Standard enthalpies of formation of some N-spiranes

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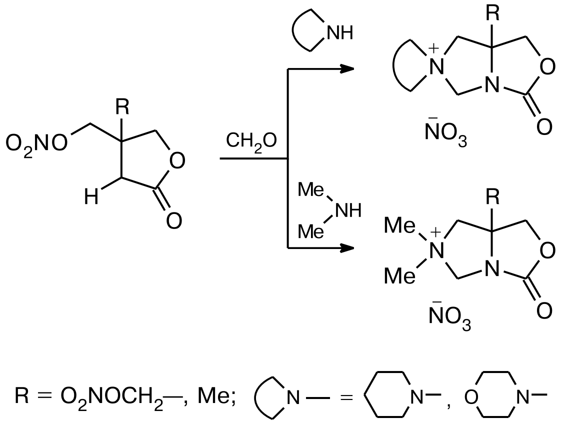
The heats of combustion of three compounds, members of a new series of N-spiranes were measured by combustion calorimetry. The molecules of the title compounds comprise condensed and N-spirofused heterocycles as well as nitroxy groups that are both NO-donors and explosophores. The enthalpies of formation and the heats of explosive transformation of these compounds are calculated. Two compounds belong to explosives with low heat of explosive transformation, whereas the third compound is inert.

Key words: N-spiranes, condensed heterocycles with nitroxyl groups, standard enthalpies of formation.

A large number of N-spiranes exhibit various types of activity including antitumorigenic one.[1,2] Recently, a new series of quaternary ammonium salts including N-spiranes was reported.[3,4] Compounds of this series were obtained by *N*-aminomethylation of heterocyclic NH-acids containing α-nitroxymethyl substituents (Scheme 1).

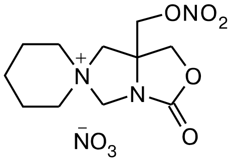
Scheme 1



A distinctive structural feature of these compounds is that their molecules contain fused cationic heterocycles bearing nitroxy groups (potential donors of nitrogen oxide). Since such groups show not only biological activity, but are also explosophores, explosive properties in some compounds can be expected as in the case of traditionally used cardiovascular drugs nitroglycerin, nitrosorbide, and erynitum.

The heat of explosive transformation is an important characteristic of the explosive properties of compounds. The heats of explosive transformation can be frequently used to assess the degree of hazard associated with technological operations with corresponding substances. The heat of explosive transformation can be quite accurately calculated based on the enthalpy of formation.[5] Despite the fact that it was proposed to use N-spiranes as components of propellants,[6] no information on the thermochemical and/or explosive properties of compounds containing N-spirane rings is available in the literature.

The aim of this work was to determine the standard enthalpies of formation and the impact sensitivities (IS) and to calculate the heats of explosive transformation of 6,6-pentamethylene-7a-(nitroxymethyl)-3-oxoperhydroimidazo[1,5-*c*]oxazol-6-ium nitrate (**1**), 6,6-(tetramethylene-3´-oxa)-7a-(nitroxymethyl)-3-oxoperhydroimidazo[1,5-*c*]oxazol-6-ium nitrate (**2**), and 6,6-(tetramethylene-3´-oxa)-7a-methyl-3-oxoperhydroimidazo[1,5-*c*]oxazol-6-ium nitrate (**3**).



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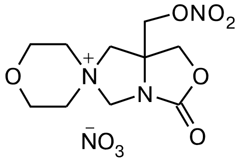

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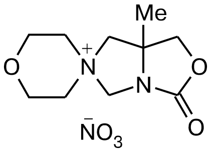

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Experimental

The enthalpies of formation of compounds **1**—**3** were determined based on the experimentally determined heats of combustion of these substances in oxygen in an automated calorimeter with isothermal jacket. The initial temperature of the main period of experiments was 25.00±0.02 °C. The changes in the temperature of the calorimeter were measured by a resistance thermometer with an accuracy of ±0.0001 °C. The temperature of water in the external jacket was 27.00±0.002 °C. The calorimeter was calibrated using a K-1 benzoic acid reference sample (nominal heat of combustion is $Q = 26417.8 \pm 3.8$ J g^{-1}). All experiments were carried out using a bomb preliminarily filled with 1 mL of distilled water at an oxygen pressure in the bomb equal to $p = 2.94$ MPa. After the completion of an experiment, the bomb was opened and washed with distilled water. The number of moles of nitric acid formed in a side reaction from nitrogen, oxygen, and water was determined by titration of the solution thus obtained by 0.1 *M* KOH solution using phenolphthalein as indicator. Based on the results of analyses, a correction to the heat of combustion was made which takes into account the formation of nitric acid from the reaction products. The samples were weighed on a VLR-20 balance with an error of $2.5 \cdot 10^{-5}$ g.

