ORGANIC
LETTERS

1999
Vol. 1, No. 5
721−724

Synthesis of 1,2,3,4-Tetrazino[5,6-*f*]benzo-1,2,3,4-tetrazine 1,3,7,9-Tetra-*N*-oxides

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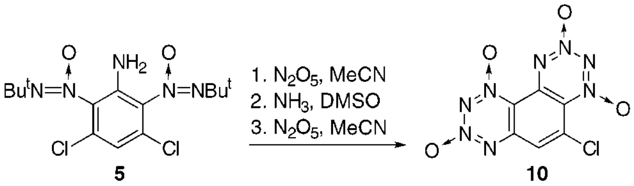
Received June 4, 1999

ABSTRACT



The novel heterocyclic system 10 with the phenanthrene type skeleton, in which the benzene ring is annulated with two 1,2,3,4-tetrazine 1,3-di-*N*-oxide rings, is of considerable interest in the context of the high nitrogen system stability and from a heteroaromaticity standpoint. The step-by-step synthetic approach to this system involves treatment of 5 with N_2O_5, resulting in the first 1,2,3,4-tetrazine 1,3-dioxide ring formation. The following displacement of the chlorine atom at the 6-position with ammonia and subsequent repeated treatment with N_2O_5 results in the second 1,2,3,4-tetrazine 1,3-dioxide ring formation. The structure of 10 was confirmed by a ^{13}C and ^{14}N NMR study.

Compounds including a maximum of adjacent nitrogen atoms have attracted significant attention in the context of high nitrogen system stability.[1] Moreover, fully conjugated cycles are of interest from a heteroaromaticity standpoint. 1,2,3,4-Tetrazine, being a six-membered aza-aromatic ring system, is one such high nitrogen cycle. The only representative of 1,2,3,4-tetrazines, i.e., 1,2,3,4-tetrazine annulated with a 1,2,3-triazole ring, the structure of which was unambiguously proved, was found to be unstable at room temperature.[2,3] At the same time, 1,3-di-*N*-oxides of 1,2,3,4-tetrazines annulated with benzene[4] or furazan[5] rings proved to be quite stable. The reasons that the stability of fully unsaturated high nitrogen heterocycles with adjacent nitrogen atoms increases in the presence of *N*-oxide oxygen atoms in particular ring positions have been discussed recently.[6] The synthetic

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(1) Benson, F. R. *The High Nitrogen Compounds*; Wiley-Interscience: New York, 1984.

(2) Kaihoh, T.; Itoh, T.; Yamaguchi, K.; Ohsawa, A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2045.

(3) For N-substituted tetrazines, which have been investigated more fully, see: Mackert, P. J.; Hafner, K.; Nimmerfroh, N.; Banert, K. *Chem. Ber.* **1994**, *127*, 1479 and references cited therein.

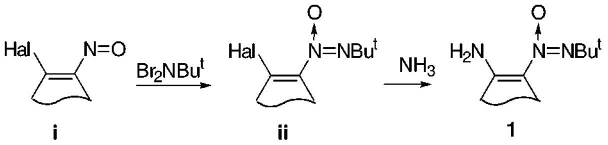
(4) Churakov, A. M.; Ioffe, S. L.; Tartakovsky, V. A. *Mendeleev Commun.* **1991**, 101.

(5) Churakov, A. M.; Ioffe, S. L.; Tartakovsky, V. A. *Mendeleev Commun.* **1995**, 227.

(6) Churakov, A. M.; Tartakovsky, V. A. 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; DWS Werbeagentur und Verlag GmbH: Karlsruhe, Germany, 1998; V7.

(7) See our next publications.

(8) Anilines **1** can be obtained in two stages starting from nitroso compounds **i**, which, according to the Kovacic method,[9] afford **ii** when treated with *N*,*N*-dibromo-*tert*-butylamine. The following displacement of halogen atom with ammonia gives anilines **1**:[10]



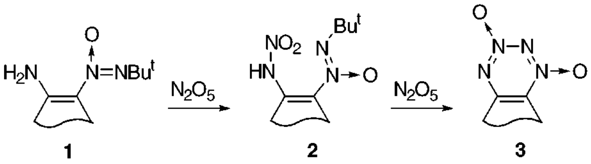
(9) Zawalski, R. C.; Kovacic, P. *J. Org. Chem.* **1979**, *44*, 2130.

