Traceless Solid-Phase Synthesis of 6-Amino- and 6-Hydroxyimino-1,3,5-triazine-2,4-diones and 1,3,5-Triazine-2,4,6-triones

Kah-Hoe Kong, Chong-Kiat Tan, and Yulin Lam*

Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore 117543

Received June 18, 2009

A traceless solid-phase synthesis of 6-amino- and 6-hydroxyimino-1,3,5-triazine-2,4-diones and 1,3,5-triazine-2,4,6-triones has been developed. The strategy comprises of linking a preformed *N*-carbamothioylcarbamate to bromomethyl resin to give a S-linked isothiourea, which then undergoes cyclization with isocynates to yield the resin-bound 1,3,5-triazine-2,4-diones. Subsequent cleavage was accomplished by either direct substitution with a suitable amine or by oxidative activation of the thioether functionality followed by nucleophilic substitution. Using this synthetic strategy, we prepared a representative set of 31 6-amino-1,3,5-triazine-2,4-diones, 10 6-hydroxyimino-1,3,5-triazine-2,4-diones, and 8 1,3,5-triazine-2,4,6-triones.

Introduction

6-Amino-1,3,5-triazine-2,4-diones **1** is a template found in a wide variety of biologically active compounds that are of pharmaceutical[1] and agricultural interests.[2] Recent works have also shown the potential use of **1** as nonpeptidic prokineticin receptor antagonists.[3] This multifaceted profile bodes well for the interaction of such heterocycles with a variety of biological targets, which has consequently led to the development of a number of synthetic strategies leading to disubstituted and trisubstituted 6-amino-1,3,5-triazine-2,4-diones.[1c,3b,4] Generally these syntheses involve multistep reactions that would limit the synthesis of large number of compounds if performed using solution-phase methodology. A solid-phase approach to the synthesis of small organic molecule libraries[5] would offer a good pathway to a large number of these analogues. To our knowledge, there is only one earlier report on the traceless solid-phase synthesis (SPS) of **1** with two points of diversification,[4a] which was achieved by treating *p*-nitrophenyl carbonate resin with *S*-methyl isothiouroium sulfate to provide the solid-supported S-methylisothiourea which then underwent reaction with isocyanates followed by base-promoted intramolecular cyclization and concomitant cleavage of **1**. As part of a continuing effort toward the development of SPS protocols for generation of small molecules, we were interested to develop a traceless approach for the SPS of fully substituted **1**. Since **1** is structurally similar to 1,3,5-triazine-2,4,6-triones **2**, a biologically interesting compound which is known to be a human gonadotropin-releasing hormone receptor antagonist[6] and cytosolic phospholipase $A_{2\alpha}$ inhibitor,[7] we were interested to design a synthetic strategy which could be applied in parallel for the traceless SPS of both **1** and **2**. We reckoned that a sulfide linker would be an attractive solid support for this synthesis as the linker is relatively stable in basic and acidic reaction conditions but is readily oxidized to a labile sulfone functionality which could then be cleaved by primary amines via a safety-catch approach.[8] Thus we herein describe a traceless approach for the solid-phase synthesis of **1** and **2** using bromomethyl resin **3**.

* To whom correspondence should be addressed. E-mail: chmlamyl@nus.edu.sg. Fax: (65)-6779-1691.

Results and Discussion

Solution-Phase Synthesis. Prior to the SPS, preliminary solution-phase studies were carried out to survey the requisite reaction conditions and establish the modifications for the solid-phase synthesis. To begin our investigation, ethyl methylcarbamathioylcarbamate **5** ($R^1 = CH_3$, Scheme 2) was prepared in quantitative yield by treating ethoxycarbonyl isothiocyanate **4** with methylamine in dichloromethane using a procedure modified from Tam and co-workers.[9] Subsequent base-promoted S-alkylation with benzyl bromide mimicked the attachment of **5** onto the solid support. For this reaction various bases like triethylamine, DBU, DiEA, and NaH were used and only reactions involving NaH with an excess of **5** provided **6**. Since compounds **6** and **5** had similar polarities, the presence of the latter in the reaction mixture made purification difficult and the yield of **6** obtained after column chromatography was only 68%. However, we reasoned that this problem should not arise on the solid-phase format where **5** could be easily separated from the solid supported **6** by filtration.

We next proceeded to cyclize **6** with various isocyanates using a procedure reported by Sanemitsu and co-workers.[10] The reaction was found to proceed well with phenyl isocyanate (Table 1, entry 4) but was less satisfactory with alkyl, *m*-tolyl and benzyl isocyanates (Table 1, entries 1, 7, and 11). Hence we investigated different reaction conditions and found that for alkyl isocynates, the reaction gave the best yield (Table 1, entry 2) when the cyclization reaction was performed at 60 °C in the presence of catalytic amounts of tetramethylguanidine (TMG) and with DMF as the solvent,

10.1021/cc900091e CCC: $40.75
Published on Web 10/09/2009

Scheme 1. Solution-Phase Synthesis

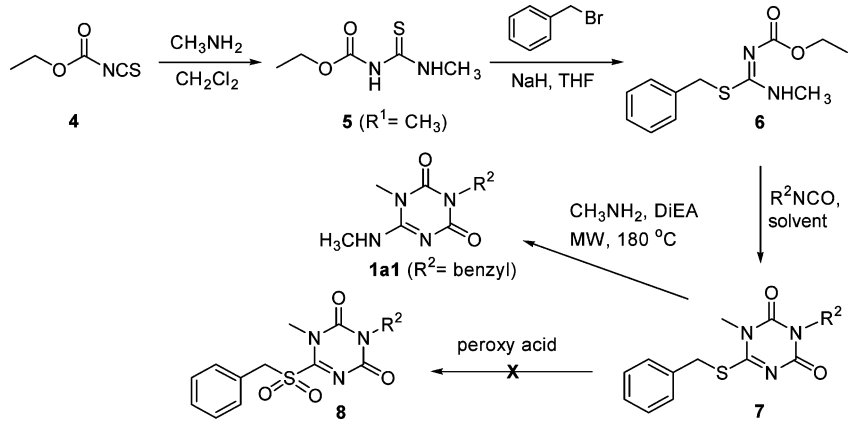


Table 1. Synthesis of **7** from **6** and Isocynates R^2NCO

entry	R^2	solvent	TMG[a] (equiv)	temp (°C)	yield (%)[b]
1[c]	phenylethyl	DMF	0.1	rt	0
2	phenylethyl	DMF	0.1	60	72
3	phenylethyl	CH_3CN	0.1	60	30
4[c]	phenyl	DMF		rt	67
5	phenyl	DMF	0.1	60	60[d]
6	phenyl	CH_3CN	0.2	60	20[d]
7	benzyl	DMF	0.1	rt	20
8	benzyl	DMF	0.1	60	40
9	benzyl	CH_3CN	0.2	rt	60
10	benzyl	THF	0.2	rt	0
11	m-tolyl	DMF	0.1	rt	30
12	m-tolyl	CH_3CN	0.2	rt	52

[a] TMG = tetramethylguanidine. [b] Yield after 24 h. [c] Reaction conditions used in ref 10. [d] Side products were observed.

while for benzyl and *m*-tolyl isocynates, the reaction surprisingly afforded a better yield when acetonitrile was used as the solvent (Table 1, entries 9 and 12). To explore if the relatively inert sulfide linkage could provide a direct nucleophilic displacement of the thiolate ion, compound **7** (R^2 = benzyl) obtained was treated with methylamine under microwave irradiation at 180 °C for 20 min. This gave **1a1** in 66% yield.

To explore other means of cleaving the sulfide linkage, we investigated the safety-catch approach by first oxidizing the thioether on **7** to a sulfone. When m-CPBA, potassium peroxymonosulfate, oxone, and magnesium monoperoxyphthalate hexahydrate (MMPP) were used as oxidants, the sulfone intermediate **8** was not isolated. Instead the hydrolyzed product, 1,3,5-triazine-2,4,6-trione **2** was obtained in 80% yield. This could be attributed to the presence of water in the peroxy acid oxidation, which readily hydrolyzed **8** to **2**. Since water is less nucleophilic than amines, this result was encouraging in the sense that it indicated that in the absence of water, it would be possible for the sulfone to be displaced by an amine.

Suckling et al. had earlier reported[11] obtaining a hydrolyzed product when Oxone® was used in the oxidation of pteridine sulfide analogs. This problem was eventually circumvented by replacing Oxone® with anhydrous dimethyldioxirane (DMDO). Encouraged by this finding, we decided to adopt Suckling's procedure for the synthesis of the sulfone. Since the sulfone linkage was highly labile and **8** could not be isolated, solution-phase validation of the reaction was therefore not performed and the oxidation and subsequent nucleophilic displacement reaction would be carried out directly on the solid-phase format.

Solid-Phase Synthesis. With the solution-phase pathway evaluated, we proceeded to synthesize **1** and **2** via SPS. Treatment of bromomethyl resin **3** in THF with carbamoyl thiourea **5** and sodium hydride gave resin **9** which was amenable to KBr FTIR monitoring for the appearance of a strong C═N stretch at 1637 cm^{-1}. Resin **9** was then reacted with the respective isocynates using the optimized solution-phase reaction conditions (Table 1) to afford resin **10** which according to FTIR analysis showed a strong C═O stretch at 1735 cm^{-1} and a blue shift of the iminium stretch to 1655−1685 cm^{-1}. Cleavage of resin **10** (R^1 = methyl) with the primary amines and DiEA in DMF under microwave irradiation at 180 °C and 5 bar for 20 min provided **1a** in generally >90% purity (by ^1H NMR and HPLC) and 39−70% overall yields, indicating an average yield of at least 70% for each step of the reaction (Figure 1). The only exception was compound **1a4** where the overall yield was much lower when a secondary isocynate was used in the synthesis of resin **10**. When a similar cleavage reaction was applied to resin **10** (R^1 = benzyl), interestingly it behaved differently to afford 1-benzyl-6-thioxo-1,3,5-triazine-2,4-dione **1a'** as the major product (28% yield). This cleavage reaction thus appears to be dependent on the R^1 substituent which therefore limits its applicability in our library synthesis. We next investigated the peroxy acid oxidation of resin **10**. As expected, reaction of resin **10** with mCPBA in CH_2Cl_2 at room temperature for 3 h gave **2** in 35−55% overall yields (Figure 1).

