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Synthesis and Scale-Up of 2,4,6,8,10,12-Hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane from 2,6,8,12-Tetraacetyl-4,10-dibenzyl-2,4,6,8,10,12-hexaazaisowurtzitane (HNIW, CL-20)

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Abstract:

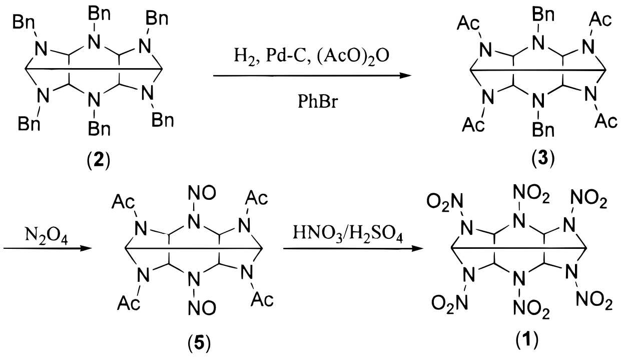
A two-stage conversion of 2,6,8,12-tetraacetyl-4,10-dibenzyl-2,4,6,8,10,12-hexaazaisowurtzitane to 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane, involving nitrosation followed by nitration, is described. It is shown that the purity of the final product obtained by this method is superior to that obtained by the reported one-pot method. Nitrosation of 2,6,8,-12-tetraacetyl-4,10-dibenzyl-2,4,6,8,10,12-hexaazaisowurtzitane in acetic acid is considered to be safer than nitrosation in pure dinitrogen tetroxide.

Introduction

One of the most interesting energetic molecules developed in recent years is the polycyclic nitramine, 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (**1**) (2,4,6,8,-10,12-hexanitro-2,4,6,8,10,12-hexaazatetracyclo$[5,5,0,0^{5,9},0^{3,11}]$-dodecane, HNIW or CL-20). Many reports have been published on its physical characteristics; these are reviewed in a recent article by Nielsen et al.[1] All known methods of producing 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (**1**) are based on the same starting material, 2,4,6,8,10,12-hexabenzyl-2,4,6,8,10,12-hexaazaisowurtzitane (**2**), which is first reductively acylated to form 2,6,8,-12-tetraacetyl-4,10-dibenzyl-2,4,6,8,10,12-hexaazaisowurtzitane (**3**).[1] The remaining benzyl groups can then be removed either by reductive formylation, with the formation of 2,6,8,-12-tetraacetyl-4,10-diformyl-2,4,6,8,10,12-hexaazaisowurtzitane (**4**),[2] or by nitrosation, leading to 2,6,8,12-tetraacetyl-4,10-dinitroso-2,4,6,8,10,12-hexaazaisowurtzitane (**5**).[1,3] Both **4** and **5** are easily converted to 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (**1**) by nitration with different nitrating systems.[1−3] Our interest in the study of the explosive and thermal characteristics of 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (**1**) prompted us to develop an acceptable synthetic procedure for this material. Since the available literature did not, at the time, contain detailed information on the synthesis of **1**, or the intermediate **5**, we initially concentrated our efforts on the method originally proposed by Nielsen et al.[1,3] This method was investigated both as a one-pot and a two-step procedure.

Results and Discussion

Our first preparations of 2,4,6,8,10,12-hexanitro-2,4,6,8,-10,12-hexaazaisowurtzitane (**1**) used a one-pot procedure, similar to that reported.[3] 2,6,8,12-Tetraacetyl-4,10-dibenzyl-2,4,6,8,10,12-hexaazaisowurtzitane (**3**) was reacted with dinitrogen tetroxide at room temperature for 20 h to give 2,6,8,12-tetraacetyl-4,10-dinitroso-2,4,6,8,10,12-hexaazaisowurtzitane (**5,** not isolated). Nitric acid and sulphuric acid were then added to the solution, which was heated at 80 °C for 2 h. The resultant reaction mixture was quenched by pouring it into ice/water. The product produced by this one-pot procedure was found to contain only 95.1% of **1** by HPLC analysis. This degree of purity was not good enough for our purposes, and we therefore decided to perform the reaction as two separate steps, with isolation of the intermediate dinitroso derivative **5**.



