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Polyaza[*n*](1,4)naphthalenophanes and polyaza[*n*](9,10)anthracenophanes

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Abstract—A series of polyaza[*n*](1,4)naphthalenophanes and polyaza[*n*](9,10)anthracenophanes have been prepared by using the Fukuyama's protecting group (2- or 4-nitrophenyl sulfonyl) in a one-pot cyclization–deprotection reaction. Global yields for the purified products are comparable with those obtained for other polyazacyclophanes using the tosyl group as the amine protecting group. Their structural study has been carried-out by NMR showing a high rigidity for the smaller cycles and a more dynamic behaviour for the largest member of the series. The free energy barrier for the rotational equilibrium for compound **25** is about 3 kcal/mol lower than that calculated for analogous *N*-tosylated macrocycles. © 2002 Elsevier Science Ltd. All rights reserved.

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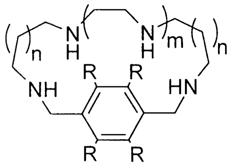
1. Introduction

In the last years, we have been involved in the preparation and study of a new family of nitrogen containing macrocycles, the polyaza[*n*]cyclophanes (Chart 1).[1,2] Those compounds combine the features of a flexible polynitrogenated moiety, having different protonation degrees depending on the pH, with the rigidity and preorganization imposed by the presence of the aromatic spacer. According to such characteristics, water soluble polyaza[*n*]cyclophanes have shown to be good ligands for metal cations as well as for biologically relevant anions such as nucleotides, pyrophosphate or barbiturates.[3,4]

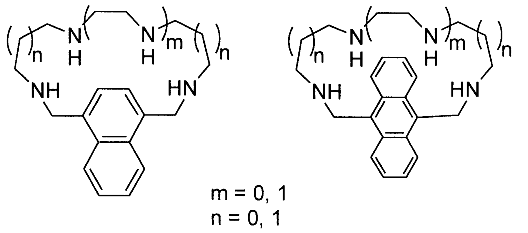
In the formation of the corresponding complexes and supramolecular species, the aromatic unit can play an important role giving place to the existence of π–π and π–cation interactions. On the other hand, aromatic subunits are also important for the potential use of those receptors as fluorescence chemosensors.[5,6] For the achievement of such properties, the introduction of extended aromatic moieties like naphthalene or anthracene seems an interesting structural feature (Chart 2).



1 R = H, Me
m = 0-3
n = 0, 1

Chart 1.

Originally, the synthesis of this family of compounds was achieved by a modification of the Richman–Atkins procedure, starting from a pertosylated polyamine that was reacted, under basic conditions, with a bis(bromomethyl)arene to give the *N*-protected macrocycles. Further removal of the protecting group led to the desired polyazamacrocycles (see Scheme 1).[1] This procedure was successful when the arene moiety was benzene or durene; however, the deprotection conditions were too drastic for the obtention of those polyazacyclophanes with naphthalene and anthracene fragments in their structure.[7] Apparently, the naphthylic and anthrylic C–N bonds were especially labile and, in most of cases, the strongly acidic or reductive



m = 0, 1
n = 0, 1

2

3

Chart 2.

Keywords: polyaza[*n*](1,4)naphthalenophane; polyaza[*n*](9,10)anthracenophane; nitrophenyl sulfonyl; polyazacyclophane.

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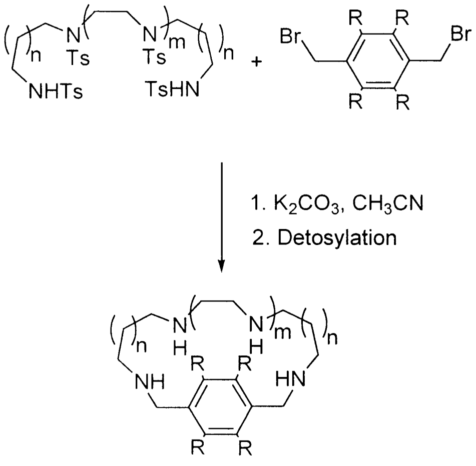


Scheme 1.

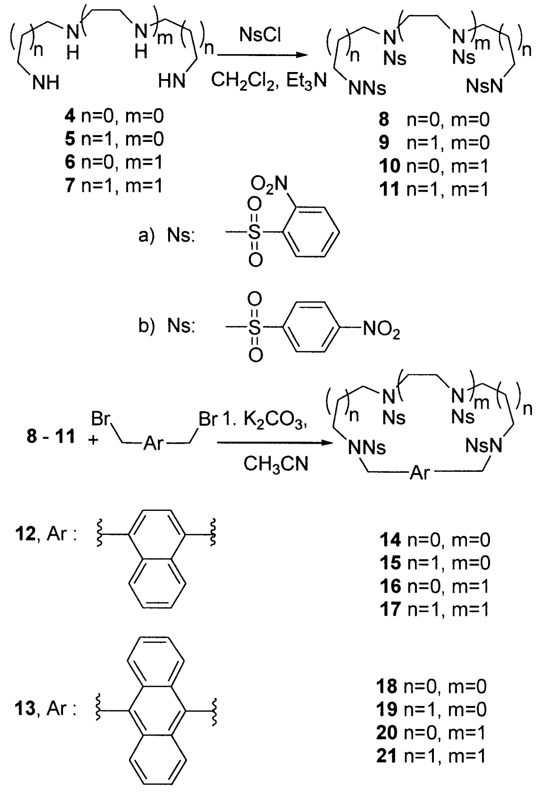
conditions used for the deprotection led to their cleavage. Only in one case, for compound N222 (m=1, n=0), the macrocyclic structure could survive the detosylation using a HBr/AcOH/PhOH mixture in a yield lower than 20%.

