

QUANTUM-CHEMICAL SIMULATION OF PYRIDINIUM  
PEROXODISULFATES  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$  COMPLEXESA. K. DOVLATYAN <sup>1\*</sup>, H. G. BADALYAN <sup>2\*\*</sup>, L. R. HARUTYUNYAN <sup>3\*\*\*</sup>,  
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The computer modeling of complexes of pyridinium peroxodisulfates  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$ , where  $n=8; 12; 15; 16; 18; 20$ , have been done. The structural and energetic parameters of complexes  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$  have been calculated by molecular-dynamic at 300 K and semi-empirical quantum-chemical methods. The values of geometric and energetic parameters of optimized complexes  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$  in vacuum and in aqueous medium, and the results of total energy quantum-chemical calculations are given. It has been established that the length of alkyl chain significantly effects on electrostatic interactions and energetically more beneficial formation of a complex with alkyl chain length  $n=16$ .

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**Keywords:** peroxodisulfates of pyridinium, complexes of quaternary ammonium salts, energetic parameters, quantum-chemical simulation.

**Introduction.** Problems of molecular interactions and complex formation in solutions are important aspects of chemistry and biology. In the modern theory of solutions more and more attention is paid to quantum-chemical and statistical methods. The results of quantum-chemical studies are giving valuable information, which is impossible and sometimes extremely difficult or too expensive to get experimentally. At the same time, quantum-chemical calculations make possible to conduct a relative analysis of the effectivity of the reagents influence.

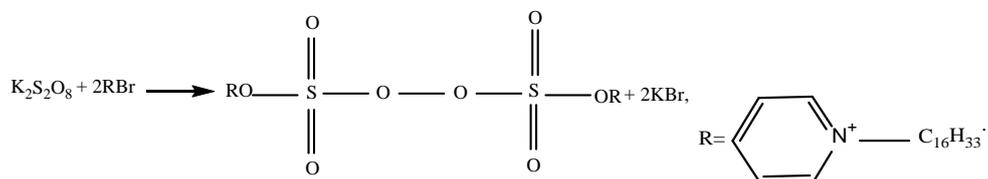
Quaternary ammonium salts (QAS) are biologically active compounds, which have bactericide activity against many gram-positive and some gram-negative organisms [1]. Studies have shown that the compounds, which are produced based on QAS, also have bactericidal properties [2, 3]. Particularly, it has been shown that cetylpyridinium peroxodisulfate (CPPDS), which has been produced by interaction of potassium persulfate (PP) with cetylpyridinium bromide (CPB) according to the reaction given below [4], also has bioactivity and can be used as an anti-inflammatory [5] and antifungal drug [6]:

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One of the important properties of complex compounds, which determines the purpose of their application, is stability, which can be obtained both experimentally and using modern methods of modeling. In the presented paper, the stability and reactivity parameters of pyridinium peroxodisulfates complexes  $(C_n\text{Pyr})_2S_2O_8$ , where  $n=8; 12; 15; 16; 18; 20$ , have been studied by quantum-chemical modeling and molecular dynamics at 300 K.

