

NITROMETHYL DERIVATIVES OF 1,3,5-TRIAZINE.

SYNTHESIS AND PROPERTIES

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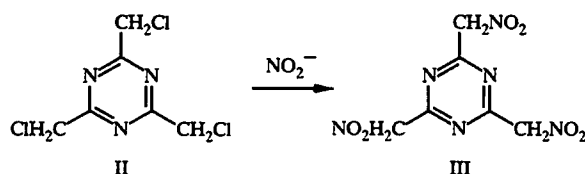
The destructive nitration of 2,4,6-tris[di(carboxy)methylene]hexahydro-1,3,5-triazine and its esters has been investigated. A first representative of the nitromethyl derivatives of 1,3,5-triazine, viz. 2,4,6-tris(nitromethyl)-1,3,5-triazine, has been synthesized.

As is evident from fundamental reviews [1, 2] and also from the studies [3-5] devoted to the 1,3,5-triazines there is no information in the literature on the nitromethyl derivatives of these compounds. Previously we reported for the first time the synthesis [6, 7] and properties [7, 8] of 2,4,6-tris(trinitromethyl)-1,3,5-triazine (I). The present paper is devoted to the synthesis of nitromethyl and dinitromethyl substituted derivatives of 1,3,5-triazine.

The reactivity of 1,3,5-triazines is linked both with the special features of the ring structure and with the nature of any substituents. The electron-accepting properties of the triazine ring in alkyl substituted triazines increase the acidity of the hydrogen atoms in an α -CH₂ group which enables alkylation, acylation, and condensation reactions to be carried out on them [2 (p. 472), 9, 10].

The nitromethyl derivatives of 1,3,5-triazine, which have a labile hydrogen atom, are of particular interest in synthesis. When checking the availability of starting materials and having analyzed the literature data on 1,3,5-triazines we selected four main approaches to the synthesis of the target compounds.

1. Nucleophilic substitution of the chlorine atoms in 2,4,6-tris(chloromethyl)-1,3,5-triazine (II) by nitro groups.



The initial triazine (II) is readily obtained from chloroacetonitrile [11].

The reaction of compound (II) with sodium and potassium nitrites was carried out in aqueous alcoholic (2:1) solution at room temperature (10 h) and on boiling (2 h). In all experiments the final product was a crystalline mass the IR spectrum of which contained no absorption bands for a nitro group but absorption bands for carboxyl groups were present.

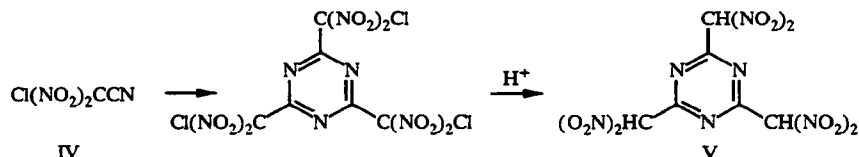
It is known from the literature [12] that the reaction of certain benzyl halides with sodium nitrite in DMF or DMSO frequently leads not to the corresponding phenylnitromethane but to benzoic acid. We carried out the reaction of benzyl chloride with sodium nitrite in water-ethanol (1:2) and isolated as main product benzoic acid in 50% yield, corresponding in its characteristics with a known specimen.

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It is possible that an analogous oxidation reaction of the CH_2Cl group to carboxyl occurred partially or completely in the case of triazine (II). Since it was obvious that the result was negative no optimization of the process or proof of the structure of the reaction products was carried out.

2. Trimerization of chlorodinitroacetonitrile (IV) with subsequent reduction of chlorine atoms.



Compound (IV) was obtained in good yield from cyanoacetic acid or its amide [13].

Two procedures were used for trimerization: 1) the nitrile was converted by known methods to the imidate hydrochloride which was treated without isolation with sodium acetate at 0°C [11]; 2) the nitrile was trimerized by the action of chlorosulfonic acid [14]. Both procedures gave negative results.

The action of sodium acetate on the product of interaction of nitrile (IV) with alcohol in the presence of HCl (20°C , 2 h) gave a violent reaction accompanied by strong heating and the evolution of nitrogen oxides. No individual substances were isolated by extraction of the reaction mixture with organic solvents. Nitrile (IV) was unchanged in the presence of chlorosulfonic acid whatever the reaction time (48 h at 0 to 20°C).

