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Serinolic Amino-*s*-triazines: Iterative Synthesis of *N*-Substituted Amino-1,3-dioxane Derivatives from *l*-(*p*-Nitrophenyl)serinols and Rotational Stereochemistry Phenomena

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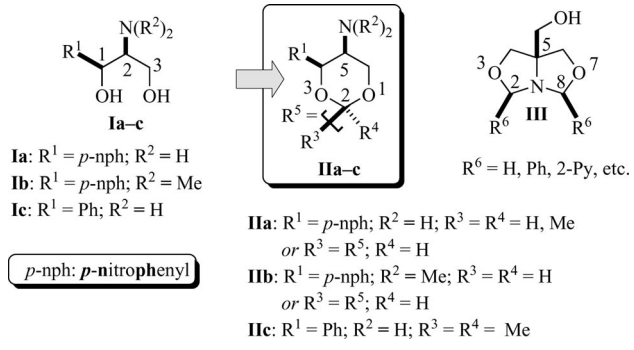
We report the first iterative and chemioselective approach towards the synthesis of highly elaborated *N*-substituted 2,4,6-triamino-*s*-triazines (melamines) and precursors, by amination of cyanuric chloride with anancomeric and enantiomerically pure primary and tertiary amino-1,3-dioxanes. The starting nucleophiles were prepared by direct diastereospecific and diastereoselective acetalization of *N*-substituted (1*S*,2*S*)-2-amino-1-(*p*-nitrophenyl)propane-1,3-diols [*l*-(*p*-nitrophenyl)serinols]. The stereochemistry of the title compounds is discussed in terms of (pro)diastereomerism originating from restricted rotation about the newly created C(*s*-triazine)–N< bonds and supported by NMR and DFT calculation data.

1. Introduction

We have previously reported a methodology by which to access enantiomerically pure primary (**IIa**) and tertiary (**IIb**) 5-amino-1,3-dioxanes (Scheme 1) by direct acetalization of the C-1-substituted serinols (2-aminopropane-1,3-diols), (1*S*,2*S*)-2-amino-1-(*p*-nitrophenyl)propane-1,3-diol [*l*-(*p*-nitrophenyl)serinol, **Ia**] and its *N*,*N*-dimethyl analogue **Ib**, on treatment with certain nonenolizable (di)carbonyl compounds in strongly acidic media.[1a–1e] The configurational stability is excellent, as evidenced by the commercially available 2,2-dimethyl acetal **IIc** of phenylserinol [(1*S*,2*S*)-2-amino-1-phenylpropane-1,3-diol, **Ic**; Scheme 1].[2] Besides this stability, primary 5-amino-1,3-dioxane derivatives **IIa** manifested useful reactivity with (aryl)(di)aldehydes and (di)acyl (di)chlorides, yielding not only the expected *N*-substituted amides,[1a–1c] but also new *C*-, *N*-substituted isoindolines[1c,1e] and 1,3-dioxanic Schiff bases.[1e,1f]



Scheme 1.

In continuation of our contributions to serinol chemistry, we have recently described the synthesis and stereochemistry of some protected *O*-, *N*-, *O*-serinolic building blocks, in the form of the 5-hydroxymethyl-3,7-dioxa-azabicyclo-[3.3.0]octanes (**III**, Scheme 1) based on TRIS [tris(hydroxymethyl)methaneamine, 2-(hydroxymethyl)serinol] anchored, by Williamson methodology, on diazine and *s*-triazine skeletons.[3] The coordination capabilities, both in solution and in the solid state, of the resulting functionalized π-deficient structures prompted us to investigate the use, described here, of an enlarged series of *O*,*O*-serinolic protected building blocks based on **Ia** and **Ib** – 1,3-dioxanes of type **IIa**, **IIb** (Scheme 1) – as amino nucleophiles with cyanuric chloride (anchorage by amination).

To the best of our knowledge, there is only one report[4] relating to the preparation and antitumor potential of 2,4,6-triamino-*s*-triazines (melamines) *N*-substituted with 1,3-dioxan-5-yl motifs as derivatives of C-2-substituted serinols. However, they were obtained in an inverted two-step strategy consisting of amination of cyanuric chloride followed by transacetalization.

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In this context, we note that the exploitation of the amino group as a selective nucleophile for substitution of a six-membered saturated heterocycle is mentioned only occasionally in syntheses of amino-*s*-triazines, and mainly in recent literature relating to dendrimeric melamines,[5a–5c] 4-aminopiperidine,[5d,5e] 4-(aminomethyl)piperidine,[5a–5c] and amino sugars.[5f] Only isolated interest has been paid to their intrinsic structural feature of restricted rotational phenomena about the C(*s*-triazine)–N< bonds.[5d,5e]

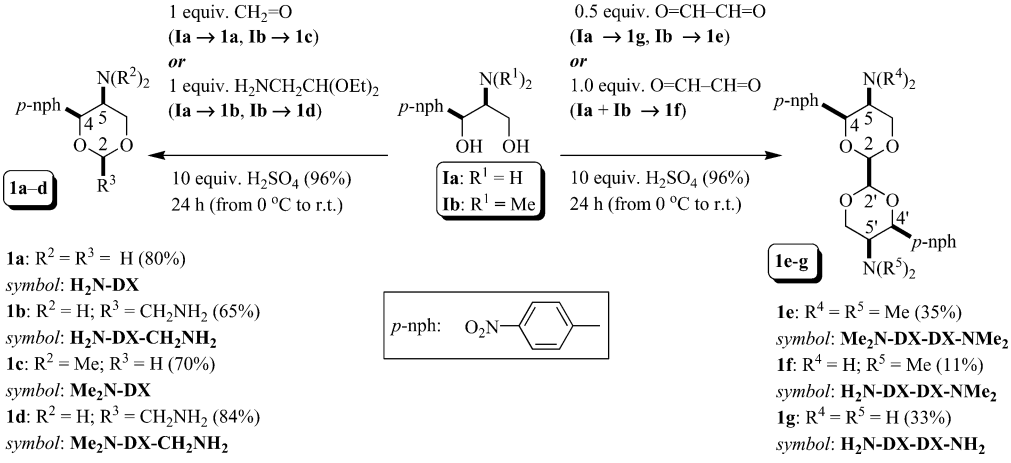
2. Results and Discussion

2.1. Synthesis and Stereochemistry of Starting Amino-1,3-dioxanes Based on *l*-(*p*-Nitrophenyl)serinols

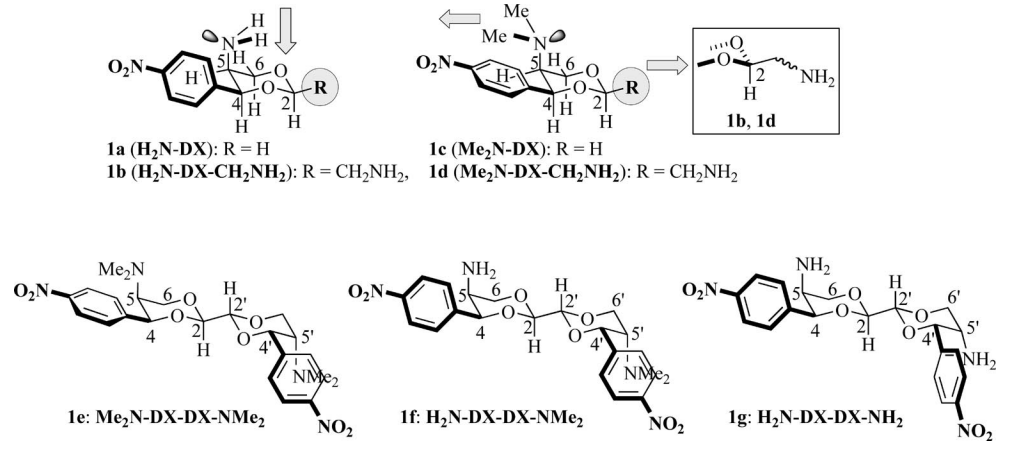
Our synthesis of 5-amino-1,3-dioxanes (Scheme 1) is summarized in Scheme 2.

As mentioned above, compounds **1a**–**d** were prepared by direct acetalization of the enantiomerically pure (1*S*,2*S*)-(*p*-nitrophenyl)serinols **Ia** and **Ib** in concentrated sulfuric acid (tenfold molar excess) at low temperature. We emphasize that only these conditions allowed the complete cancellation of the nucleophilicity of the amino group in **Ia** with respect to formaldehyde, glyoxal, and the diethyl acetal of aminoacetaldehyde. The conditions shown in Scheme 2 were also required for successful syntheses starting from **Ib**, treatment of which with the same carbonyl partners according to "classical" procedures (e.g., at reflux in an aromatic solvent with azeotropic removal of water and PTSA as catalyst) resulted in no reaction.[2e]

Our synthetic protocol, consisting of a totally diastereospecific and diastereoselective cyclocondensation, provide access to two types of 5-amino-1,3-dioxanes – "simple" (**1a**–**d**) and "double", 2,2′-dimeric (**1e**–**g**) – with yields exemplifying its overall ease (see Exp. Sect.). Indeed, despite the harsh conditions, all compounds of the series **1a**–**d** could be isolated as pure analytical samples by simple crystallization in routine workups. If **1e** and **1g** were prepared directly, by homo-coupling acetalization (2 × **Ib**) → **1e**, (2 × **Ia**) → **1g**, the disadvantages of the rather poor yields constantly obtained were offset by the structural profits gained. However, the cross-coupling acetalization (**Ia** + **Ib**) directed towards the 5,5′-diamino-2,2′-bi-1,3-dioxane **1f** gave poor selectivity, resulting in a **1e/1f/1g** mixture



Scheme 2.



Scheme 3.

(15:46:39 ratio) easily separable by column chromatography in this order (conversion of **Ia** 29% and 18% of **Ib**, yield 11% with respect to the desired **1f**).

5-Amino-1,3-dioxanes **1a**–**g** were all anancomeric structures[6] because of their overwhelmingly one-sided conformational equilibria due to the adoption of an equatorial position[1f] by the *p*-nitrophenyl (*p*-nph) ring located at C-4(′) ($A \approx 11.93$ kJ mol^{-1};[7] Scheme 3). This *A* value was greater by far than the A values of the C-5(′) amino (5.15–7.10 kJ mol^{-1}) or C-5(′) dimethylamino (6.40–8.80 kJ mol^{-1}) groups.[6]

As a result, all ^{1}H NMR spectra of compounds **1a**–**g**, displaying AMX coupling patterns in the C-4(′)–C-5(′)–C-6(′) sequences with stereospecific $^3J_{H,H}$ values of 1.0–3.0 Hz, and also 2D ^{1}H–^{1}H-NOESY experiments, allowed to assign the protons in this region to δ-4(′)-H-a > δ-6(′)-H-e > δ-6(′)-H-a > δ-5(′)-H-e.[1f] As expected, they also confirmed the equatorial C-2,–2' links between the 1,3-dioxane units in dimers **1e**–**g** and the equatorial positions of the C-2 methylene fragments in the aminomethyl groups of compounds **1b** and **1d** (*A* values up to 7.50 kJ mol^{-1}).[6] However, free orientations of amino groups with respect to the equatorial C-2 methylenes of the aminomethyl fragments in amino-1,3-dioxanes **1b** and **1d** should be pointed out (see inset in Scheme 3). This nuanced discrimination will be implied from here on throughout discussions in reference to equatorial vs. axial anchorage on the *s*-triazine ring after aminations carried out with **1b** and **1d** as nucleophiles on treatment with cyanuric chloride.

In conclusion, no epimerization occurred during acetalizations, the initial absolute configurations (1*S*,2*S*) of **Ia** and **Ib** again being identifiable as the 4(′)*S*,5(′)*S* units in all of the **1a**–**g** series, though being extended to 2(′)*R*,4(′)*S*,5(′)*S* in **1b**, **1d**, and **1e**–**g**.

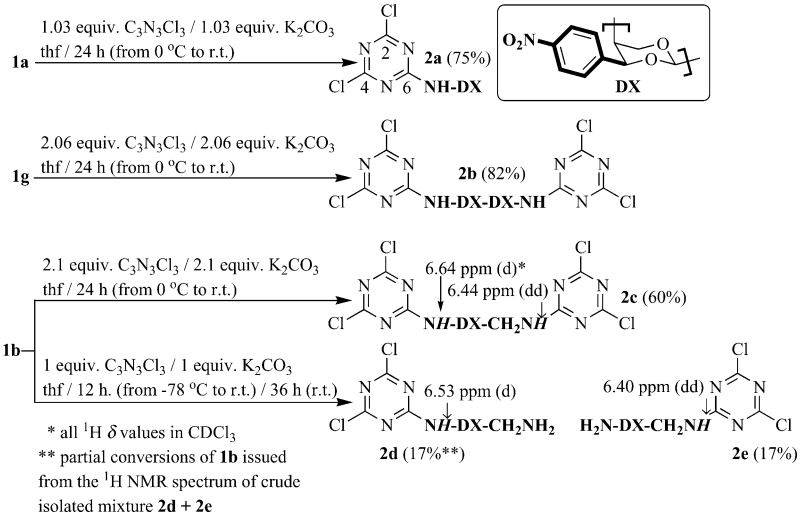
Furthermore, ^{1}H data relating to the 1,3-dioxane rings in **1a**, **1b**, **1g**, and **1f**, each bearing an axial C-5(′) amino group, in $CDCl_3$ indicated a very small geminal anisochrony of methylene C-6(′) ($\Delta\delta \approx 0.06$ ppm), with the chemical shifts of 5(′)-H-e ranging between 2.93 and 3.01 ppm. If an axial C-5(′) dimethylamino group was present instead (compounds **1c**, **1d**, **1e**, and **1f**), geminal anisochrony at C-6(′) increased dramatically ($\Delta\delta \approx 0.65$ ppm) while shielding of 5-H(′)-e was observed (2.67–2.81 ppm).

Reasonable explanation for these features, provided by manipulation of Dreiding models and by DFT calculations (Scheme 3; see later in Section 2.4.2.1., Table 4), involved differently correlated rotational preferences of substituents at C-4(′) and C-5(′). Thus, the equatorial *p*-nph group at C-4(′) was *bisectional* in the presence of an *in*-directed axial C-5(′) amino group, developing expected intramolecular hydrogen bonds with heterocyclic oxygen atoms (not depicted in Scheme 3), but was *orthogonal* if a bulkier axial NMe_2 functionality was attached at C-5(′). Its methyl groups had an *out* orientation with respect to the 1,3-dioxane ring.

2.2. Synthesis of *N*-Substituted Aminodichloro-*s*-triazines Containing the 1,3-Dioxane Motif

Test aminations were directed towards monosubstitution of chlorine in cyanuric chloride, with the use of the primary amino-1,3-dioxanes **1a**, **1b**, and **1g** as nucleophiles (Scheme 4).

Under the depicted conditions, monomeric (**2a**) and dimeric (**2b** and **2c**) *N*-substituted 6-amino-2,4-dichloro-*s*-triazines were prepared simply with good yields in a very clean procedure. Nevertheless, when we attempted to estimate the difference in reactivity (if any) between the axial C-5 amino and the equatorial C-2 aminomethyl groups in **1b**, its treatment with 1 molar equivalent of cyanuric chloride, even under very mild conditions, provided a polymeric mass from which we finally succeeded in isolating only a crude equimolar mixture of precursors of **2c**, in the form of the regioisomeric derivatives **2d** + **2e** (relevant ^{1}H NMR spectroscopic data as shown in Scheme 4). Both **2d** and **2e** were highly unstable.



Scheme 4.

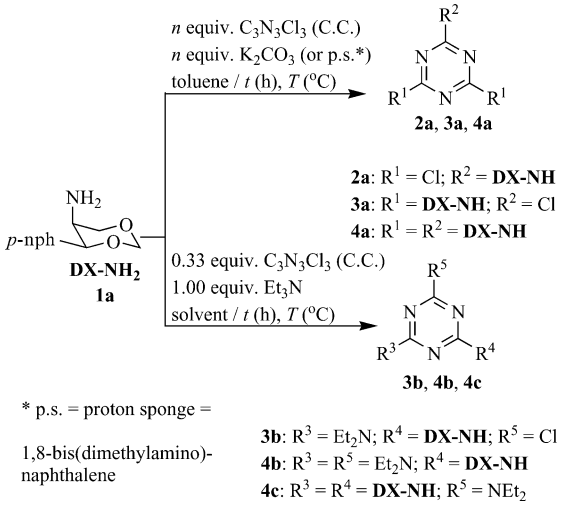
We therefore concluded that, in the first amination step, different locations of the primary amino sites on the rigid 1,3-dioxane ring had no relevance for their competitive nucleophilicity with respect to cyanuric chloride.

2.3. Synthesis of *N*-Substituted Melamines Containing 1,3-Dioxane Motifs

Encouraged by the synthetic feasibility described above, we envisaged a one-pot preparation of *N*-substituted melamines containing 1,3-dioxane motifs. For this report we limit our discussion to results obtained with amino-1,3-dioxanes **1a**, **1d**, and **1f** (Scheme 2, Scheme 3), a priori discriminated by the innate stereochemistry of their axial and/or equatorial amino sites.

2.3.1. Synthesis of N-Substituted Melamines Containing an Axial Anchorage of the 1,3-Dioxane Motif to Amino s-Triazine

The chemistry we developed starting from amino-1,3-dioxane **1a** is presented in Scheme 5, while the results are collected in Table 1.



Scheme 5.

All experiments proceeded spot-to-spot in TLC monitoring, and were stopped when no more change was observed or when thermal degradation became deleterious.

In preliminary investigations, performed in toluene (Table 1, Entries 1–3), only double amination occurred, affording chlorodiamino-*s*-triazine **3a** as the major product with satisfactory levels of conversion of **1a**. This result, obtained in the early stage of our study, implied that steric hindrance was crucial in the iterative substitution of chlorine to give an *N*-substituted melamine based entirely on axial amino nucleophile **1a**. Almost exactly the theoretically required quantity of unreacted starting material **1a** was recovered in all syntheses (Table 1, Entries 1–3). Reducing the nucleophilicity of **1a** by using more polar solvents (thf, 1,4-dioxane, Entries 4–6), resulted in diminished thermal degradation of the reaction mixture and the isolation of significant amounts of intermediate **2a** (Entries 4, 5). The overall conversion of **1a** was still up to 60%, while the partial conversions **1a**→**2a** and **1a**→**3a** were sensitive to the **1a**/cyanuric chloride molar ratio. We finally achieved the production of the desired melamine **4a** (Entry 6) but with very small levels of conversion, only to rule out this type of structure as a target molecule.

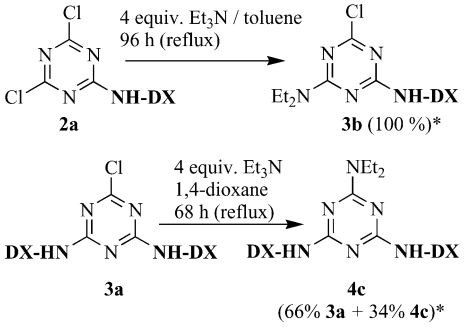
We therefore instead considered the use of triethylamine (Entries 7–9) both as a toluene-soluble proton scavenger (equimolar ratio Et_3N/**1a**) and as a potential nucleophile.[8] Indeed, competition between **1a** and triethylamine for the

Table 1. Results in the synthesis of compounds **2a**, **3a**, **3b**, and **4a**–**c** with axial anchorage of 1,3-dioxane motifs to amino-*s*-triazine (Scheme 5).

Entry	*n* equiv.	1 equiv. base	*T* [°C]	Partial conversions of **1a** (%)[a] **2a**	**3a**	**4a**	**3b**	**4b**	**4c**	% Overall conversion of **1a**
1	0.30	K_2CO_3/toluene	12 (reflux)		45					45
2	0.33	K_2CO_3/toluene	20 (reflux)		61					61
3	0.33	proton sponge/toluene	20 (70)	4	58					62
4	0.47	K_2CO_3/thf	26 (reflux)	22	50					72
5	0.48	K_2CO_3/1,4-dioxane	24 (room temp.) 22 (reflux)	18	46					64
6	0.33	K_2CO_3/1,4-dioxane	8 (room temp.) 36 (reflux)	2	54	4				60
7	0.33	Et_3N/toluene	24 (–15 to room temp.)					12	40	52
			24 (70) 9 (reflux)					*24*[b]	*20*	*44*
8	0.33	Et_3N/toluene	24 (–10 to room temp.)					6	24	30[c]
			48 (reflux)[c]					*12*	*12*	*24*
9	0.33	Et_3N/1,4-dioxane	2 (room temp.)		14		4	5	20	43
			24 (reflux)				*4*	*10*	*10*	*24*

[a] All calculations relate to effective amounts of compound isolated by column chromatography (mainly in Entries 7–9); all values are averaged from ±0.3 fluctuation. [b] *Italics format*: partial and corresponding total (overall) conversions of triethylamine. [c] Major thermal decomposition was observed.

cyanuric chloride took place, the triethylamine being *N*-dealkylated to yield melamines **4b** and **4c** with moderate degrees of conversion. They were the only products formed in toluene (Entries 7, 8); meanwhile in 1,4-dioxane (Entry 9), intermediates **3a** and **3b** were also isolated. Although no dedicated investigation of this competition chemistry was carried out, we have been able to formulate some observations based on separate syntheses (Scheme 6).



* conversions determined from ^{1}H NMR spectra of crude reaction mixtures

Scheme 6.

(i) In toluene at reflux, the isolated aminodichloro-*s*-triazine **2a** was only quantitatively converted into **3b** after 96 h upon treatment with 4 molar equivalents of triethylamine. No traces of melamine **4b** were detected under these conditions. Neither of the experiments 7 or 8 (Table 1) required such long duration and excess of triethylamine, suggesting that **2a** was not a precursor of **4b** (Scheme 5), and nor was **3a** a precursor of **4c**. If so, melamines **4c** and **4b** originated from two unisolated chloro-*s*-triazines that were mono- and diaminated by triethylamine; see Scheme 7, Equations (1) and (2).

$$Et_3N + C_3Cl_3N_3 \rightarrow C_3N_3Cl_2\text{–}NEt_2 + EtCl \quad (1)$$

$$Et_3N + C_3N_3Cl_2\text{-}NEt_2 \rightarrow C_3N_3Cl(NEt_2)_2 + EtCl \quad (2)$$

$$\underset{\mathbf{1a}}{\mathbf{DX\text{-}NH_2}} + C_3N_3Cl_2\text{-}NEt_2 \rightarrow \underset{\mathbf{3b}}{\mathbf{DX\text{-}NH}}\text{-}C_3N_3Cl\text{-}NEt_2 + HCl \quad (3)$$

not isolable in toluene
isolable in 1,4-dioxane

$$\underset{\mathbf{1a}}{\mathbf{DX\text{-}NH_2}} + C_3N_3Cl(NEt)_2 \rightarrow \underset{\mathbf{4b}}{\mathbf{DX\text{-}NH}}\text{-}C_3N_3(NEt)_2 + HCl \quad (4)$$

$$\underset{\mathbf{1a}}{\mathbf{DX\text{-}NH_2}} + \underset{\mathbf{3b}}{\mathbf{DX\text{-}NH}}\text{-}C_3N_3Cl\text{-}NEt_2 \rightarrow \underset{\mathbf{4c}}{(\mathbf{DX\text{-}NH})_2}C_3N_3\text{-}NEt_2 + HCl \quad (5)$$

Scheme 7.