Those disappointing results prompted us in the search of a different protecting group that would be able to maintain the high yields of the cyclization step and would require mild deprotection conditions. Different protecting groups have been assayed for the substitution of the tosyl group in the Richman–Atkins procedure such as mesylates, trifluoroacetates or diethoxyphosphoryl derivatives.[8] However, most of those groups have not found general application as they also require deprotection under drastic conditions, the starting materials are not prepared easily and the efficiency of the cyclization step is low. Recently, the synthesis of some anthracenophanes in a small scale has been described with the use of the β-trimethylsilylethane sulfonyl group to protect the nitrogen atoms.[9] A few years ago, Fukuyama described the use of the nosyl group (2- or 4-nitrophenyl sulfonyl) for the protection of primary amino groups and its removal under very mild conditions. Since then, its utility has been demonstrated by the use in the selective protection and activation of polyamines and other amino derivatives, both in solution and in supported media, as well as in the preparation of *N*-functionalized pyridinophanes, among others.[10]

Here we report on the synthesis of polyaza[*n*](1,4)naphthalenophanes and polyaza[*n*](9,10)anthracenophanes by the use of *o*- and *p*-nitrobenzenesulfonyl as the amine protecting groups in a one-pot macrocyclization–deprotection reaction.[11]

2. Results and discussion

2.1. Synthesis



Scheme 2.

The commercially available polyamines **4**–**7** were protected by their reaction with 2- or 4-nitrobenzenesulfonyl chloride in CH_2Cl_2 using triethylamine as a base (Scheme 2). Further reaction of **8**–**11** with different bis(bromomethyl)arenes (**12**, **13**) in acetonitrile, using anhydrous potassium carbonate as the base, gave the *N*-pernosylated polyaza[*n*](1,4)naphthalenophanes **14**–**17** and polyaza[*n*](9,10)anthracenophanes **18**–**21** (Scheme 2).

The yields obtained are collected in Table 1. As it can be seen, the *p*-nosylated polyamines (**8b**–**11b**) are obtained in slightly higher yields than the *o*-analogues (**8a**–**11a**). The pernosylated polyamines are yellowish solids sparingly soluble in most solvents, especially the *p*-nitro substituted and the longer ones.

As it happened in the case of the tosylated analogues, the protecting group seems to have multiple functions: first, protecting the amino functions from the undesired polyalkylation as well as increasing the acidity of the primary NH groups. On the other hand, the bulkiness of the aryl sulfonyl groups seems to favor the 1:1 cyclization reaction by preventing the approach of a second polyamine molecule to the arene. The high yields obtained (Table 2) in absence of high dilution conditions cannot be ascribed to any template effect as they seem to be independent of the

Table 1. Yields obtained in the preparation of pernosylated polyamines

Starting polyamine	Pernosylated polyamine	Yield (%)
4	A22oNs (**8a**)	61
	A22pNs (**8b**)	81
5	A33oNs (**9a**)	54
	A33pNs (**9b**)	63
6	A222oNs (**10a**)	53
	A222pNs (**10b**)	62
7	A323oNs (**11a**)	74
	A323pNs (**11b**)	86

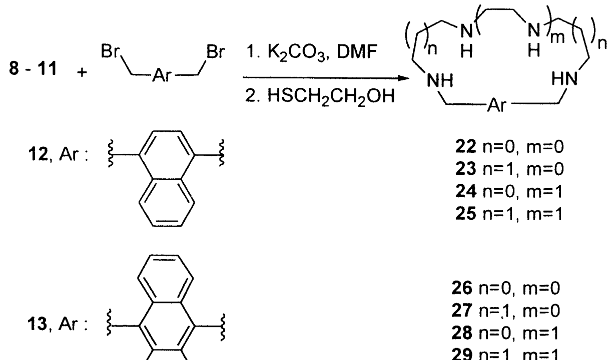
Table 2. Yields obtained in the cyclization of the pernosylated polyamines

Cyclophane	Yield (%)
N22pNs (**14b**)	92
N33pNs (**15b**)	46
N222pNs (**16b**)	88
N323oNs (**17a**)	98
N323pNs (**17b**)	90
AN22pNs (**18b**)	75
AN33pNs (**19b**)	84
AN222oNs (**20a**)	94
AN222pNs (**20b**)	80
AN323pNs (**21b**)	87

polyamine chain length and it also happened for the pertosylated analogues, independent of the metal cation used.[1a]

Finally, the deprotection of the macrocycles **14–21** was attempted via S_NAr by using the different thiol nucleophiles described in the literature (PhSH, $HSCH_2COOH$, $HSCH_2CH_2OH$) in acetonitrile with potassium carbonate as a base. The best results were, in general, obtained with the use of β-mercaptoethanol. Although the yields obtained were low and the cleavage of the labile C–N bonds was not completely suppressed, we could obtain the polyaza[*n*](1,4)naphthalenophanes **22–25** and the polyaza-[*n*](9,10)anthracenophanes **26–29**. The low solubility of the isolated pernosylated compounds, especially the *p*-nitro substituted ones in acetonitrile, could be the factor responsible for those low yields initially observed. The deprotection conditions were improved by a one-pot cyclization–deprotection sequence using DMF as the solvent (Scheme 3).

Thus, the pernosylated polyamine and the corresponding bis(bromomethyl)arene were reacted in DMF with anhydrous K_2CO_3 as the base. After 3 days of reaction at 100°C, the mixture was cooled to room temperature, the sulfur nucleophile was added and the mixture was stirred for 15 h. By this way, using $HSCH_2CH_2OH$ as the nucleophile, compounds **22–29** were obtained with the overall yields shown in Table 3 after a thorough purification process. It is important to note that for these kinds of compounds, a drastic decrease in yields is always obtained, very often to less than one-half of the yield for the crude product, when a complete purification is carried out.[1a]



Scheme 3.

Table 3. Yields obtained in the one-pot synthesis of naphthalenophanes and anthracenophanes

Cyclophane	Overall yield (%)[a]
N22 (**22**)	18
N33 (**23**)	13
N222 (**24**)	25
N323 (**25**)	28
AN22 (**26**)	27
AN33 (**27**)	25
AN222 (**28**)	11.2
AN323 (**29**)	30

[a] Yields correspond to the global three-steps route: cyclization–deprotection–conversion into the hydrochloride.