(10) Churakov, A. M.; Smirnov, O. Yu.; Ioffe, S. L.; Strelenko, Yu. A.; Tartakovsky, V. A. *Izv. Akad. Nauk, Ser. Khim.* **1994**, 1620; *Russ. Chem. Bull. (Engl. Transl.)* **1994**, *43*, 1532.

10.1021/ol990713q CCC: $18.00

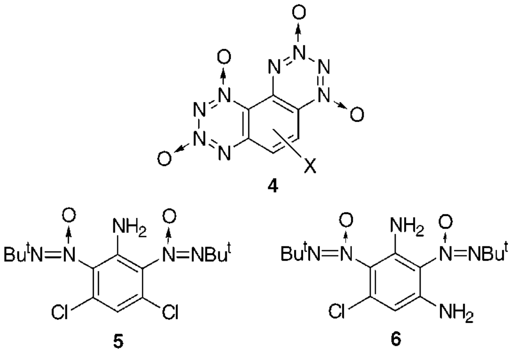
approach to benzo-1,2,3,4-tetrazine 1,3-di-*N*-oxides (BTDOs; **3**) (Scheme 1)[4,7] involves nitration of anilines **1**, bearing the *tert*-butyl-*NNO*-azoxy group in the ortho position[8], with dinitrogen pentoxide. *N*-Nitroamines **2** were found to be intermediates in this reaction.[7]

Scheme 1



The aim of the work described herein was to synthesize the novel heterocyclic system **4** (Scheme 2), constituted by a benzene ring annulated with two 1,2,3,4-tetrazine 1,3-di-*N*-oxide rings: i.e., 1,2,3,4-tetrazino[5,6-*f*]benzo-1,2,3,4-tetrazine 1,3,7,9-tetra-*N*-oxide (TBTDO).

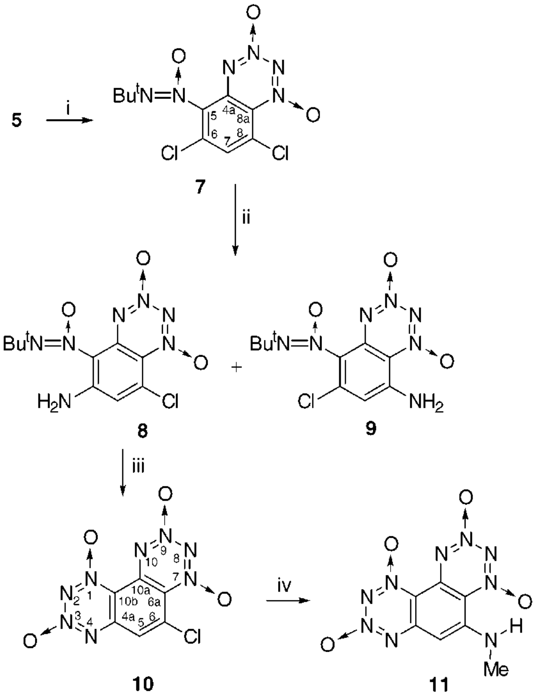
Scheme 2



Bearing in mind the synthetic approach described above, we examined the two possible routes to system **4**. The first route might involve step-by-step synthesis starting from aniline **5**, which bears the two *tert*-butyl-*NNO*-azoxy groups in meta positions. However, the second one might consist of single-stage formation of both tetrazine rings, starting from diamine **6**. The syntheses of **5** and **6** have been described recently.[11]