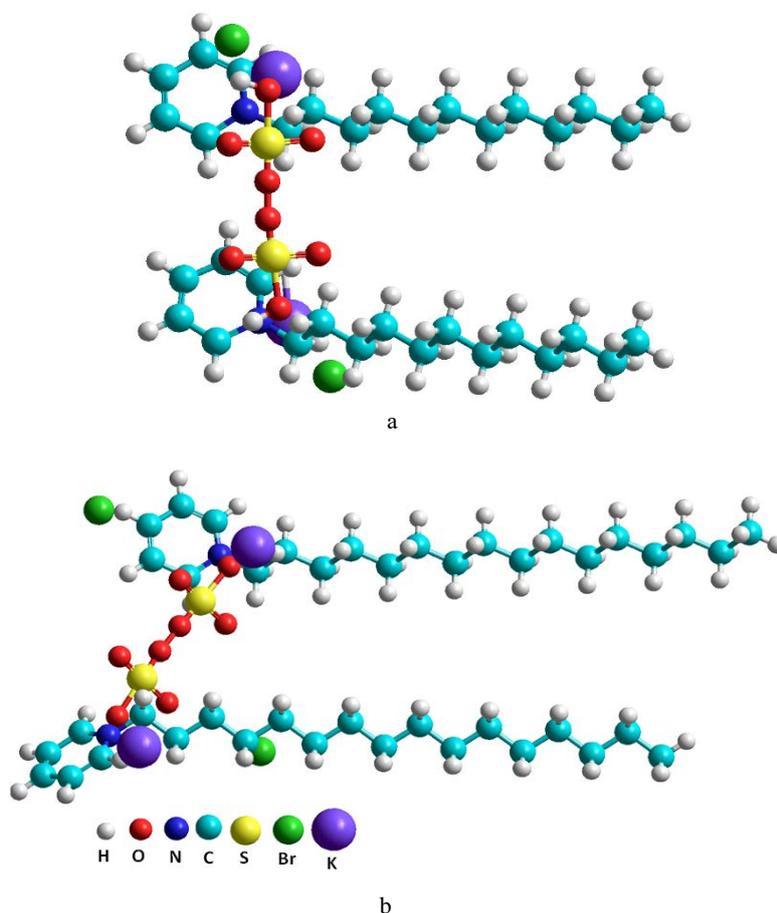


Fig. 1. Computer models of  $(C_{12}\text{Pyr})_2S_2O_8$  (a) and  $(C_{16}\text{Pyr})_2S_2O_8$  (b) in vacuum.

**Experimental Part.** The geometric optimization of the structure of complexes  $(C_n\text{Pyr})_2S_2O_8$ , where  $n=8; 12; 15; 16; 18; 20$ , has been done by semi-empirical quantum-chemical AM1 method and molecular dynamic method with applying

MM<sup>+</sup> force field in the software package HyperChem 8.5 for obtaining characteristics of pyridinium peroxodisulfates complexes (C<sub>n</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub>. The algorithm of Polak–Ribiere with a given accuracy of the energy gradient 0.01 kcal/mol has been used at geometric optimization. The Z-matrix has been built with help of HyperChem 8.5 software – a convenient and generally accepted method for determining the geometric parameters of a molecule by sequentially entering the internal coordinates of atom, i.e. bond lengths, values of valence and torsion angels, after which the initial optimization of the studied complexes has been done by semi-empirical method [7–10].

The AM1 method has been used for study of the optimized structures of complexes in vacuum and in aqueous medium, the parameters of electronic structure, the total energy and heat of formation have been calculated and the geometry has been optimized. Computer models of (C<sub>16</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> and (C<sub>12</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> are given in Fig. 1. For modeling in aqueous medium the standard model TIP-3P has been used (Fig. 2).

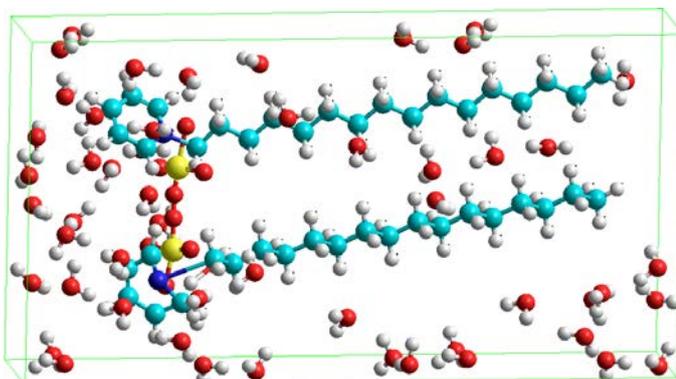


Fig. 2. Computer model of (C<sub>16</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> molecule in aqueous medium.

**Results and Discussion.** It is known that the symmetry and the density of equipotential surface characterize the stability of system [11]. The results of modeling indicate that in the case of (C<sub>16</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> negative equipotential surfaces are equally distributed between two fragments of molecules (Fig. 3) both in vacuum (a) and in an aqueous medium (b); as a result, the system is stable which is also indicated by the change in the enthalpy of the system (Tab. 1).

