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Anarchy in the solid state: structural dependence on glass-forming ability in triazine-based molecular glasses

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ABSTRACT

We have recently shown that molecular glasses, small molecules capable of readily forming glassy solids as opposed to crystals, can be designed by exploiting molecular association through strong and directional intermolecular interactions, as exemplified by several members of the bis(mexylamino)triazine family. Herein, 43 new bis(mexylamino)triazine derivatives were synthesized, 31 of which have been found to spontaneously form glassy phases and did not crystallize upon heating.

1. Introduction

One of the unsolved challenges ubiquitous to every area of materials science is the understanding of how the structure of individual molecules impacts the structure and properties of the bulk materials. Understanding these principles holds the promise of enabling the design of molecules that not only possess the desired intrinsic properties but also interact with neighboring molecules in ways that enhance those properties.[1] To this end, entire fields of chemistry have been devoted toward predicting the crystal structure[2] or liquid crystalline properties[3] of compounds based on their molecular structure. In contrast, glassy amorphous solids and how molecular structure can affect and promote their formation are still poorly understood,[4] despite amorphous materials being commonly used for a wide range of applications ranging from common glass and plastics to foods,[5] opto-electronics (OLEDs and photovoltaic cells),[6] nanolithography,[7] and pharmaceuticals (amorphous drug formulations).[8]

While most polymers readily form amorphous phases, small molecules possess the advantage of being easier to purify, characterize and process, making them an appealing alternative for applications involving amorphous materials. Furthermore, some applications require specific small molecules to exist in the amorphous state. For these reasons, the study of molecular compounds capable of forming stable glasses at ambient temperature, also called molecular glasses, has received an increasing amount of attention in the last 20 years.[4] However, the development of adequate molecular glasses for commercial applications has so far been limited by (1) the glassy phases of most small molecules being only accessible through special processing techniques (e.g., supercooling, freeze-drying),[4,8] and (2) the propensity of these glasses to revert to their more stable crystalline forms over time.[4] In various applications involving amorphous materials derived from small molecules, crystallization is undesirable and imposes limits on the shelf life of the materials,[5–9] thus making the design of superior molecular glasses a field of active research where efforts are deployed to develop compounds that spontaneously form glassy phases under ambient conditions and in which crystallization is halted at ambient temperature.[10]

Most known molecular glasses are defined by their incapability to pack efficiently in an ordered structure.[4] Strategies, which have been used to achieve this goal include increasing conformational freedom, reducing the degree of symmetry, and preventing the molecules from interacting together in a strong and directional fashion.[11–13] While these strategies have met a certain degree of success, the principles underlying glass formation are in general poorly understood, and even though some empirical relationships have been established between molecular structure and glass-forming ability,[4,11–13] and the current knowledge of molecular glasses does not yet allow one to predict the glass-forming ability or the T_g of any given compound solely from its molecular structure.

In previous studies, we have introduced an approach in molecular glass design in which structural elements are purposefully introduced to exploit association between molecules along specific and predictable patterns through strong non-covalent interactions

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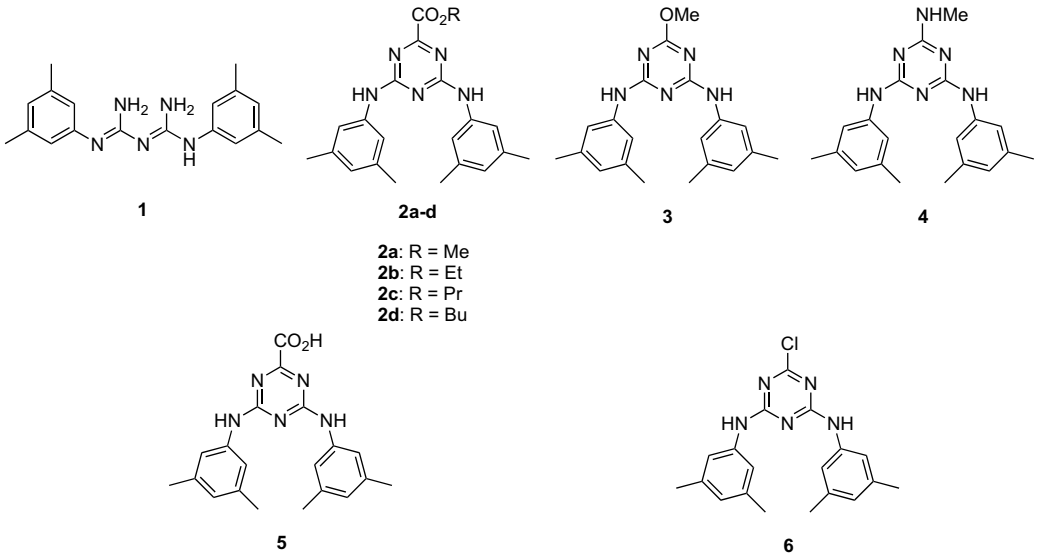


while bulky groups prevent efficient packing from other parts of the molecules.[14] 1,5-Dimexylbiguanide **1**[15] and 4,6-bis(mexylamino)-1,3,5-triazines **2**–**4**[14,16] exemplify this approach, as these compounds have been shown to readily form glassy phases that do not crystallize on standing for extended periods of time. We have shown that in this family of compounds, hydrogen bonding is present in the glassy state and contributes to glass formation by generating supramolecular aggregates that pack poorly and interact weakly, and by limiting molecular reorganization.[17] We have also demonstrated that there is a correlation between disruption of the hydrogen bonds and the macroscopic changes occurring during glass transition.

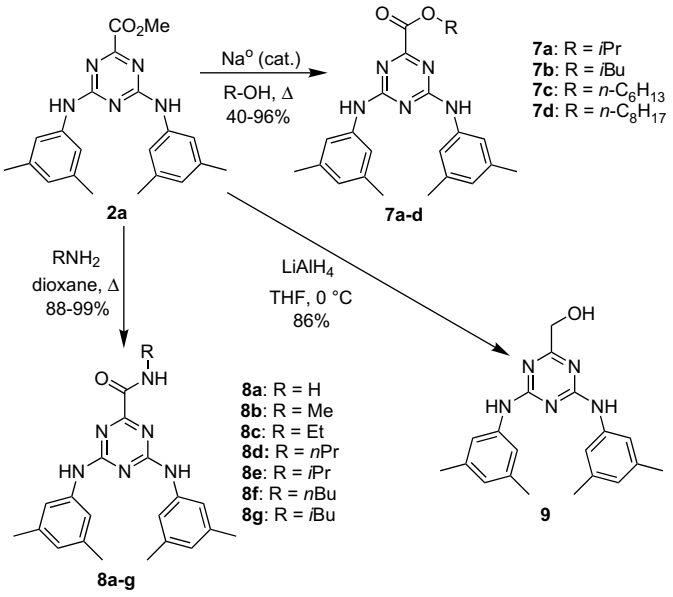
While none of the compounds reported in our previous studies without at least one mexylamino group has shown the ability to reversibly form stable glasses, some mexylamino and bis(mexylamino) compounds including carboxylic acid **5** and chlorotriazine **6** (which has been shown to pack more efficiently in the crystalline state) have also shown an incapacity to form glassy phases under ambient conditions. The group at the 2-position of the triazine ring (subsequently referred to as head group) thus influences solid-state packing, which translates on glass-forming ability. Even with glass-forming compounds, the head group has been shown to have a significant impact on glass transition temperature (T_g), as exemplified by isosteric compounds **3** and **4**, which show a difference in T_g of 36 °C.

In this study, we sought to gain a better understanding of the role of the head group on glass-forming ability and glass transition temperature (T_g) in this family of compounds. To do so, we have synthesized a series of related 4,6-bis(mexylamino)-1,3,5-triazines bearing various functional groups at the 2-position. T_g has been measured by differential scanning calorimetry (DSC) and was found to range from 26 to 97 °C. We have found that subtle structural changes can alter dramatically the thermal properties of the bulk solids, and that most compounds described herein behave as molecular glasses, showing the generality of the 4,6-bis(mexylamino)-1,3,5-triazine motif as promoting glass formation.

2. Results and discussion

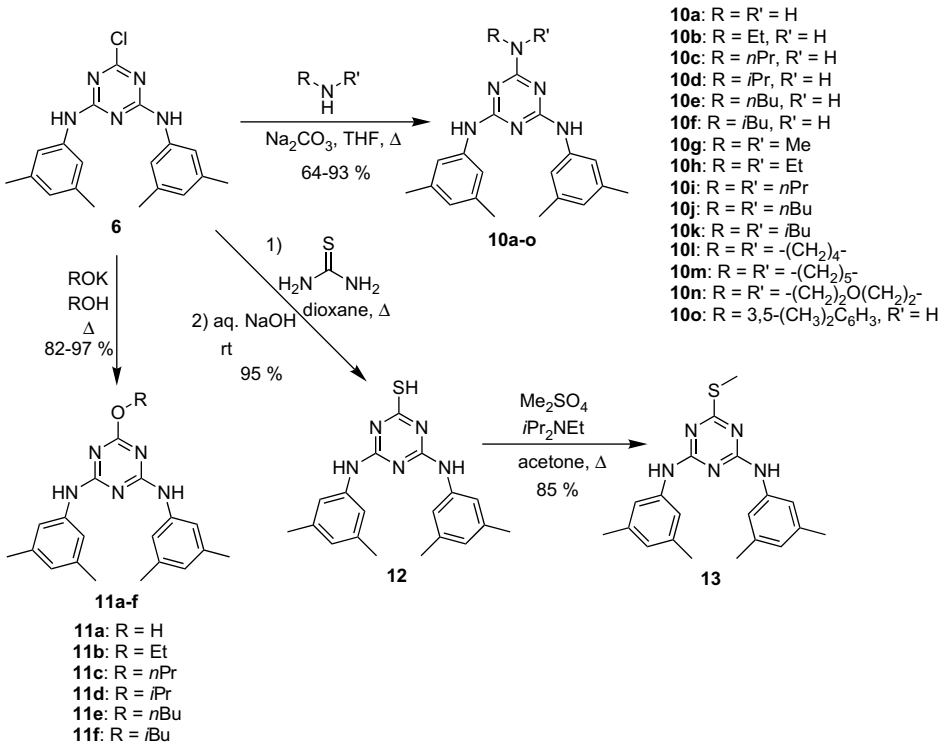
2.1. Synthesis of 4,6-bis(mexylamino)-1,3,5-triazine derivatives

The transesterification of compound **2a** with alcohols has already been reported for ethyl, *n*-propyl, and *n*-butyl esters **2b**–**d**.[14] To further expand the series to study the effect of alkyl chain branching and longer linear chains, isopropyl, isobutyl, *n*-hexyl, and *n*-octyl esters **7a**–**d** were synthesized using a similar method (Scheme 1), typically in good yields except for the isopropyl and *n*-octyl derivatives **7a** and **7d**. Ester **2a** could also be converted to the carboxamide **8a** by transamidation with aqueous ammonia in refluxing dioxane, while the same reaction with various amines gave secondary amides **8b**–**g**. Near quantitative yields were obtained for all compounds (Scheme 1). Finally, compound **2a** was reduced with $LiAlH_4$ in THF to give hydroxymethyl derivative **9** in 86% yield (Scheme 1).