It was anticipated that this would make it easier to improve the purity of the final product. The use of pure dinitrogen tetroxide as the reaction medium, proposed in the original method[1,3] and used in the one-pot method, was avoided, since such reaction mixtures, consisting of fuel and an excess of oxidizer, are known to be very powerful and sensitive explosives.[4] Instead, a small excess of dinitrogen tetroxide

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(1) Nielsen, A. T.; Chafin, A. P.; Christian, S. L.; Moore, D. W.; Nadler, M. P.; Nissan, R. A.; Vanderah, D. J.; Gilardi, R. D.; George, C. F.; Flippen-Anderson, J. L. *Tetrahedron* **1998**, *54*, 11793.

(2) Braithwaite, P. C.; Hatch, R. L.; Lee, K.; Wardle, R. B.; Mezger, M.; Nicolich, S. In *Annual ICT Conference on Energetic Materials*; Karlsruhe, Germany, 1998; pp 4−1.

(3) Bescond, P.; Graindorge, H.; Mace, H. EP913374A1, May, 1999, Example 2.

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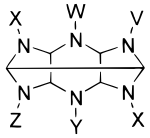
relative to the amount of **3**, dissolved in acetic acid, was used. This system seems to be more attractive since an ecologically friendly solvent is used and the reaction mixture is much safer to handle. Preliminary experiments showed that in this case the reaction, which was monitored by thin-layer chromatography, proceeds rather slowly, the rate depending on the concentration of dinitrogen tetroxide present. Full conversion of **3** to **5** was usually achieved after 2−3 days with 100−150% excess of dinitrogen tetroxide at room temperature. It was also shown by thin-layer chromatographic analysis that after the first stage of the reaction (16−18 h), the product consisted of a 1:1 mixture of two components, **5** ($R_f = 0.5$) and presumably 2,6,8,12-tetraacetyl-10-benzyl-4-nitroso-2,4,6,8,10,12-hexaazaisowurtzitane (**6**) ($R_f = 0.38$). The latter was slowly converted to **5**. **6** was not isolated and characterized, but its structure could be deduced from the proton NMR spectrum of the product mixture, which showed the presence of aromatic protons, thus indicating that a benzyl-substituent was present in the isowurtzitane structure. The presence of **6** in **5** was shown to be quite unacceptable, as the subsequent nitration of such mixtures inevitably led to **1** contaminated by nitrated isowurtzitanes containing nitrobenzyl substituents. Purification of such products was deemed to be impracticable on a large scale. To avoid this problem we preferred to use longer reaction times (3−4 days) and a larger excess of dinitrogen tetroxide (5−6 mol of dinitrogen tetroxide per mole of **3**). Under these conditions an additional by-product (10−20%, $R_f = 0.61$) was detected by thin-layer chromatography. This by-product noticeably lowered the melting point of the product (280 °C relative to 290−295 °C reported by Nielsen et al.[1]). Fortunately, the presence of this impurity, presumably 6,8,12-triacetyl-2,4,10-trinitroso-2,4,6,8,10,12-hexaazaisowurtzitane (**7**), did not affect the quality of the final product **1** obtained by this method. It was found that subsequent nitration of **5** containing up to 10% of this by-product always led to pure **1**. Nitration of **5** was successfully accomplished using ordinary "mixed acids". This system was chosen for economic reasons and the potential for scale-up. It was found that the conversion of **5** to **1** slowly takes place even in pure (99%) nitric acid at 60−75 °C, the main by-products, according to thin-layer chromatography, being 2,8-diacetyl-4,6,10,12-tetranitro-2,4,6,8,10,12-hexaazaisowurtzitane (**8**) and 2-acetyl-4,6,8,10,12-pentanitro-2,4,6,8,10,12-hexaazaisowurtzitane (**9**).



1 V = W = X = Y = Z = NO_2
2 V = W = X = Y = Z = CH_2Ph
3 V = X = Z = $COCH_3$, Y = W = CH_2Ph
4 V = X = Z = $COCH_3$, Y = W = CHO
5 V = X = Z = $COCH_3$, Y = W = NO
6 V = X = Z = $COCH_3$, Y = NO, W = CH_2Ph
7 V = X = $COCH_3$, W = Y = Z = NO
8 W = Y = V = Z = NO_2, X = $COCH_3$
9 V = W = X = Y = NO_2, Z = $COCH_3$

