QSPR approach to the calculation of rate constants of homolysis of nitro compounds in different states of aggregation

1. The gas phase

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A method for the theoretical estimation and prediction of rate constants of homolysis of nitro compounds of different chemical classes in the gas phase is proposed on the basis of the QSPR approach.

Key words: QSPR approach; rate constants; nitro compounds, homolysis, gas phase.

Earlier[1] a method for the theoretical estimation of the activation energy of the homolysis of C—N and N—N bonds of nitro compounds of different chemical classes was proposed on the basis of the QSPR (Quantitative Structure—Property Relationships) approach. Nevertheless, to obtain complete information concerning these reactions data on the preexponential factor in the Arrhenius equation for the homolysis are required. In principle, this parameter may be calculated using the vibration spectra of the transition state formed during elementary homolytic decay of the molecules. However, these calculations are very time consuming and do not have enough accuracy. Moreover, the problem of the inclusion of temperature in calculations of the rate constant of homolysis still remains unsolved. We believe that the QSPR approach could be an alternative to such calculations.

The question concerning the estimation and the prediction of the Arrhenius preexponential factor for homolysis of nitro compounds also still remains open.[1] It is known[2—9] that the logarithm of this parameter is usually varied within the range of 13—18, while the error of its calculation is equal to 1—2. These facts prevent one from calculating log A with sufficient accuracy because the calculation error is comparable to the range in which this parameter is varied. Therefore, it seems appropriate to develop a direct method for calculation of the rate constants of homolysis of nitro compounds, which is the key parameter of their thermal stability. This permits us to reveal a relationship between the chemical structure of nitro compounds of different chemical classes (aliphatic and aromatic nitro compounds, cyclic and acyclic nitramines, nitroesters, nitrates, *etc.*) and the rate constants (k) of the homolysis of C—N and N—N bonds, the radical cleavage of these bonds being the primary step of their thermolysis.

The experimental data base used for the construction of "structure—log k" models consisted of 69 compounds in the training set (Table 1) and of 10 compounds in the test set (Table 2). As previously,[1] the EMMA (Efficient Modeling of Molecular Activity) program package was used. The values of log k were recomputed using the Arrhenuis equation and the average temperature of homolysis of compounds studied (420 K).

About 3000 descriptors were computed for each structure. A set of descriptors includes topologycal indices (molecular connectivity indices, indices of molecular shape, modified Wiener indices, *etc.*); information indices (SIC_i, TIC_i, CIC_i) that are functions of charge distribution in molecules (atomic charges were calculated by the Gastieger method[10]); indices based on electronegativities of atoms; indices based on substructures; *etc.*[11] After the computed descriptors were analyzed and pairwisely highly correlated and low variable descriptors were removed a set of alternative models allowed us to calculate log k for compounds from the training set with sufficient accuracy; models were constructed based on the remaining descriptors. Finally, on the basis of compounds from the test set that had not been used for the models' construction we selected models with the lowest prediction error of log k.

Data on "structure—log k" correlations obtained using one of the most stable regression models are shown in Fig. 1. The model is constructed on 11 descriptors and is represented by the Eq. (1).

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Table 1. Experimental and calculated log *k* for homolysis of nitro compounds in the gaseous state (from the training set[14–28])

