44** and **46** (Acylation) (Schemes I-V).

A mixture of 1-pyrenebutyric acid, anthraquinone-2-carboxylic acid or 1-pyrenecarboxylic acid (3.0 mmoles) and 4-methylmorpholine (0.59 g, 5.9 mmoles), 1,3-dicyclohexylcarbodiimide (DCC) (0.62 g, 3.0 mmoles) and 1-hydroxybenzotriazole (HOBt) (0.41 g, 3.0 mmoles) in 20 ml of dimethylformamide containing 10 ml of acetonitrile was stirred at room temperature for 30 minutes. A solution of compound **15**, **23**, **28**, **37**, **41** or **42** (3.0 mmoles) in 5 ml of dimethylformamide was added and the resulting mixture was stirred at room temperature for 40 hours. The reaction mixture was filtered and the filtrate was washed with brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash chromatography on a silica gel column. Chromatographic eluents, product yields and spectral properties are listed below.

3,10-Bis(2-nitrobenzenesulfonyl)-6-(1-pyrenebutyryl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**17**) (Scheme I).

Compound **17** was purified using methylene chloride/methanol: 100/1 as an eluent and isolated as a pale yellow foam in a yield of 92%; ^1H nmr: (δ) 1.58 (m, 2H), 2.10-2.22 (m, 2H), 2.27-2.43 (m, 2H), 2.67-2.75 (m, 1H), 2.94 (m, 1H), 3.08-3.25 (m, 2H), 3.34-3.38 (m, 6H), 4.43-4.60 (m, 4H), 7.32-8.39 (m, 20H); hrms (FAB): m/z 861.235 ($M + H$) $^+$ ($C_{44}H_{41}N_6O_9S_2$ requires 861.237).

Anal. Calcd. for $C_{44}H_{40}N_6O_9S_2$: C, 61.38; H, 4.69; N, 9.77. Found: C, 61.11; H, 4.80; N, 9.81.

6-(2-Anthraquinonecarbonyl)-3,10-bis(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**18**) (Scheme I).

Compound **18** was purified using methylene chloride/methanol: 200/1 as an eluent and isolated as a pale yellow foam in a yield of 76%; ^1H nmr: (δ) 1.50-1.63 (m, 2H), 3.19-3.32 (m, 3H), 3.40-3.55 (m, 3H), 3.50-3.68 (m, 2H), 4.53-4.67 (m, 4H), 7.44-8.37 (m, 18H); hrms (FAB): m/z 825.166 ($M + H$) $^+$ ($C_{39}H_{33}N_6O_{11}S_2$ requires 825.164). A satisfactory elemental analysis result was obtained for compound **3**, a derivative of compound **18**.

3,10-Bis(2-nitrobenzenesulfonyl)-6-(1-pyrenecarbonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**19**) (Scheme I).

Compound **19** was purified using methylene chloride/methanol: 200/1 as an eluent and isolated as a pale yellow foam in a yield of 86%; ^1H nmr: (δ) 1.75-1.95 (m, 1H), 2.30-2.55 (m, 1H), 2.85-3.35 (m, 4H), 3.40-3.95 (m, 4H), 4.30-4.80 (m, 4H), 5.91 (t, 0.5 H, $J = 6.3$ Hz), 6.18 (d, 0.5H, $J = 9.5$ Hz), 6.99 (t, 0.5H, $J = 7.6$ Hz), 7.13-8.40 (m, 18.5H); hrms (FAB): m/z 819.193 ($M + H$) $^+$ ($C_{41}H_{35}N_6O_9S_2$ requires 819.189).

Anal. Calcd. for $C_{41}H_{34}N_6O_9S_2$: C, 60.13; H, 4.19; N, 10.27. Found: C, 60.30; H, 4.16; N, 10.35.

General Procedure for the Preparation of Compounds **1-13** (Final Deprotection) (Schemes I-V).

A mixture of 2-nitrobenzenesulfonyl-protected compound **16-19**, **24**, **25**, **29**, **30**, **38** or **43-46** (2.6 mmoles), thiophenol (0.87 g, 7.8 mmoles) and anhydrous potassium carbonate (3.22 g, 23.4 mmoles) in 20 ml of dimethylformamide was stirred at room temperature overnight. The solvent was evaporated and the residue was dissolved in chloroform-water. The organic phase was separated and the aqueous phase was extracted with chloroform. The combined organic phase was dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash chromatography on a silica gel column. Chromatographic eluents, product yields and spectral properties are listed below.

6-(2-Anthraquinonemethyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**1**) (Scheme I).

Compound **1** was purified using methylene chloride/methanol: 1/0 and then 1/1 as eluents, and isolated as a white foam in a yield of 73%; ^1H nmr: (δ) 1.75-1.90 (m, 2H), 2.32-2.53 (m, 6H), 2.74 (t, 2H, $J = 5.3$ Hz), 3.70 (s, 2H), 3.73 (s, 2H), 3.91 (s, 2H), 3.90-4.20 (br, 2H), 6.92 (d, 1H, $J = 7.8$ Hz), 6.99 (d, 1H, $J = 7.3$ Hz), 7.50 (t, 1H, $J = 7.5$ Hz), 7.68-7.73 (m, 2H), 7.85-7.89 (m, 1H), 8.18-8.25 (m, 4H); ^{13}C nmr: (δ) 26.7, 46.9, 49.3, 52.4, 53.5, 55.4,

55.8, 58.9, 120.4, 127.1, 127.7, 132.6, 133.6, 133.9, 134.8, 136.6, 146.5, 158.7, 159.0, 182.9, 183.1; hrms (FAB): m/z 441.230 ($M + H$) $^+$ ($C_{27}H_{29}N_4O_2$ requires 441.229).

Anal. Calcd. for $C_{27}H_{28}N_4O_2 \cdot 1.5H_2O$: C, 69.68; H, 6.67; N, 12.04. Found: C, 69.26; H, 6.80; N, 11.76.

6-(1-Pyrenebutyryl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**2**) (Scheme I).

Compound **2** was purified using methylene chloride/methanol: 1/0 and then 3/1 as eluents, and isolated as a white foam in a yield of 65%; ^1H nmr: (δ) 1.10-1.35 (m, 1H), 1.45-1.65 (m, 1H), 2.00-2.95 (m, 12H), 3.10-3.38 (m, 4H), 3.65 (s, 1H), 3.68 (s, 1H), 3.79 (s, 1H), 3.82 (s, 1H), 6.74-6.92 (m, 2H), 7.28-7.35 (m, 1H), 7.74-8.25 (m, 9H); ^{13}C nmr: (δ) 27.0, 29.1, 32.2, 32.4, 32.7, 44.3, 46.0, 46.2, 46.5, 46.9, 48.1, 48.9, 54.1, 55.0, 55.3, 120.7, 120.9, 121.3, 123.6, 124.8, 125.0, 125.8, 126.6, 127.3, 127.5, 128.8, 129.8, 131.4, 136.3, 137.1, 159.7, 160.2, 172.7; hrms (FAB): m/z 491.283 ($M + H$) $^+$ ($C_{32}H_{35}N_4O$ requires 491.281).

Anal. Calcd. for $C_{32}H_{34}N_4O \cdot H_2O$: C, 75.59; H, 7.09; N, 11.02. Found: C, 75.43; H, 7.20; N, 10.73.