Both **8** and **9** have been separated by chromatography and characterized by NMR, FTIR, DSC, and elemental analysis. The reaction was considerably accelerated by the addition of small amounts (10−15%) of sulphuric acid to the nitration mixture, which gave complete conversion of **5** to **1** in 2 h at 75−80 °C. The interesting feature of this process is that high nitration rates do not guarantee pure **1** and the absence of **8** and **9** in the final product, because of the approximately equal solubility of the three products in the nitration mixture. This leads, at low ratios of "mixed acid" to **5**, to coprecipitation of **8** and **9**, together with **1**, directly from the nitration mixture during the course of the reaction. The composition of the product remains unchanged, independent of reaction time. To avoid this phenomenon, a rather large excess of nitration mixture should be used. Under these conditions (the ratio of "mixed acid" to **5** was >15, reaction temperature 70−75 °C) practically pure **1** is formed after 2 h, according to thin-layer chromatography. Pure **1** precipitates from the reaction mixture on cooling (yield 70%), and an additional 20−22% are usually obtained by diluting the mother liquor with water. Alternatively, the whole reaction mixture may be quenched in ice/water. HPLC analysis showed that the purity of the 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane **1** obtained was 99.0%.

Conclusions

A two-step process for making **1** from **3**, involving nitrosation of **3** with dinitrogen tetroxide in acetic acid, and nitration of **5** by "mixed acid", has been developed. This method is superior to the one-pot process in terms of the purity of the final product. The main impurities which can occur in **1** under non-ideal conditions, **8** and **9**, have been isolated and characterized. Both steps in the two-step process have been scaled up to 1 kg scale.

Experimental Section

General Remarks. *Caution*: Polynitramines are powerful explosives and should be handled with appropriate precautions. Employ all standard energetic materials safety procedures in experimental operations involving such substances.

NMR spectra were recorded on a Varian XL-200 Fourier transform NMR spectrometer. The onset of melting was determined on a Mettler DSC 30. IR spectra were recorded on a Mattson 1000 Fourier transform IR spectrometer. HPLC analyses were performed on a C-8 column using MeOH/THF/H_2O (49/6/45) as eluent.[5] Elemental analyses were performed by Dornis und Kolbe, Mühlheim, Germany. Commercially available solvents and reagents were used without further purification. 2,6,8,12-Tetraacetyl-4,10-dibenzyl-2,4,6,8,10,12-hexaazaisowurtzitane (**3**) was prepared according to a published procedure.[1]

One-Pot Conversion of 2,6,8,12-Tetraacetyl-4,10-dibenzyl-2,4,6,8,10,12-hexaazaisowurtzitane (3) to 2,4,6,8,-10,12-Hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (1).

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(4) Urbanski, T. In *Chemistry and Technology of Explosives*; Pergamon Press: Elmsford, NY, 1983; Vol. 3, p 288.

(5) Persson, B.; Östmark, H.; Bergman, H. *Propellants, Explos. Pyrotech.* **1997**, *22*, 238−239.

2,6,8,12-Tetraacetyl-4,10-dibenzyl-2,4,6,8,10,12-hexaazaisowurtzitane (**3**, 57 g, 0.11mol) was added over a 10 min period to dinitrogen tetroxide (240 mL, 3.78 mol) and water (9.6 mL) at 0 °C. After maintaining the magnetically stirred solution at 0 °C for 1 h, the flask was securely stoppered and allowed to warm to 20−25 °C without stirring. The solution was re-cooled to <5 °C after 20 h, and 90% nitric acid (960 mL, 20.6 mol) was slowly added (1.5−2 h) with stirring, keeping the temperature below 5 °C. Sulphuric acid (98%, 240 mL) was then added over 10 min without external cooling; the temperature rose to about 35 °C. The resultant solution was slowly heated in an oil bath until the liquid temperature reached 80 °C. During this period, the excess of dinitrogen tetroxide and some nitric acid distilled off and was collected for reuse. The total volume of distillate was 241 mL (at 0 °C) forming two layers[6]—an upper layer (130 mL) consisting of 94.5 wt % dinitrogen tetroxide and 5.5 wt % nitric acid (this liquid can be reused for the nitrosation without further purification), and a lower layer (111 mL) consisting of 56.5 wt % dinitrogen tetroxide and 43.5 wt % nitric acid. Once the internal temperature reached 80 °C, the solution was held at this temperature for 2−2.5 h before pouring the hot solution, with stirring, into ice/water (4 kg). The white solid that separated was filtered off from the green solution, washed thoroughly with water, and then dried in vacuo over silica gel to give a pale yellow powder (**1**, 47.0 g, 97%). HPLC analysis showed that the purity of the 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (**1**) obtained was 95.1%.

