Organic Process Research & Development **2007**, *11*, 56–59

On the Synthesis of 1,1-Diamino-2,2-dinitroethene (FOX-7) by Nitration of 4,6-Dihydroxy-2-methylpyrimidine

Nikolaj V. Latypov, Martin Johansson, and Erik Holmgren
Swedish Defence Research Agency (FOI), SE-147 25 Tumba, Sweden

Ekaterina V. Sizova and Vladimir V. Sizov
St. Petersburgs State Institute of Technology, Moskovskij pr. 26. 193013, St. Petersburg, Russia

Anthony J. Bellamy*
Cranfield University, Defence Academy of the United Kingdom, Shrivenham, Swindon, SN6 8LA, UK

Abstract:

The synthesis of 1,1-diamino-2,2-dinitroethene (FOX-7) by nitration of 4,6-dihydroxy-2-methylpyrimidine and hydrolysis of the resulting intermediate 2-dinitromethylene-5,5-dinitropyrimidine-4,6-dione has been studied. By varying the reaction parameters the optimal conditions for the synthesis of FOX-7 have been identified and gave a >90% yield of the pure product. The optimised process allowed the spent acid to be recycled without loss of yield, with almost stoichiometric consumption of nitric acid. The purity of the FOX-7 has been determined using a newly developed HPLC method

Introduction

1,1-Diamino-2,2-dinitroethene (FOX-7, **4**) has become a widely known, new explosive with great potential for a variety of applications.[1,2] The first synthetic method which made the product available for study as an energetic material was a tedious, multistep procedure involving several unstable intermediates.[3] Later, an alternative route based on the nitration of the commercially available 4,6-dihydroxy-2-methylpyrimidine (**1**) was published.[4] This became the method which is now commonly used,[5,6] though information about the reaction course is limited. The only isolable intermediates are 5-nitro-4,6-dihydroxy-2-methylpyrimidine (**2**) and 2-dinitromethylene-5,5-dinitropyrimidine-4,6-dione (**3**), irrespective of the amount of nitric acid used (Scheme 1).[7] The final product, FOX-7 (**4**), is obtained by acid-catalysed hydrolysis of the tetranitro-intermediate **3**.

In Astrat'ev et al.'s original recipe,[4] and elsewhere,[5] a very large excess of nitric acid was used (10−19 equiv) compared to the stoichiometric 4 equiv, the latter being sufficient for the completion of *gem*-dinitration at both positions.[7] We here report improvements to the process for the manufacture of 1,1-diamino-2,2-dinitroethene (**4**) by nitration of 4,6-dihydroxy-2-methylpyrimidine, which demonstrates that significantly reduced amounts of nitric acid may be used and that recycling of the mixed acid is possible, without loss of both yield and product quality. Furthermore, the refined process avoids adding the whole mixed acid reaction mixture to water for the final hydrolysis of the tetranitropyrimidine **3**.

Results and Discussion

Nitration of 1 and Formation of 2. Preliminary experiments showed that the amount of sulfuric acid recommended by Astrat'ev et al.[4] is clearly insufficient for the nitration step to be performed safely. In most cases crystallisation of **3** leads to caking of the reaction mixtures and makes further workup impossible. Moreover, the poor heat transfer from such mixtures, combined with the rather low thermal stability of **3**, may create a potential for thermal explosions when performing the reaction on a larger scale. It was found in the present work that the weight ratio of sulfuric acid to **1** should be increased from 5.5−8.5 as recommended by previous workers[4−6] to at least 10 or preferably to 12−14, depending on the type of mixing device being used, in order to ensure a controllable reaction on any scale.

In the first series of experiments the optimal amount of nitric acid which furnishes formation of pure **3** was shown to be only slightly more then stoichiometric (Table 1). Moreover, it was also found that nitration of **1** proceeds in the manner described[7−9] viz. through the relatively rapid

---

* To whom correspondence should be addressed. E-mail: A.J.Bellamy@cranfield.ac.uk.

(1) Eldsäter, C.; Edvinsson, H.; Johansson, M.; Pettersson, Å.; Sandberg, C. *33rd Int. Annu. Conf. ICT*, Karlsruhe **2002**, 63−1 to 63−14.

(2) Kretschmer, A.; Gerber, P.; Happ, A. *35th Int. Annu. Conf. ICT*, Karlsruhe **2004**, 172-1 to 172-11.

(3) Latypov, N. V.; Bergman, J.; Langlet, A.; Wellmar, U.; Bemm, U. *Tetrahedron* **1998**, *54*, 11525.