6-(2-Anthraquinonecarbonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**3**) (Scheme I).

Compound **3** was purified using methylene chloride and then methanol/30% aqueous ammonium hydroxide: 1/0 and 15/1 as eluents, and isolated as a pale yellow foam in a yield of 80%; ^1H nmr: (δ) 1.30-1.52 (m, 1H), 1.55-1.82 (m, 1H), 2.27 (s, 2H), 2.55-3.02 (m, 4H), 3.07 (s, 2H), 3.45 (m, 1H), 3.64 (m, 1H), 3.94 (m, 4H), 7.08-7.12 (d, 2H, $J = 7.7$ Hz), 7.52-7.89 (m, 4H), 8.17 (s, 1H), 8.26-8.31 (m, 3H); ^{13}C nmr: (δ) 28.1, 28.4, 28.6, 29.0, 43.4, 43.6, 45.6, 47.3, 47.8, 48.1, 49.6, 54.7, 55.8, 121.1, 121.8, 125.0, 127.4, 127.5, 132.0, 133.4, 134.3, 137.5, 142.6, 160.3, 169.9, 182.5; hrms (FAB): m/z 455.207 ($M + H$) $^+$ ($C_{27}H_{27}N_4O_3$ requires 455.207).

Anal. Calcd. for $C_{27}H_{26}N_4O_3 \cdot H_2O$: C, 68.64; H, 5.93; N, 11.86. Found: C, 68.73; H, 5.87; N, 11.62.

6-(1-Pyrenecarbonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**4**) (Scheme I).

Compound **4** was purified using methylene chloride/methanol: 10/1 and then methanol/30% aqueous ammonium hydroxide: 10/1 as eluents, and isolated as a pale yellow foam in a yield of 77%; ^1H nmr: (δ) 1.18-1.40 (m, 1H), 1.72-1.95 (m, 1H), 2.36-2.43 (m, 1H), 2.63 (br, 4H), 2.85-3.06 (m, 1H), 3.03-3.35 (m, 2H), 3.32-3.56 (m, 1H), 3.72-4.12 (m, 5H), 6.87 (d, 0.5H, $J = 7.4$ Hz), 7.02 (t, 1H, $J = 6.6$ Hz), 7.46 (t, 0.5H, $J = 7.8$ Hz), 7.59 (t, 0.5H, $J = 7.8$ Hz), 7.73-8.17 (m, 9H); ^{13}C nmr: (δ) 28.3, 28.7, 43.2, 45.5, 46.7, 47.8, 48.4, 48.6, 49.4, 54.3, 54.6, 55.5, 55.9, 120.8, 121.1, 121.8, 123.5, 123.9, 124.0, 124.6, 125.5, 126.3, 127.2, 127.7, 128.0, 128.6, 130.8, 131.2, 131.4, 131.8, 137.4, 159.9, 160.3, 171.4, 171.6; hrms (FAB): m/z 449.231 ($M + H$) $^+$ ($C_{29}H_{29}N_4O$ requires 449.233).

Anal. Calcd. for $C_{29}H_{28}N_4O \cdot H_2O$: C, 75.65; H, 6.52; N, 12.17. Found: C, 75.58; H, 6.41; N, 11.94.

5-(*tert*-Butoxycarbonyl)amino-1-pentanyl Tosylate (**21**) (Scheme II).

A solution of tosyl chloride (28.6 g, 0.15 moles) in 200 ml of tetrahydrofuran was added slowly into a mixture of sodium hydroxide (24.0 g, 0.6 moles) and 5-(*tert*-butoxycarbonyl)amino-1-pentanol (**20**) [18] (20.3 g, 0.1 moles) in 200 ml of water and 300 ml of THF at 0°. After stirring at room temperature overnight, the reaction

mixture was poured onto 100 g of ice and 80 ml of hydrochloric acid (37%), and then extracted with chloroform. The combined organic phase was washed with 5% aqueous sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash chromatography on a silica gel column using methylene chloride as an eluent to give 15.6 g (46%) of compound **21** as a pale yellow oil; ^1H nmr: (δ) 1.21-1.45 (m, 4H), 1.42 (s, 9H), 1.57-1.70 (m, 2H), 2.44 (s, 3H), 3.05 (q, 2H, $J = 6.3$ Hz), 4.00 (t, 2H, $J = 6.4$ Hz), 4.50 (m, 1H), 7.33 (d, 2H, $J = 8.2$ Hz), 7.77 (d, 2H, $J = 8.2$ Hz); ^{13}C nmr: (δ) 21.5, 22.6, 28.4, 29.3, 40.1, 70.4, 78.8, 127.8, 129.8, 133.1, 144.7, 156.0; hrms (FAB): m/z 358.168 ($M + H$) $^+$ ($\text{C}_{17}\text{H}_{28}\text{NO}_4\text{S}$ requires 358.168).

Anal. Calcd. for $\text{C}_{17}\text{H}_{27}\text{NO}_4\text{S}$: C, 57.11; H, 7.62; N, 3.92. Found: C, 56.98; H, 7.59; N, 4.08.

6-[5-(*tert*-Butoxycarbonyl)amino-1-pentanyl]-3,10-bis(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**22**) (Scheme II).

A mixture of compound **15** (2.0 g, 3.4 mmoles), anhydrous potassium carbonate (1.0 g, 7.2 mmoles) and tosylate **21** (1.39 g, 4.1 mmoles) in 50 ml of anhydrous acetonitrile was refluxed for two days. The solvent was evaporated and the residue was dissolved in chloroform-water. The organic phase was separated and the aqueous phase was extracted with chloroform. The combined organic phase was washed with brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash chromatography on a silica gel column using methylene chloride/methanol: 200/1 and then 100/1 as eluents to give 1.37 g (57%) of compound **22** as a pale yellow foam; ^1H nmr: (δ) 1.11-1.51 (m, 15 H), 1.95-2.10 (m, 2H), 2.06-2.25 (m, 4H), 2.90-3.09 (m, 4H), 3.10-3.30 (m, 4H), 4.55-4.65 (br, 1H), 4.91-5.00 (s, 4H), 7.35-7.47 (m, 2H), 7.55-7.76 (m, 7H), 7.89-8.02 (m, 2H); ^{13}C nmr: (δ) 23.0, 24.4, 25.6, 26.8, 28.4, 29.9, 32.3, 40.5, 46.7, 47.5, 49.8, 50.3, 54.7, 55.3, 62.3, 78.8, 124.0, 124.3, 130.3, 132.1, 132.5, 134.0, 138.7, 148.2, 155.1, 155.7, 156.1; hrms (FAB): m/z 776.276 ($M + H$) $^+$ ($\text{C}_{34}\text{H}_{46}\text{N}_7\text{O}_{10}\text{S}_2$ requires 776.274).

Anal. Calcd. for $\text{C}_{34}\text{H}_{45}\text{N}_7\text{O}_{10}\text{S}_2$: C, 52.63; H, 5.85; N, 12.64. Found: C, 52.68; H, 6.00; N, 12.47.

6-(5-Amino-1-pentanyl)-3,10-bis(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**23**) (Scheme II).