The experimentally determined heat capacity of the calorimeter W was $(363.6 \pm 1.8) \cdot 10^{-4}$ J (arb. deg)$^{-1}$ in the experiments on the determination of the heats of combustion of compounds **1** and **3** and $(363.9 \pm 1.3) \cdot 10^{-4}$ J (arb. deg)$^{-1}$ in the experiments on the determination of the heat of formation of compound **2**. The error for a 95% confidence interval was calculated from the relation

$$\sigma = k\sqrt{\sum x^2/[n(n-1)]},$$

where x is the deviation of each result from the average value, n is the number of runs, and k is the Student coefficient.

The results of measurements of the heats of combustion and standard enthalpies of formation of compounds **1**—**3** are listed in Table 1.

The change in the internal energy ΔU_i upon combustion of compound **2** at constant volume at 25 °C was calculated using the equation[7]

$$-\Delta U_\mathrm{i} = (W\Delta T - q_\mathrm{cf} - q_\mathrm{b} - q_{\mathrm{HNO_3}})/m,$$

where m is the weight of the substance reduced to its actual value *in vacuo* by applying the buoyancy correction; ΔT is the experimentally measured temperature rise in the calorimeter due to combustion of the compound under study corrected for heat exchange between the calorimetric system and the jacket of the calorimeter (Regnault—Pfaundler correction,[8] expressed in arb. deg); q_cf is the energy of combustion of a cotton filament; q_b is the ignition energy; and q_{HNO3} is the correction for the heat of formation of nitric acid from the reaction products, which is calculated as the product of the heat of formation of a mole of a nitric acid solution by the number of moles of nitric acid found in the bomb by titration. The corrections mentioned above were calculated using the following published data: 16.336 kJ g^{-1} for the heat of combustion of cotton filament[9] and 59.789 kJ mol^{-1} for the heat of formation of nitric acid solution in the bomb.[9]

Combustion of compound **2** is described by the following equation:

$$\mathrm{C_{10}H_{16}N_4O_9\,(cr) + 9.5\,O_2\,(g) =}$$
$$\mathrm{= 8\,H_2O\,(l) + 10\,CO_2\,(g) + 2\,N_2\,(g),}$$

where cr, g, and l denote the crystalline, gas, and liquid state, respectively.

From the average value of ΔU_i for compound **2** we calculated the standard enthalpies of combustion and formation of this substance ($\Delta H^\circ_\mathrm{comb}$ and $\Delta H^\circ_\mathrm{f}$, respectively): $R_\mathrm{W} = 4.31$ kJ mol^{-1}, $\Delta nRT = 6.17$ kJ mol^{-1}, $\Delta H^\circ_\mathrm{comb} = -(5384.8 \pm 36)$ kJ mol^{-1}, $\Delta H^\circ_\mathrm{f} = -(837 \pm 36)$ kJ mol^{-1}, where R_W is the Washburn correction to the enthalpy of combustion (Washburn correction to standard state),[10] ΔnRT is the correction for the work of gas expansion in the bomb, Δn is the difference between the number of moles of gas in the right and left parts of the chemical equation describing the combustion of a mole of the substance under study. In accordance with the equation of combustion of compound **2** one gets $\Delta n = 2.5$.

The $\Delta H^\circ_\mathrm{comb}$ value was calculated using the equation

$$\Delta H^\circ_\mathrm{comb} = \Delta U_\mathrm{i} + \Delta nRT + R_\mathrm{W}.$$

The $\Delta H^\circ_\mathrm{f}$ values of the compounds under study were calculated using the following values of the standard enthalpies of formation of some known compounds: $\Delta H^\circ_\mathrm{f}(\mathrm{CO_2}^{(\mathrm{g})}) = -393.505$ kJ mol^{-1},[11] $\Delta H^\circ_\mathrm{f}(\mathrm{H_2O}^{(\mathrm{l})}) = -285.838$ kJ mol^{-1}.[11]

The changes in the internal energy upon combustion of compounds **1** and **3** at constant volume and 25 °C were calculated from the equation

$$-\Delta U_\mathrm{i} = (W\Delta T - q_\mathrm{cf} - q_\mathrm{b} - q_{\mathrm{HNO_3}} - q_\mathrm{sub})/m,$$

where q_sub is the correction for the heat of combustion of an auxiliary compound (dimethylphthalate and benzoic acid for combustion of compounds **1** and **3**, respectively). The q_sub value for compound **1** was calculated using the energy of combustion of dimethylphthalate measured in a separate series of experiments and equal to 24.089 kJ g^{-1}.