To demonstrate the thioether oxidation on resin **10**, DMDO in anhydrous acetone was prepared and its concentration was determined prior to usage.[12] Attempts to apply Suckling's procedure,[11] where the oxidation was carried out twice, each time with 2−3 equiv of DMDO in anhydrous acetone, resulted in a sluggish reaction because of the poor swelling of resin **10** in acetone. Hence CH_2Cl_2 was added as a cosolvent, and the resin mixture was shaken at room temperature for different periods of time (30, 15, 10, 5, and 4 min). Since it was apparent that the sulfone is highly reactive, the resin was carefully filtered at the end of the reaction and the filtrate was concentrated and checked by TLC for the presence of

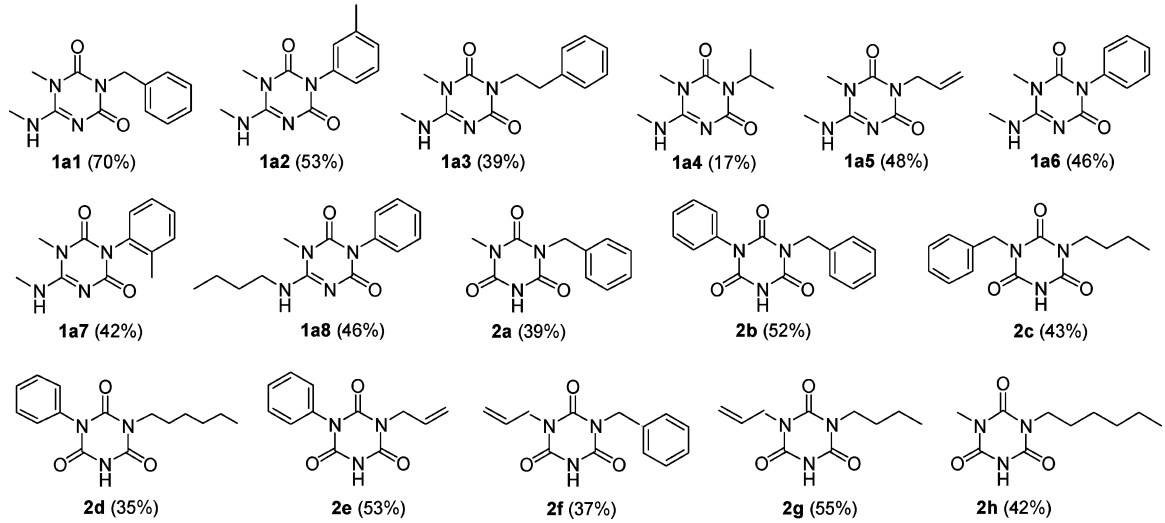
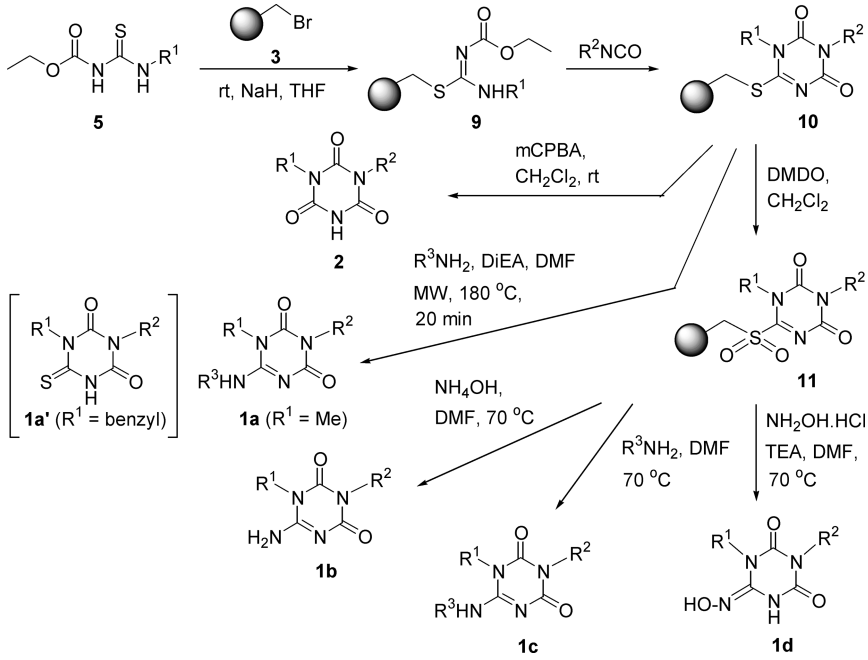


Figure 1. Library of **1** and **2** obtained from the direct substitution and peroxy acid oxidation of resin **10**. The overall yield was calculated based on the loading of resin **3**.

Scheme 2. SPS of 6-Amino-1,3,5-triazine-2,4-diones and 1,3,5-Triazine-2,4,6-triones



hydrolyzed product **2**. We found that the oxidative rate was dependent on the R^1 substituent but nevertheless the oxidation generally occurred rapidly. This is probably because the triazine moiety is sufficiently planar to allow the DMDO to access the thioether linkage easily. When R^1 was a methyl group, the oxidation was completed within 4 min but for larger R^1 substituents, the reaction required 10 min. Formation of compound **2** was not observed during these reaction times however prolong reaction gave increasing amounts of **2** which could probably be attributed to traces of water in the resin mixture even despite our best efforts to ensure an anhydrous reaction condition. The formation of resin **11** was monitored by KBr FTIR which showed a blue shift of the iminium stretch to 1675−1692 cm^{-1}.

With resin **11** in hand, we reacted it with various amino compounds as cleavage reagents. Treatment of resin **11** with ammonium hydroxide solution and the respective primary amines proceeded smoothly to give **1b** and **1c**, respectively. Reaction of resin **11** with hydroxylamine provided the oxime tautomer **1d** as the stable product, as confirmed by the X-ray crystal structure of compound **1d3**. Unlike the direct substitution of the thioether with an amine, the safety-catch approach was applicable to resin **11** containing different R^1 substituents. To demonstrate the versatility of this solid-phase methodology, a representative set of 33 members of 6-amino- and 6-hydroxyimino-1,3,5-triazine-2,4-diones was prepared in 22−63% overall yields (Figure 2).

In summary, we have described the first example of a traceless SPS route to fully substituted 6-amino-1,3,5-triazine-2,4-diones **1** and 1,3,5-triazine-2,4,6-triones **2**. In the process, we have also demonstrated an expedient thioether oxidation using anhydrous DMDO in acetone-CH_2Cl_2 mix-

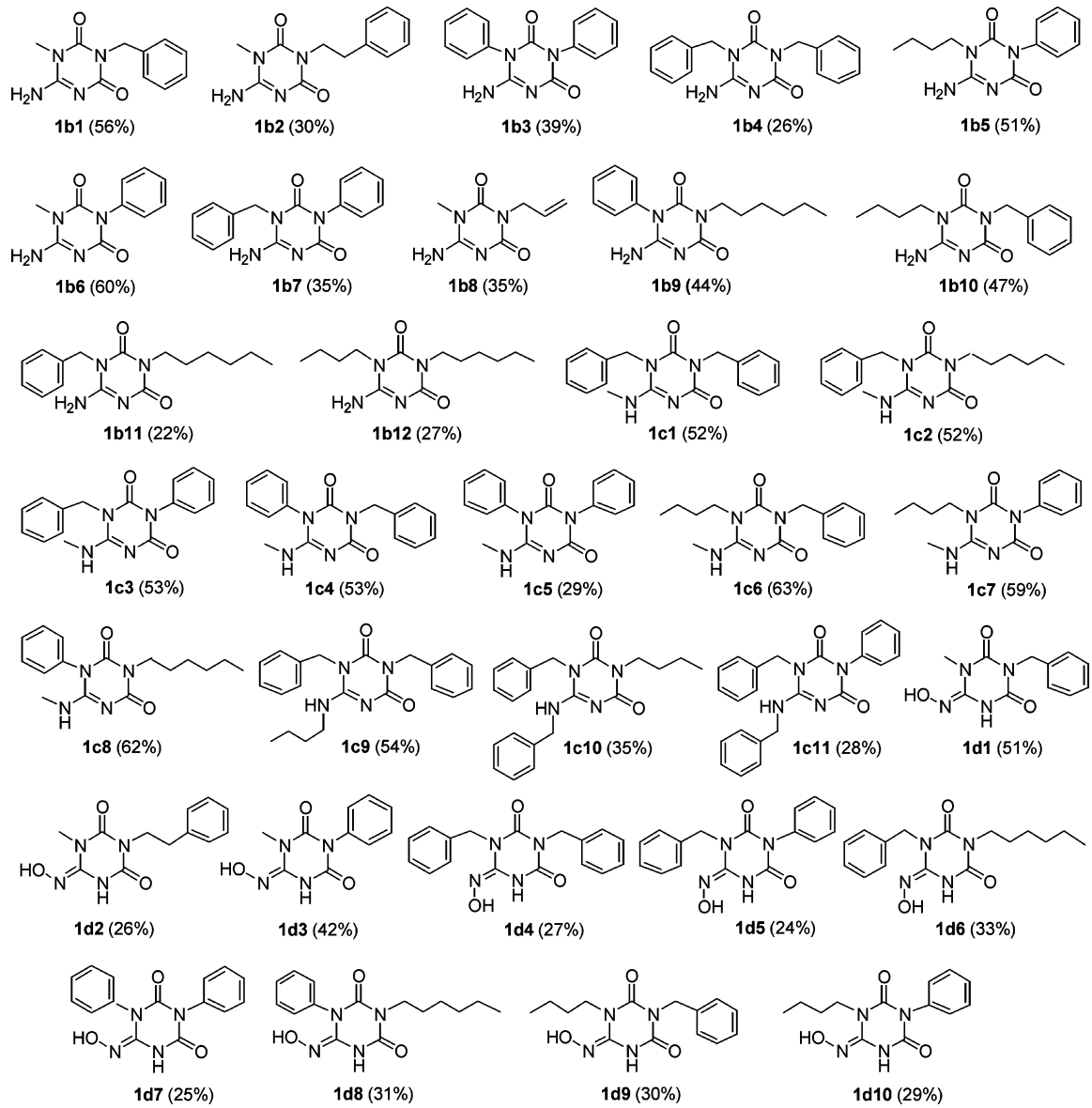


Figure 2. Library of **1** obtained by the oxidative activation followed by the nucleophilic substitution of resin **10**. The overall yield was calculated based on the loading of resin **3**.

ture to provide an activated sulfone linkage which is cleavable by nucleophilic substitution.

Experimental Section

General Procedures. Bromomethyl resin was purchased from Tianjin Nankai Hecheng Science and Technology Co. (100−200 mesh, 1.5 mmol/g, 1% divinylbenzene cross-linking). All other chemical reagents were purchased from Aldrich, Merck, Lancaster, or Fluka and were used without further purification. Moisture-sensitive experiments were carried out under nitrogen in atmosbag with commercially obtained anhydrous solvents. The solid-phase, room-temperature reactions were agitated on a flask shaker SF1 (Stuart Scientific). Microwave reactions were carried out using the Biotage Initiator microwave synthesizer. Analytical TLC was carried out on precoated plates (Merck silica gel 60, F254) and visualized with UV light or stained with iodine or Dragendorff-Munier. Flash column chromatograph was performed with silica (Merck, 70−230 mesh).