Compound **23** was purified using methylene chloride/methanol: 2/1 and then methanol/30% aqueous ammonium hydroxide: 10/1 as eluents, and isolated as a pale yellow foam in a yield of 87%; ^1H nmr: (δ) 1.18-1.55 (m, 10H), 2.05-2.14 (m, 2H), 2.26 (t, 4H, $J = 6.8$ Hz), 2.65 (t, 2H, $J = 6.8$ Hz), 3.22-3.34 (m, 4H), 4.54 (s, 2H), 4.55 (s, 2H); 7.46-7.60 (m, 2H), 7.62-7.80 (m, 7H), 8.00-8.12 (m, 2H); ^{13}C nmr: (δ) 24.5, 25.6, 27.0, 33.4, 42.0, 46.8, 47.4, 49.8, 50.4, 54.7, 55.4, 124.1, 124.3, 130.3, 132.0, 132.6, 133.9, 138.6, 148.2, 155.0, 155.7; hrms (FAB): m/z 676.224 ($M + H$) $^+$ ($\text{C}_{29}\text{H}_{38}\text{N}_7\text{O}_8\text{S}_2$ requires 676.222).

Anal. Calcd. for $\text{C}_{29}\text{H}_{37}\text{N}_7\text{O}_8\text{S}_2$: C, 51.53; H, 5.52; N, 14.52. Found: C, 51.35; H, 5.70; N, 14.36.

6-[5-(2-Anthraquinonecarbonyl)amino-1-pentanyl]-3,10-bis(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**24**) (Scheme II).

Compound **24** was purified using ethyl acetate as an eluent and isolated as a pale yellow foam in a yield of 76%; ^1H nmr: (δ) 1.40-1.75 (m, 4H), 1.91-2.11 (m, 2H), 2.12-2.32 (m, 4H), 3.14-3.30 (m,

4H), 3.30-3.51 (m, 4H), 4.20-4.35 (m, 2H), 4.52 (s, 4H), 6.96-7.10 (br, 1H), 7.31-8.49 (m, 18H); hrms (FAB): m/z 910.250 ($M + H$) $^+$ ($\text{C}_{44}\text{H}_{44}\text{N}_7\text{O}_{11}\text{S}_2$ requires 910.254). A satisfactory elemental analysis result was obtained for compound **5**, a derivative of compound **24**.

3,10-Bis(2-nitrobenzenesulfonyl)-6-[5-(1-pyrenecarbonyl)-amino-1-pentanyl]-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**25**) (Scheme II).

Compound **25** was purified using methylene chloride/methanol: 100/1 as an eluent and isolated as a pale yellow foam in a yield of 65%; ^1H nmr: (δ) 1.30-1.50 (m, 6H), 1.67 (s, 2H), 2.00-2.15 (m, 2H), 2.20-2.38 (m, 4H), 3.19-3.38 (m, 4H), 3.54-3.64 (q, 2H, $J = 6.0$ Hz), 4.46 (s, 2H), 4.48 (s, 2H), 6.35 (br, 1H), 7.38-7.74 (m, 9H), 7.89-8.23 (m, 10H), 8.50-8.55 (d, 1H, $J = 9.0$ Hz); ^{13}C nmr: (δ) 24.7, 25.7, 26.7, 29.4, 40.2, 46.8, 47.5, 49.8, 50.4, 54.6, 55.2, 123.9, 124.2, 124.4, 125.6, 126.3, 127.1, 128.3, 130.2, 130.5, 131.0, 131.5, 131.9, 132.0, 132.4, 1432.5, 133.7, 138.5, 148.1, 154.9, 155.6, 170.0; hrms (FAB): m/z 904.281 ($M + H$) $^+$ ($\text{C}_{46}\text{H}_{46}\text{N}_7\text{O}_9\text{S}_2$ requires 904.279).

Anal. Calcd. for $\text{C}_{46}\text{H}_{45}\text{N}_7\text{O}_9\text{S}_2 \cdot 2\text{H}_2\text{O}$: C, 58.78; H, 5.22; N, 10.43. Found: C, 59.06; H, 5.38; N, 10.42.

6-[5-(2-Anthraquinonecarbonyl)amino-1-pentanyl]-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**5**) (Scheme II).

Compound **5** was purified using methylene chloride/methanol: 1/1 as an eluent and isolated as a yellow foam in a yield of 34%; ^1H nmr: (δ) 1.30-1.80 (m, 10H), 2.15-2.25 (m, 2H), 2.25-2.49 (m, 6H), 3.32-3.60 (m, 4H), 3.74 (s, 2H), 3.80 (s, 2H), 6.87 (d, 2H, $J = 7.6$ Hz), 7.39 (t, 1H, $J = 7.4$ Hz), 7.75-7.80 (m, 2H), 8.05-8.38 (m, 5H), 8.60 (s, 1H); ^{13}C nmr: (δ) 24.9, 26.3, 27.2, 28.9, 40.2, 47.0, 49.8, 52.0, 53.3, 53.6, 56.0, 57.5, 120.4, 120.5, 125.4, 127.3, 127.6, 133.3, 133.4, 134.3, 136.5, 158.4, 158.7, 182.5, 182.6; hrms (FAB): m/z 540.295 ($M + H$) $^+$ ($\text{C}_{32}\text{H}_{38}\text{N}_5\text{O}_3$ requires 540.296).

Anal. Calcd. for $\text{C}_{32}\text{H}_{37}\text{N}_5\text{O}_3 \cdot 2\text{H}_2\text{O}$: C, 66.74; H, 7.13; N, 12.17. Found: C, 67.00; H, 6.77; N, 11.41.

6-[5-(1-Pyrenecarbonyl)amino-1-pentanyl]-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**6**) (Scheme II).

Compound **6** was purified using methylene chloride/methanol: 1/0 and 4:1, and then methanol/30% aqueous ammonium hydroxide: 5/1 as eluents, and isolated as a pale yellow foam in a yield of 89%; ^1H nmr: (δ) 1.42-1.65 (m, 6H), 1.65-1.82 (m, 2H), 2.01-2.14 (m, 2H), 2.15-2.48 (m, 8H), 3.30 (s, 2H), 3.53 (s, 2H), 3.56-3.65 (m, 2H), 3.50-3.95 (br, 2H), 6.56 (t, 2H, $J = 8.0$ Hz), 7.16 (t, 1H, $J = 7.6$ Hz), 7.65 (br, 1H), 7.87-8.13 (m, 8H), 8.43 (d, 1H, $J = 9.2$ Hz); ^{13}C nmr: (δ) 24.9, 26.4, 27.2, 29.3, 40.3, 47.1, 49.7, 52.1, 53.2, 53.6, 56.1, 57.0, 120.0, 124.1, 124.7, 125.5, 126.1, 127.1, 128.2, 130.7, 131.1, 132.0, 136.0, 158.3, 158.5, 170.2; hrms (FAB): m/z 534.322 ($M + H$) $^+$ ($\text{C}_{34}\text{H}_{40}\text{N}_5\text{O}$ requires 534.322).

Anal. Calcd. for $\text{C}_{34}\text{H}_{39}\text{N}_5\text{O} \cdot 2\text{H}_2\text{O}$: C, 71.70; H, 7.55; N, 12.30. Found: C, 71.61; H, 7.30; N, 12.15.

6-(5-*tert*-Butoxycarbonyl)amino-3-aza-2-carboxyl-1-pentanyl)-3,10-bis(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**27**) (Scheme III).

