Synthesis of Podands with Cyanurate or Isocyanurate Cores and Terminal Triple Bonds

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Received 11 February 2010

Abstract: The synthesis of podands with cyanuric or isocyanuric acid cores and oligoethyleneoxy pendant arms exhibiting terminal triple bonds or brominated triple bonds is reported. The starting material for cyanuric acid derived podands is commercially available cyanuric acid, while the isocyanuric derivatives are obtained by thermal isomerization of the corresponding cyanurates.

Key words: podands, cyanurates, alkynes, isomerization, heterocycles

In this work we have investigated the synthesis of tripodands with terminal triple bonds and cyanuric **I** or isocyanuric acids **II** as cores, targeted to be useful intermediates for further functionalization in order to achieve a plethora of macromolecular or supramolecular compounds (Figure 1).[1–9]

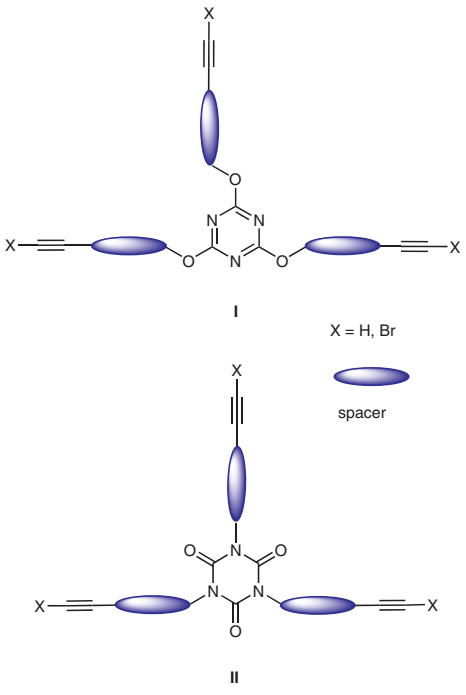


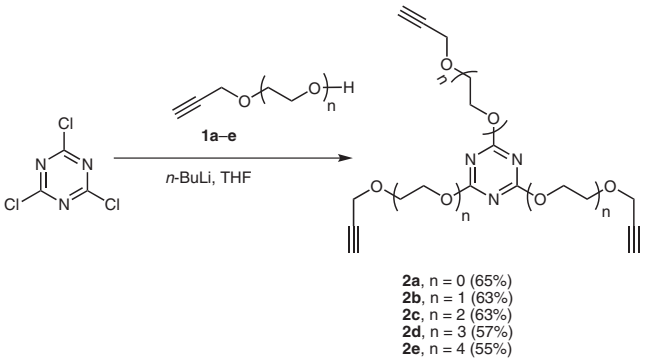
Figure 1

The core of the two series of tripodands exhibit different properties: the 1,3,5-triazine unit **I** is an electron-poor heteroaromatic system, while the isocyanurate core **II** can participate, via the oxygen atoms, as a donor for the formation of hydrogen bonds.[10] The attachment of functional groups (X = Br) to the terminal triple bonds opens the way to many other possible synthetic approaches and makes these compounds important precursors for host molecules, macromolecules, and dendrimers with C_3 symmetry.

The investigated synthetic strategies utilize consecutive reactions, they are based on an inexpensive commercially available starting compound (cyanuric chloride), and the results have been compared with other methodologies, which failed or gave poor results.

Trialkoxycyanurates have long been known,[11] their synthesis requires the reaction of silver cyanurates with alkyl halides, trimerization of imidates, and, most commonly used, the nucleophilic substitution of the chlorine in cyanuric chloride with alkoxides.

Given the availability of cyanuric chloride, we focused our investigations on the possibility of obtaining compounds **2a–e** (Scheme 1) by nucleophilic substitution of the chlorines of cyanuric chloride with alkoxides having oligoethyleneoxy chains and a terminal triple bond.



