Russian Chemical Reviews **72** (3) 279 – 287 (2003) © 2003 Russian Academy of Sciences and Turpion Ltd

DOI 10.1070/RC2003v072n03ABEH000803

Nitro derivatives of 1,3,5-triazine: synthesis and properties

A V Shastin, T I Godovikova, B L Korsunskii

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Abstract. The published data on nitro derivatives of 1,3,5-triazine, belonging to the class of high-energy substances, have been systematised for the first time. The properties of *C*-nitrotriazines, nitraminotriazines and nitroalkyltriazines are considered. The data on the synthesis of previously unknown trisubstituted 1,3,5-triazines containing various functional groups including trinitromethyl groups are generalised. The bibliography includes 69 references.

I. Introduction

1,3,5-Triazines are known for about 200 years.[1] They are used as herbicides, pesticides, coupling reagents in the peptide synthesis, modifiers, antioxidants, thermal stabilisers, antipyrenes, bleaching agents, dyes and base compounds for combinatorial libraries.[1–6] Melamine–formaldehyde resins have found broad application.[7] It was shown that 1,3,5-triazines encounter in some natural objects, such as meteorites and algae.[8,9] However, despite the great body of the published data on substituted 1,3,5-triazines,[1,7,9,10] information on nitro-, nitramino- and nitro(polynitro)methyl 1,3,5-triazine derivatives is scattered in the literature.

The aim of the present review is to generalise and systematise the published data on nitro derivatives of 1,3,5-triazines which present special interest as high-energy compounds. Some of these compounds have been synthesised as explosives or components of explosive mixtures; therefore, special emphasis in their description is given to their explosive properties and sensitivity to shock, friction, *etc*.

II. Nitro-1,3,5-triazines

There are several approaches to the synthesis of nitro-1,3,5-triazines, *viz*.:

(1) electrophilic nitration of the triazine ring;

(2) nucleophilic substitution of the nitrite ion for the halogen atom or other good leaving groups (nucleophilic nitration);

(3) oxidation of amino, nitroso, hydroxyamino or azido groups;

(4) cyclotrimerisation of nitriles containing a nitro group;

(5) nitration of heterocyclic organometallic compounds.

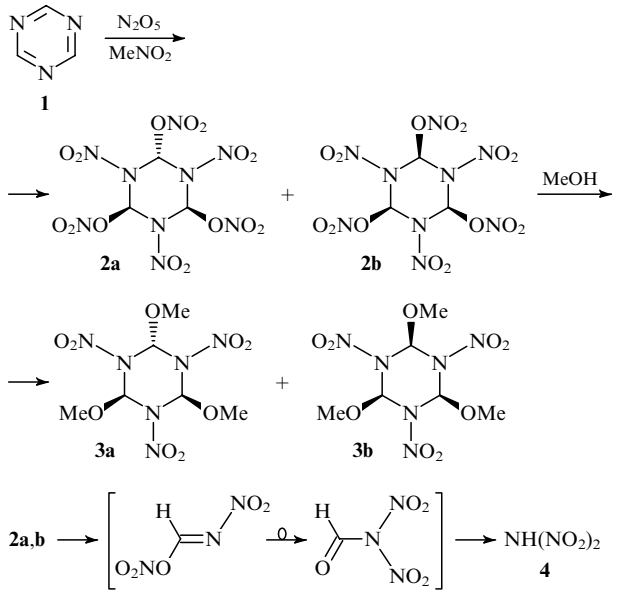
1. Electrophilic nitration

Electrophilic nitration of 1,3,5-triazine (**1**) has been described relatively recently.[11] In contrast to nitration of aromatic compounds, that of heteroaromatic compounds containing several nitrogen atoms is significantly inhibited due to the acceptor effect of the nitrogen atoms present in the ring (the nitration rate decreases 10^6-fold upon substitution of C=N for one C=C fragment).[12] Moreover, nitration in acidic media creates additional difficulties due to easier protonation of nitrogen-containing heterocycles in comparison with aromatic rings, which also reduces the nitration rate. In general, direct nitration of six-membered azines is used only if the heterocycle contains some activating groups (*e.g*., amino or hydroxy groups) or *N*-oxide groups. However, no more than two nitro groups can be incorporated simultaneously irrespective of the nature of the heterocycle.[13] Nitration of unsubstituted triazines with nitric anhydride (Scheme 1) occurs as a conjugate addition of nitronium nitrate to the N=C bond, which affords isomeric *N*-nitronitroxyhexahydro-1,3,5-triazines, *viz*., 1,3,5-trinitro-*cis*-2,4,6-trinitroxyhexahydrotriazine (**2a**) and 1,3,5-trinitro-*trans*-2,4,6-trinitroxyhexahydrotriazine (**2b**).[11] In this case, nitration proceeds similarly to the known halogenation reactions of the triazine ring and affords perhalogenohexahydrotriazines.[14] The structures of the compounds obtained were established[11] based on the analysis of the NMR spectra of the reaction mixture and the composition of their methanolysis products **3a** and **3b** (yields 14% and 10%, respectively). Nitronitroxyhexahydro-1,3,5-triazines **2a**,**b** themselves could not be isolated because of their low stability (according to the NMR spectroscopic data, they are rather stable at temperatures below 0 °C and decompose at nearly the same rates at 20 °C). Presumably,[11] dinitramide (**4**) is the final decomposition product of these compounds (see Scheme 1). This is formed as a result of retro-[2+2+2]cycloaddition of hexahydrotriazines **2a**,**b** and formation of transient imidoyl nitrate which is further rearranged into *N*,*N*-dinitroformamide to give dinitramide **4**. The reaction products **3a**,**b** represent methoxy-substituted analogues of hexogen.

A V Shastin, B L Korsunskii Institute of Problems of Chemical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax (7-096) 514 32 44. Tel. (7-096) 522 33 01. E-mail: shastin@icp.ac.ru (A V Shastin). Tel. (7-095) 939 71 10. E-mail: kors@polymer.chph.ras.ru, kor@icp.ac.ru
T I Godovikova N D Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp. 47, 119991 Moscow, Russian Federation. Fax (7-095) 135 53 28. Tel. (7-095) 134 03 76, (7-095) 938 36 27. E-mail: orakitin@ioc.ac.ru

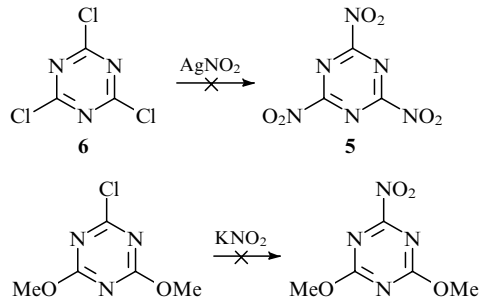
Received 18 December 2002
Uspekhi Khimii **72** (3) 311 – 320 (2003); translated by R L Birnova

