Brief Communications

On the relationship between the energy characteristics of the isodesmic reactions of polychlorinated dioxins and their toxicity

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Thermodynamic functions (ΔG_f and ΔH_f) of clorinated dibenzo-*p*-dioxins (Cl_nDD) with $n = 0$—8 were calculated at the DFT level of theory using the B3LYP functional and extended 6-31** basis sets and used to analyze possible relationship of the structures and energy characteristics of these compounds with their toxicity. A new sequence of successive isodesmic reactions, which makes it possible to calculate chemical potentials μ_G and μ_H from the ΔG_f and ΔH_f values, has been proposed. In the framework of this approach, satisfactory linear correlations between the chemical potentials μ and the logarithms of toxicity of the corresponding polychlorodioxins were obtained for the first time.

Key words: chlorobenzo-*p*-dioxins, structure, quantum chemical calculations, isodesmic reactions, thermodynamic potentials, toxicity.

Currently, one of the important ecological problems is the environmental pollution with the organic compounds that are resistant to various types of exposure and have a long period of decay. Polychlorinated dibenzo-*p*-dioxins (Cl_nDD), which are by-products of many industrial processes, belong to this type of compounds. Formation of Cl_nDD occurs in chemical processes in the temperature range from 200 to 650 °C, and the temperature range 200—450 °C is considered the most favorable for their formation.

Being well soluble in fats and organic solvents, Cl_nDD are capable to accumulate in human and animal tissues. Even in the amounts that are several orders of magnitude smaller than the doses causing acute poisoning (the minimum toxic dose is 0.5—1 μg kg^{-1} for humans),[1] chlorodioxins favor transformations of different synthetic and natural compounds to toxic substances.

Detection of dioxins in the environment and in biological objects is one of the most difficult analytical tasks. First of all, it is connected with high toxicity of Cl_nDD, which means that the limits of their detection in various matrices should be significantly lower than those typical of many organic analysis tasks, including detection of pesticides.[2]

The solution of this problem required the development and introduction to analytic practice of methods of separation and detection, which ensure the determination of picogram or even femtogram quantities of Cl_nDD against

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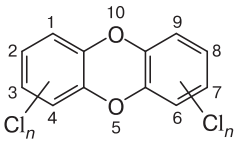
the background of substances present in the matrices in much higher concentrations. These methods include multistage sample preparation aimed at removing large amounts of interfering substances, which is followed by capillary GLC separation and detection using high-resolution or, less frequently, low-resolution mass spectrometry.[3,4]

Chemical analytical studies have shown that humans and animals are exposed to mixtures of various dioxins. For simple determination of the total biological activity of the mixtures, the concept of toxic dioxin equivalency factors (TEF) was developed in the late 1980s. Within the framework of this concept, Cl_nDD are characterized by an international toxicity coefficients (I-TEF) equal to the ratio between the toxicities of a particular compound and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-Cl_4DD), for which it is the largest. The overall toxicity of a Cl_nDD mixture is calculated as the sum of the products of the concentrations of particular compounds and the corresponding TEF values.

The purpose of the present study is the analysis of the relationship between the chemical compositions of dioxins and their toxicities using approximate calculated values of their chemical potentials.

Results and Discussion

The I-TEF values for the most toxic isomers of chlorinated dioxins were evaluated on the basis of the available data.[2,5] The logarithms of the toxicities of these compounds are presented in Table 1.



Chlorinated dioxins

To assess relative stabilities of Cl_nDD, we, like the authors of earlier studies,[6] have used isodesmic reactions.

Table 1. Logarithms of toxicities and energy characteristics of the most stable isomers of polychlorinated dioxins

Molecule	ln*I*	E_{tot}/a.u.[8]	$\Delta H_f/n$	$\Delta G_f/n$
			kcal mol^{-1}	
2-ClDD	—	−1072.133	0	0
2,7-Cl_2DD	−9.2	−1531.725	−0.12	0.70
2,3,7-Cl_3DD	−2.3	−1991.313	−1.11	1.27
2,3,7,8-Cl_4DD	0	−2450.900	−0.87	1.29
1,2,3,7,8-Cl_5DD	−0.7	−2910.484	−1.17	1.20
1,2,3,6,7,8-Cl_6DD	−2.3	−3370.067	−0.99	1.23
1,2,3,4,6,7,8-Cl_7DD	−4.6	−3829.650	−0.95	1.02
1,2,3,4,6,7,8,9-Cl_8DD	−6.9	−4289.232	−0.84	1.05

However, these reactions were considered not in statics, but in the development, *i.e.*, as a system of thermochemical equations in which each subsequent equation differs from the previous one by one chlorine atom. In fact, this allowed us to switch from the consideration of the correlation ratios between toxicities and thermodynamic functions of the compounds under consideration to approximate values of their chemical potentials, *viz.*, to the ratios $\Delta H/n$ and $\Delta G/n$, where n is the number of chlorine atoms in the chlorinated dioxin molecule.