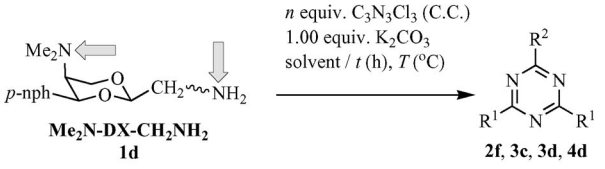
Thus, in toluene, triethylamine was the first nucleophile to aminate cyanuric chloride [Equations (1), (2)], followed, in the last steps of substitution, by **1a** [Equations (3), (4), and (5)]. Consistently with overall conversions, primary amino-1,3-dioxane **1a** was, on the whole, more nucleophilic than triethylamine (Table 1, Entries 7, 8).

(ii) In 1,4-dioxane at reflux, although the nucleophilicities of **1a** and triethylamine were diminished, as shown by the overall conversions, the difference in reactivity between them was much higher.

Hence, significant amounts of chlorodiamino-*s*-triazines **3a** and **3b** were isolated. Compound **3a** was not an intermediate in the synthesis of **4c** (Table 1, Entry 9, Scheme 5), because on treatment with a large excess of triethylamine (Scheme 6) over 68 h, only a low level of conversion **3a**→**4c** was observed, suggesting that melamine **4c** was formed, as in toluene, in reactions as depicted in Equations (3) and (5).

2.3.2. Synthesis of N-Substituted Melamines with Equatorial Anchorage of the 1,3-Dioxane Motif to Amino-s-triazine

The different chemistry we found in the case of the diamino-1,3-dioxane **1d** is summarized in Scheme 8. Quantitative and qualitative results are collected in Table 2.



2f: R^1 = Cl; R^2 = **Me$_2$N-DX-CH$_2$NH**
3c: R^1 = Cl$_2$C$_3$N$_3$-**NHCH$_2$-DX-N(Me)**; R^2 = Cl
3d: R^1 = **Me$_2$N-DX-CH$_2$NH**; R^2 = Cl
4d: R^1 = R^2 = **Me$_2$N-DX-CH$_2$NH**

Scheme 8.

The simplest experiment, consisting of treatment of **1d** with 1 molar equivalent of cyanuric chloride (Scheme 8, Table 2, Entry 1), raised unexpected synthetic and structural problems. The crude reaction mixture, with very com-

Table 2. Results for the synthesis of compounds **2f**, **3c**, **3d**, and **4d** (Scheme 8).

Entry	*n* equiv. $C_3N_3Cl_3$	Solvent	Time [h] (*T* [°C])	Partial conversions **1d** (%)[a]				% Overall conversion of **1d**
				2f	**3c**	**3d**	**4d**	
1	1.00	thf	24 (–20 to room temp.)	16	37	–	–	100
2	0.45	toluene	24 (room temp.) or 12 (70)	–	–	71	18	89
3	0.33	toluene	72 (room temp.)	–	–	52	19	71
4	0.33	toluene	24 (room temp.) or 100 (reflux)	–	–	–	36	36[b]
5	0.33	toluene	24 (room temp.) or 24 (70)	–	–	42	27	69
6	0.33	1,4-dioxane	8 (room temp.) or 36 (reflux)	–	–	34	20	54

[a] All calculations refer to effective amounts of compound isolated by column chromatography; all values were averaged from ±0.3 fluctuations. [b] Major thermal degradation was observed.

plex NMR spectra, was an almost polymeric mass from which we separated, by column chromatography, the envisaged aminodichloro-*s*-triazine **2f** with a poor degree of conversion. As observed for **2d** and **2e** (Section 2.2, Scheme 4), despite convincing NMR, IR and MS spectra, **2f** was unstable on storage even for short periods.

Along with **2f**, a stable compound **3c** was isolated. Its *m*/*z* (%) (MALDI) = 942.5 (100) $[M]^+$ was consistent with an oligomeric structure containing two *N*-mono-demethylated **1d** and three chloro-*s*-triazine fragments. We deduced that **2f** was, in fact, just a precursor of the more stable **3c**, and on treatment with cyanuric chloride, **1d** was coupled with both amino nucleophilic sites (Scheme 8). Hence, three possible formulations of oligomer **3c** (**3c**-*1*, **3c**-*2*, and **3c**-*3*) were considered (Scheme 9). We assigned **3c**-*1* as the correct structure of **3c** on the basis of the comparative ^{1}H NMR spectroscopic data below.

(i) Firstly, we figured the chemical shift of the NH proton in **2f** in $CDCl_3$ (6.33 ppm, broad dd as a triplet) to be indicative, in an AMX coupling pattern, of a CH_2NH group linked to a *dichloro*-*s*-triazine, since in **3c** the same type of resonance was at 6.26 ppm. We next observed, however, that protons of NH groups linked to a *monochloro*-*s*-triazine, as in **3d**, (Scheme 8), were also situated in the 5.62–6.33 ppm region, precluding a definite diagnosis for **3c** in $CDCl_3$.

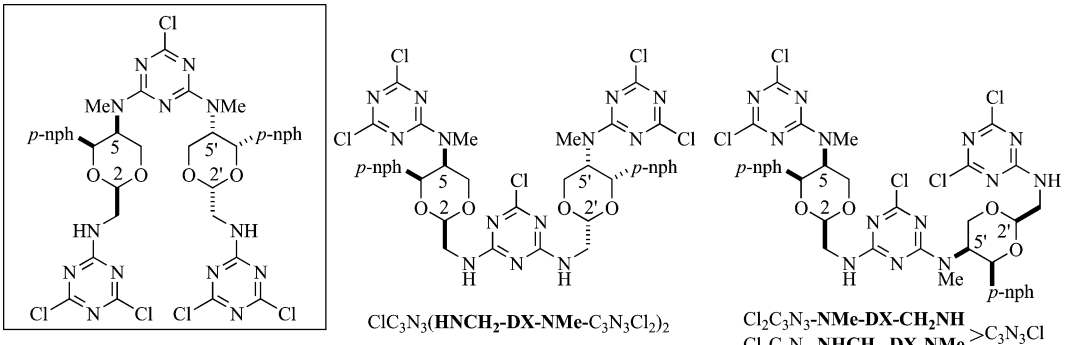
(ii) Fortunately, in $[D_6]$DMSO, a strong hydrogen bond acceptor solvent,[9f] the NH proton signals were very differently shifted downfield, to 7.73–8.06 ppm in **3d** but to 9.48 ppm in **3c**. The peripheral *s*-triazine rings in **3c** were thus far greater deshielding influences than the central *s*-triazine unit in **3d**, most probably due to the two chlorine substituents. In addition, in aminodichloro-*s*-triazine **2a** (Scheme 4), the δ(NH) value in $[D_6]$DMSO was also very comparable (9.41 ppm).

One must also observe that -(**MeN-DX-CH_2NH**) units were chemically equivalent only in **3c**-*1* and **3c**-*2*. Nevertheless, this feature was irrelevant for the purpose of this analysis, since **3c** was expected to be a mixture of frozen rotamers about the C(*s*-triazine)–N(exocyclic) bonds, causing additional chemical nonequivalence between -(**MeN-DX-CH_2NH**)- units in any of the possible oligomers **3c**-*1*, **3c**-*2*, or **3c**-*3* (see discussion later in Section 2.4.2.)

Attempted optimization of the synthesis of oligomer **3c**, seen by us as an attractive building block, yielded no improvement, as the conditions listed in Table 2 so far appear to be the most promising ones. Interestingly, attempted partial demethylation of the C-5 dimethylamino groups in amino-1,3-dioxanes **1c** and **1f** (Scheme 2, Scheme 3) gave negative results. Surprisingly, **1c** was completely inert to cyanuric chloride even in toluene at reflux; meanwhile **1f**, under conditions identical to those used for **1d**, yielded only a polymeric mass. Like it or not, at this point of our study, we had to consider the equimolar treatment of cyanuric chloride with **1d** to be best avoided as unpromising because of its modest results.

Thus, in order to speed up the first amination step, we opted to start further experiments at room temperature in the presence of an excess of nucleophile **1d** (Table 2, Entries 2–6).

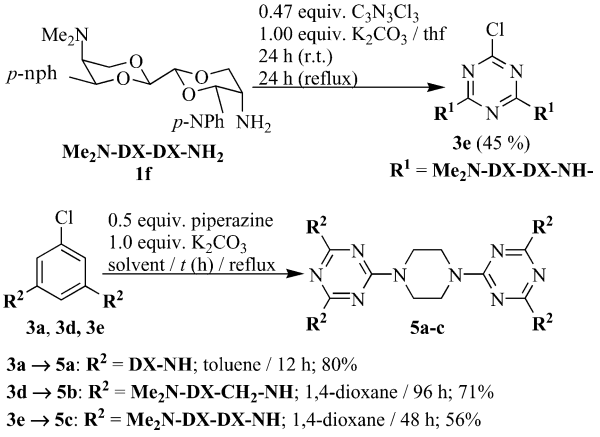
Accordingly, *N*-substituted chlorodiamino-*s*-triazine **3d** and *N*-substituted melamine **4d**, constructed exclusively from **1d**, were prepared with moderate to good overall levels of conversion. On the whole, the syntheses of **3d** and **4d** showed higher reactivity of the sterically unconstrained equatorial C-2 aminomethyl site in **1d** in the second and third steps of *s*-triazinic chlorine substitution than of its own axial C-5 dimethylamino component and of the axial C-5 amino of **1a** (Section 2.3.1.). As shown in Table 2, melamine **4d** was the single product in only one of the experiments (Entry 4), when the lowest observed conversion of **1d** (36%) was the result of thermal degradation of the reaction mixture during the long reflux time (100 h). Regardless of the solvent polarity, the data in Table 2 also demonstrate complete replacement of *s*-triazine chlorines by nucleophile **1d** to be difficult, especially in the final step (**3d**→**4d**) of substitution. In all manipulations 2–6 (Table 2), TLC monitoring detected only mixtures of compounds **3d**, **4d**, and unreacted **1d**, the last of which was recovered by column chromatography.



Scheme 9.

2.3.3. Synthesis of N-Substituted Dimeric Melamines with 1,3-Dioxane Motifs

For this discussion, we finished the synthetic explorations by preparing dimeric melamines with piperazine as a nucleophilic linker between two identical *N*,*N*′-symmetrically disubstituted chlorodiamino-*s*-triazines **3a**, **3d**, and **3e** (Scheme 10).



Scheme 10.

The synthesis of compound **5a** under the conditions illustrated was relatively straightforward. In contrast, toluene was not an appropriate solvent for the dimerization **3d**→**5b** due to thermal degradation. In 1,4-dioxane, however, although the reaction proceeded very slowly (over 4 d) as shown by spot-to-spot TLC monitoring, dimeric melamine **5b** could be routinely prepared.

Special consideration was paid to the dimeric amino-1,3-dioxane **1f** **Me_2N-DX-DX-NH_2** as starting material. We thus set out directly only for double amination of cyanuric chloride by **1f**, inspired by the already established restrictive behavior of its simpler analogues, the monomeric **H_2N-DX 1a** (steric hindrance) and **Me_2N–DX–CH_2NH_2 1d** (demethylation). Although difficulty was expected, chlorodiamino-*s*-triazine **3e** was obtainable under milder conditions than those used for **3a** (Scheme 5, Table 1) or **3d** (Scheme 8, Table 2). Next, **3e** underwent dimerization through the piperazine linker to give **5c** in moderate yield, due mainly to thermal decomposition. In attempts to avoid this (e.g., by replacing 1,4-dioxane with thf), TLC monitoring identified **5c** as a component of complex reaction mixtures, unpromising for successful separation by chromatographic methods.

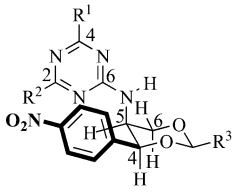
All members of series **5a**–**c** could be chromatographed on silica gel, providing stable pure analytical samples with clean and convincing IR, NMR, and MS spectra.

2.4. Rotational Stereochemistry Phenomena in *N*-Substituted Amino-s-triazines Containing 1,3-Dioxane Motifs

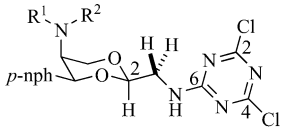
In previous structural approaches involving *N*-substituted amino-*s*-triazines and directed towards investigation of restricted rotation about C(*s*-triazine)–N< bonds,[5a,5b,9] due to lpN→π(*s*-triazine) conjugation, only minor attention had been paid until now to a specific conformation[5-d,5e,9a] defining the environment of the nitrogen atom involved in this partial double bond. The results of our iterative syntheses provided evidence of the importance of location, axial or equatorial, of the amino site in an anancomeric 1,3-dioxane in the second and third amination steps of cyanuric chloride. We therefore considered it to be of interest to complete this study with a stereochemical examination focused on the nature of rotational phenomena, mainly about the newly created C(*s*-triazine)–N(axial vs. equatorial) bonds, seen as (pro)stereogenic axes in the title compounds. For this purpose, the variety in the new family of amino-*s*-triazines presented its simplest classification, based on the increasing number of 1,3-dioxane motifs (1 to 3) *N*-monosubstituting through their exocyclic nitrogen atoms.

2.4.1. N-Substituted Amino-s-triazines Containing a Single 1,3-Dioxane Motif

A NMR investigation in this series provided the pertinent commenting data collected in Table S1 (axial anchorage; Scheme 11) and Table S2 (equatorial anchorage; Scheme 12).



Scheme 11.



Scheme 12.

Compounds **2a**–**c**, **3b**, and **4b** (Scheme 11) each possessed a *s*-triazinylamino group in an axial C-5(′) position in the rigid 1,3-dioxane ring, as demonstrated by the magnitudes of stereospecific $^nJ_{H,H}$ (n = 2, 3) values of the AMX systems in the sequence C-5(′)–C-6(′), assigned as 5(′)-H-e–6(′)-H-e–6(′)-H-a. The magnitude of $^3J_{H,H}$ coupling (9.1–10.0 Hz) N(′)H:5(′)-H-e suggested a rather *trans* relationship between these protons, and hence some limited rotation about the axial >C-5(′)–N(′)< bond. We considered a steric impediment innate to the adjacent equatorial and bisectional

C-4(′) *p*-nph ring to be responsible for this preferred geometry. From here on we refer to the arrangement of the axial C-5(′) *s*-triazinylamino substituent, also bisecting the 1,3-dioxane ring, as *s-trans-out*.

Indeed, the strongly π-deficient *N*-substituted amino-dichloro-*s*-triazines **2a**–**c**, with increased order of the C-6(′)(*s*-triazine)–N(′)(axial) bond dictating restricted rotation about this axis, revealed prodiastereomerism, since the *s*-triazine carbons C-2(′) and -4(′) were diastereotopic ($\Delta\delta$ = 0.5–0.6 ppm). As a result, coplanarity between the >C-5(′)–N(′)H sequences and *s*-triazine rings, imposed by the lpN(′)(axial)→π(*s*-triazine) conjugation, was expected. This should more readily accommodate the *s-trans-out* arrangement of the amino-*s*-triazine fragment with the presence at C-4(′) of the bulky equatorial and bisectional *p*-nph substituent. That is, in series **2a**–**c**, both steric and electronic requirements were met in conjunction to generate frozen rotational prodiastereomerism.

Compounds **2a**–**c** were not amenable to ^{13}C DNMR monitoring[9b–9d] since some decomposition occurred upon heating in [D_6]DMSO, obscuring the relevant signals for dynamic phenomena.

Appropriate changes thus having been made, the *N*,*N*′-unsymmetrically disubstituted chlorodiamino-*s*-triazine **3b** at room temperature showed two hindered rotations giving rise to diastereomerism about the stereogenic C-6(*s*-triazine)–N(axial) axis and prodiastereomerism about the prostereogenic C-4(*s*-triazine)–N($Et)_2$ axis (Figure 1).

Its ^1H NMR spectrum thus displayed two environments, blocked rotamers **3b**-*anti* (major) and **3b**-*syn* (minor). The *s*-triazine chlorine and **DX** ring were used as references for *anti* and *syn* descriptors. The *anti*-**3b**/*syn*-**3b** ratio was calculated from the resonances of protons 5-H-e and NH and from the QC NMR spectrum. Indeed, the QC NMR spectrum of **3b** (75 MHz) showed the methyl and methylene carbons in the NEt_2 groups to be diastereotopic: 13.2 and 13.4 ppm (Me in *anti*-**3b**), 13.1 and 13.6 ppm (Me in *syn*-**3b**), and 41.8. 41.9 ppm (methylene in both *anti*- and *syn*-**3b**). The diastereomers of **3b**, *anti* vs. *syn*, were then differentiated, account being taken of a reasonable dipolar interaction between their two differently substituted aromatic rings, but placed appropriately: (i) equatorial benzene by the strongly electron-withdrawing nitro group, and (ii) *s-trans-out s*-triazine by the strongly electron-releasing diethylamino group. Rotamer *anti*-**3b** was thus predicted to be stabilized by the opposite orientations of these two dipole moments, and hence dominant.

Additional observations supporting our rotameric assignments were (i) the shifting of the mixture's *anti*/*syn* composition in $CDCl_3$ vs. [D_6]DMSO (Table S1), (ii) the de-

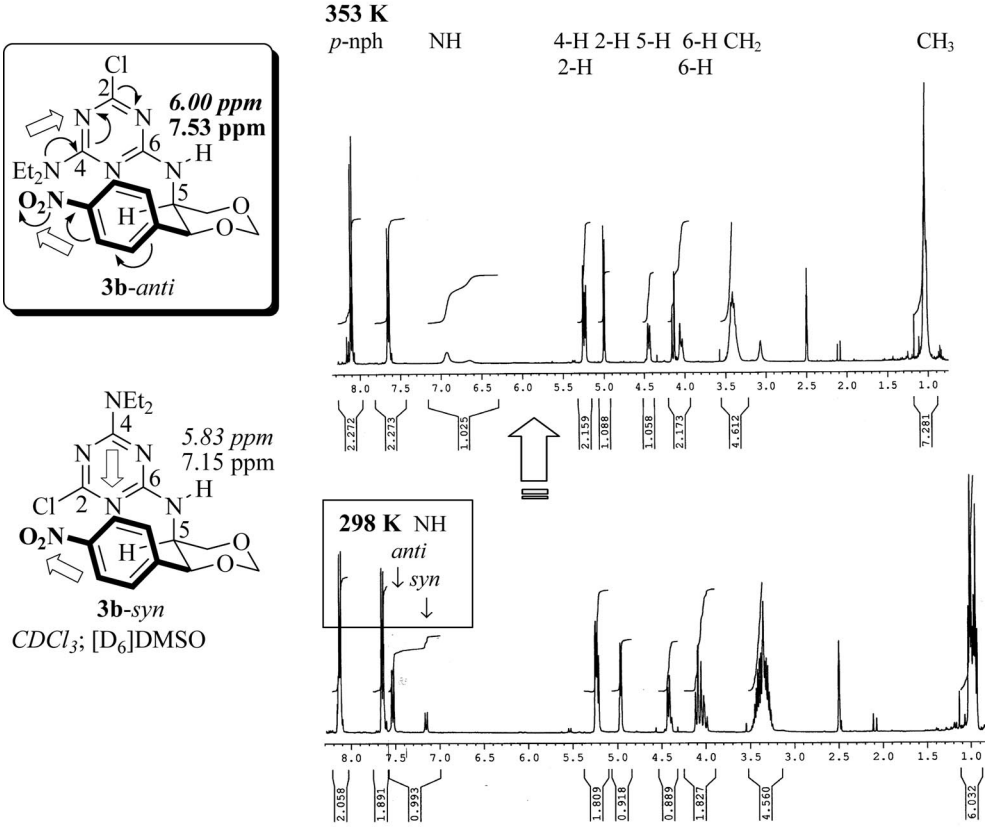


Figure 1. ^1H DNMR spectra of compound **3b** ([D_6]DMSO on 400 MHz timescale, Table S1).

shielding influence of *s*-triazine chlorine's dipole moment on some relevant ^{1}H chemical shifts[1c,10] such as δ(5-H-e, **3b**-*syn*) > δ(5-H-e, **3b**-*anti*) but δ(NH, **3b**-*anti*) > δ(NH, **3b**-*syn*) (Table S1 in the Supporting Information, Figure 1), and (iii) the weak N(CH_2CH_3)/3-, 5-H (*p*-nph) correlation found in the 2D ^{1}H–^{1}H-NOESY chart for the major diastereomer.

As can be seen in Figure 1, the ^{1}H DNMR spectra of **3b** (298–353 K) revealed that this compound existed at 353 K only in a slow exchange status between unequally populated sites (partially deblocked structure).[6] We explained this dynamic behavior on the basis of electronic, rather than steric, factors operating in the ground state of **3b**: namely the increased bond order of the C(*s*-triazine)–N< links as two lpN→π(*s*-triazine) conjugations reinforced by the electron-withdrawing *s*-triazine chlorine. We also ruled out the alternative hypothesis that a crowded rotational transition state (steric factor) of **3b** could in fact be responsible for the spectral changes shown in Figure 1 since the more congested molecule melamine **4c** was completely deblocked at 353 K (see Section 2.4.2.2.)

To our surprise, at 298 K, prodiastereomerism was also present in melamine **4b**, since despite its lowest π-deficiency in the discussed series, this molecule was still a blocked rotamer. Nevertheless, it appeared to us that the prodiastereomerism of **4b** involved only the C-6(*s*-triazine)–N(axial) bond, illustrated by diastereotopicity as $\Delta\delta$ (*s*-triazine C-2 vs. C-4) = 0.3 ppm (Table S1), because all four N(Et) groups were ^{1}H and ^{13}C chemically equivalent (i.e., as a single A_2X_3 ^{1}H coupling pattern. We therefore concluded that frozen rotamerism in the ground state of **4b** was somewhat residual and most probably due to steric obstruction promoted by the equatorial C-4 *p*-nph group and not to any noteworthy lpN(axial)→π(*s*-triazine) conjugation.