^{1}H NMR and ^{13}C NMR spectra were measured at 298 K on a Bruker DPX 300 or DPX 500 Fourier Transform spectrometer. Chemical shifts were reported in δ (ppm), relative to the residual undeuterated solvent, which was used an internal reference. The signals observed were described as: s (singlet), d (doublet), t (triplet), and m (multiplet). The number of protons (*n*) for a given resonance was indicated as *n*H. All Infrared (IR) spectra were recorded on a Bio-Rad FTS 165 spectrometer. Mass spectra were performed on Finnigan MAT 95/XL-T spectrometer under electron impact (EI), electrospray ionization (ESI) or fast atom bombardment (FAB) techniques.

Synthesis of Ethyl Methylcarbamathioylcarbamate 5 ($R^1 = CH_3$). Methylamine (100 mmol) was added to ethoxy isothiocyanate **4** (5.91 mL, 50 mmol) in anhydrous dichloromethane and stirred for 4 h. The reaction mixture was washed twice with 10% HCl to remove any nonvolatile amines, followed by additional washing with brine. The solution was then concentrated and purified by column

chromatography (EtOAc/hexane = 1:3) to obtain **5** as a white solid in quantitative yield (99%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.61 (s, NH, 1H), 8.91 (s, NH, 1H), 4.10 (q, J = 7.1 Hz, CH_2CH_3, 2H), 3.06 (d, J = 4.5, NHCH_3, 3H), 1.18 (t, J = 7.1 Hz, CH_2CH_3, 3H,). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 179.8, 152.6, 62.2, 31.6, 13.7. HRMS (ESI, $C_5H_{10}N_2O_2S$ &# x2212; H): calcd 161.0385; found 161.0387.

Synthesis of Ethyl(benzylthio)(methylamino)methylenecarbamate 6. Sodium hydride (60% dispersion in mineral oil) (0.2508 g, 6.6 mmol) was added to **5** (R^1 = CH_3, 0.3888 g, 2.4 mmol) in anhydrous THF (10 mL). Effervescence was observed. Thereafter benzyl bromide (0.2378 mL, 2.0 mmol) was added and the reaction mixture was stirred for 12 h and then quenched with deionized water at 0 °C. The reaction mixture was concentrated in vacuo, and the residue obtained was washed with brine (20 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layer was dried with $MgSO_4$, filtered, concentrated, and purified by column chromatography (EtOAc/hexane = 1:3) to give **6** (0.3774 g, 68% yield) as a pale yellowish white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.78 (s, NH, 1H), 7.37−7.24 (m, 5H, ArH), 4.37 (s, ArCH_2S, 2H), 4.17 (q, J = 7.1 Hz, $CO_2CH_2CH_3$, 2H), 2.95 (s, NHCH_3, 3H), 1.32 (t, J = 7.1 Hz, CH_2CH_3, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.9, 162.2, 135.9, 128.9, 128.3, 127.2, 61.0, 35.0, 29.7, 14.2. HRMS (ESI, $C_{12}H_{16}N_2O_2S$ + Na): calcd 275.0825; found 275.0835.

Synthesis of 6-(Benzylthio)-1,3,5-triazine-2,4-(1*H*,3*H*)-dione 7. The respective isocyanate (6 equiv) was added to **6** according to the reaction conditions listed in Table 1. The resultant reaction mixture was stirred overnight, concentrated in vacuo, and purified by column chromatography (EtOAc/hexane = 1:3) to give **7** as a white solid.

3-Benzyl-6-(benzylthio)-1-methyl-1,3,5-triazine-2,4-(1*H*,3*H*)-dione 7a. Yield: 60%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.39−7.11 (m, ArH, 10H), 4.92 (s, NCH_2Ar, 2H), 4.31 (s, SCH_2Ar, 2H), 3.20 (s, NCH_3, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.2, 152.1, 149.9, 135.9, 134.4, 129.2, 129.1, 128.9, 128.8 (2 carbons), 128.6, 45.5, 36.8, 30.9. HRMS (ESI, $C_{18}H_{17}N_3O_2S$ + Na): calcd 362.0934; found 362.0933.

6-(Benzylthio)-1-methyl-3-*m*-tolyl-1,3,5-triazine-2,4-(1*H*,3*H*)-dione 7b. Yield: 52%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.44−7.05 (m, ArH, 9H), 4.53 (s, SCH_2Ar, 2H), 3.46 (s, NCH_3, 3H), 2.39 (s, ArCH_3, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.0, 152.1, 150.2, 139.4, 134.4, 134.3, 129.8, 129.3, 129.2, 128.8, 128.3, 128.0, 124.7, 36.9, 31.2, 21.2. HRMS (ESI, $C_{18}H_{17}N_3O_2S$ + Na): calcd 362.0934; found 362.0933.

6-(Benzylthio)-1-methyl-3-phenylethyl-1,3,5-triazine-2,4-(1*H*,3*H*)-dione 7c. Yield: 72%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.35−7.15 (m, ArH, 10H), 4.40 (s, SCH_2Ar, 2H), 4.07−4.02 (m, NCH_2CH_2Ar, 2H), 3.33 (s, NCH_3, 3H), 2.91−2.85 (m, NCH_2CH_2Ar, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.3, 152.1, 150.1, 138.0, 134.6, 129.4, 128.9, 128.8, 128.4, 128.1, 126.5, 43.7, 36.8, 33.7, 31.1. ^{13}C DEPT135 NMR ($CDCl_3$, 75 MHz): δ 129.4, 128.9, 128.8, 128.5, 128.1, 126.5, 43.8, 36.9, 33.4, 31.1. HRMS (ESI, $C_{19}H_{19}N_3O_2S$ + Na): calcd 376.1090; found 376.1096.

6-(Benzylthio)-1-methyl-3-phenyl-1,3,5-triazine-2,4-(1*H*,3*H*)-dione 7d. Yield: 67%. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.36−7.13 (m, ArH, 10H), 4.40 (s, SCH_2Ar, 2H), 3.29 (s, NCH_3, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.8, 151.6, 149.9, 134.4, 134.4, 129.2, 129.1, 128.6 (2 carbons), 127.9, 127.7, 36.8, 31.0. ^{13}C DEPT135 NMR ($CDCl_3$, 75 MHz): δ 129.2, 129.1, 128.6, 127.8, 127.7, 36.7, 31.0. HRMS (ESI, $C_{17}H_{15}N_3O_2S$ + Na): calcd 348.0777; found 348.0794.

Synthesis of 3-Benzyl-1-methyl-6-(methylamino)-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1a1. DMF (15 mL), methylamine (2 M in THF, 2.5 mL, 5 mmol), and DiEA (0.870 mL, 5 mmol) were added to **7** (R^2 = benzyl, 1 mmol) in a 20 mL microwave vessel. The resultant mixture was a clear pale yellow solution. The reaction mixture was then microwave irradiated at 180 °C for 20 min at a pressure of 5 bar. After which the reaction was concentrated in vacuo to yield a pale yellow solid that was washed with diethyl ether and EtOAc to give **1a1** as a white solid (0.1723 g, 70% yield). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.72 (d, J = 3.63, *NH*CH_3, 1H), 7.27−7.21 (m, ArH, 5H), 4.88 (s, ArCH_2, 2H), 3.22 (s, NCH_3, 3H), 2.80 (d, J = 3.93 Hz, NHCH_3, 3H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 155.9, 154.7, 152.1, 138.6, 129.2, 128.5, 128.0, 45.3, 30.1, 29.3. HRMS (ESI, $C_{12}H_{14}N_4O_2$ + Na): calcd 269.1009; found 269.1009. mp: 226.2−228.4 °C.

General Procedure for the Preparation of Resin 9. Bromomethyl resin **3** (10 mmol, 1.55 mmol/g) was swollen in anhydrous THF (100 mL) for 10 min. Thereafter, compound **5** (20 mmol) and sodium hydride (60% dispersion in mineral oil, 1.2 g, 30 mmol) were added, and the reaction mixture was stirred overnight at room temperature. After which, the resin was filtered and washed thoroughly with DMF (20 mL × 3), ethanol (20 mL × 3), acetone (20 mL × 3), ethyl acetate (20 mL × 3), and THF (20 mL × 3), respectively, and dried overnight in a vacuum oven at 40 °C. FTIR: ν (C═N stretch) 1637 cm^{-1}.

General Procedure for the Preparation of Resin 10. Resin **10** was prepared according to the reaction conditions listed in Table 1. Resin **9** (3 mmol) was swollen in the reaction solvent (30 mL) for 10 min. Thereafter the respective isocyanate (15 mmol) and tetramethylguanidine (0.2 equiv, when R^2 = aliphatic or benzyl) were added, and the reaction mixture was stirred overnight After which, the resin was filtered and washed thoroughly with DMF (20 mL × 3), ethanol (20 mL × 3), acetone (20 mL × 3), ethyl acetate (20 mL × 3), and THF (20 mL × 3), respectively, and dried overnight in a vacuum oven at 40 °C. FTIR: ν (C═O stretch) 1735 cm^{-1}, ν (C═N stretch) 1685 cm^{-1}.

Synthesis of 1,3-Dibenzyl-6-thioxo-1,3,5-triazinane-2,4-dione 1a′. DMF (15 mL), methylamine (2 M in THF, 2.5 mL, 5 mmol), and DiEA (0.870 mL, 5 mmol) were added to **10** (R^1 = R^2 = benzyl, 1 mmol) in a 20 mL microwave vessel. The resultant mixture was a clear pale yellow solution. The reaction mixture was then microwave irradiated at 180 °C for 20 min at a pressure of 5 bar. After which the reaction was concentrated in vacuo to yield a pale yellow solid that was purified using column chromatography with EA/hexane (1:3) as eluent. This afforded **1a′** as a white solid (0.078 g, 24% yield). ^{1}H NMR (MeOD-d_4, 300 MHz): δ 7.37−7.24 (m, ArH, 10H), 5.50 (s, ArCH_2N, 2H), 4.85 (s, ArCH_2N, 2H). ^{13}C NMR (MeOD-d_4, 75 MHz): δ 178.6, 150.1, 147.9,

137.3, 137.2, 129.5, 129.3, 129.3, 128.8, 128.5, 51.2, 46.3. HRMS (ESI, $C_{17}H_{15}N_3O_2S_1$ − H): calcd 324.0812; found 324.0810.

General Procedure for the Synthesis of 1a from Resin 10. Resin **10** (1 mmol) and anhydrous DMF (15 mL) were placed in a 20 mL microwave vessel, and the resin was allowed to swell in DMF for 10 min. Methylamine (2 M in THF, 2.5 mL, 5 mmol) and DiEA (0.870 mL, 5 mmol) were added, and the reaction mixture was microwave irradiated at 180 °C for 20 min at a pressure of 5 bar. After which the reaction mixture was filtered through a frit and washed with DMF (2 × 10 mL). The filtrate was then concentrated in vacuo to yield a pale yellow solid that was then washed with diethyl ether and EtOAc to yield a white solid.