The following reaction was taken as a starting approximation:

$$DD + ClDD \longrightarrow ClDD + DD.$$

Clearly, the ΔH_f and ΔG_f values for this reaction are equal to zero. Then, the reactions for $n = 1$—8 were analyzed:

$$Cl_nDD + ClDD \longrightarrow Cl_{n+1}DD + DD + \Delta H_f,$$

$$Cl_nDD + ClDD \longrightarrow Cl_{n+1}DD + DD + \Delta G_f.$$

In the right-hand part of the reaction equations, the number of chlorine atoms increases by one, and in the left-hand part it decreases by one. Therefore the total number of the C—Cl bonds in the left-hand and right-hand parts remains unchanged, *i.e.*, the reactions are isodesmic.

To our opinion, this type of isodesmic reactions makes it possible to take into account the presence of both aromatic rings and ether bridges in the chlorodioxin systems more correctly since their number in the right and left parts of the reactions is always the same in contrast to earlier works, where it was different.[6]

This also makes it possible to directly take into account changes in the thermodynamic characteristics due to the changes in the chlorine atom number.

Only most stable isomers of polychlorinated dioxins Cl_nDD ($n = 0$—8) were considered in the present study. Total energies (E_{tot}) of these isomers, which were calculated on the basis of the density matrixes using density functional theory (the B3LYP functional with the 6-31** basis sets)[7] with full optimization of geometric parameters are collected in Table 1. The specific enthalpy of a particular isodesmic reaction, $\Delta H_f/n$, where n is the number of chlorine atoms in the corresponding isomer (see Table 1), was considered as a relative energy stability of this isomer. This value can be regarded as an approximate value for the chemical potential $\mu_H = \delta H/\delta n$.

The specific Gibbs free energies, which, in analogy with the above, correspond to approximate values of the chemical potentials $\mu_G = \delta G/\delta n$ and were obtained using the same isodesmic reactions on the basis of the calculations of isolated molecules,[8] are also given in Table 1.

The graphs of dependencies of the logarithms of TEFs for a series of the Cl_nDD isomers on the μ_H и μ_G values

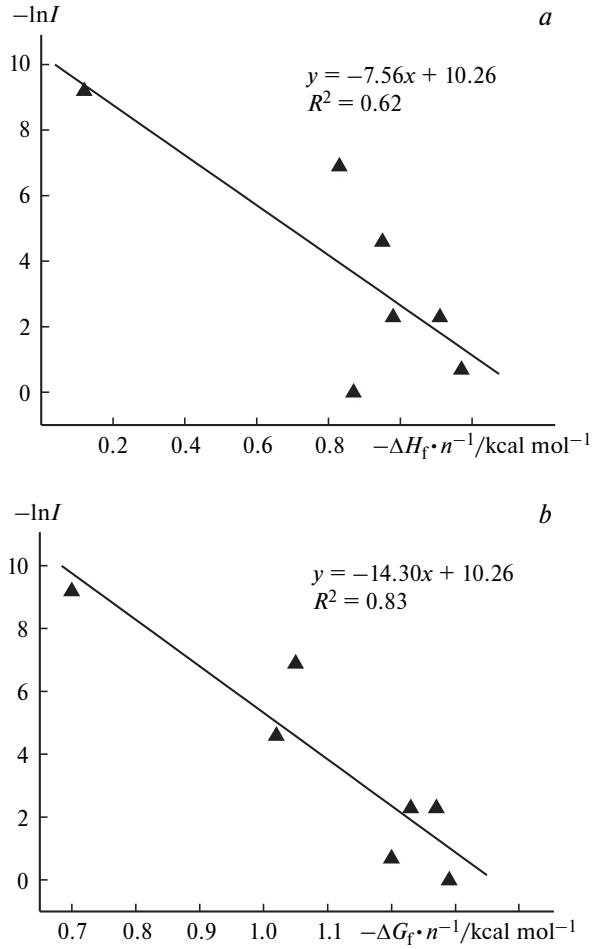


Fig. 1. Logarithms of toxicities of the Cl_nDD isomers *vs.* specific $\Delta H_f/n$ (*a*) and $\Delta G_f/n$ (*b*) values.

obtained from the corresponding isodesmic reactions were calculated by the least squares method and are shown in Fig. 1.

Correlation coefficients R^2 for enthalpies and Gibbs free energies are equal to 0.62 and 0.83, respectively, which exceeds the values of 0.59 and 0.74 that were obtained for wider object sampling, though using these thermodynamic functions themselves.[9] Note that the transition from μ_H to μ_G results in a significant increase in the R^2 values.

The obtained data indicate that the dependence of toxicity of the considered compounds on the approximate values of their chemical potentials is linear. As it follows from the experimental data, the most toxic isomer is that characterized by the maximum chemical potential ($n = 4$) in the framework of the suggested series of isodesmic reactions.

Thus, the present study is shown that there is a relationship between toxicity and chemical potentials μ_H and μ_G of chlorine atoms in the investigated series of compounds.

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