Scheme 1

The cyanurate **2a** was previously synthesized[12] from cyanuric chloride and propargyl alcohol in acetone using sodium hydroxide as base. Compound **2a** was later used as an intermediate for the construction of dendrimers.[13] Attempts to obtain **2a** and other compounds **2** of the series

SYNTHESIS 2010, No. 10, pp 1639–1644
Advanced online publication: 06.04.2010
DOI: 10.1055/s-0029-1218724; Art ID: P01810SS

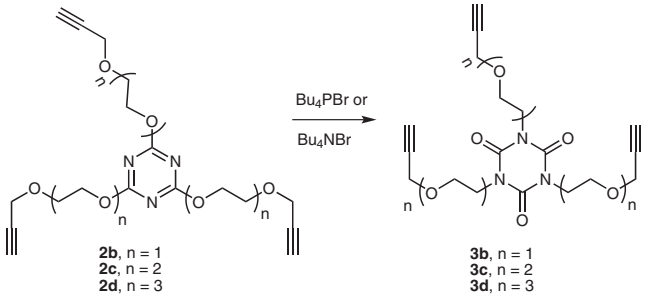
using this reported procedure gave poor or moderate yields. The other procedures reported for the formation of trialkoxycyanurates starting from cyanuric chloride with alcohols use sodium hydride,[14] sodium hydroxide, *N*,*N*-diisopropylethylamine,[15] or potassium *tert*-butoxide[16] as the base and require a large excess of alcohol. Due to the use of a large excess of alcohol, these procedures were considered unsuitable for the synthesis of **2a–e**.

The high yielding synthesis of trialkoxycyanurates starting from cyanuric chloride with alcohols using butyllithium as a base has been recently reported.[17] We adapted this method for our target compounds and carried out the synthesis of **2a–e** in tetrahydrofuran with stoichiometric amounts of the appropriate alcohol. The yields increased considerably (55–65%) when compared to other methods[12] and the separation and purification of the products was substantially facilitated (Scheme 1).

The precursor alcohols **1b–e** were synthesized using procedures described in the literature[18] while propargyl alcohol **1a** is commercially available.

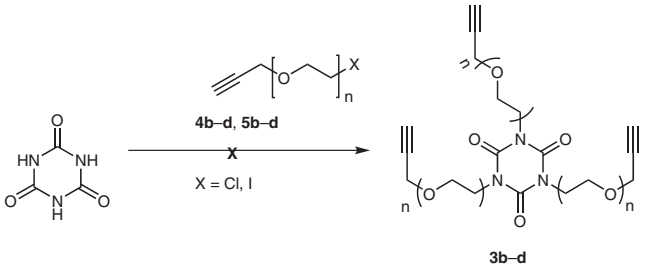
As shown in the literature, isocyanuric acid derivatives can be formed by trimerization of isocyanates,[19] by substitution under harsh conditions at cyanuric acid,[20] or by rearrangement of the corresponding cyanurates.[21,22]

The hitherto unknown isocyanurate derivatives **3b–d** (Scheme 2) were obtained by the rearrangement reaction from cyanurates **2b–d**, in a process catalyzed by tetrabutylammonium bromide or tetrabutylphosphonium bromide at 120 °C without solvent. Even though there are reports that such thermal isomerizations occur using solvents at temperatures higher than 100 °C,[22] the treatment of cyanurates **2** in toluene or xylene under reflux gave no isocyanurates **3**. This type of reaction was previously described by Harrington et al.[21] for the isomerization of other 1,3,5-triazine derivatives.



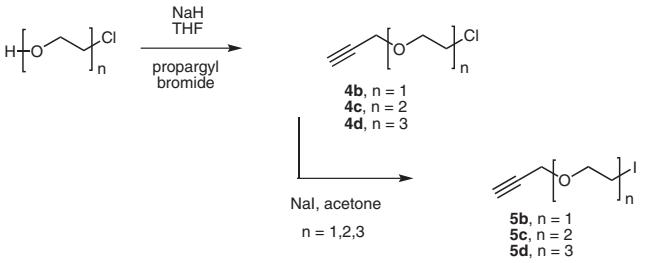
Scheme 2

As an alternative route to the isocyanurate derivatives **3b–d**, the alkylation of cyanuric acid with propargyloligo(ethyleneoxy)ethyl halides **4b–d** and **5b–d** was attempted (Scheme 3). Despite the successful synthesis reported for **3a**,[23] all attempts to alkylate cyanuric acid under various basic conditions (KOH, NaH)[24] with the chlorides **4b–d** or the iodides **5b–d** failed.