1-Methyl-6-(methylamino)-3-*m*-tolyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1a2. Overall yield: 53%. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.77 (s, NH, 1H), 7.31−6.97 (m, ArH, 4H), 3.24 (s, N*CH*$_3$, 3H), 2.85 (s, NH*CH*$_3$, 3H), 2.31(s, ArCH$_3$). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 155.0, 153.4, 150.9, 137.9, 136.3, 129.1, 128.3, 128.3, 125.7, 28.9, 28.3, 20.6. HRMS (ESI, $C_{12}H_{13}N_4O_2$ − H): calcd 245.1044; found 245.1036. mp: 329.2−331.9 °C.

1-Methyl-6-(methylamino)-3-phenylethyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1a3. Overall yield: 39%. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.66 (s, NH, 1H), 7.29−7.19 (m, ArH, 5H), 3.91−3.86 (m,, N*CH*$_2$CH$_2$Ar, 2H), 3.21(s, NCH$_3$, 3H), 2.80−2.75 (m, NCH$_2$*CH*$_2$Ar, 2H), 2.8−2.75 (m, NH*CH*$_3$, 3H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 154.7, 153.4, 150.8, 138.6, 128.5, 128.3, 126.2, 42.4, 33.3, 28.9, 28.2. HRMS (ESI, $C_{13}H_{16}N_4O_2$ + Na): calcd 283.1165; found 283.1160. mp: 212.2−217.8 °C.

3-Isopropyl-1-methyl-6-(methylamino)-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1a4. Overall yield: 17%. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 6.62 (s, NH, 1H), 5.02 (m, J = 6.95 Hz, *CH*(CH$_3$)$_2$, 1H), 3.41 (s, NCH$_3$, 3H), 3.02 (s, NHCH$_3$, 3H), 1.43−1.42 (d, J = 6.95 Hz, CH(*CH*$_3$)$_2$, 6H). ^{13}C NMR (CDCl$_3$, 125 MHz): δ 154.6, 154.3, 150.2, 47.0, 29.0, 29.0, 19.3. HRMS (ESI, $C_8H_{14}N_4O_2$ − H): calcd 197.1044; found 197.1042. mp: 216.4−218.5 °C.

3-Allyl-1-methyl-6-(methylamino)-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1a5. Overall yield: 48%. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.12 (s, NH, 1H), 5.86 (m, CH$_2$-*CH*CH$_2$, 1H), 5.20 (d, J = 17.65 Hz, 10.05 Hz, CH$_2$CH*CH*$_2$, 1H,), 5.15 (d, J = 10.05 Hz, CH$_2$CH*CH*$_2$, 1H,), 4.46 (d, J = 5.7 Hz, *CH*$_2$CHCH$_2$, 2H), 3.43 (s, N*CH*$_3$, 3H), 2.98 (s, NH*CH*$_3$, 3H). ^{13}C NMR (CDCl$_3$, 125 MHz): δ 155.2, 155.1, 150.8, 131.8, 117.5, 44.3, 29.0, 28.9. ^{13}C DEPT135 NMR (CDCl$_3$, 125 MHz): δ 131.8, 117.5, 44.3, 29.0, 28.9; HRMS (ESI, $C_8H_{12}N_4O_2$ − H): calcd 195.0887; found 195.0881. mp: 209.5−213.7 °C.

1-Methyl-6-(methylamino)-3-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1a6. Overall yield: 46%. ^{1}H NMR (MeOD, 500 MHz): δ 7.81 (s, NH, 1H), 7.43−7.18 (m, ArH, 5H), 3.25 (s, N*CH*$_3$, 3H), 2.84 (s, NH*CH*$_3$, 3H). ^{13}C NMR (MeOD, 125 MHz): δ 155.0, 153.4, 150.9, 136.5, 128.7, 128.5 127.6, 29.0, 28.4. HRMS (EI, $C_{11}H_{12}N_4O_2^+$): calcd 232.0960; found 232.0961. mp: 286.4−291.5 °C.

1-Methyl-6-(methylamino)-3-*o*-tolyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1a7. Overall yield: 42%. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.81 (s, N*H*, 1H), 7.30−7.09 (m, ArH, 4H), 3.26 (s, N*CH*$_3$, 3H), 2.86 (s, NH*CH*$_3$, 3H) 2.03 (s, Ar*CH*$_3$, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 155.2, 153.0, 150.5, 135.7, 135.5, 130.2, 128.8, 128.0, 126.3, 29.0, 28.4, 16.9. ^{13}C DEPT135 NMR (DMSO-d_6, 125 MHz): δ 130.2, 128.8, 128.0, 126.3, 29.0, 28.4, 16.9. HRMS (ESI, $C_{12}H_{14}N_4O_2$ − H): calcd 245.1044; found 245.1028. mp: 276.2−280.9 °C.

6-(Butylamino)-1-methyl-3-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1a8. Column chromatography with acetone:EtOAc (1:1) as eluent afforded **1a8** as a white solid. Overall yield: 46%. ^{1}H NMR (MeOD-d_4, 500 MHz): δ 7.47−7.23 (m, ArH, 4H), 3.49 (t, N*CH*$_2$CH$_2$CH$_2$CH$_3$, 3H), 3.37 (s, NH*CH*$_3$, 3H), 1.65 (m, NCH$_2$*CH*$_2$CH$_2$CH$_3$, 2H), 1.65 (m, NCH$_2$*CH*$_2$CH$_2$CH$_3$, 2H), 1.39 (m, NCH$_2$CH$_2$*CH*$_2$CH$_3$, 2H), 0.98 (m, NCH$_2$CH$_2$CH$_2$*CH*$_3$, 3H). ^{13}C NMR (MeOD-d_4, 125 MHz): δ 157.4, 156.8, 152.8, 137.2, 130.0, 129.7, 129.4, 42.8, 32.2, 29.6, 21.0, 14.1. HRMS (ESI) [M + H]$^+$ calcd for $C_{14}H_{19}N_4O_2^-$: 275.1503; found 275.1504.

General Procedure for the Synthesis of 2 from Resin 10. Resin **10** (0.5 mmol) was swollen in CH_2Cl_2 (20 mL) for 10 min. Thereafter mCPBA (3 equiv) was added, and the reaction mixture was shaken at room temperature for 3 h. The resin was then filtered using a frit and washed with CH_2Cl_2 (2 × 10 mL). The combined filtrate and washings were then extracted with deionized H_2O at pH 8 (50 mL, pH of the water was adjusted using saturated $NaHCO_3$). The combined organic extracts was dried over $MgSO_4$, filtered, and concentrated in vacuo to yield a colorless syrup, which was purified by column chromatography. The isolated compounds were not UV active and were visualized on TLC using I_2 vapor.

1-Benzyl-3-methyl-1,3,5-triazinane-2,4,6-trione 2a. Column chromatography with acetone/hexane (1:2) as eluent afforded **2a** as a white solid. Overall yield: 39%. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 9.62 (s, NH, 1H), 7.39−7.36 (m, 2ArH, 2H), 7.22−7.20 (m, 3ArH, 3H), 4.92 (s, N*CH*$_2$Ar, 2H), 3.21 (s, N*CH*$_3$, 3H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 149.8, 148.7, 148.6, 135.4, 129.1, 128.5, 128.2, 45.5, 28.7. HRMS (EI, $C_{11}H_{11}N_3O_3$): calcd 233.0800; found 233.0799.

1-Benzyl-3-phenyl-1,3,5-triazinane-2,4,6-trione 2b. Column chromatography with EtOAc/hexane (1:1) as eluent afforded **2b** as a white solid. Overall yield: 52%. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 7.50−7.19 (m, 10H, 10ArH), 5.04 (s, 2H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 149.6, 148.3, 147.9, 135.4, 133.0, 129.5, 129.5, 128.6, 128.3 (3 carbons), 45.83. HRMS (EI, $C_{16}H_{13}N_3O_3^+$): calcd 295.0957; found 295.0957.

1-Benzyl-3-butyl-1,3,5-triazinane-2,4,6-trione 2c. Column chromatography with EA/hexane (1:2) as eluent afforded **2c** as a white solid. Overall yield: 43%. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 7.46−7.44 (m, ArH, 2H), 7.23−7.25 (m, ArH, 3H), 4.99 (s, *CH*$_2$Ar, 2H), 3.82 (t, J = 7.32 Hz, *CH*$_2$CH$_2$CH$_2$CH$_3$, 2H), 1.60 (m, CH$_2$*CH*$_2$CH$_2$CH$_3$, 2H), 1.33 (m, CH$_2$CH$_2$*CH*$_2$CH$_3$, 2H), 0.92 (t, J = 7.29 Hz, CH$_2$CH$_2$CH$_2$*CH*$_3$, 3H). ^{13}C NMR: (CDCl$_3$, 75 MHz): δ 149.6, 148.7, 148.5, 135.6, 128.9, 128.4, 128.0, 45.3, 42.3, 29.6, 19.7, 13.5. HRMS (EI, $C_{14}H_{17}N_3O_3^+$): calcd 275.1270; found 275.1264.

1-Hexyl-3-phenyl-1,3,5-triazinane-2,4,6-trione 2d. Column chromatography with EtOAc/hexane (1:2) as eluent afforded **2d** as a white solid. Overall yield: 35%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.26 (s, br, NH, 1H), 7.53−7.42 (m, 3ArH, 3H), 7.27−7.24 (m, ArH, 2H), 3.89 (t, J = 7.32 Hz, $CH_2CH_2CH_2CH_3$, 2H), 1.65 (m, $CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 1.29 (m, $CH_2CH_2CH_2CH_2CH_2CH_3$, 6H), 0.88 (t, J = 6.6 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.4, 148.3, 148.1, 133.0, 129.3, 129.3, 128.3, 42.8, 31.2, 27.6, 22.4, 13.9. HRMS (EI, $C_{15}H_{19}N_3O_3^+$): calcd 289.1426; found 289.1430.

1-Allyl-3-phenyl-1,3,5-triazinane-2,4,6-trione 2e. Column chromatography with EtOAc/hexane (1:1) as eluent afforded **2e** as a white solid. Overall yield: 53%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.48−7.41 (m, Ar*H*, 3H), 7.23−7.21 (m, Ar*H*, 2H), 5.91 to 5.80 (m, CH_2**C***H*CH_2, 1H), 5.32 (d, J = 17.07 Hz, CH_2CH**C***H*$_2$, 1H), 5.23 (d, J =10.2 Hz, CH_2CH**C***H*$_2$, 1H), 4.45 (d, J = 5.94 Hz, CH_2CHCH_2, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.1, 148.1 (2 carbons), 132.9, 130.4, 129.2, 129.2, 128.2, 119.4, 44.4. HRMS (EI, $C_{12}H_{11}N_3O_3^+$): calcd 245.0800; found 245.0799.

