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SYNTHESIS OF ^{14}C-LABELED HEXAHYDRO-1,3,5-TRINITRO-1,3,5-TRIAZINE (RDX)

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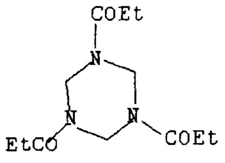
SUMMARY

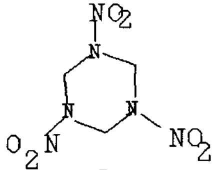
^{14}C-labeled hexahydro-1,3,5-trinitro-1,3,5-triazine (2, **RDX**) was prepared by nitrolysis of hexahydro-1,3,5-tripropionyl-1,3,5-triazine (1) for bioenvironmental studies. 1 was synthesized from paraformaldehyde and propionitrile by a modified method reported earlier.

KEYWORDS: ^{14}C-hexahydro-1,3,5-trinitro-1,3,5-triazine; ^{14}C-hexahydro-1,3,5-tripropionyl-1,3,5-triazine; nitrolysis.

INTRODUCTION



1



2

Several methods for the preparation of the high explosive **RDX** (2) on industrial as well as laboratory scale are described in the literature (1). Precursors such as hexamethylenetetramine, and tripotassium hexahydro-1,3,5-triazine 1,3,5-trisulfonate are used in manufacturing of RDX. These substances are not practical for small scale radiosynthesis and therefore a simple and straightforward method has been developed beginning with labeled

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paraformaldehyde and proceeding through a crystalline, characterized intermediate, hexahydro-1,3,5-tripropionyl-1,3,5-triazine (1) (2).

Synthesis of hexahydro-1,3,5-tripropionyl-1,3,5-triazine (1)

The preparation of 1 from trioxane, or paraformaldehyde as a formaldehyde source and propionitrile under acid catalysis, has been previously described in the literature (3).

1 was easily obtained from paraformaldehyde and propionitrile as reported by Wegler and Ballauf (3a) in 75% yield by a minor modification of the method. The reaction was carried out in closed system which prevented the escape of formaldehyde.

Diverse values are reported in the literature for the melting point of hexahydro-1,3,5-tripropionyl-1,3,5-triazine, 169° (3a,d), 173.2-174.1° (3c), and 152-154° (3e), therefore 1 was identified by elemental analysis and by ^1H, ^{13}C-NMR, and mass spectra.

Nitrolysis of hexahydro-1,3,5-tripropionyl-1,3,5-triazine

The synthesis of ^{14}C-labeled RDX reported by Castorina *et al.* (4) started from labeled formaldehyde *via* hexamethylenetetramine as intermediate, McCormick *et al.* (5) described the formation of labeled RDX from labeled paraformaldehyde, ammonium nitrate and boron trifluoride etherate. We have found that the nitrolysis reaction of hexahydro-1,3,5-tripropionyl-1,3,5-triazine (1) is an efficient alternative method for the preparation of small quantities of labeled RDX with high specific activity.

The nitrolysis of 1 was accomplished by direct nitrolysis (2) with a 6:4 (v/v) mixture of absolute nitric acid and trifluoroacetic anhydride. Using commercial fuming nitric acid no nitrolysis product was obtained; distillation from 2 parts of 98% sulfuric acid furnished suitably concentrated (absolute) nitric acid. It was not analyzed further.

The yield of ^{14}C-RDX produced on a small scale by this method was 52%, the ^1H and ^{13}C-NMR spectra of this product gave chemical shifts identical to those reported in the literature (6).

EXPERIMENTAL

The melting points are uncorrected. The NMR spectra were recorded on a GE-400 OMEGA FT NMR instrument at 400 (^1H) and 100 MHz (^{13}C), respectively. The samples were dissolved in chloroform-d_1 and dimethylsulfoxide-d_6 and tetramethylsilane was used as an internal reference. 70 eV EI-MS spectra were recorded. ^{14}C-Paraformaldehyde was purchased from American Radiolabeled Chemicals.

Hexahydro-1,3,5-tripropionyl-1,3,5-triazine (1)

Three hundred mg (9.5 mM) of paraformaldehyde was added with stirring to a mixture of 1.35 mL of propionitrile, 0.15 mL of acetic anhydride, and 0.024 mL of 98% sulfuric acid in a 10 mL glass screw cap vial. After sealing the reaction mixture with the cap the vial was heated in a boiling water bath for 3 hours and stirred continuously with a magnetic stir bar. After the reaction vial was removed from the water bath, the product immediately solidified as a yellow crystalline mass. It was triturated with ethyl ether, filtered, and washed with ethyl ether. After air drying 610 mg (75%) of crude product was obtained. This product was satisfactory for the next synthetic step but a small amount of **1** was recrystallized from 95% ethanol - ether mixture (3:2) to obtain an analytical sample. $C_{12}H_{21}N_3O_3$, 255.32 Required/found C 56.45/56.04; H 8.29/8.20; N 16.46/16.02. MS: m/z: 255, 213, 198, 182, 157, 142, 114, 101, 85, 71, 57, 43, 29 ; ^{1}H-NMR (CDCl$_3$, δ ppm) 5.29 s, 2.56 q, 1.13 t, $^3J \sim 7$ Hz; ^{13}C (CDCl$_3$, δ ppm) 173.0, 55.89, 26.16, 8.88; mp 150-152°.

^{14}C-Hexahydro-1,3,5-tripropionyl-1,3,5-triazine.

^{14}C-Hexahydro-1,3,5-tripropionyl-1,3,5-triazine was prepared by the above procedure. A mixture of 19.8 mg (1 mCi) of ^{14}C-paraformaldehyde (specific activity 50.5 μCi/mg) and 280 mg of unlabeled paraformaldehyde was used (overall 9.99 mmol) and 0.2 mL of acetic anhydride was employed to compensate for the higher water content of labeled paraformaldehyde. Yield: 594 mg (70%). ^{1}H-NMR (CDCl$_3$, δ ppm) 5.29s, 2.56q, 1.13t; ^{13}C-NMR (CDCl$_3$, δ ppm) 173.08, 55.90, 26.18, 8.88.

Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) (2)

Four mL of trifluoroacetic anhydride was added to 6 mL of absolute nitric acid in a large test tube in an ice bath and stirred. 580 mg of **1** was added and the tube was loosely closed with glass wool, placed in a water bath at 55°, and the reaction mixture was stirred at 55-65° for 45 minutes. Vigorous evolution of nitrous gases was observed. After 45 min, when the evolution of gases had subsided, the reaction mixture was poured onto about 100 g of crushed ice. The white precipitate was filtered off, washed thoroughly with water and then with 95% ethanol. The product was air dried to yield 320 mg (63%) RDX. Mp 200-203 ° lit. mp 200-203° (7); $C_3H_6N_6O_6$, 222.13, required/found: C 16.22/16.25; H 2.72/2.82; N 37.84/37.85%; ^{1}H-NMR (dimethyl sulfoxide-d_6, δ ppm) 6.10s; ^{13}C-NMR (dimethyl sulfoxide-d_6, δ ppm) 61.10.

^{14}C-Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX)

590 mg (2.31 mmol) ^{14}C-**1** yielded 265 mg (52%) of ^{14}C-**2** by the above procedure. ^{1}H-NMR (dimethyl sulfoxide-d_6, δ ppm) 6.10s; ^{13}C-NMR (dimethyl sulfoxide-d_6, δ ppm) 61.11. The specific activity of the labeled RDX: 1.35 μCi/mg. Total activity: 0.358 mCi.

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