Dipolar spirocyclic σ-complexes based on of 4,6-dinitrobenzofuroxan

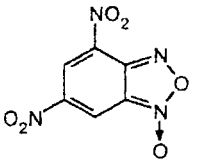
S. V. Kurbatov,[a] Z. N. Budarina,[b] G. S. Vaslyaeva,[a] N. I. Borisenko,[a] A. P. Knyazev,[a] V. I. Minkin,[b] Yu. A. Zhdanov,[a] and L. P. Olekhnovich[a]*

[a]*Rostov State University, Department of Chemistry, 7 ul. Zorge, 344090 Rostov-on-Don, Russian Federation. Fax: 007 (863 2) 64 5255. E-mail: root@chimfak.rnd.runnet.ru*
[b]*Institute of Physical Organic Chemistry, Rostov State University, 194/2 ul. Stachki, 344090 Rostov-on-Don, Russian Federation. Fax: 007 (863 2) 28 5667*

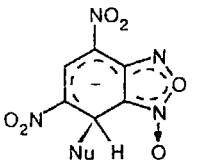
The first dipolar spiro-σ-complexes with a superelectrophilic dinintrobenzofuroxan fragment and tropolone systems with diastereotopic substituents were synthesized. The kinetics of their enantiotopomerization, which occurs *via* cleavage—formation of the C_{spiro}—heteroatom bond, was studied by dynamic ^1H NMR. The stereorigidity of dinitrobenzofuroxan spiro-complexes in this degenerated process increases in the series: tropolone < aminotropone << aminothiotropone ≈ aminotroponimine. The two last possess the highest kinetic stability compared to all known zwitterionic spiro-complexes.

Key words: tropolone, 4,6-dinitrobenzofuroxan, dipolar spiro-σ-complexes, enantiotopomerization.

It is known that 4,6-dinitrobenzofuroxan (DNBF) (**1**) with *O*-,[1] *N*-,[2] *S*-,[3] and *C*-nucleophiles[4] readily forms anionic σ-complexes of the Meisenheimer type (**2**).



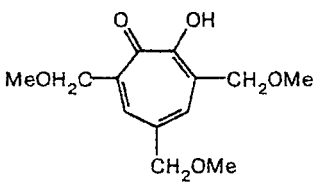
1



2

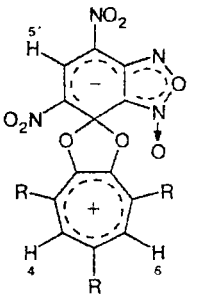
Their unique stability (approximately 10 orders of magnitude higher than that of similar derivatives of trinitrobenzene)[4] is explained by the high electron-deficiency of DNBF **1**, which is usually considered as a "superelectrophile".[5]

However, zwitterionic spirocyclic σ-complexes based on DNBF are unknown so far. One of the most convenient reagents for constructing such compounds is tropolone, *e.g.*, **3** or its heteroanalogs, which have optimal geometry of an active fragment and are able to effectively delocalize a positive charge formed.[6]



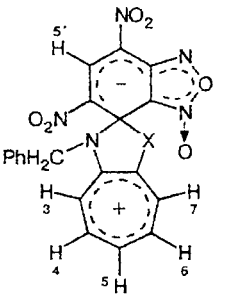
3

In the present work, spiro-σ-complexes (**4**—**8**) were synthesized by reactions of thallium salts of tropolones and aminotropones with 7-chloro-4,6-dinitrobenzofuroxan.