(4) Astrat'ev, A. A.; Dashko, D. V.; Mershin, A. Y.; Stepanov, A. I.; Urazgil'deev, N. A. *Russ. J. Org. Chem.* **2001**, *37*, 729.

(5) Chung, K. -H.; Goh, E. M.; Cho, J. R. *36th Int. Annu. Conf. ICT*, Karlsruhe **2005**, 52−1 to 52−13.

(6) Chylek, Z.; Cudzilo, S.; Bladek, J.; Pietrzyk, S. *New trends in research of energetic materials - Proceedings of the VIII Seminar*; Pardubice, Czech Republic, 2005, p 207.

(7) Bellamy, A. J.; Latypov, N. V.; Goede, P. *New trends in research of energetic materials − Proceedings of the VIII Seminar,* Pardubice, Czech Republic, 2004, p 75.

10.1021/op068010t CCC: $37.00

Scheme 1. **Nitration of 4,6-dihydroxy-2-methylpyrimidine (1)**

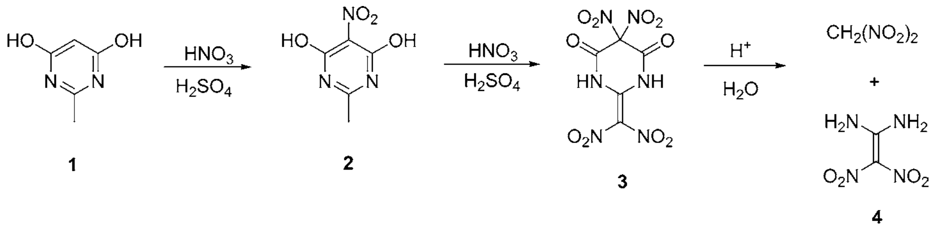

Table 1. **Product yields as a function of the amount of nitric acid used; weight ratio H_2SO_4 /1 = 12; reaction time 18 h**

	HNO$_3$/**1** (mole ratio)			
yield (%)	1.0	2.0	3.4	4.2−4.3
2[a]	72.5	42.4	8.7	not detected
4[b]	2.5−3.0	32.0	66.1	91.9
1[c]	+[d]	+[d]	+[d]	not detected
CH$_2$(NO$_2$)$_2$[e]	not estimated	12.0	40.0	56.2

[a] Estimated as the sum of the amount of solid **2**, which crystallized after filtration of **3** and dilution of spent acid by water (1:4), plus amount of **2** detected by UV absorption of the mother liquor formed. [b] Separated after aqueous hydrolysis of **3**. [c] Detected by HPLC analysis of the diluted spent acid. [d] Detected but not quantified. [e] Precipitated as the potassium salt after hydrolysis of **3** and extraction with ether.

Table 2. **Product yields as a function of the reaction time; weight ratio H_2SO_4/1 = 12; mole ratio HNO_3/1 = 4.2−4.3**

	reaction time (h)			
yield (%)	0.7	2.0	3.0	18
2[a]	31.5	10.4	<1	−
4[b]	60.6	78.9	89.9	92.0
1[c]	−	−	−	−

[a] Estimated as the sum of the amount of solid **2**, which crystallized after filtration of **3** and dilution of spent acid by water (1:4), plus amount of **2** detected by UV absorption of the mother liquor formed. [b] Separated after aqueous hydrolysis of **3**. [c] Detected by HPLC analysis of the diluted spent acid.

formation of the isolable mononitro compound **2**. The presence of the latter could be seen until the mole ratio of HNO$_3$/**1** reaches the optimal value for the formation of **3**. The presence of **3**, and hence **4**, could indeed be seen in the reaction mixture even when the amount of nitric acid used at the nitration stage favoured mononitration**.** This observation indicates that, unlike other 4,6-dihydroxy-2-methylpyrimidines,[8,9] mononitration of **1** and subsequent nitration of **2** proceed at comparable rates. However *gem*-dinitration is a noticeably slower step in the whole reaction sequence. This is also confirmed by the results presented in Table 2.

These results clearly show that an appreciable excess of nitric acid in the nitrating mixture ensures rapid transformation of **1** into a mixture of **2** and **3**, with the remaining **2** being slowly nitrated to give more of **3**. The results obtained thus far allowed the optimal parameters, such as amount of nitric acid (5−8% excess over the stoichiometric amount) and reaction time (4 h) for the process of nitration of **1** to **3** to be determined.

