First example of the formation of bipolar spiro σ-complexes from 6-bromo-5,7-dinitrobenzo[*e*]-1,2,3,4-tetrazine 1,3-di-*N*-oxide

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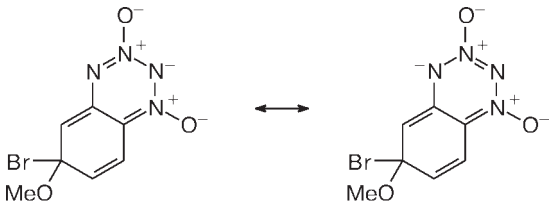
The reactions of 3,5,7-trimethyltropolone and 2-(*N*-benzylamino)tropone with 6-bromo-5,7-dinitrobenzo[*e*]-1,2,3,4-tetrazine 1,3-di-*N*-oxide afforded novel bipolar spiro σ-complexes. The kinetic and activation parameters of the *R,S*-enantiotopomerization of a chiral spiro σ-complex of 2-(*N*-benzylamino)tropone were determined using dynamic ^{1}H NMR spectroscopy.

Key words: benzo[*e*]-1,2,3,4-tetrazine 1,3-di-*N*-oxides, tropolone, bipolar spiro complexes, enantiotopomerization.

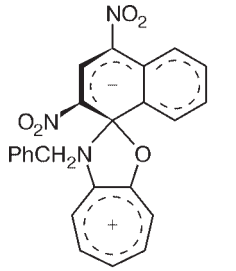
Benzo[*e*]-1,2,3,4-tetrazine 1,3-di-*N*-oxides (BTDOs) are a novel class of polynitrogen heterocyclic compounds.[1] Recently, their properties have been studied extensively.[2,3] Brominated BTDOs easily enter into substitution reactions with a methoxide ion. The substitution occurs most rapidly for the bromine atom in position 6.[2,3] This is associated with easy formation of an anionic σ-complex **A**, in which the negative charge is delocalized over the tetrazine dioxide fragment.



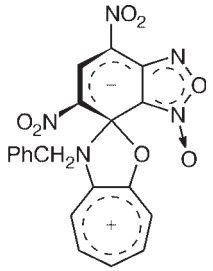
A

Quantitative data on the kinetic stability of such complexes can be obtained while studying bipolar spiro-σ-complexes **1** and **2**. The kinetic and activation parameters of the reverse cleavage—formation processes for the C_{ipso}—O bond in compounds **1** and **2**, which are determined from dynamic ^{1}H NMR data, can serve as a quantitative criterion for the stability of a σ-complex.[4,5]

In the present study, complexes based on 6-bromo-5,7-dinitrobenzo[*e*]-1,2,3,4-tetrazine 1,3-di-*N*-oxide (**3**) were chosen as objects of investigation. In their structures, the negative charge is additionally stabilized by two nitro groups. Compound **3** was prepared by the nitration of 6-bromo-BTDO **4** with an HNO_3—oleum mixture (Scheme 1).[2]

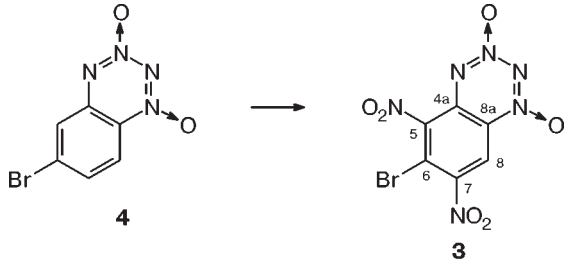


1



2

Scheme 1



4 **3**

Reagents and conditions: HNO_3—20% oleum, 90 °C, 1.5 h.

3,5,7-Trimethyltropolone **5** and 2-(*N*-benzylamino)tropone **6** were chosen as the most appropriate reaction partners in the synthesis of spiro complexes. They

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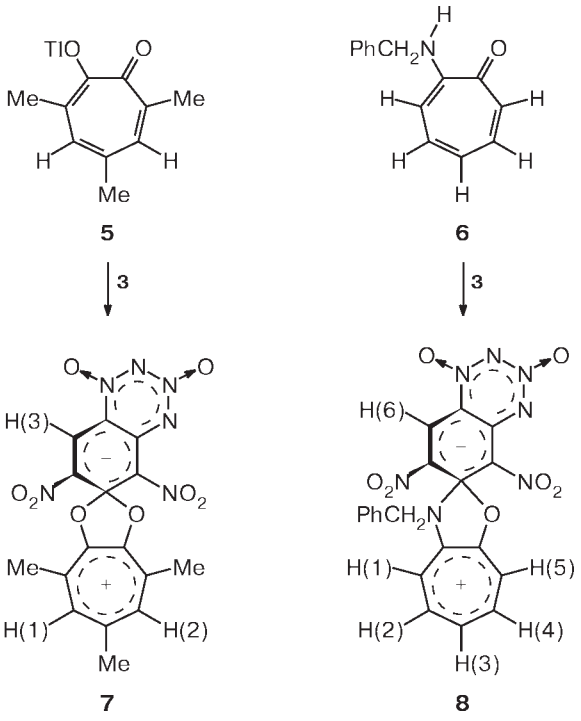
have optimum geometry of the reaction center and can effectively delocalize the positive charge in the aromatic tropylium cation.[6]