The treatment of **5** with N_2O_5 yielded the BTDO species **7** along with the 7-nitro derivative (Scheme 3). As shown in the reaction of bromo-substituted BTDOs with methoxide anions,[7] the reactivity of positions of the BTDO ring reflects a decrease of the nucleophilic substitution rates as follows: 6 > 8 > 7 > 5. This consideration allowed us to envisage that ammonia would replace the chlorine atom at the 6-position rather than the *tert*-butyl-*NNO*-azoxy group at the 5-position in BTDO **7**. We also expected that treatment of this BTDO with ammonia might predominantly result in amine **8**, but the experiment showed that the amounts of amines **8** and **9** obtained were practically equal. This mixture of amines was separated by chromatography, and treatment of **8** with N_2O_5 yielded TBTDO **10**.[13]

Scheme 3[a]



[a] Reagents and conditions: (i) N_2O_5, MeCN, −20 to 0 °C (41%); (ii) NH_3, DMSO, 1 h, chromatographic separation (silica gel, CH_2Cl_2), **8**, yield 37%, **9**, yield 43%; (iii) N_2O_5, MeCN, −30 to 0 °C (55%); (iv) $MeNH_2$, MeCN, 20 °C (61%).

TBTDO **10** was found to be sensitive to nucleophilic attack. For example, it reacts readily with methylamine, involving replacement of the chlorine atom, to give TBTDO **11**,[13] the tetrazinobenzotetrazine skeleton being left intact. Thus, the TBTDO system can be considered as a benzene

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[11] Amines **5** and **6** were synthesized from 2-bromo-4,6-dichloro-1,3-phenylenediamine via intermediate nitroso compounds by the Kovacic method[9] followed by the displacement of halogen atoms with ammonia.[12]

[12] Frumkin, A. E.; Churakov, A. M.; Strelenko, Yu. A.; Tartakovsky, V. A. *Izv. Akad. Nauk, Ser. Khim.*, in press.

[13] All new compounds gave satisfactory analytical data. The assignments of the chemical shifts are based on experiments, including proton-coupled spectroscopy, and on calculated ^{13}C chemical shifts, obtained with regard to the ^{13}C NMR data of the closely related compounds. *Caution*! BTDOs and TBTDOs are potential explosives and should be handled with care. Characterization data for **10**: yellow crystals, begins to melt with decomposition at 140 °C; IR (KBr) 1437, 1506, 1518 cm^{-1}; ^1H NMR (500 MHz, $[^2H_6]$acetone) δ 8.19 (s, 1 H); ^{13}C NMR (126 MHz, $[^2H_6]$acetone) δ 120.0 (br, C-10b), 125.8 (br, d, $^3J = 8.9$ Hz, C-6a), 126.9 (d, $^1J = 181.1$ Hz, C-5), 136.2 (d, $^2J = 4.5$ Hz, C-6), 144.0 (d, $^4J = 1.1$ Hz, C-10a), 151.6 (d, $^2J = 1.9$ Hz, C-4a); ^{14}N NMR (22 MHz, $[^2H_6]$acetone, $MeNO_2$ as a reference) δ −45 (1N, $\Delta\nu_{1/2} = 40$ Hz, N→O), −42 (2N, $\Delta\nu_{1/2} = 60$ Hz, 2 N→O), −40 (1N, $\Delta\nu_{1/2} = 45$ Hz, N→O); EI-MS *m/z* 284, 286 (3:1) (M^+). Characterization data for **11**: brown crystals, decompose without melting above 210 °C; IR (KBr) 1426, 1448, 1506, 3344 cm^{-1}; ^1H NMR (500 MHz, $[^2H_6]$acetone) δ 3.32 (d, $J = 5.1$ Hz, 3H, CH_3), 6.68 (s, 1H, CH), 9.9 (br, 1H, NH); ^{13}C NMR (126 MHz, $[^2H_6]$acetone) δ 31.8 (dq, $^1J = 140.0$, $^2J = 1.5$ Hz, Me), 95.2 (dd, $^1J = 172.1$, $^3J = 6.6$, C-5), 111.2 (br, C-10b), 118.7 (br, dd, $^3J = 9.6$, 3.1 Hz, C-6a), 143.5 (s, C-10a), 147.0 (q, $^2J = 4.1$, C-6), 150.4 (d, $^2J = 2.1$, C-4a); ^{14}N NMR (22 MHz, $[^2H_6]$acetone) δ −43 (3N, $\Delta\nu_{1/2} = 60$ Hz, 3 N→O), −39 (1N, $\Delta\nu_{1/2} = 45$ Hz, N→O); EI-MS *m/z* 279 (M^+).