Scheme 3

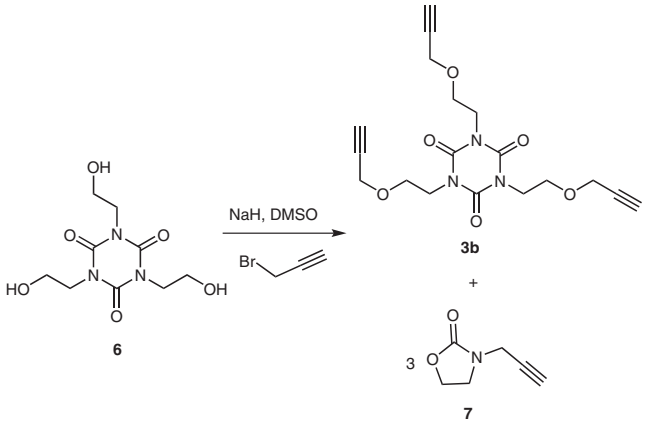
The chloro derivatives **4b** and **4d** are known compounds.[25,26] The procedure reported for **4d**[26] was used also for the synthesis of **4c**, providing **4c**,**d** in good yields (70–85%) (Scheme 4). The iodo compounds **5b–d** were synthesized (60–80% yields) by a standard procedure[27] for the halogen-exchange reaction (Scheme 4). Compounds **5c**,**d** have not been previously reported, while **5b** was recently obtained by another procedure (using $^{-}$OTs for I^{-} exchange).[28]



Scheme 4

As another alternative synthetic route to isocyanuric acid derivatives **3**, a side chain nucleophilic substitution of commercially available 1,3,5-tris(2-hydroxyethyl)cyanuric acid (**6**) with propargyl bromide and iodo derivatives **5b–d** was considered. Only the reaction with propargyl bromide in the presence of sodium hydride (DMSO, 20 °C) afforded the isocyanurate **3b**, together with the oxazolidone **7** (Scheme 5). In the other reactions (iodo derivatives **5b–d**), no isocyanurates were isolated from the reaction mixtures. The cleavage of the tris(2-hydroxyethyl)isocyanurate heterocycle involved in the formation of **7** is likely to occur by nucleophilic attack of the deprotonated side chain hydroxy group on the carbonyl site with in situ formation of the unsubstituted oxazolidone, which is further deprotonated and propargylated. Similar behavior, but without alkylation, was previously observed for 2-hydroxyethyl isocyanurates on vacuum pyrolysis[29] and on heating in *N*,*N*-dimethylformamide solution at high temperatures.[30] In our case working at 35–40 °C gave the oxazolidone **7** as the major product while the isocyanurate **3b** was formed predominantly at room temperature (20 °C).

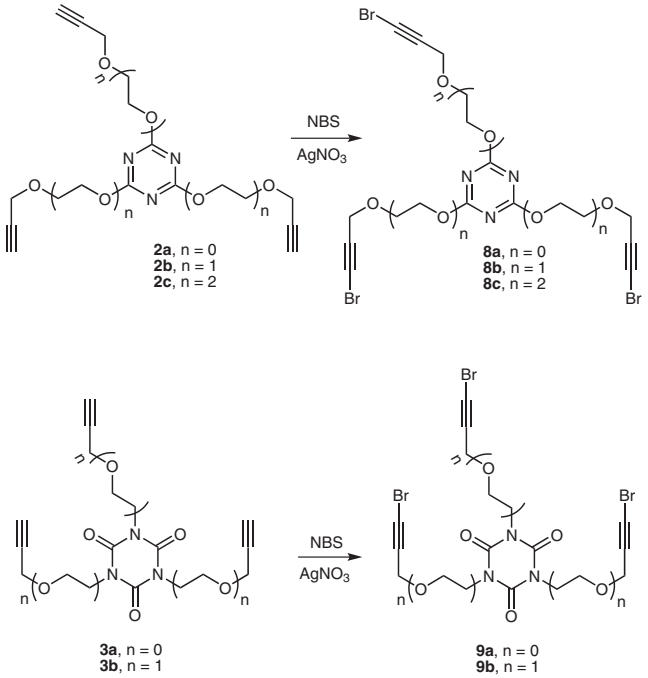
The structures of the new cyanurates **2a–e** and their isomers isocyanurates **3b–d** were confirmed by NMR spectroscopy. The main differences between the spectra of



Scheme 5

these two series were observed in the ^{13}C NMR spectra where the quaternary C=O carbons in isocyanurates give signals at δ = 148–149 compared with C–O signals of the corresponding cyanurates which are considerably more deshielded (δ = 172–173). Similarly for the CH_2N carbon atoms of the isocyanurates **3** the ^{13}C NMR signals are in the range δ = 41–42 (the corresponding protons show signals at δ = 4.10–4.15), while the signals for the CH_2O moieties of cyanurates **2** are more deshielded (^{13}C NMR, δ = 67–70 and ^1H NMR, δ = 4.51–4.55).