A mixture of compound **15** (2.0 g, 3.4 mmoles), bromo-compound **26** [25] (1.0 g, 3.57 mmoles) and anhydrous potassium carbonate (2.0 g, 14.1 mmoles) in 20 ml of anhydrous acetonitrile was stirred at room temperature overnight. The solvent was evaporated

and the residue was dissolved in chloroform-water. The organic phase was separated and the aqueous phase was extracted with chloroform. The combined organic phase was washed with brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash chromatography on a silica gel column using methylene chloride/methanol: 200/1 and 100/1 as eluents to give 2.17 g (81%) of compound **27** as a pale yellow foam; ^1H nmr: (δ) 1.38 (s, 9H), 1.35-1.50 (m, 2H), 2.22-2.45 (m, 4H), 2.95 (s, 2H), 3.13-3.42 (m, 8H), 4.54 (s, 2H), 4.56 (s, 2H), 5.03 (br, 1H), 7.10 (br, 1H), 7.48 (d, 2H, $J = 7.8$ Hz), 7.61-7.80 (m, 7H), 8.01-8.08 (m, 2H); ^{13}C nmr: (δ) 25.0, 28.4, 39.7, 40.6, 46.8, 47.4, 50.5, 51.6, 54.5, 55.2, 59.4, 79.2, 123.8, 124.3, 130.6, 132.1, 132.6, 133.8, 134.1, 138.7, 148.2, 155.4, 155.9, 156.4, 171.3; hrms (FAB): m/z 791.248 ($M + H$) $^+$ ($\text{C}_{33}\text{H}_{43}\text{N}_8\text{O}_{11}\text{S}_2$ requires 791.248).

Anal. Calcd. for $\text{C}_{33}\text{H}_{42}\text{N}_8\text{O}_{11}\text{S}_2 \cdot 2\text{H}_2\text{O}$: C, 47.92; H, 5.57; N, 13.55. Found: C, 47.86; H, 5.71; N, 13.29.

6-[5-(2-Amino-3-aza-2-carbonyl-1-pentanyl)-3,10-bis(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**28**) (Scheme III).

Compound **28** was purified using methylene chloride/methanol: 10/1 and then methanol/30% aqueous ammonium hydroxide: 20/1 as eluents, and isolated as a pale yellow foam in a yield of 82%; ^1H nmr: (δ) 1.42-1.58 (m, 2H), 1.70 (s, 2H), 2.29-2.44 (m, 4H), 2.77 (t, 2H, $J = 5.8$ Hz), 2.95 (s, 2H), 3.21-3.37 (m, 6H), 4.54 (s, 4H), 7.22 (br, 1H), 7.46 (d, 1H, $J = 7.2$ Hz), 7.62-7.81 (m, 7H), 8.00-8.05 (m, 2H); ^{13}C nmr: (δ) 24.6, 41.2, 46.8, 47.0, 50.0, 51.8, 54.0, 54.9, 59.4, 123.9, 124.3, 124.4, 130.5, 132.0, 132.1, 132.6, 133.9, 134.1, 138.7, 148.2, 155.3, 155.6, 170.9; hrms (FAB): m/z 691.198 ($M + H$) $^+$ ($\text{C}_{28}\text{H}_{35}\text{N}_8\text{O}_9\text{S}_2$ requires 691.196).

Anal. Calcd. for $\text{C}_{28}\text{H}_{34}\text{N}_8\text{O}_9\text{S}_2 \cdot 2\text{H}_2\text{O}$: C, 47.44; H, 5.08; N, 15.81. Found: C, 47.44; H, 5.19; N, 15.86.

6-[5-(2-Anthraquinonecarbonyl)amino-3-aza-2-carboxyl-1-pentanyl]-3,10-bis(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**29**) (Scheme III).

Compound **29** was purified using methylene chloride/methanol: 100/1 as an eluent and isolated as a pale yellow foam in a yield of 73%; ^1H nmr: (δ) 1.34-1.58 (m, 2H), 2.32-2.43 (m, 4H), 3.01 (s, 2H), 3.33-3.42 (m, 4H), 3.59 (s, 4H), 4.49 (s, 2H), 4.52 (s, 2H), 7.27-7.44 (m, 3H), 7.59-7.88 (m, 10H), 7.95-8.05 (m, 2H), 8.18-8.32 (m, 4H), 8.65 (d, 1H, $J = 1.8$ Hz); ^{13}C nmr: (δ) 25.0, 39.1, 41.2, 47.3, 50.9, 51.9, 54.2, 55.4, 59.2, 123.6, 123.9, 124.3, 126.0, 127.3, 127.6, 130.6, 131.8, 132.0, 132.6, 133.3, 134.1, 134.4, 134.8, 138.6, 139.4, 148.2, 155.4, 155.9, 166.0, 172.4, 182.2, 182.4; hrms (FAB): m/z 925.225 ($M + H$) $^+$ ($\text{C}_{43}\text{H}_{41}\text{N}_8\text{O}_{12}\text{S}_2$ requires 925.224).

Anal. Calcd. for $\text{C}_{43}\text{H}_{40}\text{N}_8\text{O}_{12}\text{S}_2 \cdot \text{H}_2\text{O}$: C, 53.75; H, 4.58; N, 11.66. Found: C, 53.96; H, 4.76; N, 11.64.

3,10-Bis(2-nitrobenzenesulfonyl)-6-[5-(1-pyrenecarbonyl)-amino-3-aza-2-carboxyl-1-pentanyl]-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**30**) (Scheme III).

Compound **30** was purified using methylene chloride/methanol: 100/1 as an eluent and isolated as a pale yellow foam in a yield of 81%; ^1H nmr: (δ) 1.45-1.50 (m, 2H), 2.22-2.43 (m, 4H), 2.96 (s, 2H), 3.23-3.42 (m, 4H), 3.56-3.80 (m, 4H), 4.35 (s, 2H), 4.49 (s, 2H), 7.05-7.45 (m, 6H), 7.50-7.65 (m, 5H), 7.90-8.22 (m, 10H), 8.55 (d, 1H, $J = 9.2$ Hz); ^{13}C nmr: (δ) 24.7, 24.9, 33.8, 39.4, 40.5, 47.2, 50.7, 51.8, 54.0, 55.2, 59.2, 123.3, 123.6, 123.9, 124.1, 124.3, 124.6, 124.8, 125.6, 126.3, 127.1, 128.3, 130.0, 130.3, 130.5,

130.8, 130.9, 131.5, 131.9, 132.1, 132.5, 133.5, 133.7, 138.3, 147.7, 148.1, 155.3, 155.6, 170.4, 171.7; hrms (FAB): m/z 919.253 ($M + H$) $^+$ ($\text{C}_{45}\text{H}_{43}\text{N}_8\text{O}_{10}\text{S}_2$ requires 919.253).

Anal. Calcd. for $\text{C}_{45}\text{H}_{42}\text{N}_8\text{O}_{10}\text{S}_2$: C, 58.81; H, 4.61; N, 12.20. Found: 58.88; H, 4.92; N, 11.82.

6-[5-(2-Anthraquinonecarbonyl)amino-3-aza-2-carbonyl-1-pentanyl]-3,6,10,16-tetraaza-bicyclo[10.3.1]hexadeca-1(16),12,14-triene (**7**) (Scheme III).