Table 1

Values of energetic parameters of optimized structures of (C<sub>n</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> complexes in vacuum (1) and in aqueous medium (2), calculated by AM1 method

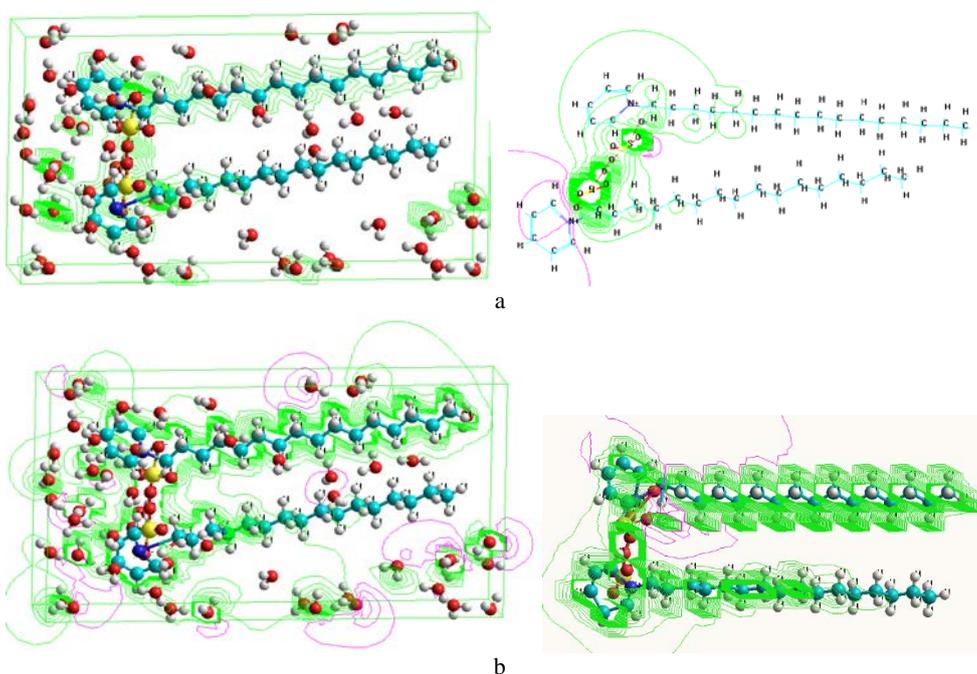
Complexes	1					2		RMS GRAD
	$E_{\text{total}}$ , kJ/mol	$E_{\text{binding}}$ , kJ/mol	$E_{\text{int}}^*$ , kJ/mol	$\Delta H$ , kJ/mol	$\Delta H_{\text{complex}}^*$ , kJ/mol	$\Delta H_{\text{complex}}^*$ , kJ/mol		
(C <sub>20</sub> Pyr) <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	-1134527.74	-62186.88	-424173.24	-2511.92	-387.65	-3993.95	0.099	
(C <sub>18</sub> Pyr) <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	-1074419.14	-57477.15	-394215.33	-2403.97	-397.20	-3822.30	0.097	
(C <sub>16</sub> Pyr) <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	-1018263.72	-56720.47	-368062.55	-6249.16	-4244.73	-9936.16	0.086	
(C <sub>15</sub> Pyr) <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	-988204.09	-54360.48	-352981.82	-6189.94	-4164.11	-9842.0	0.080	
(C <sub>12</sub> Pyr) <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	-901580.94	-47000.24	-309512.36	-5713.54	-3939.38	-9084.53	0.099	
(C <sub>8</sub> Pyr) <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	-777639.14	-37691.42	-247669.64	-5627.11	-3852.96	-6247.10	0.083	

Note:  $E_{\text{int}}^* = E(\text{complex})_{\text{total}} - E(\text{QAS})_{\text{total}} - E(\text{PP})_{\text{total}}$ ;  $\Delta H_{\text{complex}}^* = \Delta H(\text{complex}) - \Delta H(\text{QAS}) - \Delta H(\text{PP})$ ; the values of  $E(\text{QAS})_{\text{total}}$ ,  $E(\text{PP})_{\text{total}}$ ,  $\Delta H(\text{QAS})$  and  $\Delta H(\text{PP})$  are presented in Tab. 2.