Table 3. **Yield and purity of FOX-7 when using recycled spent acid as a function of number of experiments and concentration of sulfuric acid; weight ratio H_2SO_4/1 = 12−14, mole ratio HNO_3 /1 = 4.2−4.3**

no. of expt	H$_2$SO$_4$ (%)	yield (g)	yield (%)	purity (%) HPLC	dec. (°C) DSC
1	∼100	5.10	86.9	96−98	220−225
2	96.0−96.5	5.50	93.7	98−99	238−240
3	95.0−96.0	5.43	92.5	>99	236−238
4	94.0	5.40	92.0	>99	238−240
5	93.0	5.35	91.1	>99	238−240
6	93.0	5.30	90.3	>99	238−240
7	93.0	5.28	90.0	>99	238−240
8	93.0	5.30	90.3	>99	238−240

In order to reduce the rather large amount of sulfuric acid used (12−14 parts per part of **1**) the possibility of recycling the spent acid has been investigated by studying both the nitration of **1** in the spent acid and the effect of varying the concentration of sulfuric acid in the nitration medium. It was found that the optimal concentration of sulfuric acid for nitration lies between 90 and 98%. At higher concentrations of sulfuric acid, the solubility of **3** in the spent acid is increased. However this was accompanied by side reactions. In more dilute sulfuric acid (<88%) hydrolysis of **3** becomes noticeable. In both cases the yield of **4** decreases substantially. Based on these figures, the standard 95−97% sulfuric acid was chosen for the nitration, which in the reaction conditions used (12−14 parts of sulfuric acid) is transformed to an acid concentration of ca. 92%. In the recycling regime, the product **3** was filtered off, washed with fresh sulfuric acid, and subjected directly to hydrolysis. The spent acid contains very small amounts (<0.5%) of both **3** and nitric acid and is sufficiently stable for safe storage during several days. A part of this acid (70−80%) was refortified with oleum (30% SO$_3$) and used again for further nitration. This gave essentially the same yield and quality of **4**, up to 8 cycles (see Table 3), and resulted in the consumption of ∼3 parts of 30% oleum instead of the 10−14 parts of sulfuric acid normally wasted through dilution of the nitration mixture.

Hydrolysis of 3 to 4. In the original paper by Astrat'ev et al.[4] dilution of the whole reaction mixture in an excess of water was suggested in order to hydrolyse **3** to give the desired product. This approach, which was subsequently used by other workers,[5,6] makes the recycling of the spent acid impossible. Moreover, in some of our experiments, a distinct tendency for runaway reactions in such mixtures was noticed: this was clearly seen by copious frothing in the reaction mixtures and self-heating of the latter. All these phenomena are most probably caused by NOx/HNO$_3$ cata-

---

(8) Langlet, A.; Latypov, N. V.; Wellmar, U.; Goede, P. *Propellants, Explosives, Pyrotechnics* **2004**, *29*, 344.

(9) Latypov, N. V.; Bergman, J.; Langlet, A.; Wellmar, U.; Bemm, U.; Goede, P. *J. Org. Chem.* **2002**, *67*, 7833.