4, 5

4: R = Me
5: R = $MeOCH_2$



6—8

6: X = O
7: X = S
8: X = N—CH_2Ph

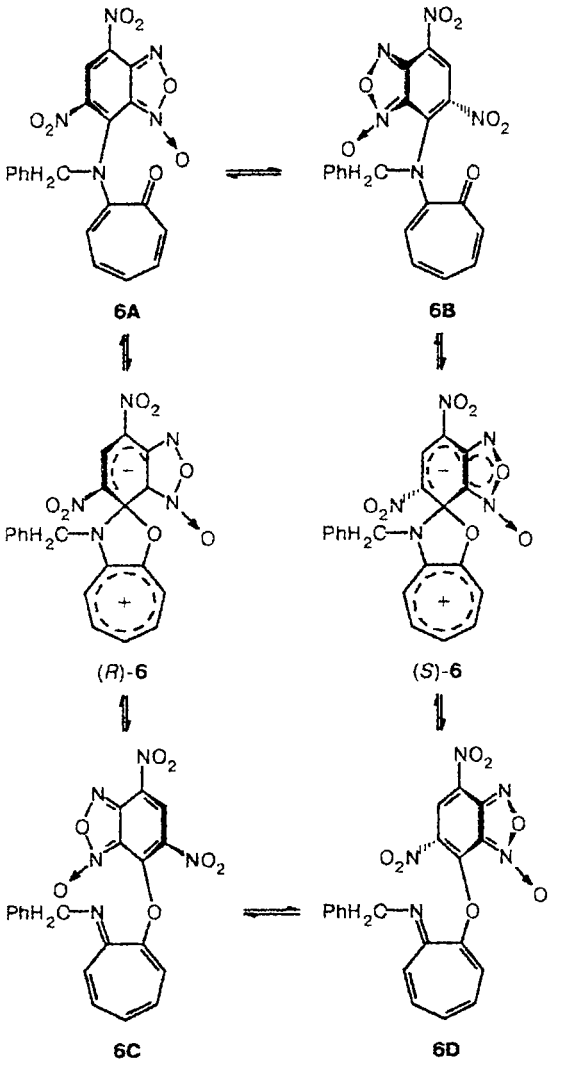
Compounds **4**—**8** are stable intermediates of reactions, *e.g.*, of intramolecular aromatic nucleophilic substitution of the **6A** ⇌ (*R*)-**6** ⇌ **6C** type (Scheme 1).

The spirocyclic structure of compounds **4**—**8** has been reliably confirmed by ^1H NMR spectra: the proton signals of the tropolone ring are significantly shifted downfield (>1 ppm), as in the case of other dipolar spirocomplexes,[7,8] compared to the initial tropolone and its heteroanalogs or to known *O*,*N*-aryl and hetaryl

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 8, pp. 1509—1512, August, 1997.

1066-5285/97/4608-1445 $18.00

Scheme 1



tropolone derivatives, open-chain isomers of the **6A** type.[7] This indicates a considerable separation of charge between tropylium and benzofuroxan fragments of the molecules of **4**—**8**. The thermodynamic stability of zwitterions **5**—**8** with a stereogenic spirocarbon center is evidenced by the presence of AB-quartets of diastereotopic methylene protons of the $MeO\underline{CH}_2$ (**5**) and $Ph\underline{CH}_2N$ groups (**6**—**8**) in the ^1H NMR spectra (Fig. 1, Table 1).

A diastereotopic label in the neighborhood of a chiral or prochiral spirocenter[9] allows one to investigate enantiotopomerization (*R*)-**6** ⇌ (*S*)-**6** (see Scheme 1) occurring through dissociation—recombination of carbon—heteroatomic spirobonds, using dynamic ^1H NMR spectroscopy.[10] One can conclude from the analysis of data given in Table 2 that kinetic and activation parameters of degenerated stereoconversion of the tetrahedral spirocenter strongly depend on the type of

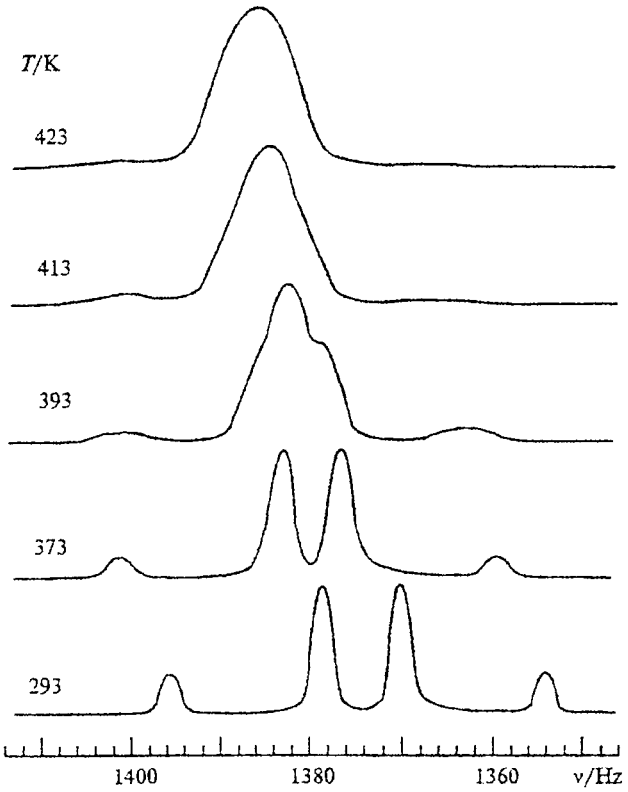


Fig. 1. Temperature dependence of the line shape of proton signals ($C(3)H_2$ + $C(7)H_2$) of compound **5** (300 MHz).