Scheme 1.

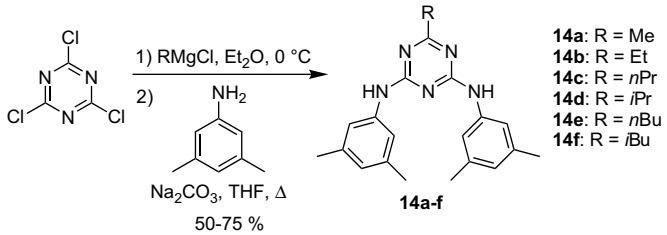
Compound **6** constitutes another appealing precursor, which can be substituted with various nucleophiles to give a wide range of derivatives; methoxy derivative **3** and methylamino compound **4** have both already been reported and exhibited glass-forming ability.[14] Other amino compounds were synthesized using a slightly different procedure starting from chlorotriazine **6**. Reaction with aqueous ammonia gave amino compound **10a** while reaction with various primary and secondary amines gave substituted amino



Scheme 2.

derivatives **10b**–**n** in excellent yields (Scheme 2). Symmetrically substituted 2,4,6-tris(mexylamino)-1,3,5-triazine **10o** was synthesized in one step in 90% yield from 3,5-dimethylaniline and cyanuric chloride. Hydroxy compound **11a** was synthesized by treating precursor **6** with KOH in dioxane, while alkoxy compounds **11b**–**f** were obtained in good yields by substituting the chloro group of compound **6** with the corresponding potassium alkoxides generated in situ from potassium and the corresponding alcohols (Scheme 2). Thiol-substituted triazine **12** was synthesized in excellent yield by refluxing chlorotriazine **6** with thiourea in dioxane followed by a basic treatment;[18] compound **12** could be *S*-methylated with dimethyl sulfate in acetone in the presence of DIEA to give methyl thioether **13** in 85% yield (Scheme 2).

Alkyltriazines **14a**–**f** were synthesized in global 50–75% yield by reacting cyanuric chloride with the corresponding alkylmagnesium chlorides in ether under inert atmosphere[19] followed by reaction of the two other chloride groups with 3,5-dimethylaniline in refluxing THF (Scheme 3).



Scheme 3.

By heating compound **1** in DMF it is possible to generate compound **15**, which is unsubstituted at the 2-position of the triazine ring, with a yield of 76% (Scheme 4). Condensation of biguanide **1** with methyl chloroacetate in refluxing MeOH for 2 h[20] yielded chloromethyl derivative **16**, albeit in low yield (39%) (Scheme 4).

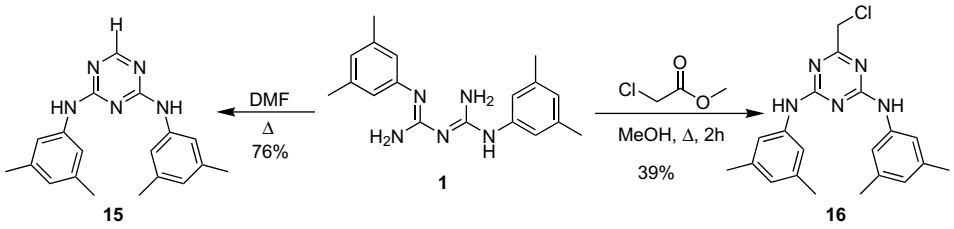
2.2. Thermal behavior of molecular glasses

The thermal behavior of all compounds described herein has been studied by DSC. The glass transition temperatures (T_g), crystallization temperatures (T_c), and melting points (T_m) are reported in Table 1. Most compounds show a glass transition on slow cooling (5 °C/min) with no crystallization upon heating (representative thermograms of compound **7a** is shown in Fig. 1). Conducting the DSC on several heating/cooling cycles consistently gave similar T_g values both upon heating and upon cooling. All compounds are stable up to 250 °C except for ester derivatives **2a** and **7a**–**d**, which decompose upon prolonged heating over 160 °C.

Aside from compounds **5** and **6**, only 5 of the 43 newly reported compounds did not show any glass formation: primary amide **8a**, hydroxyl and thiol-substituted compounds **11a** and **12**, symmetric trimexyl derivative **10o**, and unsubstituted **15**. For these compounds, the head group possesses features that facilitate efficient packing between molecules, favoring crystallization: strong hydrogen bonding motifs for carboxylic acid **5** and carboxamide **8a**, higher symmetry for trimexylamino derivative **10o**, tautomerism for compounds **11a** and **12**, or a smaller substituent, which is less disruptive to packing for compounds **6**, **11a**, **12**, and **15**.

Alkyl chains, which are too long or too short result in compounds showing poor stability of the glassy phase exemplified by rapid crystallization upon heating at 5 °C/min (a representative thermogram of poor glass-former **8f** is shown in Fig. 2).

The optimal alkyl chain length depends on the functional group: for example, ester derivatives with *n*-hexyl or longer chains and *n*-butyl amide **8f** have shown poor glass-forming ability as evidenced by crystallization upon heating, which can be observed by DSC (octyl ester **7d** did not show any crystallization during the DSC experiment but crystallizes overnight on standing at room temperature). For tertiary amines, derivatives with linear chains smaller than butyl all crystallize rapidly upon heating, and for alkyltriazines **14a**–**f**, the methyl-substituted compound crystallizes



Scheme 4.

Table 1
Glass transition temperatures (T_g) for bis(mexylamino)triazines **2**–**16**, measured at 5 °C/min (or 10 °C/min for compounds **11b**–**f**)

Compound	R	T_g (°C)	T_c (°C)	T_m (°C)	Ref.	Compound	R	T_g (°C)	T_c (°C)	T_m (°C)	Ref.
15	–H	—	—	251 (dec)		**10g**	$-NMe_2$	65	101	181	
6	–Cl	—	—	191	14	**10h**	$-NEt_2$	57	79	174	
5	$-CO_2H$	—	—	143 (dec)	16	**10i**	$-NPr_2$	40	81	149	
2a	$-CO_2Me$	75	—	—	16	**10j**	$-NBu_2$	26	—	119	
2b	$-CO_2Et$	62	—	—	14	**10k**	$-N^iBu_2$	45	—	—	
2c	$-CO_2Pr$	58	—	—	14	**10l**	–Pyrrolidinyl	72	—	180	
7a	$-CO_2{}^iPr$	57	—	164		**10m**	–Piperidinyl	67	—	165	
2d	$-CO_2Bu$	54	—	—	14	**10n**	–Morpholinyl	72	—	165	
7b	$-CO_2{}^iBu$	51	—	152		**10o**	–NHMexyl	—	—	327 (dec)	
7c	$-CO_2C_6H_{13}$	41	117	138		**11a**	–OH	—	—	>350 (dec)	
7d	$-CO_2C_8H_{17}$	34	—	122		**3**	–OMe	58	—	168	14 (54 °C)
8a	$-CONH_2$	—	—	285 (dec)		**11b**	–OEt	53	—	188	
8b	–CONHMe	84	—	—		**11c**	–OPr	49	—	161	
8c	–CONHEt	76	—	—		**11d**	$-O^iPr$	63	—	—	
8d	–CONHPr	63	—	—		**11e**	–OBu	43	—	124	
8e	$-CONH^iPr$	78	—	—		**11f**	$-O^iBu$	52	—	—	
8f	–CONHBu	59	112	170		**12**	–SH	—	—	286 (dec)	
8g	$-CONH^iBu$	72	—	173		**13**	–SMe	54	—	159	
9	$-CH_2OH$	59	—	—		**14a**	–Me	59	103	168	
10a	$-NH_2$	97	—	203		**14b**	–Et	41	—	135	
4	–NHMe	94	—	—	14	**14c**	–Pr	39	—	135	
10b	–NHEt	85	—	—		**14d**	$-{}^iPr$	43	—	—	
10c	–NHPr	80	—	—		**14e**	–Bu	31	—	105	
10d	$-NH^iPr$	94	—	—		**14f**	$-{}^iBu$	38	—	—	
10e	–NHBu	65	—	162		**16**	$-CH_2Cl$	44	—	—	
10f	$-NH^iBu$	83	—	—							

readily. In these cases, we propose that alkyl chains of improper size allow a more optimal solid-state packing, which favors crystallization, and the chain length range for optimal glass-forming ability varies from one functional group to the other. However, for all functional groups, T_g decreases with increasing alkyl chain length (Fig. 3), and in most cases, branched alkyl groups exhibit T_g 8–12 °C higher than their linear counterparts. The effect of increasing alkyl chain length on T_g is more pronounced on series of compounds with higher T_g, as evidenced in Figure 3.

The stability toward crystallization of glass-forming compounds varies from one compound to another; in all cases, heating the compounds over T_g for a prolonged period of time will cause the sample to crystallize, but this process can take between a few hours (compounds **2a** and **3**, for example) to several weeks or even months (an amorphous sample of compound **4** left in an oven at 120 °C only showed the first signs of crystallization after 3 weeks, while a sample of ethylamino derivative **10b** under the same conditions did not show any crystallization after 4 months!).

3. Conclusion

Our approach to design novel molecular glasses, which exploit hydrogen bonding has allowed us to develop a whole family of compounds that can readily form glassy phases and that show an increased resistance to crystallization. In these studies, we have identified the bis(mexylamino)triazine moiety as a general structural motif capable of promoting glass formation. The glass-forming properties of this molecular building block were shown to be tolerant of a wide variety of functional groups, making the bis(mexylamino)triazine group an attractive candidate as a glass-inducing unit to be attached to more complex molecules otherwise incapable of glass formation. The extreme resistance toward crystallization shown by some compounds of this family, even at temperatures above T_g, makes this even more compelling. The lessons learned herein hold the promise of helping develop strategies toward the design of improved molecular glasses, which will lead to the design of functional glasses for practical applications. To reach this goal, however, a greater understanding of the correlations between molecular structure and T_g will need to be achieved; the relationship between molecular structure and glass-forming ability will thus be probed in greater depth in future studies.