2.2. Structural studies

NMR spectroscopy was used to analyze the structural features of compounds **22–29** and similar trends to the previously described pertosylated precursors were found. The main structural characteristic of these ansa compounds is the possibility of rotation of the aromatic moiety that will depend on the polyamine chain length.[7a,12] As it can be seen in Fig. 1, for naphthalenophane **24** (N222) the rotation of the polyamine chain around the naphtyl moiety is precluded, leading to a loss of symmetry in the molecule and thus to the nonequivalence of the different geminal protons. This can be clearly seen for the naphthylic protons that appear as an AB system and also for the polyamine methylene protons that split into two different signals for each geminal proton. The same trends were also observed for the smaller cycles of the series **22** (N22) and **23** (N33) that, obviously, presented a higher rigidity. 2D NMR experiments (^1H–^{13}C HMQC and HMBC) were carried out for the full assignation of all the signals and the summary of the selected signals appears collected in Table 4.

The rigidity introduced by the aromatic moiety fixes the conformation of the polyamine chain arching above the aromatic plane. In this situation, the protons located over the B ring will be magnetically shielded as is the case, for example, of protons 3 in compound **24** (N222): proton H3′ (1.79 ppm) is shifted 0.21 ppm upfield from its geminal proton H3 (2.0 ppm). The same effect can be observed for protons 4, with an upfield shift of 0.24 ppm. However, in the case of protons 2 and 2′ there is not an appreciable magnetic difference between them, probably because both are oriented to the outside of the macrocyclic cavity. The observed field effects depend on the macrocycle size, namely, on the distance between the proton and the aromatic moiety. Thus, the upfield shifts observed for protons H2′ and H3′ in compound **22** (N22) are 1.21 and 0.82 ppm, respectively, both values clearly larger than those observed for naphthalenophane **24**.

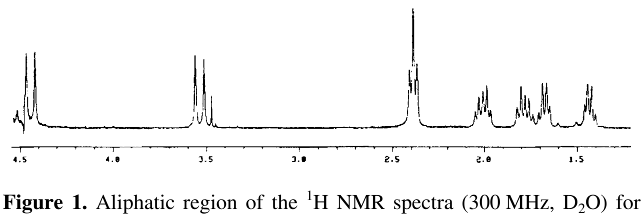
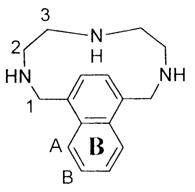
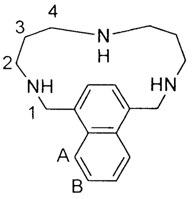


Figure 1. Aliphatic region of the ^1H NMR spectra (300 MHz, D_2O) for naphthalenophanes **24**.

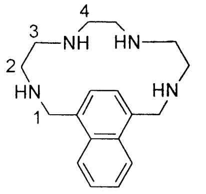
Table 4. Assignation of the ^{1}H NMR signals for naphthalenophanes **22–24**



22



23



24

Naphthalenophane	Proton[a]	^{1}H δ (ppm)[b]	$\Delta\delta$[c]
N22 (**22**)	1, 1′	3.79, 4.82	1.03
	2, 2′	2.3, 1.09	1.21
	3, 3′	2.82, 2.0	0.82
	A, B, C	8.18, 7.59, 7.45	–
N33 (**23**)	1, 1′	3.56, 4.77	1.21
	2, 2′	2.7	–
	3, 3′	1.0–1.4	–
	4, 4′	1.5–1.8	–
	A, B, C	8.17, 7.54, 7.2	–
N222 (**24**)	1, 1′	3.55, 4.45	0.89
	2, 2′	2.4	–
	3, 3′	2.0, 1.79	0.21
	4, 4′	1.67, 1.43	0.24
	A, B, C	8.03, 7.47, 7.27	–

[a] 1′, 2′,… correspond to the geminal protons of each methylene oriented towards the B-ring of naphthalene.

[b] CDCl$_3$, 200 MHz.

[c] Difference of the chemical shifts between the geminal protons.

On the other hand, all the protons of the polyamine chain, with the exception of the naphthylic ones, are shifted upfield, in general, with respect to the analogues bearing benzene as the aromatic group, as a consequence of the presence of an extra aromatic ring. The naphthylic protons, as pointed out before, appear as an AB system. In this case, the low field signal corresponds to a proton unshielded ca. 1 ppm with respect to the other one, as a consequence of being located in the proximity of the *peri* protons of the B ring of naphthalene. The aromatic signals for H_A and H_B appear as an AA′BB′ system also reflecting the loss of symmetry.

Naphthalenophane **25** shows a different situation: the chain length is large enough to allow the free rotation around the aromatic system at room temperature and its spectrum showed the expected average signals (see Table 5). VT NMR experiments were carried out in order to measure the energy barrier associated to this rotational process. As it can be seen in Fig. 2 for compound **25** the coalescence of the naphthylic signals occurs at ca. −65°C, the ΔG_c value being 9.3 kcal/mol.[13] This value is 3 kcal/mol lower than that found for the pertosylated derivative reported before and confirms the importance of the steric hindrance caused by the nitrogen protecting group that plays a fundamental role in the conformations adopted by the macrocyclic compounds and probably also in the macrocyclization reaction.

Table 5. Compared ^{1}H NMR chemical shifts for some selected signals of compounds **25** and **29** and the related *p*-cyclophanes B323(**1**, n=1, m=1, R=H) and D323(**1**, n=1, m=1, R=CH$_3$)

Compound	Proton	^{1}H δ (ppm)[a]
B323(**1**)	1	3.8
D323(**1**)	1	4.03
N323(**25**)	1	4.3
AN323(**29**)	1	4.9
B323(**1**)	3	1.31
D323(**1**)	3	1.50
N323(**25**)	3	1.45
AN323(**29**)	3	0.9
B323(**1**)	5	2.30
D323(**1**)	5	2.47
N323(**25**)	5	2.2
AN323(**29**)	5	1.7

[a] CDCl$_3$, 200 MHz.