1-Allyl-3-benzyl-1,3,5-triazinane-2,4,6-trione 2f. Column chromatography with EtOAc/hexane (1:2) as eluent afforded **2f** as a white solid. Overall yield: 37%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.46−7.43 (m, Ar*H*, 2H), 7.34−7.25 (m, Ar*H*, 3H), 5.90−5.77 (m, CH_2CHCH_2, 1H), 5.31 (dd, J = 17.25 Hz, J = 1.14 Hz, CH_2CHCH_2, 1H), 5.26 (dd, J = 10.2 Hz, J = 0.99 Hz, CH_2CHCH_2, 1H), 5.00 (s, CH_2Ar, 2H), 4.43 (d, J = 5.91 Hz, CH_2CHCH_2, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.3, 148.6, 148.2, 135.4, 130.5, 129.0, 128.5, 128.1, 119.1, 45.4, 44.3. HRMS (EI, $C_{13}H_{13}N_3O_3^+$): calcd 259.0957; found 259.0962.

1-Allyl-3-butyl-1,3,5-triazinane-2,4,6-trione 2g. Column chromatography with EtOAc/hexane (3:1) as eluent afforded **2g** as a white solid. Overall yield: 55%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.91−5.78 (m, CH_2**C***H*CH_2, 1H), 5.29 (d, J = 17.4 Hz, NCH_2CHCH_2, 1H), 5.22 (d, J = 10.44 Hz, NCH_2CHCH_2, 1H), 4.45 (d, J = 5.58 Hz, NCH_2CHCH_2, 2H), 3.85 (t, J = 7.32 Hz, **C***H*$_2CH_2CH_2CH_3$, 2H,), 1.62 (q, J = 6.99 Hz, CH_2**C***H*$_2CH_2CH_3$, 2H,), 1.35 (m, CH_2CH_2**C***H*$_2CH_3$, 2H), 0.92 (t, J = 7.29 Hz, **C***H*$_2CH_2CH_2CH_3$, 3H,). ^{13}C NMR (CDCl3, 75 MHz): δ 149.3, 148.5, 148.3, 130.6, 119.0, 44.2, 42.3, 29.7, 19.8, 13.5. HRMS (EI, $C_{10}H_{15}N_3O_3^+$): calcd 225.1113; found 225.1113.

1-Hexyl-3-methyl-1,3,5-triazinane-2,4,6-trione 2h. Column chromatography with acetone/hexane (1:1) as eluent afforded **2h** as a white solid. Overall yield: 42%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.59 (s, NH, 1H), 3.84 (t, J = 7.56 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 3.31 (s, NCH_3, 3H), 1.62 (m, $CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 1.30 (m, $CH_2CH_2CH_2CH_2CH_2CH_3$, 6H), 0.87 (t, J = 6.72 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.7, 148.8, 148.4, 42.5, 31.3, 28.7, 27.6, 26.2, 22.4, 13.9. HRMS (EI, $C_{10}H_{17}N_3O_3^+$): calcd 227.1270; found 227.1273.

General Procedure for the Preparation of Resin 11. Resin **10** (0.5 mmol) was swollen in dichloromethane (3 mL) for 10 min. Thereafter DMDO (2.5 equiv.) was added and the reaction mixture was shaken at room temperature for 10 min (except when $R^1 = CH_3$ where the reaction mixture was shaken at room temperature for 4 min). The resin was then filtered, washed with acetone and THF, and dried overnight in a vacuum oven at 40 °C.

General Procedure for the Synthesis of 1b. Resin **11** (0.5 mmol) was swollen in DMF (20 mL) for 10 min. Thereafter 33% ammonium hydroxide (5 mL) was added, and the reaction mixture was stirred at 70 °C for 6 h. After which, the reaction mixture was filtered through a reaction frit, and the resin was washed with DMF (2 × 10 mL).

6-Amino-3-benzyl-1-methyl-1,3,5-trazine-2,4(1*H*,3*H*)-dione 1b1. The filterate and washings were combined and concentrated to yield a white solid as product without further purification. Overall yield: 56%. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.28−7.24 (m, ArH, 5H), 4.86 (s, NCH_2Ar, 2H), 3.22 (s, $NHCH_3$, 3H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 156.7, 153.9, 151.2, 137.6, 128.2, 127.5, 126.9, 44.3, 29.7. ^{13}C DEPT135 NMR (DMSO-d_6, 75 MHz): δ 128.2, 127.5, 126.9, 44.3, 29.7. HRMS (ESI, $C_{11}H_{12}N_4O_2$ − H): calcd 231.0887; found 231.0882.

6-Amino-3-benzyl-1-methyl-1,3,5-trazine-2,4(1*H*,3*H*)-dione 1b2. The filtrate and washings were combined and concentrated to yield a white solid as product without further purification. Overall yield: 30%. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.32−7.18 (m, ArH, 5H), 3.87 (t, J = 8.01 Hz, NCH_2CH_2Ar, 2H), 3.21 (s, NCH_3, 3H), 2.77 (t, J = 8.37, NCH_2CH_2Ar, 2H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 156.6, 153.7, 150.9, 138.7, 128.5, 128.4, 126.2, 42.5, 33.4, 29.5. ^{13}C DEPT135 NMR (DMSO-d_6, 75 MHz): δ 128.5, 126.2, 42.5, 33.4, 29.5. HRMS (ESI, $C_{12}H_{14}N_4O_2$ − H): calcd 245.1044; found 245.1028.

6-Amino-1,3-diphenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1b3. Column chromatography with acetone/EtOAc/hexane (1:1:1) as eluent afforded **1b3** as a white solid. Overall yield: 39%. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.00, (s, 1H, N−H), 7.99 to 7.26, (m, 10H, 10ArH), 6.35, (s, 1H, N−H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 156.2, 153.9, 150.6, 136.2, 133.9, 129.7, 129.5, 129.0, 128.8, 128.4, 127.6. HRMS (ESI, $C_{15}H_{12}N_4O_2$ + H): calcd 281.1033; found 281.1039.

6-Amino-1,3-dibenzyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1b4. Column chromatography with acetone/EtOAc/hexane (1:1:1) as eluent afforded **1b4** as a white solid. Overall yield: 26%. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.36−7.23 (m, ArH, 10H), 5.06 (s, NCH_2Ar, 2H), 4.91 (s, NCH_2Ar, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 156.0, 153.7, 151.3, 137.5, 135.6, 128.5, 128.2 (2 carbons), 127.3, 127.0, 126.4, 45.1, 44.4. DEPT 135 (DMSO-d_6, 125 MHz): δ 128.5, 128.2, 127.3, 127.0, 126.4, 45.1, 44.4. ^{13}C DEPT135 NMR (DMSO-d_6, 125 MHz): δ 128.5, 128.2, 127.3, 127.0, 126.4, 45.1, 44.4. HRMS (ESI, $C_{17}H_{16}N_4O_2$ + H): calcd 309.1346; found 309.1343.

6-Amino-1-butyl-3-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1b5. Column chromatography with acetone/EtOAc/hexane (1:1:3) as eluent afforded **1b5** as a white solid. Overall yield: 51%. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.41−7.37 (m, ArH, 3H), 7.21−7.19 (d, J = 6.99 Hz, ArH, 2H), 3.77, (t, J = 7.32 Hz, $NCH_2CH_2CH_2CH_3$, 2H), 1.55 (m, $NCH_2CH_2CH_2CH_3$, 2H), 1.32 (m, $NCH_2CH_2CH_2CH_3$, 2H), 0.89 (t, J = 7.32 Hz, $NCH_2CH_2CH_2CH_3$, 3H). ^{13}C NMR: (DMSO-d_6, 75 MHz): δ 156.1, 153.4, 150.9, 136.3,

128.7, 128.4, 127.5, 42.0, 29.2, 19.1, 13.5. ^{13}C DEPT135 NMR (DMSO-d_6, 125 MHz): δ 128.7, 128.4, 127.5, 42.0, 29.1, 19.1, 13.5. HRMS (ESI, $C_{13}H_{16}N_4NaO_2$ + Na): calcd 283.1165; found 283.1178.

6-Amino-1-methyl-3-phenyl-1,3,5-trazine-2,4(1*H*,3*H*)-dione 1b6. The filterate and washings were combined and concentrated to yield a white solid as product without further purification. Overall yield: 60%. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.44−7.18 (m, ArH, 5H), 3.25 (s, NCH_3, 3H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 156.9, 153.7, 151.1, 136.5, 128.8, 128.6, 127.6, 29.6. ^{13}C DEPT135 NMR (DMSO-d_6, 125 MHz): δ 128.8, 128.6, 127.6, 29.6. HRMS (ESI, $C_{10}H_{10}N_4O_2$ − H): calcd 217.0731; found 217.0726.

6-Amino-1-benzyl-3-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1b7. Column chromatography with acetone/EtOAc/hexane (1:1:1) as eluent afforded **1b7** as a white solid. Overall yield: 35%. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.43−7.25 (m, ArH, 10H), 5.09 (s, NCH_2Ar, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 156.2, 153.4, 151.2, 136.3, 135.5, 128.8, 128.5, 128.4, 127.7, 127.3, 126.5, 45.0. ^{13}C DEPT135 NMR (DMSO-d_6, 125 MHz): δ 128.8, 128.5, 128.4, 127.7, 127.3, 126.5, 45.0. HRMS (ESI, $C_{16}H_{14}N_4O_2$ + H): calcd 295.1190; found 295.1190.

3-Ally-6-amino-1-methyl-1,3,5-trazine-2,4(1*H*,3*H*)-dione 1b8. The filterate and washings were combined and concentrated to yield a white solid as product without further purification. Overall yield: 35%. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.73 (br, N*H*, 1H), 5.84−5.71 (m, $CH_2CH$$CH_2$, 1H), 5.08−5.04 (ddd, J = 2.07 Hz, 2.46 Hz, 13.74 Hz, NCH_2CHCH_2, 2H), 4.27 (d, J = 5.22 Hz, NCH_2CHCH_2, 2H,), 3.21 (s, NCH_3, 3H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 156.7, 153.6, 150.9, 133.0, 116.1, 43.2, 29.6. ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 133.8, 116.9, 44.0, 30.4. HRMS (ESI, $C_7H_{10}N_4O_2$ − H): calcd 181.0731; found 181.0720.

