

Synthesis and characterization of 1,3,5-tris((1/2*H*-tetrazol-5-yl)methyl)-1,3,5-triazinane-2,4,6-trione

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Abstract 2,2',2''-(2,4,6-Trioxo-1,3,5-triazinane-1,3,5-triyl) triacetonitrile (or tris-(cyanomethyl)-isocyanurate) and 1,3,5-tris((1/2*H*-tetrazol-5-yl)methyl)-1,3,5-triazinane-2,4,6-trione (or tris-(5-tetrazolylmethyl)-isocyanurate) were synthesized with new methods. High yields, simple methodology, and cheapness are advantages of the methods. Furthermore, 1,3,5-tris((1/2*H*-tetrazol-5-yl)methyl)-1,3,5-triazinane-2,4,6-trione was synthesized in the less hazardous condition. The compounds were characterized by elemental analysis, IR, ¹HNMR, ¹³CNMR and mass spectroscopic analysis. In addition, DSC/TGA measurements were carried out to determine the thermal behavior of the final product.

Keywords Isocyanuric acid · *N*-Alkylation · Tetrazole · Mass spectroscopy · DSC/TGA

Introduction

Isocyanuric acid or 1,3,5-triazinane-2,4,6-trione is a six-membered heterocyclic compound containing alternative C and N atoms (Wojtowicz 2004). Spectroscopic studies have been indicated an aromatic character of the ring structure

of isocyanuric acid. This compound exists in two isomeric forms (enol–keto tautomers) (Fig. 1). The keto structure prevails in the solid state, acidic or neutral solutions (Burakevich 1979).

Isocyanuric acid derivatives have been found numerous industrial applications, such as industrial cleaners and industrial polymer applications (as cross-linking agents and curing agents) (Huthmacher and Most 2005). Recently, tris-(cyanomethyl)-isocyanurate (*I*) has been applied to prepare the polydentate organic chelating agents. In addition, tris-(5-tetrazolylmethyl)-isocyanurate (*III*) has been synthesized as blowing agent for thermoplastic resins (Illy and Fussenegger 1979).

Tetrazoles are commonly used in a wide range of applications, such as medicinal chemistry, explosives (Aboudi et al. 2015), agriculture, (Sandmann et al. 1996) and in the photography and photo imaging (Koldobskii et al. 1981). Several methods have been developed for the synthesis of tetrazoles, including the use of hydrazoic acid (HN₃) (Světlik et al. 1979), metal salts (Nasrollahzadeh et al. 2009), tin and silicon-mediated (Herr 2002).

Trisubstituted isocyanurates have previously been synthesized in a variety of methods, such as the reaction of cyanuric acid metal salt with alkylating agents and trimerization reaction of cyanurate derivatives or isocyanates. Chiron-Charrier and Caubère (1993) synthesized tris-(cyanomethyl)-isocyanurate (*I*) by using chloro acetonitrile/NaH/HMPA system, and Burdick et al. (1966) synthesized it by using trisodium cyanurate salt/chloro acetonitrile/DMF system. However, these methods suffer from low yield, expensive starting materials and the use of the toxic reagents and solvents (Tazuuia 1963).

Herein, tris-(cyanomethyl)-isocyanurate was synthesized in a new one-pot method using cyanurate/chloro acetonitrile/DMF system. Tris-(5-tetrazolylmethyl)-

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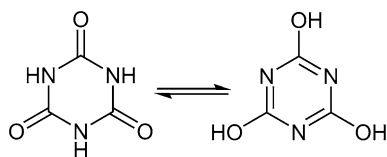


Fig. 1 The enol–keto tautomers of isocyanuric acid

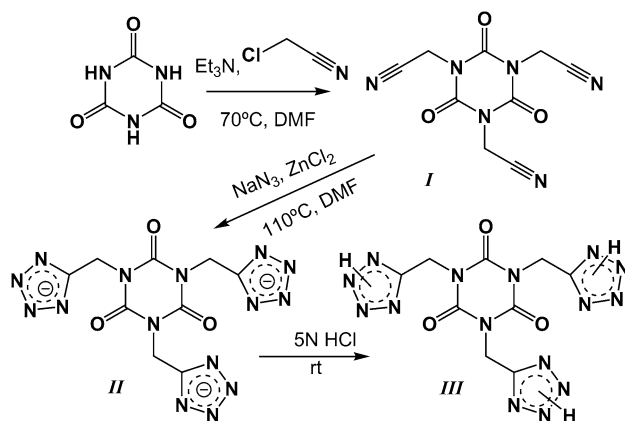


Fig. 2 Synthetic route of 1,3,5-tris((1/2*H*-tetrazol-5-yl)methyl)-1,3,5-triazinane-2,4,6-trione from isocyanuric acid

isocyanurate was also synthesized in a new method using tris-(cyanomethyl)-isocyanurate/ NaN_3 /DMF in the presence of ZnCl_2 as a Lewis acid catalyst (Fig. 2). All products were characterized.