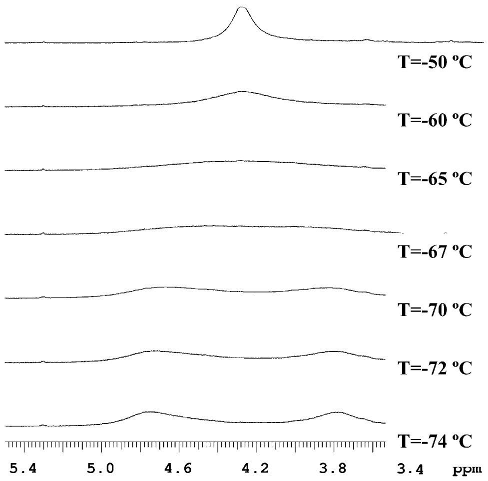


Figure 2. VT ^{1}H NMR spectra (300 MHz, CDCl$_3$) of the naphthylic protons for naphthalenophane **25**.

In the case of polyaza[n](9,10)anthracenophanes **26** (AN22), **27** (AN33), **28** (AN222) and **29** (AN323) a new symmetry plane is present and no splitting of the NMR signals was observed. Anyway, the rotation of the polyamine chain around the aromatic moiety is precluded by the presence of an extra aromatic ring. The chemical shifts for some selected signals of anthracenophane AN323, naphthalenophane N323, and related paracyclophanes B323 and D323 are compared in Table 5. As can be seen, the presence of the anthryl moiety enhances dramatically the field effects observed before.

Molecular mechanics calculations were carried out using the Monte Carlo conformational search method implemented in Macromodel V7.0 program. The AMBER* and MM2* force fields were used in a chloroform continuous solvent simulation (GB/SA).[14] The results obtained in the conformational search were in agreement with the NMR studies. In all cases, energy minimum conformers were found showing the polyamine chain arching over the aromatic system (Fig. 3). The smaller cycles, **22** and **23**, presented more strained structures with larger energy differences between the conformers found. In particular, within the energy gap considered, 12 kcal/mol, for those cyclophanes, no conformers were found for which the chain was significantly deviated from the plane perpendicular to the aromatic unit. However, for larger cycles, **24** and especially **25**, a higher degree of flexibility was found, namely, several conformers were found in a small energy range. Thus, for naphthalenophane **25**, conformations

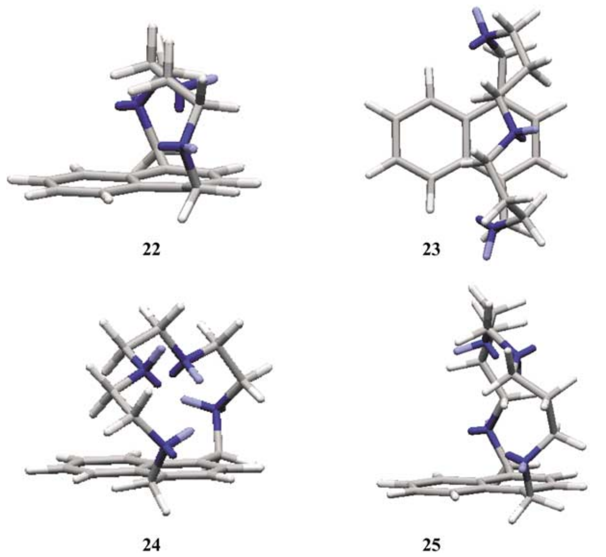


Figure 3. Calculated MM2* energy minimum conformations for naphthalenophanes **22**–**25**.

showing considerable chain mobility, often deviated from the perpendicular plane, were found even at ca. 2 kJ/mol above the minimum energy conformer.

3. Conclusions

In conclusion, the present results clearly confirm the high potential of the nosyl group as an alternative to the tosyl group for the protection of amino functionalities and removal under mild conditions. The problems associated in many cases with the low solubility of compounds containing several nosyl groups have been reduced, in our case, with the use of one-pot procedures that do not require isolation of the intermediate nosylated macrocycles. Using this one-pot methodology we have been able to prepare a series of polyaza[*n*]naphthalenophanes and polyaza[*n*]-anthracenophanes even in a gram scale. Structural analyses have shown the versatility of their dynamic characteristics upon selection of the chain length. The study of these compounds as receptors for different cationic and anionic guests is currently under investigation and they seem to have a great potential in metal coordination as well as in fluorescence sensing.[6b,15]

4. Experimental section

4.1. General

^{1}H NMR spectra were recorded either with a 200 MHz Varian Gemini spectrometer or a 300 MHz Varian Mercury spectrometer. ^{13}C NMR spectra were recorded at 50.3 and 75.4 MHz using the same spectrometers. Elemental analysis was carried out in a Carlo Erba EA-1108 CHNS-O analyzer. 1,4-Bis(bromomethyl)naphthalene (**12**) and 9,10-bis(bromomethyl)anthracene (**13**) were prepared as previously described.[7]

