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Synthesis of Tetrazino-tetrazine 1,3,6,8-Tetraoxide (TTTO)

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Abstract: This study presents the first synthesis and characterization of a new high energy compound [1,2,3,4]tetrazino[5,6e][1,2,3,4]tetrazine 1,3,6,8-tetraoxide (TTTO). It was synthesized in ten steps from 2,2-bis(tert-butyl-NNO-azoxy)acetonitrile. The synthetic strategy was based on the sequential closure of two 1,2,3,4-tetrazine 1,3-dioxide rings by the generation of oxodiazonium ions and their intramolecular coupling with tertbutyl-NNO-azoxy groups. The TTTO structure was confirmed by single-crystal X-ray.

Cyclic high-nitrogen systems with *N*-oxide oxygen atoms are of significant interest as a new generation of high energy density materials (HEDM).[1] One of the most promising compounds of this type is [1,2,3,4]tetrazino[5,6-e]-[1,2,3,4]tetrazine 1,3,6,8-tetraoxide (TTTO)^[2,3] **1** (Figure 1 a).

Figure 1. a) Resonance structures of TTTO 1. b) Y-type structural unit of "compounds with alternating charges".

It belongs to the so-called "compounds with alternating charges" family. We introduced this term^[4] to denote cyclic conjugated compounds with nitrogen catenation having a specific Y-type arrangement of atoms in nitrogen chains (Figure 1b). These high nitrogen compounds exhibit enhanced stability. Principles of construction of "compounds with alternating charges" based on the PMO theory^[5] were published previously.^[4]

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We initiated theoretical studies of TTTO 1 back in 1999. [6] This molecule has gained much attention in the scientific community due to its high energetic characteristics and the aesthetic perfection of the butterfly-like structure. Since then, a number of theoretical studies on TTTO 1 have been published.^[7] By theoretical data, the TTTO 1 heat of formation is about 206 kcal mol⁻¹, [7b] density 1.98 g cm⁻³, [3a,7c] estimated detonation velocity 9.71 km s⁻¹, [7b] and detonation pressure 432 kbar, [7b] which puts it on a par with the most powerful explosives known. Similar estimated data were obtained for [1,2,3,4]tetrazino[5,6-e][1,2,3,4]tetrazine 1,3,5,7tetraoxide (iso-TTTO).[3a,7,8]

Herein we report the first synthesis of TTTO 1. The synthetic strategy is based on the sequential closure of two 1,2,3,4-tetrazine 1,3-dioxide (TDO) rings. As shown previously, [9] aromatic compounds containing amino and (tertbutyl-NNO-azoxy) groups in the neighboring positions serve as direct precursors of annulated TDOs. TDO 2 could be such a precursor for TTTO 1 (Scheme 1). It could be obtained

Scheme 1. Retrosynthesis of TTTO 1.

from TDOs 3a-c bearing leaving groups X. Recently, we have developed a synthesis of compound 3c (X = SMe).^[10] However, its overall yield was low [3% yield if sourced from 2,2bis(tert-butyl-NNO-azoxy)acetonitrile (4)] and the synthesis per se appeared hardly scalable. Preliminary studies showed that the SMe group substitution with ammonia in compound 3c gave TDO 2 but in a low yield (18-20%) and the reaction was accompanied by the formation of a number of byproducts.[11] Taking this into account, we developed a more efficient method for the synthesis of TDO 2 (Scheme 2) from TDOs with electron withdrawing substituents SO₂Me (3a) and SO₂Et (3b).

The overall yield of TDO 2 prepared from TDO 3a (5%) was higher than that in the synthesis from TDO 3b (2%) (see



Scheme 2. Synthesis of TDO **2.** (i) for R = Me: MeSH, NEt₃, tBuOMe, 5 °C, 48 h; for R = Et: EtSH, NEt₃, CH_2Cl_2 , 25 °C, 24 h. (ii) HNO₃, H_2SO_4 , Ac_2O , -5-0 °C, 1.5 h. (iii) for R = Me: tBuOK, tBuOH, 30 °C, 10 minutes; for R = Et: MeONa, MeOH, 20 °C, 5 minutes. (iv) AgNO₃, MeCN. (v) iPrBr, Et_2O , 25 °C, 30 d. (vi) mCPBA, CH_2Cl_2 , 25 °C, 3 h. (vii) mCPBA, CH_2Cl_2 , 25 °C, 24 h. (viii) BF₃· Et_2O , CH_2Cl_2 , 25 °C, 4 d. (ix) NH₃, MeCN, 20 °C, 5 minutes. mCPBA = m-chloroperoxybenzoic acid.

Supporting Information). In this regard, below we only discuss the first variant. Nevertheless, Scheme 2 shows the yields in each step of the synthetic chain for both variants.