4. Experimental section

4.1. General

1,5-Dimexylbiguanide (**1**) and its hydrochloride salt,[15] methyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxylate (**2a**),[16] 2-methoxy-4,6-bis(mexylamino)-1,3,5-triazine (**3**),[14] 2-methylamino-4,6-bis(mexylamino)-1,3,5-triazine (**4**),[14] and 2-chloro-4,6-bis(mexylamino)-1,3,5-triazine (**6**)[14] were prepared according to literature procedures, while all other reagents were commercial products purchased from Aldrich and were used without further purification. ACS reagent grade solvents were purchased from Caledon

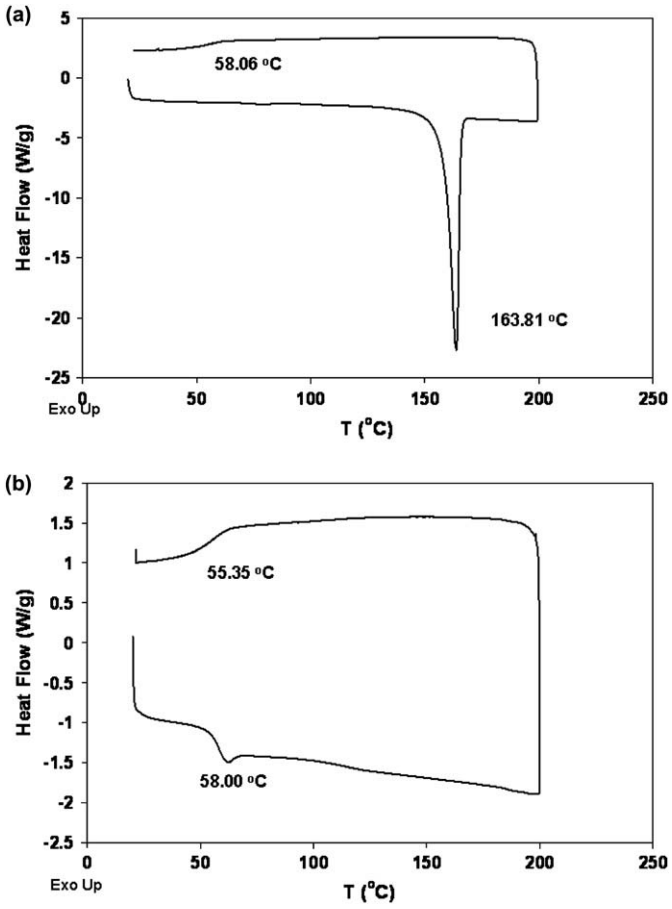


Figure 1. Representative thermograms obtained by differential scanning calorimetry (DSC) of a crystalline sample of molecular glass **7a**, recorded at a heating/cooling rate of 5 °C/min. (a) First heating/cooling cycle. (b) Second heating/cooling cycle. T_g and T_m are indicated in each case. After the initial melting of the crystalline sample, no further melting or crystallization can be observed.

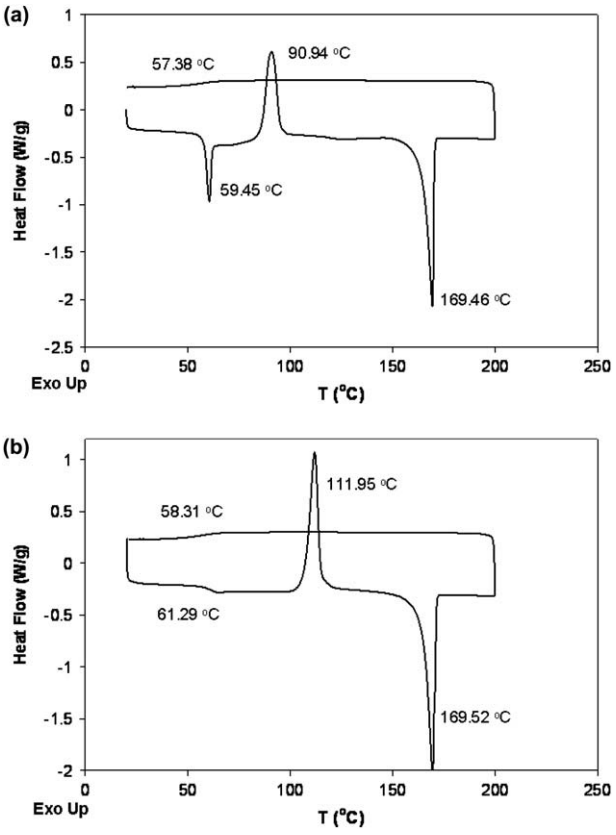


Figure 2. Representative thermograms obtained by differential scanning calorimetry (DSC) of an amorphous sample of compound **8f**, recorded at a heating/cooling rate of 5 °C/min. (a) First heating/cooling cycle. (b) Second heating/cooling cycle. T_g, T_c, and T_m are indicated in each case. The sharp signal observed as the sample undergoes glass transition in the initial heating run can be attributed to loss of solvent present in the sample. In both heating cycles, the sample undergoes crystallization followed by melting, showing poor glass-forming ability.

Laboratories and were used without further purification. SiliaFlash P60 grade silica gel and TLC plates were purchased from SiliCycle. Unless otherwise noted, the reactions were performed under ambient atmosphere. NMR spectra were recorded on a Bruker Avance 400 MHz or a Varian Mercury 300 MHz spectrometer at 298 K unless otherwise noted. Infrared spectra were recorded on a Perkin Elmer Spectrum GX spectrometer as thin films deposited from $CHCl_3$ solution on KBr windows or as solids in KBr. T_g, T_c, and T_m were recorded by DSC with a TA Instruments Q100 calorimeter (see Section 4.3).

4.2. Synthesis of 4,6-bis(mexylamino)-1,3,5-triazine derivatives

*4.2.1. Isopropyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxylate **7a***

A small chunk of sodium metal was dissolved in isopropanol (30 mL) in a round-bottomed flask equipped with a magnetic stirrer. Methyl ester **2a** (0.377 g, 1.00 mmol) was added, then a water-jacketed condenser was fitted on the flask and the mixture was refluxed for 18 h. After evaporation of the volatiles, the crude product was purified by flash chromatography on silica with 20% AcOEt/Hexanes as eluent. The fractions containing the desired product were collected and the solvent was evaporated to yield 0.231 g pure **7a** (0.570 mmol, 57%); T_g 57 °C, T_m 164 °C; IR ($CHCl_3$/KBr) 3413, 3272, 3190, 2985, 2923, 2855, 1737, 1614, 1580, 1561, 1523, 1439, 1388, 1377, 1363, 1325, 1302, 1263, 1173, 1106, 1054, 994, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 2H), 7.13 (s, 4H), 6.77 (s, 2H), 5.32 (m, ^3J=6.4 Hz, 1H), 2.28 (s, 12H), 1.44 (d, ^3J=6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 163.1, 138.6, 137.4, 126.1, 119.0, 70.8, 21.6, 21.3; HRMS (ESI) calcd for $C_{23}H_{28}N_5O_2$ *m/z*: 406.2238, found: 406.2239.

Compounds **7b**–**d** were synthesized by the same procedure with the corresponding alcohols as solvents, and the crude products were purified by filtration on a short silica pad with $CHCl_3$ as eluent.

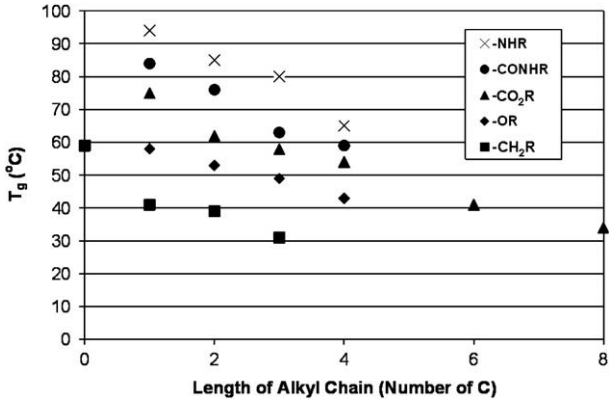


Figure 3. Graph of T_g as a function of alkyl chain length for series of molecular glasses with –NHR, –CONHR, $–CO_2R$, –OR, and $–CH_2R$ as the head group, where R is methyl, ethyl, propyl, butyl, *n*-hexyl, and *n*-octyl.

4.2.2. Isobutyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxylate **7b**

Yield: 69%; T_g 51 °C; IR ($CHCl_3$/KBr) 3402, 3271, 3232, 3187, 3102, 2960, 2918, 2873, 2849, 1745, 1616, 1585, 1560, 1526, 1435, 1394, 1377, 1346, 1336, 1303, 1262, 1172, 1054, 1001, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 2H), 7.14 (s, 4H), 6.77 (s, 2H), 4.18 (d, ^3J=6.9 Hz, 2H), 2.27 (s, 12H), 2.15 (m, ^3J=6.8 Hz, 1H), 1.03 (br s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 163.3, 138.3, 137.2, 125.9, 118.9, 72.2, 27.5, 21.1, 18.9; HRMS (ESI) calcd for $C_{24}H_{30}N_5O_2$ *m*/*z*: 420.2394, found: 420.2398.

4.2.3. n-Hexyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxylate **7c**

Yield: 77%; T_g 41 °C, T_c 117 °C, T_m 138 °C; IR ($CHCl_3$/KBr) 3406, 3272, 3233, 3192, 3108, 2956, 2922, 2870, 2859, 1745, 1615, 1589, 1559, 1528, 1439, 1392, 1379, 1344, 1304, 1263, 1170, 1056, 997, 889 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (s, 2H), 7.15 (s, 4H), 6.78 (s, 2H), 4.42 (t, ^3J=6.9 Hz, 2H), 2.28 (s, 12H), 1.82 (quint, ^3J=6.9, 2H), 1.43 (m, 2H), 1.34 (m, 4H), 0.90 (t, ^3J=6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 163.3, 138.3, 137.2, 125.9, 118.9, 66.7, 31.2, 28.2, 25.2, 22.3, 21.1, 13.8; HRMS (ESI) calcd for $C_{26}H_{34}N_5O_2$ *m*/*z*: 448.2707, found: 448.2708.