6-Amino-3-hexyl-1-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1b9. Column chromatography with acetone/EtOAc/hexane (1:1:2) as eluent afforded **1b9** as a white solid. Overall yield: 44%. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.82, (s, 1H, N−H), 7.53−7.51, (m, ArH, 3H), 7.40−7.38, (m, ArH, 2H), 6.18, (s, 1H, N−H), 3.68 (t, J = 7.55 Hz, N$CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 1.52 (m, $NCH_2CH_2CH_2CH_2CH_2CH_3$,2H), 1.26 (m, $NCH_2CH_2CH_2CH_2CH_2CH_3$, 6H), 0.86 (t, J = 6.35 Hz, $NCH_2CH_2CH_2CH_2CH_2CH_3$, 3H). ^{13}C NMR (DMSO-$d_6$, 125 MHz): δ 155.8, 154.0, 150.7, 134.0, 129.7, 129.4, 128.9, 41.0, 30.8, 27.2, 25.8, 21.9, 13.8. ^{13}C DEPT 135 NMR (DMSO-d_6, 125 MHz): δ 129.7, 129.5, 128.9, 41.0, 30.9, 27.2, 25.9, 21.9, 13.8. HRMS (ESI, $C_{15}H_{20}N_4O_2$ − H): calcd 287.1513; found 287.1504.

6-Amino-3-benzyl-1-butyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1b10. Column chromatography with acetone/EtOAc/hexane (1:1:3) as eluent afforded **1b10** as a white solid. Overall yield: 47%. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.30−7.21 (m, ArH, 5H), 4.87 (s, N$\mathbf{CH_2}$Ar, 2H), 3.76 (t, J = 7.55 Hz, N$CH_2CH_2CH_2CH_3$, 2H), 1.48 (m, $NCH_2CH_2CH_2CH_3$, 2H), 1.26 (m, $NCH_2CH_2CH_2CH_3$, 2H), 0.87 (t, J = 7.55 Hz, $NCH_2CH_2CH_2CH_3$, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 155.9, 153.7, 151.0, 137.6, 128.1, 127.3, 126.9, 44.2, 42.0, 29.1, 19.1, 13.5. ^{13}C DEPT 135 NMR (DMSO-d_6, 125 MHz): δ 128.1, 127.3, 126.9, 44.2, 42.0, 29.1, 19.1, 13.5. HRMS (ESI, $C_{14}H_{18}N_4O_2$ + H): calcd 275.1503; found 275.1512.

6-Amino-1-benzyl-3-hexyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1b11. Column chromatography with acetone/EtOAc/hexane (1:1:2) as eluent afforded **1b11** as a white solid. Overall yield: 22%. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.68 (s, NH, 1H), 7.37 to 7.20 (m, ArH, 5H), 5.03 (s, NCH_2Ar, 2H), 3.69 (t, J = 7.32 Hz, N$CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 1.49 (m, $NCH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 1.23 (m, $NCH_2CH_2CH_2CH_2CH_2CH_3$, 6H), 0.83 (t, J = 5.91 Hz, $NCH_2CH_2CH_2CH_2CH_2CH_3$, 3H). ^{13}C NMR (DMSO-$d_6$, 75 MHz): δ 155.9, 153.7, 151.2, 135.7, 128.5, 127.4, 126.4, 44.9, 41.2, 30.9, 27.2, 25.9, 21.9, 13.8. ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 128.5, 127.4, 126.4, 44.9, 41.2, 30.9, 27.2, 25.9, 22.0, 13.8. HRMS (ESI, $C_{16}H_{22}N_4O_2$ + Na): calcd 325.1635; found 325.1627.

6-Amino-1-butyl-3-hexyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1b12. Column chromatography with acetone/EtOAc/hexane (1:1:3) as eluent afforded **1b12** as a white solid. Overall yield: 27%. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.61 (s, 2H, NH), 3.75 (t, J = 6.95 Hz, N$\mathbf{C}H_2CH_2CH_2CH_3$, 2H), 3.65, (t, J = 6.95 Hz, N$CH_2CH_2CH_2CH_3$, 2H,), 1.46 (m, $2CH_2$, 4H), 1.24 (m, $4CH_2$, 8H), 0.88 (m, $2CH_3$, 6H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 155.8, 153.8, 150.9, 41.9, 41.0, 30.9, 29.2, 27.2, 25.8, 21.9, 19.1, 13.8, 13.6. HRMS (ESI, $C_{13}H_{24}N_4O_2$ + Na): calcd 291.1791; found 291.1783.

General Procedure for the Synthesis of 1c. Resin **11** (0.5 mmol) was swollen in DMF (10 mL) for 10 min. Thereafter the respective primary amine (5 equiv.) was added and the reaction mixture was stirred at 70 °C for 6 h. After which, the reaction mixture was filtered through a reaction frit, and the resin was washed with DMF (2 × 10 mL). The combined filtrate and washings wwere then concentrated in vacuo and purified using column chromatography to afford **1c** as a white solid.

1,3-Dibenzyl-6-(methylamino)-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c1. Column chromatography with acetone/EtOAc/hexane (1:1:2) as eluent afforded **1c1** in 52% overall yield. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.79 (s, N*H*, 1H), 7.36−7.20 (m, ArH, 10H), 5.07 (s, NCH_2Ar, 2H), 4.93 (s, NCH_2Ar, 2H), 2.77 (s, NCH_3, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 154.1, 153.5, 151.2, 137.5, 135.5, 128.6, 128.2, 127.3 (2 carbons) 127.0, 126.2, 44.5, 44.4, 28.5. ^{13}C DEPT 135 NMR (DMSO-d_6, 125 MHz): δ 128.6, 128.2, 127.3, 127.0, 126.2, 44.5, 44.4, 28.5. HRMS (ESI, $C_{18}H_{18}N_4O_2$ − H): calcd 321.1357; found 321.1353.

1-Benzyl-3-hexyl-6-(methylamino)-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c2. Column chromatography with acetone/EtOAc/hexane (1:1:4) as eluent afforded **1c2** in 52% overall yield. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.68 (d, J = 4.4 Hz, NH, 1H), 7.36−7.33 (m, ArH, 2H), 7.29−7.26 (m, ArH, 1H), 7.20−7.19 (m, ArH, 2H), 5.05 (s, NCH_2Ar, 2H), 3.71 (t, J = 7.55 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 2.75 (d, J = 3.75 Hz, NHCH_3, 3H), 1.50 (m, $CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 1.24 (s, $CH_2CH_2CH_2CH_2CH_2CH_3$, 6H), 0.84 (t, J = 6.30 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, 3H,). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 154.0, 153.4, 151.0, 135.5, 128.5, 127.2, 126.1, 44.3, 41.1, 30.8, 28.4, 27.2, 25.8, 21.9, 13.8. ^{13}C DEPT

135 NMR (DMSO-d_6, 125 MHz): δ 134.5, 133.2, 132.1, 50.3, 47.1, 36.8, 34.4, 33.1, 31.8, 27.9, 19.8. HRMS (ESI, $C_{17}H_{24}N_4O_2$ − H): calcd 315.1826; found 315.1819.

1-Benzyl-6-(methylamino)-3-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c3. Column chromatography with acetone/EtOAc/hexane (1:1:2) as eluent afforded **1c3** in 53% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.84 (s, N*H*, 1H), 7.46−7.25 (m, ArH, 10H), 5.10 (s, NCH_2Ar, 2H), 2.82 (s, NHCH_3, 3H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 154.3, 153.3, 151.1, 136.3, 135.4, 128.8, 128.6, 128.5, 127.8, 127.3, 126.3, 44.5, 28.6. ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 128.8, 128.6, 128.5, 127.8, 127.3, 126.3, 44.5, 28.6. HRMS (ESI, $C_{17}H_{16}N_4O_2$ − H): calcd 307.1200; found 307.1202.

3-Benzyl-6-(methylamino)-1-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c4. Column chromatography with acetone/EtOAc/hexane (1:1:2) as eluent afforded **1c4** in 53% overall yield. ^{1}H NMR (MeOD-d_4, 300 MHz): δ 7.55 (m, ArH, 3H,), 7.41−7.24 (m, ArH, 7H), 5.03 (s, NCH_2AR, 2H), 2.82 (s, NHCH_3, 3H). ^{13}C NMR (MeOD-d_4, 75 MHz): δ 154.7, 154.3, 151.2, 137.9, 133.8, 130.3, 130.1, 129.7, 128.5, 127.9, 127.3, 44.6, 28.9. ^{13}C DEPT 135 NMR (MeOD, 75 MHz): δ 130.4, 130.2, 129.8, 128.6, 128.0, 127.4, 44.7, 29.0. HRMS (ESI, $C_{17}H_{16}N_4O_2$ − H): calcd 307.1200; found 307.1198.

6-(Methylamino)-1,3-diphenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c5. Column chromatography with acetone/EtOAc/hexane (1:1:1) as eluent afforded **1c5** in 29% overall yield. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.57−7.26 (m, ArH, 10H), 6.66 (d, J = 4.4 Hz, N*H*, 1H), 2.75 (d, J = 4.4 Hz, NHCH_3, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 154.6, 153.7, 150.5, 136.1, 133.3, 129.9, 129.7, 129.3, 128.8, 128.5, 127.6, 28.6. ^{13}C DEPT 135 NMR (DMSO-d_6, 125 MHz): δ 129.9, 129.7, 129.3, 128.8, 128.5, 127.6, 28.6. HRMS (ESI, $C_{16}H_{14}N_4O_2$ + H): calcd 295.1190; found 295.1192.

3-Benzyl-1-butyl-6-(methylamino)-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c6. Column chromatography with acetone/EtOAc/hexane (1:1:3) as eluent afforded **1c6** in 63% overall yield. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.69 (d, J = 3.75 Hz, NH, 1H), 7.69−7.21 (m, Ar*H*, 5H), 4.88 (s, NCH_2Ar, 2H), 3.76 (t, J = 7.55 Hz, N$CH_2CH_2CH_2CH_3$, 2H), 2.81 (d, J = 3.15 Hz, NHCH_3, 3H), 1.49 (m, $NCH_2CH_2CH_2CH_3$, 2H), 1.28 (m, $NCH_2CH_2CH_2CH_3$, 2H), 0.88 (t, J = 7.55 Hz, $NCH_2CH_2CH_2CH_3$, 3H,). ^{13}C NMR: (DMSO-d_6, 125 MHz): δ 153.9, 153.5, 150.9, 137.6, 128.1, 127.3, 126.9, 44.2, 41.4, 29.1, 28.4, 19.1, 13.5. ^{13}C DEPT 135 NMR (DMSO-d_6, 125 MHz): δ 128.1, 127.3, 126.9, 44.2, 41.4, 29.1, 28.4, 19.1, 13.5. HRMS (ESI, $C_{15}H_{20}N_4O_2$ − H): calcd 287.1513; found 287.1515.