Scheme 1



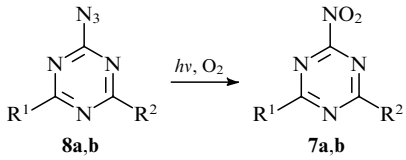
2. Nucleophilic nitration

Nucleophilic nitration is not virtually applied to aromatic compounds because of the high mobility of the aromatic nitro group and the ambident nature of the nitrite ion.[15] Nevertheless, alkali metal nitrites were used as efficient nucleophiles for the replacement of halogen atoms in 1-halogeno-4-nitro-, 1-halogeno-4,6-dinitro- and 1-chloro-2,4,6-trinitrobenzenes under conditions of phase transfer catalysis (solid phase – liquid) in the presence of 18-crown-6 ether.[16] Nucleophilic nitration of some halogen-substituted pyridazinones also gives acceptable yields.[17] It is not therefore surprising that nucleophilic nitration of cyanuric chloride (**6**) with silver nitrite was the first, albeit unsuccessful, attempt to synthesise 2,4,6-trinitro-1,3,5-triazine (**5**).[18] A similar reaction of 4,6-dimethoxy-2-chloro-1,3,5-triazine with potassium nitrite was unsuccessful also.[19]

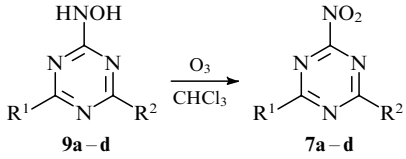


3. Oxidation of nitrogen-containing groups

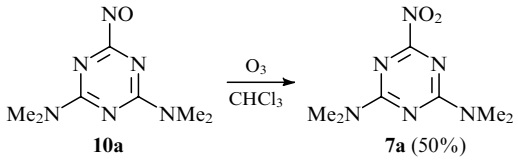
Oxidation of exocyclic nitrogen-containing groups is a convenient method for the synthesis of nitroazines.[13] Few mononitro-1,3,5-triazines **7** were prepared by photochemical oxidation of azido-1,3,5-triazines **8** in the presence of oxygen [20] (similar to oxidation of azidopyrimidines [21]) or by ozonisation of the corresponding hydroxyaminotriazines **9** or nitrosotriazines **10**, *e.g.*, the bisdimethylamino-substituted derivative **10a**.[22,23] The yields of mononitrotriazines **7** are 15% – 50%. Photooxidation includes the formation of a transient triplet nitrene. Ozonisation is very sensitive to the electronic properties of the substituents in the triazine ring; thus the reaction is only successful if one or two dialkylamino groups are present in the ring.



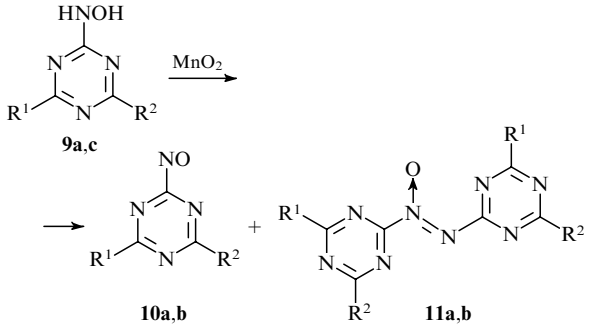
a: $R^1 = R^2 = NMe_2$ (29%); **b**: $R^1 = OMe$, $R^2 = NMe_2$ (15%).



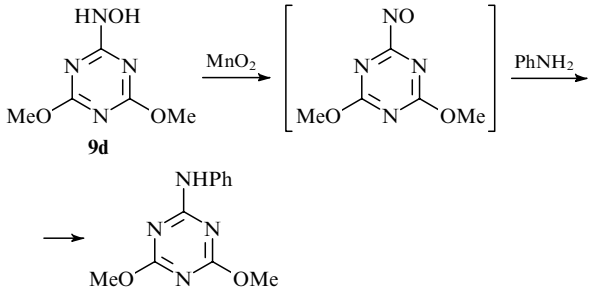
a: $R^1 = R^2 = NMe_2$ (28%); **b**: $R^1 = OMe$, $R^2 = NMe_2$ (30%); **c**: $R^1 = R^2 = N(CH_2)_5$ (50%); **d**: $R^1 = R^2 = OMe$ (0%).



However, this method cannot be used for the introduction of several nitro groups into the triazine ring. The oxidation of hydroxyaminotriazines **9a**,**c** with manganese oxide in chloroform gives only nitrosotriazines **10a**,**b** and their condensation products with the starting hydroxylamines **11a**,**b**.[24] The oxidation of 2-hydroxyamino-4,6-dimethoxy-1,3,5-triazine (**9d**) under identical conditions resulted in the formation of solutions with the greenish colour typical of nitrosoazines, but the attempts to isolate the corresponding triazine or to identify its adduct with aniline failed. 2-Anilino-4,6-dimethoxy-1,3,5-triazine formed as a result of substitution of aniline for a mobile nitroso group was the only compound identified.[24]

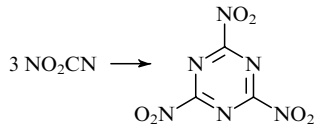


Compounds	R^1, R^2	Yield of **10** (%)	Yield of **11** (%)
9a, **10a**, **11a**	NMe_2	35	0
9c, **10b**, **11b**	$N(CH_2)_5$	30	30



4. Cyclotrimerisation

The trimerisation of hypothetical nitrocyanogen into 2,4,6-trinitro-1,3,5-triazine (**5**) is discussed in a study[25] devoted to the energy characteristics of trinitrotriazine as a representative of a novel class of high-energy compounds of the general formula $C_nN_{2n}O_{2n}$.



5

This scheme looks rather attractive: according to the calculations [*ab initio* calculations with optimisation of geometrical parameters using the HF/6-31G* and MBPT(2)/6-31G* basis sets and the ACES II software], the trimerisation of hypothetical nitrocyanogen can be energetically favourable: $\Delta E = -70.2$ kcal mol^{-1} as calculated by MBPT(2). However, it has been shown[26] that the reaction of HCN with NO_2BF_4 in nitromethane, tetrahydrothiophene 1,1-dioxide or in the absence of a solvent is not accompanied by trimerisation of the intermediate, structurally similar and less sterically hindered neutral $CN-NO_2$.

In the calculated trinitrotriazine structure with the symmetry C_3 corresponding to the minimum energy, the aromatic triazine ring is planar and the nitro groups are rotated 40° to the ring plane. Such a spatial arrangement of the nitro groups compensates for their conjugation with the ring and the mutual repulsion of the negatively charged oxygen atoms and the nitrogen atoms of the triazine ring (the minimum value corresponds to the angle 90°). The length of the C–N bond in the triazine ring is equal to 1.331 Å, the NCN angle is equal to 128.4° (according to the electron diffraction spectroscopy data, the length of the C–N bond in unsubstituted 1,3,5-triazine is 1.338 Å, while the NCN angle is equal to 126.2°). The standard enthalpy of formation (ΔH_f°), the heat of explosive degradation (ΔE_r) and specific impulse (I_{sp}) of compound **5** were calculated to be equal to $\Delta H_f^\circ = 46$ kcal mol^{-1}, $\Delta E_r = 304$ kcal mol^{-1}, I_{sp} is 269 s at ambient pressure and 294 s in vacuum. These characteristics are similar to the corresponding values for hexogen, but the calculated density (ρ_0) of trinitrotriazine **5** is higher (1.82 and 2.1 g cm^{-3} for hexogen and compound **5**, respectively).[27] Korkin and Bartlett[25] expect to prepare trinitrotriazine **5** using an original scheme which includes trimerisation of nitrocyanogen. The following characteristics of compound **5** have been calculated[28] (for comparison, the corresponding parameters for hexanitrobenzene are given in parentheses): detonation rate (D), 9530 (9413) m s^{-1}; $\Delta H_f^\circ = 18$ (36) kcal mol^{-1}, $\rho_0 = 1.973$ (1.973) g cm^{-3}.