4.2.4. n-Octyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxylate **7d**

The remaining octanol was distilled on Kugelrohr. Yield: 40%; T_g 34 °C, T_m 122 °C; IR ($CHCl_3$/KBr) 3409, 3271, 3233, 3190, 3106, 2956, 2924, 2856, 1745, 1615, 1590, 1561, 1528, 1438, 1393, 1379, 1344, 1322, 1304, 1262, 1170, 1055, 997, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 2H), 7.13 (s, 4H), 6.77 (s, 2H), 4.36 (t, ^3J=6.9 Hz, 2H), 2.27 (s, 12H), 1.78 (quint, ^3J=7.4 Hz, 2H), 1.40 (br s, 2H), 1.27 (m, 8H), 0.88 (t, ^3J=6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 163.3, 138.4, 137.2, 126.1, 119.0, 66.8, 31.6, 29.0 (29.03), 29.0 (28.96), 28.3, 25.6, 22.5, 21.1, 13.9; HRMS (ESI) calcd for $C_{28}H_{38}N_5O_2$ *m*/*z*: 476.3020, found: 476.3025.

4.2.5. 4,6-Bis(mexylamino)-1,3,5-triazine-2-carboxamide **8a**

To a solution of **2a** (0.5 g, 1.325 mmol) in dioxane (15 mL) in a round-bottomed flask was added 30% aqueous NH_4OH (10 mL) and the reaction was refluxed overnight. After the reaction mixture was brought back to room temperature, H_2O was added, then the precipitate was filtered, washed with toluene and dried on the vacuum pump to yield 0.42 g of **8a** (1.16 mmol, 88%); mp 285 °C; IR (KBr) 3402, 3306, 3238, 2945, 2915, 2853, 1708, 1665, 1617, 1576, 1541, 1475, 1427, 1374, 1360, 1300, 1173, 1124, 1073, 1037, 996, 930, 886, 871, 840 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 9.93 (s, 2H), 7.76 (s, 1H), 7.73 (s, 1H), 7.30 (s, 4H), 6.70 (s, 2H), 2.21 (s, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.4, 164.8, 164.2, 138.7, 137.4, 124.6, 118.6, 21.0; HRMS (ESI) calcd for $C_{20}H_{23}N_6O$ *m*/*z*: 363.1928, found: 363.1940.

Compounds **8b** and **8c** were synthesized by similar procedures with the corresponding amines in aqueous solution, and the crude products were purified on silica using acetone as eluent.

4.2.6. N-Methyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxamide **8b**

Compound **2a** was reacted with a 40 wt % aqueous methylamine solution. Yield: 99%; T_g 84 °C; IR ($CHCl_3$/KBr) 3373, 3281, 3192, 3103, 2953, 2918, 2850, 1683, 1615, 1585, 1524, 1435, 1378, 1320, 1302, 1264, 1234, 1175, 1074, 1034, 988, 886, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (br s, 1H), 7.40 (s, 2H), 7.13 (s, 4H), 6.77 (s, 2H), 3.01 (d, ^3J=5.0 Hz, 3H), 2.27 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 164.8, 163.3, 138.8, 137.7, 126.3, 119.3, 26.7, 21.6; HRMS (ESI) calcd for $C_{21}H_{25}N_6O$ *m*/*z*: 377.2089, found: 377.2086.

4.2.7. N-Ethyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxamide **8c**

A 70 wt % aqueous ethylamine solution was used. Yield: 98%; T_g 76 °C; IR ($CHCl_3$/KBr) 3373, 3283, 3194, 3142, 3106, 2975, 2918, 2874, 2851, 1685, 1615, 1587, 1524, 1435, 1379, 1356, 1321, 1302, 1266, 1176, 1039, 993, 968, 928, 886, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (br s, 1H), 7.34 (s, 2H), 7.15 (s, 4H), 6.78 (s, 2H), 3.50 (t, ^3J=6.5 Hz, 2H), 2.28 (s, 12H), 1.26 (t, ^3J=6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 165.0, 162.5, 139.0, 137.9, 126.5, 119.4, 35.0, 21.8, 15.0; HRMS (ESI) calcd for $C_{22}H_{27}N_6O$ *m*/*z*: 391.2246, found: 391.2277.

4.2.8. N-Propyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxamide **8d**

To a stirred solution of compound **2a** (0.377 g, 1.00 mmol) in dioxane (10 mL) in a 50 mL round-bottomed flask equipped with a water-jacketed condenser was added *n*-propylamine (10 mL) then the mixture was refluxed for 18 h. After cooling down to room temperature, the volatiles were removed under reduced pressure, and the crude product was filtered on a short silica pad with acetone as eluent and the recovered fraction was dried in vacuo to yield 0.380 g **8d** (0.940 mmol, 94%); T_g 63 °C; IR ($CHCl_3$/KBr) 3373, 3280, 3193, 3143, 2964, 2919, 2874, 2850, 1686, 1615, 1587, 1524, 1465, 1436, 1321, 1304, 1264, 1176, 1037, 987, 964, 936, 886, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (br s, 1H), 7.34 (s, 2H), 7.15 (s, 4H), 6.78 (s, 2H), 3.43 (q, ^3J=6.1 Hz, 2H), 2.29 (s, 12H), 1.65 (q, ^3J=7.0 Hz, 2H), 1.00 (t, ^3J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 164.8, 162.5, 138.8, 137.7, 126.3, 119.2, 41.6, 22.9, 21.6, 11.7; HRMS (ESI) calcd for $C_{23}H_{29}N_6O$ *m*/*z*: 405.2402, found: 405.2410.

Compounds **8e**–**g** were synthesized by similar procedures with the corresponding amines.

4.2.9. N-Isopropyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxamide **8e**

Yield: 91%; T_g 78 °C; IR ($CHCl_3$/KBr) 3372, 3278, 3194, 3142, 2972, 2920, 2872, 2852, 1688, 1615, 1585, 1523, 1435, 1391, 1321, 1303, 1267, 1259, 1175, 1129, 1060, 1038, 978, 922, 885, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, ^3J=7.9 Hz, 1H), 7.42 (s, 2H), 7.15 (s, 4H), 6.77 (s, 2H), 4.26 (m, ^3J=7.0 Hz, 2H), 2.28 (s, 12H), 1.26 (d, ^3J=7.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 164.8, 161.5, 138.8, 137.7, 126.3, 119.1, 42.0, 22.8, 21.6; HRMS (ESI) calcd for $C_{23}H_{29}N_6O$ *m*/*z*: 405.2402, found: 405.2427.

4.2.10. N-Butyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxamide **8f**

Yield: 92%; T_g 59 °C, T_c 112 °C, T_m 170 °C; IR ($CHCl_3$/KBr) 3374, 3279, 3194, 3138, 2960, 2919, 2873, 2862, 2851, 1687, 1615, 1585, 1524, 1464, 1435, 1321, 1303, 1266, 1175, 1037, 971, 885, 843 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (t, ^3J=5.2 Hz, 1H), 7.30 (s, 2H), 7.15 (s, 4H), 6.79 (s, 2H), 3.47 (q, ^3J=8.0 Hz, 2H), 2.29 (s, 12H), 1.61 (m, 2H), 1.43 (m, 2H), 0.96 (t, ^3J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.7, 164.5, 162.0, 138.4, 137.3, 126.0, 118.8, 39.3, 31.3, 21.2, 20.0, 13.6; HRMS (ESI) calcd for $C_{24}H_{31}N_6O$ *m*/*z*: 419.2554, found: 419.2557.

4.2.11. N-Isobutyl 4,6-bis(mexylamino)-1,3,5-triazine-2-carboxamide **8g**

Yield: 96%; T_g 72 °C, T_m 173 °C; IR ($CHCl_3$/KBr) 3373, 3279, 3192, 3139, 2960, 2921, 2871, 1687, 1615, 1586, 1524, 1468, 1434, 1321, 1303, 1270, 1174, 1039, 996, 971, 933, 886, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (br s, 2H), 7.63 (br s, 1H), 7.15 (s, 4H), 6.78 (s, 2H), 3.29 (t, ^3J=6.4 Hz, 2H), 2.28 (s, 12H), 1.90 (m, ^3J=6.4 Hz, 1H), 0.99 (d, ^3J=6.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 165.0, 162.6, 139.0, 137.9, 126.5, 119.4, 47.4, 28.9, 21.8, 20.6; HRMS (ESI) calcd for $C_{24}H_{31}N_6O$ *m*/*z*: 419.2554, found: 419.2575.

4.2.12. 2-Hydroxymethyl-4,6-bis(mexylamino)-1,3,5-triazine **9**

To a suspension of $LiAlH_4$ (0.754 g, 19.87 mmol) in dry THF (50 mL) in a round-bottomed flask under inert atmosphere was added dropwise a solution of **2a** (5.0 g, 13.25 mmol) in dry THF

(50 mL) at 0 °C. The reaction was stirred for 1 h while letting it warm to room temperature, then H_2O was added dropwise until hydrogen evolution had stopped. Aqueous HCl (1 M, 20 mL) and AcOEt were added and the two phases were extracted. The organic phase was extracted with saturated aqueous K_2CO_3, and then the combined aqueous phases were extracted with AcOEt. The combined organic phases were then dried over $MgSO_4$, filtered, and the solvent was evaporated, then the crude product was purified on silica using acetone as eluent to yield 3.98 g of **9** (11.4 mmol, 86%); T_g 59 °C; IR ($CHCl_3$/KBr) 3378, 3283, 3232, 3192, 2950, 2919, 2851, 1613, 1588, 1524, 1434, 1394, 1378, 1320, 1302, 1267, 1177, 1116, 1093, 1055, 996, 973, 930, 884, 841 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.23 (s, 2H), 7.13 (s, 4H), 6.77 (s, 2H), 4.51 (s, 2H), 3.76 (br s, 1H), 2.28 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$, 278 K) δ 176.7, 163.6, 138.5, 137.6, 125.9, 119.1, 63.7, 21.5; HRMS (ESI) calcd for $C_{20}H_{24}N_5O$ m/z: 350.1975, found: 350.1978.

4.2.13. 2-Amino-4,6-bis(mexylamino)-1,3,5-triazine **10a**

To a stirred solution of chlorotriazine **6** (32.4 g, 91.6 mmol) in THF (250 mL) in a round-bottomed flask was added 30 wt% aqueous NH_4OH (25 mL) and the reaction was refluxed overnight. After letting the reaction cool down to room temperature, AcOEt and H_2O were added, and the two layers were separated. The organic layer was then extracted with aqueous K_2CO_3 then with brine. The organic layer was then dried over $MgSO_4$ and the solvent was evaporated, yielding 28.0 g **10a** (83.8 mmol, 91%); T_g 97 °C; IR ($CHCl_3$/KBr) 3486, 3392, 3295, 3171, 2952, 2918, 2850, 1614, 1590, 1551, 1518, 1433, 1377, 1359, 1324, 1302, 1257, 1192, 1178, 1148, 1069, 1036, 982, 957, 885, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 2H), 7.11 (s, 4H), 6.70 (s, 2H), 5.29 (s, 2H), 2.25 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 164.6, 138.4, 138.3, 125.3, 118.9, 21.3; HRMS (ESI) calcd for $C_{19}H_{23}N_6$ m/z: 335.1979, found: 335.1970.