Experimental

Materials and methods

Isocyanuric acid, chloro acetonitrile, triethylamine, DMF, NaN_3 , ZnCl_2 and HCl (37%) were purchased from Merck Chemical Company. Isocyanuric acid was recrystallized from water prior to use. ^1H NMR and ^{13}C NMR Spectroscopy was recorded on a Bruker FT-100 and 500 MHz instrument (Bruker Biosciences, USA). Melting points were determined with an Electrothermal 9100 apparatus. Infrared spectra were recorded on a Shimadzu FT-IR-8400 spectrophotometer. Mass spectroscopy was recorded on an Agilent Electron Impact (EI) 70 eV with quadrupole analyzer at 230 °C. The element analysis measurements were performed on a Perking-Elmer 2400 Elemental analyzer. Prior to the measurements, samples were dried under vacuum at 60 °C (overnight). TGA and DSC curves were obtained using a Mettler Toledo thermo analyzer under a dynamic nitrogen atmosphere (heating rate: 10 °C/min, temperature ranging from 30 to 600 °C, aluminum oxide crucible).

Synthesis of 2,2',2''-(2,4,6-trioxo-1,3,5-triazinane-1,3,5-triyl) triacetonitrile (*I*)

In a 10 mL round bottom flask, 0.2 g (1.55 mmol) isocyanuric acid was added to the 2 mL DMF and magnetically stirred for 10 min. Then, 0.7 mL (5.02 mmol) triethylamine was added to the mixture and heated at 70 °C for 3 h to generate isocyanurate salt. Subsequently, 0.32 mL (5.05 mmol) chloro acetonitrile was added gradually to it and heated with vigorously stirring at 70 °C for 7 h. After cooling it to room temperature, 20 mL water was added to the mixture and stirred for 5 min. The white precipitate was collected by filtration to give 0.37 g of *I* (1.5 mmol, 97%) as an amorphous, off-white solid. This solid was crystallized by dissolution in hot DMF (3 mL) and 7 mL of water. The solid that precipitated upon cooling of the mixture to room temperature was collected by filtration, was washed with water and dried under vacuum at 60 °C (overnight) to give 0.35 g of *I* (1.42 mmol, 92%) as a white amorphous solid (Tables 1, 2).

Synthesis of 1,3,5-tris((1/2*H*-tetrazol-5-yl)methyl)-1,3,5-triazinane-2,4,6-trione anion (*II*)

In a 10 mL round bottom flask, 0.4 g NaN_3 (6.15 mmol) and 0.6 g ZnCl_2 (4.40 mmol) was added to 10 mL DMF and stirred. Then, 0.3 g (1.22 mmol) compound *I* was added to the mixture and heated at 110 °C. After 5 h, the yellow precipitate was generated in the mixture. The reaction mixture was vigorously stirred and heated overnight to complete the reaction. Then, the mixture was cooled down to room temperature. Subsequently, 40 mL of water was added. The pale yellow precipitate was filtered by sinter glass (4 mesh) and washed with 5 mL of DMF and 10 mL of water then dried in an oven to give 0.45 g *II* (1.02 mmol, 84%) (decomposition temperature: 325 °C) (Table 2).

Synthesis of 1,3,5-tris((1/2*H*-tetrazol-5-yl)methyl)-1,3,5-triazinane-2,4,6-trione (*III*)

Compound *II* [0.3 g (0.80 mmol)] was added to 5 N HCl (10 mL) and stirred for 5 min. The crystals were collected by filtration and washed with 30 mL of water. It was dried under vacuum at 60 °C for 15 h to give 0.34 g (0.90 mmol, 74%) a colorless crystalline solid (Tables 1, 2).