Compound	Empirical formula	−log*k*		References
		calculated	experimental	
Nitromethane	CH_3NO_2	8.4	7.8	14
Nitrotrichloromethane	CNO_2C_5	−0.2	0.3	14
Dinitrofluoromethane	$CHN_2O_4F_4$	2.0	3.6	14
Dinitrochloromethane	CHN_2O_4Cl	1.4	0.8	14
Dinitrodichloromethane	$CN_2O_4Cl_2$	0.1	−0.8	14
Dinitrofluorochloromethane	CN_2O_4FCl	1.9	1.7	14
Dinitrofluorobromomethane	CN_2O_4FBr	1.6	1.2	14
Dinitrofluoroiodomethane	CN_2O_4FI	1.4	0.9	14
Dinitrodifluoromethane	$CN_2O_4F_2$	2.5	3.9	14
Dinitrofluoromethyldifluoramine	$CN_3O_4F_3$	1.2	1.8	14
Dimethyldinitromethane	$C_3H_6N_2O_4$	2.6	2.6	15
Trinitrofluoromethane	CN_3O_6F	1.1	2.1	14
Trinitrochloromethane	CN_3O_6Cl	−0.13	−0.4	16
Trinitrobromomethane	CN_3O_6Br	−1.1	−0.9	14
Trinitroiodomethane	CN_3O_6I	−1.13	−0.8	14
Trinitromethylthiomethane	$C_2H_3N_3O_6S$	−3.6	−3.2	17
Tetranitromethane	CN_4O_8	−0.8	−0.3	14
1-Nitro-1,1-dichloroethane	$C_2H_3NO_2Cl_2$	2.8	2.6	14
1,1-Dinitroethane	$C_2H_4N_2O_4$	3.2	3.1	14
1,1-Dinitro-1-chloroethane	$C_2H_3N_2O_4Cl$	1.1	0.9	18
1,1-Dinitro-1-methylthioethane	$C_3H_6N_2O_4S$	0.8	0.8	17
1,1-Dinitro-1-methylsulfoethane	$C_3H_6N_2O_6S$	1.1	1.2	
1,1,1-Trinitroethane	$C_2H_3N_3O_6$	0.13	0.9	14
1,1,2,2-Tetranitro-1,2-difluoroethane	$C_2N_4O_8F_2$	0.7	−0.3	14
Pentanitrofluoroethane	$C_2N_{13}O_{10}F$	−0.8	−1.9	14
Hexanitroethane	$C_2N_6O_{12}$	−0.9	−2.2	14
1,1-Dinitropropane	$C_3H_6N_2O_4$	2.6	2.6	14
1,1,1-Trinitropropane	$C_3H_{13}N_3O_6$	0.2	0.8	14
2,1,1-Trinitro-3-bromopropane	$C_3H_4N_3O_6Br$	0.1	0.3	17
1,1-Dinitrobutane	$C_4H_8N_2O_4$	2.7	3.2	14
1,1,1-Trinitrobutane	$C_4H_7N_3O_6$	0.4	0.6	14
4,4,4-Trinitrobutyronitrile	$C_4H_4N_4O_6$	0.3	0.13	19
3,3,3-Trinitropropyl methyl ketone	$C_{13}H_7N_3O_7$	0.1	0.13	17
Methyl(4,4,4-trinitro)butyrate	$C_{13}H_7N_3O_8$	0.4	0.3	19
1-Methoxy-3,3,3-trinitro-2,2-dimethylbutane	$C_7H_{11}N_3O_7$	−1.7	−0.4	19
Trinitromethylthiobenzene	$C_7H_5N_3O_6S$	−3.8	−2.7	17
1-(Trinitromethylthio)-2,4-dinitrobenzene	$C_7H_3N_5O_{10}S$	−1.6	−3.0	17
1,1-Dinitroethylsulfobenzene	$C_8H_8N_2O_6S$	3.3	2.8	17
(1,1-Dinitroethylthio)benzene	$C_8H_8N_2O_4S$	−1.7	−1.6	17
2-Nitropyridine	$C_5H_4N_2O_2$	12.0	11.3	20
4-Nitropyridine	$C_5H_4N_2O_2$	12.1	11.6	20
2-Amino-5-nitropyridine	$C_5H_5N3O_2$	12.13	12.0	20
3,5-Dinitropyridine	$C_5H_3N_3O_4$	11.2	10.8	20
Nitrobenzene	$C_6H_5NO_2$	12.4	11.9	20
p-Nitrochlorobenzene	$C_6H_4NO_2Cl$	11.8	12.6	21
o-Nitrochlorobenzene	$C_6H_4NO_2Cl$	11.8	11.2	21
p-Nitrobromobenzene	$C_6H_4NO_2Br$	11.7	12.8	21
m-Nitrobromobenzene	$C_6H_4NO_2Br$	11.7	12.3	21
p-Nitroiodobenzene	$C_6H_4NO_2I$	11.6	12.5	21
m-Nitrophenol	$C_6H_5NO_3$	12.5	12.4	21
m-Nitroaniline	$C_6H_6N_2O_2$	12.8	20.6	21
p-Nitroaniline	$C_6H_6N_2O_2$	12.8	13.3	21
m-Nitrotoluene	$C_7H_7NO_2$	9.8	11.5	22
p-Nitrotoluene	$C_7H_7NO_2$	9.8	11.3	21
2-Nitrodiphenyl	$C_{12}H_9NO_2$	11.3	10.3	21
3-Nitrodiphenyl	$C_{12}H_9NO_2$	10.6	9.1	21
4-Nitrodiphenyl	$C_{12}H_9NO_2$	10.6	10.4	21
Methyldinitramine	$CH_3N_3O_4$	−2.3	−2.7	23
Dimethyldinitramine	$C_2H_6N_2O_8$	2.13	2.6	24