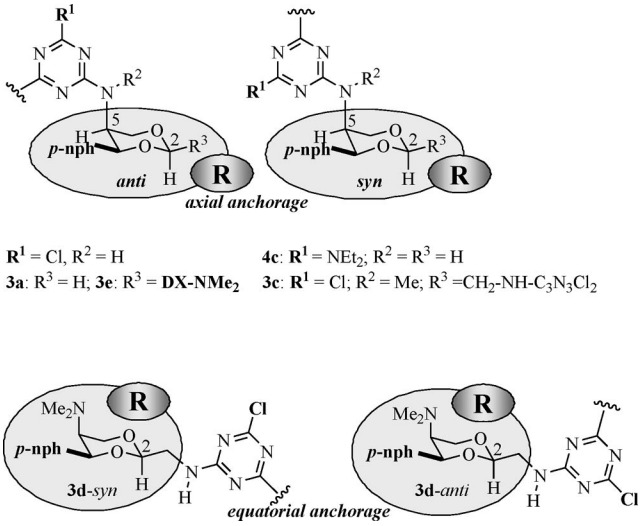
In compounds **2c**, **2f**, and **3c** (Scheme 12, Table S2) a (2,4-dichloro-*s*-triazin-6-yl)aminomethyl fragment was linked to the 1,3-dioxanic ring at C-2(′) in an equatorial position.

NMR spectroscopic data relating to this anchorage showed the features we expected: ^{1}H diastereotopicity in the equatorial C-2(′) methylene group and prodiastereomerism due to the C-6(′) (*s*-triazine)–N(′)H partial double bonds (prostereogenic axis), as well as the ^{13}C implying diastereotopicity across the *s*-triazine carbons C-2(′) and -4(′).

We note the smaller $^3J_{H,H}$ value (5.5–6.4 Hz) between protons CH_2 and NH, denoting the lack of any constraint to rotation about the *C*H_2–*N*H bond, which is believed to be independent of the equatorial anchorage.

2.4.2. N,N′-Symmetrically Disubstituted Diamino-s-triazines Containing Two 1,3-Dioxane Motifs

The stereochemistry of restricted rotational phenomena about C(*s*-triazine)–N(′)< bonds in the title compounds **3a**, **3c**–**e**, and **4c** was analyzed by starting from ^{1}H NMR spectroscopic data (Table 3), DFT calculations (Table 4) and, fortuitously, assignments already made in the case of simpler structures in Section 2.4.1. The descriptors *syn* and *anti* (1,3-dioxane ring and *s*-triazine substituent R^1 = Cl, NEt_2 as references; Scheme 13) were used to depict the three rotamerism terms that we encountered in this series of *N*,*N*′-symmetrically disubstituted diamino-*s*-triazines.[9f]



Scheme 13.

2.4.2.1. Analysis of Frozen Equilibria

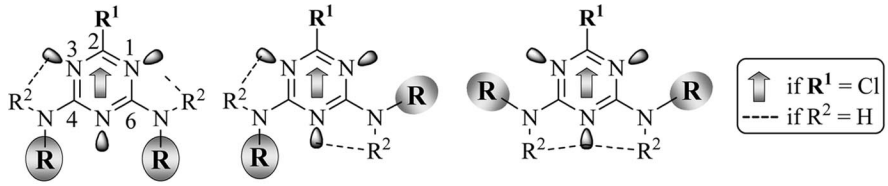
At room temperature, each of **3a**, **3c**–**e**, and **4c** (Table 3) exists as a rotameric mixture (frozen equilibria) of three possible diastereomers about two C(*s*-triazine)–N(exocyclic) bonds, two stereogenic axes, *anti*-*anti* (*a*-*a*), *syn*-*syn* (*s*-*s*) and *anti*-*syn* (*a*-*s*).[9f,10] Despite the complicated NMR spectra, their abundances could be established, since well separated ^{1}H signals of what from here on are named "indicative protons", isochronous in each of the rotamers (*a*-*a*) and (*s*-*s*) but equally intense and anisochronous (*syn* vs. *anti*) in rotamers (*a*-*s*) were exhibited. Usually, N(′)H protons played the basic indicative role (compounds **3a**, **3d**, **3e** and **4c**; see later discussion).

Distinction between (*a*-*a*) and (*s*-*s*) rotamers in chlorodiamino-*s*-triazines **3a**, **3c**, **3e**, and **3d** by direct NMR experimentation was not possible. Therefore, in the case of differently anchored – double axial (**3a**) and double equatorial (**3d**) – compounds we applied computational methods, both in gas phase and in solution (chloroform). The results are collected in Table 4.

The lowest-energy gas-phase conformers generated by Spartan′04 with the MMFF force field were thus subjected to full geometry optimization at the B3LYP/6-31G(d) level of theory by use of the same package.[11] Further, the effect of solvent was taken into account by performing SCRF single-point calculation at the gas-phase optimum geometries in the COSMO[11e] model implemented in NWChem.[12]

Initial inspection of calculated stereoisomers (Table 4) confirmed our earlier NMR basic conformation considerations about anancomeric serinolic 1,3-dioxanes (Section 2.1., Scheme 3) connected to a *s*-triazinyl moiety by substitution through the axial C-5 amino group in **3a** (bisectional *s*-*trans*-*out* arrangement, Section 2.4.1, Scheme 11) or

Table 3. Relevant ^{1}H NMR spectroscopic data for *N*,*N*′-symmetrically disubstituted diamino-*s*-triazines **3a**, **3c**–**e**, and **4c** containing two 1,3-dioxane motifs (Scheme 13).



anti-anti (*a*-*a*) *anti-syn* (*a*-*s*) *syn-syn* (*s*-*s*)

No.	Solvent	*T* (K)	Indicative protons	Discriminating signals as d (ppm) values in rotamers (*a*-*a*)	(*a*-*s*) = (*s*-*a*)	(*s*-*s*)	Content of blocked rotamers (%)[a] (*a*-*a*)	(*a*-*s*) = (*s*-*a*)	(*s*-*s*)
3a	$CDCl_3$	298	N(′)H[b]	5.97	5.95 5.75	5.77	23	52	25
			5(′)-H-e	4.06	4.28 4.42	4.42			
	[D_6]benzene	298	N(′)H	6.48	5.78 5.57	5.85	53	24	23
			5(′)-H-e	3.87	3.77 3.87	3.77			
	[D_6]DMSO	298	N(′)H	7.55	7.55 7.13	7.10	34	53	13
			5(′)-H-e	4.25	4.41 4.25	4.22			
	[D_6]DMSO	353	NH	6.70 (br. s) and 7.06 (d, ^3J = 8.0 Hz) → *partially deblocked structure*					
3c	$CDCl_3$	298	*p*-NPh	7.49, 8.16	7.49, 8.16, 7.67, 8.22	7.45, 8.09	68	24	8
			5(′)-H-e	5.30	5.30 5.71	5.71			
			CH_3	3.31	3.31 3.22	3.22			
			N(′)H		6.26				
	[D_6]DMSO	298	*p*-NPh	7.63, 8.15	7.63, 7.88 8.15, 8.23	–	66	34	–
			N(′)H		9.48				
		353	*p*-NPh	7.62, 8.11	7.62, 7.85 8.15, 8.23	–	66	34	–
			N(′)H		9.19				
3d	$CDCl_3$	298	N(′)H	6.36	6.21 5.62	6.03	50	42	8
	[D_6]benzene	298	N(′)H	7.47	7.54 5.49	6.63	41	47	12
			2(′)-H-a	4.80	4.71 4.63	4.63			
	[D_6]DMSO	298	N(′)H	8.13	8.09 8.03	7.79	43	47	10
		353	N(′)H	7.69 (br. s) → *single mediated structure (slow exchange)*					
3e	$CDCl_3$	298	N(′) H	5.97	5.82 5.68	5.71	23	43	34
			5(′)-H-e	4.12	4.34 4.49	4.49			
	[D_6]DMSO	298	N(′)H	7.51	7.51 7.04	6.98	61	29	10
			5(′)-H-e	4.50	4.40 4.38	4.30			
		353	NH	6.53 (br. s) and 6.87 (d, ^3J = 8.4 Hz) → *partially deblocked structure*					
4c	$CDCl_3$	298	*p*-NPh	–	7.45, 7.47, 7.95, 8.18	7.45, 8.06	–	12	88
			6(′)-H-e	–	4.24, 4.26	4.09			
			6(′)-H-a	–	3.87, 3.87	3.98			
	[D_6]DMSO	298	N(′)H	5.72	5.67 5.57	5.62	20	40	40
			p-NPh	7.55, 7.98; 7.58, 8.07; 7.58, 8.09; 7.60, 8.11					
		353	N(′)H	5.42 (d, ^3J = 9.0 Hz) → *single mediated structure*					

[a] Averaged values determined from signals of the depicted *indicative protons*. [b] Doublets ($^3J_{H,H}$ = 9.0–9.8 Hz) in **3a**, **3e**, and **4c**; overlapped doublets of doublets as triplets ($^3J_{H,H}$ around 6.0 Hz) in **3c** and **3d** with clear connectivities in 2 D ^{1}H–^{1}H-COSY charts: N(′)H:5(′)-H-e in **3a**, **3e** and N(′)H/CH_2 in **3d**.

Table 4. Relative energies (ΔE, kJ mol^{-1}) of the blocked rotamers of compounds **3a** and **3d** vs. their ^{1}H NMR abundance (Scheme 13).

Compound	Gas phase[a] relative energy (ΔE [kJ mol^{-1}])			Solution ($CHCl_3$) relative energy (ΔE [kJ mol^{-1}])[b] assigned ^{1}H NMR abundance ($CDCl_3$) (%)[c]		
Rotamer	(*a*-*a*)	(*a*-*s*)	(*s*-*s*)	(*a*-*a*)	(*a*-*s*)	(*s*-*s*)
3a	4.12	1.55	0.00	2.89	0.69	0.00
				31	35	34
3d	0.00	9.00	4.57	0.00	8.84	5.72
				63	27	10

[a] Spartan, B3LYP/6-31G(d) implemented in Gaussian 98. [b] (COSMO model) Single-point calculations on the Spartan geometries run at B3LYP/6-31G(d) within NWChem. [c] Percentages corrected for symmetry starting from abundance of rotamers (*a*-*s*) ≡ (*s*-*a*) twice favored with respect to (*a*-*a*) and (*s*-*s*); e.g., for **3a**, percentages deduced from ^{1}H NMR spectrum were: 23% (*a*-*a*), 52% (*a*-*s* ≡ *s*-*a*), 25% (*a*-*a*) (Table 3); ratios corrected for symmetry: 23 (*a*-*a*)/26 (*a*-*s* or *s*-*a*)/25 (*s*-*s*) respectively; corrected abundances: 31% (*a*-*a*), 35% (*a*-*s*), 34% (*s*-*s*).

through the equatorial C-2 aminomethyl group in **3d** (Section 2.4.1, Schemes 12 and 13).

Next, the statistical content of rotamers of compound **3a** in $CDCl_3$, deduced from its ^1H NMR spectrum (Table 3), was also predicted by calculation (Table 4), since the difference between their relative energies was sufficiently small (0.69–0.16 kcal mol^{-1}). A definite environment (*a*-*a*) vs. (*s*-*s*) energetic diagnosis of double axial anchored compound **3a** by calculations was thus precluded.

Computation on the doubly equatorially anchored compound **3d** determined its rotamer **3d** (*a*-*a*) to be the most stable. The orientation of its two N(′)H protons was in the direction of the C-2-*s*-triazine chlorine (R^1 = Cl, Table 3), allowing us the following indirect ^1H NMR assignment of *syn*:*anti* rotamerism in this class of chlorodiamino-*s*-triazines.

As in the case of the simpler chlorodiamino-*s*-triazine **3b** (Figure 1, Section 2.4.1), we considered the strong dipole moments induced by the *s*-triazine chlorine[5c,10] in **3a**, **3c**, **3d**, and **3e** to be a useful discriminating factor in the NMR spectra, causing, along with the *s*-triazine N-1 and -3 hydrogen-bonding lone pairs, the deshielding of protons N(′)H [or N(′)Me groups of **3c**] in rotamers (*a*-*a*) in comparison with (*s*-*s*) and in the *anti* site of rotamers (*a*-*s*) against the *syn* (*a*-*s*) counterpart. To resume, in $CDCl_3$, we assigned signals located as δN(′)H(*a*-*a*) ≈ δN(′)H(*a*-*s*) > δN(′)H(*s*-*a*) ≈ δN(′)H(*s*-*s*) to be doubly indicative of (i) rotamer assignment and (ii) composition calculation. Subsequently, consistently with the specific *s*-*trans*-*out* orientation of the axial C-5(′) *s*-triazinylamino fragment bisecting the 1,3-dioxane ring (Section 2.4.1, Scheme 11), the 5(′)-H-e protons in chlorodiamino-*s*-triazines **3a**, **3c**, **3e** in $CDCl_3$ were also doubly indicative (Table 3). Since they were s-*trans* coupled with the N(′)H protons (Scheme 13, Table 3, Table 4 and 2D ^1H–^1H-COSY charts), with regard to recognition of rotamerism, the same deshielding influence of the *s*-triazine chlorine was expected, and indeed found, in $CDCl_3$, as δ[5(′)-H-e, (*a*-*a*)] < δ[5(′)-H-e, (*s*-*s*)] and δ[5(′)-H-e, (*a*-*s*)] < δ[5(′)-H-e, (*a*-*s*)].

As one can see in Table 3, other well separated signals – *p*-nph, 6(′)-H-e, 2(′)-H-a, Me and 5(′)-H-e (in solvents other than $CDCl_3$) – were also *indicative* but only for checking rotameric calculation. In other NMR solvents (Table 3), calculation of the rotameric distribution was also made by starting from the assumption that the most strongly downfield shifted location of NH protons referred to environment (*a*-*a*); then, different but equally intense signals revealed, whenever possible, the two sites, *anti* vs. *syn*, in rotamers (*a*-*s*) etc.

The rotameric distribution in the series of *N*,*N*′-symmetrically disubstituted diamino-*s*-triazines containing two 1,3-dioxane motifs was strongly dependent on the type of anchorage to central *s*-triazine unit and solvent (Table 3).

The rotameric abundance of the less crowded compound **3d**, in which the two 1,3-dioxane fragments were attached by equatorial linkages, were less sensitive to various solvents. The same, almost zero, influence of solvent modification was manifested by the oligomeric compound **3c**.

In contrast, while identically based on a double axial connection to an *s*-*trans*-*out* diamino-*s*-triazine unit, only in $CDCl_3$ were both compounds **3a** and **3e** roughly statistical mixtures of rotamers. In [D_6]DMSO, the rotational equilibrium of **3a** was somewhat shifted as **3a** (*a*-*a*, 23→34%), **3a** (*a*-*s*, 52 ≈ 53%), **3a** (*s*-*s*, 25→13%); meanwhile, for **3e**, rotamer **3e** (*a*-*a*) became noticeably dominant (23→61%), followed by **3e** (*a*-*s*, 43→29%) and **3e** (*s*-*s*, 34→10%). In addition, in the case of **3a**, important π–π interactions such as A.S.I.S. (*Aromatic Solvent-Induced Shifts*) phenomena[13] involving its (*a*-*a*) rotamer (23% in $CDCl_3$) were assumed to play a major role in [D_6]benzene (53%, Figure S1 in the Supporting Information).

Melamine **4c** showed a dramatic influence of the solvent in rotamerism. In $CDCl_3$, the 2D ^1H–^1H-NOESY chart (Figure S2, Table 3) showed rotamer **4c** (*s*-*s*) greatly predominating (88%) over **4c** (*a*-*s*, 12%).

In [D_6]DMSO, equal abundance of **4c** (*s*-*s*, 40%) and **4c** (*a*-*s*, 40%) was found (Table 3).

2.4.2.2. Analysis of Dynamic Equilibria

When explored by ^1H DNMR, run in [D_6]DMSO on a 400 MHz timescale with heating (298–353 K), the behavior of our *N*,*N*′-symmetrically disubstituted diamino-*s*-triazines containing two 1,3-dioxane motifs (Table 3) showed varied effects of electronic factors vs. steric factors.

Compound **3c** remained a rigid structure with respect to all C(*s*-triazine)–NH (or –NMe) bonds (Table 3). We explained this rotational stability in two different ways, as (i) electronic influence at peripheral level, but (ii) steric factors in the central part of the oligomer. Thus, the highly π-deficient terminal dichloro-*s*-triazines units reinforced the local conjugations lpN(exocyclic)→π(*s*-triazine), hence the bond order of these connections. In contrast, steric hindrance to rotation as represented by the double *s*-*trans*-*out* relationship in the central bis(methylamino)-*s*-triazinediyl linker (R^2 = Me, Table 3) substituted with two axial C-5(′) anacomeric 1,3-dioxane motifs and additionally crowded at C-4(′) by the equatorial and orthogonal *p*-nph rings decisively prevailed in the transition vs. ground state of **3c**.

When the temperature was increased, compound **3a** and its dimeric analogue **3e** reached only a slow exchange status between unequal populated sites (Table 3, Figure S3, compound **3a**).[14] The ^1H DNMR transformations of the **DX-NH** rings in **3a** were almost the same as those of the inner **DX-NH** ones in **3e**. Indeed, in **3e** the peripheral **Me_2N-DX** rings in the dimeric 1,3-dioxane sequence **Me_2N-DX-DX-NH** were normally freely rotating about the equatorial C-2–C-2′ bonds with an expected *s*-*trans* (antiperiplanar) preferred orientation of protons 2-H-a and 2(′)-H-a (Scheme 3).[6]

In comparison with **3c**, the sterically less congested transition states of **3a** and **3e**, involving the same double axial *s*-*trans*-*out* arrangement (Scheme 13) of the central but smaller diamino-*s*-triazinediyl unit (R^2 = H, Table 3), was, however, just a partial explanation for this evolution, as we had to deduce from the analysis of the last two items in this series, **3d** and **4c**.

Indeed, **3d** could be deblocked almost completely at 353 K (Figure S3), demonstrating the relevance, in rotational phenomena, of its far less crowded transition state involving two equatorial arrangements about the C(*s*-triazine)–N(′)< partial double bonds.

Compound **3d** was considered appropriate for estimation of its free enthalpy of activation to rotation ($\Delta G^{\neq}$) by application of Eyring Equations (6) and (7).[14]

$$k_c \approx k_{-c} = 2.22\ \Delta\nu\ [s^{-1}] \quad (6)$$

$$\Delta G^{\neq} = 19.14\ T_c\ (10.32 + \log T_c/k_c)\ [J\,mol^{-1}] \quad (7)$$

where T_c [K] is the coalescence temperature, $\Delta\nu$ [Hz] is the frequency separation between two analyzed signals at room temperature belonging, in the absence of exchange, to two equally populated sites, and k_c (s^{-1}) is the rate constant of the first-order exchange dynamic process occurring at T_c.

As in the case of *N*-substituted chlorodiamino-*s*-triazines with open-chain serinolic motifs[10] we had to simplify the problem considerably by considering rotational equilibria of **3d** to be limited to a simple topomerization **3d** (*a*-*s*) ⇆ **3d** (*s*-*a*) presumably via rotamer **3d** (*a*-*a*) (Table 3). Furthermore, in Equations (6) and (7) we cautiously used[9,14] the resonances of "mobile protons" N(′)H (Figure S3) and obtained $\Delta\nu$ = 24 Hz, k_c = 53 s^{-1}, and hence $\Delta G^{\neq}$ = 71.10 kJ mol^{-1} (T_c = 343 K). We note that in Equation (7), the value of k_c was multiplied by 2, since rotamers of type (*a*-*s*) ≡ (*s*-*a*) were statistically twice favored.[9f,14]

The barrier to rotation in **3d** was plausible, since it was smaller than those previously reported for two more lpN→π conjugated and crowded 2-chloro-4,6-bis(dialkylamino)-*s*-triazines with normal chains (*n*Bu, 74.22 kJ mol^{-1}, *n*-octyl 75.17 kJ mol^{-1}) but significantly higher if the alkyl chain was branched (*i*Pr, 65.33 kJ mol^{-1}).[8c]

^{1}H DNMR analysis of melamine **4c** (Figure S3) gave information concerning the electronic influence of substituents in rotational phenomena. Formally, **4c** derived from **3a** by replacement of the *s*-triazine electron acceptor chlorine with a strong donor diethylamino group. A significant lower double bond character of its C(*s*-triazine)–N(′)< bonds was expected, and indeed, **4c** became an almost freely rotating structure at 353 K, with some remaining decoalescences in the N(′)H–5(′)-H-e–6(′)-H-a zones. Calculations based on the Eyring Equation with use of protons N(′)H ($\Delta\nu$ = 58 Hz, k_c = 129 s^{-1}, T_c = 328 K) gave a rotational barrier about the C(*s*-triazine)–N(′)(axial) bonds as $\Delta G^{\neq}$ = 65.44 kJ mol^{-1}. ^{1}H NMR resolution of the Et_2N group was poor, preventing us from ascertaining the rotamerism about the C(*s*-triazine)–N(Et_2) bond. Hence, in melamine **4c**, despite its steric relationships between diamino-*s*-triazine and 1,3-dioxane rings being identical to those in **3a** and **3e** (Scheme 13), favorable electronic factors dominated steric hindrance, determining a low energetic level of the rotational transition state.

We therefore finished by defining the "versatile effect of electronic against steric factors" in this series as (i) **3c** > **3a** ≈ **3e** > **3d** > **4c** in decreasing order of double bond character of their C(*s*-triazine)–N< linkages, and (ii) **3c** > **4c** > **3a** ≈ **3e** > **3d** as progressively diminished steric hindrance in the transitions states associated with rotations about these junctions.

2.4.3. N,N′,N′′-Trisubstituted Triamino-s-triazines Containing 1,3-Dioxane Motifs – Melamines and Dimeric Melamines

The rotational behavior of *N*,*N*′,*N*′′-symmetrically trisubstituted melamines **4a** (Scheme 5) and **4d** (Scheme 8), containing 1,3-dioxane motifs, and in the dimeric **5a**–**c** (Scheme 10) was analyzed by ^{1}H DNMR, their two types of anchorage, axial or equatorial, to amino-*s*-triazine being kept in mind.

Relevant ^{1}H NMR supporting data for melamines **4a** and **4d** are collected in Table 5.

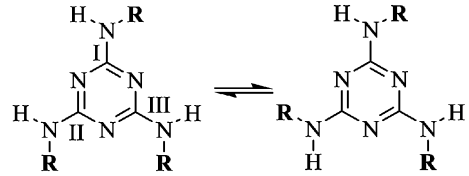
At room temperature, on a 300 MHz timescale in $CDCl_3$, melamine **4a** consisted of a statistic mixture of two predictable frozen rotamers about bonds I–III: "asymmetric" and "propeller".[9f,10] Their ratio was established from the signals of protons N(′)(′′)H, again indicative, since involved in similar steric relations seen in axial monoanchored (Section 2.4.1.) or doubly anchored compounds (Section 2.4.2). On increasing the temperature in [D_6]DMSO on a 400 MHz ^{1}H NMR timescale to 353 K, this triple axial anchored structure could not be totally deblocked, exhibiting two unassignable diastereomers and therefore named simply **4a**-major and **4a**-minor.