The synthetic chain started with nitrile 4 to which we had recently discovered a pathway.^[10] The reaction with MeSH/ Et₃N afforded thioimidate 5a in a high yield. Nitration of 5a with HNO₃ in Ac₂O gave N-nitroamine **6a** in the 42 % yield. Deprotonation of the latter followed by the reaction with AgNO₃ vielded Ag salt and its alkylation with iPrBr in Et₂O taken as a solvent resulted in azoxyalkene 7a (55% yield, three steps). Oxidation of azoxyalkene 7a with mCPBA in CH₂Cl₂ as a solvent gave sulfoxide **8a**. [12] The crude product contained impurities and needed chromatographic purification. Subsequent oxidation of azoxyalkene 8a yielded practically pure sulfone 9a (97% yield). Excess BF₃·Et₂O was used for the cyclization of sulfone 9a to TDO 3a. We failed to isolate the latter in a pure form. The structure of TDO 3a was confirmed by 1H, 13C and 14N NMR spectra. The reaction of TDO 3a with a saturated solution of NH3 in MeCN for 5 minutes resulted in the MeSO₂ group substitution giving TDO **2** (60 % yield) as colorless crystals, m.p. 185–187 °C (decomp.). Its structure was confirmed by X-ray crystallography^[13] (Figure 2), 1 H, 13 C, and 14 N NMR spectroscopy, HRMS, and IR spectroscopy.

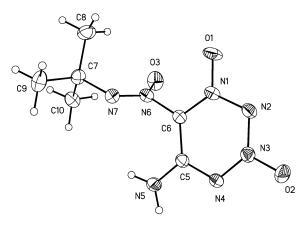


Figure 2. General view of one of the two crystallographically independent molecules of TDO **2** in a crystal. Anisotropic displacement parameters for non-hydrogen atoms are drawn at 50%.

To convert TDO **2** to TTTO **1** we used a HNO₃/H₂SO₄/Ac₂O system of reagents. This system was successfully used earlier for the TDO ring formation on benzene, furazane, and triazole substrates.^[14] The reaction proceeded at 0–5 °C for 30 minutes resulting in TTTO **1** in 22 % yield. It was purified by column chromatography on silica gel. The eluent contained 1 % of trifluoroacetic acid.

Surprisingly, the main reaction product proved to be triazole **10** (77% yield) characterized as Ag salt **11** (54% yield; cf. Ref. [15]). We did not expect that, because triazoles had never been observed in such reaction conditions.

A plausible mechanism for the formation of TTTO 1 (Scheme 3) and triazole 10 is presented in Scheme 4. At first, TDO 2 is converted to nitramine 12 which is acetylated at the oxygen atom of the nitro group to afford compound A. After protonation, the latter eliminates the AcOH molecule to give oxodiazonium ion B. We suppose that its intramolecular coupling with the neighboring *tert*-butyl-*NNO*-azoxy group should proceed in two directions. In the first case, the *NNO*-cation attacks the nitrogen atom of the azoxy group to give intermediate C which eliminates the *tert*-butyl cation to afford TTTO 1. In the second case, the *NNO*-cation attacks the oxygen atom of the azoxy group to give cyclic cation D. The following ring opening can afford cation E that eliminates

2
$$\xrightarrow{(i)}$$
 $\xrightarrow{N_{5}^{2}}$ $\xrightarrow{N_{6}^{8}}$ $\xrightarrow{N_{5}^{1}}$ $\xrightarrow{N_{1}^{2}}$ $\xrightarrow{N_{1}^$

Scheme 3. Synthesis of TTTO 1. (i) HNO $_3$, H $_2$ SO $_4$, Ac $_2$ O, 0–5 °C, 30 minutes. (ii) AgNO $_3$, H $_2$ O.





2
$$\frac{\text{HNO}_3}{\text{N}^2 \text{N}^2 \text{N}^2$$

Scheme 4. Plausible mechanism of formation of compounds 1 and 10.

the *tert*-butyl cation with the formation of diazoketone \mathbf{F} . The subsequent cyclization followed by the hydrolysis of N-nitrotriazole \mathbf{G} yields triazole $\mathbf{10}$.

