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Research Article

BIOLOGICAL ACTIVITY OF CHLORINATED COMPOUNDS AND INTERMOLECULAR INTERACTIONS

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Abstract

Biological activity of chlorinated compounds has been analyzed in relation to their electron parameters. It is established that the toxic and narcotic actions chlorinated chemical compounds due to their ability to intermolecular interactions. General regression equations are given for electron parameter – dependent changes in the bioactivity of molecules. Statistical comparison of qualitative indexes has revealed that the energetic parameters of the molecules that define the intermolecular interactions are the most informative characteristics of the chlorinated compounds responsible for the toxicity and narcotic effects. Molecular mechanisms of the toxic effect of chlorinated compounds are discussed in terms of intermolecular interactions. It is discussed the influence on bioactivity of the formation donor – acceptor complexes and hydrogen bonds.

Keywords: Biological activity, chlorinated compounds, toxicity, intermolecular interaction

INTRODUCTION

Recently, much attention is paid to seek different quantitative relations which link variations in the molecular structure of chemical compounds and their biological activity. For these purposes, commonly used either abstract statistical models (the mechanism of biological activity remains unsolved), or known physical and chemical conceptions of the behavior of chemical compounds in biological systems. In this study, we performed analysis of the dependence of the biological activity of derivatives of chlorobenzene on the number, type and position of substituent on the benzene ring. According to current knowledge the bioactivity of chemical compounds is determined by physical and chemical properties at the macroscopic level (solubility, distribution, permeability), as well as at the microscopic level (electronic parameters of molecules, conformational transitions). Analyzed a series of derivatives of chlorobenzene is interesting from the point of view that they are not involved in the metabolic transformations.

Analyzed a series of derivatives of chlorobenzene is interesting from the point of view that they are not involved in the metabolic transformations. In literature[1,2] attempts were made to obtain an equation that takes into account these effects and could describe the toxic properties of the homologous series. However, these equations were not informative even in the case of disubstituted benzenes. In addition, in papers[3,4] pointed out the difficulties of physical-chemical interpretation of constants, which are included in the equations.

MATERIALS AND METHODS

Hansch model is most propagation[5]. This model connects the bioactivity of chemical compounds with their lipophilic properties. In many practical cases, this model has proved useful. Therefore, we investigated whether a bioactivity (lethal dose of chlorine derivatives of benzene for rats after oral administration[6]) is due to the distribution of substance ($\pi = \log P$) in octanol - water. We will use the well-known equation of Hansch

$$A = B_0 + B_1\pi + B_2\pi^2, \quad (1)$$

here parameter $A = 1000 / LD_{50}$ is bioactivity; B_0, B_1 and B_2 are some parameters." Bioactivity values and values for the series of substituted benzenes are given in Table 1. It is important to note that the parameter of the hydrophobicity is linearly related to the information function of the molecule[7]. Information function can be calculated if we know only the chemical formula of the molecule[8].

We have defined the coefficient of determination $\rho = 0.237$ for the equation (1). The low value of the coefficient ρ confirms the lack of linkage between the model and the biological response. Moreover, as demonstrated analysis, the use of different versions of equation (1) (see, for example, paper[9]) or the use of the Hammett constants σ also did not improve the quality of the model. Apparently, the relationships of the molecular structure - bioactivity to search using the other features of this series of compounds. The mathematical model should not only reflect the existence of correlations, but the model has to explain the mechanism of action of chemical compounds on the biological system. In molecular pharmacology known that the biological effect of a chemical compound is dependent on its ability to accumulate in the organisms by interacting with some sensitive local structures of the body.