In order to access C_3 podands with extended capacity for further applications (e.g., cross-coupling reactions), bromination of the terminal CH of the triple bonds in compounds **2a**–**c** and **3a**,**b** was envisaged (Scheme 6). The reactions were carried out in fair to good yields (30–70%) with *N*-bromosuccinimide in the presence of silver nitrate. An excess of *N*-bromosuccinimide (250%) was used in order to enhance the ratio of triple substitution products.



Scheme 6

The structure of the brominated products **8a**–**c** and **9a**,**b** was elucidated by NMR spectroscopy. Thus, the absence of signals for the protons of the terminal triple bonds in ^1H NMR spectra, the upfield shift of the signals belonging to the *sp* carbon atoms in ^{13}C NMR and the specific pattern for the tribrominated peaks in MS were noted (see experimental section).

An efficient synthesis of C_3 symmetry podands with pendant arms of different lengths (n = 0–4) bearing at their extremities triple bonds, either brominated or not, and exhibiting 1,3,5-triazine or 1,3,5-triazinane-2,4,6-trione cores is reported. Starting from cyanuric chloride, an inexpensive commercially available compound, diverse podands could be obtained in a few consecutive steps. The compounds described in this paper represent promising versatile starting materials for functionalized podands and/or cryptands by subsequent reactions, such as copper-catalyzed [2+3] cycloaddition with azides or oxidative copper-catalyzed homocoupling, Sonogshira, and other palladium-catalyzed cross-coupling reactions.

^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 spectrometer operating at 300 MHz (^1H) and 75 MHz (^{13}C) relative to TMS. MS were recorded on an ESI ion trap mass spectrometer (Agilent 6320) in positive mode and in EI mode (70eV) on a VG-Autospec mass spectrometer or in positive ionization on a Thermo-Finnigan MSQ mass spectrometer. Solvents were dried and distilled under argon using standard procedures before use. Chemicals of commercial grade were used without further purification. Melting points are uncorrected. Column chromatography purifications were carried out on Merck silica gel Si 60 (40–63 μm). TLC was carried out on aluminum plates coated with silica gel 60 F254 using UV lamp (254 nm) and $KMnO_4$ visualization.

Podands 2 with 1,3,5-Triazine Units; General Procedure

A soln of 15% *n*-BuLi in hexane (3.34 mL, 5.32 mmol) was slowly added to the soln of hydroxy alkyne **1b**–**e** (5.32 mmol) in anhyd THF (40 mL) under an argon atmosphere at –78 °C. The lithium alkoxide soln was stirred at this temperature for 15 min and then cyanuric chloride (327.2 mg, 1.77 mmol) in anhyd THF (10 mL) was added dropwise over 5 min. The mixture was stirred overnight at r.t. The solvent was removed and the residue was washed with H_2O (50 mL), extracted with CH_2Cl_2, dried (Na_2SO_4), and concentrated.

2,4,6-Tris(prop-2-ynyloxy)-1,3,5-triazine (2a)

Following the general procedure with purification by column chromatography (silica gel, pentane–EtOAc, 9:1); white solid (65%); mp 69–70 °C (Lit.[13] 69–70 °C); R_f = 0.35 (pentane–EtOAc, 9:1).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.53 (t, *J* = 2.4 Hz, 3 H), 5.04 (d, *J* = 2.4 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 58.8 (CH_2), 75.8 (CH), 76.8 (C), 172.3 (CO).

Anal. Calcd for $C_{12}H_9N_3O_3$: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.43; H, 3.58; N, 17.44.