2,6,8,12-Tetraacetyl-4,10-dinitroso-2,4,6,8,10,12-hexaazaisowurtzitane (5). To a mixture of acetic acid (400−450 mL), dinitrogen tetroxide (240 mL, 3.78mol), and water (20 mL) in a round-bottomed flask equipped with a reflux condenser was added 2,6,8,12-tetraacetyl-4,10-dibenzyl-2,4,6,8,10,12-hexaazaisowurtzitane (**3**, 400 g, 0.78mol) with vigorous stirring over a 20 min period at 20−25 °C. The reaction was monitored by thin-layer chromatography (ethyl acetate/triethylamine 1/1). After 24 and 48 h additional dinitrogen tetroxide (20 mL, 31.5 mmol) was added. After 72 h, thin-layer chromatography showed no remaining (**6**) ($R_f = 0.38$). Instead, two spots were observed, the major one corresponding to 2,6,8,12-tetraacetyl-4,10-dinitroso-2,4,6,8,10,12-hexaazaisowurtzitane (**5**) (≅90%, $R_f = 0.5$), and the minor one most probably corresponding to 6,8,12-triacetyl-2,4,10-trinitroso-2,4,6,8,10,12-hexaazaisowurtzitane (**7**) (≅10%, $R_f = 0.61$). The reaction mixture was transferred to a crystallising dish where it was stirred for 3 h to remove the remaining oxides of nitrogen. Ethanol (3 L) was added with vigorous stirring and the product was allowed to precipitate for 3 h. The precipitate was filtered off and then washed with ethanol (3 × 300 mL) to remove all traces of benzaldehyde. After drying (50 °C for 12 h) the product was obtained as a yellowish powder (250 g, 0.635 mol, 82% based on **3**), mp 280 °C (lit.[1] mp 290−295 °C). This product was used without further purification in the subsequent nitration step. In a smaller scale reaction dinitrogen tetroxide (3.8 mL, 0.06 mol) was added to **3** (5.16 g, 0.01mol) in 50 mL of acetic acid; the reaction mixture was stirred for 24 h when additional dinitrogen tetroxide (4.0 mL, 0.063mol) was added. After the reaction mixture was stirred for a total of 72 h, the excess of acetic acid was removed under reduced pressure, and the reaction mixture was worked up as above. After recrystallization from ethyl acetate/acetic acid **5** with a decomposition temperature (290−295 °C), FTIR and NMR spectra identical to those reported[1] was obtained.

2,4,6,8,10,12-Hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (1). To a solution of 2,6,8,12-tetraacetyl-4,10-dinitroso-2,4,6,8,10,12-hexaazaisowurtzitane (**5**, 500 g, 1.27 mol) in 99% nitric acid (6 L) was added 96% sulphuric acid (750 mL) over a 5 min period. The reaction mixture was heated to 75−80 °C, maintained at this temperature for 2 h, and then poured into ice/water (30 kg) with vigorous stirring, the temperature being kept below 35 °C during the addition. The precipitated product was filtered off and washed with water (4−5 times) until neutral washings were obtained. The product was isolated in the hydrated alpha form after drying to constant weight at 40 °C. HPLC analysis showed that the purity of the 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (**1**) obtained was 99.0%, (520 g, 93%). The decomposition temperature (240 °C) and FTIR and NMR spectra were identical to those reported,[3,7,8] respectively.

A reaction mixture quenched after 20 min gave a mixture of **1**, **8**, and **9**. This mixture was resolved into the three components by chromatography using the Chromatotron system with heptane/ethyl acetate 3/1 → 3/2 as eluent.

2,8-Diacetyl-4,6,10,12-tetranitro-2,4,6,8,10,12-hexaazaisowurtzitane (8). The decomposition temperature (233−234 °C) and FTIR and NMR spectra were identical to those reported.[9]

2-Acetyl-4,6,8,10,12-pentanitro-2,4,6,8,10,12-hexaazaisowurtzitane (9). The decomposition temperature (203.5 °C) and FTIR and NMR spectra were identical to those reported.[10]

Acknowledgment

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