Compound **7** was purified using methylene chloride/methanol: 10/1 and 0/1, and then methanol/30% aqueous ammonium hydroxide: 5/1 as eluents, and was isolated as a pale yellow foam in a yield of 68%; ^1H nmr: (δ) 1.69-1.75 (m, 2H), 2.37-2.52 (m, 4H), 2.61-2.80 (m, 4H), 2.65-3.05 (br, 2H), 3.11 (s, 2H), 3.53-3.69 (m, 4H), 3.78 (s, 2H), 3.93 (s, 2H), 6.95 (d, 2H, $J = 7.6$ Hz), 7.49 (t, 1H, 7.6 Hz), 7.78-7.83 (m, 2H), 8.27-8.34 (m, 4H), 8.34-8.45 (br, 1H), 8.64 (s, 1H), 9.00-9.18 (br, 1H); ^{13}C nmr: (δ) 27.1, 29.7, 38.9, 40.7, 46.8, 48.4, 52.4, 53.4, 53.7, 58.2, 120.7, 125.6, 127.4, 127.7, 133.2, 133.5, 134.3, 134.9, 135.0, 136.9, 139.9, 158.5, 159.1, 166.0, 172.6, 182.5; hrms (FAB): m/z 555.273 ($M + H$) $^+$ ($\text{C}_{31}\text{H}_{35}\text{N}_6\text{O}_4$ requires 555.272).

Anal. Calcd. for $\text{C}_{31}\text{H}_{34}\text{N}_6\text{O}_4 \cdot 1.5\text{HCl}$: C, 61.11; H, 5.83; N, 13.79. Found: C, 61.18; H, 5.58; N, 13.53.

6-[5-(1-Pyrenecarbonyl)amino-3-aza-2-carboxyl-1-pentanyl]-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**8**) (Scheme III).

Compound **8** was purified using methanol/30% aqueous ammonium hydroxide: 1/0 and then 2:1 as eluents, and isolated as a pale yellow foam in a yield of 85%; ^1H nmr: (δ) 1.42-1.61 (m, 2H), 1.70 (br, 2H), 2.21-2.41 (m, 6H), 2.46-2.65 (m, 2H), 3.10 (s, 4H), 3.48 (s, 2H), 3.62-3.85 (m, 4H), 6.24 (d, 1H, $J = 8.0$ Hz), 6.45 (d, 1H, $J = 7.4$ Hz), 7.00 (t, 1H, $J = 7.6$ Hz), 7.96-8.25 (m, 8H), 8.40 (d, 1H, $J = 9.2$ Hz), 8.45 (br, 1H), 8.59 (br, 1H); ^{13}C nmr: (δ) 27.2, 38.3, 40.4, 46.4, 48.2, 52.0, 53.0, 53.2, 57.8, 58.3, 119.8, 120.0, 124.3, 124.4, 125.6, 126.2, 127.1, 128.2, 128.3, 128.4, 130.7, 131.1, 132.0, 136.0, 157.9, 159.4, 171.9; hrms (FAB): m/z 549.295 ($M + H$) $^+$ ($\text{C}_{33}\text{H}_{37}\text{N}_6\text{O}_2$ requires 549.297).

Anal. Calcd. for $\text{C}_{33}\text{H}_{36}\text{N}_6\text{O}_2 \cdot \text{H}_2\text{O}$: C, 69.93; H, 6.71; N, 14.83. Found: C, 70.07; H, 6.78; N, 14.71.

Methyl 4-[5-(*tert*-Butoxycarbonyl)amino-1-pentanoxy]pyridine-2,6-dicarboxylate (**32**) (Scheme IV).

To a stirred solution of 5-(*tert*-butoxycarbonyl)amino-1-pentanol **20** [18] (4.06 g, 20.0 mmoles) and triphenylphosphine (5.76 g, 20.0 mmoles) in 50 ml of anhydrous tetrahydrofuran was added the solution of diethyl azodicarboxylate (3.85 g, 20.0 mmoles) at 0°. A solution of dimethyl 4-hydroxypyridine-2,6-dicarboxylate **31** [26] (4.22 g, 20.0 mmoles) in 20 ml of tetrahydrofuran was added dropwise to the above solution at 0° and the resulting solution was stirred at room temperature for 24 hours. The solvent was evaporated and the residue was partially dissolved in ethanol. After filtration, the solid was recrystallized from ethanol/hexanes: 1/1 to give 6.15 g (78%) of compound **32** as white crystals; mp 98-99°; ^1H nmr: (δ) 1.43 (s, 9H), 1.48-1.62 (m, 4H), 1.80-1.95 (m, 2H), 3.09-3.11 (m, 2H), 4.00 (s, 6H), 4.12 (t, 2H, $J = 6.0$ Hz), 7.78 (s, 2H); ^{13}C nmr: (δ) 23.0, 28.3, 29.6, 40.2, 53.0, 66.9, 68.8, 78.8, 114.3, 149.6, 156.0, 165.0, 166.9; hrms (FAB): m/z 397.198 ($M + H$) $^+$ ($\text{C}_{19}\text{H}_{29}\text{N}_2\text{O}_7$ requires 397.197).

Anal. Calcd. for $C_{19}H_{28}N_2O_7$: C, 57.55; H, 7.12; N, 7.07. Found: C, 57.56; H, 7.32; N, 7.33.

4-[5-(*tert*-Butoxycarbonyl)amino-1-pentanoxy]pyridine-2,6-dimethanol (**33**) (Scheme IV).

Sodium borohydride (1.89 g, 50.0 mmoles) was added in portions to a stirred solution of compound **32** (4.0 g, 10.0 mmoles) in 200 ml of ethanol. The resulting reaction mixture was stirred at room temperature for 2 hours and refluxed for 2 hours. The solvent was evaporated and the residue was dissolved in chloroform-water. The organic phase was separated and the aqueous phase was extracted with chloroform. The combined organic phase was dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash chromatography on a silica gel column using methylene chloride/methanol: 50/1 as an eluent to give 2.59 g (76%) of compound **33** as a white solid; mp 83.5–84.0°; 1H nmr: (δ) 1.36–1.62 (m, 13H), 1.75–1.90 (m, 2H), 3.06–3.21 (m, 2H), 4.02 (t, 2H, $J = 6.4$ Hz), 4.55–4.70 (br, 2H), 4.67 (s, 4H), 6.70 (s, 2H); ^{13}C nmr: (δ) 22.8, 28.4, 29.7, 40.3, 64.2, 67.8, 77.0, 105.5, 156.3, 161.4, 166.7, 227.8; hrms (FAB): m/z 341.207 ($M + H$) $^+$ ($C_{17}H_{29}N_2O_5$ requires 341.207).

Anal. Calcd. for $C_{17}H_{28}N_2O_5$: C, 59.96; H, 8.29; N, 8.23. Found: C, 59.84; H, 8.38; N, 8.08.

4-[5-(*tert*-Butoxycarbonylamino)-1-pentanoxy]pyridine-2,6-dimethyl Ditosylate (**34**) (Scheme IV).