5. Nitration of organometallic compounds

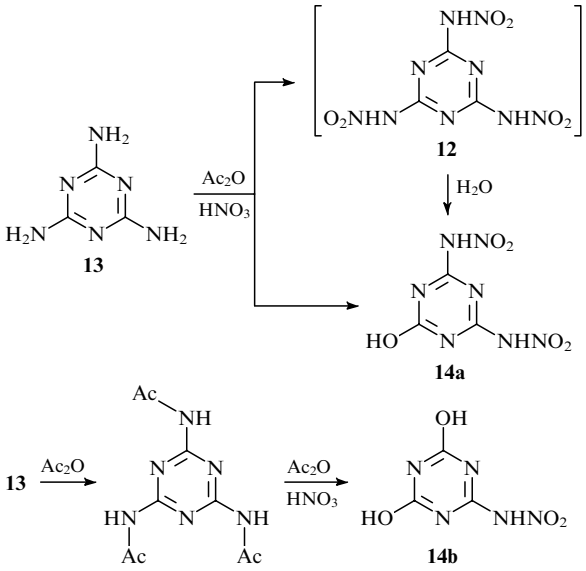
Nitration of 1,3,5-triazine stannyl derivatives is yet another, hitherto non-explored method for the synthesis of nitro-substituted triazines. Recently, this approach has been used in the synthesis of 2-nitro derivatives from 2-trimethylstannylated benzo[*b*]furan, benzo[*b*]thiophene, substituted indoles and 2-, 3- and 4-trimethylstannylpyridines under the action of tetranitromethane or dinitrogen tetraoxide (in the case of 3- and 4-trimethylstannylpyridines, the yields did not exceed 2%).[29]

Thus, 2,4,6-trinitro-1,3,5-triazine, a heterocyclic analogue of one of the most potent explosives, *viz.*, hexanitrobenzene,[30] could not be prepared so far.

III. Nitramino-1,3,5-triazines

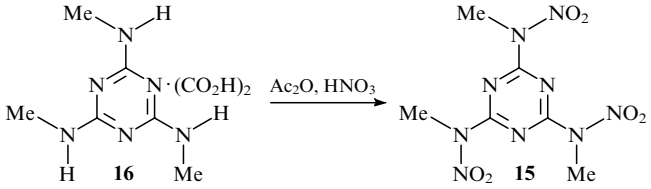
Both substituted and unsubstituted nitramines based on heterocyclic compounds are usually prepared by nitration of the corresponding amines, sometimes with preliminary protection of the NH_2 group. Primary and secondary (*i.e.*, containing the $NHNO_2$ and $NRNO_2$ groups, respectively) nitramines of the 1,3,5-triazine series are documented. Numerous attempts at the synthesis of 2,4,6-tris(nitramino)-1,3,5-triazine (**12**), which is the first member of this series, failed.[31,32]

It was shown[33] that nitration of melamine (**13**) gives dinitroammeline (**14a**) in 44% – 52% yield. Presumably, the transient compound **12** formed in this reaction is hydrolysed to dinitroammeline with the loss of a nitramino group, which is typical of nitramino derivatives of six-membered heterocycles.[32] It is of note that nitration of triacetylmelamine at higher temperatures yields nitroammelide (**14b**). The feasibility of dinitroammeline as a high-energy compound is being investigated.[33,34] Dinitroammeline rapidly decomposes on heating to 228 °C, while nitroammelide decomposes at 248 °C and slowly sublimates at 200 °C (1 Torr).



Melamine salts with nitramide and nitric acid are considered to be promising candidates for high-energy compounds.[35]

The data on substituted nitraminotriazines, *i.e.*, triazines containing secondary nitramino groups as substituents, are more numerous. Thus the synthesis and properties of 2,4,6-tris(methylnitramino)-1,3,5-triazine (**15**) have been described.[36] This compound is prepared by nitration of a complex of 2,4,6-tris(methylamino)-1,3,5-triazine with oxalic acid (**16**) with acetyl nitrate (40 °C, 5 h) (the yield of the product **15** is 72%).

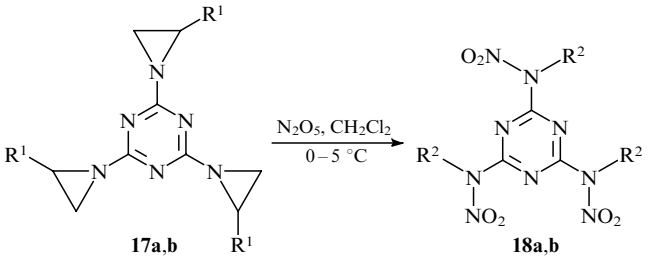


According to derivatography data, triazine **15** decomposes at 210 °C. This compound has the following characteristics (for comparison, some parameters of tetryl are given in parentheses): single crystal density (ρ_m), 1.67 g cm^{-3}, $\Delta H_f^\circ = 275.1$ (33.9) kJ mol^{-1}, friction sensitivity > 36 (36), impact sensitivity, 12.5 (6.5–12.5),† detonation rate, 7228 m s^{-1} at the charge density of $\rho = 1.53$ g cm^{-3} (7575 m s^{-1} at $\rho = 1.71$ g cm^{-3}).[36]

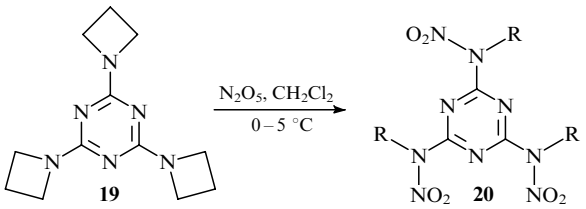
The nitration of such melamine derivatives as 2,4,6-triaziridino-1,3,5-triazine (**17a**) and 2,4,6-tris(methylaziridino)-1,3,5-

† There are many ways for expressing the sensitivity of explosives. As a rule, this is determined as a ratio of the number of explosions of a standard amount of a substance for a given number of trials to the total number of trials at a given mass and load fall height. In this case, they represent relative values.[36] In the Russian literature, the sensitivity is traditionally expressed on a per cent basis; the mass and load fall height separated by an oblique stroke are given in parentheses: x% (M kg/N cm).

triazine (**17b**) with N_2O_5 in dichloromethane at 0 – 5 °C (the molar ratio **17** : N_2O_5 is 1.0 : 3.3) afforded nitramines **18a**,**b** (yields 95% and 78%, respectively).[37] The nitration of 2,4,6-triazetidino-1,3,5-triazine (**19**) under analogous conditions yields a mixture of products which contains nitramine nitrate **20** (60%) and non-identified compounds.[38]



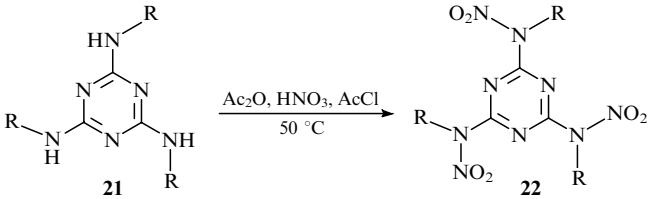
R^1 = H (**a**), Me (**b**); R^2 = $CH_2CHR^1ONO_2$.