3. Reduction of triazine (I). The conversion of a trinitromethyl fragment of an aliphatic compound to dinitromethyl under various conditions has been described in the literature. Thus 1,1-dinitroethane is formed from 1,1,1-trinitroethane by the action of potassium cyanide [15], potassium hydroxide [16], potassium ethylate [16, 17], the potassium salts of 2-nitropropane, 2,4-pentanedione, or 1-butanethiol [18], or *n*-butyllithium [18]. Hydrogen peroxide in alkaline medium has been used for the reduction of 1,1,1-trinitropropane, 1,1,1-trinitropentane, and 4,4,4-trinitrobutyric acid to gem-dinitromethyl compounds [19]. The reaction of 1,1-dimethylhydrazine or its hydrochloride salt with trinitroacetonitrile leads to dinitroacetonitrile [20]. An analogous result was also obtained with hydrobromic acid [21]. Potassium iodide in methanol reduces 1,1,1-trinitroethane, 1,1,1,3-tetranitropropane, 4,4,4-trinitrobutyric acid amide and methyl ester, 5,5,5-trinitropentan-2-one, and 3,3,3-trinitropropyl phenyl ketone to the corresponding compounds containing a dinitromethyl grouping [22].

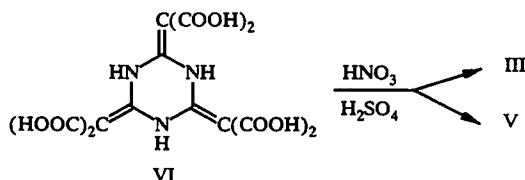
In view of the high reactivity towards nucleophiles (water, alcohols, amines) of the trinitromethyl groups in triazine (I) [7, 8] and the literature data on the conversion of the trinitromethyl fragment into a dinitromethyl, we remodeled the conditions for reducing compound (I). 1) It is impossible to carry out the reduction in a nucleophilic medium, such as water, alcohol, or amine solution. 2) The reducing agent must be a weak nucleophile in order to reduce the substitution process of the trinitromethyl groups to a minimum. 3) The reducing agent must be a bulky molecule in order to use steric hindrance to avoid substitution.

As reducing agents we used tetrabutylammonium bromide and iodide, hydrogen bromide, a system of potassium bromide and iodide in trifluoroacetic acid, hydrazine hydrate, hydrazine sulfate, 2-nitropropane sodium salt, trimethyliodosilane, and metallic zinc and copper. Absolute chloroform, carbon tetrachloride, and tetrahydrofuran were used as solvents.

The results of the investigations showed that triazine (I) was unaffected on using potassium bromide and iodide in trifluoroacetic acid, hydrogen bromide, and hydrazine sulfate as reducing agent. In all other experiments complete decomposition of the starting material was observed. Demonstration (by TLC) of the formation of an individual compound in the reaction mixture was unsuccessful.

We also studied the electrochemical reduction of compound (I) with the aim of obtaining triazines (III) and (V). This method is used for the reduction of polynitroalkanes, including some containing a trinitromethyl fragment [23, 24]. However it transpired that triazine (I) decomposed under the experimental conditions.

4. Destructive nitration of 2,4,6-tris[di(carboxy)methylene]hexahydro-1,3,5-triazine (VI) or its esters.

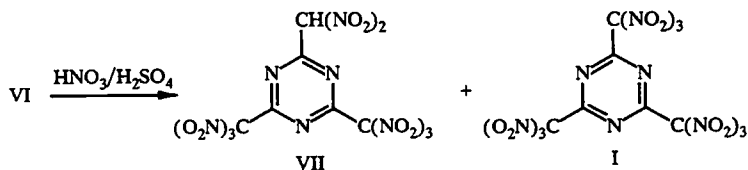


The hexacarboxylic acid (VI) and its t-butyl ester became available from our own work [6, 7].

Purpose-directed systematic investigations on the destructive nitration of hexaacid (VI) were carried out previously in the synthesis of triazine (I) using a mixture of concentrated sulfuric and nitric acids (molar ratio 1:1) taken at a tenfold excess over stoichiometric [6, 7]. The formation of compounds (III) or (V) was not recorded in any experiment.