2,4,6-Tris(3-oxahexa-5-ynyloxy)-1,3,5-triazine (2b)

Following the general procedure with purification by column chromatography (silica gel, Et_2O–acetone–hexane, 4:1:1); white solid (63%); mp 96–97 °C; R_f = 0.35 (Et_2O–acetone–hexane, 4:1:1).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.43 (t, *J* = 2.4 Hz, 3 H), 3.86 (t, *J* = 4.8 Hz, 6 H), 4.21 (d, *J* = 2.4 Hz, 6 H), 4.55 (t, *J* = 4.8 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 58.4 (CH_2), 67.1, 67.2 (CH_2CH_2), 74.8 (CH), 79.1 (C), 172.8 (CO).

MS (ESI): *m*/*z* = 376.1 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{21}N_3O_6$: C, 57.59; H, 5.64; N, 11.19. Found: C, 57.37; H, 5.48; N, 11.35.

2,4,6-Tris(3,6-dioxanona-8-ynyloxy)-1,3,5-triazine (2c)
Following the general procedure with purification by column chromatography (silica gel, Et_2O–acetone–hexane, 4:1:1); colorless liquid (63%); R_f = 0.35 (Et_2O–acetone–hexane, 4:1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.40 (t, *J* = 2.4 Hz, 3 H), 3.65–3.67 (m, 12 H), 3.78–3.81 (m, 6 H), 4.16 (d, *J* = 2.4 Hz, 6 H), 4.48–4.52 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 58.3 (CH_2), 67.3, 68.7, 68.9, 70.4 (CH_2CH_2), 74.5 (CH), 79.4 (C), 172.8 (CO).

MS (ESI): *m*/*z* = 508.2 $[M + H]^+$.

Anal. Calcd for $C_{24}H_{33}N_3O_9$: C, 56.80; H, 6.55; N, 8.28. Found: C, 56.96; H, 6.78; N, 8.19.

2,4,6-Tris(3,6,9-trioxadodeca-11-ynyloxy)-1,3,5-triazine (2d)
Following the general procedure with purification by column chromatography (silica gel, Et_2O–acetone–hexane, 4:1:1); colorless liquid (57%); R_f = 0.3 (Et_2O–acetone–hexane, 4:1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (t, *J* = 2.4 Hz, 3 H), 3.65–3.66 (m, 24 H), 3.76–3.82 (m, 6 H), 4.17 (d, *J* = 2.4 Hz, 6 H), 4.49–4.52 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 58.3 (CH_2), 67.4, 68.8, 69.0, 70.4, 70.5, 70.6 (CH_2CH_2), 74.4 (CH), 79.4 (C), 172.9 (C–O).

MS (ESI): *m*/*z* = 640.3 $[M + H]^+$, 662.3 $[M + Na]^+$.

Anal. Calcd for $C_{30}H_{45}N_3O_{12}$: C, 56.33; H, 7.09; N, 6.57. Found: C, 56.51; H, 6.98; N, 6.76.

2,4,6-Tris(3,6,9,12-tetraoxapentadec-14-ynyloxy)-1,3,5-triazine (2e)
Following the general procedure with purification by column chromatography (silica gel, Et_2O–acetone–hexane, 4:1:1); colorless liquid (55%); R_f = 0.35 (Et_2O–acetone–hexane, 4:1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (t, *J* = 2.4 Hz, 3 H), 3.64–3.67 (m, 36 H), 3.80–3.83 (m, 6 H), 4.18 (d, *J* = 2.4 Hz, 6 H), 4.49–4.53 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 58.3 (CH_2), 67.4, 68.8, 69.1, 70.3, 70.5 (3 C) (CH_2CH_2), 70.6 (CH_2), 74.4 (CH), 79.6 (C), 172.9 (CO).

MS (ESI): *m*/*z* = 772.3 $[M + H]^+$, 794.3 $[M + Na]^+$.

Anal. Calcd for $C_{36}H_{57}N_3O_{15}$: C, 56.02; H, 7.44; N, 5.74. Found: C, 55.88; H, 7.59; N, 5.57.

Isocyanurate Podands 3; General Procedure
Derivatives **2b–d** (0.66 mmol) and Bu_4NBr (53 mg, 0.2 mmol) or Bu_4PBr (67.8 mg, 0.2 mmol) were stirred at 125 °C for 48 h. The mixture was extracted with CH_2Cl_2 and, after washing with H_2O, the organic layer was concentrated.