Table 2

Values of energetic parameters of QAS and PP in vacuum, calculated by AM1 method

Compound	$E_{total}$ , kJ/mol	$E_{binding}$ , kJ/mol	$\Delta H$ , kJ/mol	RMS GRAD
C <sub>20</sub> PyrBr	-424244.38	-28866.70	-392.79	0.0931
C <sub>18</sub> PyrBr	-394093.56	-26448.31	-275.29	0.0998
C <sub>16</sub> PyrBr	-364090.91	-24145.09	-272.96	0.0972
C <sub>15</sub> PyrBr	-349112.15	-23016.05	-264.36	0.0734
C <sub>12</sub> PyrBr	-305958.48	-20137.14	-246.71	0.0957
C <sub>8</sub> PyrBr	-243859.38	-14711.27	-42.68	0.0903
PP	-286110.13	-4458.6	-1731.48	0.0812

Fig. 3. Distribution of electrostatic potential (2D contour) of (C<sub>16</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> optimized structure in aqueous medium (a) and in vacuum (b).

Compared with the data in Fig. 3, a and b, it can be concluded that the location of equipotential surfaces does not change around atoms of studied molecule (for example, around nitrogen atom). At the same time, in aqueous medium the equipotential surfaces are thicker than in vacuum. It means that in the aqueous medium value of the potential is higher than in vacuum. For obtaining the difference of numerical values the distribution of electrostatic potential presented at 3D display (Fig. 3), from which it follows that the maximum potential near atom changes from  $-2.298$  to  $+2.298$  in vacuum and from  $-4.277$  to  $+4.277$  in the aqueous medium. It means that water shows itself as an external force field, which is increasing the value of surface potential, but the location of equipotential surface does not change. This result makes possible to carry out an experiment in vacuum in a pre-calculated external force field. It facilitates the conditions of the computer simulation process save computer resources and significantly reduce the experimental time.

The energetic parameters of the optimized structures of (C<sub>n</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> complexes in vacuum in an external force field, calculated by AM1 method, are presented in Tab. 1. From that data it follows, that in vacuum the formation of complexes with different alkyl chain length is possible. However, taking into consideration that the energy of interaction of complexes ( $E_{\text{int}}$ ) in absolute values increases in the order C<sub>8</sub><C<sub>12</sub><C<sub>15</sub><C<sub>16</sub><C<sub>18</sub><C<sub>20</sub>, the relatively stable are complexes which have long alkyl chain. The obtained results of quantum-chemical modeling are in good agreement with earlier obtained experimental data (IR-spectroscopy, NMR, X-ray analysis) [4, 12].

The obtained results of distribution of energetic potential of complexes by 3D display indicate that the length of alkyl chain has significant effect on electrostatic interactions at the complex formation.

The results of calculations by molecular dynamic method with application of MM<sup>+</sup> force field show that the dipole moment of (C<sub>20</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> and (C<sub>8</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> is equal 3.354 D and 3.430 D, respectively, i.e. the repulsive forces also play significant role, which also indicates that mentioned complexes are less stable compared with (C<sub>16</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (3.200 D). The results of calculation by semi-empirical method and method of molecular dynamics are in good agreement. The total energy of interaction has minimum at  $n=16$ , which corresponds to the complex (C<sub>16</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (Fig. 4).