Table 1. Physicochemical properties of compounds **1**—**3**

Compound	Empirical formula	M.p./°C (with decomp.)	Picnometric density /g cm^{-3}	$-\Delta H^\circ_\mathrm{comb}$	$-\Delta H^\circ_\mathrm{f,exp}$	$-\Delta H^\circ_\mathrm{f,calc}$	Q_expl /kJ kg^{-1}	IS (%)
				kJ mol^{-1}				
1	$\mathrm{C_{11}H_{18}N_4O_8}$	137	1.51	6166.4±9.0	735±9.0	740.1	2930	96
2	$\mathrm{C_{10}H_{16}N_4O_9}$	170	1.64	5384.8±36	837±36	841.8	3310	100
3	$\mathrm{C_{10}H_{17}N_3O_6}$	208	1.49	5587.5±3.5	778±3.5	752.7	2180	0

Combustion of compound **1** is described by the following reaction equation:

$$C_{11}H_{18}N_4O_8\,(cr) + 11.5\,O_2\,(g) =$$
$$= 9\,H_2O\,(l) + 11\,CO_2\,(g) + 2\,N_2\,(g),$$

R_W = 3.88 kJ mol^{-1}, ΔnRT = 3.70 kJ mol^{-1}, $\Delta H°_{comb}$ = = –(6166.4±9.0) kJ mol^{-1}, and $\Delta H°_f$ = –(734.8±9.0) kJ mol^{-1}.

Combustion of compound **3** is described by the following reaction equation:

$$C_{10}H_{17}N_3O_6\,(cr) + 11.25\,O_2\,(g) =$$
$$= 8.5\,H_2O\,(l) + 10\,CO_2\,(g) + 1.5\,N_2\,(g),$$

R_W = 3.51 kJ mol^{-1}, ΔnRT = 0.62 kJ mol^{-1}, $\Delta H°_{comb}$ = = –(5587.5±3.5) kJ mol^{-1}, and $\Delta H°_f$ = –(777.7±3.5) kJ mol^{-1}.

To evaluate the contributions of interactions between functional groups to the enthalpies of formation of the compounds under study, the $\Delta H°_{f,calc}$ values were calculated using the group additivity scheme for organic substances in the condensed state with allowance for the ring corrections.[12–14] The contribution of the fragment $N^+NO_3^-$(4C) preliminarily estimated from the heats of formation of dimethylammonium nitrate, trimethylammonium nitrate, and tetramethylammonium nitrate equals –142.3 kJ mol^{-1}. Based on this value, the calculated enthalpies of formation compounds of **1**, **2**, and **3** are –740.1, –841.8, and –752.7 kJ mol^{-1}, respectively.

The heat of explosive transformation Q_{expl}, which correlates with the calorimetric heat of explosion under the conditions of quenching equilibrium reactions between the explosion products, was calculated from the relation[5]

$$Q_{expl} = K_r Q_{max},$$

where Q_{max} is the maximum possible heat of explosion for a given explosive and K_r is the realization coefficient. The initial data for Q_{max} calculations include the empirical formula of an explosive, the enthalpy of its formation, the charge density, and the scheme of formation of explosion products.[15] The coefficient K_r is calculated from the oxygen balance for the explosive and the composition of explosion products[16] which takes into account the equilibrium constant of water gas.

The IS as a confirmation of explosiveness or inertness of the compound studied was determined according to state standart (GOST 4545-88). The Q_{expl} and IS values obtained are listed in Table 1.

Results and Discussion

There are two essential aspects of the present study. On the one hand, our aim was to obtain thermochemical data for the N-spiranes synthesized. On the other hand, a practical aspect of the work was to assess the risk of explosion when working with compounds whose molecules contain explosophores.

According to the results of determination of the IS values and heats of explosive transformation (see Table 1), compound **3** (Q_{expl} = 2180 kJ kg^{-1}) containing no nitroxy groups can be considered inert, whereas compounds **1** and **2** can be treated as explosives with low heats of explosive transformation (Q_{expl} = 2930 and 3310 kJ kg^{-1}, respectively). Compounds **1** and **2** are characterized by a high IS (see Table 1); this is quite unexpected because the corresponding Q_{expl} values are relatively low. The IS values of **1** and **2** approach those of such polynitrate high-explosives as pyroxylin (100%) and pentaerythrytol tetranitrate (100%)[17] whose Q_{expl} values (4600 and 6120 kJ kg^{-1}, respectively)[18] are much larger than those of compounds **1** and **2**. To date, no solid explanation for this fact can be offered. One can assume that the increased IS values of compounds **1** and **2** can be due to, *e.g.*, specific features of the molecular packing in the crystal lattice. Elucidation of the nature of this phenomenon deserves additional investigations.

If the search for new pharmaceuticals involves the synthesis of N-spiranes similar to those described above, one should (i) take special care when working with such compounds and (ii) study the possibility to design molecules with nitroxy groups in such a manner that their ability to undergo explosive transformation be reduced. In this connection, it seems realistic to introduce some substituents into molecules in order to reduce the oxygen balance and, thus, Q_{expl}.

Summing up, we have experimentally determined and calculated the standard enthalpies of formation of N-spiranes **1**—**3** using the group additivity scheme. Good agreement between theory and experiment suggests no contribution from the interactions between functional groups in the molecules of the compounds under study. Using the experimentally determined $\Delta H°_f$ values, we calculated the heats of explosive transformation of the N-spiranes studied. Compounds **1** and **2** whose molecules contain a nitroxy group should be treated as explosives with low heats of explosive transformation. Correctness of this consideration is confirmed by high IS values.

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