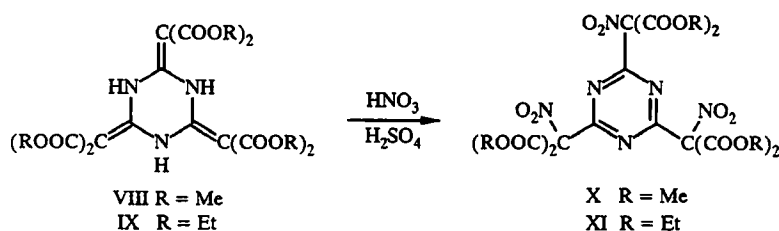
Attempts to obtain these triazines by the nitration of (VI) under milder conditions $[(\text{CH}_3\text{CO})_2\text{O} + \text{HNO}_3, (\text{CF}_3\text{CO})_2\text{O} + \text{HNO}_3, \text{CF}_3\text{COOH} + \text{HNO}_3]$ were not crowned with success. The hexaacid did not react with these mixtures, unlike the sulfuric-nitric acid mixture which we used at various ratios.

At a molar ratio H_2SO_4 (d 1.84)– HNO_3 (d 1.51)–triazine (VI) equal to 1:4:0.4 2-dinitromethyl-4,6-bis(trinitromethyl)-1,3,5-triazine (VII) was isolated containing from 10 to 20% triazine (I) depending on the duration of the reaction (6-7 h at 18°C). The content of compound (VII) was reduced and of triazine (I) increased at more extended times under the same conditions. This may indicate that compound (VII) is possibly the immediate precursor of compound (I).



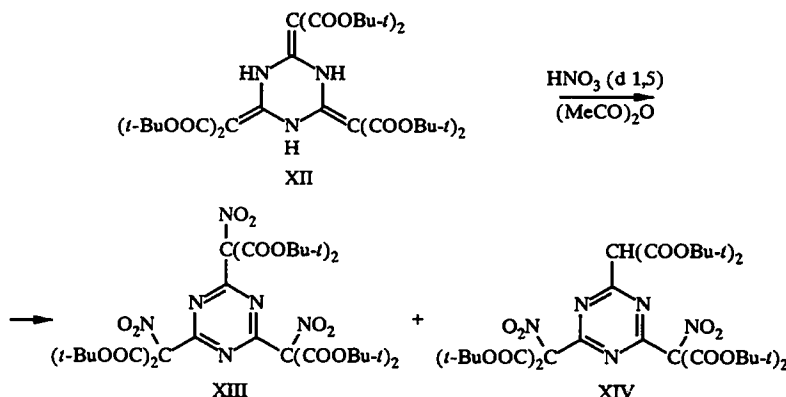
A signal was present in the PMR spectrum of this mixture for the proton of the dinitromethyl group which indicates the absence of the enamine form of triazine (VII). The ^{13}C NMR spectrum contained characteristic signals for the carbon atoms of the triazine ring, and the dinitromethyl, and trinitromethyl groups. Signals were present for the nitro groups in the ^{14}N NMR spectrum. Attempts to purify compound (VII) by recrystallization led to decomposition. Judging from our data the nitration of the hexaacid (VI) is unlikely to give triazines (III) and (V).

We showed previously that esters (VIII) and (IX) of hexaacid (VI) are converted in good yield by a mixture of concentrated nitric and sulfuric acids into the corresponding 2,4,6-tris[di(alkoxycarbonyl)nitromethyl]-1,3,5-triazines (X) and (XI) [6] which might be precursors for triazine (III).



Attempts to saponify esters (X) and (XI) under acidic or alkaline conditions were unsuccessful.

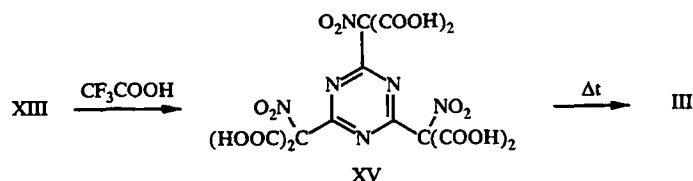
The corresponding t-butyl ester (XII) of hexaacid (VI) gave a mixture of triazines (XIII) and (XIV) in an overall yield of 95% on nitration with conc. $\text{HNO}_3 + \text{Ac}_2\text{O}$.



Attempts to increase the yield of product (XIII) by increasing the duration of the reaction or the quantity of HNO_3 led only to decomposition of the reaction mixture. Milder nitration conditions using HNO_3 (d 1.42) enabled decomposition to be avoided, however the overall yield of compounds (XIII) and (XIV) was reduced by 5-10% and the content of triazine (XIV) in the reaction products grew by up to 15-20%.

The mixture of triazines (XIII) and (XIV) was readily separated by recrystallization from ethanol in which ester (XIII) is insoluble. On saponifying triazine (XIII) with trifluoroacetic acid the corresponding hexaacid (XV) was formed, decarboxylation of which on heating in ethanol or methanol led to the desired product (III) in 80% yield.