Compounds **10b–n** were synthesized by the same procedure from the corresponding amines, and then the crude products were purified by filtration on a short silica pad with $CHCl_3$ as eluent.

4.2.14. 2-Ethylamino-4,6-bis(mexylamino)-1,3,5-triazine **10b**

A 70 wt% aqueous ethylamine solution was used. Yield: 79%; T_g 85 °C; IR ($CHCl_3$/KBr) 3391, 3277, 3159, 2972, 2919, 2872, 1590, 1558, 1516, 1428, 1376, 1357, 1323, 1301, 1245, 1188, 1096, 1037, 997, 979, 958, 937, 885, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.43 (s, 1H), 7.20 (s, 2H), 7.16 (s, 2H), 6.67 (s, 2H), 5.49 (s, 1H), 3.43 (quint, ^3J=6.9 Hz, 2H), 2.26 (s, 12H), 1.18 (t, ^3J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 164.3, 138.9, 138.7, 138.2, 124.8, 124.4, 118.5, 118.0, 35.6, 21.3, 14.8; HRMS (ESI) calcd for $C_{21}H_{27}N_6$ m/z: 363.2292, found: 363.2292.

4.2.15. 2-Propylamino-4,6-bis(mexylamino)-1,3,5-triazine **10c**

Yield: 78%; T_g 80 °C; IR ($CHCl_3$/KBr) 3388, 3279, 3156, 2963, 2919, 2874, 1590, 1559, 1517, 1427, 1378, 1361, 1325, 1300, 1260, 1244, 1187, 1156, 1098, 1037, 884, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.48 (s, 1H), 7.21 (s, 2H), 7.15 (s, 2H), 6.67 (s, 2H), 5.61 (s, 1H), 3.34 (q, ^3J=7.9 Hz, 2H), 2.26 (s, 12H), 1.59 (sex, ^3J=7.3 Hz, 2H), 0.94 (t, ^3J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 164.3, 164.0, 138.9, 138.6, 138.2, 124.9, 124.4, 118.6, 117.9, 42.7, 22.9, 21.3, 11.4; HRMS (ESI) calcd for $C_{22}H_{29}N_6$ m/z: 377.2448, found: 377.2467.

4.2.16. 2-Isopropylamino-4,6-bis(mexylamino)-1,3,5-triazine **10d**

Yield: 64%; T_g 94 °C; IR ($CHCl_3$/KBr) 3387, 3281, 2969, 2919, 2867, 1593, 1559, 1512, 1426, 1384, 1361, 1325, 1300, 1245, 1193, 1181, 1128, 1098, 1036, 932, 883, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (br s, 1H), 7.53 (br s, 1H), 7.21 (s, 2H), 7.18 (s, 2H), 6.67 (s, 2H), 5.46 (s, 1H), 4.19 (m, ^3J=6.8 Hz, 1H), 2.26 (s, 12H), 1.18 (d, ^3J=6.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 164.6, 139.1, 138.6, 138.5, 125.1, 124.7, 118.7, 118.2, 42.8, 23.0, 21.6; HRMS (ESI) calcd for $C_{22}H_{29}N_6$ m/z: 377.2448, found: 377.2435.

4.2.17. 2-Butylamino-4,6-bis(mexylamino)-1,3,5-triazine **10e**

Yield: 85%; T_g 65 °C, T_m 162 °C; IR ($CHCl_3$/KBr) 3386, 3278, 2958, 2919, 2871, 2861, 2850, 1590, 1559, 1516, 1426, 1360, 1324, 1301, 1186, 1036, 884, 840 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (br s, 1H), 7.51 (br s, 1H), 7.21 (s, 2H), 7.15 (s, 2H), 6.67 (s, 2H), 5.62 (s, 1H), 3.38 (q, ^3J=6.6 Hz, 2H), 2.25 (s, 12H), 1.52 (quint, ^3J=7.2 Hz, 2H), 1.36 (sex, ^3J=7.4 Hz, 2H), 0.92 (t, ^3J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 164.3, 164.1, 139.0, 138.7, 138.2, 124.8, 124.3, 118.5, 117.9, 40.6, 31.6, 21.3, 20.1, 13.7; HRMS (ESI) calcd for $C_{23}H_{31}N_6$ m/z: 391.2605, found: 391.2600.

4.2.18. 2-Isobutylamino-4,6-bis(mexylamino)-1,3,5-triazine **10f**

Yield: 93%; T_g 83 °C; IR ($CHCl_3$/KBr) 3389, 3280, 3145, 2957, 2920, 2870, 1597, 1560, 1517, 1426, 1386, 1359, 1324, 1300, 1277, 1262, 1244, 1187, 1158, 1100, 884, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (br s, 1H), 7.40 (br s, 1H), 7.21 (s, 2H), 7.14 (s, 2H), 6.68 (s, 2H), 5.60 (s, 1H), 3.21 (t, ^3J=6.4 Hz, 2H), 2.26 (s, 12H), 1.87 (m, ^3J=6.4 Hz, 1H), 0.93 (d, ^3J=6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 164.6, 164.5, 139.3, 139.0, 138.6, 138.4, 125.2, 124.7, 118.9, 118.2, 48.8, 28.8, 21.6, 20.5; HRMS (ESI) calcd for $C_{23}H_{31}N_6$ m/z: 391.2605, found: 391.2625.

4.2.19. 2-Dimethylamino-4,6-bis(mexylamino)-1,3,5-triazine **10g**

Yield: 75%; T_g 65 °C, T_c 101 °C, T_m 181 °C; IR ($CHCl_3$/KBr) 3387, 3287, 3211, 3102, 2943, 2918, 2863, 1601, 1555, 1530, 1425, 1403, 1328, 1301, 1272, 1247, 1181, 1081, 1037, 978, 903, 881, 840 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 2H), 7.22 (s, 4H), 6.68 (s, 2H), 3.22 (s, 6H), 2.28 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 139.1, 138.2, 124.3, 117.9, 36.3, 21.4; HRMS (ESI) calcd for $C_{21}H_{27}N_6$ m/z: 363.2292, found: 363.2298.

4.2.20. 2-Diethylamino-4,6-bis(mexylamino)-1,3,5-triazine **10h**

Yield: 84%; T_g 57 °C, T_c 79 °C, T_m 174 °C; IR ($CHCl_3$/KBr) 3386, 3290, 3211, 3159, 3102, 2971, 2928, 2919, 2867, 2851, 1606, 1553, 1519, 1458, 1425, 1377, 1358, 1329, 1306, 1249, 1222, 1179, 1098, 881, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 2H), 7.25 (s, 4H), 6.67 (s, 2H), 3.68 (q, ^3J=7.0 Hz, 4H), 2.28 (s, 12H), 1.30 (t, ^3J=7.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 164.4, 139.7, 138.4, 124.2, 117.8, 42.1, 21.7, 13.6; HRMS (ESI) calcd for $C_{23}H_{31}N_6$ m/z: 391.2610, found: 391.2622.

4.2.21. 2-Dipropylamino-4,6-bis(mexylamino)-1,3,5-triazine **10i**

Yield: 82%; T_g 40 °C, T_c 82 °C, T_m 149 °C; IR ($CHCl_3$/KBr) 3387, 3288, 3212, 3096, 2965, 2931, 2920, 2872, 1606, 1553, 1518, 1428, 1380, 1328, 1300, 1275, 1247, 1179, 1105, 978, 934, 882, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (s, 2H), 7.19 (s, 4H), 6.66 (s, 2H), 3.55 (t, ^3J=7.6 Hz, 4H), 2.28 (s, 12H), 1.72 (sex, ^3J=7.4 Hz, 4H), 0.98 (t, ^3J=7.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 164.3, 139.7, 138.4, 124.3, 117.8, 49.8, 21.7, 21.4, 11.9; HRMS (ESI) calcd for $C_{25}H_{35}N_6$ m/z: 419.2923, found: 419.2929.

4.2.22. 2-Dibutylamino-4,6-bis(mexylamino)-1,3,5-triazine **10j**

The crude product was solubilized in a minimal amount of toluene, then EtOH was added, causing compound **10j** to crystallize. The crystals were collected by filtration. Yield: 69%; T_g 26 °C, T_m 119 °C; IR ($CHCl_3$/KBr) 3343, 3280, 3244, 3212, 3099, 2958, 2929, 2873, 2861, 1610, 1592, 1563, 1517, 1443, 1429, 1373, 1355, 1328, 1302, 1239, 1180, 1113, 913, 884, 845 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (s, 4H), 6.72 (s, 2H), 6.67 (s, 2H), 3.56 (t, ^3J=7.6 Hz, 4H), 2.30 (s, 12H), 1.64 (quint, ^3J=7.6 Hz, 4H), 1.39 (sex, ^3J=7.5 Hz, 4H), 0.96 (t, ^3J=7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 164.0, 139.4, 138.1, 124.0, 117.5, 47.3, 30.1, 21.4, 20.4, 14.0; HRMS (ESI) calcd for $C_{27}H_{39}N_6$ m/z: 447.3231, found: 447.3219.

4.2.23. 2-Diisobutylamino-4,6-bis(mexylamino)-1,3,5-triazine ***10k***

Yield: 88%; T_g 45 °C; IR ($CHCl_3$/KBr) 3393, 3291, 3212, 3162, 3099, 2960, 2922, 2869, 1606, 1552, 1515, 1465, 1429, 1387, 1366, 1330, 1289, 1248, 1180, 1107, 1036, 980, 880, 839 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 (s, 2H), 7.20 (s, 4H), 6.67 (s, 2H), 3.50 (d, ^3J=7.3 Hz, 4H), 2.28 (s, 12H), 2.26 (m, ^3J=6.7 Hz, 2H), 0.97 (d, ^3J=6.5 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 164.1, 139.7, 138.4, 124.3, 117.8, 55.6, 27.2, 21.7, 20.7; HRMS (ESI) calcd for $C_{27}H_{39}N_6$ *m*/*z*: 447.3231, found: 447.3241.

4.2.24. 2-Pyrrolidinyl-4,6-bis(mexylamino)-1,3,5-triazine ***10l***

Yield: 81%; T_g 72 °C, T_m 180 °C; IR ($CHCl_3$/KBr) 3422, 3388, 3282, 3204, 3161, 3099, 2969, 2950, 2919, 2872, 2850, 1595, 1551, 1515, 1480, 1427, 1367, 1339, 1325, 1301, 1246, 1198, 1178, 1037, 913, 883, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 4H), 7.06 (s, 2H), 6.66 (s, 2H), 3.64 (t, ^3J=6.7 Hz, 4H), 2.28 (s, 12H), 1.98 (t, ^3J=6.8 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 164.1, 139.8, 138.6, 124.5, 118.2, 46.5, 25.8, 21.9; HRMS (ESI) calcd for $C_{23}H_{29}N_6$ *m*/*z*: 389.2453, found: 389.2425.