Analysis of the relationship of chemical compounds toxicity with their physicochemical properties are shown[10,11] that most of the correlations found with molecular properties that are associated with the interaction energy of the molecules. The presence of long-range component of the interaction energy should lead to a concentration gradient of chemical compounds in biological substrates. This may be

accompanied by the appearance of the diffusion flow of chemical compounds in the direction to the active site. Binding to the active site is determined by the short-range intermolecular interactions in condensed media. Intermolecular interactions are usually divided into two groups, namely, specific and nonspecific (universal) interactions. The first group includes the anisotropic pair quasi-chemical associations (donor-acceptor complexes, hydrogen bonds), which are formed when there is overlap of the electron shells of interacting molecules. Nonspecific interactions include various isotropic long-range multipole interactions, and dispersion forces. These interactions are determined both the individual properties of chemical compounds, and properties of the biosystem.

It is known[11,12] that the chlorinated compounds have acceptor properties. This allows the molecules to form a donor-acceptor complexes with charge-transfer. Change in the total energy (ΔE) for the bonding between atom s donor molecule and the atom t acceptor molecule has the following form

$$\Delta E = -\frac{q_s q_t}{\varepsilon R_{st}} + 2\sum_m \sum_n \frac{(C_s^m C_t^n \Delta\beta_{st})^2}{\varepsilon_m - \varepsilon_n}, \quad (2)$$

where m is occupied molecular orbital (MO) of the donor; n is unoccupied MO of acceptor; ε_m and ε_n are single particles MO of donor and acceptor, respectively; $\Delta\beta_{st}$ is the change of the resonance integral for interaction of atoms s and t for the distance R_{st}; C_s^m and C_t^n are the coefficients of the expansion of MO. The first term in equation (2) determines the electrostatic interaction between the atoms, which have a full charges q_s and q_t. ε is the static permittivity of biosystem. Electrostatic forces are favorable to the interaction of donor and acceptor atoms, but they usually do not determine the stability of complex. The second term in equation (2) characterizes the covalent binding, that is defines a partial electron transfer from the donor to the acceptor and characterizes the stability of the complex. The interaction between donor and acceptor lowers the energy of the ground state of the system below the initial levels of donor and acceptor. Measure of acceptor activity of a chemical compound is the position of lowest unoccupied MO (ε_{lumo}^0) along the scale energy. To determine the MO energies we used the quantum chemistry method CNDO/S'[13], which takes into account the interaction of the electron configurations. Bond distances and bond angles for all chemicals were taken from the handbook[14].

The values of the self-energies ε_{lumo}^0 correspond to the state of the molecule in a vacuum. In a condensed polar medium electronic levels are shifted relative to their vacuum state. Using the ideas developed in molecular spectroscopy of the condensed state[15], we can write for the displacement of energy the following equation

$$\varepsilon_{lumo} = \varepsilon_{lumo}^0 - \frac{f_R \mu_1^2}{2a^3} + \frac{\alpha_1}{2a^6} f_R^2 \mu_1^2 - \frac{3I_1 I_3 \alpha_1}{2(I_1 + I_3)a^3}\left(\frac{n_3^2 - 1}{n_3^2 + 2}\right),$$
$$f_R = 2(\varepsilon - 1)/(2\varepsilon + 1), \quad (3)$$

where a, μ_1, α_1 and I_1 are the effective size of the molecules of a chemical compound, its dipole moment, static polarizability and the ionization potential, respectively. Subscript 1 refers to a molecule of a chemical compound, the index 2 refers to a molecule of biosystem and index 3 refers to the polar dielectric medium; the optical index of refraction is equal n_3. The second and third terms of Eq. (3) describe the interaction of the dipole moment of a chemical compound with the reactive moment of polar media and the effect of the polarization of the molecule by this field, respectively. The fourth term of Eq. (3) determines the effect of dispersion interactions on the energy levels of chlorine compounds. Thus, under the influence of the reactive moment the energy of complex is changed. In the macroscopic scale the role of reactive moment is manifested in that the liquid is compressed, thereby increasing the potential energy of a polar medium. This phenomenon is one of the reasons for the increase of boiling-point (T_b) and low melting temperature (T_m) of polar liquids. Therefore it is not surprising that the correlation coefficients between the bioactivity and the parameters T_b, T_m and μ_1 close in magnitude[10]." In this case, the correlation equations are not enough informative, since the behavior of molecules in the polar medium is not fully taken into account.