In contrast, at 298 K in $CDCl_3$, melamine **4d** (Table 5) was a slow rotational molecule on the ^{1}H NMR 300 MHz timescale and free rotating on the ^{13}C NMR 75 MHz timescale. Its blocked rotamers, **4d** (asymmetric) and **4d** (propeller), could be detected only in [D_6]benzene or [D_6]DMSO in slightly different occurrence. In [D_6]DMSO, clean ^{1}H DNMR transformation of **4d** into a free rotating molecule, suitable for kinetic calculations with the aid of the Eyring Equation, was observed (Table S3). Three barriers to rotation – $\Delta G^{\neq}_{I-III}$ [kJ mol^{-1}] – about the C(*s*-triazine)–NH bonds I–III in **4d** could be estimated[9f] from the chemical shifts corresponding to the three broad singlets of the N(′)(′′)H protons in rotamer **4d** asymmetric (298 K, Table 5).

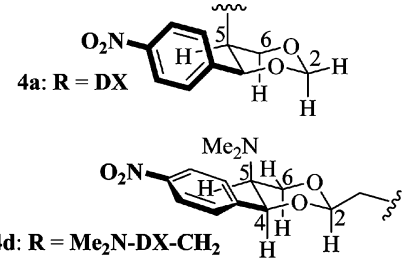
We related the decreasing magnitudes of the $\Delta G^{\neq}_{III}$ > $\Delta G^{\neq}_{II}$ > $\Delta G^{\neq}_{I}$ values (Table 5, Table S3) to progressively diminished steric hindrance III > II > I in the three transition states of **4d** when each R–NH- group rotates out of plane about bonds III, II, and I, respectively.[9f] They all were higher than the $\Delta G^{\neq}$ value for melamine **4c** (65.44 kJ mol^{-1}, Section 2.4.2.2.). We thus again concluded that the effect of electron-donor substituents, reducing the double bond character of C(*s*-triazine)–N< linkages either to a lesser (in **4d**) or a greater degree (in **4c**), prevailed over steric hindrance in the corresponding transition states, which were more congested in **4c** than in **4d**.

However, the possibility that additional solvation in [D_6]-DMSO might have a greater stabilizing effect on the ground state[9f] of the more basic **4d** over **4c** was also considered. This solvation might not only increase the magnitude of all

Table 5. Relevant ^{1}H NMR spectroscopic data for *N*,*N*′,*N*″-symmetrically trisubstituted melamines containing 1,3-dioxane motifs attached through axial (**4a**) or equatorial anchorages (**4d**).



$\Delta G_{III}^{\neq} > \Delta G_{II}^{\neq} > \Delta G_{I}^{\neq}$ (kJ/mol)
69.43 67.76 66.53
Asymmetric *Propeller*



No.	Solvent	*T* (K)	Indicative protons	Discriminating signals as δ (ppm) values in rotamers		Content of blocked rotamers (%)	
				Asymmetric	*Propeller*	*Asymmetric*	*Propeller*
4a	$CDCl_3$	298	N(′)(″)H[a]	5.36, 5.52, 5.62	5.36[b]	75	25
			5(′)(″)-H-e[c]	4.06, 4.06, 4.26	4.14		
	[D$_6$]DMSO	298	N(′)(″)H[a]	5.60, 5.69, 5.78	5.69[d]	67	33
		353		*Major*	*Minor*	*Major*	*Minor*
			p-NPh	8.01, 7.57	8.20, 7.59	83	17
			2(′)(″)-H-a	4.95	4.91		
			6(′)(″)-H-e	4.04	4.20		
			6(′)(″)-H-a	3.80	3.93		
			N(′)(″)H	5.46 (br. s) → *partially deblocked structure*			
4d	$CDCl_3$	298	N(′)(″)H	5.27, 5.84 (2 × br. s 1:1) → *partially deblocked structure*			
	[D$_6$]benzene	298		*Asymmetric*	*Propeller*	*Asymmetric*	*Propeller*
			N(′)(″)H	5.49, 5.61, 6.79, 6.89 (4 × br. s, 1:1:1:1)		75	25
	[D$_6$]DMSO	298	N(′)(″)H	6.97, 6.55, 6.70 (3 × br. s, 1:1:1)	6.80	69	31
		353	N$^{(′)(″)}$H	6.33 (br. s) → *single mediated structure*			

[a] Doublets with $^3J_{H,H}$ = 8.6–9.9 Hz. [b] Assignment based on the equal intensities of doublets located at δ = 5.52 and 5.62 ppm, which normally belong to the asymmetric rotamer. [c] Assignments deduced from the 2 D ^{1}H–^{1}H-COSY chart as N(′)(″)H:5(′)(″)-H-e. [d] Assignment based on the equal intensities of doublets located at δ = 5.60 and 5.78 ppm, which normally belong to the asymmetric rotamer.

$\Delta G^{\neq}$ barriers in **4d** vs. **4c**, but also their significantly greater values in relation to a $\Delta G^{\neq}$ value of 60.90 ± 0.84 kJ mol^{-1} previously obtained from reported molecular mechanics in the case of 2,4,6-tris(cyclohexylamino)-*s*-triazine,[9a] with an authentic equatorial orientation of amino-*s*-triazine group against cyclohexane ring.

NMR analyses of the dimeric melamines **5a**–**c** were run at room temperature in $CDCl_3$ (300 MHz timescale) and then in [D$_6$]DMSO at higher temperature (298–353 K on 400 MHz timescale). Their evolutions were compared (Figure 2).

At 298 K in $CDCl_3$, the axially quadruply anchored **5a** and **5c** showed only ^{1}H broad multiplets. It was not possible to establish whether this appearance was due to a slow motion mediating unequal populations or simply to overlapped signals belonging to an exacerbated number of rotational conformers [we had previously shown that seven rotational diastereomers are possible in linearly connected double melamines of type **5a**–**c**, due to six restricted rotations about C(*s*-triazine)-N< partial double bonds[10]].

On the 75 MHz timescale, **5a** and **5c** showed some residual frozen rotamerism, as more than one ^{13}C line was recorded for some homo- or enantiotopic positions, with respect to a freely rotating structure (see Exp. Sect.). Under the same ^{1}H timescale conditions, the equatorially quadruply anchored compound **5b**, like melamine **4d**, was a partially deblocked molecule since, except for the four protons N(′)H (two distinct broad singlets at δ = 5.29 and 5.79 ppm), unique signals were detected for all other identically numbered nuclei. In addition, the QC NMR spectrum of **5b** was also consistent with a single mediated structure.

In [D$_6$]DMSO at room temperature, we observed that all compounds **5a**–**c** were partially frozen mixtures of better solvated rotamers exhibiting a great number of overlapped ^{1}H multiplets. Indeed, with increasing temperature (Figure 2), diverse modifications were revealed.

At 353 K, the quadruply axially anchored dimeric melamine **5a** still displayed outstanding decoalescence in the zones 3(′)-H–5(′)-H (*p*-nph) and NH–5(′)-H-e–6(′)-H-a, so it was not completely deblocked.

Similar ^{1}H DNMR transformations were observed for the inner 1,3-dioxane rings **A** of dimer **5c**. They were assigned as slowly rotating at 353 K; meanwhile the peripheral 1,3-dioxane rings **B** indicated their fast-exchange status about the equatorial bonds C-2–C-2-(′). We note that discrimination between the two environments **A** vs. **B** of **5c** was not possible at 298 K.

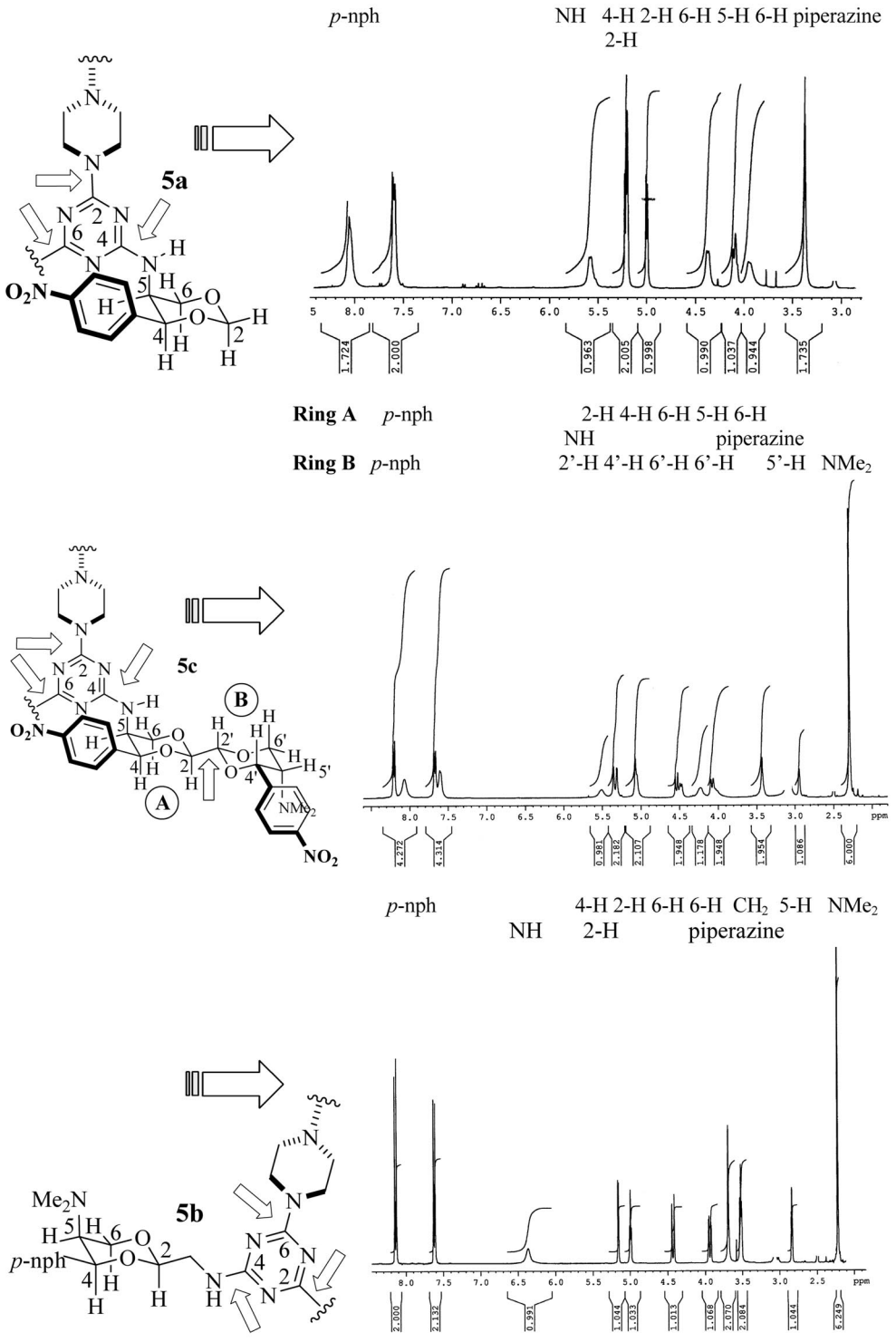


Figure 2. ^{1}H NMR spectra of compounds **5a**–**c** (353 K, on 400 MHz timescale, [D$_6$]DMSO).

When the above ^{1}H DNMR results for **5a** and **5c** were compared with those provided by the simpler melamine **4c** (free-rotating structure at 353 K; Figure S3, Section 2.4.2.2.) we concluded that this different behavior could be caused by:

(i) better solvation in [D$_6$]DMSO of **5a** and **5c**, stabilizing their ground states,

(ii) a greater ability of the diethylamino group in **4c** to accommodate the transition state, by simple rotation out of plane of the *s*-triazine ring, than the chair–chair flipping piperazine linker in **5a** and **5c**, or

(iii) a greater electron-donating effect of the diethylamino group as a free open-chain substituent, reducing the *s*-tri-

azine π-deficiency, in relation to its inclusion in a six-membered saturated diaza-heterocycle.

As expected, very clean ^{1}H DNMR evolution, encountered earlier in the spectra of the doubly equatorially anchored compound **3d** (Figure S3) and the triply equatorially anchored melamine **4d** (Table 5; Table S2 in the Supporting Information) also occurred upon heating the quadruply equatorially anchored compound **5b** (Figure 2).

3. Conclusion

Amination of cyanuric chloride with anancomeric amino-1,3-dioxane obtained by complete diastereospecific and diastereoselective acetalization of two enantiomerically pure *l*-*p*-nitrophenylserinols yielded *N*-substituted amino-*s*-triazines in moderate to good yields. When double or triple amination was carried out, quantitative results essentially depended on the orientation of the nucleophilic site with respect to the 1,3-dioxane ring, an axial C-5 amino group being less reactive than an equatorial C-2 aminomethyl one. In competitive aminations, however, a rigid axial C-5amino group was more effective than triethylamine.

Restricted rotations about the C(*s*-triazine)–N(exocyclic) bonds were found in all compounds under consideration. The highest double bond character of this linkage was shown by *N*-substituted aminodichloro-*s*-triazines with 1,3-dioxane motifs, regardless of the axial or equatorial natures of their attachment. In *N*-substituted doubly and triply anchored structures, specifically assignable frozen rotamerism (*syn*/*anti* or "asymmetric/propeller") was basically influenced by the nature of anchorage, solvents, and substituents. The dynamic behavior of these new *N*-substituted amino-*s*-triazines revealed, on the whole, higher rotational ability in the equatorially constructed compounds.

Experimental Section

General: Melting points are uncorrected; they were carried out on an ELECTROTHERMAL® instrument. Conventional NMR spectra were recorded on a Bruker® AM 300 instrument operating at 300 and 75 MHz for ^{1}H and ^{13}C nuclei, respectively. ^{1}H DNMR spectra were performed on a Bruker® AM 400 instrument operating at 400 and 100 MHz for ^{1}H and ^{13}C nuclei, respectively, with 10 K increases in temperature for each step. All NMR spectra were measured in commercially available anhydrous deuteriated solvents. No $SiMe_4$ was added; chemical shifts were measured against the solvent peak. All chemical shifts (δ values) are given throughout in ppm; all coupling patterns ($^nJ_{H,H}$ values) are given throughout in Hz. NMR descriptions of compounds exhibiting three or more frozen rotamers at room temperature have been done by considering each compound as one overall structure. Multiple values of chemical shifts and coupling constants for the same labeled ^{1}H or ^{13}C position means a mixture of rotamers, as described in Tables 3, 4, and 5. Abbreviations used: br. d (br. doublet), br. dd (br. doublet of doublets), br. t (br. triplet,) and br. m (br. multiplet). TLC was performed on aluminium sheets coated with silica gel 60 F_{254} (Merck®); flash column chromatography was conducted on silica gel Si 60 (40–63 μm, Merck®). IR spectra were measured on a Perkin–Elmer® Paragom FT-IR spectrometer. Only relevant absorptions are listed [throughout in cm^{-1}: weak (w), medium (m) or (s) strong]. Microanalyses were performed on a Carlo–Erba® CHNOS 1160 apparatus. Mass spectra (MS) were recorded as follows: FAB Spectra on a JEOL® AX 500 instrument fitted with a DEC DA 5000 computer, and ionization was produced with a FAB JEOL® Cannon (fascicle of Xenon accelerated under 4 kV/10 μA). MALDI Spectra were acquired on a Micromass TOF-SpecE MALDI® Instrument fitted with a time of flight analyzer and a nitrogen pulsed laser (337 nm). ESI spectra were measured on a Bruker® Esquire Instrument with ion trapping in electrospray mode. Computational details: the lowest-energy gas-phase conformers generated by Spartan′04 with the MMFF force field were subjected to full geometry optimization at the B3LYP/6-31G(d)[11] level of theory by use of the same package. Further, the effect of solvent (chloroform) was taken into account by performing SCRF single-point calculations at the gas-phase optimum geometries with the COSMO[11e] model implemented in NWChem.[12] The synthesis and stereochemistry of compound **1a** and related derivatives we discussed in detail elsewhere.[1a,1c,1d,1f,2a]

Typical Procedure for the Synthesis of Compounds 1a–g (Scheme 2). Simultaneous Preparation of Compounds 1e–g by Cross Acetalization Between *l*-(*p*-Nitrophenyl)serinols Ia and Ib: Glyoxal monohydrate (1.83 g, 24.06 mmol) was suspended in concd. sulfuric acid (96%, 24.56 g, 13.35 mL, 240.60 mmol) with vigorous stirring and then cooled at 0 °C. Finely powdered (1*S*,2*S*)-2-amino-1-(*p*-nitrophenyl)propane-1,3-diol (**Ia**, as hydrochloride, 6.00 g, 24.06 mmol) was added portionwise (5 × 1.20 g, each 3 h) at 0 °C. The reaction mixture was diluted with additional concd. sulfuric acid (96%, 24.56 g, 13.35 mL, 240.6 mmol) at 0 °C. Finely powdered (1*S*,2*S*)-2-(dimethylamino)-1-(4-nitrophenyl)propane-1,3-diol (**Ib**) (5.80 g, 24.06 mmol) was finally added, and the reaction mixture was stirred and allowed to reach room temperature gradually overnight. The mixture was carefully poured into dichloromethane (300 mL) and aq. NH_3 (1:1, 200 mL of 25% aq. NH_3 and 200 g of ice). The organic layer was recovered, filtered, washed with water (50 mL) to neutrality, dried with $CaCl_2$, and evaporated in vacuo. The resulted crude solid (3.70 g) was separated by flash column chromatography on silica gel (eluent MeOH/dichloromethane, 3:1, v/v) to yield the following three fractions: **1e** (0.40 g), **1f** (1.20 g), and **1g** (1.00 g). Each fraction was additionally crystallized from ether.

(2*R*,4*S*,5*S*)-5-Amino-2-(aminomethyl)-4-(4-nitrophenyl)-1,3-dioxane (1b): Yield 65% (6.60 g, 26.00 mmol **1b** starting from 8.48 g, 40.00 mmol, **Ia**), yellow crystalline powder, R_f(75% MeOH/dichloromethane) = 0.20; m.p. 101–102 °C (direct crystallization from Et_2O/ligroin, 1:1). $[\alpha]_D^{20}$ = +25.0 (0.5% thf); +85.3 (0.2% MeOH). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.37 (br. s, 4 H, 2 × NH_2), 2.93 (ddd, $^3J_{H,H}$ = 1.8, 1.8, 1.8 Hz, 1 H, 5-H-e), 2.96 (d, $^3J_{H,H}$ = 4.5 Hz, 2 H, C$H_2$$NH_2$), 4.12 (dd, $^2J_{H,H}$ = 11.6, $^3J_{H,H}$ = 1.8 Hz, 1 H, 6-H-a), 4.16 (dd, $^2J_{H,H}$ = 11.6, $^3J_{H,H}$ = 1.8 Hz, 1 H, 6-H-e), 4.76 (dd, $^3J_{H,H}$ = 4.5, 4.5 Hz, 1 H, 2-H-a), 5.01 (s, 1 H, 4-H-a), 7.49 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, 2-, 6-H, *p*-nph), 8.23 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 46.0 (1 C, CH_2NH_2), 50.1 (1 C, C-5), 73.1 (1 C, C-6), 80.5 (1 C, C-4), 103.0 (1 C, C-2), 124.1 (2 C, C-2, -6, *p*-nph), 126.8 (2 C, C-3, -5, *p*-nph), 146.8 (1 C, C-1, *p*-nph), 147.7 (1 C, C-4, *p*-nph) ppm. IR (KBr): $\tilde{\nu}$ = 3378 (s), 2980 (m), 2918 (m), 2857 (m), 1606 (m), 1515 (s), 1350 (s), 1145 (m), 1092 (m), 1053 (s), 1018 (s), 903 (m), 874 (s), 810 (m), 741 (s), 710 (m), 623 (w), 526 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 252.8 (7) $[M]^+$, 218.0 (78), 188.0 (98), 164.1 (100), 119.9 (73). $C_{11}H_{15}N_3O_4$ (253.26): calcd. C 52.17, H 5.97, N 16.59; found C 51.89, H 6.22, N 16.65.

(4*S*,5*S*)-5-(Dimethylamino)-4-(4-nitrophenyl)-1,3-dioxane (1c): Yield 70% (7.00 g, 28.00 mmol **1c** starting from 9.60 g, 40.00 mmol **Ib**), yellow crystalline powder, R_f(75% MeOH/dichloromethane) = 0.50; m.p. 131–132 °C (direct crystallization from Et_2O/ligroin, 1:1). $[\alpha]_D^{20}$ = +115.0 (1% $CDCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.01 [s, 6 H, $N(CH_3)_2$], 2.74 (s, 1 H, 5-H-e), 3.93 (dd, $^2J_{H,H}$ = 12.4, $^3J_{H,H}$ = 2.7 Hz, 1 H, 6-H-a), 4.55 (d, $^2J_{H,H}$ = 12.4 Hz, 1 H, 6-H-e), 4.96 (d, $^2J_{H,H}$ = 6.2 Hz, 1 H, 2-H-a), 5.03 (d, $^3J_{H,H}$ = 3.0 Hz, 1 H, 4-H-a), 5.28 (d, $^3J_{H,H}$ = 6.2 Hz, 2-H-e), 7.54 (d, $^3J_{H,H}$ = 8.6 Hz, 2 H, 2-, 6-H, *p*-nph), 8.21 (d, $^3J_{H,H}$ = 8.6 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 43.9 [2 C, $N(CH_3)_2$], 60.2 (1 C, C-5), 65.3 (1 C, C-6), 81.0 (1 C, C-4), 94.1 (1 C, C-2), 123.3 (2 C, C-2, -6, *p*-nph), 126.3 (2 C, C-3, -5, *p*-nph), 147.4 (1 C, C-1, *p*-nph), 147.8 (1 C, C-4, *p*-nph) ppm. IR (KBr): $\tilde{\nu}$ = 3000 (s), 2943 (s), 2834 (s), 2784 (s), 1609 (s), 1517 (s), 1475 (s), 1348 (s), 1316 (s), 1299 (s), 1165 (s), 1080 (s), 1040 (s), 1010 (s), 982 (s), 962 (s), 896 (m), 849 (s), 822 (s), 722 (s), 708 (s), 692 (m), 583 (m) cm^{-1}. MS (CI, isobutane): *m*/*z* (%) = 253 (100) $[M + 1]^+$, 209 (<10), 193 (<10). $C_{12}H_{16}N_2O_4$ (252.27): calcd. C 57.13, H 6.39, N 11.10; found C 56.88, H 6.11, N 10.96.