4.2. General procedure for the preparation of pernosylated polyamines

4.2.1. *N*,*N*′,*N*″,*N*‴-Tetrakis(*o*-nitrobenzenesulfonyl)-1,5,8,12-tetraazadodecane (11a). A solution of 8.4 g (38 mmol) of *o*-nitrobenzenesulfonyl chloride in dry CH_2Cl_2 was added to a mixture of 1,5,8,12-tetraazadodecane (1.66 g, 9.5 mmol) and 5.6 mL of Et_3N in 100 mL of dry CH_2Cl_2. The reaction mixture was stirred at room temperature for 30 h. The resulting suspension was filtered, washed several times with NH_4Cl and water, and the solution was vacuum evaporated. The resulting waxy solid was further purified by column chromatography on silica-gel (CH_2Cl_2/acetone, 9:1). 74%. ^{1}H NMR (200 MHz, DMSO-d_6): 1.7 (m, 4H, $-CH_2-CH_2-CH_2-$), 2.9 (m, 4H, CH_2-N), 3.3 (m, 4H, CH_2-NH), 3.48 (s, 4H, $N-(CH_2)_2-N$), 7.7–8.25 (m, 16H, Ar–*H*). ^{13}C NMR: 28.3, 40.1, 46.0, 46.5, 124.5, 129.4, 129.7, 131.3, 132.6, 134.0, 134.7, 147.7. Anal. Calcd for $C_{32}H_{34}N_8S_4O_{16}$: C, 42.0; H, 3.8; N, 12.3; S, 14.0. Found: C, 42.4; H, 3.7; N, 12.4; S, 14.3.

4.2.2. *N*,*N*′,*N*″,*N*‴-Tetrakis(*p*-nitrobenzenesulfonyl)-1,5,8,12-tetraazadodecane (11b). 86%. ^{1}H NMR (200 MHz, DMSO-d_6): 1.7 (m, 4H), 2.8 (t, 4H), 3.3 (t, 4H), 7.9 (d, 4H, J=9.2 Hz), 8.11 (m, 4H), 8.3 (d, 4H, J=9.2 Hz), 8.46 (m, 4H). ^{13}C NMR: 28.8, 46.6, 47.1, 123.5, 124.5, 125.0, 127.1, 128.1, 144.2, 147.4, 150.0, 154.4. Anal. Calcd for $C_{32}H_{34}N_8S_4O_{16}$: C, 42.0; H, 3.8; N, 12.3; S, 14.0. Found: C, 42.3; H, 4.0; N, 12.2; S, 14.2.

4.2.3. *N*,*N*′,*N*″-Tris(*o*-nitrobenzenesulfonyl)-1,4,7-triaza heptane (8a). 61%. ^{1}H NMR (200 MHz, DMSO-d_6): 3.35 (q, 4H, J_1=5.9 Hz, J_2=6.1 Hz), 3.56 (t, 4H, J=6.1 Hz), 5.78 (t, 2H, J=5.9 Hz), 7.6–7.9 (m, 9H), 8.0–8.15 (m, 3H). ^{13}C NMR: 42.2, 48.9, 124.4, 125.5, 131.0, 131.2, 132.9, 133.1, 133.8, 134.3, 147.8. Anal. Calcd for $C_{22}H_{22}N_6S_3O_{12}$: C, 40.1; H, 3.4; N, 12.8; S, 14.6. Found: C, 40.2; H, 3.5; N, 12.7; S, 14.8.

4.2.4. *N*,*N*′,*N*″-Tris(*p*-nitrobenzenesulfonyl)-1,4,7-triaza heptane (8b). 81%. ^{1}H NMR (200 MHz, DMSO-d_6): 2.5–3.4 (m, 8H), 7.8–8.0 (m, 6H), 8.1–8.4 (m, 6H). ^{13}C NMR: 40.2, 44.1, 123.4, 127.7, 129.2, 144.2, 145.9, 148.7. Anal. Calcd for $C_{22}H_{22}N_6S_3O_{12}$: C, 40.1; H, 3.4; N, 12.8; S, 14.6. Found: C, 40.3; H, 3.7; N, 12.5; S, 14.5.

4.2.5. *N*,*N*′,*N*″-Tris(*o*-nitrobenzenesulfonyl)-1,5,9-triaza nonane (9a). 54%. ^{1}H NMR (200 MHz, DMSO-d_6): 1.82 (q, 4H, J_1=6.9 Hz, J_2=7.3 Hz), 3.14 (q, 4H, J_1=7.3 Hz, J_2=6.1 Hz), 3.38 (t, 4H, J_1=6.9 Hz), 5.6 (t, 2H, J=6.1 Hz), 7.6–7.9 (m, 9H), 8.0 (m, 1H), 8.1 (m, 2H). ^{13}C NMR: 28.9, 40.8, 45.4, 124.3, 125.5, 130.8, 131.0, 132.1, 132.9, 133.4, 133.8, 134.0, 148.0. Anal. Calcd for $C_{24}H_{26}N_6S_3O_{12}$: C, 42.0; H, 3.8; N, 12.2; S, 14.0. Found: C, 41.9; H, 3.7; N, 12.1; S, 14.1.

4.2.6. *N*,*N*′,*N*″-Tris(*p*-nitrobenzenesulfonyl)-1,5,9-triaza nonane (9b). 63%. ^{1}H NMR (200 MHz, DMSO-d_6): 1.57 (m, 4H), 2.76 (m, 4H), 3.07 (m, 4H), 7.9–8.1 (m, 6H), 8.3–8.5 (m, 6H). ^{13}C NMR: 28.5, 40.2, 45.8, 124.6, 124.7, 128.0, 128.4, 144.4, 146.1, 149.5. Anal. Calcd for $C_{24}H_{26}N_6S_3O_{12}$: C, 42.0; H, 3.8; N, 12.2; S, 14.0. Found: C, 42.2; H, 3.9; N, 12.4; S, 14.2.

4.2.7. *N*,*N*′,*N*″,*N*‴-Tetrakis(*o*-nitrobenzenesulfonyl)-1,4,7,10-tetraazadecane (10a). 53%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 3.35 (m, 4H), 3.5–3.6 (m, 8H), 5.75 (t, 2H), 7.6–7.9 (m, 12H), 8.0–8.15 (m, 4H). ^{13}C NMR: 42.4, 47.8, 49.0, 124.4, 124.8, 125.4, 131.0, 131.1, 131.6, 132.4, 132.5, 132.6, 132.9, 133.1, 133.9, 134.2, 135.9, 147.8, 147.9. Anal. Calcd for $C_{30}H_{30}N_8S_4O_{16}$: C, 40.6; H, 3.4; N, 12.6; S, 14.5. Found: C, 41.0; H, 3.6; N, 12.5; S, 14.4.