If the molecule is close to the receptor, it comes into contact with the receptor. The effectiveness of this interaction is approximated by the following additive components:

The dipole - dipole interaction, which after averaging over all orientations has the following form

$$E_{dip} = -\frac{2\mu_1^2 \mu_2^2}{3R_0^6 k_B T}; \quad (4)$$

The induction interaction

$$E_{ind} = -\frac{\alpha_2 \mu_1^2 \alpha_1 \mu_2^2}{\varepsilon^2 R_0^6}; \quad (5)$$

The dispersion interaction

$$E_{disp} = -\frac{3\alpha_2 \alpha_1 I_1 I_2}{2R_0^6 (I_1 + I_2)}. \quad (6)$$

Here, R_0 is the effective distance between the interacting molecules. The zero of energy taken the energies of non-interacting molecules. Equations (4) - (6) were obtained in the approximation when the overlap of the electron shells of the interacting molecules is small. That is, the distance between the molecules, such that holds a multipole expansion in inverse powers of the distance. Approximate equations (4) - (6) reflect correctly changes in the potential energy of the interaction of molecules depending on the distance between the molecules and their individual parameters.

Equation (2) can be simplified. For a homologous series of compounds that interact with the same donor, the energy of the complex is determined by the parameter ε_{lumo} of the acceptor: $\Delta E_{d-a} = f(\varepsilon_{lumo})$. For the purposes of the regression analysis and, in particular, for the homologous series of chemical compounds, the change of energy can be written in the form $\Delta E_{d-a} \approx \varepsilon_{lumo}$.

Table 1: Physical - chemical parameters of Chlorobenzene derivatives and their lethal dose (LD_{50}) for rats after oral administration of the drugs

Chemical compounds	$\log P$ [5]	ε_{lumo}^{0}, eV	I^{*}, eV	μ_1, D [19]	α^{**}, 10^{-24}cm^3	A, $1000/LD_{50}$ [6]	A_{calcul}
Chlorobenzene	2.84	-0.971	9.15	1.69	13.2	0.303	0.242
n- Dichlorobenzene	3.39	-1.441	9.11	0	15.0	0.398	0.546
o- Dichlorobenzene	3.39	-1.356	9.23	2.51	15.9	0.468	0.799
1,2,4,5- Tetrachlorobenzene	4.89	-2.097	9.31	0	19.7	0.667	1.193
2,4,6- Trichlorophenol	3.06	-1.751	9.02	1.62	19.0	1.299	0.998
1,2,4- Trichlorobenzene	4.13	-1.764	9.26	1.25	18.3	1.323	0.953
3,4- Dichloroaniline	2.69	-1.292	8.24	4.16*	17.8	1.429	1.317
n- Nitrochlorobenzene	2.39	-3.112	10.21	2.52	16.5	1.802	1.521
m- Nitrochlorobenzene	2.46	-3.077	10.00	3.38	17.9	2.326	2.698
o- Nitrochlorobenzene	2.53	-2.987	9.95	4.25	16.7	2.949	2.949
2,4- Dinitrochlorobenzene	2.45	-3.657	10.86	3.29	19.1	3.571	3.226
2,3,5,6- Tetrachloronitrobenzene	4.55	-3.576	9.86	5.34*	24.1	4.00	4.094

* Dipole moments of molecules and their ionization potentials calculated by the MINDO/ 3 method, which gives the most accurate values of these parameters.
**Polarizability of the molecules was calculated using the additive scheme of the method[20].

Table 2: Physico-chemical parameters of Chlorinated compounds and Isotoxic concentration (C, mM/l) of vapor chemicals.