Table 1. (*Continued*)

Compound	Empirical formula	$-\log k$ calculated	$-\log k$ experimental	References
n-Propyldinitramine	$C_3H_7N_3O_6$	−2.9	−3.4	23
N-Nitrotetrahydroxazine	$C_4H_4N_2O_3$	1.7	0.8	24
Diethylnitramine	$C_4H_{10}N_2O_2$	2.7	2.3	24
n-Butyldinitramine	$C_4H_9N_3O_4$	−2.8	−3.1	23
1-Nitropiperidine	$C_5H_{10}N_2O_2$	2.13	2.8	24
Methyl nitrate	CH_3NO_3	1.8	2.1	25
1,3,5,7-Tetraaza-1,3,5,7-tetranitrocyclooctane	$C_4H_8N_8O$	1.4	3.1	24
1,2-Ethyl dinitrate	$C_2H_4N_2O_6$	0.6	0.6	26
1,2-Propyl dinitrate	$C_3H_6N_2O_6$	0.4	0.4	27
1,4-Butene-2 dinitrate	$C_4H_6N_2O_6$	1.7	0.7	27

Table 2. Experimantal and calculated log *k* for homolysis of nitro compounds in the gaseous state (from the test set[16,28])

Compound	Empirical formula	$-\log k$ calculated	$-\log k$ experimental
Trinitromethane	CHN_3O_6	−0.2	1.8
1,1-Dinitro-1-fluoroethane	$C_2H_3N_2O_4F$	2.9	3.0
1,1-Dinitro-1-bromoethane	$C_2H_3N_2O_4Br$	0.9	0.8
1-Nitro-1,1-dichloropropane	$C_3H_5NO_2Cl_2$	2.9	2.8
N,N,N′,N′-Tetrafluoro-2-(3,3-dinitro-3-fluoropropyl)-2-methylmethylenediamine	$C_5H_7N_4O_4F_5$	3.3	2.8
1-(1,1-Dinitroethylthio)-2,4-dinitrobenzene	$C_8H_6N_4O_8$	−0.8	−1.8
m-Nitrochlorobenzene	$C_6H_4NO_2Cl$	11.7	12.0
Ethyldinitramine	$C_2H_{13}N_3O_4$	−3.1	−3.0
1,3,5-Trinitrohexahydro-1,3,5-triazine	$C_3H_6N_6O_6$	0.8	1.4
Ethyl nitrate	$C_2H_{13}NO_3$	0.9	0.5

$$\begin{aligned}\log k = {} & -6.92 - 0.56\mathrm{SDM_H} + 0.96\,{}^3\chi_c^s - 18.45\sum_{\mathrm{fr_1}}(\max q_\mathrm{H}) + \\ & + 1.77\sum_{\mathrm{fr_2}}(\sum \mathrm{S}_i) - 0.53\max_{\mathrm{fr_3}}(\sum \mathrm{S}_i) - 0.73\max_{\mathrm{fr_4}}(\sum \mathrm{S}_i) + \\ & + 0.41\min_{\mathrm{fr_5}}(\sum \mathrm{S}_i) + 0.06\sum_{\mathrm{fr_6}}(\sum \mathrm{S}_i) - 0.12\max_{\mathrm{fr_7}}(\sum \mathrm{S}_i) + \\ & + 0.37\max_{\mathrm{fr_8}}(\sum \mathrm{S}_i) + 26.05\sum_{\mathrm{fr_9}}(\sum q),\end{aligned} \tag{1}$$