The reactions of a Tl salt of trimethyltropolone **5** and aminotropone **6** with compound **3** afforded zwitterionic spirans **7** and **8** (Scheme 2).

Scheme 2



Their structures were confirmed by ^{1}H NMR spectra showing an upfield shift of a signal from the proton of the BTDO fragment, which is characteristic of both the anionic[7] and bipolar[8] σ-complexes. Signals from the protons of the tropylium ring are shifted downfield ($\Delta\delta > 1$ ppm) relative to the starting compounds **5** and **6**, which indicates a considerable charge separation between the tropylium and BTDO fragments in compounds **7** and **8**. The spirocyclic structure of zwitterion **8** is evidenced by the AB quartet from the methylene protons of diastereotopic $PhCH_2N$ group.

When spiran **8** is heated in $C_6D_5NO_2$, the AB quartet is reversibly converted to a singlet, indicating the (*R*)-**8** ⇌ (*S*)-**8** enantiotopomerization, whose kinetic and activation parameters can be used for quantitative estimation of the relative stability of spiro σ-complexes. The kinetic data obtained in the present study are given in Table 1 in comparison with the literature data for structurally close spirans **1** [4] and **2**.[5]

The *R,S*-conversion rate of compound **8** is lower by two orders of magnitude than that of **1**, which is quite expected because the benzene ring is replaced by tetrazine 1,3-di-*N*-oxide (TDO). At the same time, the significantly higher kinetic stability of **2** compared to compound **8** is not so evident *a priori*. The relative stability of compounds **8** and **2** is probably determined by a higher aromaticity of the BTDO system as a whole relative to dinitrobenzofuroxane rather than by a difference in the electron-withdrawing properties of annelated furoxane and TDO rings. Dinitrobenzofuroxane can behave like a heterodiene,[9] which accounts for its superelectrophilicity.[10]

Table 1. Kinetic and activation enantiotopomerization parameters for compounds **1**, **2**, and **8**

Compound	Solvent	k_{298} /s^{-1}	$\Delta G^{\neq}_{298}$	$\Delta H^{\neq}$	$\Delta S^{\neq}$
			kJ mol^{-1}		
1 [4]	$CDCl_3$	$1.2 \cdot 10^3$	55.0	46.0	−31.4
	Acetone-d_6	$9.2 \cdot 10^2$	56.0	48.0	−26.8
2 [5]	DMSO-d_6	$5.0 \cdot 10^{-5}$	97.6	97.6	0.0
8	$C_6D_5NO_2$	$1.2 \cdot 10^1$	66.7	76.7	33.5

Note. $\Delta S^{\neq}$ is expressed in J mol^{-1} deg^{-1}.

Experimental

IR spectra were recorded on a Perkin—Elmer 577 spectrometer. Mass spectra were recorded on a Kratos MS-30 instrument (EI, 70 eV). ^{1}H NMR spectra were recorded on a Bruker DPX-250 instrument; ^{13}C and ^{14}N NMR spectra were taken on a Bruker AM-300 spectrometer (75.5 and 21.5 MHz, respectively). ^{14}N chemical shifts are given on the δ scale with nitromethane as a standard. Kinetic and activation parameters of the (*R*)-**8** ⇌ (*S*)-**8** rearrangement were determined from the temperature dependence of a signal shape for a methylene group in the ^{1}H NMR spectrum by analyzing a computer-assisted simulation of signal shapes for indicator protons using the gNMR program. The course of the reactions was monitored by TLC (Silufol UV-254). Preparative chromatography was carried out on silica gel.