R = $(CH_2)_3ONO_2$.

Some characteristics of triazine **18a** (its commercial name is 'Tris-X') have been reported:[39] m.p. = 68 – 69 °C, ρ_m = 1.73 g cm^{-3} (data from X-ray diffraction analysis), impact sensitivity, 57, detonation rate, 8700 m s^{-1}. The latter value suggests that compound **18a** is a high-energy low-melting explosive despite its relatively low density.

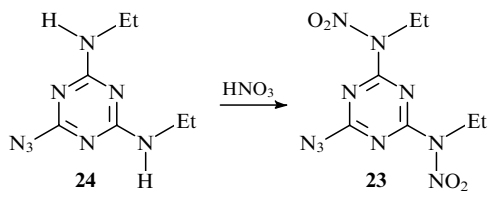
2,4,6-Tris(picrylnitramino)-1,3,5-triazine (**21**) gave 2,4,6-tris(picrylnitramino)-1,3,5-triazine (**22**) in 95% yield.[40]



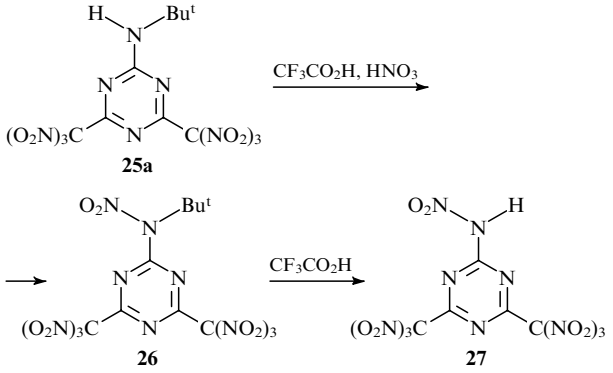
R = 2,4,6-$(NO_2)_3C_6H_2$.

Unlike nitramines **18a**,**b**, which dissociate at 177 – 197 °C, compound **22** is unstable: this slowly decomposes at 0 °C and rapidly decomposes at 100 °C.[39]

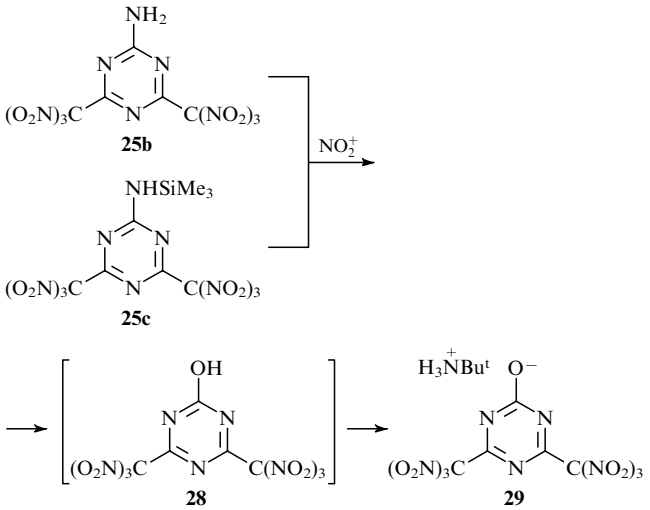
Synthesis of 2-azido-4,6-bis(ethylnitramino)-1,3,5-triazine (**23**) from 2-azido-4,6-bis(ethylamino)-1,3,5-triazine (**24**) has been described.[41] The characteristics of compound **23** obtained in 20% yield are as follows: m.p. = 40 – 41 °C, ρ_m = 1.375 g cm^{-3}, ΔH_f = 540.2 kJ mol^{-1}, initial decomposition temperature, 207 °C. Presumably,[41] elimination of nitrogen from the azido group is the initial step in the decomposition of azidotriazine **23**.



The use of *tert*-butyl protection in the nitration of bistrinitromethyl-substituted triazine **25a** and subsequent removal of the protective group in the *tert*-butylnitraminotriazine **26** formed with trifluoroacetic acid has enabled the preparation of nitraminotriazine **27**,[42] which possesses low thermal stability.



Attempts at direct nitration of unprotected aminotriazine **25b** and introduction of the trimethylsilyl protective group (compound **25c**) were ineffective: the amino group of triazine underwent oxidative hydroxylation. 2-Hydroxy-4,6-bis(trinitromethyl)-1,3,5-triazine (**28**) formed in this reaction was isolated and characterised as *tert*-butylammonium salt **29** (for the synthesis of trinitromethyl-substituted aminotriazines see Section IV.1).

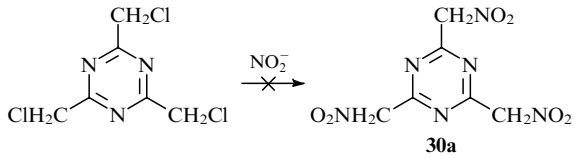


IV. Nitromethyl-, dinitromethyl- and trinitromethyl-1,3,5-triazine derivatives

The synthesis of these 1,3,5-triazine derivatives includes nucleophilic substitution, nitration, destructive nitration and cyclotrimerisation.

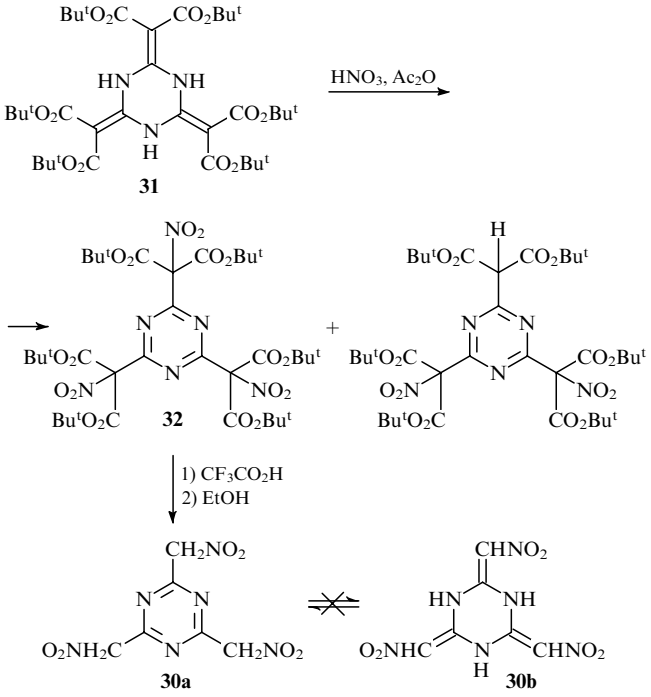
1. Nitromethyl derivatives

The attempts to synthesise 2,4,6-tris(nitromethyl)-1,3,5-triazine (**30a**), the first representative of nitromethyl-substituted 1,3,5-triazines, by nucleophilic substitution of the chlorine atom in 2,4,6-tris(chloromethyl)-1,3,5-triazine were unsuccessful.[43]