4.2.25. 2-Piperidinyl-4,6-bis(mexylamino)-1,3,5-triazine ***10m***

Yield: 77%; T_g 67 °C, T_m 165 °C; IR ($CHCl_3$/KBr) 3383, 3278, 3158, 3101, 2933, 2919, 2851, 1594, 1548, 1510, 1431, 1377, 1360, 1326, 1286, 1248, 1182, 1107, 1026, 997, 976, 955, 881, 840 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (s, 4H), 6.82 (s, 2H), 6.68 (s, 2H), 3.80 (m, 4H), 2.29 (s, 12H), 1.68 (m, 2H), 1.62 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 164.8, 139.6, 138.6, 124.7, 118.4, 45.0, 26.3, 25.3, 21.9; HRMS (ESI) calcd for $C_{24}H_{31}N_6$ *m*/*z*: 403.2610, found: 403.2623.

4.2.26. 2-Morpholinyl-4,6-bis(mexylamino)-1,3,5-triazine ***10n***

Yield: 74%; T_g 72 °C, T_m 165 °C; IR ($CHCl_3$/KBr) 3375, 3283, 3231, 3196, 3163, 3124, 2963, 2918, 2856, 1614, 1591, 1548, 1511, 1434, 1376, 1354, 1326, 1301, 1279, 1253, 1178, 1116, 1070, 1024, 978, 888, 840 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.16 (s, 4H), 7.00 (s, 2H), 6.69 (s, 2H), 3.84 (t, ^3J=4.6 Hz, 4H), 3.74 (t, ^3J=4.8 Hz, 4H), 2.28 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 164.6, 139.1, 138.6, 124.9, 118.4, 67.0, 44.1, 21.7; HRMS (ESI) calcd for $C_{23}H_{29}N_6O$ *m*/*z*: 405.2402, found: 405.2392.

4.2.27. 2,4,6-Tris(mexylamino)-1,3,5-triazine ***10o***

To a stirred solution of cyanuric chloride (0.922 g, 5.0 mmol) in THF (30 mL) in a round-bottomed flask were added successively 3,5-dimethylaniline (1.875 mL, 1.819 g, 15.0 mmol) and K_2CO_3 (1.037 g, 7.5 mmol) at room temperature. The reaction mixture was refluxed overnight, then the precipitate was filtered and washed with water to yield 1.97 g **10o** (4.49 mmol, 90%) in acceptable purity; T_m 327 °C (dec); IR (KBr) 3394, 3280, 3251, 3208, 3076, 3005, 2939, 2915, 2851, 1741, 1626, 1591, 1558, 1508, 1429, 1319, 1299, 1239, 1179, 1036, 880, 839 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53 (s, 3H), 7.11 (s, 6H), 6.72 (s, 3H), 2.25 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 138.4, 138.0, 125.7, 119.2, 21.4; HRMS (ESI) calcd for $C_{27}H_{31}N_6$ *m*/*z*: 439.2605, found: 439.2610.

4.2.28. 2-Hydroxy-4,6-bis[(3,5-dimethylphenyl)amino]-1,3,5-triazine ***11a***

KOH (0.281 g, 5.00 mmol) was added to a stirred solution of chlorotriazine **6** (0.354 g, 1.00 mmol) in dioxane (25 mL)/H_2O (5 mL) in a 100 mL round-bottomed flask equipped with a magnetic stirrer and a water-jacketed condenser. The mixture was refluxed for 18 h, then, after cooling down to room temperature, 1 M aqueous HCl was added and the precipitate filtered and abundantly washed with H_2O and acetone. Subsequent drying of the product under vacuum gave 0.343 g **11a** (0.970 mmol, 97%); T_m>350 °C (dec); IR (KBr) 3420, 3237, 3105, 3017, 2917, 2858, 1747, 1688, 1625, 1596, 1501, 1439, 1365, 1262, 1182, 1123, 1090, 1035, 983, 928, 892, 848 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 9.86 (s, 2H), 7.15 (s, 4H), 6.79 (s, 2H), 2.21 (s, 12H); HRMS (ESI) calcd for $C_{19}H_{22}N_5O$ *m*/*z*: 336.1824, found: 336.1819. Anal. Calcd for $C_{19}H_{21}N_5O$: C, 68.04; H, 6.31; N, 20.88. Found: C, 67.65; H, 6.37; N, 20.72.

4.2.29. 2-Ethoxy-4,6-bis(mexylamino)-1,3,5-triazine ***11b***

Potassium ethoxide was prepared by dissolving potassium metal (0.0430 g, 1.10 mmol) in ethanol (30 mL) in a 100 mL round-bottomed flask equipped with a magnetic stirrer and a water-jacketed condenser. Chlorotriazine **6** (0.354 g, 1.00 mmol) was added, and then the mixture was refluxed for 2 h. The solvent was evaporated under reduced pressure, and then the residue was partitioned between ethyl acetate and H_2O. Both layers were separated, and then the organic layer was recovered, dried over Na_2SO_4, and filtered. Removal of the solvent in vacuo and subsequent filtration of the crude product on a short silica pad with $CHCl_3$ as eluent gave 0.360 g **11b** (0.990 mmol, 99%); T_g 53 °C, T_m 188 °C; IR ($CHCl_3$/KBr) 3420, 3274, 3230, 3129, 3099, 2981, 2956, 2919, 2850, 1618, 1589, 1563, 1516, 1471, 1429, 1381, 1360, 1330, 1302, 1182, 1118, 1102, 1038, 1008, 884, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 2H), 7.17 (s, 4H), 6.73 (s, 2H), 4.43 (q, ^3J=7.1 Hz, 2H), 2.28 (s, 12H), 1.41 (t, ^3J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 165.8, 138.7, 138.6, 125.6, 119.1, 63.3, 21.6, 14.8; HRMS (ESI) calcd for $C_{21}H_{26}N_5O$ *m*/*z*: 364.2137, found: 364.2114.

Compounds **11c–f** were synthesized by the same procedure using the corresponding alcohols as solvents.

4.2.30. 2-Propoxy-4,6-bis(mexylamino)-1,3,5-triazine ***11c***

Yield: 94%; T_g 49 °C, T_m 161 °C; IR ($CHCl_3$/KBr) 3373, 3276, 3231, 3190, 3131, 2968, 2920, 2878, 2858, 1619, 1590, 1562, 1518, 1429, 1368, 1327, 1301, 1276, 1245, 1185, 1116, 1040, 988, 960, 931, 885, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (s, 2H), 7.17 (s, 4H), 6.73 (s, 2H), 4.32 (t, ^3J=6.7 Hz, 2H), 2.28 (s, 12H), 1.82 (sex, ^3J=7.0 Hz, 2H), 1.03 (t, ^3J=7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 165.8, 138.7, 138.6, 125.6, 119.1, 69.0, 22.4, 21.6, 10.6; HRMS (ESI) calcd for $C_{22}H_{28}N_5O$ *m*/*z*: 378.2293, found: 378.2299.

4.2.31. 2-Isopropoxy-4,6-bis(mexylamino)-1,3,5-triazine ***11d***

Yield: 93%; T_g 63 °C; IR ($CHCl_3$/KBr) 3417, 3373, 3274, 3230, 3190, 3129, 2981, 2920, 2864, 2850, 1618, 1588, 1560, 1516, 1470, 1426, 1386, 1337, 1317, 1181, 1144, 1115, 1098, 1037, 985, 956, 918, 885, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 2H), 7.16 (s, 4H), 6.72 (s, 2H), 5.30 (sept, ^3J=6.4 Hz, 1H), 2.28 (s, 12H), 1.40 (d, ^3J=6.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 166.0, 138.8, 138.6, 125.8, 119.1, 70.6, 22.4, 21.8; HRMS (ESI) calcd for $C_{22}H_{28}N_5O$ *m*/*z*: 378.2293, found: 378.2286.

4.2.32. 2-Butoxy-4,6-bis(mexylamino)-1,3,5-triazine ***11e***

Yield: 82%; T_g 43 °C, T_m 124 °C; IR ($CHCl_3$/KBr) 3374, 3274, 3231, 3191, 3130, 2959, 2918, 2873, 2850, 1619, 1590, 1562, 1517, 1428, 1371, 1335, 1303, 1182, 1118, 1106, 1035, 929, 883, 842 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29 (s, 2H), 7.17 (s, 4H), 6.73 (s, 2H), 4.36 (t, ^3J=7.0 Hz, 2H), 2.28 (s, 12H), 1.77 (quint, ^3J=7.0 Hz, 2H), 1.48 (sex, ^3J=7.3 Hz, 3H), 0.97 (t, ^3J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 165.8, 138.6, 138.4, 125.6, 119.0, 67.3, 31.1, 21.6, 19.4, 14.0; HRMS (ESI) calcd for $C_{23}H_{30}N_5O$ *m*/*z*: 392.2450, found: 392.2470.

4.2.33. 2-Isobutoxy-4,6-bis(mexylamino)-1,3,5-triazine ***11f***

Yield: 97%; T_g 52 °C; IR ($CHCl_3$/KBr) 3412, 3370, 3275, 3231, 3190, 3131, 2960, 2919, 2873, 2850, 1618, 1588, 1562, 1517, 1428, 1386, 1367, 1331, 1300, 1275, 1185, 1117, 1036, 993, 978, 932, 885, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 2H), 7.17 (s, 4H), 6.73 (s, 2H), 4.17 (d, ^3J=6.8 Hz, 2H), 2.28 (s, 12H), 2.12 (m, ^3J=6.7 Hz, 1H), 1.02 (d, ^3J=6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 166.0, 138.8, 138.6, 125.8, 119.2, 73.9, 28.3, 21.8, 19.6; HRMS (ESI) calcd for $C_{23}H_{30}N_5O$ *m*/*z*: 392.2450, found: 392.2438.