The triazine (III) exists exclusively in the nitromethyl form judging by NMR spectra. This compound is a strong CH -acid and readily gives a trilithium salt (XVI) on treatment with lithium methylate or ethylate in the corresponding alcohol.



We made numerous attempts to nitrate triazine (III) or its trilithium salt (XVI) but this did not give product (V). In all cases a polymeric compound of unestablished structure was isolated.

EXPERIMENTAL

The IR spectra were taken on a Specord instrument in KBr disks. The ^1H , ^{13}C , and ^{14}N NMR spectra were obtained on a Bruker 300 instrument (300, 75.5, and 21.67 MHz respectively), internal standard was TMS. Melting points were determined on a Boetius hot stage with a rate of heating $4^\circ\text{C}/\text{min}$ close to the melting point.

The synthesis of 2,4,6-tris[di(t-butoxycarbonylmethylene)]hexahydro-1,3,5-triazine (XII) has been described in [7].

Nitration of Hexaacid (VI) with a Mixture of Concentrated Nitric and Sulfuric Acids. The hexaacid (VI), prepared from hexaester (XII) (2.9 g, 4 mmole), was added with stirring to a mixture of nitric (d 1.51) (10 ml) and sulfuric (d 1.84) acids (40 ml) cooled to 0°C . Stirring was continued for 6 h at room temperature. The precipitated solid was filtered off, washed with conc. H_2SO_4 , and extracted with hot CCl_4 (60-80 ml). The extract was purified from traces of H_2SO_4 by shaking over freshly calcined magnesium sulfate. The crystals which precipitated on cooling the filtrate were filtered off and air dried. Compound (VII) (0.7 g) was obtained containing (judging by spectral characteristics) up to 10% triazine (I) and had mp $67-72^\circ\text{C}$ (with decomposition). IR spectrum: 1620, 1605, 1560, 1300, 1280, 1000, 980 cm^{-1} . PMR spectrum (CDCl_3): 7.54 ppm (1H, s, CH). ^{13}C NMR spectrum (CDCl_3): 166.87 (N-C-CH, $^2J_{\text{CH}} = 3.5$ Hz; 164.95 (-C=N); 120.86 [$\text{C}(\text{NO}_2)_3$]; 107.58 ppm [$\text{CH}(\text{NO}_2)_2$, $^1J_{\text{CH}} = 173.1$ Hz]. ^{14}N NMR spectrum (CDCl_3): -42.78 [NO_2 in $\text{C}(\text{NO}_2)_3$]; -32.70 ppm [NO_2 in $\text{CH}(\text{NO}_2)_2$]. Found, %: C 15.75; H 2.02; N 33.22. $\text{C}_6\text{H}_1\text{N}_{11}\text{O}_{16}$. Calculated, %: C 14.91; H 0.20; N 31.89.

2,4,6-Tris[di(t-butyloxycarbonyl)nitromethyl]-1,3,5-triazine (XIII) and 2,4-Bis[di(t-butyloxycarbonyl)nitromethyl-6-di-(t-butyloxycarbonyl)methyl-1,3,5-triazine (XIV). The hexaester (XII) (14.5 g, 20 mmole) in CHCl_3 (40 ml) was added with stirring and cooling ($0-10^\circ\text{C}$) to a mixture of acetic anhydride (120 ml), abs. CCl_4 (120 ml), and HNO_3 (d 1.51) (45 ml). The mixture was stirred at this temperature for 1.5-2 h, the cooling removed, and then stirred 30 min further at $18-20^\circ\text{C}$. The reaction mixture was poured into ice water (500 ml), stirred for 1 h, the organic layer separated, and the aqueous layer extracted with CHCl_3 (3×100 ml). The extracts were combined with the organic layer, washed with water (3×100 ml), and once with aqueous sodium bicarbonate solution. The organic solution was dried over calcium chloride, the solvent evaporated in vacuum, and ethanol (150 ml) added to the residue. The contents of the flask were heated to 60°C , the solid filtered off, washed with alcohol, and air-dried. Triazine (XIII) (14.6 g, 85%) was obtained. Triazine (XIV) precipitated from the filtrate on cooling, and was filtered off, washed with alcohol, and dried in the air. Yield was 1.1 g (10%).