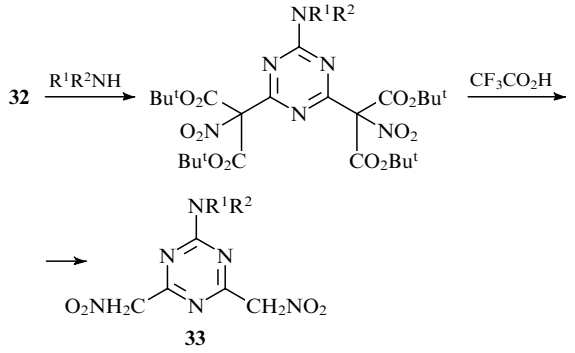


Compound **30a** could be synthesised[43] starting from 2,4,6-tris[di(*tert*-butoxycarbonyl)methylidene]hexahydro-1,3,5-triazine (**31**). 2,4,6-Tris(nitromethyl)-1,3,5-triazine (**30a**) represents a solid yellow-coloured substance (decomposition temperature is 155 °C). According to NMR spectroscopic data (acetone-d_6), it

exists in solution exclusively in a nitromethyl form (the potential tautomer **30b** was not found).[43]

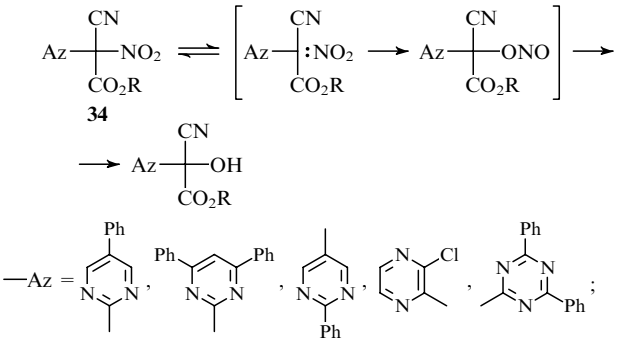


A convenient method for the synthesis of substituted 2-amino-4,6-bis(nitromethyl)-1,3,5-triazines **33** based on 2,4,6-tris[di(*tert*-butoxycarbonyl)nitromethyl]-1,3,5-triazine (**32**) has been developed.[44, 45]



R^1, R^2 = H, Alk.

As can be seen from the scheme, the bulky di(*tert*-butoxycarbonyl)nitromethyl group in triazine **32** acts as a pseudo-halogen. It is noteworthy that reactions involving compounds of the type **34** (triazine, pyrimidine and pyrazine derivatives) are documented,[46] where the nitro group plays the role of a leaving group. Such a



R = Me, Et.

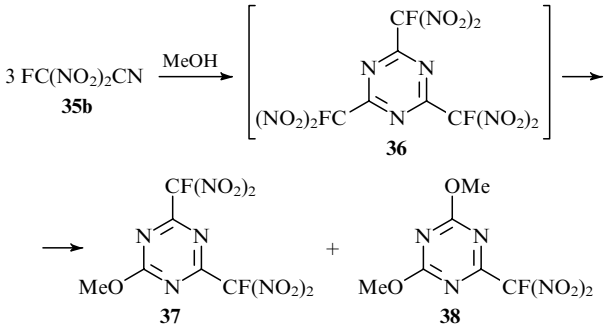
substitution proceeds by a mechanism which involves the initial formation of a radical pair.

Apparently, substitution of di(*tert*-butoxycarbonyl)nitromethyl group (rather than the nitro group) in triazine **32** is due to both the high electrophilicity of the triazine ring and the shielding of the nitro group with bulky *tert*-butoxycarbonyl substituents.

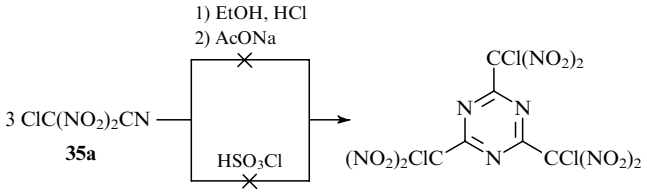
To the best of our knowledge, no methods for the synthesis of nitromethyl-1,3,5-triazines based on destructive nitration or cyclisation of the corresponding nitroacetonitriles have been reported so far.

2. Dinitromethyl derivatives

The known methods for the synthesis of dinitromethyltriazine derivatives are based on cyclotrimerisation of dinitrochloroacetonitrile (**35a**) under conditions of acidic and basic catalyses [43] and cyclotrimerisation of fluorodinitroacetonitrile [47] (**35b**) in methanol at 60 °C and 0.8 GPa. It is assumed [47] that the target 2,4,6-tris(dinitrofluoromethyl)-1,3,5-triazine (**36**) is formed but is converted into the corresponding mono- and dialkoxy derivatives **37** and **38** under the reaction conditions. These compounds could not be isolated in a pure state and their existence was judged from the respective transformation products, mass and NMR spectra. According to mass spectrometry data, the yields of the target triazines **37** and **38** were 45% and 19%, respectively, along with non-identified products.



The attempts at trimerisation of dinitrochloroacetonitrile (**35a**) in basic and acidic media were unsuccessful.[43] Two approaches were used, *viz*., preparation of the corresponding imidate hydrochloride and *in situ* treatment with anhydrous sodium acetate at 0 °C and trimerisation of the nitrile with chlorosulfonic acid. Both methods gave negative results: a vigorous reaction with heating and evolution of nitrogen oxides occurred when the reaction product of the nitrile with ethanol was treated with sodium acetate; no trimerisation occurred in the presence of chlorosulfonic acid.

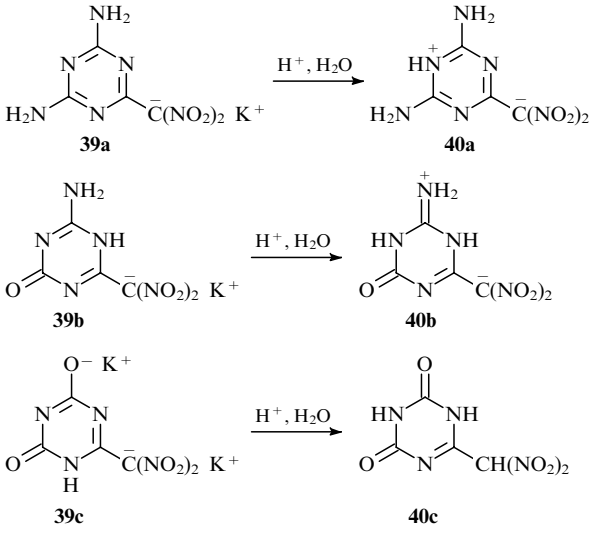


The known method for the synthesis of dinitromethyl derivatives from oximes of aromatic and heteroaromatic carbonyl compounds [48–51] was not applied to triazine derivatives, although the synthesis of 1,3,5-triazine-2,4,6-tricarboxaldehyde trioxime had been reported.[52] The authors of the review are unaware of the attempts to use dinitromethane salts for the synthesis of dinitromethyltriazine derivatives, although this method is applied in the case of halogenobenzenes activated by nitro groups.[53] 1,3,5-Triazines containing a dinitromethyl group together with amino and hydroxyl(oxo) groups have been described, but their synthesis has not been detailed.[54, 55] Acidification of potassium salts of 2,4-diamino-6-dinitromethyl-1,3,5-triazine (**39a**),