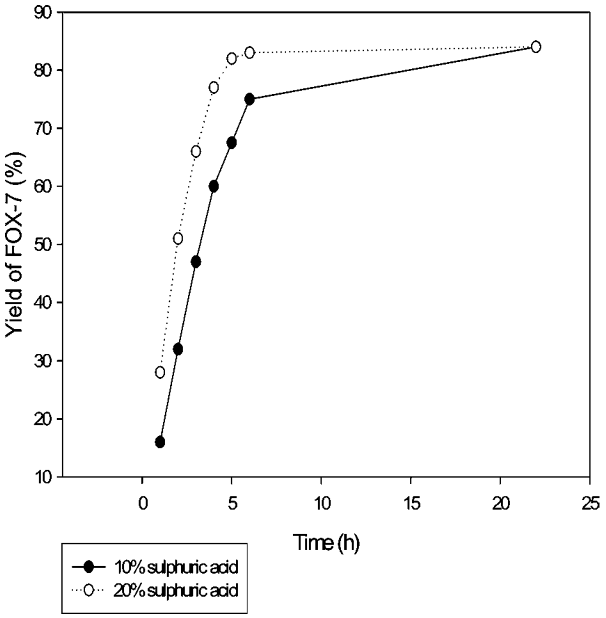

Figure 1. **Hydrolysis of 3 to form FOX-7 (4).**

lyzed thermal decomposition of dinitromethane. To solve both problems, separation of **3**, which is insoluble in the spent acid, by filtration, followed by hydrolysis of the product in water was studied. Preliminary experiments, involving the isolation of **3** free from sulfuric acid, showed that the yield of **3** under optimal reaction conditions (vide supra) was $>$96%. Dry **3** was shown to have low hydrolytic stability, being easily hydrolyzed in a humid atmosphere. Moreover, it was found to be very sensitive to mechanical stimuli (compared to PETN). By contrast, **3** containing more than 30% of sulfuric acid is quite stable and can be kept in the open air for up to 2 days; the sensitivity of such a product is also substantially lower (intermediate between TNT and tetryl). That is why all further work on the hydrolysis of **3** was performed in such a manner that **3**, separated from the nitrating mixture and containing 40−45% of sulfuric acid from the sulfuric acid washing process, was transferred at once to the required amount of water. It was shown that the rate of hydrolysis depends strongly on the amount of water used or, more probably, on the concentration of sulfuric acid formed (Figure 1). Under these conditions the hydrolysis proceeded in a controllable manner: in no experiments were frothing or self-heating observed. Preparative reactions, run without isolation and analysis of intermediates and using 20% sulfuric acid as the hydrolysis medium (reaction time 8-10h), gave a 90−92% yield of **4**. This is about a 5−7% higher yield than the maximum values shown in Figure 1. This is probably due to losses when the isolation/filtration of **3** is involved. The resulting product was more than 99% pure by HPLC.

The data obtained for both the nitration and the hydrolysis steps resulted in the development, to the kilogram scale, of a more economic process for making FOX-7 (Figure 2), giving the final product in both high yield and high purity and with the enhanced possibility for recycling of the spent acid.

Conclusions

A two-step process for making **4** by nitration of **1** in refortified spent acid, followed by the hydrolysis of **3** separated from the spent acid, has been developed.

This method has several advantages over the original procedure *viz.* a high purity product facilitating its use without further purification, controllable reaction conditions at both stages, minimal amounts of the reagents used, and the possibility for the recycling of the spent acid, obviating the need to dispose of/treat highly corrosive waste.

Experimental Section

General Remarks. *Caution*: The polynitro compounds described in this section are powerful explosives and should be handled with appropriate precautions. Standard safety procedures for energetic materials should be employed in all experimental operations involving these substances. All of the reaction products were identified as described previously.[3,4,9]

General Procedure for the Nitration of 4,6-Dihydroxy-2-methylpyrimidine (1): Isolation of 5-Nitro-4,6-dihydroxy-2-methylpyrimidine (2) and 2-Dinitromethylene-5,5-dinitropyrimidine-4,6-dione (3). Finely divided **1** (12.6 g, 0.1mol) was added in small portions ($\sim$0.5 g) to vigorously stirred concentrated ($\sim$95%) sulfuric acid (85 mL), keeping the temperature of the reaction mixture below 30 °C. After the solid had dissolved, the necessary amount of concentrated (99%) nitric acid was added to the solution, keeping the temperature below 20 °C. After maintaining the vigorously stirred solution at 15−20 °C for the necessary period of time, the precipitate of **3** was filtered off, washed with concentrated sulfuric acid (15 mL), and subjected to hydrolysis (vide

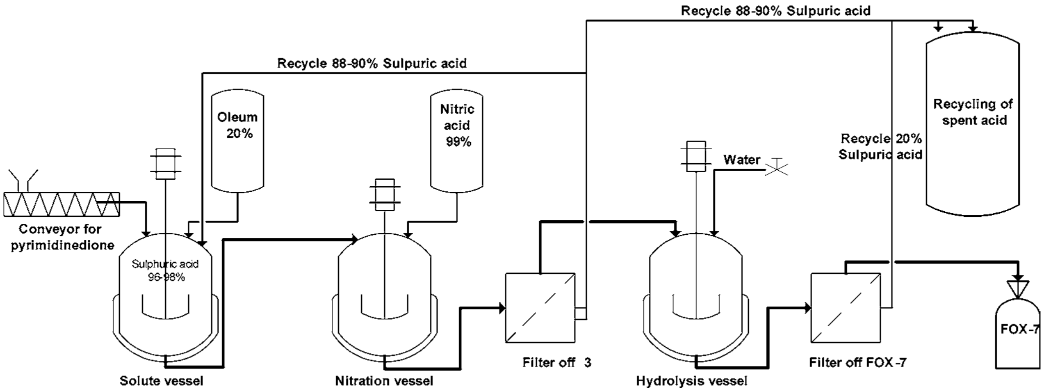

Figure 2. **Plant for the synthesis of FOX-7.**

infra). The filtrate was diluted with ice−water (1:4), and the precipitate of **2** was filtered off and dried at 100 °C; the amount of **2**, remaining dissolved in the diluted acid, was estimated by a UV technique.[4] The results are presented in Table 1.