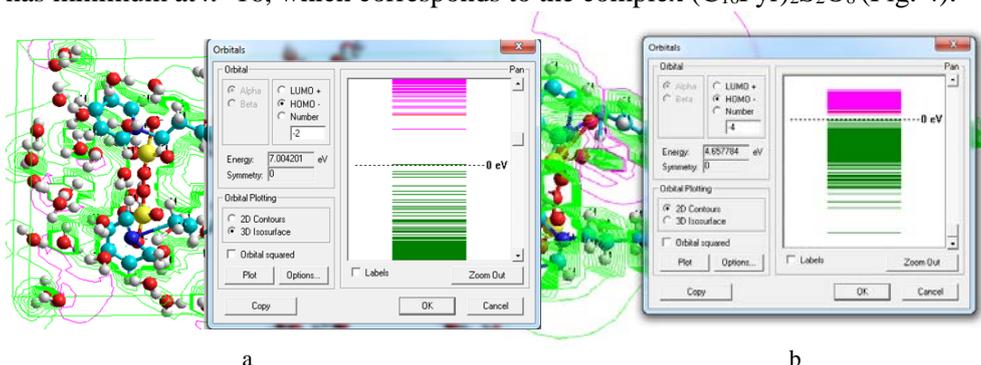


Fig. 4. Energies of molecular orbitals (C<sub>16</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> in aqueous medium (a) and in vacuum (b).

Energies of molecular orbitals (MO) (Tab. 3) in semi-empirical methods, as well as in *ab initio* methods, are directly determined as eigenvalues of one-electron operators of Fock. Of much greater interest are the values of the highest occupied ( $E_{\text{HOMO}}$ ) and lowest unoccupied ( $E_{\text{LUMO}}$ ) MO, because many properties of molecules depend on the degree of occupation of these orbitals. Particularly, using Koopmans' theorem, based on the values of  $E_{\text{HOMO}}$  and  $E_{\text{LUMO}}$ , the first ionization potential ( $I_M = -E_{\text{HOMO}}$ ), electron affinity ( $A_M = -E_{\text{LUMO}}$ ) and energy gap ( $\Delta E_g = -E_{\text{LUMO}} - E_{\text{HOMO}}$ ) can be obtained, which reflect the donor-acceptor and redox properties of the molecule [13, 14]. The value of the frontier MO allows to make discussion about mechanism of organic reactions with participation of studied compounds [13, 14] as an electrophilic attack often occurs at the maximum values of  $E_{\text{HOMO}}$  and the nucleophilic at the highest values of  $E_{\text{LUMO}}$ . Besides it, two molecules prefer to react at maximum overlap of  $E_{\text{HOMO}}$  and  $E_{\text{LUMO}}$  [13, 14]. For the complexes (C<sub>n</sub>Pyr)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> the quantum-chemical calculations of chemical potential ( $\chi$ ), molecular hardness ( $\eta$ ) and molecular softness ( $S$ ) by Pearson and Parr [13, 14] have been done:

$$\chi = \frac{I_M + A_M}{2}, \quad \eta = \frac{I_M - A_M}{2}, \quad S = \frac{1}{\eta}.$$

The results of quantum-chemical calculations of reactionability parameters for complexes  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$  are given in Tab. 3. By analyzing obtained data (Tab. 3), it must be noted that the studied systems are characterized by low values of molecular hardness (the high value of molecular hardness of reagent must be no less than 8 eV [13, 14]). The obtained values indicate the chemical activity of the complexes and the tendency of nucleophilic properties. According to the results presented in Tab. 3, the complexes  $(C_{20}\text{Pyr})_2\text{S}_2\text{O}_8$  and  $(C_{16}\text{Pyr})_2\text{S}_2\text{O}_8$  are characterized by low values of molecular softness (0.232 and 0.249 eV, respectively) compared with other studied complexes, high values of  $E_{\text{HOMO}}$ , which are  $-8.200$  eV and  $-8.469$  eV, and high values of molecular hardness (4.305 eV and 4.022 eV, respectively), which make possible to classify them as “hard” nucleophiles capable of effective interaction with “hard” substrates [13, 14]. It must be noted that the obtained results are in good agreement with the experimental data [4, 12].