heteroatoms bonded with this center. Thus, replacing one of oxygen atoms of spiro-complex **5** by the $PhCH_2N$ group increases the activation barrier of the process (*R*)-**6** ⇌ (*S*)-**6** by almost 15 kJ mol^{-1}, while replacing two oxygen atoms by more nucleophilic N and S atoms decelerates the enantiotopomerization of compounds **7**, **8** to such an extent that it is not observed at all in the time scale of dynamic ^1H NMR spectroscopy. Dipolar spirocycles (which are close in structure to compounds **6**—**8**) that contain[9] 2,4-dinitrophenyl and 3,5-dinitropyridyl fragments instead of 4,6-dinitrobenzofuroxan one are much less stereorigid. Under the same conditions, the rate of their stereoconversion is 7—10 orders of magnitudes higher than that of compounds **6**—**8**, which confirms the superelectrophilic properties of DNBF and the unique stability of spiro-σ-complexes based on it.

Experimental

The ^1H NMR spectra were recorded on a Varian Unity-300 instrument (300 MHz) with tetramethylsilane as the internal standard. Kinetic and activation parameters of rearrangements were determined by analyzing the temperature dependence of the shape of lines of methylene groups in the ^1H NMR spectra (see Fig. 1) using computer simulation of a shape of the line of the indicator proton on a Varian-620L

Table 1. The parameters of the ^1H NMR spectra of the compounds synthesized

Compound	Solvent	^1H NMR, δ, J/Hz
3	Aceton-d_6	7.68 (s, 2 H, H(4,6)); 4.49 (s, 4 H, C(3,7)H_2); 4.38 (s, 2 H, C(5)H_2); 3.38 (s, 6 H, MeO(3,7)); 3.30 (s, 3 H, MeO(5))
4	$CDCl_3$	9.19 (s, 1 H, H(5')); 8.20 (s, 2 H, H(4,6)); 2.86 (s, 3 H, Me(5)); 2.69 (s, 6 H, Me(3,7))
5	$CDCl_3$	9.15 (s, 1 H, H(5')); 8.81 (s, 2 H, H(4,6)); 4.82 (s, 2 H, C(5)H_2); 4.74 (d, 2 H, C(3,7)H_2); 4.66 (d, 2 H, C(3,7)H_2, J_{CH_2HH} = 14.4); 3.60 (s, 3 H, Me(5)O); 3.58 (s, 6 H, Me(3,7)O)
	C_6D_5Br	9.38 (s, 1 H, H(5')); 8.60 (s, 2 H, H(4,6)); 4.67 (d, 2 H, C(3,7)H_2); 4.56 (d, 2 H, C(3,7)H_2, J_{CH_2HH} = 18.0); 4.28 (s, 2 H, C(5)H_2); 3.43 (s, 6 H, Me(3,7)O); 3.38 (s, 3 H, Me(5)O)
6	DMSO-d_6	8.80 (s, 1 H, H(5')); 8.40 (dd, 1 H, H(4)); 8.32 (d, 1 H, H(3)); 8.20 (dd, 1 H, H(6)); 7.90 (d, 1 H, H(7)); 7.81 (dd, 1 H, H(5), $J_{3,4}$ = 11.5, $J_{4,5}$ = 10.8, $J_{5,6}$ = 10.8, $J_{6,7}$ = 11.5); 7.1—7.2 (m, 5 H, Ph); 5.32 (d, 1 H, CH_2); 4.66 (d, 1 H, CH_2, J_{CH_2HH} = 18.0)
7	DMSO-d_6	8.74 (s, 1 H, H(5')); 8.35 (d, 1 H, H(3)); 8.11 (dd, 1 H, H(4)); 7.86 (dd, 1 H, H(6)); 7.82 (d, 1 H, H(7)); 7.68 (dd, 1 H, H(5), $J_{3,4}$ = 10.8, $J_{4,5}$ = 10.5, $J_{5,6}$ = 10.5, $J_{6,7}$ = 11.5); 7.05—7.25 (m, 5 H, Ph); 5.12 (d, 1 H, CH_2); 4.74 (d, 1 H, CH_2, J_{CH_2HH} = 18.0)
8	DMSO-d_6	8.79 (s, 1 H, H(5')); 7.92 (dd, 2 H, H(4,6)); 7.68 (d, 2 H, H(3,7)); 7.34 (dd, 1 H, H(5)); 7.0—7.2 (m, 10 H, 2 Ph); 5.03 (d, 2 H, 2 CH_2); 4.47 (d, 2 H, 2 CH_2, J_{CH_2HH} = 17.0)