1,3,5-Tris(3-oxahexa-5-ynyl)-1,3,5-triazinane-2,4,6-trione (3b)
Following the general procedure with purification by column chromatography (silica gel, pentane–EtOAc, 1:2); colorless liquid (20%); R_f = 0.4 (EtOAc–pentane, 1:2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (t, *J* = 2.4 Hz, 3 H), 3.78 (t, *J* = 5.4 Hz, 6 H), 4.13 (t, *J* = 5.4 Hz, 6 H), 4.16 (d, *J* = 2.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.7 (NCH_2), 57.8 (OCH_2), 65.9 (OCH_2), 74.7 (CH), 79.2 (C), 148.9 (C=O).

MS (APCI): *m*/*z* = 376.3 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{21}N_3O_6$: C, 57.59; H, 5.64; N, 11.19. Found: C, 57.80; H,5.41; N, 11.03.

1,3,5-Tris(3,6-dioxanona-8-ynyl)-1,3,5-triazinane-2,4,6-trione (3c)
Following the general procedure with purification by column chromatography (silica gel, pentane–EtOAc, 1:1); yellow liquid (33%); R_f = 0.64 (EtOAc–pentane, 1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (t, *J* = 2.4 Hz, 3 H), 3.68 (m, 12 H), 3.71 (t, *J* = 4.5 Hz, 6 H), 4.10 (t, *J* = 4.5 Hz, 6 H), 4.17 (d, *J* = 2.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.6 (NCH_2), 58.3 (OCH_2), 67.4 (OCH_2), 69.0, 69.8 (CH_2CH_2), 74.5 (CH), 79.6 (C), 149.0 (C=O).

MS (ESI): *m*/*z* = 508.4 $[M + H]^+$, 530.4 $[M + Na]^+$, 546.3 $[M + K]^+$.

Anal. Calcd for $C_{24}H_{33}N_3O_9$: C, 56.80; H, 6.55; N, 8.28. Found: C, 56.65; H, 6.81; N, 8.39.

1,3,5-Tris(3,6,9-trioxadodeca-11-ynyl)-1,3,5-triazinane-2,4,6-trione (3d)
Following the general procedure with purification by column chromatography (silica gel, pentane–EtOAc, 1:1); yellow liquid (20%); R_f = 0.5 (EtOAc–pentane, 1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (t, *J* = 2.4 Hz, 3 H), 3.61–6.71 (m, 30 H), 4.09 (t, *J* = 4.5 Hz, 6 H), 4.19 (d, *J* = 2.4 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.6 (NCH_2), 58.4 (OCH_2), 67.4, 69.1, 69.9, 70.4, 70.6 (CH_2CH_2), 74.5 (CH), 149.0 (C=O).

MS (ESI): *m*/*z* = 640.4 $[M + H]^+$.

Anal. Calcd for $C_{30}H_{45}N_3O_{12}$: C, 56.33; H, 7.09; N, 6.57. Found: C, 56.29; H, 7.21; N, 6.51.

Chloroalkynes 4; General Procedure
Chloropoly(ethoxy)ethanol (20 mmol) was added dropwise to a soln of 95% NaH (0.97 g, 40 mmol) in anhyd THF (50 mL) at –20 °C under an argon atmosphere. After 15 min at –78 °C, 80% propargyl bromide soln (2.97 g, 20 mmol) was added dropwise and the mixture was refluxed for 2 h. The mixture was concentrated by evaporation in vacuo, washed with H_2O (50 mL), and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and concentrated and the resulting residue was purified by chromatography (silica gel, pentane–Et_2O, 4:1).

1-Chloro-3,6-dioxanona-8-yne (4c)
Following the general procedure; colorless liquid (70%); R_f = 0.56 (pentane–Et_2O, 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (t, *J* = 2.1 Hz, 1 H), 3.61–3.77 (m, 8 H), 4.20 (d, *J* = 2.4 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.3 (ClC), 57.1 (OC), 68.5, 69.9, 70.8 (CH_2CH_2), 74.3 (CH), 78.1 (C).

Anal. Calcd for $C_7H_{11}ClO_2$: C, 51.70; H, 6.82; Cl, 21.80. Found: C, 51.98; H, 6.74; Cl, 21.93.

Iodoalkynes 5; General Procedure
Chloroalkynes **4b–d** (17 mmol) and anhyd NaI powder (10.2 g, 68 mmol) were refluxed in anhyd acetone (170 mL) for 48–68 h. The solvent was removed and the crude mixture was washed with H_2O and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure. The products were purified by chromatography (silica gel, pentane–Et_2O, 4:1).