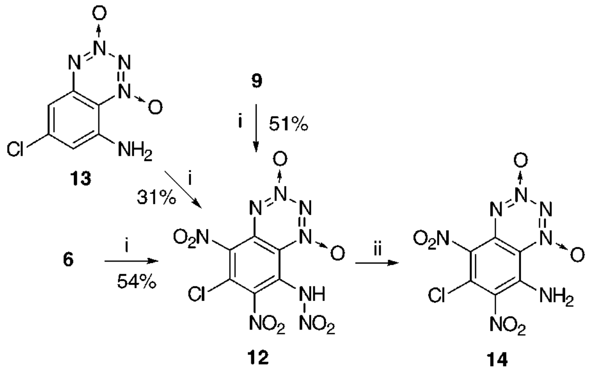
ring with strongly electron withdrawing substituents, which do not take part in substitution reactions but facilitate such reactions at the 6- and, probably, 5-positions. The possibility of the C(5)−C(6) double-bond reactivity increase, as is the case with phenanthrene, is yet to be studied.

The structures of TBTDOs **10** and **11** were confirmed by NMR studies. The ^{14}N NMR spectra of **10** and **11** showed that four signals due to the *N*-oxide nitrogen atoms are present in the expected region.[4,7] The ^{13}C NMR chemical shifts of both TBTDOs are in good agreement with chemical shifts, calculated with regard to the ^{13}C NMR data for the closely related BTDOs.[4,7] The broadening of C-6a and C-10b signals due to coupling with the ^{14}N nucleus confirms the arrangement of the *N*-oxide oxygen atoms in the system. In addition, both **10** and **11** gave the molecular ion in their mass spectra.

The second synthetic route to TBTDOs might involve the treatment of diamine **6** with N_2O_5. However, this reaction furnished the *N*-nitroamine **12** instead.[14]

To confirm the structure of **12**, this compound was synthesized by nitration of BTDO **13**[7] (Scheme 4). The structure of **12** was further confirmed by its conversion to amine **14** when treated with an acid in the presence of toluene.

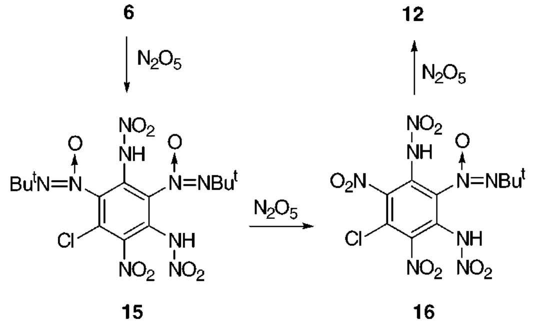
Scheme 4[a]



[a] Reagents and conditions: (i) N_2O_5, MeCN, −20 to 0 °C; (ii) toluene, 1 drop of TfOH, room temperature (57%).

The formation of **12** can be rationalized by the intermediate production of the di-*N*-nitroamino species **15** followed by electrophilic displacement of one of the *tert*-butyl-*NNO*-azoxy groups by the nitro group[15] and the subsequent ring closure of the symmetrical species **16** (Scheme 5).

Scheme 5



At the same time, one could not disregard another possible sequence of reactions, the first step being tetrazine ring formation and the second being the displacement of the *tert*-butyl-*NNO*-azoxy group by the nitro group. In any case, BTDO **9** afforded **12** when treated with N_2O_5 under similar conditions (Scheme 4). The electrophilic displacement of the *tert*-butyl-*NNO*-azoxy group is rather unusual. It implies the ipso attack of the nitronium cation at the C-5 carbon of BTDO, bearing the strongly electron withdrawing *tert*-butyl-*NNO*-azoxy group. To clarify this point, amine **14** was treated with an excess of labeled $K^{15}NO_3$ in sulfuric acid to afford nitramine **12′**, in which the *N*-nitro group was ca. 80% ^{15}N-labeled and one of the *C*-nitro groups was ca. 50% ^{15}N-labeled. This clearly indicates that the exchange of the *C*-nitro groups took place via the intermediate σ-adduct. This adduct is similar to the one produced from BTDO **9**, although in the case of **9**, the substitution of the *tert*-butyl-*NNO*-azoxy group should be irreversible. Actually, this σ-adduct can eliminate either the *tert*-butyl cation and N_2O or the $t\text{-BuN}{=}N{=}O^+$ cation followed by its decomposition to give the same species.