TTTO **1** was obtained as a yellow powder, m.p. 183–186 °C (decompostion). Its structure was confirmed by X-ray, ¹³C and ¹⁴N NMR spectra, IR spectrum, EI MS, and HRMS. Crystals suitable for X-ray diffraction were grown from dry benzene. According to the X-ray study^[13] a molecular complex of TTTO **1** with benzene in the ratio 1:1 was formed (Figure 3)

Our attempts to grow single crystals of TTTO 1 were unsuccessful and even indexing of TTTO 1 from powder was not feasible due to possible full-molecule disorder, common for such symmetric structures. However, the benzene complex obtained by crystallization from benzene is ordered. The part of crystal structure is shown in Figure 4. The molecules of TTTO 1 and benzene are packed into stacks with average distances between the planes of molecular rings equal to 3.242(3) Å and 3.244(2) Å from two sides of TTTO 1 molecule. Such short distances imply relatively strong donoracceptor interactions and charge transfer between the molecules. The angles C(8a)-N(1)-O(1) and C(8a)-N(8)-O(8)equal to 123.74(18) and 123.61(19)°, as well as very short distance between the oxygen atoms O(1) and O(8) in peri positions equal to 2.619(2) Å indicate possible transannular interaction between these oxygens. The alternation of bond lengths in TTTO 1 molecule: N(1)-N(2) 1.348(2), N(2)-N(3)

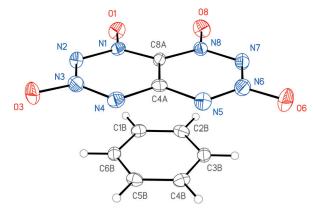
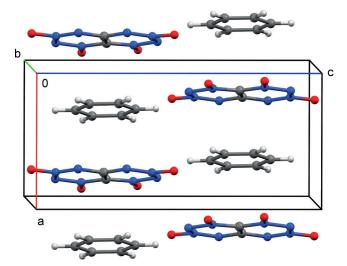


Figure 3. General view of TTTO 1 and solvating benzene molecules in a crystal. Anisotropic displacement parameters for non-hydrogen atoms are drawn at 50% probability.



 $\it Figure~4.~$ A fragment of crystal packing in complex of TTTO 1 with benzene.

1.390(2), N(3)-N(4) 1.328(3) Å) is similar to benzo- TDOs. [16] In contrast, in non-annulated TDO bearing CO_2Me substituents in the 5- and 6-positions [17] all N-N bonds are almost of the same length, that supports more effective conjugation between the fragments. The same trend is observed, for example, for benzene/naphthalene pair.

The 13 C NMR spectrum of TTTO **1** shows two signals at $\delta = 129.0$ ppm (br, C-8a) and 158.9 ppm (C-4a). Two narrow 14 N NMR signals were found at $\delta = -39$ ppm (N-3 and N-6, $\Delta \nu_{1/2} = 32$ Hz) and -54 ppm (N-1 and N-8, $\Delta \nu_{1/2} = 13$ Hz). An additional broad signal at $\delta = -90$ ppm $\Delta \nu_{1/2} = 430$ Hz) was assigned to N-4 and N-5. The mass spectrum (EI, 70 eV) of TTTO **1** shows a peak of the molecular ion [M⁺⁺]. The HRMS spectrum (ESI, negative mode) displays a corresponding peak of the anion radical [M⁻⁺].

The hydrolytic stability of TTTO 1 and its complex with benzene is sufficient to maintain both in open air for a short time. The hydrolysis of TTTO 1 in 50% aqueous EtOH at 20°C was completed within 2 h and resulted in triazole 10 with 86% yield. The plausible mechanism of hydrolysis involves an attack of H_2O at the N-3 atom with the subsequent TDO cycle opening to give intermediate H





Scheme 5. Plausible mechanism of the TTTO 1 hydrolysis.

(Scheme 5). After protonation, the azoxy group of this intermediate is supposed to eliminate the H₂O molecule to afford diazonium cation I.[18] It could react with the neighboring nitramine group yielding N-nitrotriazole G and its hydrolysis would give triazole 10.

It should be noted that triazole 10 formed directly in the reaction of compound 2 with the HNO₃/H₂SO₄/Ac₂O system cannot be a product of the TTTO 1 hydrolysis, because the reaction was carried out in the anhydrous medium. Moreover, a special experiment was performed which showed that TTTO 1 remained unchanged in the HNO₃/H₂SO₄/Ac₂O system for more than an hour at room temperature.

Detailed studies on the sensitivity of TTTO 1 to external impulses have not been so far undertaken. In the preliminary experiments, it did not detonate when rubbed in an agate mortar, but exploded in unglazed porcelain one.

In conclusion, the synthesis of TTTO 1 was accomplished in ten steps with 1% overall yield from 2,2-bis(tert-butyl-NNO-azoxy)acetonitrile (4). TTTO 1 has acceptable thermal stability; however, a low resistance to hydrolysis may limit its practical use.

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[1] a) P. Politzer, P. Lane, J. S. Murray, Mol. Phys. 2014, 112, 719-725; b) P. Yin, Q. Zhang, J. M. Shreeve, Acc. Chem. Res. 2016, 49, 4 - 16.