Table 2. The kinetic and activation parameters of the enantiotopomerization of compounds 5—8

Compound	Solvent	k_{298} /s^{-1}	$\Delta G^{\neq}_{298}$ /kJ mol^{-1}	$\Delta H^{\neq}$ /kJ mol^{-1}	$\Delta S^{\neq}$ /J $mol^{-1} \cdot deg^{-1}$
5	C_6D_5Br	$1.7 \cdot 10^{-2}$	83.0	58.2	−20.0
6	DMSO-d_6	$5.0 \cdot 10^{-5}$	97.6	97.6	0.0
7	DMSO-d_6	$<10^{-9}$	>110	—	—
8	DMSO-d_6	$<10^{-9}$	>110	—	—

computer. Melting points, yields, and data of elemental analysis are given in Table 3. The solvents used were purified according to standard procedures.

3,5,7-Tris(methoxymethyl)tropolone (3). A mixture of 3,5,7-tris(hydroxymethyl)tropolone[11] (6.36 g, 0.03 mol), Me_2SO_4 (14 mL, 0.15 mol), 50 mL of 50% aqueous KOH solution, 50 mL of CH_2Cl_2, and triethylbenzylammonium chloride (0.7 g, 10 mol. %) was stirred vigorously at ~20 °C for 12 h. The mixture was then poured into 200 mL of ice water, acidified with AcOH to pH 4—5, and extracted with ether (3×50 mL). The extract was washed with water, dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel 40/100, $CHCl_3$) and recrystallized from petroleum ether.

Dipolar spirocomplex 4. A mixture of the thallium salt of 3,5,7-trimethyltropolone[11] (0.2 g, 0.5 mmol) obtained according to the known procedure,[12] 7-chloro-4,6-dinitrobenzofuroxan[13] (0.14 g, 0.5 mmol), and 10 mL of toluene was refluxed for 1 h. After cooling, the precipitate containing the reaction product and TlCl was filtered off. Three mL of $CHCl_3$ was added, and TlCl was separated by filtration. Yellow crystals of **4** were isolated from the filtrate by chromatography (silica gel 40/100, $CHCl_3$).

Dipolar spirocomplex 5. A mixture of the thallium salt of 3,5,7-tris(methoxymethyl)tropolone **3** (0.25 g, 0.55 mmol) obtained according to the known procedure,[12] 7-chloro-4,6-dinitrobenzofuroxan (0.145 g, 0.55 mmol), and 10 mL of MeCN was refluxed for 0.5 h. The precipitate of TlCl was separated by filtration, and the filtrate was concentrated *in vacuo*. The residue was purified twice by column chromatography (silica gel 40/100, MeCN—$CHCl_3$, 1 : 6).

Table 3. The characteristics of compounds 3—8

Compound	Yield (%)	M.p. /°C	Found / Calculated (%) H	N	C	Molecular formula
3	33	92	61.20	7.18	—	$C_{13}H_{18}O_5$
			61.41	7.13	—	
4	35	260—263 (decomp.)	49.65	3.07	14.26	$C_{16}H_{12}N_4O_8$
			49.49	3.12	14.43	
5	75	186—188 (decomp.)	48.02	3.68	11.50	$C_{19}H_{18}N_4O_{11}$
			47.77	3.79	11.71	
6	40	277—280 (decomp.)	55.42	3.14	15.87	$C_{20}H_{13}N_5O_7$
			55.18	3.01	16.09	
7	85	302—305 (decomp.)	53.10	2.74	15.67	$C_{20}H_{13}N_5O_6S$
			53.22	2.90	15.51	
8	90	308—310 (decomp.)	61.72	3.53	16.30	$C_{27}H_{20}N_6O_6$
			61.83	3.84	16.02	

Dipolar spirocomplex 6. A mixture of 7-chloro-4,6-dinitrobenzofuroxan (0.1 g, 0.4 mmol), 2-benzylaminotropone (0.08 g, 0.4 mmol),[14] and 5 mL of MeCN was refluxed for 0.5 h. After cooling, the crystals formed were separated by filtration and dissolved in 1 mL of DMSO, and the solution was poured into 10 mL of ice water. A yellow precipitate obtained was purified by column chromatography (Al_2O_3, $CHCl_3$).