In conclusion, TBTDOs **10** and **11** were found to be rather stable: **10** begins to melt with decomposition at 140 °C, and **11** begins to decompose without melting above 210 °C. Such stability can be considered as comparatively high in view of the fact that 1,2,3,4-tetrazines lacking the *N*-oxide oxygen atoms are unstable at room temperature.[2] The actual arrangement of the oxygen atoms in the cycles under consideration forms the so-called “structure with alternating charges”.[6] This fact is responsible for the stability of these systems. The higher stability of **11** as compared with that of **10** can also be explained in terms of the “structures with alternating charges”[6] concept.

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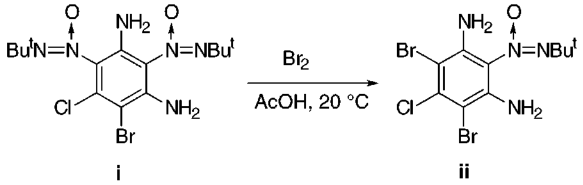
(14) Characterization data for **12**: red crystals, mp 116−118 °C dec; IR (KBr) 3430, 3230, 1550, 1510, 1450, 1410, 1335 cm^{-1}; ^{13}C NMR (76 MHz, [^{2}H$_6$]acetone) δ 123.4 (br, C-8a); 126.5 (C-8); 132.2 (C-6); 139.5 (br, C-5 and C-7); 141.0 (C-4a); ^{14}N NMR (22 MHz, [^{2}H$_6$]acetone, $MeNO_2$ as a reference) δ −42 (1N, $\Delta\nu_{1/2} = 60$ Hz, N→O), −38 (1N, $\Delta\nu_{1/2} = 50$ Hz, N→O), −21 (1N, $\Delta\nu_{1/2} = 70$ Hz, NO_2,), −18 (1N, $\Delta\nu_{1/2} = 90$ Hz, NO_2), −13 (1N, $\Delta\nu_{1/2} = 50$ Hz, N*NO*$_2$). Characterization data for **12′**: ^{15}N NMR (51 MHz, [^{2}H$_6$]acetone, $MeNO_2$ as a reference) δ −18.6 (NO_2), −13.9 (N*NO*$_2$); ^{14}N NMR (22 MHz, [^{2}H$_6$]acetone, $MeNO_2$ as a reference) δ −42 (1N, N→O), −38 (1N, N→O), −21 (1N, NO_2), −18 (0.5N, NO_2), −13 (0.2N, N*NO*$_2$).

(15) A similar electrophilic displacement of the *tert*-butyl-*NNO*-azoxy group by bromine atom in the closely related diamine **i** was observed when **i** was treated with bromine in acetic acid as solvent to yield **ii**:[16]



(16) Frumkin, A. E.; Churakov, A. M.; Tartakovsky, V. A. *Izv. Akad. Nauk, Ser. Khim.*, in press.

To summarize, the step-by-step synthesis of TBTDO **10** was accomplished by starting from amine **5**. The single-stage synthesis of **10** starting from diamine **6** failed, owing to the facile replacement of the *tert*-butyl-*NNO*-azoxy group by the nitro group. The development of a synthetic route to TBTDOs offers the possibility of studying the chemical and physicochemical properties of this novel class of heterocycles. It is anticipated that TBTDOs could be employed as precursors for the unknown nonannulated 1,2,3,4-tetrazine 1,3-di-*N*-oxide ring system.

Supporting Information Available: Characterization data for compounds **7**−**9** and **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL990713Q