Table 1. Physicochemical and explosive characteristics of compounds **40a–c**.[54, 55]

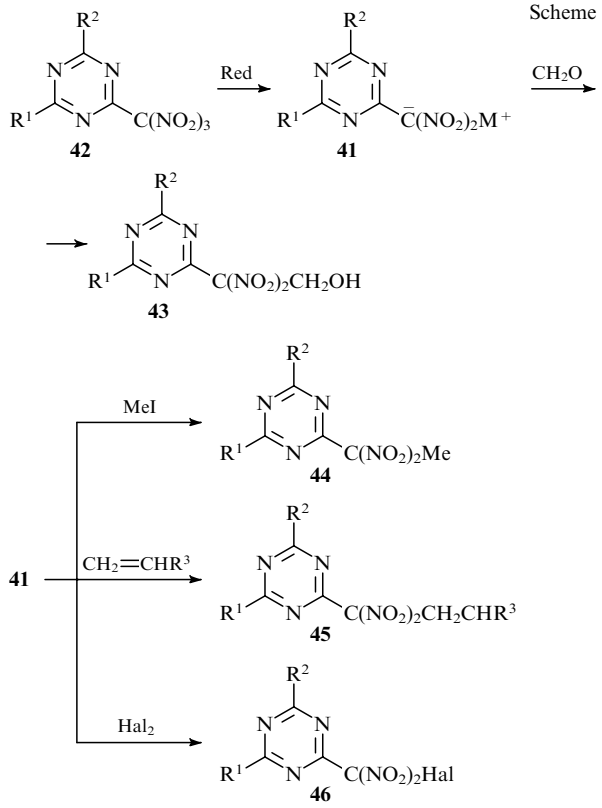
Parameter	**40a**	**40b**	**40c**
Single crystal density ρ_m /kg m^{-3}	1880	1910	2020
Initial temperature of intense decomposition T_d /°C	265	253	170
Enthalpy of formation ΔH_f° /kJ mol^{-1}	−86.9	−291.3	−446.4
Ultimate stress σ_{lim} /MPa	91.2	86.3	94.2
Critical explosive stress p_{cr} /MPa	1500	1400	1500
Critical layer thickness Δ_{cr} /mm	2.2	1.6	2.5
Detonation rate D /m s^{-1} (at experimental charge density ρ /kg m^{-3})	7350 (1.73)	7200 (1.76)	7320 (1.83)
Detonation rate determined by extrapolation of ρ to ρ_m, D_{max} /m s^{-1}	7760	7680	8000

2-amino-6-dinitromethyl-4-oxodihydro-1,3,5-triazine (**39b**) and the dipotassium salt of 2-hydroxy-6-dinitromethyl-4-oxodihydro-1,3,5-triazine (**39c**) afforded dinitromethyl-substituted triazines **40a–c** in the zwitter-ionic (**40a**,**b**) or dioxotetrahydrotriazine form (**40c**).[54, 55] The compounds synthesised possess high energy and high density and represent low-sensitivity explosives (Table 1).



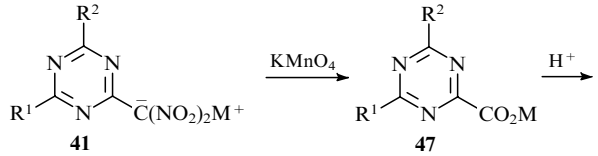
Salts of dinitromethyl-1,3,5-triazine derivatives (**41**) prepared by reduction of the corresponding *C*-trinitromethyltriazines **42** with conventional reducing agents were used in the synthesis of functionalised dinitromethyl-1,3,5-triazines.[56] It was shown that under conditions of acid catalysis formaldehyde enters into the Henry reaction with the salts **41** to give (2-hydroxy-1,1-dinitroethyl)-1,3,5-triazine derivatives **43** (Scheme 2). The same authors performed the alkylation of the salts **41** with methyl iodide in aprotic solvents to the corresponding dinitroethyl derivatives **44** (yields 70%–90%). Salts of *C*-dinitromethyl-1,3,5-triazine derivatives **41** enter into the Michael reaction with various derivatives of acrylic acid, particularly with methyl acrylate and acrylonitrile, to give 4-(2-R^1-4-R^2-1,3,5-triazin-6-yl)-4,4-dinitrobutyric acid derivatives **45**. The halogenation of the salts **41** proceeds differently depending on the halogen used. Chloro- and bromodinitromethyl-1,3,5-triazine derivatives **46** are formed in good yields (80%–95%) in reactions with chlorine and bromine; fluorination gives a complex mixture of products.

Scheme 2

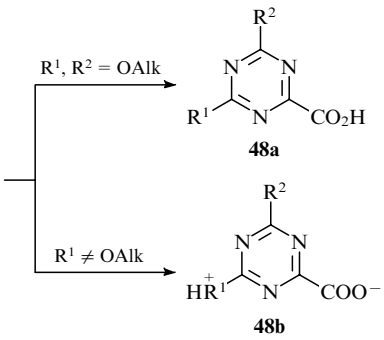


Red is a reducing agent; M = Na, K, NH_4 *etc.*; R^1, R^2 = OAlk, OAr, NH_2, NHAlk, $NAlk_2$, N_3 *etc.*; R^3 = CO_2H, CO_2Me, CN, COMe; Hal = Cl, Br.

The oxidation of the salts **41** with potassium permanganate in an aqueous medium yields the carboxylic acid salts **47**; depending on the substituents in the triazine ring, their acidification gives either the carboxylic acids **48a** (R^1 and R^2 are the alkoxy groups), or the zwitter-ionic compounds **48b** (if at least one of the substituents represents an amino group). This can be attributed to the differences in the basicities of dialkoxy- and alkoxyaminotriazines. The interest in the synthesis of dinitromethyl-1,3,5-triazines is due to the fact that these compounds manifest diverse biological activities including the cytotoxic (antitumour) activity.[57, 58] It was shown that the level of the cytotoxic effects of the most active synthetic compounds is commensurate with that of clinically important 1,3,5-triazines;[57] the highest activity (GI_{50} = 10–80 μmol litre^{-1}) is manifested by some representatives of *C*-(2-hydroxy-1,1-dinitroethyl)-1,3,5-triazines (**43**: R^1 = R^2 = OMe; R^1 = $C(NO_2)_2CH_2OH$, R^2 = NMe_2).‡

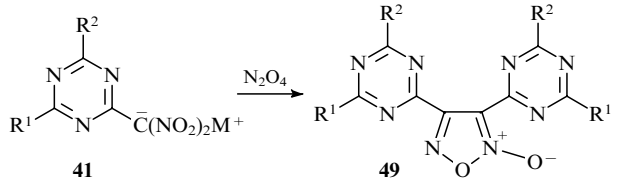


‡ GI_{50} is the concentration of the tested substance which causes 50% inhibition of growth of tumour cell cultures under standard conditions *in vitro* (this methodology was developed at the National Cancer Institute).



