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Reactions of Trinitromethyl-1,3,5-triazines with Triphenylphosphine in the Presence of Hydrogen Donors and a Dipolarophile

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Abstract—2-Dialkylamino-4-methoxy-6-trinitromethyl-1,3,5-triazines reacted with triphenylphosphine in toluene in the presence of primary aliphatic alcohols as proton donors to give the corresponding 6-[hydroxyimino(nitro)methyl)-1,3,5-triazines. Analogous reactions in the presence of prop-2-yn-1-ol at elevated temperature resulted in the formation of [3+2]-dipolar cycloaddition products, 3-(1,3,5-triazinyl)-5-hydroxymethylisoxazoles.

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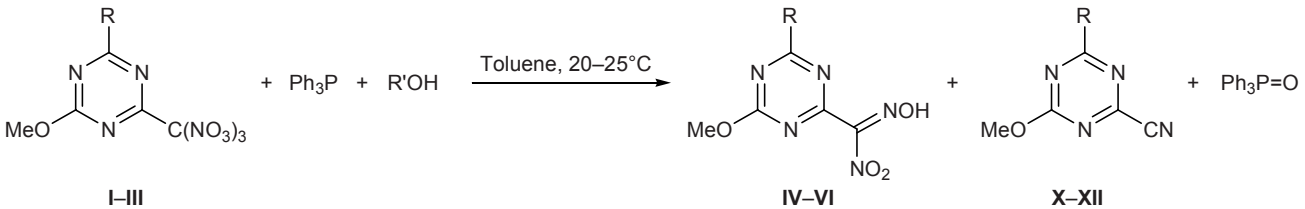
We previously found that trinitromethyl-1,3,5-triazines react with triphenylphosphine to give 1,3,5-triazinecarbonitriles [1]. We proposed a mechanism involving intermediate formation of 1,3,5-triazinecarbonitrile oxide via elimination of two nitrogen dioxide molecules from initially formed dinitro(nitroso)methyl-1,3,5-triazine. In order to prove the proposed scheme we made an attempt to trap intermediate compounds.

1,3,5-Triazinecarbonitrile oxide is a 1,3-dipole, and it should be active in [3+2]-dipolar cycloaddition reactions [2]. Therefore, we used prop-2-yn-1-yl alcohol as dipolarophile to trap 1,3,5-triazinecarbonitrile oxide. The reactions of substituted trinitromethyl-1,3,5-triazines **I**–**III** with triphenylphosphine in the presence of prop-2-yn-1-yl alcohol (the molar ratio prop-2-yn-1-yl alcohol–trinitromethyl-1,3,5-triazine was 5:1) at 20–25°C required 2 equiv of triphenylphosphine to ensure complete conversion of the trinitromethyl compound. However, instead of expected [3+2]-dipolar cycloaddition products we isolated the corresponding hydroxyimino(nitro)methyl-1,3,5-triazines **IV**–**VI** (yield 70–80%), as well as minor amounts of 1,3,5-triazinecarbonitriles **X**–**XII** (yield 5–7%, Scheme 1). Analogous results were obtained when the reactions were carried out in the presence of other aliphatic alcohols (such as MeOH, EtOH, and *i*-PrOH. These findings may be rationalized assuming successive elimination of two NO_2 molecules from initially formed dinitro(nitroso)methyl-1,3,5-triazine. Intermediate 1,3,5-triazinyl(nitro)nitrosomethyl radical reacts with hydrogen donor (alcohol) present in the reaction mixture to give oximes **IV**–**VI** that are stable at 20–25°C (Scheme 2). Here, one equivalent of Ph_3P is consumed for initial abstraction of oxygen atom from the $C(NO_2)_3$ group, and the second equivalent reacts with nitrogen dioxide.