Chemical compounds	d_{20}, g/ml [20]	n_{20}^{20}	ε_{lumo}^{0}, eV	I_1^{*}, eV	μ_1, D,	α^{**}, 10^{-24} cm^3	A, $100/C$ [10]	A_{calcul}
Ethyl chloride	0.8978	1.3676	0.151	10.70	2.0[18]	6.4	0.71	0.55
Propyl chloride	0.8909	1.3879	0.445	10.44	1.8[18]	8.24	1.23	2.02
Vinyl chloride	0.9999	1.4046	-0.522	9.82	1.44[18]	7.83[20]	1.56	1.01
1,1- Dichlorovinyl	1.2180	1.4249	-1.216	9.59	1.13	8.07	2.50	1.17
1,2- Dichlorovinyl	1.2837	1.4490	-1.214	9.15	1.77	7.78[20]	2.50	2.20
1,1- Dichloroethane	1.1757	1.4164	-1.206	10.60	1.80[18]	8.38	3.08	3.90
Methylene chloride	1.3255	1.4242	-1.215	10.79	2.40[18]	6.48[20]	3.08	3.63
Trivinylchloride	1.4642	1.4773	-2.276	9.48	1.01	10.06	4.00	4.53
Chloroform	1.4832	1.4459	-2.467	11.00	1.51	8.23	5.00	4.25
Tetra chlorovinyl	1.6227	1.5053	-2.623	9.66	0	12.03	5.00	6.70
1,2- Dichloroethane	1.2531	1.4476	-0.089	10.92	2.43	8.45	5.71	5.51
1,2- Dichloropropane	1.1559	1.4394	0.099	10.60	2.82	10.20	9.52	9.45
1,1,2- Trichloroethane	1.4714	1.4940	-1.264	10.89	2.72	10.28	10.00	10.46
1,1,2,2- Tetrachloroethane	1.5953	1.4940	-1.680	10.89	2.17	12.15	11.76	11.15
Pentachloroethane	1.6796	1.5025	-2.753	10.88	1.37	14.11	13.33	14.11

* We calculated dipole moments and ionization potentials by the MINDO/3 method. "**Polarizability of the molecules we calculated by using equation of Clausius-Mossotti: $\alpha = (n_{20}^2 - 1)(n_{20}^2 + 2)^{-1} 3M\ (4\pi d_{20} N_A)^{-1}$; d_{20} and n_{20}^2 are the density and refractive index at 20^{0}C, respectively.

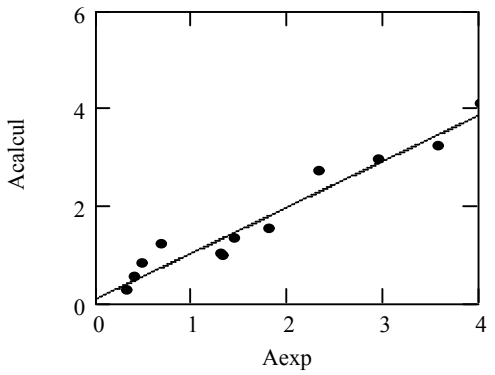

Figure 1: **Field of correlations of the experimental data and calculated bioactivities using equation (9a). ● is the values of bioactivity are taken from Table 1, ── is the linear correlation equation: A_{calcul} = 0.098 + 0.948A_{exp}; linear correlation coefficient equal to R = 0.97 >**

$R_{9;0.05}^{(cr)} = 0.60$.

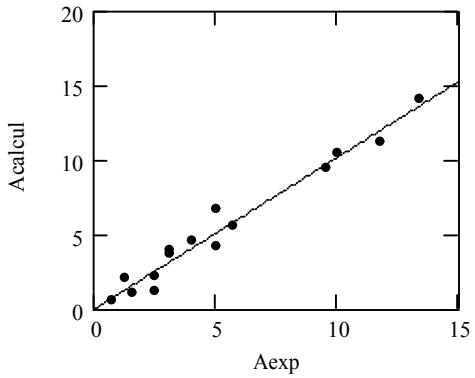

Figure 2: **Field of correlations of the experimental data and calculated bioactivities using equation (12a). ● is the values of bioactivity are taken from Table 2, ── is the linear correlation equation: A_{calcul} = 0.0104 + 1.02A_{exp}; linear correlation coefficient equal to R = 0.98 >**

$R_{14;0.05}^{(cr)} = 0.50$.