4.2.34. 2-Mercapto-4,6-bis(mexylamino)-1,3,5-triazine ***12***

Thiourea (1.55 g, 20.3 mmol) was added to a solution of chlorotriazine **6** (6.85 g, 19.4 mmol) in dioxane (100 mL) in a round-bottomed flask equipped with a magnetic stirring bar and a water-jacketed condenser. The reaction mixture was refluxed for 3 h, allowed to cool down to room temperature, then aqueous NaOH (2.5 M, 35 mL) was added and the mixture was stirred at room temperature for 15 min. Aqueous HCl (1 M) was added until the formation of a white precipitate. The precipitate was then filtered off, abundantly washed with H_2O, CH_2Cl_2 and acetone, and allowed to dry to yield 6.45 g **12** (18.4 mmol, 95%); T_m 286 °C (dec); IR (KBr) 3082, 3010, 2917, 1675, 1619, 1600, 1559, 1477, 1430, 1341, 1303, 1260, 1197, 1178, 1104, 1033, 944, 881, 840 cm^{-1}; ^1H NMR (400 MHz, DMF-d_7) δ 11.36 (s, 2H), 7.26 (s, 4H), 6.94 (s, 2H), 2.28 (s, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.9, 138.2, 137.4, 135.2, 127.5, 120.0, 20.8; HRMS (ESI) calcd for $C_{19}H_{22}N_5S$ m/z: 352.1590, found: 352.1589.

4.2.35. 2-Methylthio-4,6-bis(mexylamino)-1,3,5-triazine ***13***

Compound **12** (6.45 g, 18.4 mmol) was suspended in acetone (100 mL) in a round-bottomed flask equipped with a magnetic stirring bar and a water-jacketed condenser. Diisopropylethylamine (3.84 mL, 2.85 g, 22.0 mmol) was added and the mixture was allowed to stir at room temperature for 15 min. Dimethyl sulfate (3.47 mL, 4.63 g, 36.7 mmol) was then added, and the mixture was refluxed for 12 h. After cooling down to room temperature, the solvent was concentrated in vacuo, and then H_2O was added. The resulting precipitate was filtered, washed with H_2O and hexanes, suspended in CH_2Cl_2 and extracted with 1 M aqueous NaOH. The organic layer was then recovered, dried over Na_2SO_4, filtered, and the solvent was evaporated, then the crude product was filtered on a short silica pad using $CHCl_3$ as eluent to yield 5.76 g **13** (15.5 mmol, 85%); T_g 54 °C, T_m 159 °C; IR ($CHCl_3$/KBr) 3369, 3268, 3229, 3115, 2949, 2919, 2849, 1615, 1581, 1535, 1508, 1466, 1432, 1397, 1367, 1321, 1301, 1278, 1247, 1175, 1112, 1050, 990, 965, 886, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 2H), 7.17 (s, 4H), 6.74 (s, 2H), 2.56 (s, 3H), 2.28 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.6, 162.8, 138.4, 138.0, 125.6, 118.8, 21.5, 13.3; HRMS (ESI) calcd for $C_{20}H_{24}N_5S$ m/z: 366.1752, found: 366.1745.

4.2.36. 2-Methyl-4,6-bis(mexylamino)-1,3,5-triazine ***14a***

To a stirred solution of cyanuric chloride (1.00 g, 5.42 mmol) in 30 mL dry Et_2O in a 100 mL round-bottomed flask kept under nitrogen atmosphere was added 2.17 mL methylmagnesium chloride in 3.0 M THF solution (6.51 mmol) dropwise at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 12 h. AcOEt and H_2O were then added and both layers were separated. The organic layer was extracted with 0.1 M aqueous NaOH and H_2O, dried over Na_2SO_4, filtered, and then the solvent was evaporated in vacuo. The crude product was dissolved in 50 mL THF in a 100 mL round-bottomed flask, then Na_2CO_3 (1.21 g, 11.4 mmol) and 3,5-dimethylaniline (1.42 mL, 1.38 g, 11.4 mmol) were successively added, the flask was equipped with a magnetic stirrer and water-jacketed condenser and the mixture was refluxed for 18 h. After cooling down to room temperature, AcOEt, and H_2O were added, and both layers were separated. The organic layer was then extracted three times with 0.1 M aqueous HCl, then with aqueous $NaHCO_3$. The organic extracts were dried over Na_2SO_4, filtered, then the solvent was evaporated to give 0.938 g **14a**, which was of acceptable purity but which can be further purified by filtration through a short silica pad with $CHCl_3$ as eluent (2.81 mmol, 61%); T_g 59 °C, T_c 103 °C, T_m 168 °C; IR ($CHCl_3$/KBr) 3374, 3274, 3225, 3186, 3088, 2949, 2918, 2850, 1616, 1590, 1519, 1431, 1376, 1321, 1302, 1264, 1176, 1066, 1037, 976, 887, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 2H), 7.17 (s, 4H), 6.74 (s, 2H), 2.36 (s, 3H), 2.28 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 164.6, 138.7, 138.3, 125.9, 119.4, 25.8, 21.6; HRMS (ESI) calcd for $C_{20}H_{24}N_5$ m/z: 334.2031, found: 334.2010.

Compounds **14b–f** were synthesized by the same procedure using commercial 2.0 M in Et_2O solutions of the corresponding alkylmagnesium chloride reagents.

4.2.37. 2-Ethyl-4,6-bis(mexylamino)-1,3,5-triazine ***14b***

Yield: 75%; T_g 41 °C, T_m 135 °C; IR ($CHCl_3$/KBr) 3380, 3270, 3228, 3188, 3124, 3099, 2974, 2938, 2919, 2877, 2861, 2851, 1615, 1589, 1552, 1518, 1464, 1428, 1377, 1347, 1323, 1301, 1266, 1177, 1122, 1061, 1038, 986, 959, 885, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 2H), 7.19 (s, 4H), 6.74 (s, 2H), 2.64 (q, ^3J=7.3 Hz, 2H), 2.28 (s, 12H), 1.32 (t, ^3J=7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.3, 164.7, 138.6, 138.6, 125.7, 119.3, 32.3, 21.7, 11.8; HRMS (ESI) calcd for $C_{21}H_{26}N_5$ m/z: 348.2188, found: 348.2173.

4.2.38. 2-Propyl-4,6-bis(mexylamino)-1,3,5-triazine ***14c***

Yield: 69%; T_g 39 °C, T_m 135 °C; IR ($CHCl_3$/KBr) 3380, 3269, 3227, 3187, 3099, 2964, 2920, 2873, 1616, 1589, 1550, 1518, 1430, 1379, 1323, 1303, 1267, 1204, 1177, 1122, 1071, 1038, 976, 935, 885, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 2H), 7.18 (s, 4H), 6.74 (s, 2H), 2.56 (t, ^3J=7.3 Hz, 2H), 2.28 (s, 12H), 1.82 (sex, ^3J=7.2 Hz, 2H), 0.99 (t, ^3J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.5, 164.9, 138.8, 138.7, 125.9, 119.5, 41.2, 21.8, 21.3, 14.4; HRMS (ESI) calcd for $C_{22}H_{28}N_5$ m/z: 362.2344, found: 362.2342.

4.2.39. 2-Isopropyl-4,6-bis(mexylamino)-1,3,5-triazine ***14d***

Yield: 64%; T_g 43 °C; IR ($CHCl_3$/KBr) 3416, 3379, 3271, 3228, 3125, 3097, 2969, 2920, 2868, 1616, 1584, 1549, 1517, 1471, 1427, 1377, 1347, 1325, 1300, 1266, 1180, 1165, 1121, 1081, 1048, 997, 885, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (s, 4H), 7.15 (s, 2H), 6.73 (s, 2H), 2.83 (m, ^3J=6.5 Hz, 2H), 2.29 (s, 12H), 1.32 (d, ^3J=7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.8, 164.9, 138.8, 138.6, 125.6, 119.1, 37.4, 21.7, 21.3; HRMS (ESI) calcd for $C_{22}H_{28}N_5$ m/z: 362.2344, found: 362.2315.

4.2.40. 2-Butyl-4,6-bis(mexylamino)-1,3,5-triazine ***14e***

Yield: 50%; T_g 31 °C, T_m 105 °C; IR ($CHCl_3$/KBr) 3375, 3267, 3226, 3096, 2958, 2921, 2871, 2861, 1616, 1590, 1549, 1518, 1431, 1377, 1325, 1301, 1199, 1176, 841, 819 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.28 (s, 2H), 7.18 (s, 4H), 6.74 (s, 2H), 2.59 (t, ^3J=7.3 Hz, 2H), 2.28 (s, 12H), 1.77 (quint, ^3J=7.1 Hz, 2H), 1.41 (sex, ^3J=7.3 Hz, 2H), 0.97 (t, ^3J=7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.5, 164.7, 139.0, 138.6, 125.8, 119.5, 38.9, 29.9, 22.8, 21.7, 14.3; HRMS (ESI) calcd for $C_{23}H_{30}N_5$ m/z: 376.2501, found: 376.2500.

4.2.41. 2-Isobutyl-4,6-bis(mexylamino)-1,3,5-triazine ***14f***

Yield: 66%; T_g 38 °C; IR ($CHCl_3$/KBr) 3420, 3266, 3225, 3094, 2957, 2919, 2869, 2851, 1615, 1588, 1549, 1517, 1431, 1322, 1302, 1206, 1175, 1038, 979, 886, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 2H), 7.18 (s, 4H), 6.75 (s, 2H), 2.46 (br s, 2H), 2.29 (s, 12H), 2.25 (m, ^3J=6.4 Hz, 1H), 1.00 (d, ^3J=6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 164.7, 138.8, 138.6, 125.9, 119.3, 48.2, 27.9, 23.0, 21.8; HRMS (ESI) calcd for $C_{23}H_{30}N_5$ m/z: 376.2501, found: 376.2494.

4.2.42. 4,6-Bis(mexylamino)-1,3,5-triazine ***15***

In a round-bottomed flask was added **1** hydrochloride (0.5 g, 1.45 mmol) in DMF (20 mL). A methanolic NaOMe solution (25%, 0.44 mL, 1.6 mmol) was added then the reaction was heated to 120 °C overnight. After the reaction mixture was brought to room temperature, H_2O was added, then the precipitate was filtered and thoroughly washed with H_2O to remove any remaining DMF. The product was dried overnight on a vacuum pump to yield 0.352 g **15** (1.102 mmol, 76%); mp 251 °C (dec); IR (KBr) 3263, 3228, 3189, 3093, 3011, 2928, 2860, 1637, 1598, 1538, 1417, 1320, 1304, 1265, 1226, 1167, 1036, 994, 956, 886, 865, 843 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 9.58 (s, 2H), 8.32 (s, 1H), 7.32 (s, 4H), 6.67 (s, 2H), 2.21 (s, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.9, 163.4, 138.9, 137.3, 124.3, 118.4, 21.0; HRMS (ESI) calcd for $C_{19}H_{22}N_5$ m/z: 320.1870, found: 320.1869.