Triazine (XIII). mp $155-157^\circ\text{C}$. IR spectrum: 1760, 1570, 1550, 1250, 820 cm^{-1} . PMR spectrum (CDCl_3): 1.48 ppm (54H, s, 18CH_3). ^{13}C NMR spectrum (CDCl_3): 169.45 (C=N); 157.36 (COO); 100.53 (C- NO_2); 67.26 [$\text{C}(\text{CH}_3)_3$]; 27.36 ppm (CH_3). ^{14}N NMR spectrum (CDCl_3): -17.93 ppm (NO_2). Found, %: C 50.44; H 6.66; N 9.42. $\text{C}_{36}\text{H}_{54}\text{N}_6\text{O}_{18}$. Calculated, %: C 50.34; H 6.33; N 9.78.

Triazine (XIV). mp 108-110°C. IR spectrum: 1760, 1550, 1250, 820 cm^{-1} . PMR spectrum (CDCl_3): 1.42 ppm (54H, s, 18CH_3). ^{13}C NMR spectrum (CDCl_3): 173.49 ($\text{CH}-\text{C}=\text{N}$, $^2J_{\text{CH}} = 10.2$ Hz); 169.21 ($\text{CNO}_2-\text{C}=\text{N}$); 163.32 ($\text{CH}-\text{C}-\text{OOC}$, $^2J_{\text{CH}} = 8.2$ Hz); 157.71 (CNO_2COOC); 100.71 (CNO_2); 83.48 [$\text{C}(\text{CH}_3)_3$]; 63.12 (CH , $^1J_{\text{CH}} = 134.04$ Hz); 27.87 and 27.44 ppm (CH_3). ^{14}N NMR spectrum (CDCl_3): -17.68 ppm (NO_2). Found, %: C 53.27; H 6.50; N 8.49. $\text{C}_{36}\text{H}_{55}\text{N}_5\text{O}_{16}$. Calculated, %: C 53.12; H 6.81; N 8.60.

2,4,6-Tris(nitromethyl)-1,3,5-triazine (III). Triazine (XIII) (30.8 g, 36 mmole) triazine (XIII) was added with stirring to a mixture of CF_3COOH (70 ml) and dry CHCl_3 (70 ml). The reaction mixture was stirred at room temperature for 2 h. The precipitate was filtered off, dried in the air, then dissolved in methanol or ethanol (100 ml), and heated to boiling. The mixture was cooled with ice, the precipitated solid filtered off, and dried in the air. Triazine (III) (7.43 g, 80%) was obtained having mp 155°C (with decomposition). IR spectrum: 3020, 2960, 1530, 1410, 1350, 1300, 900 cm^{-1} . PMR spectrum [$(\text{CD}_3)_2\text{CO}$]: 6.06 ppm (6H, s, 3CH_2). ^{13}C NMR spectrum [$(\text{CD}_3)_2\text{CO}$]: 171.71 ($\text{C}=\text{N}$, d, $^2J_{\text{CH}} = 6.3$ Hz); 80.94 ppm (CH_2 , t, $^1J_{\text{CH}} = 150.2$ Hz). ^{14}N NMR spectrum [$(\text{CD}_3)_2\text{CO}$]: -8.57 ppm (NO_2). Found, %: C 27.96; H 2.29; N 32.30. $\text{C}_6\text{H}_6\text{N}_6\text{O}_6$. Calculated, %: C 27.91; H 2.34; N 32.56.

Trilithium Salt of 2,4,6-Tris(nitromethyl)-1,3,5-triazine (XVI). Triazine (III) (0.26 g, 10 mmole) was added with stirring at 18°C to a reaction mixture containing ethanol or methanol (50 ml) and lithium hydride (30-50 mg, an excess). After 2 h at this temperature the reaction mixture was heated at 50°C for 15 min, and cooled. The precipitated solid was filtered off, washed with alcohol, and dried at 100-150°C. Yield was 0.27 g (~100%), mp > 250°C (with decomposition). PMR spectrum (D_2O): 6.77 ppm (3H, s, CH). ^{13}C NMR spectrum (D_2O): 165.84 ($\text{C}=\text{N}$, $^2J_{\text{CH}} = 4.9$ Hz); 122.57 ppm (CH, $^1J_{\text{CH}} = 186.38$ Hz). ^{14}N NMR spectrum (D_2O): -46.71 ppm (NO_2). Found, %: C 26.08; H 0.98; N 30.39. $\text{C}_6\text{H}_3\text{N}_6\text{O}_6\text{Li}_3$. Calculated, %: C 26.11; H 1.09; N 30.45.

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