In general, the equation that determines the stabilization energy of the complex can be written in the form

$$\Delta E_{d-a} = k_0 + k\varepsilon^0_{lumo} + \mu_1^2\left\{-\frac{k_1 f_R}{2a^3} + \frac{k_2\alpha_1 f_R^2}{2a^6} - \frac{2\mu_2^2}{3R_0^6\varepsilon k_B T} - \frac{\alpha_2}{\varepsilon^2 R_0^6}\right\} +$$

$$+\alpha_1\left\{-\frac{\mu_2^2}{\varepsilon^2 R_0^6} - \frac{3\alpha_2 I_1 I_2}{2R_0^6(I_1+I_2)}\right\} - \frac{3I_1 I_2\alpha_1}{(I_1+I_2)a^3}\left(\frac{n_3^2-1}{n_3^2+2}\right), \quad (7)$$

where k, k_0, k_1, and k_2 are some constants. Usually, the induction interaction is much smaller than the dispersion interaction: $E_{ind} << E_{disp}$. Therefore, in the fourth term of equation (7) the first addend in the curly brackets can be neglected in comparison with the second addend. In the future, we will assume that the parameters are related to biological system and polar medium are permanent. These parameters can be replaced by some a constants.

RESULTS AND DISCUSSION

Our goal is to provide to obtaining an explanatory regression equation. Coefficients of regression equation are selected by statistical methods. Therefore, this approximation is quite satisfactory. Thus, using equation (7) we can write the general regression equation in the following form:

$$A = B_0 + B_1\varepsilon^0_{lumo} + B_2\mu_1^2 + B_3\alpha_1 I_1(I_1+I_2)^{-1}, \quad (8)$$

This equation relates the activity of molecules (A) with their electronic characteristics that determine the ability of molecules to the formation of donor-acceptor complexes. Since we do not particularize receptor, for further analysis we take $I_2 = 10eV$ [12]. This value of the potential is typical for most organic molecules. Using equation (8), we obtain the following regression equation for the molecules of chlorobenzene (Table 1):

$$A = 1000/LD_{50} = -0.903 - 0.938\varepsilon^0_{lumo} + 0.052\mu_1^2 + 0.014\alpha_1 I_1(I_1+I_2)^{-1}. \quad (9)$$

Equation (9) has the following statistical data:

$$n = 12, \quad \rho_1 = R_1^2 = 0.942, \quad S_1^2 = 0.1249, \quad F_1 = 43.67 > F_{3,8;0.99} = 15.8,$$

$$t(B_1) = 4.73 > t(B_2) = 3.33 > t^{(cr)}_{9;0.95} = 2.26 >> t(B_3) = 0.11. \quad (10)$$

Here are the values of the coefficient of determination (ρ_1), standard deviation (S^2), Fisher-test (F), and t-test values for each coefficients B_i (i = 1, 2, 3); n is the number of chemical compounds. From the statistical data (10) follows that the coefficient B_3 is not statistically significant. Hence, Eq. (9) can be replaced by the following regression equation:

$$A = 1000/LD_{50} = -0.819 - 0.953\varepsilon^0_{lumo} + 0.052\mu_1^2 \quad (9a)$$

Equation (9a) has the following statistical data:

$$n = 12, \quad \rho_2 = R_2^2 = 0.942, \quad S_1^2 = 0.1112,$$

$$F_1 = 73.56 > F^{(cr)}_{2,9;0.95} = 4.26.$$

Correlation range of experimental and theoretical values of the biological activity of the molecules (Table 1) shown in Figure 1. The terms in equation (9) correspond to the actual energy contributions in the total energy of the molecular interactions in accordance with inequalities

$$E_{d-a} >> E_{react} \approx E_{disp} \approx E_{dip} \quad (11)$$

If chemical compounds are able to form hydrogen bonds, it must be in the equation (8) to take into account the energy contribution due to hydrogen bonds. The hydrogen bond is essentially a weak chemical interaction, and therefore the properties of the hydrogen bond is difficult to describe using the properties of isolated molecules. However, some estimates we can be made. The additives of Eq. (9a) proportional their contributions to the binding energy and satisfies to inequalities (11). Hence taking into account that the binding energy of the donor-acceptor complex is approximately equal to the energy of formation of hydrogen bonds, it can be assumed that the contributions to the bioactivity of these effects are also approximately equal.