Table 3

Values of reactionability of parameters of  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$  complexes

Complexes	$E_{\text{HOMO}}$ , eV	$E_{\text{LUMO}}$ , eV	$\Delta E_{\text{gap}}$ , eV	$I_M$ , eV	$A_M$ , eV	$\chi$ , eV	$\eta$ , eV	$S$ , eV <sup>-1</sup>
$(C_{20}\text{Pyr})_2\text{S}_2\text{O}_8$	-8.200	0.409	8.609	8.200	-0.409	3.896	4.305	0.232
$(C_{18}\text{Pyr})_2\text{S}_2\text{O}_8$	-7.380	-0.880	6.500	7.380	0.880	4.130	3.250	0.308
$(C_{16}\text{Pyr})_2\text{S}_2\text{O}_8$	-8.469	-0.425	8.044	8.469	0.425	4.450	4.022	0.249
$(C_{15}\text{Pyr})_2\text{S}_2\text{O}_8$	-7.746	0.189	7.935	7.746	-0.189	3.779	3.968	0.252
$(C_{12}\text{Pyr})_2\text{S}_2\text{O}_8$	-7.699	-1.900	5.799	7.699	1.900	4.799	2.899	0.345
$(C_8\text{Pyr})_2\text{S}_2\text{O}_8$	-7.040	-1.110	5.930	7.040	1.110	4.075	2.965	0.337

**Conclusion.** Based on the quantum-chemical simulation data, it is concluded that the more stable state has  $(C_{16}\text{Pyr})_2\text{S}_2\text{O}_8$ , which also has antibacterial properties. It is shown that the results of quantum-chemical simulation in vacuum in practice do not qualitatively differ from the results of quantum-chemical simulation in an aqueous medium, but the quantitative values of calculated parameters differ, particularly, the values of the electrostatic potential close to the atoms of the studied complexes increase.

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( $C_n\text{Pyr}$ )<sub>2</sub>S<sub>2</sub>O<sub>8</sub> ՊԻՐԻԴԻՆԻՈՒՄԻ ՊԵՐՕՔՍՈՂԻՍՈՒՄՈՒՄԻ ՖԼՖԱՏԱՑԻՆ  
ԿՈՄՊԼԵՔՍՆԵՐԻ ԲՎԱՆՏԱԶԻՄԻԱԿԱՆ ՄՈԴԵԼԿՈՆՍՏՐԱԿՏ

Իրականացվել է պիրիդինիումի պերօքսոդիսուլֆատների ( $C_n\text{Pyr}$ )<sub>2</sub>S<sub>2</sub>O<sub>8</sub> կոմպլեքս միացությունների համակարգային մոդելավորում, որտեղ  $n = 8; 12; 15; 16; 18; 20$ : Մոլեկուլային-դինամիկ և կիսաէմպիրիկ քվանտաքիմիական եղանակներով հաշվարկվել են ( $C_n\text{Pyr}$ )<sub>2</sub>S<sub>2</sub>O<sub>8</sub> կոմպլեքսների կառուցվածքային և էներգետիկ պարամետրերը: Ներկայացված են ( $C_n\text{Pyr}$ )<sub>2</sub>S<sub>2</sub>O<sub>8</sub> օպտիմալացված կոմպլեքսների երկրաչափական և էներգետիկ պարամետրերի արժեքները վակուումում և ջրային միջավայրում, ինչպես նաև ամբողջ էներգիայի քվանտաքիմիական հաշվարկի արդյունքները: Հաստատված է, որ էներգետիկորեն առավել շահավետ է  $n = 16$  ակիլ շղթայով կոմպլեքսի առաջացումը:

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КВАНТОВО-ХИМИЧЕСКОЕ МОДЕЛИРОВАНИЕ КОМПЛЕКСОВ  
ПЕРОКСОДИСУЛЬФАТОВ ПИРИДИНА  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$

Проведено компьютерное моделирование комплексных систем пероксодисульфатов пиридина  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$ , где  $n = 8; 12; 15; 16; 18; 20$ . С помощью молекулярно-динамических и полуэмпирических квантово-химических методов рассчитаны структурные и энергетические параметры комплексов  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$ . Приведены значения геометрических и энергетических параметров оптимизированных комплексов  $(C_n\text{Pyr})_2\text{S}_2\text{O}_8$  в вакууме и водной среде, а также результаты квантово-химического расчета полной энергии. Установлено, что энергетически более выгодно образование комплекса с длиной алкильной цепи  $n = 16$ .