The reactions of trinitromethyl-1,3,5-triazines **I**–**III** with triphenylphosphine in the presence of prop-2-yn-

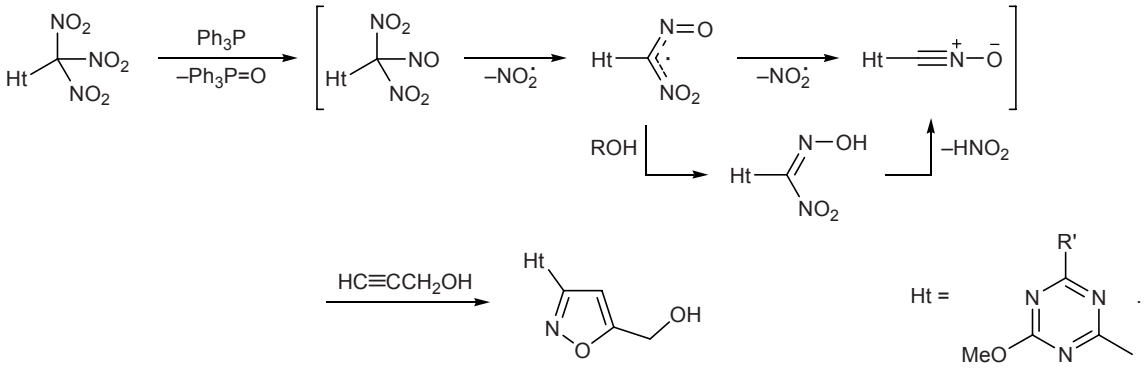
Scheme 1.



I–III **IV–VI** **X–XII**

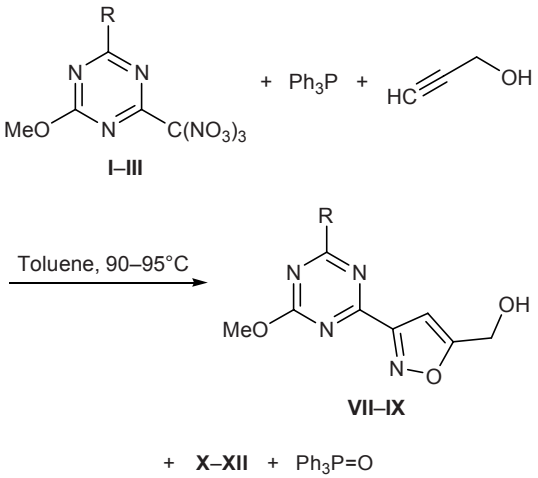
I, **IV**, **X**, R = NMe_2; **II**, **V**, **XI**, R = pyrrolidin-1-yl; **III**, **VI**, **XII**, R = piperidino; R′ = Me, Et, *i*-Pr, $HC{\equiv}CCH_2$.

Scheme 2.



1-yl alcohol (molar ratio prop-2-yn-1-yl alcohol–trinitromethyl-1,3,5-triazine 5:1) at 90–95°C required 3 equiv of triphenylphosphine. In this case we isolated [3+2]-dipolar cycloaddition products of intermediate 1,3,5-triazinecarbonitrile oxides, 5-hydroxymethyl-3-(1,3,5-triazin-2-yl)isoxazoles **VII**–**IX** in 60–75% yield and small amounts of 1,3,5-triazinecarbonitriles **X**–**XII** (yield 8–10%, Scheme 3).

Scheme 3.

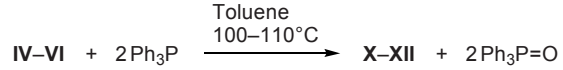


I, **VII**, **X**, R = NMe_2; **II**, **VIII**, **XI**, R = pyrrolidin-1-yl; **III**, **IX**, **XII**, R = piperidino.