1-Iodo-3,6-dioxanona-8-yne (5c)
Following the general procedure; brown liquid (60%); R_f = 0.5 (pentane–Et_2O, 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (t, *J* = 2.1 Hz, 1 H), 3.27 (t, *J* = 6.9 Hz, 2 H), 3.65–3.76 (m, 6 H), 4.19 (d, *J* = 2.4 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 2.7 (ICH_2), 58.2 (OCH_2), 68.8, 69.7, 71.7 (CH_2CH_2), 74.5 (CH), 79.3 (C).

Anal. Calcd for $C_7H_{11}IO_2$: C, 33.09; H, 4.36; I, 49.95. Found: C, 33.27; H, 4.29; I, 50.11.

1-Iodo-3,6,9-trioxadodec-11-yne (5d)

Following the general procedure; brown liquid (79%); R_f = 0.38 (pentane–Et_2O, 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (t, *J* = 2.1 Hz, 1 H), 3.24 (t, *J* = 6.6 Hz, 2 H), 3.64–3.76 (m, 10 H), 4.19 (d, *J* = 2.4 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 2.8 (ICH_2), 58.1 (OCH_2), 68.8, 69.9, 70.2, 70.3, 71.6 (CH_2CH_2), 74.4 (CH), 79.4 (C).

Anal. Calcd for $C_9H_{15}IO_3$: C, 36.26; H, 5.07; I, 42.57. Found: C, 36.61; H, 4.88; I, 42.69.

3-(Prop-2-ynyl)oxazolidin-2-one (7)

NaH 95% (1.72 g, 8.4 mmol) was slowly added to a soln of 1,3,5-tris(2-hydroxyethyl)cyanuric acid (6 g, 22.8 mmol) in anhyd DMSO (50 mL) under an argon atmosphere and cooling with ice, without freezing the solvent. The mixture was stirred at r.t. for 1 h and then 80% propargyl bromide in toluene (10.17 g, 68.4 mmol) was added dropwise at 35–40 °C and the mixture was stirred for 2 h. The mixture was washed with H_2O (3 × 50 mL) and extracted with CH_2Cl_2. The organic layer was concentrated and the crude product was purified by column chromatography (silica gel, EtOAc–pentane, 1:2). The first collected fraction was compound **3b**, colorless liquid (20%), R_f = 0.40 (EtOAc–pentane, 1:2), followed by compound **7**, colorless liquid (31%), R_f = 0.30 (EtOAc–pentane, 1:2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.30 (t, *J* = 2.4 Hz, 1 H), 3.62–3.89 (m, 2 H), 4.07 (d, *J* = 2.4 Hz, 2 H), 4.33–4.38 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.0 (NCH_2), 43.8 (NCH_2), 61.9 (OCH_2), 73.3 (CH), 76.81 (C), 157.8 (C=O).

Anal. Calcd for $C_6H_7NO_2$: C, 57.59; H, 5.64; N, 11.19. Found: C, 57.77; H, 5.44; N,11.35.

Bromination Reaction; General Procedure

NBS (34.6 mmol) and $AgNO_3$ (4.9 mmol) were added to a soln of cyanurates **2** (3.3 mmol) or isocyanurates **3** (3.3 mmol) in degassed acetone (75 mL) under stirring at r.t. under an argon atmosphere. The mixture was stirred at r.t. overnight, extracted with CH_2Cl_2, and washed with brine. The oily crude product was purified by column chromatography (silica gel, toluene–acetone).

2,4,6-Tris(3-bromoprop-2-ynyloxy)-1,3,5-triazine (8a)

Following the general procedure with purification by column chromatography (silica gel, toluene–acetone, 20:1); white solid (36%); mp 94–95 °C; R_f = 0.7 (toluene–acetone, 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.05 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.5 (CBr), 56.7 (CH_2), 73.3 (C), 172.3 (CO).

MS (ESI): *m*/*z* (%) = 477.9 (33), 479.9 (100), 481.8 (99), 483.8 (35) ($[M + H]^+$).

Anal. Calcd for $C_{12}H_6Br_3N_3O_3$: C, 30.03; H, 1.26; Br, 49.95; N, 8.76. Found: C, 30.27; H, 1.42; Br, 50.15; N, 8.64.