A solution of tosyl chloride (5.26 g, 27.6 mmoles) in 100 ml of tetrahydrofuran was added dropwise into a solution of compound **33** (2.35 g, 6.90 mmoles) and sodium hydroxide (1.66 g, 41.4 mmoles) in 50 ml of tetrahydrofuran and 50 ml of water at 0°. The resulting reaction mixture was stirred at room temperature for 4 hours and was then poured into 30 g of ice. The organic phase was separated and the aqueous phase was extracted with chloroform. The combined organic phase was washed with 5% aqueous sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash chromatography on a silica gel column using methylene chloride as an eluent to give 4.29 g (96%) of compound **34** as a white oil; 1H nmr: (δ) 1.35–1.65 (m, 13H), 1.69–1.85 (m, 2H), 2.43 (s, 6H), 3.14 (q, 2H, $J = 6.0$ Hz), 3.98 (t, 2H, $J = 6.2$ Hz), 4.98 (s, 4H), 4.70–4.95 (br, 1H), 6.82 (s, 2H), 7.33 (d, 4H, $J = 7.8$ Hz), 7.80 (d, 4H, $J = 8.2$ Hz); ^{13}C nmr: (δ) 21.5, 13.1, 28.4, 29.7, 40.3, 68.2, 71.3, 78.8, 107.8, 127.9, 129.9, 132.6, 145.2, 155.0, 156.1, 166.6; hrms (FAB): m/z 649.226 ($M + H$) $^+$ ($C_{31}H_{41}N_2O_9S_2$ requires 649.225).

Anal. Calcd. for $C_{31}H_{40}N_2O_9S_2$: C, 57.38; H, 6.22; N, 4.32. Found: C, 57.34; H, 6.23; N, 4.44.

14-[5-(*tert*-Butoxycarbonyl)amino-1-pentanoxy]-3,6,10-tris(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**36**) (Scheme IV).

A mixture of ditosylate **34** (4.01 g, 6.2 mmoles), tri-protected triamine **35** [18] (4.20 g, 6.2 mmoles) and anhydrous cesium carbonate (8.10 g, 24.8 mmoles) in 450 ml of anhydrous dimethylformamide was stirred at room temperature overnight. The solvent was evaporated and the residue was dissolved in chloroform-water. The organic phase was separated and the aqueous phase was extracted with chloroform. The combined organic phase was washed with brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by flash chromatography on a silica gel column using methylene chloride/methanol: 200/1 and then 100/1 as eluents to give 5.4 g (89%) of compound **36** as a white foam; 1H nmr: (δ)

1.44 (s, 9H), 1.47–1.58 (m, 4H), 1.72–2.02 (m, 4H), 2.82–2.93 (m, 2H), 3.10–3.60 (m, 8H), 4.44 (t, 2H, $J = 6.2$ Hz), 4.46 (s, 2H), 4.50 (s, 2H), 4.50–4.62 (br, 1H), 7.00 (d, 1H, $J = 2.2$ Hz), 7.08 (d, 1H, $J = 2.2$ Hz), 7.86–8.15 (m, 12H); ^{13}C nmr: (δ) 23.2, 27.2, 28.5, 29.8, 40.4, 46.1, 46.3, 46.7, 49.0, 55.6, 68.3, 79.0, 110.0, 110.6, 124.3, 130.5, 130.7, 130.9, 131.7, 131.9, 132.1, 132.3, 133.0, 133.9, 134.1, 147.9, 148.3, 156.1, 157.2, 158.1, 167.1; hrms (FAB): m/z 977.248 ($M + H$) $^+$ ($C_{40}H_{49}N_8O_{15}S_3$ requires 977.248).

Anal. Calcd. for $C_{40}H_{48}N_8O_{15}S_3$: C, 49.17; H, 4.96; N, 11.48. Found: C, 48.96; H, 5.09; N, 11.68.

14-(5-Amino-1-pentanoxy)-3,6,10-tris(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**37**) (Scheme IV).

Compound **37** was purified using methylene chloride/methanol: 200/1 as an eluent and isolated as a white foam in a yield of 28%; 1H nmr: (δ) 1.41–1.70 (m, 6H, 2H), 1.70–2.00 (m, 4H), 2.78–2.95 (m, 4H), 3.20–3.38 (m, 4H), 3.49–3.54 (m, 2H), 4.06 (t, 2H, $J = 5.8$ Hz), 4.37 (s, 2H), 4.40 (s, 2H), 7.01 (d, 1H, $J = 2.0$ Hz), 7.09 (d, 1H, $J = 2.2$ Hz), 7.60–7.78 (m, 10H), 7.91–8.11 (m, 2H); ^{13}C nmr: (δ) 22.9, 27.1, 27.7, 28.3, 29.7, 40.0, 46.3, 46.7, 46.9, 55.5, 68.0, 110.1, 110.6, 124.4, 130.2, 130.6, 130.9, 131.9, 132.2, 132.3, 133.9, 134.1, 147.7, 147.9, 148.3, 157.2, 158.1, 167.1; hrms (FAB): m/z 877.197 ($M + H$) $^+$ ($C_{35}H_{41}N_8O_{13}S_3$ requires 877.195).

Anal. Calcd. for $C_{35}H_{40}N_8O_{13}S_3 \cdot 2H_2O$: C, 46.04; H, 4.82. Found: C, 45.77; H, 4.91.

14-[5-(1-Pyrenecarbonyl)amino-1-pentanoxy]-3,6,10-tris(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**38**) (Scheme IV).

Compound **38** was purified using methylene chloride/methanol: 1/0 and then 100/1 as eluents, and isolated as a pale yellow foam in a yield of 71%; 1H nmr: (δ) 1.30–1.48 (m, 2H), 1.50–1.75 (m, 6H), 2.81–3.09 (m, 4H), 3.25–3.55 (m, 6H), 3.81–3.95 (m, 2H), 4.42 (s, 2H), 4.44 (s, 2H), 6.81 (s, 1H), 6.88 (s, 1H), 7.20–8.05 (m, 21H); ^{13}C nmr: (δ) 22.0, 26.0, 26.3, 27.4, 39.3, 45.5, 46.8, 48.3, 54.8, 67.5, 109.2, 109.6, 116.6, 117.9, 123.9, 124.2, 129.5, 129.6, 132.0, 132.2, 134.0, 134.2, 157.1, 158.0; hrms (FAB): m/z 1105.251 ($M + H$) $^+$ ($C_{52}H_{49}N_8O_{14}S_3$ requires 1105.253). A satisfactory elemental analysis result was obtained for compound **9**, a derivative of compound **38**.

14-[5-(1-Pyrenecarbonyl)amino-1-pentanoxy]-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**9**) (Scheme IV).

Compound **9** was purified using methylene chloride/methanol: 5/1 and then methanol/30% aqueous ammonium hydroxide: 2/1 as eluents, and isolated as a pale yellow oil in a yield of 41%; 1H nmr: (δ) 1.52–2.01 (m, 8H), 1.80–2.40 (br, 3H), 2.43–2.71 (m, 8H), 3.60–3.75 (m, 2H), 3.73 (s, 2H), 3.75 (s, 2H), 4.04 (t, 2H, $J = 6.2$ Hz), 6.50 (s, 2H), 8.01–8.25 (m, 8H), 8.65 (d, 1H, $J = 9.4$ Hz); ^{13}C nmr: (δ) 23.5, 28.6, 29.1, 29.5, 40.0, 47.9, 48.3, 48.7, 49.2, 52.9, 53.8, 67.6, 106.7, 107.2, 124.5, 124.8, 125.7, 126.4, 127.1, 128.6, 130.7, 131.2, 142.3, 161.4, 165.8, 170.1; hrms (FAB): m/z 550.316 ($M + H$) $^+$ ($C_{34}H_{40}N_5O_2$ requires 550.318).