Two ways of formation of 1,3,5-triazinecarbonitrile oxide are possible. The first of these involves successive elimination of two nitrogen dioxide molecules from dinitro(nitroso)methyl-1,3,5-triazine with formation of 1,3,5-triazinecarbonitrile oxide which reacts preferentially with the dipolarophile (prop-2-yn-1-yl alcohol) rather than with triphenylphosphine; as a result, 1,3,5-triazinecarbonitriles **X**–**XII** are obtained. The second pathway may be elimination of HNO_2 molecule via thermal decomposition of intermediate oxime **IV**–**VI** (Scheme 2). It is known [3] that thermolysis of hydroxyimino(nitro)methyl-1,3,5-triazines in toluene at 90–110°C leads to 3,4-bis(1,3,5-triazinyl)-furoxans through intermediate 1,3,5-triazinylcarbonitrile oxides. In this case, one equivalent of triphenylphosphine is consumed for initial abstraction of oxygen from the trinitromethyl group, while the remaining amount of Ph_3P (2 equiv) is involved in reaction with two molecules of nitrogen dioxide or one molecule of nitrogen dioxide and one molecule of nitrous acid (when oximes **IV**–**VI** are formed as intermediates).

According to the scheme proposed in [1], one step in the reaction of trinitromethyl-1,3,5-triazines with triphenylphosphine was reduction of 1,3,5-triazinecarbonitrile oxide to final 1,3,5-triazinecarbonitrile by the action of 1 equiv of triphenylphosphine. In the present work 1,3,5-triazinecarbonitrile oxides were generated *in situ* via thermolysis of hydroxyimino(nitro)methyl-1,3,5-triazines [3]. Thermal decomposition of oximes **IV**–**VI** in toluene at 100–110°C in the presence of 2 equiv of Ph_3P (1 equiv of Ph_3P is consumed for the reaction with nitrous acid) gave 1,3,5-triazinecarbonitriles **X**–**XII** in 82–90% yield (Scheme 4).

Scheme 4.



Thus, the formation of hydroxyimino(nitro)methyl-1,3,5-triazines suggests intermediacy of 1,3,5-triazinyl-(nitro)nitrosomethyl radical, while the formation of 3-(1,3,5-triazinyl)isoxazoles indicates intermediate generation of 1,3,5-triazinecarbonitrile oxides. We also confirmed that 1,3,5-triazinecarbonitrile oxides can be reduced to 1,3,5-triazinecarbonitrile with triphenylphosphine. The reaction of substituted trinitromethyl-1,3,5-triazines with triphenylphosphine involves initial

abstraction of oxygen atom from the trinitromethyl group and successive elimination of two nitrogen dioxide molecules through 1,3,5-triazinyl(nitro)nitrosomethyl radical with formation of 1,3,5-triazinecarbonitrile oxide.

EXPERIMENTAL

The progress of reactions was monitored by TLC on Silufol UV-254 plates. The IR spectra were measured in KBr on an Avatar 360 ESP spectrometer. The ^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 MHz), and the ^{13}C NMR spectra were obtained on a Bruker AC-200 instrument (50.32 MHz); the chemical shifts were determined relative to tetramethylsilane as internal reference.

Compounds **I–III** were synthesized according to the procedure described in [4].

(Hydroxyimino)(nitro)methyl-1,3,5-triazines IV–VI (*general procedure***).** Trinitromethyl-1,3,5-triazine **I–III**, 0.01 mol, was dissolved in 40 ml of toluene, 0.05 mol of methanol, ethanol, propan-2-ol, or prop-2-yn-1-ol was added under stirring at 20–25°C, and 5.76 g (0.022 mol) of triphenylphosphine was added in portions over a period of 1–1.5 h. The mixture was stirred at 20–25°C until the initial trinitromethyl-1,3,5-triazine disappeared (~0.5 h), the precipitate of triphenylphosphine oxide was filtered off, the solvent was distilled off from the filtrate under reduced pressure, and compounds **IV–VI** were isolated by column chromatography on silica gel using ethyl acetate as eluent. In addition, 1,3,5-triazinecarbonitriles **X–XII** were isolated (yield 5, 5, and 7%, respectively); their melting points, elemental analyses, and IR and ^{1}H NMR spectra were consistent with published data [1].