M = Na, K, NH_4 *etc.*; R^1 = NH_2, NHAlk, $NAlk_2$, OAlk; R^2 = OAlk, R^1.

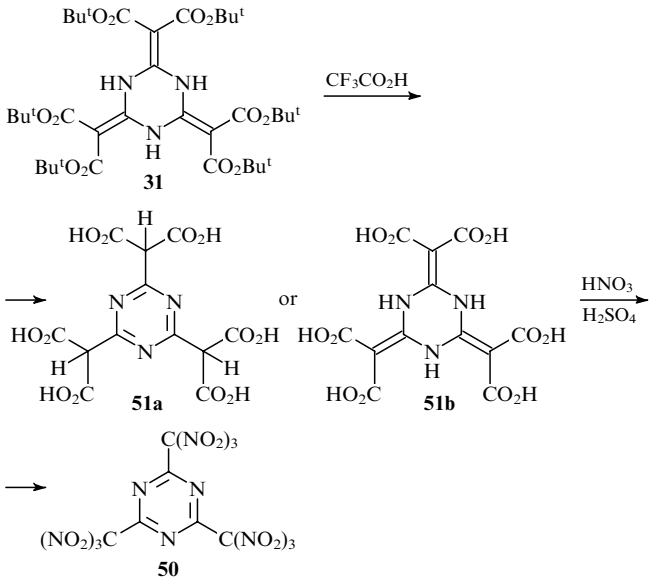
Reactions of the salts of the dinitromethyl-1,3,5-triazine derivatives **41** with nitrogen dioxide in organic solvents afford furoxanes **49**.[56]



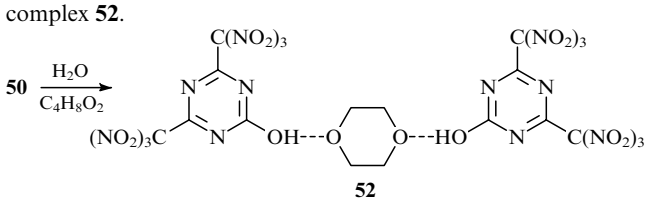
M = Na, K, NH_4 *etc.*; R^1 = R^2 = OMe, NMe_2.

3. Trinitromethyl derivatives

Trinitromethyl-1,3,5-triazine derivatives are synthesised by methods developed by Khmel'nitskii for aromatic and heteroaromatic compounds containing trinitromethyl groups.[48–51,59] 2,4,6-Tris-(trinitromethyl)-1,3,5-triazine (**50**) presents the greatest interest among other 1,3,5-triazines both in the academic and practical aspects; however, numerous attempts at its synthesis did not give any positive results until recently.[60] This compound could be obtained only after the synthesis of 2,4,6-tris(dicarboxymethyl)-1,3,5-triazine (**51a**),[60] which presumably exists in the ylidene form **51b**. Its destructive nitration with a mixture of sulfuric and nitric acids results in tris(trinitromethyl)triazine **50**.



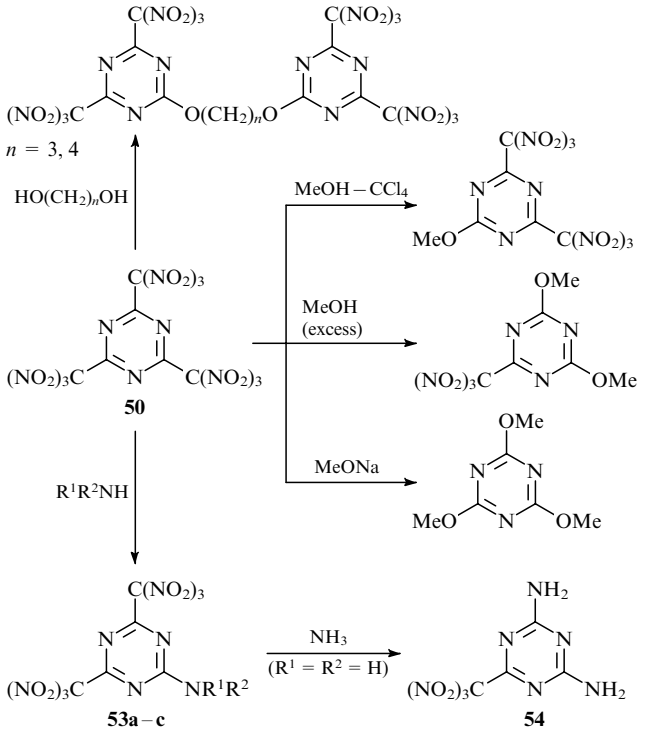
2,4,6-Tris(trinitromethyl)-1,3,5-triazine (**50**) is a colourless crystalline substance, which is stable infinitely at room temperature (in the absence of water vapour). Its pycnometric density is equal to 1.91 g cm^{-3}, m.p. = 91–92 °C (with decomposition), ΔH_f = 93 kcal kg^{-1}, impact sensitivity is 90% (2 kg/20 cm), α = 1.5. The hydrolytic stability of this compound is rather low: after dissolution in aqueous dioxane, the hydroxy group is substituted for one trinitromethyl group to give a stable dioxane complex **52**.



The following characteristics of the complex **52** have been determined: decomposition temperature, 150–152 °C, impact sensitivity, 90% (2 kg/20 cm), ρ_m = 1.764 g cm^{-3} (X-ray diffraction data).[60]

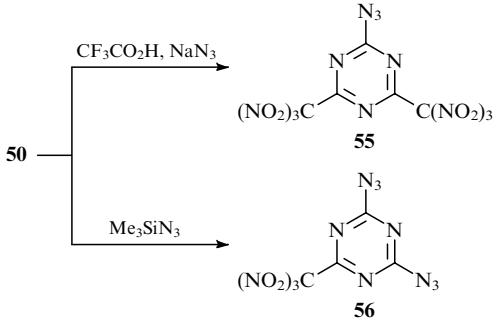
Reaction of compound **50** with nucleophiles can occur with the substitution of one, two or three trinitromethyl groups (Scheme 3).[61,62] Thus reaction with ammonia or amines gives the monoamino derivatives **53a–c**; treatment of triazine **50** with an excess of ammonia gives the diamino derivative **54**.

Scheme 3



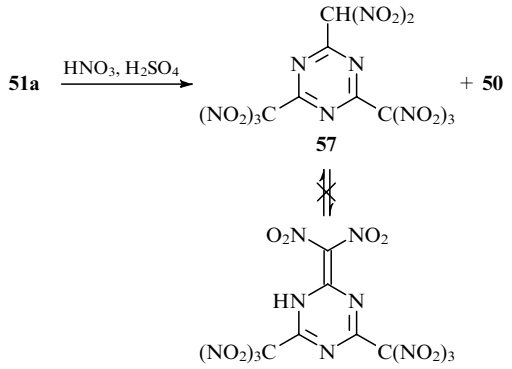
53: R^1 = R^2 = H (**a**), Me (**b**); R^1 = H, R^2 = Ph (**c**).