General Procedure for the Hydrolysis of 3 to 4 and Separation of Dinitromethane. Acid-contaminated **3** (40-42 g) produced by nitration of 10 g of **1** in the manner described above, containing ∼40−45% of sulfuric acid, was added in small portions to water (100−200 mL) with vigorous stirring, keeping the temperature below 20 °C. After certain time intervals the precipitate of **4** was filtered off, washed with water until neutral, and dried. After the hydrolysis was complete, the filtrate was extracted with ether (3 × 50 mL) and the extract was neutralised with 5% alcoholic KOH (ca 50 mL) to pH 6−7. The precipitate of potassium dinitromethane was washed with a minimal amount of cold water and dried. The results are presented in Figure 1 and Table 1.

Nitration of 2-Methyl-4,6-dihydroxypyrimidine in the Pilot Plant Scale. 2-Methyl-4,6-dihydroxypyrimidine (**1**, 2.10 kg) was added in small portions (∼100 g) to vigorously stirred concentrated sulfuric acid (95−97%; 10 L) placed in a 16 L glass reactor, at such a rate that the temperature in the reaction mixture did not exceed 30 °C. After the addition had been completed the mixture was kept for an additional 2 h until the solid had dissolved. The solution of **1** in sulfuric acid (11.5 L) was then transferred to a stainless steel 20 L reactor. The temperature in the reactor was lowered to 15 °C, and the stirring (six blade turbine stirrer) was set at 800 rpm.

Nitric acid (99.5%, 2.97 L) was added slowly to the sulfuric acid solution, keeping the temperature below 20 °C. The reaction mixture was kept at 20−25 °C for an additional 4 h and then was poured onto a stainless steel filter (10 μm). Most of the acid was removed by filtration, and the solid product was washed with concd sulfuric acid (ca. 2 L). The solid **3**, containing 30−40% by weight of sulfuric acid, was transferred in small amounts to a 90 L stainless steel reactor containing vigorously stirred water (20 L) at $<$20 °C. The mixture was left overnight, and the product **4**, which had separated after this period, was then filtered off, washed with pure water (2 × 2 L), and dried. Pure **4** (2.22−2.25 kg, 90−91%) was usually obtained.

Isolation of 3 Free from Sulfuric Acid. Acid-contaminated **3** produced under the optimal conditions described above (mole ratio HNO_3/**1** = 4.3, reaction time 4 h) was washed with trifluoroacetic acid (TFA) until all of the sulfuric acid had been removed (checked by the absence of precipitated $BaSO_4$ on addition of barium nitrate solution to the diluted washing TFA) and then dried at 0 °C under a vacuum to give purified **3** (∼30 g, 95%). Elemental analysis showed this to be a hemi-hydrate. Calculated for $C_5N_6O_{10}H_2 \cdot 0.5\ H_2O$: C, 19.05%; N, 26.67%; H, 0.95%. Found: C, 19.15%; N, 26.38%; H, 1.05%. The product decomposed vigorously without melting at ∼90 °C.

General Procedure for the Nitration of 1 with Recycling of the Spent Acid. Compound **1** (5.0 g) was nitrated in concentrated sulfuric acid (40 mL). The resulting **3** was washed with concd sulfuric acid (5 mL) and subjected to hydrolysis as described above. The filtrate plus the washing acid (30 mL) was fortified with 30% oleum (ca. 10 mL) and used for the next nitration experiment. The results for a series of eight experiments are presented in Table 3.

Instrumentation. A Waters 2695 Quaternary HPLC System (Waters, Milford, MA) was used to deliver the solvent. HPLC separation was carried out on a Hypercarb porous graphitic carbon (PGC) 100 mm × 4.6 mm column (3 μm particles) (Thermo Quest, Cheshire, UK) using a gradient mobile phase. Eluent A 100% water, eluent B 93.3% acetonitrile, 4.7% water, and 2% aq. NH_3 (v/v). The analysis starts with A/B 95/5 for 2 min with a flow rate of 1 mL min^{-1}; during the next 10 min the mixture is changed to A/B 0/100 and then held there for 3 min. The temperature was maintained at 55 °C. UV detection was by a Waters UV detector model 996 photodiode array detector operating at 250 nm. The mass spectrometer used was a Bruker Esquire 3000+ ion trap mass spectrometer (Bruker Daltonics, Bremen, Germany) equipped with an electrospray ionization interface. Interface conditions were set to the following values: Nebulizer Gas 60 psi, dry temp 365 °C, dry gas 10 L min^{-1}, HV 4000 V, Trap Drive 74.4, Octopole RF Amplitude 114.6 Vpp.

Received for review July 6, 2006.

OP068010T