4-[(Hydroxyimino)(nitro)methyl]-6-methoxy-*N*,*N*-dimethyl-1,3,5-triazin-2-amine (IV). Yield 80%, mp 109–111°C (decomp.). IR spectrum, ν, cm^{-1}: 3145, 3049, 3004, 2933, 2879, 2811, 1608, 1587, 1552, 1511, 1417, 1382, 1268, 1224, 1149, 1074, 1051, 1002, 902, 864, 806, 727, 646. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 3.12 s and 3.20 s (3H each, NCH_3, Δν = 16 Hz), 3.96 s (3H, OCH_3), 12.46 br.s (1H, NOH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 36.44 and 36.63 (NCH_3), 55.00 (OCH_3), 151.26 (C=NOH), 163.00 (C^4), 166.51 (C^2), 171.52 (C^6). Found, %: C 34.82; H 4.28; N 34.59. $C_7H_{10}N_6O_4$. Calculated, %: C 34.71; H 4.16; N 34.70.

***N*-Hydroxy[4-methoxy-6-(pyrrolidin-1-yl)-1,3,5-triazin-2-yl]nitromethanimine (V).** Yield 73%, mp 119–121°C (decomp.). IR spectrum, ν, cm^{-1}: 3104, 2973, 2887, 2802, 2780, 1596, 1562, 1508, 1477, 1457, 1380, 1340, 1245, 1054, 1008, 970, 806, 727. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 2.15 m (4H, CH_2CH_2), 3.56 m and 4.00 m (2H each, CH_2N), 3.97 s (3H, OCH_3), 12.81 s (1H, NOH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 25.47 and 25.56 (CH_2CH_2), 47.17 and 47.37 (CH_2N), 54.99 (OCH_3), 151.31 (C=NOH), 162.93 (C^2), 164.39 (C^6), 171.40 (C^4). Found, %: C 40.37; H 4.62; N 31.28. $C_9H_{12}N_6O_4$. Calculated, %: C 40.30; H 4.51; N 31.33.

***N*-Hydroxy[4-methoxy-6-piperidino-1,3,5-triazin-2-yl]nitromethanimine (VI).** Yield 71%, mp 113–114°C (decomp.). IR spectrum, ν, cm^{-1}: 3131, 3043, 3010, 2937, 2861, 2806, 1589, 1560, 1508, 1473, 1450, 1382, 1295, 1234, 1099, 1052, 1016, 993, 889, 856, 831, 808, 786, 721. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 1.62 m (6H, $CH_2CH_2CH_2$), 3.82 m (4H, CH_2N), 3.96 s (3H, OCH_3), 12.64 s (1H, =NOH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 25.02, 26.25, 26.29 (CH_2); 45.12, 45.50 (CH_2N); 55.09 (OCH_3); 151.44 (C=NOH); 163.52 (C^2); 165.71 (C^6); 171.99 (C^4). Found, %: C 42.68; H 5.07; N 29.64. $C_{10}H_{14}N_6O_4$. Calculated, %: C 42.55; H 5.00; N 29.77.

3-(1,3,5-Triazin-2-yl)isoxazol-5-ylmethanols VII–IX (*general procedure***).** Prop-2-yn-1-ol, 0.29 ml (0.05 mol), was added to a solution of 0.01 mol of trinitromethyl-1,3,5-triazine **I–III** in 40 ml of toluene, the mixture was heated to 90–95°C, and 7.86 g (0.03 mol) of triphenylphosphine was added in portions under stirring over a period of 1–1.5 h. The mixture was stirred at 90–95°C until the initial trinitromethyl-1,3,5-triazine disappeared (~0.5 h), cooled to 20–25°C, and filtered from partially separated triphenylphosphine oxide, the solvent was distilled off from the filtrate under reduced pressure, and the residue was subjected to column chromatography on silica gel using dichloroethane–ethyl acetate as eluent to isolate 3,5-disubstituted isoxazoles **VII–IX**. In addition, 1,3,5-triazinecarbonitriles **X–XII** were isolated (yield 9, 8, and 10%, respectively); their melting points, elemental analyses, and IR and ^{1}H NMR spectra were consistent with published data [1].