Anal. Calcd. for $C_{34}H_{39}N_5O_2 \cdot CHCl_3$: C, 62.80; H, 5.98; N, 10.46. Found: C, 62.79; H, 6.51; N, 10.19.

14-Piperazinyl-3,6,10-tris(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**41**) (Scheme V).

Compound **41** was obtained as pale yellow crystals in a yield of 81% by recrystallizing the crude product from methanol containing

2% of acetonitrile, mp 195–197°; silica gel tlc R_f 0.35 (methanol/30% aqueous ammonium hydroxide: 50/1); ^1H nmr (dimethyl sulfoxide- d_6): (δ) 1.42–1.64 (m, 2H), 3.00–3.68 (m, 16H), 4.48 (s, 4H), 6.82 (s, 1H), 7.01 (s, 1H), 7.80–8.15 (m, 12H), 9.60 (br, 1H); hrms (FAB): m/z for $\text{C}_{34}\text{H}_{37}\text{N}_9\text{O}_{12}\text{S}_3 \cdot 3\text{H}_2\text{O}$: C, 44.68; H, 4.73; N, 13.97. Found: C, 44.74; H, 4.65; N, 13.48.

16-Piperazinyl-3,7,12-tris(2-nitrobenzenesulfonyl)-3,7,12,18-tetraazabicyclo[12.3.1]octadeca-1(18),14,16-triene (**42**) (Scheme V).

Compound **42** was purified using ethyl acetate/methanol: 9/1, 8/5, and then 1/5 as eluents, and isolated as a yellow foam in a yield of 92%; silica gel tlc R_f 0.53 (methylene chloride/methanol: 9/1); ^1H nmr (acetonitrile- d_3): (δ) 1.22–1.40 (m, 4H), 1.65–1.79 (m, 2H), 3.00–3.15 (m, 4H), 3.20–3.30 (m, 6H), 3.32–3.40 (m, 2H), 3.54–3.60 (m, 4H), 4.30 (s, 2H), 4.49 (s, 2H), 6.77 (s, 2H), 7.64–7.82 (m, 10H), 7.96–8.02 (m, 2H), 9.20 (br, 1H); ^{13}C nmr (acetonitrile- d_3): (δ) 14.5, 19.2, 21.1, 26.7, 27.2, 29.5, 43.5, 44.0, 47.4, 48.3, 50.0, 51.0, 54.0, 55.1, 60.9, 108.5, 108.7, 118.3, 125.1, 125.2, 130.6, 131.0, 131.2, 132.1, 132.7, 133.1, 133.2, 135.1, 135.2, 135.3, 149.1, 149.2, 156.8, 157.0; hrms (FAB): m/z 888.211 ($\text{M} + \text{H}^+$) ($\text{C}_{36}\text{H}_{42}\text{N}_9\text{O}_{12}\text{S}_3$ requires 888.211).

Anal. Calcd. for $\text{C}_{36}\text{H}_{41}\text{N}_9\text{O}_{12}\text{S}_3 \cdot \text{H}_2\text{O}$: C, 44.72; H, 4.79. Found: C, 44.31; H, 4.72.

14-[N^4 -(2-Anthraquinonemethyl)piperazin- N^1 -yl]-3,6,10-tris(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**43**) (Scheme V).

Compound **43** was purified using hexanes/ethyl acetate: 2/1, 1/1, and then 0/1 as eluents, and isolated as a yellow foam in a yield of 89%; silica gel tlc R_f 0.60 (ethyl acetate); ^1H nmr (acetonitrile- d_3): (δ) 1.53–1.68 (m, 2H), 2.48–2.59 (m, 4H), 2.93–3.05 (m, 2H), 3.22–3.50 (m, 10H), 3.69 (s, 2H), 4.33 (s, 2H), 4.35 (s, 2H), 6.67 (d, 1H, $J = 1.8$ Hz), 6.76 (d, 1H, $J = 1.8$ Hz), 7.68–7.98 (m, 15H), 8.15–8.26 (m, 4H); hrms (FAB): m/z 1080.229 ($\text{M} + \text{H}^+$) ($\text{C}_{49}\text{H}_{46}\text{N}_9\text{O}_{14}\text{S}_3$ requires 1080.232).

Anal. Calcd. for $\text{C}_{49}\text{H}_{45}\text{N}_9\text{O}_{14}\text{S}_3$: C, 54.48; H, 4.19; N, 11.67. Found: C, 54.31; H, 4.15; N, 11.86.

14-[N^4 -(1-Pyrenebutyryl)piperazin- N^1 -yl]-3,6,10-tris(2-nitrobenzenesulfonyl)-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**44**) (Scheme V).

Compound **44** was purified using hexanes/ethyl acetate: 1/1 and 0/1, and then ethyl acetate/methanol: 20/1, 10/1 and 5/1 as eluents, and isolated as a pale yellow foam in the yield of 97%; silica gel tlc R_f 0.44 (ethyl acetate); ^1H nmr: (δ) 1.86–2.02 (m, 2H), 2.15–2.33 (m, 2H), 2.36–2.49 (m, 2H), 2.82–2.98 (m, 2H), 3.18–3.60 (m, 14H), 3.68–3.80 (m, 2H), 4.39 (s, 2H), 4.42 (s, 2H), 6.76 (d, 1H, $J = 1.8$ Hz), 6.87 (d, 1H, $J = 1.8$ Hz), 7.52–7.78 (m, 9H), 7.85–8.20 (m, 11H), 8.34 (d, 1H, $J = 9.2$ Hz); hrms (FAB): m/z 1130.288 ($\text{M} + \text{H}^+$) ($\text{C}_{54}\text{H}_{52}\text{N}_9\text{O}_{13}\text{S}_3$ requires 1130.289).

Anal. Calcd. for $\text{C}_{54}\text{H}_{51}\text{N}_9\text{O}_{13}\text{S}_3 \cdot 5\text{H}_2\text{O}$: C, 53.15; H, 5.03; N, 10.33. Found: C, 52.87; H, 4.83; N, 10.02.

16-[N^4 -(2-Anthraquinonemethyl)piperazin- N^1 -yl]-3,7,12-tris(2-nitrobenzenesulfonyl)-3,7,12,18-tetraazabicyclo[12.3.1]octadeca-1(18),14,16-triene (**45**) (Scheme V).

Compound **45** was purified using ethyl acetate/methanol: 1/0 and then 9/1 as eluents, and isolated as a yellow foam in a yield of 87%; silica gel tlc R_f 0.64 (methylene chloride/methanol: 95/5); ^1H nmr (acetonitrile- d_3): (δ) 1.20–1.42 (m, 6H), 1.69–1.78 (m, 2H), 2.48–2.55 (m, 4H), 2.98–3.15 (m, 4H), 3.20–3.40 (m, 8H), 3.71 (s, 2H), 4.26 (s,

2H), 4.44 (s, 2H), 6.64–6.68 (m, 2H), 7.68–8.02 (m, 15H), 8.20–8.40 (m, 4H); hrms (FAB): m/z 1108.260 ($\text{M} + \text{H}^+$) ($\text{C}_{51}\text{H}_{50}\text{N}_9\text{O}_{14}\text{S}_3$ requires 1108.263). A satisfactory elemental analysis result was obtained for compound **12**, a derivative of compound **45**.