$$n = 83,\ R = 0.99,\ s = 0.87,\ F = 265,\ \Delta = 0.62,$$

where *n* is the number of structures in the training set; *R* is the correlation coefficient; *s* is the standard deviation; *F* is the Fischer criterion; Δ is the average square error; $\mathrm{SDM_H}$ is the sum of differences between the electronegativities of nonhydrogen and adjacent hydrogen atoms (the sum is taken over all atom—H bonds); ${}^3\chi_c{}^s$ is the solvation index of the third order[12]; S_i is the sum of electrotopological states of atoms in fragment fr_i; Σ is the sum for all fragments (fr) in the molecule; max and min are the highest and lowest values for all fragments (fr) in the molecule, respectively; $\max\limits_{\mathrm{fr}}$ is the highest value for all atoms in the fragment (fr) in the molecule; $\sum\limits_{\mathrm{fr}}$ is the sum for all atoms in the fragment (fr) in the molecule.

Fragments used in the model are given below (· is an arbitrary nonhydrogen atom):

$$-\mathrm{C}-\mathrm{C}-\mathrm{N}- \qquad \mathrm{fr_1}$$

$$-\mathrm{C}-\mathrm{NO_2} \qquad \mathrm{fr_2}$$

$$-\mathrm{C}-\mathrm{N}{=}\mathrm{O} \qquad \mathrm{fr_3}$$

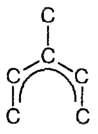
$$-\mathrm{N}-\mathrm{C}-\mathrm{N}{=}\mathrm{O} \qquad \mathrm{fr_4}$$

$$\cdot-\cdot-\cdot\equiv\cdot \qquad \mathrm{fr_5}$$

$$-\mathrm{C}-\mathrm{S}-\mathrm{C}-\mathrm{N}{=}\mathrm{O} \qquad \mathrm{fr_6}$$

$$\cdot-\cdot-\cdot-\cdot\equiv\cdot \qquad \mathrm{fr_7}$$

$$-\cdot\equiv\cdot-\cdot-\cdot\equiv\cdot \qquad \mathrm{fr_8}$$



$\mathrm{fr_9}$

The results of log *k* calculations obtained using the best "structure—log *k*" model for nitro compounds from the training set are presented in Table 1. As can be seen the error in calculated log *k* values for 11 compounds from the experimental training set exceeds 1.

As a whole, from Eq. (1) follows that this model has a high value of the correlation coefficient and a low value of the average absolute error. Nine of eleven descriptors used in the model are the descriptors of electrotopological states of atoms in different fragments.

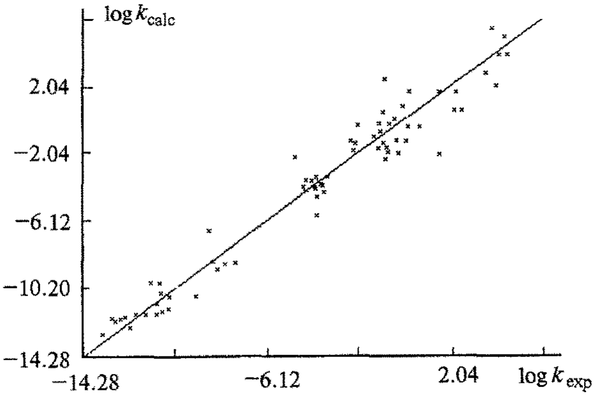


Fig. 1. Scattering diagram of experimental and recomputed $\log k$ for the training set involving 69 nitro compounds from different chemical classes.

They are known to reflect the electron density distribution at atoms. Obviously, for nitro compounds in the gas state these descriptors are of the most informative and determine the relationship between the structures and the rate constants of the homolysis of nitro compounds.

The prediction capability of the model was estimated on the basis of test compounds (Table 2) selected so as to represent compounds that belong to different chemical classes. According to data presented in Table 2 the model obtained shows a high prediction ability (see Eq. (1)). Only for one compound (trinitromethane) from the test set the prediction error of the rate constant of homolysis is considerable.

Thus a method for estimation and prediction of the rate constants of homolysis of nitro compounds of different chemical classes in the gas state is proposed on the basis of the QSPR approach, and the correlation model is obtained.

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