4.2.43. 2-Chloromethyl-4,6-bis(mexylamino)-1,3,5-triazine ***16***

To a solution of **1** (4.60 g, 14.87 mmol) in MeOH (100 mL) in a round-bottomed flask was added methyl chloroacetate (2.62 mL, 3.23 g, 29.74 mmol) and the reaction mixture was refluxed for 2 h with constant stirring. After cooling down to room temperature, the solvent was evaporated, then the residue was solubilized in a small amount of ethyl acetate and filtered on a short silica pad using ethyl acetate as eluent. The solvent was then evaporated, yielding 2.14 g **19** (5.81 mmol, 39%); T_g 41 °C; IR ($CHCl_3$/KBr) 3382, 3272, 3232, 3190, 3098, 2954, 2919, 2860, 1655, 1616, 1586, 1557, 1521, 1436, 1379, 1323, 1303, 1265, 1175, 1153, 1037, 974, 936, 887, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 2H), 7.15 (s, 4H), 6.77 (s, 2H), 4.37 (s, 2H), 2.29 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 164.9, 139.0, 138.0, 126.4, 119.5, 46.4, 21.8; HRMS (ESI) calcd for $C_{20}H_{23}ClN_5$ m/z: 368.1637, found: 368.1637.

4.3. Measurement of T_g by differential scanning calorimetry (DSC)

Measurements were made with a TA Instruments Q100 calorimeter, using heating/cooling rates of 5 °C/min or 10 °C/min for compounds **11a–f**. Starting temperatures ranged from 0 to 20 °C, and the samples were heated up to 200 to 350 °C depending on the compound. The results reported were recorded after an initial cycle of heating and cooling.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.07.026.

References and notes

1. For example see: (a) Bushey, M. L.; Nguyen, T.-Q.; Zhang, W.; Horoszewski, D.; Nuckolls, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 5446; (b) Facchetti, A.; Annoni, E.; Beverina, L.; Morone, M.; Zhu, P.; Marks, T. J.; Pagani, G. A. *Nat. Mater.* **2004**, *3*, 910; (c) Huang, C.-H.; McClenaghan, N. D.; Kuhn, A.; Hofstraat, J. W.; Bassani, D. M. *Org. Lett.* **2005**, *7*, 3409; (d) Murphy, A. R.; Chang, P. C.; VanDyke, P.; Liu, J.; Fréchet, J. M. J.; Subramanian, V.; DeLongchamp, D. M.; Sambasivan, S.; Fischer, D. A.; Lin, E. K. *Chem. Mater.* **2005**, *17*, 6033; (e) Miao, Q.; Chi, X.; Xiao, S.; Zeis, R.; Lefenfeld, M.; Siegrist, T.; Steigerwald, M. L.; Nuckolls, C. *J. Am. Chem. Soc.* **2006**, *128*, 1340.
2. For example see: (a) Dunitz, J. D. *Chem. Commun.* **2003**, 545; (b) Desiraju, G. R. *Crystal Engineering: the Design of Organic Solids*; Elsevier: Amsterdam, 1989; (c) Wuest, J. D. *Chem. Commun.* **2005**, 5830.
3. For example, see: Chandrasekhar, S. *Liquid Crystals*, 2nd ed.; Cambridge University: New York, NY, 1993.
4. For example, see: (a) Ediger, M. D.; Angell, C. A.; Nagel, S. R. *J. Phys. Chem.* **1996**, *100*, 13200; (b) Shirota, Y. *J. Mater. Chem.* **2000**, *10*, 1; (c) Strohriegl, P.; Grazulevicius, J. V. *Adv. Mater.* **2002**, *14*, 1439; (d) Shirota, Y. *J. Mater. Chem.* **2005**, *15*, 75; (e) Shirota, Y.; Kageyama, H. *Chem. Rev.* **2007**, *107*, 953.
5. For example, see: Hartel, R. W. *Crystallization in Foods*; Springer: Boston, 2001.
6. For example see: (a) Burroughes, J. H.; Bradley, D. D. C.; Brown, A. R.; Marks, R. N.; Mackay, K.; Friend, R. H.; Burn, P. L.; Holmes, A. B. *Nature* **1990**, *347*, 539; (b) Nazeeruddin, M. K.; Kay, A.; Roddicio, I.; Humphry, R.; Müller, E.; Liska, P.; Vlachopoulos, N.; Grätzel, M. *J. Am. Chem. Soc.* **1993**, *115*, 6382; (c) Bach, U.; Lupo, D.; Comte, P.; Moser, J. E.; Weissörtel, F.; Salbeck, J.; Spreitzer, H.; Grätzel, M. *Nature* **1998**, *395*, 583; (d) Irie, M. *Chem. Rev.* **2000**, *100*, 1685; (e) Dimitrakopoulos, C. D.; Malenfant, P. R. L. *Adv. Mater.* **2002**, *14*, 99; (f) Bendikov, M.; Wudl, F.; Perepichka, D. F. *Chem. Rev.* **2004**, *104*, 4891.
7. Tsuchiya, K.; Chang, S. W.; Felix, N. M.; Ueda, M.; Ober, C. K. *J. Photopolym. Sci. Technol.* **2005**, *18*, 431.
8. (a) Hancock, B. C.; Zografi, G. *J. Pharm. Sci.* **1997**, *86*, 1; (b) Yu, L. *Adv. Drug Delivery Rev.* **2001**, *48*, 27.
9. For example see: (a) Han, E. M.; Do, L. M.; Yamamoto, N.; Fujihira, M. *Mol. Cryst. Liq. Cryst. Sci. Technol. A: Mol. Cryst. Liq. Cryst.* **1995**, *267*, 411; (b) Adachi, C.; Tsutsui, T.; Saito, S. *Appl. Phys. Lett.* **1990**, *56*, 799; (c) Han, E. M.; Do, L. M.; Niidome, Y.; Fujihira, M. *Chem. Lett.* **1994**, 969.
10. For example see: (a) Cho, M. J.; Lee, S. K.; Choi, D. H.; Jim, J.-I. *Dyes Pigm.* **2008**, *77*, 335; (b) Guo, M.; Xu, Z.; Wang, X. *Opt. Mater.* **2008**, *31*, 412; (c) Nakano, H. *J. Photopolym. Sci. Technol.* **2008**, *21*, 545; (d) Bubniene, G.; Malinauskas, T.; Getautis, V.; Stanisauskaite, A.; Jankauskas, V.; Sidaravicius, J. *Synth. Met.* **2008**, *158*, 670; (e) De Silva, A.; Lee, J.-K.; Andre, X.; Felix, N. M.; Cao, H. B.; Deng, H.; Ober, C. K. *Chem. Mater.* **2008**, *20*, 1606; (f) Chien, C.-H.; Kung, L.-R.; Wu, C.-H.; Shu, C.-F.; Chang, S.-Y.; Chi, Y. *J. Mater. Chem.* **2008**, *18*, 3461; (g) Zondervan, R.; Xia, T.; van der Meer, H.; Storm, C.; Kulzer, F.; van Saarloos, W.; Orrit, M. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 4993.
11. For example see: (a) Chen, S. H.; Mastrangelo, J. C.; Shi, H.; Bashir-Hashemi, A.; Li, J.; Gelber, N. *Macromolecules* **1995**, *28*, 7775; (b) Mastrangelo, J. C.; Conger, B. M.; Chen, S. H.; Bashir-Hashemi, A. *Chem. Mater.* **1997**, *9*, 227; (c) Fuhrmann, T.; Tsutsui, T. *Chem. Mater.* **1999**, *11*, 2226; (d) Okumoto, K.; Ohara, T.; Noda, T.; Shirota, Y. *Synth. Met.* **2001**, *121*, 1655; (e) Chan, L.-H.; Lee, R.-H.; Hsieh, C.-F.; Yeh, H.-C.; Chen, C.-T. *J. Am. Chem. Soc.* **2002**, *124*, 6469; (f) Kinoshita, M.; Kita, H.; Shirota, Y. *Adv. Funct. Mater.* **2002**, *12*, 780; (g) Jeong, J.-M.; Abe, K.; Sato, H.; Pretula, J.; Kaluzynski, K.; Ogino, K. *Synth. Met.* **2003**, *139*, 11; (h) Shi, J.; Huang, M.; Xin, Y.; Chen, Z.; Gong, Q.; Xu, S.; Cao, S. *Mater. Lett.* **2005**, *59*, 2199; (i) Sonntag, M.; Kreger, K.; Hanft, D.; Strohriegl, P.; Setayesh, S.; de Leeuw, D. *Chem. Mater.* **2005**, *17*, 3031.
12. While several molecular glasses can form multiple intermolecular interactions such as hydrogen bonds, in most cases the interactions are not directional and the multitude of possible self-assembly motifs makes it more difficult for molecules to converge towards an ordered structure: (a) Kim, S.-J.; Karis, T.E.J. Mater. Res. 195, 10, 2128. (b) Boileau, S.; Bouteiller, L.; Foucat, E.; Lacoudre, N. *J. Mater. Chem.* **2002**, *12*, 195; (c) Boils, D.; Perron, M.-È.; Monchamp, F.; Duval, H.; Maris, T.; Wuest, J. D. *Macromolecules* **2004**, *37*, 7351; (d) Dirama, T. E.; Carri, G. A.; Sokolov, A. P. *J. Chem. Phys.* **2005**, *122*, 114505.
13. Naito, K. *Chem. Mater.* **1994**, *6*, 2343.
14. Lebel, O.; Maris, T.; Perron, M.-È.; Demers, E.; Wuest, J. D. *J. Am. Chem. Soc.* **2006**, *128*, 10372.
15. Lebel, O.; Maris, T.; Duval, H.; Wuest, J. D. *Can. J. Chem.* **2005**, *83*, 615.
16. Lebel, O.; Perron, M.-È.; Maris, T.; Zalzal, S. F.; Nanci, A.; Wuest, J. D. *Chem. Mater.* **2006**, *18*, 3616.
17. Wang, R.; Pellerin, C.; Lebel, O. *J. Mater. Chem.* **2009**, *19*, 2747.
18. Hayase, Y.; Morita, K.; Ide, K.; Takahashi, T. Eur. Pat. Appl. EA 171708, 1986.
19. (a) Menicagli, R.; Samaritani, S.; Zucchelli, V. *Tetrahedron* **2000**, *56*, 9705; (b) Thakur, V. V.; Kim, J. T.; Hamilton, A. D.; Bailey, C. M.; Domaoal, R. A.; Wang, L.; Anderson, K. S.; Jorgensen, W. L. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5664.
20. Brzozowski, Z.; Saczewski, F.; Gdaniec, M. *Eur. J. Med. Chem.* **2000**, *35*, 1053.