The use of various azide ion sources has enabled the synthesis of mono- and diazido derivatives **55** and **56**, respectively.[63]



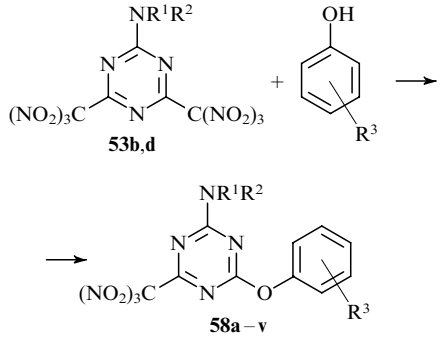
Under certain conditions,[43] nitration of the hexaoic acid **51a** yields, along with 2,4,6-tris(trinitromethyl)-1,3,5-triazine (**50**), the

dinitromethyl derivative, 2-dinitromethyl-4,6-bis(trinitromethyl)-1,3,5-triazine **57**, which exists in the dinitromethyl form.



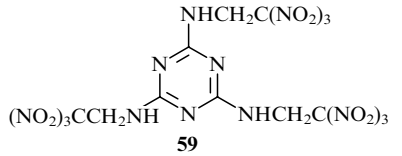
Compound **57** is thermally and hydrolytically unstable. Attempts have been undertaken to reduce 2,4,6-tris(trinitromethyl)-1,3,5-triazine and to perform selective nitration of 2,4,6-tris(nitromethyl)-1,3,5-triazine;[43] however, no reducing agent could be found that did not cause nucleophilic substitution of the trinitromethyl group.

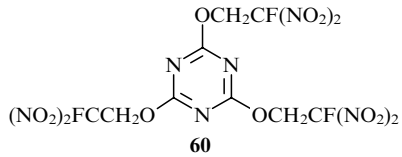
It was found [64] that substitution of phenols for the $C(NO_2)_3$ group in the bis(trinitromethyl)-1,3,5-triazine derivatives **53b**,**d** in the presence of a base occurs in a selective manner and results in 4-aryloxy-2-dimethyl(diethyl)amino-6-trinitromethyl-1,3,5-triazines **58a**–**v**.



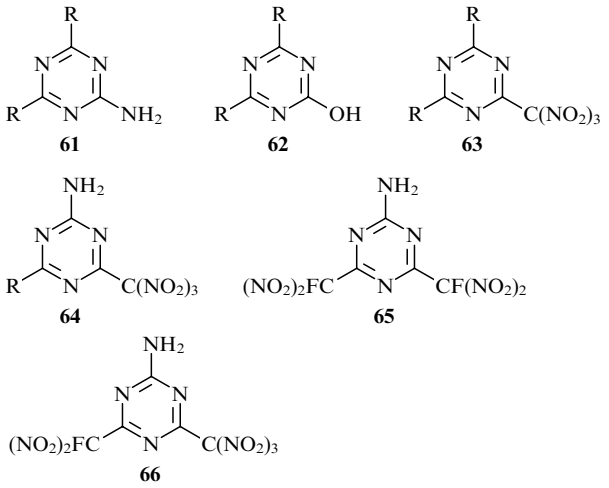
53: $R^1 = R^2$ = Me (**b**), Et (**d**);
58: $R^1 = R^2$ = Me: R^3 = *o*-Me (**a**), *m*-Me (**b**), *p*-Me (**c**), *o*-NO_2 (**d**), *m*-NO_2 (**e**), *p*-NO_2 (**f**), *o*-Cl (**g**), *m*-Cl (**h**), *p*-Cl (**i**), *o*-OMe (**j**), *m*-OMe (**k**), *p*-OMe (**l**), *o*-CO_2Me (**m**), *m*-CO_2Me (**n**), *p*-CO_2Me (**o**); $R^1 = R^2$ = Et: R^3 = *o*-Me (**p**), *p*-OMe (**q**), *m*-CO_2Me (**r**), *p*-NO_2 (**s**), *o*-Cl (**t**), 2,4-$(NO_2)_2$ (**u**), H (**v**).

The substituted 1,3,5-triazines **59** and **60** containing trinitromethyl and fluorodinitromethyl groups linked to the triazine ring through the aminomethyl or oxymethyl bridge have been described.[65–67]





Compound **59** has the following characteristics:[65] detonation rate, 7700 m s^{-1} at ρ = 1.54 g cm^{-3}, impact sensitivity, 50% (2 kg/20 cm). For compound **60,** m.p. = 76–77 °C, ρ_m = 1.795 g cm^{-3};[66] however, its synthesis has not been detailed. 1,3,5-Triazines containing both trinitro(fluorodinitro)-methyl and 2,2,2-trinitro(2-fluoro-2,2-dinitro-)ethoxy groups are reported;[68] some physicochemical and thermodynamic characteristics of these compounds are given, but the methods for their synthesis are omitted.[68] These include 6-amino-2,4-bis(2-fluoro-2,2-dinitro-ethoxy)-1,3,5-triazine (**61**), 6-hydroxy-2,4-bis(2-fluoro-2,2-dinitroethoxy)-1,3,5-triazine (**62**), tri-2,4-bis(2-fluoro-2,2-dinitroethoxy)-1,3,5-triazine (**63**), 6-amino-4-trinitromethyl-2-(2-fluoro-2,2-dinitroethoxy)-1,3,5-triazine (**64**), [4,6-bis(fluoro-dinitromethyl)-1,3,5-triazin-2-yl]amine (**65**) and [6-trinitro-methyl-4-(fluoro-dinitromethyl)-1,3,5-triazin-2-yl]amine (**66**).



R = $OCH_2CF(NO_2)_2$.

Compound	M.p. /°C	ρ_m /g cm^{-3}	Compound	M.p. /°C	ρ_m /g cm^{-3}
61	91–92 (with decomposition)	1.78	**64**	94–95	1.84
			65	109–111	1.86
62	144–145	1.89	**66**	73–75	1.83
63	113–114	1.82			

* * *

Some nitro-substituted 1,3,5-triazines considered in this review (*e.g.*, nitramino-1,3,5-triazines, trinitromethyl-1,3,5-triazines) belong to the class of high-energy compounds and present potential as explosives or components of explosive mixtures. Many of them are promising chemical reagents for the synthesis of novel representatives of 1,3,5-triazines, such as trinitromethyl-1,3,5-triazines and nitromethyl-1,3,5-triazines. All nitro-substituted triazines can be used as NO donors;[69] some dinitromethyl-substituted 1,3,5-triazines were found to manifest high cytotoxic activity.[57,58] An interesting feature of trinitromethyl-1,3,5-triazines is the ease of substitution of various nucleophiles for the trinitromethyl group. Since the major part of these compounds has been obtained relatively recently, in-depth investigation of 1,3,5-triazine nitro derivatives is a topical matter.

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