(2*R*,4*S*,5*S*)-2-(Aminomethyl)-5-(dimethylamino)-4-(4-nitrophenyl)-1,3-dioxane (1d): Yield 84% (9.45 g, 33.60 mmol **1d** starting from 9.60 g, 40.00 mmol **Ib**), yellow crystalline powder, R_f(75% MeOH/dichloromethane) = 0.25; m.p. 91–92 °C (direct crystallization from Et_2O/ligroin 1:1). $[\alpha]_D^{20}$ = +115.0 (0.3% MeOH). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.41 (br. s, 2 H, NH_2), 2.25 [s, 6 H, $N(CH_3)_2$], 2.67 (dd, $^3J_{H,H}$ = 3.0, 3.0 Hz, 1 H, 5-H-e), 2.92 (d, $^3J_{H,H}$ = 4.1 Hz, 2 H, CH_2NH_2), 3.95 (dd, $^2J_{H,H}$ = 12.6, $^3J_{H,H}$ = 3.0 Hz, 1 H, 6-H-a), 4.55 (d, $^2J_{H,H}$ = 12.6 Hz, 1 H, 6-H-e), 4.77 (dd, $^3J_{H,H}$ = 4.1, 4.1 Hz, 1 H, 2-H-a), 5.06 (d, $^3J_{H,H}$ = 3.0 Hz, 1 H, 4-H-a), 7.50 (d, $^3J_{H,H}$ = 8.7 Hz, 2 H, 2-, 6-H, *p*-nph), 8.17 (d, $^3J_{H,H}$ = 8.7 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 44.1 [2 C, $N(CH_3)_2$], 46.2 (1 C, CH_2NH_2), 59.6 (1 C, C-5), 65.3 (1 C, C-6), 81.2 (1 C, C-4), 102.6 (1 C, C-2), 123.6 (2 C, C-2, -6, *p*-nph), 126.6 (2 C, C-3, -5, *p*-nph), 147.3 (1 C, C-1, *p*-nph), 147.8 (1 C, C-4, *p*-nph) ppm. IR (KBr): $\tilde{\nu}$ = 3378 (m), 2937 (m), 2862 (m), 2773 (m), 1602 (m), 1516 (s), 1464 (w), 1349 (s), 1148 (s), 1107 (m), 1061 (s), 1048 (s), 1008 (s), 905 (s), 852 (m), 717 (m), 710 (m), 580 (w), 462 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 282.2 (100) $[M + 1]^+$, 267.9 (12), 251.1 (19), 223.6 (23), 223 (77), 221 (<10), 209.1 (<10), 192.8 (<10), 178.8 (<10), 160.8 (<10), 149.1 (<10), 126.2 (<10). $C_{13}H_{19}N_3O_4$ (281.31): calcd. C 55.51, H 6.81, N 14.94; found C 55.61, H 7.11, N 15.15.

(2*R*,2′*R*,4*S*,4′*S*,5*S*,5′*S*)-5,5′-Bis(dimethylamino)-4,4′-bis(4-nitrophenyl)-2,2′-bi-1,3-dioxane (1e): Yield 33% (3.32 g, 6.60 mmol **1e** starting from 9.60 g, 40.00 mmol **Ib**), yellow crystalline powder, R_f(75% MeOH/dichloromethane) = 0.75; m.p. 123–124 °C (flash column chromatography; methanol/dichloromethane 3:1 or direct crystallization from Et_2O). $[\alpha]_D^{20}$ = –12.14 (1% MeOH). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.35 [s, 12 H, 2×$N(CH_3)_2$], 2.81 (dd, $^3J_{H,H}$ = 3.1, 3.1 Hz, 2 H, 5-, 5′-H-e), 4.07 (dd, $^2J_{H,H}$ = 12.5, $^3J_{H,H}$ = 3.1 Hz, 2 H, 6-, 6′-H-a), 4.70 (d, $^2J_{H,H}$ = 12.5 Hz, 2 H, 6-, 6′-H-e), 5.01 (s, 2 H, 2-, 2′-H-a), 5.19 (d, $^3J_{H,H}$ = 3.1 Hz, 2 H, 4-, 4′-H-a), 7.54 (d, $^3J_{H,H}$ = 8.4 Hz, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 8.21 (d, $^3J_{H,H}$ = 8.4 Hz, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 43.8 [4 C, 2×$N(CH_3)_2$], 59.3 (2 C, C-5, -5′), 65.3 (2 C, C-6, -6′), 80.7 (2 C, C-4, -4′), 99.8 (2 C, C-2, -2′), 123.3 (4 C, C-2, -2′, -6, -6′, *p*-nph), 126.2 (4 C, C-3, -3′, -5, -5′, *p*-nph), 147.0 (2 C, C-1, -1′, *p*-nph), 147.3 (2 C, Cq, C-4, -4′, *p*-nph) ppm. IR (KBr): $\tilde{\nu}$ = 3354 (s), 2934 (w), 2886 (w), 1660 (s), 1607 (w), 1519 (s), 1472 (m), 1453 (m), 1348 (s), 1214 (w), 1108 (w), 1076 (m), 1048 (m), 1014 (w), 856 (m), 737 (s), 592 (w) cm^{-1}. MS (CI, isobutane): *m*/*z* (%) = 463 (<10) $[M - 39]^+$, 445 (30), 329 (100), 311 (<5), 180 (<5), 135 (30). $C_{24}H_{30}N_4O_8$ (502.52): calcd. C 57.36, H 6.02, N 11.15; found C 57.41, H 5.77, N 10.85.

(2*R*,2′*R*,4*S*,4′*S*,5*S*,5′*S*)-5-Amino-5′-(dimethylamino)-4,4′-bis(4-nitrophenyl)-2,2′-bi-1,3-dioxane (1f): Yield 11% (1.20 g, 2.53 mmol **1f** starting from **Ia** hydrochloride, 6.00 g, 24.06 mmol and **Ib** 5.80 g, 24.06 mmol), yellow crystalline powder, R_f(75% MeOH/dichloromethane) = 0.50; m.p. 134–135 °C (flash column chromatography; methanol/dichloromethane, 3:1). $[\alpha]_D^{20}$ = –3.18 (1% MeOH). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.42 (br. s, 2 H, NH_2), 2.2 [s, 6 H, $N(CH_3)_2$], 2.68 (s, 1 H, 5′-H-e), 2.90 (s, 1 H, 5-H-e), 3.95 (dd, $^2J_{H,H}$ = 12.4, $^3J_{H,H}$ = 2.3 Hz, 1 H, 6′-H-a), 4.09 (d, $^2J_{H,H}$ = 11.3 Hz, 1 H, 6-H-a), 4.15 (d, $^2J_{H,H}$ = 11.3 Hz, 6-H-e), 4.58 (d, $^2J_{H,H}$ = 12.4 Hz, 1 H, 6′-H-e), 4.84 (d, $^3J_{H,H}$ = 4.1 Hz, 2-H-a), 4.91 (d, $^3J_{H,H}$ = 4.1 Hz, 2′-H-a), 4.99 (s, 1 H, 4-H-a), 5.06 (d, $^3J_{H,H}$ = 2.6 Hz, 1 H, 4′-H-a), 7.40, 7.43 (2×d, $^3J_{H,H}$ = 9.0, 9.0 Hz, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 8.08, 8.11 (2×d, $^3J_{H,H}$ = 9.0, 9.0 Hz, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 44.1 [2 C, $N(CH_3)_2$], 50.1 (1 C, C-5), 59.6 (1 C, C-5′), 65.3 (1 C, C-6′), 73.4 (1 C, C-6), 80.4 (1 C, C-4), 81.1 (1 C, C-4′), 100.2 (1 C, C-2′), 100.5 (1 C, C-2), 123.6, 124.1 (4 C, C-2, -2′, -6, -6′, *p*-nph), 126.7, 126.8 (4 C, C-3, -3′, -5, -5′, *p*-nph), 146.4, 147.2 (2 C, C-1, -1′, *p*-nph), 147.4, (2 C, C-4, -4′, *p*-nph) ppm. IR (KBr): $\tilde{\nu}$ = 3378 (m), 2931 (m), 2865 (m), 2789 (m), 1604 (m), 1518 (s), 1464 (w), 1348 (s), 1149 (m), 1108 (m), 1058 (m), 1014 (m), 852 (m), 742 (m), 712 (m) cm^{-1}. MS (EI): *m*/*z* (%) = 474.0 (42) $[M]^+$, 279.9 (12), 240.3 (26), 222.0 (100), 204.3 (23), 157.8 (17). $C_{22}H_{26}N_4O_8$ (474.47): calcd. C 55.69, H 5.52, N 11.81; found C 55.88, H 5.61, N 12.15.

(2*R*,2′*R*,4*S*,4′*S*,5*S*,5′*S*)-5,5′-Diamino-4,4′-bis(4-nitrophenyl)-2,2′-bi-1,3-dioxane (1g): Yield 33% (2.95 g, 6.60 mmol **1 g** starting from 8.48 g, 40.00 mmol **Ia**) yellow crystalline powder, R_f(75% MeOH/dichloromethane) = 0.25; m.p. 141–142 °C (flash column chromatography; methanol/dichloromethane 3:1 or direct crystallization from Et_2O). $[\alpha]_D^{20}$ = –11.5 (1% MeOH). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.40 (br. s, 4 H, 2×NH_2), 3.01 (s, 2 H, 5-, 5′-H-e), 4.21 (d, $^2J_{H,H}$ = 11.5 Hz, 2 H, 6-, 6′-H-a), 4.26 (d, $^2J_{H,H}$ = 11.5 Hz, 2 H, 6-, 6′-H-e), 4.98 (s, 2 H, 2-, 2′-H-a), 5.10 (s, 2 H, 4-, 4′-H-a), 7.51 (d, $^3J_{H,H}$ = 8.6 Hz, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 8.21 (d, $^3J_{H,H}$ = 8.6 Hz, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 49.7 (2 C, C-5, -5′), 73.1 (2 C, C-6, -6′), 80.2 (2 C, C-4, -4′), 100.1 (2 C, C-2, -2′), 123.7 (4 C, C-2, -2′, -6, -6′, *p*-nph), 126.5 (4 C, C-3, -3′, -5, -5′, *p*-nph), 146.1 (2 C, C-1, -1′, *p*-nph), 147.3 (2 C, C-4, -4′, *p*-nph) ppm. IR (KBr): $\tilde{\nu}$ = 3372 (m), 3313 (m), 3108 (w), 3061 (m), 2925 (m), 2866 (m), 1603 (s), 1514 (s), 1458 (m), 1348 (s), 1294 (s), 1250 (m), 1144 (s), 1094 (s), 1041 (s), 1015 (s), 963 (s), 877 (s), 843 (s), 812 (s), 741 (s), 713 (s), 690 (w), 558 (w) cm^{-1}. MS (CI, isobutane): *m*/*z* (%) = 503 (<5) $[M + 56]^+$, 447 (100) $[M]^+$, 294 (<5), 235 (10), 154 (5), 116 (<5). $C_{20}H_{22}N_4O_8$ (446.42): calcd. C 53.81, H 4.97, N 12.55; found C 54.05, H 5.11, N 12.77.

Typical Procedure for the Synthesis of Compounds 2a–c (Scheme 4). Preparation of Compound 2c: Anhydrous potassium carbonate (0.570 g, 4.14 mmol) was suspended with vigorous stirring in a dry thf (40 mL) solution containing cyanuric chloride (0.780 g, 4.14 mmol), cooled to 0 °C. At this temperature, (2*R*,4*S*,5*S*)-5-amino-2-(aminomethyl)-4-(4-nitrophenyl)-1,3-dioxane (**1b**, 0.500 g, 1.97 mmol) in a dry thf (15 mL) solution was added portionwise (2.5 mL each 60 min). The reaction mixture was then allowed to reach room temperature overnight (about 12 h). After filtering and thorough washing of solid residues with dry thf (50 mL), the organic filtrate was evaporated under reduced pressure to dryness, yielding the crude product, which was crystallized by trituration from ligroin/Et_2O. Yield 0.650 g **2c** (60%).

2,4-Dichloro-6-{[(4*S*,5*S*)-4-(4-nitrophenyl)-1,3-dioxan-5-yl]amino}-*s*-triazine (2a): Yield 75% (11.10 g, 30.00 mmol **2a** starting from 8.92 g, 40.00 mmol **1a**) yellowish crystalline powder, R_f(60% ligroin/acetone) = 0.80; m.p. 192–193 °C (direct crystallization from Et_2O/ligroin 1:1). $[\alpha]_D^{20}$ = +39.3 (0.18% DMSO), +20.4 (0.2% MeOH). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.08 (dd, $^2J_{H,H}$ = 12.0, $^3J_{H,H}$ = 1.3 Hz, 1 H, 6-H-a), 4.17 (d, $^2J_{H,H}$ = 12.0 Hz, 1 H, 6-H-e), 4.50 (dd, $^3J_{H,H}$ = 9.7, 1.3 Hz, 1 H, 5-H-e), 4.96 (d, $^2J_{H,H}$ = 6.4 Hz, 1 H, 2-H-a), 5.05 (s, 1 H, 4-H-a), 5.29 (d, $^2J_{H,H}$ = 6.4 Hz, 1 H, 2-H-e), 6.56 (d, $^3J_{H,H}$ = 9.7 Hz, 1 H, NH), 7.62 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, 2-, 6-H, *p*-nph), 8.12 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 4.04 (d, $^2J_{H,H}$ = 11.3 Hz, 1 H, 6-H-a), 4.13 (dd, $^2J_{H,H}$ = 11.3, $^3J_{H,H}$ = 1.1 Hz, 1 H, 6-H-e), 4.42 (dd, $^3J_{H,H}$ = 9.1, 1.1 Hz, 1 H, 5-H-e), 4.97 (d, $^2J_{H,H}$ = 6.2 Hz, 1 H, 2-H-a), 5.23 (d, $^2J_{H,H}$ = 6.2 Hz, 1 H, 2-H-e), 5.28 (s, 1 H, 4-H-a), 7.66 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 2-, 6-H, *p*-nph), 8.15 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 3-, 5-H, *p*-nph), 9.41 (d, $^3J_{H,H}$ = 9.1 Hz, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 50.2 (1 C, C-5), 70.5 (1 C, C-6), 78.9 (1 C, C-4), 94.9 (1 C, C-2), 124.0 (2 C, C-2, -6, *p*-nph), 126.8 (2 C, C-3, -5, *p*-nph), 144.4 (1 C, C-1, *p*-nph), 148.0 (1 C, C-4, *p*-nph), 165.8 (1 C, C-6, *s*-triazine), 170.6, 171.1 (2 C, C-2, -4, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3305 (s), 1585 (s), 1557 (s), 1410 (s), 1346 (s), 1325 (s), 1240 (s), 1183 (s), 1167 (s), 1103 (s), 1043 (m), 1029 (m), 964 (m), 852 (m), 842 (m), 798 (m), 745 (m), 713 (m), 684 (w), 652 (w), 558 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 370.7 (40) [M – 1]$^+$, 340.7 (25), 310.7 (100), 276.7 (18), 217.8 (40), 189.6 (25), 163.9 (26). $C_{13}H_{11}Cl_2N_5O_4$ (372.17): calcd. C 41.96, H 2.98, N 18.82; found C 41.77, H 3.18, N 19.05.

(2*R*,2′*R*,4*S*,4′*S*,5*S*,5′*S*)-5,5′-Bis[(2,4-dichloro-*s*-triazin-6-yl)amino]-4,4′-bis(4-nitrophenyl)-2,2′-bi-1,3-dioxane (2b): Yield 82% (0.610 g, 0.82 mmol **2b** starting from 0.446 g, 1.00 mmol **1 g**), yellowish crystalline powder, R_f(75% ligroin/acetone) = 0.50; m.p. 216–218 °C (direct crystallization from Et_2O/ligroin 1:1). $[\alpha]_D^{20}$ = +75.1 (0.3% DMSO). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.28 (dd, $^2J_{H,H}$ = 13.0, $^3J_{H,H}$ = 1.1 Hz, 2 H, 6-, 6′-H-a), 4.33 (dd, $^2J_{H,H}$ = 13.0, $^3J_{H,H}$ = 1.5 Hz, 2 H, 6-, 6′-H-e), 4.61 (dd, $^3J_{H,H}$ = 9.5, 1.3 Hz, 2 H, 5-, 5′-H-e), 5.07 (s, 2 H, 2-, 2′-H-a), 5.24 (s, 2 H, 4-, 4′-H-a), 6.49 (d, $^3J_{H,H}$ = 9.5 Hz, 2 H, N-, N′-H), 7.52 (d, $^3J_{H,H}$ = 8.9 Hz, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 8.18 (d, $^3J_{H,H}$ = 8.9 Hz, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 49.5 (2 C, C-5, -5′), 70.5 (2 C, C-6, -6′), 79.1 (2 C, C-4, -4′), 100.0 (2 C, C-2, -2′), 124.0 (4 C, C-2, -2′, -6, -6′, *p*-nph), 126.9 (4 C, C-3, -3′, -5, -5′, *p*-nph), 143.7 (2 C, C-1, -1′, *p*-nph), 148.1 (2 C, C-4, -4′, *p*-nph), 165.8 (2 C, C-6, 6′, *s*-triazine), 170.7, 171.2 (4 C, C-2, -2′, -4, -4′ *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3400 (m), 2870 (m), 1752 (m), 1579 (s), 1510 (s), 1349 (s), 1327 (s), 1239 (s), 1166 (s), 1110 (s), 1033 (m), 852 (m), 743 (w), 715 (w), 526 (w) cm^{-1}. MS (FAB+, 3-nitrobenzyl alcohol): *m*/*z* (%) = 743 (30) [M + 1]$^+$, 400 (30), 382 (20), 355 (15), 342 (35), 324 (27), 312 (35), 296 (15), 289 (28), 261 (65), 245 (100), 219 (38), 191 (47), 165 (40). $C_{26}H_{20}Cl_4N_{10}O_8$ (742.32): calcd. C 42.07, H 2.72, N 18.87; found C 41.91, H 2.98, N 18.77.

(2*R*,4*S*,5*S*)-5-[(2,4-Dichloro-*s*-triazin-6-yl)amino]-2-[(2,4-dichloro-*s*-triazin-6-yl)aminomethyl]-4-(4-nitrophenyl)-1,3-dioxane (2c): Yield 60% (0.650 g, 1.18 mmol **2c**, starting from 0.500 g, 1.97 mmol **1b**), yellowish crystalline powder, R_f(60% ligroin/acetone) = 0.80; m.p. 287 °C (dec., direct crystallization from Et_2O/ligroin, 1:1). $[\alpha]_D^{20}$ = +55.5 (0.15% MeOH). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.81 (ddd, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 5.5, 6.2 Hz, 1 H, C*H*$_2$NH), 3.93 (ddd, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 5.5, 6.2 Hz, 1 H, C*H*$_2$NH), 4.22 (d, $^2J_{H,H}$ = 11.7 Hz, 1 H, 6-H-a), 4.26 (d, $^2J_{H,H}$ = 11.7 Hz, 1 H, 6-H-e), 4.59 (dd, $^3J_{H,H}$ = 9.5, 1.3 Hz, 1 H, 5-H-e), 5.10 (dd, $^3J_{H,H}$ = 4.3, 4.9 Hz, 1 H, 2-H-a), 5.21 (s, 1 H, 4-H-a), 6.44 (dd, $^3J_{H,H}$ = 5.5, 6.2 Hz, 1 H, CH$_2$N*H*), 6.64 (d, $^3J_{H,H}$ = 9.5 Hz, 1 H, C-5-N*H*), 7.50 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, 2-, 6-H, *p*-nph), 8.19 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 44.4 (1 C, CH_2NH), 49.2 (1 C, C-5), 70.7 (1 C, C-6), 79.1 (1 C, C-4), 99.7 (1 C, C-2), 124.1 (2 C, C-2, -6, *p*-nph), 126.8 (2 C, C-3, -5, *p*-nph), 143.6 (1 C, C-1, *p*-nph), 148.1 (1 C, C-4, *p*-nph), 165.8, 166.6 (2 C, C-6, -6′, *s*-triazine), 168.9, 170.7, 171.2, 171.6 (4 C, C-2, -2′, -4, -4′, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3326 (m), 3054 (m), 1752 (m), 1725 (m), 1589 (s), 1555 (s), 1511 (s), 1400 (m), 1349 (s), 1324 (m), 1168 (m), 1105 (w), 1055 (w), 950 (m), 799 (m), 745 (w), 713 (m), 536 (m) cm^{-1}. MS (EI): *m*/*z* (%) = 550.1 (<10) [M – 1]$^+$, 529.0 (10), 528.1 (20), 526.2 (38), 490.3 (75), 476.3 (100), 459.2 (10), 447.3 (18), 433.1 (20), 404.2 (27), 390.1 (13), 386.1 (<10), 364.9 (11), 338.1 (16), 324.1 (19), 320.1 (35), 290.1 (48), 282.0 (26), 277.8 (15), 250.1 (10), 233.6 (17), 223.1 (27), 204.7 (13), 192.8 (16), 185.0 (38), 166.9 (82), 153.0 (53), 135.7 (22), 124.3 (15), 110.4 (18). $C_{17}H_{13}Cl_4N_9O_4$ (549.16): calcd. C 37.18, H 2.39, N 22.96; found C 36.85, H 2.55, N 23.11.

2,4-Dichloro-6-{[(2*R*,4*S*,5*S*)-5-(dimethylamino)-4-(4-nitrophenyl)-1,3-diox-2-yl]methylamino}-*s*-trazine (2f): Yield 16% (0.137 g, 0.32 mmol **2f**, starting from 0.565 g, 2.00 mmol **1d**), yellowish crystalline powder, R_f(66% ligroin/acetone) = 0.55, (66% AcOEt/ligroin) = 0.45; m.p. 260 °C (dec., flash column chromatography; ligroin/acetone 2:1 or AcOEt/ligroin 2:1). $[\alpha]_D^{20}$ = +57.3 (0.05% MeOH). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.27 [s, 6 H, N(CH$_3$)$_2$], 2.75 (s, 1 H, 5-H-e), 3.82 (br. dd, 2 H, C*H*$_2$NH), 3.99 (d, $^2J_{H,H}$ = 12.3 Hz, 1 H, 6-H-a), 4.59 (d, $^2J_{H,H}$ = 12.3 Hz, 1 H, 6-H-e), 5.00 (s, 1 H, 2-H-a), 5.10 (s, 1 H, 4-H-a), 6.33 (br. dd, 1 H, NH), 7.48 (d, $^3J_{H,H}$ = 8.3 Hz, 2 H, 2-, 6-H, *p*-nph), 8.22 (d, $^3J_{H,H}$ = 8.3 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 44.1 [2 C, N(CH$_3$)$_2$], 44.8 (1 C, CH_2NH), 59.5 (1 C, C-5), 65.6 (1 C, C-6), 81.3 (1 C, C-4), 98.9 (1 C, C-2), 123.7 (2 C, C-2, -6, *p*-nph), 126.5 (2 C, C-3, -5, *p*-nph), 146.7 (1 C, C-1, *p*-nph), 147.5 (1 C, C-4, *p*-nph), 166.6 (1 C, C-6, *s*-triazine), 171.0 (2 C, C-2, -4, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3229 (s), 3083 (s), 2928 (s), 2875 (s), 1784 (m), 1702 (s), 1609 (s), 1521 (s), 1402 (s), 1349 (s), 1323 (s), 1238 (s), 1146 (s), 1035 (s), 984 (m), 851 (m), 800 (m), 708 (w), 533 (w) cm^{-1}. MS (CI): *m*/*z* (%) = 443.2 [M + 14]$^+$, 429.2 [M]$^+$ (70), 411.1 (17), 223.0 (28), 171.1 (13), 126.6 (17), 125.9 (29). $C_{16}H_{18}Cl_2N_6O_4$ (429.27) (as a result of product instability no satisfactory microanalysis could be obtained).