Results and discussion

Isocyanuric acid undergoes *N*-alkylation and *O*-alkylation. According to literature, alkylation from the N site or O site depends on bases and solvents used in the reaction media (Chiron-Charrier and Caubère 1993). Tris-(cyanomethyl)

Table 1 Characterization data of newly prepared compounds

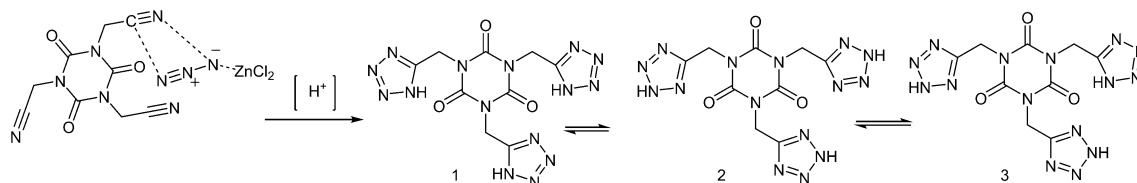
Compound	Formula	M_r	w_i (calc.)/% w_i (found)/%			Yield (%)	m.p. (°C)
			C	H	N		
<i>I</i>	$C_9H_6N_6O_3$	246.05	43.91	2.46	34.15	92	227–228
			44.06	2.53	34.19		
<i>III</i>	$C_9H_9N_{15}O_3$	375.1	28.81	2.42	55.99	74	296 (dec)
			28.94	2.49	55.81		

Table 2 Spectral data of newly prepared compounds

Compound	Spectral data
<i>I</i>	IR, $\bar{\nu}/\text{cm}^{-1}$: 3483, 3416, 3028, 2958, 2261 (CN), 1713 (C=O), 1446, 1170, 904, 766, 591, ^1H NMR (100 MHz, DMSO- d_6), δ : 4.87(s, 6H), S1 ^{13}C NMR (125 MHz, DMSO- d_6), δ : 30.6, 114.8, 147.3, S2
<i>II</i>	IR, $\bar{\nu}/\text{cm}^{-1}$: 2900–3500 (NH, CH), 1689 (CO), 1316 (–N=N=N–) ^1H NMR (500 MHz, CDCl_3 and D_2SO_4), δ : 5.62 (s, 6H), S3
<i>III</i>	IR, $\bar{\nu}/\text{cm}^{-1}$: 3418, 2479, 2625, 2710, 2752, 2884, 3002, 3051, 3142 (NH, CH), 1709 (CO), 1571 (C=N tetrazole ring stretching band), 1676 (CO), 1293 (–N=N=N–) ^1H NMR (500 MHz, DMSO- d_6), δ : 5.33 (s, 6H), S4 ^{13}C NMR (125 MHz, DMSO- d_6), δ : 36.5, 148.3, 152.8, S5 MS, m/z (I_r %): 375 (0.94) (M^+), S6

cyanurate which is the *O*-substituted cyanurate was synthesized by cyanuric chloride/glyconitrile and pyridine (Dudley et al., 1951). *N*-substituted isocyanuric acid can be obtained in aprotic solvents, such as DMF and triethylamine as the base. In addition, the alkyl halide is the key factor affects the alkylation (soft–hard acid/base theory). In comparison to previous methods of synthesis of compound *I*, the present method reduces the number of reaction steps but increases the purity and yield of reaction without the need of dry condition or expensive and toxic solvent which is mentioned in the introduction section.

In the synthesis of compound *II*, by utilizing ZnCl_2 instead of NH_4Cl makes this method less hazardous, because the explosive and toxic HN_3 (generated from the reaction of NH_4Cl with NaN_3) is avoided. In addition, the yield of this reaction is high.

**Fig. 3** Some of 1*H*, 2*H* and 1*H*/2*H* tetrazole tautomers of *III*

The mechanism of the formation of compound *III* is shown in Fig. 3. First, ZnCl_2 as a Lewis acid makes the N_3^- more reactive (metal-azide complexes) for the [2 + 3] cycloaddition condensation reaction with tris-(acetonitrile)-isocyanurate (*I*). It is assumed that 1*H* and 2*H* tautomeric forms of tetrazoles are nearly in 1:1 ratio, however; calculations of Mazurek and Sadlej-Sosnowska (2000) and Sadlej-Sosnowska (2001) determined that 2*H*-forms of 5-substituted tetrazoles are more stable isomers. Consequently, the probability of the existence of product 1 (Fig. 3) is lower than the other forms. Furthermore, the ring chain isomers (imidoyl azides) of 5-substituted tetrazoles are known (Herr et al. 2002).