- [2] In the literature TTTO is also referred to as DTTO.
- [3] a) K. O. Christe, D. A. Dixon, M. Vasiliu, R. I. Wagner, R. Haiges, J. A. Boatz, H. L. Ammon, Propellants Explos. Pyrotech. 2015, 40, 463-468; b) S. G. Zlotin, A. M. Churakov, O. A. Luk'yanov, N. N. Makhova, A. Y. Sukhorukov, V. A. Tartakovsky, Mendeleev Commun. 2015, 25, 399-409.
- A. M. Churakov, V. A. Tartakovsky, "New high nitrogen heterocycles with the alternation of charges: Stability and strategy of synthesis", Energetic Materials. Production, Processing and Characterization; 29th International Annual Conference of ICT, Karlsruhe, Germany, 1998, V7.
- [5] M. J. S. Dewar, R. C. Dougherty, The PMO Theory of Organic Chemistry, Plenum press, New York, 1975.
- K. I. Rezchikova, A. M. Churakov, V. A. Shlyapochnikov, V. A. Tartakovsky, Russ. Chem. Bull. 1999, 48, 870-872.
- a) K. R. Jorgensen, G. A. Oyedepo, A. K. Wilson, J. Hazard. Mater. 2011, 186, 583-589; b) P. Politzer, P. Lane, J. S. Murray, Cent. Eur. J. Energ. Mater. 2013, 10, 37-52; c) J. L. Mendoza-Cortes, Q. An, W. A. Goddard III, C. Ye, S. Zybin, J. Comput. Chem. 2016, 37, 163-167; d) C.-C. Ye, Q. An, W. A. Goddard III, T. Cheng, W.-G. Liu, S. V. Zybin, X.-H. Ju, J. Mater. Chem. A 2015, 3, 1972-1978.
- [8] a) H. Östmark, New Trends Res. Energ. Mater., Proc. Semin., 9th, Part I, University of Pardubice, Czech Republic, 2006, pp. 231-250; b) X. Song, J. Li, H. Hou, B. Wang, J. Comput. Chem. 2009, 30, 1816-1820; c) B. Tan, M. Huang, H. Huang, X. Long, J. Li, F. Nie, J. Huang, Propellants Explos. Pyrotech. 2013, 38, 372-378.
- [9] A. M. Churakov, V. A. Tartakovsky, Chem. Rev. 2004, 104, 2601 -2616.
- [10] M. S. Klenov, O. V. Anikin, A. M. Churakov, Yu. A. Strelenko, I. V. Fedyanin, I. V. Ananyev, V. A. Tartakovsky, Eur. J. Org. Chem. 2015, 6170-6179.
- A detailed study of this reaction will be published elsewhere.
- [12] We failed to obtain the 1,2,3,4-tetrazine 1,3-dioxide cycle from sulfoxide 8a. For details see our further publications.
- [13] CCDC 1482531 (2) and CCDC 1482532 (1.PhH) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
- [14] a) M. S. Klenov, V. P. Zelenov, A. M. Churakov, Yu. A. Strelenko, V. A. Tartakovsky, Russ. Chem. Bull. 2011, 60, 2040-2045; b) V. P. Zelenov, A. A. Lobanova, S. V. Sysolyatin, N. V. Sevodina, Russ. J. Org. Chem. 2013, 49, 455-465; c) A. A. Voronin, V. P. Zelenov, A. M. Churakov, Y. A. Strelenko, I. V. Fedyanin, V. A. Tartakovsky, Tetrahedron 2014, 70, 3018-3022.
- [15] A. A. Voronin, V. P. Zelenov, A. M. Churakov, Y. A. Strelenko, V. A. Tartakovsky, Russ. Chem. Bull. 2015, 64, 699-703.
- [16] a) T. M. Klapötke, D. G. Piercey, J. Stierstorfer, M. Weyrauther, Propellants Explos. Pyrotech. 2012, 37, 527-535; b) K. Yamaguchi, H. Takahashi, T. Kaihoh, T. Itoh, M. Okada, K. Nagata, G. Matsumura, A. Ohsawa, Acta Crystallogr. Sect. C 1992, 48, 1237 -1239.
- [17] M. S. Klenov, A. M. Churakov, Y. A. Strelenko, I. V. Ananyev, K. A. Lyssenko, V. A. Tartakovsky, Tetrahedron Lett. 2015, 56, 5437 - 5444.
- [18] For the same reaction see: A. Y. Tyurin, A. M. Churakov, S. L. Ioffe, Yu. A. Strelenko, V. A. Tartakovsky, Russ. Chem. Bull. **1997**, 46, 592-594.

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