Typical Procedure for the Synthesis of Compounds 3a–e (Schemes 5–9). Preparation of Compound 3a (Table 1, Entry 2): Anhydrous potassium carbonate (0.414 g, 3 mmol) was suspended with vigorous stirring in a dry toluene (25 mL) solution containing cyanuric chloride (0.184 g, 1 mmol), and fine powdered (4*S*,5*S*)-5-amino-4-(4-nitrophenyl)-1,3-dioxane (**1a**, 0.673 g, 3 mmol) was then added. The resulted suspension was heated and kept at reflux until TLC monitoring indicated no more evolution (20 h). The reaction mixture was cooled to room temperature and filtered, and solid residues were well washed with dry toluene. The organic filtrate was evaporated to dryness under reduced pressure, providing the crude reaction mixture, which was separated by flash column chromatography on silica gel. The desired **3a** was eluted with ligroin/acetone (1:1, v/v) to give **3a** (0.515 g, 61% conversion of **1a**). Complete elution of the column with pure acetone yielded unreacted **1a** (0.170 g, 87% recovery of the unreacted **1a**).

Preparation of Compound 3d (Table 2, Entry 2): Anhydrous potassium carbonate (0.980 g, 7.1 mmol) was suspended with vigorous stirring in a dry toluene (50 mL) solution containing cyanuric chloride (0.589 g, 3.2 mmol), and finely powdered **1d** (2.000 g, 7.1 mmol) was then added. The resulted suspension was kept at

room temperature for 24 h and was then heated at 70 °C until TLC monitoring indicated no more change (12 h). The reaction mixture was cooled to room temperature and filtered, and solid residues were well washed with dry toluene. The organic filtrate was evaporated to dryness under reduced pressure, providing the crude reaction mixture, which was separated by flash column chromatography on silica gel (eluent acetone/ligroin, 2:1, v/v) as follows: first fraction **3d** (1.700 g, 71% conversion of **1d**), then **4d** (0.400 g, 18% conversion of **1d**) as the second fraction.

2-Chloro-4,6-bis{[(4*S*,5*S*)-4-(4-nitrophenyl)-1,3-dioxan-5-yl]amino}-*s*-triazine (3a): Yield 61% (0.515 g, 0.92 mmol **3a**, starting from 0.673 g, 3.00 mmol **1a**) yellowish crystalline powder, R_f(60% ligroin/acetone) = 0.40; m.p. 153.2–155.0 °C (flash column chromatography; ligroin/acetone 1.5:1). $[\alpha]_D^{20}$ = –4.0 (0.5% thf). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.90–4.22 (m, 4 H, 6-, 6′-H-a, 6-, 6′-H-e), 4.06, 4.28, 4.42 (3 × d, $^3J_{H,H}$ = 8.3, 9.4, 9.8 Hz, 5-, 5′-H-e, 2 H,), 5.00 (d, $^3J_{H,H}$ = 3.0 Hz, 2 H, 4-, 4′-H-a), 4.95, 5.00 (2 × d, $^2J_{H,H}$ = 6.4 Hz, 2 H, 2-, 2′-H-a), 5.25, 5.27, 5.28, 5.33 (4 × d, $^2J_{H,H}$ = 5.7, 6.0, 6.4, 6.4 Hz, 2 H, 2-, 2′-H-e), 5.75, 5.77, 5.95, 5.97 (4 × d, $^3J_{H,H}$ = 9.8, 9.4, 9.4, 9.4 Hz, 2 H, N-, N′-H), 7.43–7.48 (m, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 8.09–8.15 (m, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 80 °C): δ = 4.19–3.79 (br. m, 4 H, 6-, 6′-H-a, 6-, 6′-H-e), 4.25–4.46 (br. m, 2 H, 5-, 5′-H-e), 4.99 (d, $^2J_{H,H}$ = 5.2 Hz, 2 H, 2-, 2′-H-a), 5.20 (d, $^2J_{H,H}$ = 5.2 Hz, 2 H, 2-, 2′-H-e), 5.21 (s, 2 H, 4-, 4′-H-a), 6.70, 7.06 (br. s and d, $^3J_{H,H}$ = 8.0 Hz, 2 H, N-, N′-H), 7.61–7.63 (br. m, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 7.97–8.09 (br. m, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 49.2, 49.3, 49.4, 49.6 (2 C, C-5, -5′), 70.5, 70.6, 70.9, 71.1 (2 C, C-6, -6′), 79.1, 79.2, 79.4 (2 C, C-4, -4′), 94.8, 94.9, 95.7 (2 C, C-2, -2′), 123.7, 123.8 (4 C, C-2, -2′, -6, -6′, *p*-nph), 126.66, 126.71, 126.9 (4 C, C-3, -3′, -5, -5′, *p*-nph), 142.9, 144.85, 144.94, 145.1 (2 C, C-1, -1′, *p*-nph), 147.85, 147.90 (2 C, C-4, -4′, *p*-nph), 165.2, 165.3, 165.4, 165.8 (2 C, C-4, -6, *s*-triazine), 169.2, 169.4, 169.7 (1 C, C-2, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3404 (m), 3315 (m), 2859 (m), 1573 (s), 1519 (s), 1347 (s), 1174 (s), 1105 (w), 1094 (s), 1026 (s), 987 (s), 956 (s), 902 (m), 875 (m), 852 (s), 805 (s), 744 (m), 711 (m), 582 (w), 530 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 558.9 (100) [M]$^+$, 540.9 (27), 528.8 (20), 510.8 (12), 498.8 (7). $C_{23}H_{22}ClN_7O_8$ (559.92): calcd. C 49.34, H 3.96, N 17.51; found C 49.40, H 4.33, N 17.21.

2-Chloro-4-(diethylamino)-6-{[(4*S*,5*S*)-4-(4-nitrophenyl)-1,3-dioxan-5-yl]amino}-*s*-triazine (3b): Yield 80% (0.327 g, 0.80 mmol **3b** starting from 0.372 g, 1.00 mmol **2a**, Scheme 6), yellowish crystalline powder, R_f(66% ligroin/acetone) = 0.75; m.p. 109–110 °*C* (flash column chromatography; ligroin/acetone, 2:1). $[\alpha]_D^{20}$ = –6.25 (0.5% thf). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) **3b**-*anti*: δ = 1.01–1.07 [m, 6 H, N(CH$_2$C*H*$_3$)$_2$], 3.31–3.46 [m, 4 H, N(C*H*$_2$CH$_3$)$_2$], 4.06 (dd, $^2J_{H,H}$ = 11.7, $^3J_{H,H}$ = 1.3 Hz, 6-H-a), 4.20 (d, $^2J_{H,H}$ = 11.7 Hz, 1 H, 6-H-e), 4.42 (d, $^3J_{H,H}$ = 9.8 Hz, 1 H, 5-H-e), 4.95 (d, $^2J_{H,H}$ = 6.1 Hz, 1 H, 2-H-a), 5.02 (s, 1 H, 4-H-a), 5.27 (d, $^2J_{H,H}$ = 6.1 Hz, 1 H, 2-H-e), 6.00 (d, $^3J_{H,H}$ = 9.8 Hz, 1 H, NH), 7.48 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 2-, 6-H, *p*-nph), 8.10 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) **3b**-*syn* (only distinct peaks are listed): δ = 4.16 (d, $^3J_{H,H}$ = 11.7 Hz, 1 H, 6-H-e), 4.53 (d, $^3J_{H,H}$ = 9.9 Hz, 1 H, 5-H-e), 4.97 (d, $^2J_{H,H}$ = 5.9 Hz, 1 H, 2-H-a), 5.29 (d, $^2J_{H,H}$ = 5.9 Hz, 1 H, 2-H-e), 5.83 (d, $^3J_{H,H}$ = 9.9 Hz, 1 H, NH), 7.51 (d, $^3J_{H,H}$ = 9.0 Hz, 2 H, 2-, 6-H, *p*-nph), 8.12 (d, $^3J_{H,H}$ = 9.0 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 80 °C): δ = 1.03 [t, $^3J_{H,H}$ = 7.8 Hz, 6 H, N(CH$_2$C*H*$_3$)$_2$], 3.41 [t, $^3J_{H,H}$ = 7.8 Hz, 4 H, N(C*H*$_2$CH$_3$)$_2$], 4.05 (br. d, $^2J_{H,H}$ = 9.8 Hz, 1 H, 6-H-a), 4.14 (dd, $^2J_{H,H}$ = 9.8, $^3J_{H,H}$ = 2.0 Hz, 1 H, 6-H-e), 4.44 (d, $^3J_{H,H}$ = 9.6 Hz, 1 H, 5-H-e), 5.00 (d, $^2J_{H,H}$ = 6.2 Hz, 1 H, 2-H-a), 5.23 (d, $^2J_{H,H}$ = 6.2 Hz, 1 H, 2-H-e), 5.25 (s, 1 H, 4-H-a), 6.65, 6.93 (2 × bs 1 H, NH), 7.65 (d, $^3J_{H,H}$ = 8.6 Hz, 2 H, 2-, 6-H, *p*-nph), 8.10, 8.38 (2 × d, $^3J_{H,H}$ = 8.4, 8.6 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. QC NMR (75 MHz, $CDCl_3$, 25 °C) **3b**-*anti*: δ = 13.2, 13.4 [2 C, N(CH$_2$*C*H$_3$)$_2$], 41.8, 41.9 [2 C, N(*C*H$_2$*C*H$_3$)$_2$], 49.4 (1 C, C-5), 70.9 (1 C, C-6), 79.4 (1 C, C-4), 94.8 (1 C, C-2), 123.8 (2 C, C-2, -6, *p*-nph), 126.9 (2 C, C-3, -5, *p*-nph), 145.5 (1 C, C-1, *p*-nph), 147.7 (1 C, C-4, *p*-nph), 164.1 (1 C, C-4, *s*-triazine), 165.3 (1 C, C-6, *s*-triazine), 169.2 (1 C, C-2, *s*-triazine) ppm. QC NMR (75 MHz, $CDCl_3$, 25 °C) **3b**-*syn*: δ = 13.1, 13.6 [2 C, N(CH$_2$*C*H$_3$)$_2$], 41.8 [2 C, N(*C*H$_2$*C*H$_3$)$_2$], 48.9 (1 C, C-5), 71.5 (1 C, C-6), 79.9 (1 C, C-4), 94.8 (1 C, C-2), 123.7 (2 C, C-2, -6, *p*-nph), 127.0 (2 C, C-3, -5, *p*-nph), 145.4 (1 C, C-1, *p*-nph), 147.5 (1 C, C-4, *p*-nph), 164.1 (1 C, C-4, *s*-triazine), 165.8 (1 C, C-6, *s*-triazine), 169.3 (1 C, C-2, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3321 (w), 2966 (s), 2933 (m), 2961 (w), 1579 (s), 1523 (s), 1439 (s), 1346 (s), 1319 (m), 1262 (s), 1174 (s), 1094 (s), 1024 (s), 851 (w), 802 (s), 710 (w), 690 (w), 585 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 408 (<1) [M – 1]$^+$, 227 (100), 212 (40), 198 (65), 184 (20). $C_{17}H_{21}ClN_6O_4$ (408.84): calcd. C 49.93, H 5.19, N 20.56; found C 50.11, H 4.95, N 20.22.

2-Chloro-4,6-bis[{(2*R*,4*S*,5*S*)-{2-[(2,4-dichloro-*s*-triazin-6-yl)aminomethyl]-4-(4-nitrophenyl)-1,3-dioxan-5-yl}(methyl)amino]-*s*-triazine (3c): Yield 37% (0.242 g, 0.257 mmol **3c**, starting from 0.565 g, 2.000 mmol **1d** and 0.395 g, 2.100 mmol cyanuric chloride), yellowish crystalline powder, R_f(66% ligroin/acetone) = 0.75 (66% AcOEt/ligroin) = 0.85; m.p. 111–112 °C (flash column chromatography; ligroin/acetone 2:1 or AcOEt/ligroin 2:1). $[\alpha]_D^{20}$ = –132.0 (0.5% thf). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.22, 3.31 (2 × s, 6 H, 2 × CH$_3$), 3.90, 3.97 (2 × dd, $^2J_{H,H}$ = 14.0, $^3J_{H,H}$ = 6.4 Hz, 4 H, 2 × C*H*$_2$NH), 4.34 (d, $^2J_{H,H}$ = 12.8 Hz, 2 H, 6-, 6′-H-a), 4.46 (dd, $^2J_{H,H}$ = 12.8, $^3J_{H,H}$ = 3.4 Hz, 2 H, 6-, 6′-H-e), 5.13, 5.20 (2 × dd, $^3J_{H,H}$ = 4.7, 4.0, 4.7, 4.0 Hz, 2 H, 2-, 2′-H-a), 5.30, 5.31, 5.707, 5.714 (4 × d, $^3J_{H,H}$ = 3.0, 2.6, 3.6, 3.6 Hz, 2 H, 5-, 5′-H-e), 5.36 (d, $^3J_{H,H}$ = 3.0 Hz, 2 H, 4-, 4′-H-a), 6.26 (dd, $^3J_{H,H}$ = 6.4, 6.4 Hz, 2 H, N-, N′-H), 7.45, 7.49, 7.67 (3 × d, $^3J_{H,H}$ = 8.7, 8.7, 9.0 Hz, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 8.09, 8.16, 8.22 (3 × d, $^3J_{H,H}$ = 8.7, 9.0, 9.0 Hz, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 30.7, 34.2, 37.4 (2 C, 2 × CH$_3$), 44.1, 44.5 (2 C, 2 × CH$_2$NH), 50.4 (2 C, C-5, -5′), 64.9, 66.2, 70.2 (2 C, C-6, -6′), 79.5 (2 C, C-4, -4′), 96.0, 99.5, 101.8, 103.5 (2 C, C-2, -2′), 123.8, 124.1, 125.2, 125.9, 126.6 (8 C, CH, *p*-nph), 143.8 (2 C, C-1, -1′, *p*-nph), 147.9, 148.1, 149.3 (2 C, C-4, -4′, *p*-nph), 165.7 [2 C, 2 × *C*-N(CH$_3$), *s*-triazine], 166.7 (2 C, 2 × C-NH, *s*-triazine), 169.8, 170.5, 170.6, 170.7, 171.6 (5 C, 5 × C-Cl, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3277 (m), 2966 (m), 1745 (m), 1692 (m), 1565 (s), 1521 (s), 1479 (s), 1415 (m), 1349 (s), 1326 (m), 1239 (m), 1175 (m), 1149 (m), 1030 (m), 847 (m), 798 (m), 743 (w), 709 (w), 570 (w), 534 (w) cm^{-1}. MS (MALDI α-cyano-4-hydroxycinnamic acid): *m*/*z* (%) = calcd. abundances: 948.1 (5), 947.1 (9), 946.1 (36), 945.1 (38), 944.1 (69), 943.1 (41), 942.1 (100), 941.1 (26), 940.1 (58); found: 948.5 (35), 947.4 (35), 946.6 (50), 945.5 (50), 944.5 (75), 943.6 (60), 942.5 (100) [M]$^+$, 941.4 (50), 940.6 (70). $C_{33}H_{30}Cl_5N_{15}O_8$ (941.96): calcd. C 42.08, H 3.21, N 22.30; found C 42.22, H 3.39, N 21.98.

2-Chloro-4,6-bis{[(2*R*,4*S*,5*S*)-5-(dimethylamino)-4-(4-nitrophenyl)-1,3-dioxan-2-yl]methylamino}-*s*-triazine (3d): Yield 71% (1.70 g, 2.52 mmol **3d**, starting from 2.00 g, 7.10 mmol **1d**), yellowish crystalline powder, R_f(66% acetone/ligroin) = 0.80; m.p. 126–127 °C (flash column chromatography; acetone/ligroin (2:1) then crystallization from Et$_2$O). $[\alpha]_D^{20}$ = +189.4 (0.05% DMSO). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.24 [s, 12 H, 2 × N(CH$_3$)$_2$], 2.66–2.71 (m, 2 H, 5-, 5′-H-e), 3.58–3.81 (m, 4 H, 2 × C*H*$_2$NH), 3.87–3.98 (m, 2 H 6-, 6′-H-a), 4.51–4.59 (m, 2 H, 6-, 6′-H-e), 4.93 (s, 2 H, 4-, 4′-H-a), 4.88–5.08 (m, 2 H, 2-, 2′-H-a), 5.62, 6.03, 6.21, 6.36

(4×dd as br. t, 2 H, N-, N′-H), 7.39–7.49 (m, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 8.12–8.20 (m, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 80 °C): δ = 2.21 [s, 12 H, 2×N-(CH$_3$)$_2$], 2.86 (s, 2 H, 5-, 5′-H-e), 3.53 (br. s, 4 H, 2×C*H*$_2$NH), 3.95 (d, $^2J_{H,H}$ = 11.4 Hz, 2 H, 6-, 6′-H-a), 4.43 (d, $^2J_{H,H}$ = 11.4 Hz, 2 H, 6-, 6′-H-e), 5.00 (br. s, 2 H, 2-, 2′-H-a), 5.18 (br. s, 2 H, 4-, 4′-H-a), 7.63 (d, $^3J_{H,H}$ = 8.6 Hz, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 7.69 (br. s, 2 H, N-, N′-H), 8.14 (d, $^3J_{H,H}$ = 8.6 Hz, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, CDCl$_3$, 25 °C): δ = 44.1 [4 C, 2×N(CH$_3$)$_2$], 44.4 (2 C, CH$_2$NH), 59.5 (2 C, C-5, -5′), 65.4 (2 C, C-6, -6′), 81.1 (2 C, C-4, -4′), 99.5, 99.6 (2 C, C-2, -2′), 123.6 (4 C, C-2, -2′, -6, -6′, *p*-nph), 126.5 (4 C, C-3, -3′, -5, -5′, *p*-nph), 147.25, 147.29 (2 C, C-4, -4′, *p*-nph), 161.1, 166.3, 166.7 (2 C, C-4, -6, *s*-triazine), 169.1 (1 C, C-2, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3432 (m), 3268 (m), 2939 (m), 2865 (m), 2789 (m), 1576 (s), 1519 (s), 1464 (m), 1412 (m), 1348 (s), 1153 (m), 1113 (m), 1057 (m), 1013 (m), 852 (m), 806 (m), 709 (m), 587 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 672.9 (100) [M – 1]$^+$, 636.9 (<10), 483.8 (<10), 221.7 (100). C$_{29}$H$_{36}$ClN$_9$O$_8$ (674.11): calcd. C 51.67, H 5.38, N 18.70; found C 51.89, H 5.55, N 19.02.

2-Chloro-4,6-bis{(2*R*,4*S*,5*S*)-2-[(2′*R*,4′*S*,5′*S*)-5′-(dimethylamino)-4′-(4′-nitrophenyl)-1′,3′-dioxan-2′-yl]-4-(4-nitrophenyl)-1,3-dioxan-5-ylamino}-*s*-triazine (3e): Yield 45% (0.360 g, 0.34 mmol **3e**, starting from 0.712 g, 1.50 mmol **1f**), yellowish crystalline powder, R_f(55% ligroin/acetone) = 0.30; m.p. 210–212 °C (flash column chromatography; ligroin/acetone 1.2:1 then crystallization from Et$_2$O). $[\alpha]_D^{20}$ = +4.0 (0.5% thf). ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): δ = 2.29, 2.30, 2.34 [3×s, 12 H, 2×N(CH$_3$)$_2$], 2.77, 2.81 (2×br. s, 2 H, 2×5′-H-e), 4.01–4.28 [br. m, 6 H, 2×(6-H-a, -e), 2×6′-H-a], 4.12, 4.34, 4.49 [3×d, $^3J_{H,H}$ = 10.8, 9.2, 8.8 Hz, 2 H, 2×5-H-e], 4.66, 4.71 (2×d, $^2J_{H,H}$ = 13.6 Hz, 2 H, 2×6′-H-e), 4.93–5.06 [br. m, 4 H, 2×(2-, 2′-H-a)], 5.14 [br. m, 4 H, 2×(4-, 4′-H-a)], 5.68, 5.71, 5.82, 5.97 (4×d, $^3J_{H,H}$ = 8.8, 8.8, 9.2, 10.8 Hz, 2 H, N-, N′-H), 7.43–7.58 [m, 8 H, 2×(2-, 2′-, 6-, 6′-H, *p*-nph)], 8.03–8.11, 8.18–8.23 [2×m, 8 H, 2×(3-, 3′-, 5-, 5′-H, *p*-nph)] ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 80 °C): δ = 2.28 [s, 12 H, 2×N(CH$_3$)$_2$], 2.94 (s, 2 H, 2×5′-H-e), 3.92 (d, $^2J_{H,H}$ = 12.4 Hz, 2 H, 2×6-H-a), 4.05 (d, $^2J_{H,H}$ = 10.8 Hz, 2 H, 2×6′-H-a), 4.21–4.27 (br. m, 2 H, 2×6-H-e), 4.30–4.38 (br. m, 2 H, 2×5-H-e), 4.54 (d, $^3J_{H,H}$ = 12.4 Hz, 2 H, 2×6′-H-e), 5.07 [s, 4 H, 2×(2-, 2′-H-a)], 5.38 (s, 2 H, 2×4′-H-a), 5.41 (s, 2 H, 2×4-H-a), 6.53, 6.87 (br. s and d, $^3J_{H,H}$ = 8.4 Hz, 2 H, N-, N′-H), 7.62 [br. s, 4 H, 2×(2-, 6-H, *p*-nph)], 7.66 [d, $^3J_{H,H}$ = 8.8 Hz, 4 H, 2×(2′-, 6′-H, *p*-nph)], 8.11–8.15 [br. d, 4 H, 2×(3-, 5-H, *p*-nph)], 8.19 [d, $^3J_{H,H}$ = 8.8 Hz ppm. 4 H, 2×(3′-, 5′-H, *p*-nph)] ppm. ^{13}C NMR (75 MHz, CDCl$_3$, 25 °C): δ = 42.7 [4 C, 2×N(CH$_3$)$_2$], 47.1, 47.2, 47.5 (2 C, 2×C-5), 56.5, 58.2 (2 C, 2×C-5′), 64.3 (2 C, 2×C-6′), 68.5, 69.3, 69.8 (2 C, 2×C-6), 77.4, 77.7, 77.9 (2 C, 2×C-4′), 79.8, 80.5 (2 C, 2×C-4), 98.5 (2 C, 2×C-2′), 99.1 (2 C, 2×C-2), 122.25, 122.34 [8 C, 2×(C-2, -2′, -6, -6′, *p*-nph)], 125.3, 125.5 [8 C, 2×(C-3, -3′, -5, -5′, *p*-nph)], 143.1, 143.3, 143.4 [4 C, 2×(C-1, -1′, *p*-nph)], 145.7, 145.8, 145.9, 146.4, 146.5 [4 C, 2×(C-4, -4′, *p*-nph)], 163.9, 164.0, 164.3 (2 C, C-4, -6, *s*-triazine), 167.9, 168.1, 168.4 (1 C, C-2, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3419 (m), 2971 (m), 2867 (m), 1700 (w), 1605 (s), 1575 (s), 1520 (s), 1415 (w), 1348 (s), 1150 (m), 1110 (s), 1063 (m), 1014 (m), 852 (m), 713 (m), 585 (w) cm^{-1}. MS (FAB+, 3-nitrobenzyl alcohol): *m*/*z* (%) = 1060.9 (100) [M]$^+$, 1015.4 (18), 965.5 (17), 857.9 (19), 838.1 (30), 780.3 (22), 717.8 (23). C$_{47}$H$_{50}$ClN$_{11}$O$_{16}$ (1060.43): calcd. C 53.23, H 4.75, N 14.53; found C 52.95, H 4.44, N 14.79.