1-Butyl-6-(methylamino)-3-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c7. Column chromatography with acetone/EtOAc/hexane (1:1:3) as eluent afforded **1c7** in 59% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.77 (s, NH, 1H), 7.44−7.18 (m, ArH, 5H), 3.78 (t, J = 7.29 Hz, N$CH_2CH_2CH_2CH_3$, 2H) 2.85 (s, NHCH_3, 3H), 1.52 (m, $CH_2CH_2CH_2CH_3$, 2H), 1.30 (m, $CH_2CH_2CH_2CH_3$, 2H), 0.89 (t, J = 6.96 Hz, $CH_2CH_2CH_2CH_3$, 3H,). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 154.1, 153.2, 150.8, 136.3, 128.7, 128.4, 127.5, 41.3, 29.1, 28.4, 19.1, 13.5. HRMS (ESI, $C_{14}H_{18}N_4O_2$ + Na): calcd 297.1322; found 297.1323.

3-Hexyl-6-(methylamino)-1-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c8. Column chromatography with acetone/EtOAc/hexane (1:1:4) as eluent afforded **1c7** in 62% overall yield. ^{1}H NMR: (DMSO-d_6, 300 MHz) δ 7.56−7.52 (m, ArH, 3H), 7.40−7.38, (m, ArH, 2H), 6.50 (d, J = 4.26 Hz, N*H*, 1H), 2.68 (t, J = 7.41 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 2.67 (d, J = 4.29 Hz, NHCH_3, 3H), 1.51 (m, $CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 1.25 (m, $CH_2CH_2CH_2CH_2CH_2CH_3$, 6H), 0.85 (t, J = 6.57 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 154.2, 153.8, 150.5, 133.5, 129.8, 129.6, 129.3, 41.0, 30.9, 28.4, 27.2, 25.9, 21.9, 13.8. ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 129.8, 129.6, 129.3, 41.0, 30.9, 28.4, 27.2, 25.9, 21.9, 13.8. HRMS (ESI, $C_{16}H_{22}N_4O_2$ + Na): calcd 325.1635; found 325.1648.

1,3-Dibenzyl-6-(butylamino)-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c9. Column chromatography with acetone/hexane (1:1) as eluent afforded **1c9** in 54% overall yield. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.78 (t, J = 5.05 Hz, NH, 1H), 7.78−7.21 (m, ArH, 10H), 5.13 (s, NCH_2Ar, 2H), 4.92 (s, NCH_2Ar, 2H), 3.27 (m, N$CH_2CH_2CH_2CH_3$, 2H), 1.42 (m, $NCH_2CH_2CH_2CH_3$, 2H), 1.12 (m, $NCH_2CH_2CH_2CH_3$, 2H), 0.79 (t, J = 6.95 Hz, $NCH_2CH_2CH_2CH_3$, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 153.5(2 carbons), 151.2, 137.5, 135.5, 128.4, 128.1, 127.3, 127.3, 126.9, 126.2, 44.4, 44.3, 40.8, 30.3, 19.1, 13.5. HRMS (EI, $C_{21}H_{24}N_4O_2^+$): calcd 364.1899; found 364.1902.

1-Benzyl-6-(benzylamino)-3-hexyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c10. The filtrate and combined washings were concentrated in vacuo to yield a yellowish syrup which was then dissolved in 30 mL EtOAC and extracted with 20 mL 1 M $CuSO_4$ to remove the residual benzylamine. The organic phase was dried over $MgSO_4$ and concentrate to yield a clear syrup as crude product, which was then purified using column chromatography with acetone/hexane (1:3) as eluent afforded **1c10** in 35% overall yield. ^{1}H NMR: ($CDCl_3$, 300 MHz) δ 7.32- 6.90 (m, ArH, 10H), 5.12 (s, NCH_2Ar, 2H), 4.46 (d, J = 5.25 Hz, NHCH_2Ar, 2H), 3.84 (t, J = 7.32 Hz, N$CH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 1.62 (m, $NCH_2CH_2CH_2CH_2CH_2CH_3$, 2H), 1.29 (m, $NCH_2CH_2CH_2CH_2CH_2CH_3$, 6H), 0.87 (t, J = 6.42 Hz, $NCH_2CH_2CH_2CH_3$, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 154.7, 153.9, 151.4, 136.6, 134.1, 129.2, 128.5, 128.4, 127.5, 127.2, 126.5, 45.5, 45.3, 42.6, 31.4, 27.6, 22.5, 13.9. ^{13}C DEPT 135 NMR ($CDCl_3$, 75 MHz): δ 129.2, 128.5, 128.4, 127.5, 127.2, 126.5, 45.5, 45.3, 42.6, 31.4, 27.6, 22.5, 13.9. HRMS (ESI, $C_{23}H_{20}N_4O_2$ + Na): calcd 407.1478; found 407.1491.

1-Benzyl-6-(benzylamino)-3-phenyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione 1c11. The filtrate and combined washings were concentrated in vacuo to yield a yellowish syrup, which was then dissolved in 30 mL of EtOAC and extracted with 20 mL of 1 M $CuSO_4$ to remove the residual benzylamine. The organic phase was dried over $MgSO_4$ and concentrate to yield a clear syrup as crude product which was then purified using column chromatography with acetone/hexane (1:2) as eluent afforded **1c11** in 28% overall yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.47 (s, NH, 1H), 7.46−7.13 (m, ArH, 15H), 5.23 (s, NCH_2Ar, 2H), 4.57 (s, J = 5.25 Hz, NHCH_2Ar, 2H. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 154.1, 153.3, 151.2, 138.3, 136.3, 135.4, 128.8, 128.6, 128.5, 128.1, 127.8, 127.3 (2 carbons), 126.8, 126.5, 44.4, 44.1. ^{13}C DEPT 135

NMR ($CDCl_3$, 75 MHz): δ 128.8, 128.6, 128.5, 128.1, 127.8, 127.3, 126.8, 126.5, 44.4, 44.1. HRMS (ESI, $C_{23}H_{28}N_4O_2$ + Na): calcd 15.2104; found 415.2100.

General Procedure for the Synthesis of 1d. Resin **11** (0.5 mmol) was swollen in DMF (5 mL) for 10 min; thereafter, hydroxylamine hydrochloride (0.1739 g, 2.5 mmol) and TEA (5 equiv.) were added, and the reaction mixture was stirred at 70 °C for 6 h. After which, the reaction mixture was filtered through a reaction frit, and the resin was washed with DMF (2 × 10 mL). The combined filtrate and washings were then concentrated in vacuo and purified using column chromatography.

3-Benzyl-6-(hydroxyimino)-1-methyl-1,3,5-triazine-2,4-dione 1d1. Column chromatography with acetone/EtOAc/hexane (1:1:4) to provide **1d1** as an off white solid in 51% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.70 (s, OH, 1H), 9.82 (s, NH, 1H), 7.30−7.24 (m, ArH, 5H), 4.84 (s, N*CH*$_2$Ar, 2H), 3.08 (s, N*CH*$_3$, 3H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 149.2, 147.7, 140.9, 137.3, 128.3, 127.2, 127.1, 43.9, 28.7. ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 128.3, 127.3, 43.9, 28.7. HRMS (EI, $C_{11}H_{12}N_4O_3^+$): calcd 248.0909; found 248.0914.

6-(Hydroxyimino)-1-methyl-3-phenylethyl-1,3,5-triazine-2,4-dione 1d2. Column chromatography with acetone: EtOAc/hexane (1:1:4) to yield **1d2** as an off white solid in 26% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.65 (s, br, NH), 9.78 (s, OH, 1H), 7.29−7.18 (m, ArH, 5H), 3.85 (m, N*CH*$_2$CH$_2$Ar, 2H), 3.07 (s, N*CH*$_3$, 3H), 2.79 (m, NCH$_2$*CH*$_2$Ar, 2H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 149.0, 147.4, 141.0, 138.4, 128.6, 128.4, 126.3, 42.1, 33.6, 28.5; ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 128.6, 128.4, 126.3, 42.1, 33.6, 28.5. HRMS (EI, $C_{12}H_{14}N_4O_3^+$): calcd 262.1066; found 262.1064.

6-(Hydroxyimino)-1-methyl-3-phenyl-1,3,5-triazine-2,4-dione 1d3. Column chromatography with acetone/EtOAc/hexane (1:1:4) to yield **1d3** as an off white solid in 42% overall yield. ^{1}H NMR (acetone-d_6, 300 MHz): δ 9.37 (s, NO***H***, 1H), 9.20 (s, N***H***, 1H), 7.44−7.33 (m, ArH, 5H), 3.17 (s, N***CH*$_3$**, 3H). ^{13}C NMR (acetone-d_6, 75 MHz): δ 150.8, 148.8, 143.5, 136.9, 130.8, 130.1, 129.7, 29.5. ^{13}C DEPT 135 NMR (acetone-d_6, 75 MHz): δ 130.8, 130.1, 129.7, 29.6. HRMS (EI, $C_{10}H_{10}N_4O_3^+$): calcd 234.0753; found 234.0753.

1,3-Dibenzyl-6-(hydroxyimino)-1,3,5-triazine-2,4-dione 1d4. Column chromatography with acetone:EtOAc: hexane (1:1:6) as eluent afforded **1d4** as a white solid in 27% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.74 (s, NH, 1H), 9.84 (s, OH, 1H), 7.32−7.26 (m, ArH, 10H), 4.90 (s, N*CH*$_2$Ar, 2H), 4.89 (s, N*CH*$_2$Ar, 2H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 149.4, 147.6, 140.2, 137.2, 136.6, 128.3, 128.2, 128.1, 127.3, 127.2, 127.1, 127.0, 126.8, 44.8, 44.1. HRMS (ESI, $C_{17}H_{16}N_4O_3$ − H): calcd 323.1150; found 323.1133.

1-Benzyl-6-(hydroxyimino)-3-phenyl-1,3,5-triazine-2,4-dione 1d5. Column chromatography with acetone/EtOAc/hexane (1:1:6) as eluent afforded **1d5** as a white solid in 24% overall yield. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.73 (s, NOH, 1H), 9.86 (s, N**H** 1H), 7.44−7.25 (m, 10H, 10ArH), 4.92 (s, N*CH*$_2$Ar, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 149.4, 147.5, 140.5, 136.6, 135.0, 129.4, 128.6 (2 carbons), 128.2 (2 carbons), 126.9, 44.8. HRMS (ESI, $C_{16}H_{14}N_4O_3$ − H): calcd 309.0993; found 309.0986.