From equation (9a) follows that the bioactive molecule 2,4-dichlorophenol is A = 0.651 (ε^0_{lumo} = - 1.4 eV, $\mu_1 = 1.5$ D). This bioactivity is markedly lower than the experimental value equal to 2.08. In the molecule of 2,4-dichlorophenol exists an intramolecular hydrogen bond between proton of the hydroxyl group and atom of chlorine in the *ortho*-position of the benzene ring. In a condensed polar medium an intramolecular hydrogen bond is broken due to the effect of the reactive moment of polar media. This state of the molecule is energetically more stable. The hydroxyl group of molecules can take part in the formation of intermolecular hydrogen bonds. In a polar medium with the increase of the dipole moment of molecules balance of the molecular forms with an intramolecular hydrogen bond and without an intramolecular hydrogen bond is shifted to the molecular state with a large dipole moment, that is, without an intramolecular hydrogen bond. Indeed this situation is indeed observed experimentally[16,17]. The formation of intermolecular hydrogen bond leads to an additional contribution to the biological activity of molecule equal to 1.31. Consequently, the total bioactivity of the molecule is equal 1.96, which is close to the experimental value of bioactivity: A_{exp} = 2.08. However, this reasoning can not be applied to the molecule 2,4,6-trichlorophenol. The molecule has a hydroxyl group, but the hydroxyl group can not involved in the formation of intermolecular hydrogen bonds. This is due to the fact that the proton of the hydroxyl group oscillates between the chlorine atoms by the tunnel migration through a potential barrier. Spectroscopic experimental studies of 2,4,6-trichloro-, 2,4,5,6-tetrachloro- and pentachlorophenol confirmed the migration of the proton[18].

As a result of intermolecular interactions of the biologically active substances shield the receptor, thereby hindering access of normal substances. In addition, for chemicals that block the receptors may exist radical and ion states of the molecules forming the complex. As a result, the physical state of the receptor changes.

With regard to the specificity of the donor-acceptor interaction, it is necessary to point out one important fact. The significant interaction between two molecules occurs when the resonance integral quasi-chemical bond is large enough. This is achieved when the atomic orbitals are adequate to each other. That is, the interaction is limited by the ability to make optimal geometry of the molecules with respect to one another. If the mutual spatial arrangement of the molecules optimal, then the interacting molecular orbitals will be a maximum splitting. The splitting of the energy levels leads to the stabilization of the complex. Therefore, molecules that may have a potentially strong acceptor properties, but does not meet the requirements of an optimal geometric matching, do not give the expected large biological response. In addition, it is essential that the electron transfer to the acceptor of different classes can be controlled by either the charge states, or their orbital states. Energetically favorable only those interactions that include both acceptors and donors that react the same way, that is, either by type of charge, or by the type of orbital control (see, for example, paper[12]). For a homologous series of chemical compounds such restrictions are usually leveled. The correctness of the interpretation of the biological response by using simple equation (9a), conditioned the fact that the center of interaction of the molecules in the formation of the donor-acceptor complex is atom of chlorine. This essentially is simplified the equation (2).