Typical Procedure for the Synthesis of Compounds 4a–d (Schemes 5, 6, and 7). Preparation of Compound 4c (Table 1, Entry 7): Cyanuric chloride (0.247 g, 1.333 mmol) was introduced as a dry toluene (10 mL) solution with vigorous stirring into a dry toluene (50 mL) solution containing triethylamine (0.563 mL, 0.405 g, 4 mmol) and (4*S*,5*S*)-5-amino-4-(4-nitrophenyl)-1,3-dioxane (**1a**) (0.897 g, 4 mmol), cooled to –15 °C. The reaction mixture was then allowed to reach room temperature (about 24 h) and was then heated at 70 °C and finally at reflux for an additional 9 h until TLC monitoring indicated no more change. The reaction mixture was cooled to room temperature and filtered, and solid residues were well washed with dry toluene. The organic filtrate was evaporated to dryness under reduced pressure, providing the crude reaction mixture, which was separated by flash column chromatography on silica gel (eluent ligroin/acetone 2:1 *v*/*v*) as follows: first fraction **4b** (0.214 g, 12% conversion of **1a**) then **4c** (0.477 g, 40% conversion of **1a**) as a second fraction. Complete elution of the column with pure acetone yielded recovered **1a** (0.420 g, 90% recovery of the unreacted **1a**).

2,4,6-Tris{[(4*S*,5*S*)-4-(4-nitrophenyl)-1,3-dioxan-5-yl]amino}-*s*-triazine (4a): Yield 4% (0.097 g, 0.13 mmol **4a** starting 2.24 g, 10.00 mmol **1a**) as a yellowish crystalline powder, R_f(63% ligroin/acetone) = 0.45; m.p. 164.4–166.5 °C (flash column chromatography; ligroin/acetone 1.7:1). $[\alpha]_D^{20}$ = +4.0 (0.5% thf). ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): δ = 3.77–4.01 (m, 6 H, 6-, 6′-, 6′′-H-a, 6-, 6′-, 6′′-H-e), 4.06, 4.14, 4.26 (s, s, d, $^3J_{H,H}$ = 7.9 Hz, 3 H, 5-, 5′-, 5′′-H-e), 4.87–4.92 (m, 6 H, 2-, 2′-, 2′′-H-a, 4-, 4′-, 4′′-H-a), 5.12–5.22 (m, 3 H, 2-, 2′, 2′′-H-e), 5.36, 5.52, 5.62 (3×d, $^3J_{H,H}$ = 9.9, 9.2, 8.6 Hz, 3 H, N-, N′-, N′′-H), 7.36–7.48 (m, 6 H, 2-, 2′-, 2′′-, 6-, 6′-, 6′′-H, *p*-nph), 7.93–8.08 (m, 6 H, 3-, 3′-, 3′′-, 5-, 5′-, 5′′-H, *p*-nph) ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 80 °C): **4a**-major δ = 3.80 (br. s, 3 H, 6-, 6′-, 6′′-H-a), 4.04 (dd, $^2J_{H,H}$ = 11.0, $^3J_{H,H}$ = 1.8 Hz, 3 H, 6-, 6′-, 6′′-H-e), 4.20 (br. s, 3 H, 5-, 5′-, 5′′-H-e), 4.95 (d, $^2J_{H,H}$ = 6.2 Hz, 3 H, 2-, 2′-, 2′′-H-a), 5.15 (s, 3 H, 4-, 4′-, 4′′-H-a), 5.18 (d, $^2J_{H,H}$ = 6.2 Hz, 3 H, 3 H, 2-, 2′-, 2′′-H-e), 5.46 (br. s, 3 H, N-, N′-, N′′-H), 7.57 (d, $^3J_{H,H}$ = 9.2 Hz, 6 H, 2-, 2′-, 2′′-, 6-, 6′-, 6′′-H, *p*-nph), 8.01 (d, $^3J_{H,H}$ = 9.2 Hz, 6 H, 3-, 3′-, 3′′-, 5-, 5′-, 5′′-H, *p*-nph) ppm; **4a**-minor (only distinct peaks are listed): δ = 3.94 (d, $^2J_{H,H}$ = 11.0 Hz, 3 H, 6-, 6′-, 6′′-H-a), 4.20 (br. s, 6 H, 6-, 6′-, 6′′-H-e, 5-, 5′-, 5′′-H-e), 4.91 (d, $^2J_{H,H}$ = 6.2 Hz, 3 H, 2-, 2′-, 2′′-H-a), 7.59 (d, $^3J_{H,H}$ = 6.8 Hz, 6 H, 2-, 2′-, 2′′-, 6-, 6′-, 6′′-H, *p*-nph), 8.20 (d, $^3J_{H,H}$ = 6.8 Hz, 6 H, 3-, 3′-, 3′′-, 5-, 5′-, 5′′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, CDCl$_3$, 25 °C): δ = 48.5, 48.9, 49.2, 50.6 (3 C, C-5, -5′, -5′′), 69.9, 70.7, 71.1, 73.1 (3 C, C-6, -6′, -6′′), 79.3, 79.6, 80.5 (3 C, C-4, -4′, -4′′), 94.7 (3 C, C-2, -2′, -2′′), 123.4, 123.8, 124.1 (6 C, C-2, -2′, -2′′, -6, -6′, -6′′, *p*-nph), 126.4, 126.8, 126.9, 127.1 (6 C, C-3, -3′, -3′′, -5, -5′, -5′′, *p*-nph), 145.3, 145.7, 145.8, 146.0, 147.6 (6 C, C-1, -1′, -1′′, -4, -4′, -4′′, *p*-nph), 165.2, 165.3 (3 C, C-2, -4, -6, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3422 (w), 2856 (w), 1719 (w), 1578 (s), 1518 (s), 1347 (s), 1174 (s), 1094 (m), 1028 (s), 986 (m), 852 (w), 811 (w), 742 (w), 711 (w), 582 (w) cm^{-1}. MS (FAB+, 3-nitrobenzyl alcohol): *m*/*z* (%) = 748.9 (100) [M + 1]$^+$, 613.1 (15), 541.2 (20), 481.1 (15), 460.0 (47), 415.2 (18), 378.1 (33), 351.0 (27). C$_{33}$H$_{33}$N$_9$O$_{12}$ (747.68): calcd. C 53.01, H 4.45, N 16.86; found C 52.75, H 4.33, N 17.05.

2,4-(Diethylamino)-6-{[(4*S*,5*S*)-4-(4-nitrophenyl)-1,3-dioxan-5-yl]-amino}-*s*-triazine (4b): Yield 12%, (0.214 g, 0.48 mmol **4b** starting from 0.897 g, 4.00 mmol **1a**) yellowish crystalline powder, R_f(66% ligroin/acetone) = 0.85; m.p. 75–76 °C (flash column chromatography; ligroin/acetone, 2:1). $[\alpha]_D^{20}$ = +6.7 (0.5% thf). ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): δ = 1.06 [t, $^3J_{H,H}$ = 6.9 Hz, 12 H, 2×N(CH$_2$C*H*$_3$)$_2$], 3.42 [q, $^3J_{H,H}$ = 6.9 Hz, 8 H, 2×N(C*H*$_2$CH$_3$)$_2$], 4.04 (dd, $^2J_{H,H}$ = 11.3, $^3J_{H,H}$ = 1.4 Hz, 1 H, 6-H-a), 4.19 (d, $^2J_{H,H}$ = 11.3 Hz, 1 H, 6-H-e), 4.58 (dd, $^3J_{H,H}$ = 10.0, 1.4 Hz, 1 H, 5-H-e), 4.97 (d, $^2J_{H,H}$ = 6.2 Hz, 1 H, 2-H-a), 4.99 (s, 1 H, 4-H-a), 5.28 (d, $^2J_{H,H}$ = 6.2 Hz, 1 H, H-2-e), 5.37 (d, $^3J_{H,H}$ = 10.0 Hz, 1 H,

NH), 7.53 (d, $^3J_{H,H}$ = 8.7 Hz, 2 H, 2-, 6-H, *p*-nph), 8.10 (d, $^3J_{H,H}$ = 8.7 Hz, 2 H, 3-, 5-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 13.8 [4 C, 2×N(CH_2CH_3)$_2$], 41.2 [4 C, 2×N(CH_2-CH_3)$_2$], 48.6 (1 C, C-5), 71.8 (1 C, C-6), 80.0 (1 C, C-4), 94.8 (1 C, C-2), 123.5 (2 C, C-2, -6, *p*-nph), 127.1 (2 C, C-3, -5, *p*-nph), 146.3 (1 C, C-1, *p*-nph), 147.5 (1 C, C-4, *p*-nph), 164.5, 164.8 (2 C, C-2, -4, *s*-triazine), 166.1 (1 C, C-6, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3330 (w), 2966 (m), 2930 (m), 2855 (m), 1604 (m), 1567 (s), 1530 (s), 1502 (s), 1458 (s), 1431 (s), 1374 (s), 1309 (m), 1238 (w), 1176 (s), 1102 (s), 1074 (m), 1027 (m), 989 (m), 852 (m), 812 (s), 747 (w), 589 (w) cm^{-1}. MS (CI, isobutane): *m*/*z* (%) = 446 (100) [M]$^+$, 430 (<5). $C_{21}H_{31}N_7O_4$ (445.52): calcd. C 56.61, H 7.01, N 22.01; found C 56.88, H 6.79, N 22.25.

2-(Diethylamino)-4,6-bis{[(4*S*,5*S*)-4-(4-nitrophenyl)-1,3-dioxan-5-yl]amino}-*s*-triazine (4c): Yield 40% (0.477 g, 0.80 mmol **4c** starting from 0.897, 4.00 mmol **1a**), yellow crystalline powder, R_f(66% ligroin/acetone) = 0.45; m.p. 115.3–117.5 °C (flash column chromatography; ligroin/acetone, 2:1). $[\alpha]_D^{20}$ = +9.9 (0.15% MeOH). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) **4c** (*s*-*s*): δ = δ = 0.95 [t, $^3J_{H,H}$ = 6.8 Hz, 6 H, N(CH_2CH_3)$_2$], 3.28 [q, $^3J_{H,H}$ = 6.8 Hz, 4 H, 4 H, N(CH_2CH_3)$_2$], 3.98 (d, $^2J_{H,H}$ = 10.9 Hz, 2 H, 6-, 6′-H-a), 4.09 (d, $^2J_{H,H}$ = 10.9 Hz, 2 H, 6-, 6′-H-e), 4.38 (d, $^3J_{H,H}$ = 9.5 Hz, 2 H, 5-, 5′-H-e), 4.91 (d, $^2J_{H,H}$ = 6.0 Hz, 2 H, 2-, 2′-H-a), 4.95 (s, 2 H, 4-, 4′-H-a), 5.22 (d, $^2J_{H,H}$ = 6.0 Hz, 2 H, 2-, 2′-H-e), 5.31 (d, $^3J_{H,H}$ = 9.5 Hz, 2 H, N-, N′-H), 7.45 (d, $^3J_{H,H}$ = 8.3 Hz, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 8.06 (d, $^3J_{H,H}$ = 8.3 Hz, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. **4c** (*a*-*s*) (only distinct signals are listed): δ = 3.87 (dd, $^2J_{H,H}$ = 11.5, $^3J_{H,H}$ = 1.3 Hz, 2 H, 6-, 6′-H-a), 4.24 (d, $^2J_{H,H}$ = 11.7 Hz, 1 H, 6-H-e), 4.26 (d, $^2J_{H,H}$ = 9.2 Hz, 1 H, 6′-H-e), 7.45, 7.47 (2×d, $^3J_{H,H}$ = 7.4 Hz, 4 H, 2-, 2′- 6-, 6′-H, *p*-nph), 7.95 (br. s, 2 H, 3-, 5-H, *p*-nph), 8.18 (d, $^3J_{H,H}$ = 8.7 Hz, 2 H, 3′-, 5′-H, *p*-nph) ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 80 °C): δ = 0.93 [t, $^3J_{H,H}$ = 6.8 Hz, 6 H, N(CH_2CH_3)$_2$], 3.27, 3.33 [2×dq, $^2J_{H,H}$ = 14.5, $^3J_{H,H}$ = 6.8 Hz, 4 H, N(CH_2CH_3)$_2$], 3.93 (d, $^2J_{H,H}$ = 11.4 Hz, 2 H, 6-, 6′-H-a), 4.08 (d, $^2J_{H,H}$ = 11.4 Hz, 2 H, 6-, 6′-H-e), 4.35 (d, $^3J_{H,H}$ = 9.0 Hz, 2 H, 5-, 5′-H-e), 4.98 (d, $^2J_{H,H}$ = 6.2 Hz, 2 H, 2-, 2′-H-a), 5.19 (s, 2 H, 4-, 4′-H-a), 5.21 (d, $^2J_{H,H}$ = 6.2 Hz, 2 H, 2-, 2′-H-e), 5.42 (d, $^3J_{H,H}$ = 9.0 Hz, 2 H, N-, N′-H), 7.59 (d, $^3J_{H,H}$ = 8.8 Hz, 4 H, 2-, 2′-, 6-, 6′-H, *p*-nph), 8.04 (d, $^3J_{H,H}$ = 8.8 Hz, 4 H, 3-, 3′-, 5-, 5′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 13.5 [2 C, N(CH_2CH_3)$_2$], 41.0 [2 C, N(CH_2CH_3)$_2$], 48.7 (2 C, C-5, -5′), 71.4 (2 C, C-6, -6′), 79.1, 80.8 (2 C, C-4, -4′), 94.7 (2 C, C-2, -2′), 123.5 (4 C, C-2, -2′, -6, -6′, *p*-nph), 127.0 (4 C, C-3, -3′, -5, -5′, *p*-nph), 146.1 (2 C, C-1, -1′, *p*-nph), 147.5 (2 C, C-4, -4′, *p*-nph), 164.0 (1 C, C-2, *s*-triazine), 165.4 (2 C, C-4, -6, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3431 (w), 2973 (w), 2859 (w), 1582 (s), 1545 (s), 1502 (s), 1346 (s), 1174 (s), 1106 (m), 1027 (s), 986 (w), 852 (w), 811 (w), 742 (w), 586 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 596.2 (100) [M]$^+$, 580 (< 5), 388.9 (< 1). $C_{27}H_{32}N_8O_8$ (596.60): calcd. C 54.36, H 5.41, N 18.78; found C 53.99, H 5.33, N 19.05.

2,4,6-Tris{[(2*R*,4*S*,5*S*)-5-(dimethylamino)-4-(4-nitrophenyl)-1,3-dioxan-2-yl]methylamino}-*s*-triazine (4d): Yield 36% (0.165 g, 0.18 mmol **4d** starting from 0.422 g, 1.50 mmol **1d**) yellowish crystalline powder, m.p. 148–150 °C (flash column chromatography; acetone/ligroin, 2:1, then crystallization from Et_2O). R_f(66% acetone/ligroin) = 0.25. $[\alpha]_D^{20}$ = +49.0 (0.5% DMSO). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.23 [s, 18 H, 3×N(CH_3)$_2$], 2.65 (s, 3 H, 5-, 5′-, 5′′-H-e), 3.64 (br. s, 6 H, 3×CH_2NH), 3.88 (d, $^2J_{H,H}$ = 11.7 Hz, 3 H, 6-, 6′-, 6′′-H-a), 4.53 (d, $^2J_{H,H}$ = 11.7 Hz, 3 H, 6-, 6′-, 6′′-H-e), 4.91 (s, 3 H, 2-, 2′-, 2′′-H-a), 4.99 (s, 3 H, 4-, 4′-, 4′′-H-a), 5.27, 5.84 (2×brs, 3 H, N-, N′-, N′′-H), 7.44 (d, ^3J = 7.0 Hz, 6 H, 2-, 2′-, 2′′-, 6-, 6′-, 6′′-H, *p*-nph), 8.14 (d, $^3J_{H,H}$ = 7.0 Hz, 6 H, 3-, 3′-, 3′′-, 5-, 5′-, 5′′-H, *p*-nph) ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 80 °C): δ = 2.21 [s, 18 H, 3×N(CH_3)$_2$], 2.83 (dd, $^3J_{H,H}$ = 3.0, 3.0 Hz, 3 H, 5-, 5′, 5′′-H-e), 3.50 (dd, $^3J_{H,H}$ = 5.0, 5.0 Hz, 6 H, 3×CH_2NH), 3.92 (dd, $^2J_{H,H}$ = 12.4, $^3J_{H,H}$ = 3.2 Hz, 3 H, 6-, 6′-, 6′′-H-a), 4.43 (dd, $^2J_{H,H}$ = 12.4, $^3J_{H,H}$ = 5.2 Hz, 3 H, 6-, 6′-, 6′′-H-e), 5.00 (dd, $^3J_{H,H}$ = 5.0, 5.0 Hz, 3 H, 2-, 2′-, 2′′-H-a), 5.15 (d, ^3J = 3.6 Hz, 3 H, 4-, 4′-, 4′′-H-a), 6.33 (br. s, 3 H, N-, N′-, N′′-H), 7.62 (d, $^3J_{H,H}$ = 8.8 Hz, 6 H, 2-, 2′-, 2′′-, 6-, 6′-, 6′′-H, *p*-nph), 8.13 (d, $^3J_{H,H}$ = 8.8 Hz, 6 H, 3-, 3′-, 3′′-, 5-, 5′-, 5′′-H, *p*-nph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 44.1 [6 C, 3×N(CH_3)$_2$], 44.3 (3 C, 3×CH_2NH), 59.6 (3 C, C-5, -5′, -5′′), 65.3 (3 C, C-6, -6′, -6′′), 90.5 (3 C, C-4, -4′, -4′′), 100.3 (3 C, C-2, -2′, -2′′), 123.6 (6 C, C-2, -2′, -2′′, -6, -6′, -6′′, *p*-nph), 126.6 (6 C, C-3, -3′, -3′′, -5, -5′, -5′′, *p*-nph), 147.2 (3 C, C-1, -1′, -1′′, *p*-nph), 147.6 (3 C, C-3, -3′, -3′′, -5, -5′, -5′′, *p*-nph), 166.7 (3 C, C-2, -4, -6, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3400 (m), 2938 (m), 2863 (m), 1602 (s), 1575 (s), 1517 (s), 1464 (m), 1412 (m), 1348 (s), 1152 (m), 1111 (m), 1043 (m), 1013 (m), 852 (m), 753 (w), 709 (m), 586 (w) cm^{-1}. MS (FAB+, 3-nitrobenzyl alcohol): *m*/*z* (%) = 918.0 (100) [M – 1]$^+$, 832.0 (19), 797.1 (15), 766.3 (20), 739.2 (19), 697.0 (65), 588.7 (30), 530.2 (22), 474.4 (47), 413.1 (25). $C_{42}H_{54}N_{12}O_{12}$ (918.96): calcd. C 54.89, H 5.92, N 18.29; found C 54.77, H 6.15, N 17.98.

Typical Procedure for the Synthesis of Compounds 5a–c (Scheme 10). Preparation of Compound 5c: Anhydrous potassium carbonate (0.069 g, 0.500 mmol) was added with vigorous stirring to a dry 1,4-dioxane (25 mL) solution containing **3e** (0.530 g, 0.500 mmol) and anhydrous piperazine (0.021 g, 0.245 mmol). The reaction mixture was heated at reflux until TLC monitoring indicated no more change (about 56 h). The reaction mixture was cooled to room temperature and filtered, and solid residues were well washed with dry 1,4-dioxane. The organic filtrate was evaporated to dryness under reduced pressure, providing the crude reaction mixture, which was purified by flash column chromatography on silica gel (eluent acetone/ligroin, 5:1, v/v) to give **5c** (0.300 g, 56% yield).