According to the literature, one of the fragmentation observed in the mass spectroscopy of tetrazoles is the expulsion of N_2 , followed by the lost of the hydrogen radical (appeared in m/z 288). Another important fragmentation obtains with the loss of HN_3 (appeared in m/z 228) (Liu et al., 2008). The other detected products during the decomposition of compound *III* is HN_3 (m/z 43). The mass spectrum of compound *III* is presented in Supplementary data (S6). Considering to ^1H NMR, proton chemical shift of $-\text{CH}_2-$ in the compound *III* has appeared in the δ 5.33 ppm may due to anisotropic effects of the tetrazole rings (Table 2).

The thermal stability of tris-(5-tetrazolomethyl)-isocyanurate was examined. According to the differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) results, decomposition proceeded in two main steps. However, the strong exothermic peak was only released during the first decomposition step with one exothermal peak at 302 °C. The TGA revealed that weight loss (65%) had occurred at 240–330 °C. Further weight loss was observed at the temperature higher than 330 °C (Fig. 4).

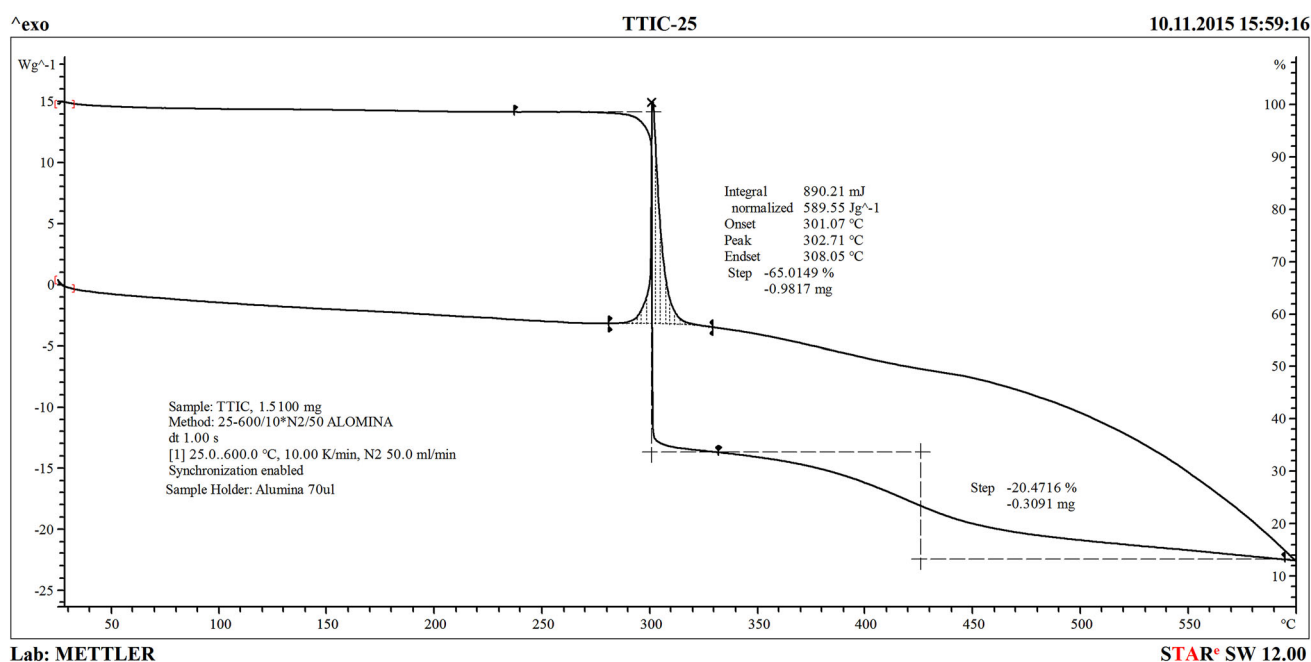


Fig. 4 DSC and TGA thermographs of compound *III* (10 °C/min)

Conclusions

Tris-(cyanomethyl)-isocyanurate and tris-(5-tetrazolylmethyl)-isocyanurate were synthesized in the efficient new methods. The full-scan mass spectrum shows the exact mass peak at 375 m/z of compound *III* (Fig. 3). In addition, one characteristic and remarkable fragment ions were observed at 288 m/z (Supplementary data) that formed by ring cleavage and elimination of three N_2 of tetrazole rings. TGA/DSC of compound *III* showed one exothermic peak at 302 °C with 65% weight loss mainly from ring opening and decomposition of tetrazoles.

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