However, to reduce the biological activity of chemical compounds only to specific interactions would not be quite true. We will demonstrate this. We apply equation (8) to interpret of narcotic action of the series saturated and unsaturated chlorinated compounds. As a biological response we choose isotoxic concentration (C, mM/l)[10] vapor compounds that cause 50% of the lateral position of the white mice (Table 2). Applying the method of least squares to general equation (2) we have obtained the following regression equation:

$$A = 100/C = -11.936 - 0.971\varepsilon^{0}_{lumo} + 0.904\mu_1^2 + 2.723\alpha_1 I_1 (I_1 + 10)^{-1}. \quad (12)$$

Equation (12) has the following statistical data:

$$n = 15, \quad \rho_1 = R_1^2 = 0.960, \quad S_1^2 = 0.8132, \quad F_1 = 88.69 > F^{(cr)}_{3,11;0.95} = 3.59,$$

$$t(B_1) = 1.8 < t^{(cr)}_{12;0.95} = 2.18 < t(B_2) = 7.03 < t(B_3) = 10.29. \quad (13)$$

The analysis of the regression coefficients (12) showed that the coefficient B_1 statistically insignificant. This follows from inequalities (13). Consequently, general equation (12) can be replaced by the following regression equation

$$A = 100/C = -12.124 + 0.685\mu_1^2 + 3.175\alpha_1 I_1 (I_1 + 10)^{-1}. \quad (12a)$$

Equation (12a) has the following statistical data:

$$n = 15, \quad \rho_1 = R_1^2 = 0.932, \quad S_2^2 = 1.286, \quad F_1 = 81.63 > F^{(cr)}_{2,12;0.95} = 3.88. \quad (14)$$

Variance reduction of (12) in comparison with equation (12a) is due to an increase in the number of connections in equation (12). That is, a random. Indeed, comparison of the two variances by Fisher-test gives the following inequality: $S_2^2 / S_1^2 = 1.58 < F^{(cr)}_{12,11;0.95} = 2.79$. Correlation range of experimental and theoretical values of the biological activity of the molecules (Table 2) shown in Figure 2.

Of the two possible structures of the molecule 1,2-dichlorvinyl in a polar medium (Table 2), we chose the structure of the *cis*-isomer, which corresponds to the state of the molecule with a lower energy (assuming for the static dielectric constant of the polar media value equal to ε = 80, and the index of refraction has value = 1.777). Using the method of CNDO/2, we have calculated the energy of the *trans*-isomer and *cis*-isomer: E_{trans} = - 1295.97 eV and E_{cis} = - 1295,952 eV, respectively. In polar dielectric medium the energy of *cis*-isomer is decreased to the value E_R:

$$E_R = -(\varepsilon - 1)(2\varepsilon + n_3^2)^{-1}(n_3^2 + 2)\mu_1^2 / 3a^2 = -0.08 \text{ eV},$$

here $\mu_1 = 1.77$ D, $a = 2.5$ Å are the dipole moment of molecule and effective size of molecule, respectively. We can define the number of molecules that are in the *cis* - and *trans*-configurations:

$$N_{cis} = N_{trans} \exp[(E_{trans} - E_{cis} - E_R)/k_B T] = 13 N_{trans},$$

that is, most of the molecules will be in the *cis*-configuration.

Comparing equations (9a) and (11a), we can make some assumptions about the action of chlorinated compounds at the molecular level and about the properties of the biosystem active center also. In the first case (Table 1) chemical chlorine compounds interact with the receptors of the body, which are characterized by strong donor properties. In the second case (see Table 2) biosystem forms molecular complexes due to the dispersion and dipolar interactions, this is characteristic of the active sites that have high polarization properties (α has higher value).

Thus, the bioavailability of chlorinated hydrocarbons associated with the accumulation of chemicals in the active centers of the body, is determined solely by the electronic structure of molecules and are characterized by their ability to form molecular complexes by a different types of molecular interactions. Apparently, chlorine compounds to associate with the active sites of receptors, alter the normal functioning of the body, irreversibly disturbing its living processes. Also, if the level of donor ε_{don} is above the acceptor level ε_{acc}, then exist the possibility of a real transfer of an electron from the molecule to molecule[19-20]. In the local area of biosystem through nonradiative electron relaxation mechanisms it is possible producing energy, approximately equal to the difference of $\varepsilon_{don} - \varepsilon_{acc}$ which is expended on destroying the equilibrium ordered structure of the receptor. The more

energy $\varepsilon_{don} - \varepsilon_{acc}$, the lower the energy of the acceptor level.

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