1-Benzyl-3-hexyl-6-(hydroxyimino)-1,3,5-triazine-2,4-dione 1d6. Column chromatography with acetone/EtOAc/hexane (1:1:8) as eluent afforded **1d6** as a white solid in 33% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.56 (s, NH, 1H), 9.78 (s, NOH, 1H), 7.30−7.25 (m, ArH, 5H), 4.89 (s, N*CH*$_2$Ar, 2H), 3.70 (t, J = 6.96 Hz, N*CH*$_2$CH$_2$CH$_2$CH$_2$CH$_2$-CH$_3$, 2H), 1.52 (m, NCH$_2$*CH*$_2$CH$_2$CH$_2$CH$_2$CH$_3$, 2H), 1.25 (m, NCH$_2$*CH*$_2$*CH*$_2$*CH*$_2$*CH*$_2$CH$_3$, 6H), 0.85 (t, J = 6.27 Hz, NCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$*CH*$_3$, 3H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 149.3, 147.5, 140.3, 136.7, 128.2, 127.0, 126.8, 44.6, 41.0, 30.9, 27.5, 25.8, 22.0, 13.8. ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 128.2, 127.0, 126.8, 44.6, 41.0, 30.9, 27.5, 25.8, 22.0, 13.8. HRMS (EI, $C_{16}H_{22}N_4O_3^+$): calcd 318.1692; found 318.1702.

6-(Hydroxyimino)-1,3-diphenyl-1,3,5-triazine-2,4-dione 1d7. Column chromatography with acetone/EtOAc/hexane (1:1:5) as eluent afforded **1d7** as a white solid in 25% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.82 (s, NO*H*, 1H), 9.77 (s, NH, 1H), 7.44−7.35 (m, 10ArH, 10H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 148.9, 147.8, 142.2, 138.4, 135.0, 129.3 (2 carbon), 129.3, 128.8, 128.5, 128.1. HRMS (ESI, $C_{15}H_{12}N_4O_3$ − H): calcd 295.0837; found 295.0826.

3-Hexyl-6-(hydroxyimino)-1-phenyl-1,3,5-triazine-2,4-dione 1d8. Column chromatography with acetone/EtOAc/hexane (1:1:8) as eluent afforded **1d8** as a white solid in 31% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.69 (s, NOH 1H,), 9.70 (s, NH, 1H), 7.43−7.30 (m, ArH, 5H), 3.68 (t, J = 7.32 Hz, N*CH*$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$, 2H), 1.53 (m, NCH$_2$*CH*$_2$-CH$_2$CH$_2$CH$_2$CH$_3$, 2H), 1.26 (m, NCH$_2$CH$_2$*CH*$_2$*CH*$_2$*CH*$_2$CH$_3$, 6H), 0.86 (t, J = 6.27 Hz, NCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$*CH*$_3$, 3H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 148.8, 147.8, 142.0, 135.4, 129.3 128.8, 128.2, 40.9, 30.9, 27.5, 25.8, 21.9, 13.8. ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 129.3, 128.8, 128.2, 40.4, 30.9, 27.5, 25.8, 21.9, 13.8. HRMS (ESI, $C_{15}H_{20}N_4O_3$ − H): calcd 303.1463; found 303.1445.

3-Benzyl-1-butyl-6-(hydroxyimino)-1,3,5-triazine-2,4-dione 1d9. Column chromatography with acetone/EtOAc/hexane (1:1:8) as eluent afforded **1d9** as a white solid in 30% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.64 (s, NO*H*, 1H), 9.82 (s, N*H*, 1H), 7.33 to 7.24 (m, ArH, 5H), 4.84 (s, N*CH*$_2$Ar, 2H), 3.68 (t, J =7.38 Hz, N*CH*$_2$CH$_2$CH$_2$CH$_2$CH$_3$, 2H), 1.54, (m, NCH$_2$*CH*$_2$CH$_2$CH$_2$CH$_2$CH$_3$, 2H), 1.27 (m, NCH$_2$-CH$_2$*CH*$_2$*CH*$_2$*CH*$_2$CH$_3$, 6H), 0.87 (t, J = 7.08 Hz, NCH$_2$-CH$_2$CH$_2$CH$_2$CH$_2$*CH*$_3$, 3H). ^{13}C NMR: (DMSO-d_6, 75 MHz): δ 149.0, 147.6, 140.1, 137.3, 128.3, 127.2 (2 carbons), 43.9, 41.6, 28.5, 19.4, 13.6. ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 128.3, 127.2, 43.9, 41.6, 28.5, 19.4, 13.6. HRMS (ESI, $C_{14}H_{18}N_4O_3$ − H): calcd 289.1306; found 289.1290.

1-Butyl-6-(hydroxyimino)-3-phenyl-1,3,5-triazinane-2,4-dione 1d10. Column chromatography with acetone/EtOAc/hexane (1:1:8) as eluent afforded **1d10** as a white solid in 29% overall yield. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.57 (s, NOH, 1H), 9.84 (s, NH, 1H), 7.43−7.28 (m, ArH, 5H), 3.70 (t, J = 7.23 Hz, N*CH*$_2$CH$_2$CH$_2$CH$_3$, 2H), 1.58 (m, NCH$_2$*CH*$_2$-CH$_2$CH$_3$, 2H), 1.29 (m, NCH$_2$CH$_2$*CH*$_2$CH$_3$, 2H), 0.89 (t, J = 7.23 Hz, NCH$_2$CH$_2$CH$_2$*CH*$_3$, 3H). ^{13}C NMR (DMSO-d_6, 75

MHz): δ 148.9, 147.4, 140.4, 135.0, 129.3, 128.5, 128.1, 41.6, 28.6, 19.5, 13.6. ^{13}C DEPT 135 NMR (DMSO-d_6, 75 MHz): δ 129.3, 128.5, 128.1, 41.6, 28.6, 19.5, 13.6. HRMS (ESI, $C_{13}H_{16}N_4O_3$ − H): calcd 275.1150; found 275.1137.

Acknowledgment. We thank the A*Star Biomedical Research Council for financial support of this work (Grant R-143-000-348-305).

Supporting Information Available. ^{1}H and ^{13}C NMR spectra of compounds **1a′**, **1a1**−**1a8**, **1b1**−**1b12**, **1c1**−**1c11**, **1d1**−**1d10**, **2a**−**2h**, **5**, **6**, **7a**−**7d**, ^{13}C DEPT135 spectra of compounds **5**, **7b**−**7d**, **1a2**, **1a5**−**1a8**, **2a**, **2d**−**2f, 1b2**, **1b5**−**1b12**, **1c1**−**1c11**, **1d1**−**1d4**, **1d6**, **1d8**−**1d10**, IR spectra of resin **3** and **9**−**11**, the crystallographic file in CIF format of **1c9** and **1d3**, and HPLC and ESI spectra of **1a** and **1b**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Pawlak, D.; Adamkiewicz, M.; Malyszko, J.; Takada, A.; Mysliwiec, M.; Buczko, W. *J. Cardiovasc. Pharmacol.* **1998**, *32*, 266–273. (b) Brown, E. D. Eur. Pat. Appl. EP 300756, 1979. (c) Gopalsamy, A.; Yang, H. Y. U.S. Patent US 2002049320, 2002. (d) Hall, I. H.; Taylor, K.; Izydore, R. A.; Coleman, D. E.; Mitchell, J. A.; Cummings, R. *Pharmazie* **1998**, *53*, 398–405. (e) Momparler, R. L.; Bovenzi, V. *J. Cell. Physiol.* **2000**, *183*, 145–154.

(2) (a) Schallner, O.; Luerssen, K.; Schmidt, R. R.; Santel, H.; Erdelen, C. Eur. Pat. Appl. EP 120820, 1993. (b) Collings, D. J. U.S. Patent. US 4,105,433, 1976.

(3) (a) Balboni, G.; Lazzari, I.; Trapella, C.; Negri, L.; Lattanzi, R.; Giannini, E.; Nicotra, A.; Melchiorri, P.; Visentin, S.; Nuccio, C. D.; Salvadori, S. *J. Med. Chem.* **2008**, *51*, 635–7639. (b) Coats, S. J.; Dyatkin, A. B.; He, W.; Lisko, J.; Miskowski, T. A.; Ralbovsky, J. L.; Schulz, M. J. PCT Int. Appl. WO 2007/079214 A2, 2007. (c) Coats, S. J.; Dyatkin, A. B.; He, W.; Lisko, J.; Ralbovsky, J. L.; Schultz, M. J. PCT Int. Appl. WO 2006104715, 2006. (d) Coats, S. J.; Dyatkin, A. B.; He, W.; Lisko, J.; Ralbovsky, J. L.; Schultz, M. J. PCT Int. Appl. WO 2006104713, 2006.

(4) (a) Yu, Y. P.; Ostresh, J. M.; Houghten, R. A. *J. Comb. Chem.* **2004**, *6*, 83–85. (b) Hagemann, H. *Angew. Chem.* **1977**, *89*, 789–96. (c) Gopalsamy, A.; Yang, H. *J. Comb. Chem.* **2001**, *3*, 278–283. (cc) Shibuya, I.; Honda, K.; Gama, Y.; Shimizu, M. *Heterocycles* **2000**, *53*, 929–934. (d) Shibuya, I.; Kaba, Y.; Shimizu, M.; Honda, K. Jpn. Kokai Tokkyo Koho JP 2000072757, 2000. (e) Akteries, B.; Jochims, J. C. *Chem. Ber.* **1986**, *119*, 669–682. (f) Fischer, E.; Kuhn, B.; Rembarz, G. *Z. Chem.* **1977**, *17*, 59–60.

(5) Blaney, P.; Grigg, R.; Sridharan, V. *Chem. Rev.* **2002**, *102*, 2607–2624.

(6) Guo, Z.; Wu, D.; Chen, C.; Tucci, F. C.; Regan, C. PCT Int. Appl. WO/2003/011839, 2003.

(7) Gopalsamy, A.; Yang, H.; Ellingboe, J. W.; McKew, J. C.; Tam, S.; Joseph-McCarthy, D.; Zhang, W.; Shen, M.; Clark, J. D. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2978−2981.

(8) (a) Gayo, L. M.; Suto, M. J. *Tetrahedron Lett.* **1997**, *38*, 211–214. (b) Backes, B. J.; Virgilio, A. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1996**, *118*, 3055–3056. (c) Bork, J. T.; Lee, J. W.; Khersonsky, S. M.; Moon, H.-S.; Chang, Y.-T. *Org. Lett.* **2003**, *5*, 117–120. (d) Ding, S.; Gray, N. S.; Ding, Q.; Wu, X.; Schultz, P. G. *J. Comb. Chem* **2002**, *4*, 183–186. (e) Khersonsky, S. M.; Chang, Y.-T. *J. Comb. Chem* **2004**, *6*, 474–477.

(9) Tam, S. Y. K.; Klein, R. S.; Wempen, I.; Fox, J. J. *J. Org. Chem.* **1979**, *44*, 4547–4553.

(10) Sanemitsu, Y.; Nakayama, Y. *Synthesis* **1984**, 770−771.

(11) Gibson, C. L.; La Rosa, S.; Suckling, C. J. *Org. Biomol. Chem.* **2003**, *1*, 1909–1918.

(12) (a) Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377. (b) Adam, W.; Chan, Y. Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800–2803.

CC900091E