The general procedure of the synthesis of spirocomplexes 7 and 8. A solution of 7-chloro-4,6-dinitrobenzofuroxan (0.04 mmol) and benzylaminothiotropone (0.08 mmol) or *N,N'*-dibenzylaminotroponimine[15] in 0.5 mL of $CHCl_3$ was applied as a narrow band onto the start line of a wide chromatographic plate with Al_2O_3. After 12 h, the reaction mixture was separated on the same plate in $CHCl_3$. After $CHCl_3$ was evaporated, an orange zone was collected, and the product was eluted with $CHCl_3$. Crystals obtained upon evaporation of $CHCl_3$ were washed with a minimal amount of benzene.

This work was financially supported by the Russian Foundation for Basic Research (Project Nos. 96-03-33902 and 96-03-32024).

References

1. R. J. Spear, W. P. Norris, and R. W. Read, *Aust. J. Chem.*, 1983, **36**, 297.
2. A. J. Boulton and D. P. Clifford, *J. Chem. Soc.*, 1965, 5414.
3. M. J. Strauss, A. De Fusco, and F. Terrier, *Tetrahedron Lett.*, 1981, **22**, 1945.
4. F. Terrier, E. Kizilian, J.-Cl. Halle, and E. Buncel, *J. Am. Chem. Soc.*, 1992, **114**, 1740.
5. V. N. Drozd and V. N. Knyazev, *Zh. Org. Khim.*, 1995, **31**, 3 [*Russ. J. Org. Chem.*, 1995, **31** (Engl. Transl.)].
6. V. I. Minkin, L. P. Olekhnovich, and Yu. A. Zhdanov, *Molecular Design of Tautomeric Compounds*, Reidel Dordrecht, Boston—Tokyo, 1988.
7. L. P. Olekhnovich, S. V. Kurbatov, A. V. Lesin, Z. N. Budarina, Yu. A. Zhdanov, and V. I. Minkin, *Zh. Org. Khim.*, 1991, **27**, 6 [*J. Org. Chem. USSR*, 1991, **27** (Engl. Transl.)].
8. S. V. Kurbatov, Z. N. Budarina, L. P. Olekhnovich, N. G. Furmanova, A. V. Lesin, O. E. Kompan, L. M. Yagupol'skii, V. I. Minkin, and Yu. A. Zhdanov, *Zh. Org. Khim.*, 1988, **24**, 913 [*J. Org. Chem. USSR*, 1988, **24** (Engl. Transl.)].
9. L. P. Olekhnovich, Z. N. Budarina, A. V. Lesin, S. V. Kurbatov, G. S. Borodkin, and V. I. Minkin, *Mendeleev Commun.*, 1994, 162.
10. S. Toyota and M. Oki, *Bull. Chem. Soc. Jpn.*, 1991, **64**, 1563.
11. T. Nozoe, T. Mikai, and K. Takase, *Science Rep. Tohoku Univ.*, 1952, **36**, 40; *Chem. Abstrs.*, 1954, **48**, 3964d.
12. L. P. Olekhnovich, S. V. Kurbatov, Z. N. Budarina, V. I. Minkin, and Yu. A. Zhdanov, *Zh. Org. Khim.*, 1985, **21**, 2550 [*J. Org. Chem. USSR*, 1985, **21** (Engl. Transl.)].
13. W. P. Norris and R. J. Spear, *Heterocycles*, 1984, **22**, 271.
14. N. Soma, J. Nakazawa, T. Watanabe, Y. Sato, and G. Sunagawa, *Chem. Pharm. Bull.* (Tokyo), 1965, **13**, 457.
15. C. E. Forbes and R. H. Holm, *J. Am. Chem. Soc.*, 1970, **92**, 2297.

Received February 11, 1997