3-(4-Dimethylamino-6-methoxy-1,3,5-triazin-2-yl)isoxazol-5-ylmethanol (VII). Yield 74%, mp 140–143°C. IR spectrum, ν, cm^{-1}: 3347, 3133, 3012, 2996, 2933, 2875, 1604, 1593, 1525, 1473, 1415, 1373, 1138, 1261, 1216, 1105, 1066, 1037, 981, 921, 900, 815, 802. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.19 s and 3.27 s (3H each, NCH_3, Δν = 16 Hz), 3.78 br.s (1H,

OH), 4.00 s (3H, OCH_3), 4.82 s (2H, CH_2), 6.81 s (1H, CH). Found, %: C 47.90; H 5.27; N 27.94. $C_{10}H_{13}N_5O_3$. Calculated, %: C 47.81; H 5.22; N 27.87.

3-[4-Methoxy-6-(pyrrolidin-1-yl)-1,3,5-triazin-2-yl]isoxazol-5-ylmethanol (VIII). Yield 62%, mp 181–183°C. IR spectrum, ν, cm^{-1}: 3347, 3155, 3025, 2973, 2925, 2877, 1587, 1565, 1521, 1473, 1434, 1369, 1336, 1236, 1184, 1164, 1110, 1056, 1039, 981, 912, 844, 819, 804. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.02 m (4H, CH_2CH_2), 2.72 br.s (1H, OH), 3.65 m and 3.76 m (2H each, CH_2N), 4.05 s (3H, OCH_3), 4.85 s (2H, CH_2), 6.89 s (1H, CH). Found, %: C 52.06; H 5.49; N 25.14. $C_{12}H_{15}N_5O_3$. Calculated, %: C 51.98; H 5.45; N 25.26.

3-(4-Methoxy-6-piperidino-1,3,5-triazin-2-yl)isoxazol-5-ylmethanol (IX). Yield 66%, mp 125–127°C. IR spectrum, ν, cm^{-1}: 3330, 3128, 3000, 2933, 2861, 1577, 1521, 1475, 1434, 1375, 1290, 1261, 1226, 1110, 1043, 995, 979, 912, 817, 794. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.68 m (6H, $CH_2CH_2CH_2$), 2.49 br.s (1H, OH), 3.87 m and 3.95 m (2H each, CH_2N), 4.07 s (3H, OCH_3), 4.83 s (2H, CH_2), 6.88 s (1H, CH). Found, %: C 53.54; H 5.95; N 24.17. $C_{13}H_{17}N_5O_3$. Calculated, %: C 53.60; H 5.88; N 24.04.

1,3,5-Triazine-2-carbonitriles X–XII. Triphenylphosphine, 5.24 g (0.02 mol), was added to a solution of 0.01 mol of compound **IV–VI** in 20 ml of toluene, and the mixture was stirred on heating at 100–110°C until the initial compound disappeared (~3–4 h). The mixture was cooled to 20–25°C and filtered from partially separated triphenylphosphine oxide, and the solvent was distilled off from the filtrate under reduced pressure. The residue was dissolved in dichloroethane, and the solution was passed through a 1–1.5-cm layer of silica gel. The solvent was distilled off under reduced pressure, the residue was treated with water, and the precipitate was filtered off. Yield of **X–XII** 90, 86, and 82%, respectively; their melting points, elemental analyses, and IR and ^{1}H NMR spectra were consistent with those reported in [1].

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