6-Bromo-5,7-dinitrobenzo[*e*]-1,2,3,4-tetrazine 1,3-di-*N*-oxide (3). Concentrated HNO_3 (0.5 g, 8 mmol, $d = 1.5$ g cm^{-3}) was added at 0 °C to a stirred solution of 6-bromobenzo[*e*]-1,2,3,4-tetrazine 1,3-di-*N*-oxide (**4**)[1] (0.25 g, 1 mmol) in 2.5 mL of conc. H_2SO_4, and the reaction mixture was kept at ~20 °C for 1.5 h. 20% Oleum (1 mL) was added at 0 °C, and the resulting solution was heated to 90 °C and kept at this temperature for 1.5 h. On cooling to ~20 °C, the reaction mixture was poured into ice. The precipitate that formed was filtered off, washed with water, and dried *in vacuo* to give compound **3** (0.27 g, 83%) as yellow crystals, m.p. 207—211 °C (from $CHCl_3$). Found (%): C, 21.31; H, 0.42; Br, 23.58; N, 25.37. $C_6HBrN_6O_6$. Calculated (%): C, 21.63; H, 0.30; Br, 23.99; N, 25.24. IR (KBr), ν/cm^{-1}: 1435, 1515 (N(O)NN(O)N); 1340, 1550 (NO_2). ^{1}H NMR (acetone-d_6), δ: 9.25. ^{13}C NMR (acetone-d_6), δ: 118.0 (C(6), ^3J = 8.5 Hz); 119.2 (C(8)); 128.7 (br, C(8a)); 139.3 (C(4a), ^3J = 6.0 Hz); 145.1 (br, C(5)); 149.6

(br, C(7)). ^{14}N NMR (acetone-d_6), δ: –45 (N(O), $\Delta\nu_{1/2}$ = 100 Hz); –42 (N(O), $\Delta\nu_{1/2}$ = 70 Hz); –23 (NO_2, $\Delta\nu_{1/2}$ = 60 Hz); –21 (NO_2, $\Delta\nu_{1/2}$ = 150 Hz). MS, *m/z*: 332, 334 $[M]^+$ (1 : 1).

4,6,8-Trimethyl-5´,7´-dinitrospiro[cycloheptatrienylio[*d*]-1,3-dioxolane-2,6´-(2´,6´-dihydrobenzo[*e*]-1´,2´,3´,4´-tetrazinate 1´,3´-di-*N*-oxide)] (7). A mixture of a Tl salt of 3,5,7-trimethyltropolone (**5**)[11] (44 mg, 0.12 mmol) and compound **3** (40 mg, 0.12 mmol) in 6 mL of toluene was kept at 50—60 °C for two days. The precipitate of TlBr that formed was filtered off, and the filtrate was concentrated. The residue was purified using column chromatography (acetone—chloroform, 1 : 6, as an eluent) to give spiro compound **7** (18 mg, 36%) as red crystals, m.p. 200—205 °C (decomp.). Found (%): C, 45.95; H, 2.93; N, 20.46. $C_{16}H_{12}N_6O_8$. Calculated (%): C, 46.15; H, 2.88; N, 20.19. ^{1}H NMR (acetone-d_6), δ: 2.3 (s, 6 H, 2 CH_3); 2.67 (s, 3 H, CH_3); 7.98 (s, 2 H, H(1), H(2)); 8.96 (s, 1 H, H(3)).

3-Benzyl-5´,7´-dinitrospiro[cycloheptatrienylio[*d*]-1,3-oxazole-2,6´-(2´,6´-dihydrobenzo[*e*]-1´,2´,3´,4´-tetrazinate 1´,3´-di-*N*-oxide)] (8). A mixture of 2-benzylaminotropone **6** [12] (32 mg, 0.15 mmol) and compound **3** (50 mg, 0.15 mmol) in 6 mL of toluene was kept at 70—80 °C for three days; the precipitate of TlBr was filtered off, and the filtrate was concentrated. The residue was suspended in chloroform (3×5 mL), filtered off, and washed with methanol to give spiro compound **8** (19 mg, 27%) as red crystals, m.p. 210—220 °C (decomp.). Found (%): C, 51.52; H, 2.96; N, 24.07. $C_{20}H_{13}N_7O_7$. Calculated (%): C, 51.83; H, 2.80; N, 23.55. ^{1}H NMR (acetone-d_6), δ: 4.95 (d, 1 H, CH_2, J = 16.4 Hz); 5.28 (d, 1 H, CH_2, J = 16.3 Hz); 7.23—7.40 (m, 5 H, Ar); 7.74 (d, 1 H, H(5), J = 10.1 Hz); 7.83 (dd, 1 H, H(3), J = 9.8 Hz, J = 10.0 Hz); 8.03 (d, 1 H, H(1), J = 11.1 Hz); 8.21 (dd, 1 H, H(4), J = 9.3 Hz, J = 10.5 Hz); 8.37 (s, 1 H, H(6)); 8.43 (dd, 1 H, H(2), J = 8.7 Hz, J = 11.8 Hz).

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