16-[N^4 -(1-Pyrenebutyryl)piperazin- N^1 -yl]-3,7,12-tris(2-nitrobenzenesulfonyl)-3,7,12,18-tetraazabicyclo[12.3.1]octadeca-1(18),14,16-triene (**46**) (Scheme V).

Compound **46** was purified using ethyl acetate/methanol: 1/0 and 9/1 as eluents and isolated as a pale yellow foam in a yield of 72%; silica gel tlc R_f 0.31 (ethyl acetate/methanol: 5/1); ^1H nmr (acetonitrile- d_3): (δ) 1.20–1.27 (m, 2H), 1.30–1.38 (m, 2H), 1.65–1.78 (m, 2H), 2.09–2.18 (m, 2H), 2.46 (t, 2H, $J = 7.0$ Hz), 2.96 (t, 2H, $J = 6.2$ Hz), 3.07 (t, 2H, $J = 6.4$ Hz), 3.15–3.28 (m, 6H), 3.30–3.40 (m, 4H), 3.45–3.51 (m, 2H), 3.58–3.64 (m, 2H), 4.24 (s, 2H), 4.44 (s, 2H), 6.61–6.65 (m, 2H), 7.58–7.81 (m, 10H), 7.90–7.97 (m, 1H), 7.98–8.08 (m, 5H), 8.10–8.21 (m, 4H), 8.42 (d, 1H, $J = 9.4$ Hz); hrms (FAB): m/z 1158.320 ($\text{M} + \text{H}^+$) ($\text{C}_{56}\text{H}_{56}\text{N}_9\text{O}_{13}\text{S}_3$ requires 1158.316).

Anal. Calcd. for $\text{C}_{56}\text{H}_{55}\text{N}_9\text{O}_{13}\text{S}_3$: C, 58.07; H, 4.78; N, 10.88. Found: C, 57.89; H, 5.00; N, 10.80.

14-[N^4 -(2-Anthraquinonemethyl)piperazin- N^1 -yl]-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**10**) (Scheme V).

Compound **10** was purified using methanol/30% aqueous ammonium hydroxide: 1/0, 10/1 and then 5/1 as eluents, and isolated as a pale yellow foam in a yield of 79%; silica gel tlc R_f 0.10 (methanol/30% aqueous ammonium hydroxide: 5/1); ^1H nmr: (δ) 1.60–1.75 (m, 2H), 2.48–2.76 (m, 12H), 3.25–3.40 (m, 4H), 3.41–3.65 (br, 3H), 3.69 (s, 2H), 3.73 (s, 2H), 6.38 (s, 2H), 7.71–7.84 (m, 3H), 8.18–8.32 (m, 4H); hrms (FAB): m/z 525.300 ($\text{M} + \text{H}^+$) ($\text{C}_{31}\text{H}_{37}\text{N}_6\text{O}_2$ requires 525.298).

Anal. Calcd. for $\text{C}_{31}\text{H}_{36}\text{N}_6\text{O}_2 \cdot 2.5\text{H}_2\text{O}$: C, 65.36; H, 7.24; N, 14.75. Found: C, 65.49; H, 7.07; N, 14.88.

16-[N^4 -(2-Anthraquinonemethyl)piperazin- N^1 -yl]-3,7,12,18-tetraazabicyclo[12.3.1]octadeca-1(18),14,16-triene (**11**) (Scheme V).

Compound **11** was purified using methanol/30% aqueous ammonium hydroxide: 1/0 and 9/1 as eluents, and isolated as a pale yellow foam in a yield of 70%; silica gel tlc R_f 0.19 (methanol/30% aqueous ammonium hydroxide: 4/1); ^1H nmr: (δ) 1.20–1.50 (m, 6H), 2.50–2.78 (m, 16H), 3.30–3.42 (m, 4H), 3.72 (s, 2H), 3.74 (s, 2H), 3.80 (s, 2H), 6.46 (d, 2H, $J = 6.8$ Hz), 7.76–7.88 (m, 3H), 8.24–8.38 (m, 4H); hrms (FAB): m/z 553.331 ($\text{M} + \text{H}^+$) ($\text{C}_{33}\text{H}_{41}\text{N}_6\text{O}_2$ requires 553.329).

Anal. Calcd. for $\text{C}_{33}\text{H}_{40}\text{N}_6\text{O}_2 \cdot 0.5\text{HCl}$: C, 69.44; H, 7.10. Found: C, 69.70; H, 6.87.

14-[N^4 -(1-Pyrenebutyryl)piperazin- N^1 -yl]-3,6,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**12**) (Scheme V).

Compound **12** was purified using methanol/30% aqueous ammonium hydroxide: 1/0, 20/1, 5/1, and then 2/1 as eluents, and isolated as a white foam in a yield of 93%; ^1H nmr: (δ) 1.53–1.67 (m, 2H), 2.12–2.25 (m, 2H), 2.25–2.37 (m, 2H), 2.46–2.80 (m, 10H), 2.97–3.08 (m, 2H), 3.16–3.30 (m, 4H), 3.39 (t, 2H, $J = 6.8$ Hz), 3.69 (s, 2H), 3.70 (s, 2H), 6.25 (s, 2H), 7.28 (d, 1H, $J = 8.9$ Hz), 7.90–8.16 (m, 7H), 8.29 (d, 1H, $J = 7.8$ Hz); ^{13}C nmr: (δ) 26.7, 29.2, 32.1, 32.6, 40.7, 44.4, 45.7, 47.7, 48.3, 48.5, 49.3, 53.3, 54.2, 105.3, 123.4, 124.5, 124.8, 125.9, 126.3, 126.7, 127.1, 127.4, 128.8, 129.8, 130.8, 131.3, 136.0, 155.3, 160.5, 160.6, 171.1; hrms (FAB): m/z 575.352 ($\text{M} + \text{H}^+$) ($\text{C}_{36}\text{H}_{43}\text{N}_6\text{O}$ requires 575.349).

Anal. Calcd. for $C_{36}H_{42}N_6O \cdot HCl$: C, 70.74; H, 7.08; N, 13.75. Found: C, 70.70; H, 6.82; N, 13.46.

16-[N^4 -(1-Pyrenebutyl)piperazin- N^1 -yl]-3,7,12,18-tetraazabicyclo[12.3.1]octadeca-1(18),14,16-triene (**13**) (Scheme V).

Compound **13** was purified using methanol/30% aqueous ammonium hydroxide: 20/1 and then 5/1 as eluents, and isolated as a white foam in a yield of 68%; silica gel tlc R_f 0.10 (methanol/30% aqueous ammonium hydroxide: 4/1); 1H nmr (δ) 1.60–1.80 (m, 4H), 2.22–2.50 (m, 4H), 2.65–3.00 (m, 8H), 3.12–3.50 (m, 10H), 3.70–3.80 (m, 2H), 3.82 (s, 2H), 3.90 (s, 2H), 6.35–6.41 (m, 2H), 7.86 (d, 1H, $J = 8.0$ Hz), 7.95–8.20 (m, 7H), 8.35 (d, 1H, $J = 8.0$ Hz); hrms (FAB): m/z 603.382 ($M + H$)⁺ ($C_{38}H_{47}N_6O$ requires 603.380).

Anal. Calcd. for $C_{38}H_{46}N_6O \cdot HCl$: C, 71.42; H, 7.36; N, 13.15. Found: C, 71.37; H, 7.46; N, 12.95.

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