2,4,6-Tris(6-bromo-3-oxahexa-5-ynyloxy)-1,3,5-triazine (8b)

Following the general procedure with purification by column chromatography (silica gel, toluene–acetone, 9:1); white solid (36%); mp 103–105 °C; R_f = 0.7 (toluene–acetone, 9:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.86 (t, *J* = 3.6 Hz, 6 H), 4.25 (s, 6 H), 4.56 (t, *J* = 3.6 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.6 (CBr), 59.4 (OCH_2), 67.1, 67.4 (CH_2CH_2), 75.8 (C), 172.9 (CO).

MS (ESI): *m*/*z* (%) = 610.0 (42), 612.0 (100), 614.0 (91), 616.0 (31) ($[M + H]^+$), 631.9 (19), 633.9 (53), 635.9 (54), 637.9 (18) ($[M + Na]^+$).

Anal. Calcd for $C_{18}H_{18}Br_3N_3O_6$: C, 35.32; H, 2.96; Br, 39.16; N, 6.87. Found: C, 35.17; H, 3.08; Br, 39.39; N, 6.93.

2,4,6-Tris(9-bromo-3,6-dioxanona-8-ynyloxy)-1,3,5-triazine (8c)

Following the general procedure with purification by column chromatography (silica gel, toluene–acetone, 4:1); colorless liquid (20%); R_f = 0.31 (toluene–acetone, 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.68–3.71 (m, 12 H), 3.82–3.84 (m, 6 H), 4.22 (s, 6 H), 4.53–4.55 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.1 (CBr), 59.4 (OCH_2), 67.4, 68.8, 69.2, 70.5 (CH_2CH_2), 76.1 (C), 172.9 (CO).

MS (ESI): *m*/*z* (%) = 742.1 (35), 744.0 (100), 746.0 (90), 747.9 (31) ($[M + H]^+$), 763.9 (6), 765.9 (10), 767.9 (11), 770.0 (3) $[M + Na]^+$.

Anal. Calcd for $C_{24}H_{30}Br_3N_3O_9$: C, 38.73; H, 4.06; Br, 32.21; N, 5.65. Found: C, 38.55; H, 4.19; Br, 32.34; N, 5.49.

1,3,5-Tris(3-bromoprop-2-ynyl)-1,3,5-triazinane-2,4,6-trione (9a)

Following the general procedure with purification by column chromatography (silica gel, toluene–acetone, 9:1); white solid (45%); mp 79–81 °C; R_f = 0.6 (toluene–acetone, 9:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.70 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.5 (NCH_2), 44.8 (CBr), 72.8 (C), 147.1 (C=O).

MS (ESI): *m*/*z* (%) = 477.9 (29), 479.9 (100), 482.0 (95), 483.9 (27) $[M + H]^+$.

Anal. Calcd for $C_{12}H_6Br_3N_3O_3$: C, 30.03; H, 1.26; Br, 49.95; N, 8.76. Found: C, 30.16; H, 1.34; Br, 49.77; N, 8.81.

1,3,5-Tris(6-bromo-3-oxahexa-5-ynyl)-1,3,5-triazinane-2,4,6-trione (9b)

Following the general procedure with purification by column chromatography (silica gel, toluene–acetone, 4:1); white solid (73%); R_f = 0.56 (toluene–acetone, 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.77 (t, *J* = 4.2 Hz, 6 H), 4.13 (t, *J* = 4.2 Hz, 6 H), 4.20 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.8 (NCH_2), 46.3 (CBr), 58.9 (OCH_2), 66.1 (CH_2), 75.9 (C), 148.9 (C=O).

MS (ESI): *m*/*z* (%) = 610.0 (37), 611.9 (96), 613.9 (100), 615.9 (34) ($[M + H]^+$).

Anal. Calcd for $C_{18}H_{18}Br_3N_3O_6$: C, 35.32; H, 2.96; Br, 39.16; N, 6.87. Found: C, 35.40; H, 3.09; Br, 39.02; N, 6.73.

Acknowledgment

We are grateful to Professor Jürgen Liebscher from Humboldt University, Berlin for fruitful discussions. We acknowledge the financial support of this work by PNCDI II program (UEFISCSU; projects IDEAS 570/2007 and 2358/2008 and TD82).

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