4.2.8. *N*,*N*′,*N*″,*N*‴-Tetrakis(*p*-nitrobenzenesulfonyl)-1,4,7,10-tetraazadecane (10). 62%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 2.93 (m, 4H), 3.1–3.5 (m, 8H), 7.9–8.5 (m, 16H). ^{13}C NMR: 45.6, 47.6, 48.6, 123.3, 124.6, 125.0, 127.0, 128.1, 128.6, 129.7, 149.6, 150.0. Anal. Calcd for $C_{30}H_{30}N_8S_4O_{16}$: C, 40.6; H, 3.4; N, 12.6; S, 14.5. Found: C, 40.4; H, 3.5; N, 12.7; S, 14.4.

4.3. General procedure for the preparation of pernosylated cyclophanes

4.3.1. *N*,*N*′,*N*″,*N*‴-Tetrakis(*p*-nitrobenzenesulfonyl)-2,6,9,13-tetraaza[14](1,4)naphthalenophane (17b). Pernosylated polyamine **7** (3 g, 3.2 mmol) and K_2CO_3 (4.5 g, 32 mmol) were suspended in refluxing acetonitrile (250 mL). To this mixture, a solution of 1,4-bis(bromomethyl)naphthalene (**8**) (1 g, 3.2 mmol) was added dropwise. After the addition was complete, the suspension was refluxed for 72 h and then filtered. The solution was vacuum evaporated to dryness to give the crude product as a yellowish solid which was purified by column chromatography on silica gel (CH_2Cl_2/acetone, 9:1). (3.4 g, 90%). ^{1}H NMR (200 MHz, DMSO-d$_6$): 1.25 (m, 4H, –CH$_2$–*CH$_2$*–CH$_2$–), 2.5–3.2 (m, 12H, *CH$_2$*–N), 4.8 (s broad, 4H, Ar–*CH$_2$*–N), 7.5 (s, 2H, Ar–*H*), 7.9 (d, 4H, Ar–*H*), 8.0–8.5 (m, 12 H, Ar–*H*). ^{13}C NMR: 28.5, 46.4, 46.7, 47.0, 53.2, 124.3, 124.7, 127.5, 128.0, 130.8, 131.1, 131.2, 131.8, 132.0, 132.2, 132.4, 132.6, 134.0, 134.2, 147.7, 148.6. IR: 3106, 1701, 1598, 1530, 1350, 1159, 853, 739. Anal. Calcd for $C_{44}H_{42}N_8S_4O_{16}$: C, 49.5; H, 4.0; N, 10.5; S, 12.0. Found: C, 49.8; H, 3.8; N, 10.3; S, 12.2.

4.3.2. *N*,*N*′,*N*″,*N*‴-Tetrakis(*o*-nitrobenzenesulfonyl)-2,6,9,13-tetraaza[14](1,4)naphthalenophane (17a). 98%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 1.2 (m, 4H), 2.9–3.3 (m, 8H), 3.5 (s, 4H), 4.9 (s broad), 4H), 7.7 (s, 2H), 7.7–8.2 (m, 14H), 8.45 (m, 2H). ^{13}C NMR: 27.8, 44.7, 45.2, 46.0, 52.3, 124.5, 124.6, 129.8, 131.0, 132.6, 134.7, 135.0, 147.9, 148.1. Anal. Calcd for $C_{44}H_{42}N_8S_4O_{16}$: C, 49.5; H, 4.0; N, 10.5; S, 12.0. Found: C, 49.6; H, 3.9; N, 10.3; S, 12.2.

4.3.3. *N*,*N*′,*N*″-Tris(*p*-nitrobenzenesulfonyl)-2,5,8-triaza-[9](1,4)naphthalenophane (14b). 92%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 1.45 (m, 2H), 2.6–3.0 (m, 6H), 4.45 (d, 2H, J=13.5 Hz), 5.54 (d, 2H, J=13.5 Hz), 7.48 (m, 2H), 7.5–7.8 (m, 12H), 8.0 (m, 2H), 8.25 (dd, 2H, J_1= 3.4 Hz, J_2=6.5 Hz). ^{13}C NMR: 44.8, 49.4, 51.8, 124.0, 124.2, 124.5, 128.1, 130.3, 131.0, 131.3, 132.0, 132.3, 132.6, 134.1, 147.8, 148.2. Anal. Calcd for $C_{34}H_{30}N_6S_3O_{12}$: C, 50.4; H, 3.7; N, 10.4; S, 11.9. Found: C, 50.7; H, 3.8; N, 10.6; S, 11.8.

4.3.4. *N*,*N*′,*N*″-Tris(*p*-nitrobenzenesulfonyl)-2,6,10-triaza-[11]-(1,4)naphthalenophane (15b). 46%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 1.3 (m, 4H), 1.9 (m, 4H), 2.8 (m, 4H), 4.4 (m, 2H), 5.1 (m, 2H), 7.4 (s, 2H), 7.7 (m, 2H), 8.0–8.6 (m, 14H). ^{13}C NMR: 27.1, 42.6, 42.9, 50.5, 124.0, 124.3, 124.5, 126.2, 127.1, 131.9, 146.0, 150.2. Anal. Calcd for $C_{36}H_{34}N_6S_3O_{12}$: C, 51.5; H, 4.1; N, 10.0; S, 11.5. Found: C, 51.3; H, 4.3; N, 9.8; S, 11.7.