1,4-Bis[4,6-bis{[(4*S*,5*S*)-4-(4-nitrophenyl)-1,3-dioxan-5-yl]amino}-*s*-triazin-2-yl]piperazine (5a): Yield 80% (0.226 g, 0.20 mmol **5a** starting from 0.280 g, 0.50 mmol **3a**), yellowish crystalline powder, R_f(55% ligroin/acetone) = 0.40; m.p. 222–225 °C (flash column chromatography; ligroin/acetone 1.25:1). $[\alpha]_D^{20}$ = +3.3 (0.5% thf). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.35 (br. s, 8 H, piperazine), 4.00–4.33 [br. m, 8 H, 2×(6-, 6′-H-a, -e)], 4.93 [br. s, 8 H, 2×(2-, 2′-H-a, 4-, 4′-H-a)], 5.22 [br. s, 4 H, 2×(2-, 2′-H-e)], 5.42 [br. s, 4 H, 2×(N-, N′-H)], 7.42 [br. s, 8 H, 2×(2-, 2′-, 6-, 6′-H, *p*-nph)], 7.93–8.03 [br. m, 8 H, 2×(3-, 3′-, 5-, 5′-H, *p*-nph)] ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 80 °C): δ = 3.36 (s, 8 H, piperazine), 3.94 [br. d, $^2J_{H,H}$ = 7.6 Hz, 4 H, 2×(6-, 6′-H-a)], 4.10 [d, $^2J_{H,H}$ = 10.4 Hz, 4 H, 2×(6-, 6′-H-e)], 4.37 [d, $^3J_{H,H}$ = 7.6 Hz, 4 H, 2×(5-, 5′-H-e)], 4.99 [d, $^2J_{H,H}$ = 6.0 Hz, 4 H, 2×(2-, 2′-H-a)], 5.20 [s, 4 H, 2×(4-, 4′-H-a)], 5.22 [d, $^2J_{H,H}$ = 6.0 Hz, 4 H, 2×(2-, 2′-H-e)], 5.58 [d, $^3J_{H,H}$ = 7.6 Hz, 4 H, 2×(N-, N′-H)], 7.59 [d, $^3J_{H,H}$ = 7.6 Hz, 8 H, 2×(2-, 2′-, 6-, 6′-H, *p*-nph)], 8.06 [br. s, 8 H, 2×(3-, 3′-, 5-, 5′-H, *p*-nph)] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 42.8 (4 C, piperazine), 49.0 [4 C, (2×C-5, -5′)], 71.4 [4 C, (2×C-6, -6′)], 79.5, 79.8 [4 C, (2×C-4, -4′)], 94.7 [4 C, 2×(C-2, -2′)], 123.4 [8 C, 2×(C-2, -2′, -6, -6′, *p*-nph)], 127.0 [8 C, 2×(C-3, -3′, -5, -5′, *p*-nph)], 146.0 [4 C, 2×(C-1, -1′, *p*-nph)], 147.6 [4 C, 2×(C-4, -4′, *p*-nph)], 165.5, 165.7 (6 C, C-2, -2′, -4, -4′, -6, -6′, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3414 (w), 2855 (w), 1577 (s), 1520 (s), 1492 (s), 1442 (s), 1346 (s), 1174 (s), 1095 (m), 1027 (m), 985 (m), 852 (w), 810 (m), 743 (w), 711 (w), 586 (w) cm^{-1}. MS (FAB+, 3-nitrobenzylalcohol): *m*/*z* (%) = 1132.3 (95) [M+ 1]$^+$, 951.9 (20), 723.0 (20), 662.7 (33), 612.4 (25), 550.5 (33), 459.4 (100).

$C_{50}H_{52}N_{16}O_{16}$ (1133.06): calcd. C 53.00, H 4.63, N 19.78; found C 53.33, H 4.81, N 19.96.

1,4-Bis[4,6-bis{[(2*R*,4*S*,5*S*)-5-(dimethylamino)-4-(4-nitrophenyl)-1,3-dioxan-2-yl]methylamino}-*s*-triazin-2-yl]piperazine (5b): Yield 71% (0.721 g, 0.53 mmol **5b** starting from 1.000 g, 1.48 mmol **3d**), yellowish crystalline powder, R_f(100% acetone) = 0.55; m.p. 198–199 °C (flash column chromatography; acetone then crystallization from Et_2O). $[\alpha]_D^{20}$ = +222.7 (0.30% DMSO). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.27 [s, 24 H, 4×N(CH_3)$_2$], 2.68 [br. s, 4 H, 2×(5-, 5′-H-e)], 3.66–3.73 (br. s, 8 H, piperazine, 8 H, 4×CH_2NH), 3.92 [br. d, $^2J_{H,H}$ = 11.9 Hz, 4 H, 2×(6-, 6′-H-a)], 4.56 [d, $^2J_{H,H}$ = 11.9 Hz, 4 H, 2×(6-, 6′-H-e)], 4.92 [br. s, 4 H, 2×(2-, 2′-H-a)], 5.01 [br. s, 4 H, 2×(4-, 4′-H-a)], 5.29, 5.79 [br. s, 4 H, 2×(N-, N′-H)], 7.48 [d, $^3J_{H,H}$ = 8.5 Hz, 8 H, 2×(2-, 2′-, 6-, 6′-H, *p*-nph)], 8.18 [d, $^3J_{H,H}$ = 8.5 Hz, 8 H, 2×(3-, 3′-, 5-, 5′-H, *p*-nph)] ppm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 80 °C): δ = 2.21 [s, 24 H, 4×N(CH_3)$_2$], 2.85 [dd, $^3J_{H,H}$ = 2.8, 2.8 Hz, 4 H, 2×(5-, 5′-H-e)], 3.52 (dd, $^3J_{H,H}$ = 5.1, 5.1 Hz, 8 H, 4×CH_2NH), 3.67 (br. s, 8 H, piperazine), 3.94 [dd, $^2J_{H,H}$ = 12.4, $^3J_{H,H}$ = 2.8 Hz, 4 H, 2×(6-, 6′-H-a)], 4.43 [d, $^2J_{H,H}$ = 12.4 Hz, 4 H, 2×(6-, 6′-H-e)], 4.99 [dd, $^3J_{H,H}$ = 5.1, 5.1 Hz, 4 H, 2×(2-, 2′-H-a)], 5.16 [d, $^3J_{H,H}$ = 3.2 Hz, 4 H, 2×(4-, 4′-H-a)], 6.37 [br. s, 4 H, 2×(N-, N′-H)], 7.62 [d, $^3J_{H,H}$ = 8.8 Hz, 8 H, 2×(2-, 2′-, 6-, 6′-H, *p*-nph)], 8.14 [d, $^3J_{H,H}$ = 8.8 Hz, 8 H, 2×(3-, 3′-, 5-, 5′-H, *p*-nph)] ppm. ^{13}QC NMR (75 MHz, $CDCl_3$, 25 °C): δ = 43.4 (4 C, piperazine), 44.1 [8 C, 4×N(CH_3)$_2$], 44.4 (4 C, 4×CH_2NH), 59.6 [4 C, 2×(C-5, -5′)], 63.4 [4 C, 2×(C-6, -6′)], 81.1 [4 C, 2×(C-4, -4′)], 100.3 [4 C, 2×(C-2, -2′)], 123.6 [8 C, 2×(C-2, -2′, -6, -6′, *p*-nph)], 126.6 [8 C, 2×(C-3, -3′, -5, -5′, *p*-nph)], 147.3 [4 C, 2×(C-1, -1′, *p*-nph)], 147.6 [4 C, 2×(C-4, -4′, *p*-nph)], 165.4 (2 C, C-2, -2′, *s*-triazine),166.6 (4 C, C-4, -4′, -6, -6′, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3434 (m), 2935 (m), 2858 (m), 2787 (m), 1552 (s), 1519 (s), 1441 (s), 1412 (m), 1348 (s), 1279 (m), 1151 (s), 1110 (m), 1054 (s), 1003 (s), 851 (m), 810 (m), 709 (m), 570 (w) cm^{-1}. MS (MALDI+, α-cyano-4-hydroxycinnamic acid): *m*/*z* (%) = 1361.8 (100) [M]$^+$, 1208.7 (50), 1192.7 (20), 1163.6 (17), 1139.7 (40), 986.6 (25), 956.5 (<10), 917.6 (15), 901.6 (18), 885.7 (12), 837.4 (10). $C_{62}H_{80}N_{20}O_{16}$ (1361.44): calcd. C 54.70, H 5.92, N 20.58; found C 55.02, H 5.88, N 20.55.

1,4-Bis[4,6-bis{[(2*R*,4*R*,5*S*)-2-[(2′*R*,4′*S*,5′*S*)-5′-(dimethylamino)-4′-(4′-nitrophenyl)-1′,3′-dioxan-2′-yl]-4-(4-nitrophenyl)-1,3-dioxan-5-yl]amino}-*s*-triazin-2-yl]piperazine (5c): Yield 56%, (0.300 g, 0.14 mmol **5c** starting from 0.530 g, 0.50 mmol **3e**) yellowish crystalline powder, m.p. 234–236 °C (flash column chromatography; acetone/ligroin 5:1 then crystallization from Et_2O). R_f(83% acetone/ligroin) = 0.55. $[\alpha]_D^{20}$ = +8.8 (0.5% thf). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.32, 2.36 [2×s, 24 H, 4×N(CH_3)$_2$], 2.79 (br. s, 4 H, 4×5′-H-e), 3.46–3.56 (br. m, 8 H, piperazine), 4.07 (d, $^3J_{H,H}$ = 13.3 Hz, 4 H, 4×6′-H-a), 4.22 (br. s, 4 H, 4×5-H-e), 4.05–4.48 [br. m, 8 H, 4×(6-H-a, -e)], 4.68 (d, $^2J_{H,H}$ = 13.3 Hz, 4 H, 2×6′-H-e), 5.02–5.08 [br. m, 8 H, 4×(2-, 2′-H-a)], 5.18 [br. s, 8 H, 4×(4-, 4′-H-a)], 5.42 [br. s, 4 H, 2×(N-, N′-H)], 7.53–7.61 [br. m, 16 H, 4×(2-, 2′-, 6-, 6′-H, *p*-nph)], 8.03–8.22 [br. m, 16 H, 4×(3-, 3′-, 5-, 5′-H, *p*-nph)] ppm. ^{1}H NMR (400 MHz, [D$_6$] DMSO, 80 °C): δ = 2.29 [s, 24 H, 4×N(CH_3)$_2$], 2.94 (s, 4 H, 4×5′-H-e), 3.43 (s, 8 H, piperazine), 4.02 (br. s, 4 H, 4×6-H-a), 4.08 (d, $^3J_{H,H}$ = 11.2 Hz, 4 H, 4×6′-H-a), 4.24 (br. s, 4 H, 4×6-H-e), 4.48 (br. d, $^3J_{H,H}$ = 9.2 Hz, 4 H, 4×5-H-e), 4.54 (d, $^3J_{H,H}$ = 11.2 Hz, 4 H, 4×6′-H-e), 5.05 (s, 4 H, 4×2′-H-a), 5.07 (s, 4 H, 4×2-H-a), 5.31 (d, $^3J_{H,H}$ = 2 Hz, 4 H, 4×4′-H-a), 5.35 (s, 4 H, 4×4-H-a), 5.52 [br. s, 4 H, 2×(N-, N′-H)], 7.60 [br. s, 8 H, 4×(2-, 6-H, *p*-nph)], 7.67 [d, $^3J_{H,H}$ = 8.6 Hz, 8 H, 4×(2′-, 6′-H, *p*-nph)], 8.07 [br. s, 8 H, 4×(3-, 5-H, *p*-nph)], 8.20 [d, $^3J_{H,H}$ = 8.6 Hz. 8 H, 4×(3′-, 5′-H, *p*-nph)] ppm. ^{13}QC NMR (75 MHz, $CDCl_3$, 25 °C): δ = 41.5 (4 C, piperazine), 42.7 [8 C, 4×N(CH_3)$_2$], 46.8 (4 C, 4×C-5), 58.2 (4 C, 4×C-5′), 64.3 (4 C, 4×C-6′), 69.6, 70.3 (4 C, 4×C-6), 77.6, 78.2 (4 C, 4×C-4′), 79.4, 79.7 (4 C, 4×C-4), 98.0 (4 C, 4×C-2′), 98.8, 99.0 (4 C, 4×C-2), 121.9, 122.2 [16 C, 4×(C-2, -2′, -6, -6′, *p*-nph)], 125.3, 125.8 [16 C, 4×(C-3, -3′, -5, -5′, *p*-nph)], 144.1, 144.7, 145.9, 146.3 [16 C, 4×(C-1, -1′, -4, -4′, *p*-nph)], 163.0, 163.7, 164.1, 164.3 (6 C, C-2, -2′, -4, -4′, -6, -6′, *s*-triazine) ppm. IR (KBr): $\tilde{\nu}$ = 3428 (m), 2926 (m), 2859 (m), 1607 (s), 1578 (s), 1522 (s), 1492 (s), 1441 (s), 1348 (s), 1148 (m), 1109 (s), 1064 (s), 1012 (s), 851 (m), 810 (m), 712 (m), 583 (w) cm^{-1}. MS (MALDI+, α-cyano-4-hydroxycinnamic acid): *m*/*z* (%) = 2135.3 (38) [M + 1]$^+$, 1894.2 (19), 877.3 (15), 453.4 (42), 212.1 (100). $C_{98}H_{108}N_{24}O_{32}$ (2134.07): calcd. C 55.16, H 5.10, N 15.75; found C 55.33, H 4.88, N 16.05.

Supporting Information (see also the footnote on the first page of this article): Table S1 listing relevant NMR spectroscopic data of *N*-substituted amino-*s*-triazines containing a single 1,3-dioxane motif by axial anchorage describing the (pro)diastereomerism of compounds **2a–c**, **3b** and **4b**. Table S2 listing relevant NMR-spectroscopic data of *N*-substituted amino-*s*-triazines containing a single 1,3-dioxane motif by equatorial anchorage describing the (pro) diastereomerism of compounds **2c**, **2f** and **3c**. Figure S1 illustrating the dependence on solvent of rotameric distribution of compound **3a**. Figure S2 showing the 2D ^{1}H–^{1}H-NOESY chart of compound **4c** as major (*s*-*s*) rotamer. Figure S3 describing the ^{1}H DNMR evolution of compounds **3a**, **3d** and **4c**. Table S3 listing the ^{1}H DNMR data used for calculation of $\Delta G^{\neq}$ rotational barriers in the a*symmetric* rotamer of melamine **4d**.

Acknowledgments

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[1] Methodology restricted, so far, to C-1-(*p*-nitrophenyl)-substituted serinols, see: a) M. Darabantu, S. Mager, C. Puscas, M. Bogdan, E. Cotora, G. Plé, I. Bratu, *Rev. Rom. Chim.* **1994**, *39*, 955–965; b) M. Darabantu, S. Mager, C. Puscas, M. Bogdan, G. Plé, E. Cotora, D. Kovacs, *Rev. Rom. Chim.* **1995**, *40*, 453–461; c) M. Darabantu, S. Mager, C. Puscas, G. Plé, M. Bogdan, E. Cotora, *Rev. Rom. Chim.* **1995**, *40*, 907–915; d) M. Darabantu, C. Maiereanu, G. Plé, C. Berghian, E. Condamine, Y. Ramondenc, *Heterocycl. Commun.* **2001**, *7*, 593–596; e) M. Darabantu, G. Plé, S. Mager, C. Puscas, E. Cotora, *Tetrahedron* **1997**, *53*, 1909–1922; f) M. Darabantu, G. Plé, S. Mager, L. Gaina, E. Cotora, A. Mates, L. Costas, *Tetrahedron* **1997**, *53*, 1891–1908.

[2] a) M. Darabantu, S. Mager, G. Plé, C. Puscas, *Heterocycles* **1995**, *41*, 2327–2356 and literature cited therein referring to the synthesis of **IIc** under strong dehydrating conditions; for other developments in the use of amino-1,3-dioxanes based on *l*-phenylserinol see: b) K. Weinges, K. P. Klotz, H. Droste, *Chem. Ber.* **1980**, *113*, 710–721; c) D. Enders, J. Schankat, *Helv. Chim. Acta* **1995**, *78*, 970–992; d) M. D. Rozwadowska, *Tetrahedron* **1997**, *53*, 10615–10622; e) In these "classical" procedures and essentially depending on the carbonyl electrophile, *l*-(*p*-nitrophenyl)serinol (**Ia**, Scheme 1) affords Schiff bases, 1,3-oxazolidines or 3,7-dioxa-1-azabicyclo[3.3.0]octanes[1e,1f,2].

[3] a) M. Darabantu, C. Maiereanu, I. Silaghi-Dumitrescu, L. Toupet, E. Condamine, Y. Ramondenc, C. Berghian, G. Plé, N. Plé, *Eur. J. Org. Chem.* **2004**, 2644–2661; b) C. Berghian, M. Darabantu, P. Lameiras, N. Plé, A. Turck, *Heterocycl. Com-*

mun. **2005**, *11*, 517–522; c) C. Berghian, P. Lameiras, L. Toupet, E. Condamine, N. Plé, A. Turck, C. Maiereanu, M. Darabantu, *Tetrahedron* **2006**, *62*, 7319–7338; d) C. Berghian, E. Condamine, N. Plé, A. Turck, I. Silaghi-Dumitrescu, C. Maiereanu, M. Darabantu, *Tetrahedron* **2006**, *62*, 7339–7354.

[4] B. O. Kraiz, A. L. Remizov, *Zh. Org. Khim.* **1979**, *15*, 1282–1289.

[5] a) M. B. Steffensen, E. E. Simanek, *Angew. Chem. Int. Ed.* **2004**, *43*, 5178–5180; b) H. T. Chen, M. F. Neerman, A. R. Parrish, E. E. Simanek, *J. Am. Chem. Soc.* **2004**, *126*, 10044–10048; c) J. Lim, E. E. Simanek, *Mol. Pharmaceutics* **2005**, *2*, 273–277; d) M. Amm, N. Platzer, J. Guilhem, J. P. Bouchet, J. P. Volland, *Magn. Reson. Chem.* **1998**, *36*, 587–596; e) M. Amm, N. Platzer, J. P. Bouchet, J. P. Volland, *Magn. Reson. Chem.* **2001**, *39*, 77–84; f) G. Sandford, *Chem. Eur. J.* **2003**, *9*, 1465–1469.

[6] E. L. Eliel, H. S. Wilen, *Stereochemistry of the Organic Compounds*, John Wiley & Sons, New York, **1994**, pp. 1191, 696, 697, 21, 466.

[7] M. J. O. Anteunis, D. Tavernier, F. Borremans, *Heterocycles* **1976**, *4*, 293–371.

[8] a) R. C. Galesworthy, R. M. Show, B. C. Smith, *J. Chem. Soc.* **1962**, 1507–1508; b) R. M. Show, P. Ward, *J. Chem. Soc.* **1965**, 5446–5451; c) B. I. Stepanov, G. I. Migachev, E. F. Ilina, *Zh. Obshch. Khim.* **1967**, *37*, 2140; d) R. M. Show, P. Ward, *J. Chem. Soc.* **1968**, *12*, 1431–1435; e) G. I. Migachev, E. F. Ilina, B. I. Stepanov, *Zh. Obsch. Khim.* **1968**, *38*, 1370–1371; f) R. M. Show, P. Ward, *J. Chem. Soc.* **1969**, *6*, 596–599; g) G. Boncic-Caricic, Z. D. Tadic, M. D. Muskatirovic, *J. Serb. Chem. Soc.* **1994**, *59*, 929–933; h) N. D. Reddy, A. J. Elias, A. Vij, *J. Chem. Res. (S)* **1998**, 504–505; i) W. R. Alder, *Chem. Rev.* **1989**, *89*, 1215–1223; j) Like triethylamine, proton sponge (p. s., Table 1, Entry 3) also met the condition of solubility in toluene. It behaved, as expected, only as a hindered base although partial *N*-dealkylation of *N*,*N*-dialkylarylamines was known as early as 1962 (refs. 8a–8f). *N*-Dealkylation of aliphatic tertiary amines appeared to be a later development of this methodology (refs. 8g, 8h).

[9] a) I. Willner, J. Rosengaus, Y. Eichen, *J. Phys. Org. Chem.* **1993**, *6*, 29–43; b) A. R. Katritzky, I. Ghiviriga, D. Oniciu, A. Barkock, *J. Chem. Soc. Perkin Trans. 2* **1995**, 785–792; c) A. R. Katritzky, I. Ghiviriga, P. G. Steel, D. C. Oniciu, *J. Chem. Soc. Perkin Trans. 2* **1996**, 443–447; d) S. A. Brewer, H. T. Burnell, I. Holpen, G. B. Jones, R. C. Willis, *J. Chem. Soc. Perkin Trans. 2* **1999**, *6*, 1231–1234; e) H. E. Birkett, R. K. Harris, P. Hodgkinson, K. Carr, M. H. Charlton, J. C. Cherryman, A. M. Chippendale, R. P. Glover, *Magn. Reson. Chem.* **2000**, *38*, 504–511; f) I. Ghiviriga, D. C. Oniciu, *Chem. Commun.* **2002**, *22*, 2718–2719; g) H. E. Birkett, J. C. Cherryman, A. M. Chippendale, J. S. O. Evans, R. K. Harris, M. James, I. J. King, G. McPherson, *Magn. Reson. Chem.* **2003**, *41*, 324–336.

[10] a) M. Darabantu, M. Pintea, M. Fazekas, P. Lameiras, C. Berghian, I. Delhom, I. Silaghi-Dumitrescu, N. Plé, A. Turck, *Lett. Org. Chem.* **2006**, *3*, 905–910; b) M. Fazekas, M. Darabantu, M. Pintea, P. Lameiras, C. Bele, C. Berghian, N. Plé, *Heterocycl. Commun.* **2006**, *12*, 151–156.

[11] a) S. H. Vosko, L. Wilk, M. Nusair, *Can. J. Phys.* **1980**, *58*, 1200–1211; b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789; c) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652; d) P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. J. Frisch, *J. Phys. Chem.* **1994**, *98*, 11623–11627; e) A. Klamt, G. Schüürmann, *J. Chem. Soc. Perkin Trans. 2* **1993**, 799–805.

[12] T. P. Straatsma, E. Aprà, T. L. Windus, E. J. Bylaska, W. de Jong, S. Hirata, M. Valiev, M. Hackler, L. Pollack, R. Harrison, M. Dupuis, D. M. A. Smith, J. Nieplocha, V. Tipparaju, M. Krishnan, A. A. Auer, E. Brown, G. Cisneros, G. Fann, H. Früchtl, J. Garza, K. Hirao, R. Kendall, J. Nichols, K. Tsemekhman, K. Wolinski, J. Anchell, D. Bernholdt, P. Borowski, T. Clark, D. Clerc, H. Dachsel, M. Deegan, K. Dyall, D. Elwood, E. Glendening, M. Gutowski, A. Hess, J. Jaffe, B. Johnson, J. Ju, R. Kobayashi, R. Kutteh, Z. Lin, R. Littlefield, X. Long, B. Meng, T. Nakajima, S. Niu, M. Rosing, G. Sandrone, M. Stave, H. Taylor, G. Thomas, J. van Lenthe, A. Wong, Z. Zhang, NWChem, *A Computational Chemistry Package for Parallel Computers*, Version 4.6 (**2004**), Pacific Northwest National Laboratory, Richland, Washington 99352–0999, USA. *High Performance Computational Chemistry: an Overview of NWChem* a Distributed Parallel Application, R. A. Kendall, E. Aprà, D. E. Bernholdt, E. J. Bylaska, M. Dupuis, G. I. Fann, R. J. Harrison, J. Ju, J. A. Nichols, J. Nieplocha, T. P. Straatsma, T. L. Windus, A. T. Wong, *Computer Phys. Commun.* **2000**, *128*, 260–283.

[13] a) P. Laszlo, *Bull. Soc. Chim. Fr.* **1964**, *10*, 2558–2561; b) K. Nikki, *Magn. Res. Chem.* **1990**, *28*, 385–388.

[14] H. Friebolin, *Basic One- and Two-Dimensional NMR Spectroscopy*, VCH Verlagsgesellschaft, Weinheim, New York, **1991**, pp. 93, 263–291.

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