4.3.5. *N*,*N*′,*N*′,*N*‴-Tetrakis(*p*-nitrobenzenesulfonyl)-2,5,8,11-tetraaza[12](1,4)naphthalenophane (16b). 88%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 1.8 (m, 4H), 2.4 (m broad, 6H), 3.1 (m, 2H), 4.0 (s broad, 2H), 5.4 (s broad, 2H), 7.27 (s, 2H), 7.64 (m, 2H), 7.85–8.3 (m broad, 16H), 8.4 (m, 2H). ^{13}C NMR: 44.1, 45.3, 45.6, 50.7, 124.2, 124.6, 128.3, 130.3, 131.3, 132.0, 132.3, 134.3, 147.9, 148.3. Anal. Calcd for $C_{42}H_{38}N_8S_4O_{16}$: C, 48.5; H, 3.7; N, 10.8; S, 12.3. Found: C, 48.3; H, 3.6; N, 10.7; S, 12.2.

4.3.6. *N*,*N*′,*N*″-Tris(*p*-nitrobenzenesulfonyl)-2,5,8-triaza[9](9,10)anthracenophane (18b). 75%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 3.1 (m, 4H), 3.6 (m, 4H), 5.4 (s, 4H), 7.3–8.5 (m, 20H). ^{13}C NMR: 45.3, 45.9, 51.8, 123.3, 124.7, 125.6, 126.9, 127.8, 129.1, 134.5, 148.3, 151.5. Anal. Calcd for $C_{38}H_{32}N_6S_3O_{12}$: C, 53.0; H, 3.8; N, 9.8; S, 11.2. Found: C, 52.8; H, 3.9; N, 9.7; S, 11.3.

4.3.7. *N*,*N*′,*N*″-Tris(*p*-nitrobenzenesulfonyl)-2,6,10-triaza[11](9,10)anthracenophane (19b). 84%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 0.85 (m, 4H), 1.7 (m, 4H), 2.9 (m, 4H), 5.25 (s, 4H), 7.5 (m, 2H), 7.7 (m, 4H), 8.0–8.6 (m, 14H). ^{13}C NMR: 29.7, 45.1, 45.8, 52.0, 124.6, 125.0, 125.6, 126.7, 128.0, 128.9, 129.5, 130.4, 131.4, 132.3, 133.6, 142.8, 144.0, 149.9. Anal. Calcd for $C_{40}H_{36}N_6S_3O_{12}$: C, 54.1; H, 4.1; N, 9.4; S, 10.8. Found: C, 54.3; H, 4.0; N, 9.6; S, 10.6.

4.3.8. *N*,*N*′,*N*″,*N*‴-Tetrakis(*p*-nitrobenzenesulfonyl)-2,5,8,11-tetraaza[12](9,10)anthracenophane (20b). 80%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 2.6–3.1 (m, 12H), 5.4 (s broad), 4H), 7.3–7.8 (m, 8H), 7.9–8.7 (m, 16H). ^{13}C NMR: 45.3 (broad), 46.0, 47.6, 51.1, 124.7 (broad), 126.9, 127.8, 129.0, 129.9, 130.5, 142.4, 143.5, 149.9. Anal. Calcd for $C_{46}H_{40}N_8S_4O_{16}$: C, 50.7; H, 3.7; N, 10.3; S, 11.8. Found: C, 50.6; H, 3.8; N, 10.1; S, 11.9.

4.3.9. *N*,*N*′,*N*″,*N*‴-Tetrakis(*p*-nitrobenzenesulfonyl)-2,6,9,13-tetraaza[14](9,10)anthracenophane (21b). 87%. ^{1}H NMR (200 MHz, DMSO-d$_6$): 0.8 (m, 4H), 1.23 (s, 4H), 2.7 (m, 4H), 3.0 (m, 4H), 5.3 (s, 4H), 7.6 (m, 4H), 7.85 (d, 4H, J=9.3 Hz), 8.2–8.4 (m, 8H), 8.6 (d, 4H, J=8.1 Hz), 8.7 (m, 4H). ^{13}C NMR: 29.7, 45.1, 46.2, 46.4, 56.0, 124.8, 125.1, 125.6, 125.9, 126.8, 128.0, 128.4, 129.5, 130.8, 142.3, 143.9, 150.0, 150.4. Anal. Calcd for $C_{48}H_{44}N_8S_4O_{16}$: C, 51.6; H, 4.0; N, 10.0; S, 11.5. Found: C, 51.5; H, 4.1; N, 10.1; S, 11.4.

4.3.10. One-pot synthesis of naphthalenophanes and anthracenophanes: 2,6,9,13-tetraaza[14](9,10)anthracenophane (29). A solution of 9,10-bis(bromomethyl)anthracene (**13**) (1.4 g, 3.8 mmol) in DMF (100 mL) was added dropwise to a mixture of *N*,*N*′,*N*″,*N*‴-tetrakis(*o*-nitrobenzenesulfonyl)-1,5,8,12-tetraazadodecane (**11a**) (3.5 g, 3.8 mmol) and anhydrous K_2CO_3 (5.2 g, 38 mmol) in dry

DMF (300 mL) at 90°C. After stirring at 90°C for 3 days, the mixture was cooled to room temperature and 3 mL (42.9 mmol) of β-mercaptoethanol were added. The mixture was stirred for 15 h and then filtered, and the solvent was evaporated under reduced pressure. The sticky solid obtained was poured into 50 mL of 3 M HCl and washed several times with CH_2Cl_2. The aqueous layer was basified, extracted several times with $CHCl_3$ and dryed with anhydrous $MgSO_4$. The solvent was vacuum evaporated to dryness and the yellow solid obtained was further purified by column chromatography ($MeOH:NH_3$, 10:0.5) giving a waxy solid that, after bubbling HCl(g) through its methanolic solution, was characterized as its hydrochloride salt. 30%. ^{1}H NMR (300 MHz, D_2O): 1.63 (m, 4H, $-CH_2-$ CH_2-CH_2-), 2.53 (t, 4H, CH_2–N), 2.7 (t+s, 8H, CH_2–N), 4.9 (s, 4H, Ar–CH_2–N), 7.7 (m, 4H, Ar–H), 8.1 (m, 4H, Ar–H). ^{13}C NMR (D_2O): 22.9, 42.5, 43.5, 44.3, 45.0, 124.9, 128.8, 131.0. Anal. Calcd for $C_{24}H_{32}N_4\cdot 4HCl$: C, 55.2; H, 6.9; N, 10.7. Found: C, 54.8; H, 6.8; N, 10.9.

4.3.11. 2,5,8-Triaza[9](1,4)naphthalenophane (22). 18%. ^{1}H NMR (300 MHz, D_2O): 1.09 (m, 2H), 2.0 (m, 2H), 2.3 (m, 2H), 2.82 (m, 2H), 3.79 (d, J=13.2 Hz, 2H), 4.82 (d, J=13.2 Hz, 2H), 7.45 (s, 2H), 7.59 (dd, J_1=3.3 Hz, J_2=3.2 Hz, 2H), 8.18 (dd, J_1=3.3 Hz, J_2=3.2 Hz, 2H). ^{13}C NMR (D_2O): 49.8, 51.0, 54.6, 124.3, 124.7, 127.3, 132.8. Anal. Calcd for $C_{16}H_{21}N_3\cdot 3HCl$: C, 52.7; H, 6.6; N, 11.5. Found: C, 52.2; H, 6.9; N, 10.9.

4.3.12. 2,6,10-Triaza[11](1,4)naphthalenophane (23). 13%. ^{1}H NMR (300 MHz, D_2O): 1.26 (m, 4H), 2.25 (m, 4H), 2.67 (m, 4H), 3.56 (d, J=13.6 Hz, 2H), 4.77 (d, J=13.6 Hz, 2H), 7.2 (s, 2H), 7.54 (m, 2H), 8.17 (m, 2H). ^{13}C NMR (D_2O): 30.4, 47.0, 48.0, 53.6, 125.1, 126.1, 132.5, 138.1. Anal. Calcd for $C_{18}H_{25}N_3\cdot 3HCl$: C, 55.0; H, 7.2; N, 10.7. Found: C, 54.6; H, 6.9; N, 10.3.

4.3.13. 2,5,8,11-Tetraaza[12](1,4)naphthalenophane (24). 25%. ^{1}H NMR (300 MHz, D_2O): 1.43 (m, 2H), 1.67 (m, 2H), 1.79 (m, 2H), 2.0 (m, 2H), 2.4 (m, 2H), 3.55 (d, J=16 Hz, 2H), 4.45 (d, J=16 Hz, 2H), 7.27 (s, 2H), 7.47 (dd, J_1=4.4 Hz, J_2=6.6 Hz, 2H), 8.03 (dd, J_1=4.4 Hz, J_2=6.6 Hz, 2H). ^{13}C NMR (D_2O): 45.8, 46.3, 47.8, 50.0, 125.6, 127.6, 128.6, 133.0, 137.0. Anal. Calcd for $C_{18}H_{26}N_3\cdot 3HBr$: C, 34.8; H, 4.9; N, 9.0. Found: C, 34.1; H, 4.9; N, 8.8.

4.3.14. 2,6,9,13-Tetraaza[14](1,4)naphthalenophane (25). 28%. ^{1}H NMR (300 MHz, D_2O): 1.45 (m, 4H), 2.23 (s, 4H), 2.45–2.5 (m, 8H), 4.29 (s, 4H), 7.37 (s, 2H), 7.55 (dd, J_1=4.4 Hz, J_2=6.6 Hz, 2H), 8.25 (dd, J_1=4.4 Hz, J_2=6.6 Hz, 2H). ^{13}C NMR (D_2O): 27.4, 45.3, 46.9, 47.2, 49.8, 125.4, 127.6, 128.5, 132.7, 135.5. Anal. Calcd for $C_{20}H_{30}N_4\cdot 4HCl$: C, 50.9; H, 7.3; N, 11.9. Found: C, 50.7; H, 7.5; N, 11.1.

4.3.15. 2,5,8-Triaza[9](9,10)anthracenophane (26). 27%. ^{1}H NMR (300 MHz, D_2O): 1.2 (m, 4H), 2.3 (m, 4H), 5.0 (s, 4H), 7.6 (dd, J_1=3.5 Hz, J_2=3.2 Hz, 4H), 8.2 (dd, J_1=3.5 Hz, J_2=3.2 Hz, 4H). ^{13}C NMR (D_2O): 51.0, 51.2, 54.5, 124.0, 124.4, 131.3, 133.5. Anal. Calcd for $C_{20}H_{23}N_3\cdot 3HCl$: C, 57.9; H, 6.3; N, 10.1. Found: C, 57.3; H, 6.7; N, 9.8.

4.3.16. 2,6,10-Triaza[11](9,10)anthracenophane (27). 25%. ^{1}H NMR (300 MHz, D_2O): 0.4 (m, 4H), 1.85 (m, 4H), 2.9 (m, 4H), 5.1 (s, 4H), 7.8 (m, 4H), 8.3 (m, 4H). ^{13}C NMR (D_2O): 21.55, 40.9, 41.5, 42.5, 43.5, 124.4, 124.9, 129.1, 130.4. Anal. Calcd for $C_{22}H_{27}N_3\cdot 3HCl$: C, 59.7; H, 6.8; N, 9.5. Found: C, 59.4; H, 6.5; N, 9.8.

4.3.17. 2,5,8,11-Tetraaza[12](9,10)anthracenophane (28). 11.2%. ^{1}H NMR (300 MHz, D_2O): 3.2–3.6 (m broad, 12H), 4.9 (s broad, 4H), 7.76 (m, 4H), 8.1 (m, 4H). ^{13}C NMR (D_2O): 42.3, 45.2, 46.3, 47.1, 124.4, 128.3, 129.3, 130.2, 137.7. Anal. Calcd for $C_{24}H_{35}N_4\cdot 4HCl$: C, 54.9; H, 7.5; N, 10.7. Found: C, 54.2; H, 7.3; N, 10.8.

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