Optics and Spectroscopy, 2025, Vol. 133, No. 2

02

The photolysis of paracetamol in aqueous solution influenced by ultraviolet radiation

© O.K. Bazyl'[1], O.N. Tchaikovskaya[1,2], E.N. Bocharnikova[1,2,¶], N.P. Bezlepkina[1,2], A.V. Spirina[2], G.V. Mayer[1]

[1] Tomsk State University,
Tomsk, Russia
[2] Institute of Electrophysics, Ural Branch, Russian Academy of Sciences,
Yekaterinburg, Russia
¶ e-mail: bocharnikova.2010@mail.ru

Received November 15, 2024
Revised February 02, 2025
Accepted February 02, 2025

Experimental and theoretical studies of electronic spectra of paracetamol in water after exposure to UV radiation are presented. Theoretical studies were performed using the quantum-chemical modified INDO/s method. Paracetamol-water complexes in a 1 : 1 ratio were determined. Chemical bonds of paracetamol were revealed, the rupture of which leads to the formation of several photoproducts. To interpret changes in the absorption spectra of paracetamol after exposure to UV radiation, electronic absorption spectra of the identified photoproducts and their complexes with the paracetamol anion were calculated. It was shown that the rupture of chemical bonds and the formation of paracetamol photoproducts occurs in the singlet state by the predissociation mechanism. The calculation results are confirmed by experimental data. Three photoproducts (2-amino-5-hydroxyacetophenone, para-aminophenol, peroxyether) formed as a result of the rupture of single bonds in the $CNHCOCH_3$ fragment were proven. It has been shown that the band in the absorption spectrum in the region of $\lambda_{max} = 380$ nm after UV irradiation of paracetamol in water is formed by a structure composed of hydrogen-bonded complex at the oxygen of the carboxyl group of the paracetamol anion with the main photoproduct of its decay 2-amino-5-hydroxyacetophenone.

Keywords: paracetamol, absorption, photolysis, fluorescence, H-bonded complexes.

DOI: 10.61011/EOS.2025.02.61022.7330-24

1. Introduction

Paracetamol is an over-the-counter household analgesic due to its analgesic and antipyretic properties, it is safe and effective in recommended doses for the treatment of fever and acute pain. However, its overdose can lead to hepatotoxicity, acute liver failure and other disorders that develop as a result of the accumulation of para-aminophenol — a metabolite of paracetamol in the body [1–6]. Environmental pollution with paracetamol occurs due to waste emissions from pharmaceutical enterprises, hospitals, agricultural production and humans themselves, which is confirmed by the detection of the substance in surface, wastewater and drinking waters around the world [7–11]. This leads to the need to create various technologies for the destruction (or reduction of harm) of pollutants [12,13]. Wastewater containing paracetamol is mainly purified by chemical oxidation processes [14]. Although modern chemical treatment methods, such as using multifunctional magnetic composite (Ma-MgMnLDO-a) [14] are available to remove these pollutants, the harsh reaction conditions, the formation of secondary pollutants, and the high operating costs associated with these methods often make them an undesirable choice. The authors of Ref. [10] studied the degradation of paracetamol in natural conditions in the soil and found that it is converted into other metabolites. Eleven other metabolites were found in the soil samples after incubation, in addition to paracetamol itself, including para-aminophenol, maleic acid, aniline, hydroquinone, 3-hydroxyacetaminophen, N-acetyl-p-benzoquinonymine, catechol, a dimeric form of paracetamol, metacetin, 4-methoxyphenol, and phenol [10]. Intermediate by-products of the degradation of paracetamol can have different toxicity, some of which are even more harmful than the parent compound, therefore, the control and identification of degradation products is an important task in the study of various degradation processes in order to reduce the toxicological burden. In this way of solving environmental problems, it is impossible to do without an in-depth study of the physico-chemical properties of both the pollutants themselves and the products of their transformation under the influence of various external factors, among which the UV VIS radiation occupies an important place. Thus, solving the problems of drug destruction by the light radiation of various energies is part of the environmental problem of preserving conditions for the normal functioning of the environment and human health.

Based on the above, the purpose of our study of the properties of photolysis products of the studied molecule becomes clear and necessary. This study can be conducted using various methods. Detection of electron absorption spectra in case of exposure to UV radiation sources with different excitation wavelengths and power makes it possible to identify the formation of paracetamol photoproducts, their temporal changes, absorption regions, as well as changes of the energy patterns of photoproducts, manifested in the presence of fluorescence, its flaring or fading, as well as a shift in the wavelength of radiation. However, these studies cannot determine the structure of the resulting photoproducts. The physical methods of NMR, EPR, and chromatography [15,16] help to establish the chemical structure of a photoproduct, although the processes of decoding these spectra take a long time and do not always give unambiguous results in interpretation. An important place in the process of interpreting photolysis products is occupied by quantum chemical methods for calculating the properties of initial compounds and their photoproducts, which are fixed but poorly living, as well as those properties of molecules that cannot be directly measured. The use of an integrated approach in the study of paracetamol photolysis makes it possible to bridge the gap between the results of previous and new studies.

2. Research methodology

2.1. Experimental

An experimental study of the electronic spectra of paracetamol used a compound synthesized by company CDH (product code 001205) with a guaranteed purity of 99%. A dry sample was dissolved in distilled water using an ultrasonic stirrer to obtain a matrix solution of paracetamol at a concentration of 1 mM. Absorption and fluorescence spectra of the studied solutions were recorded using VARIAN Cary 5000 Scan UV-VIS-NIR spectrophotometer and VARIAN Cary Eclipse spectrofluorometer (AgilentTech., USA–Netherlands–Australia) at room temperature within the spectral band of 190 - 600 nm. A quartz cell with the pathway of 10 mm was used for the measurement. The error of measurement of the absorption and fluorescence wavelengths is ± 1 nm.

An experimental study of the photolysis of paracetamol was conducted under irradiation conditions in a stationary photoreactor, which is an experimental installation for studying the mechanisms of the effects of UV radiation of various wavelengths and power on organic compounds, a detailed description of which was presented in Ref. [17]. An excilamp KrCl (222 nm) and an ultraviolet bactericidal irradiator OUFb-04 (spectral range from 180 to 275 nm) with a quartz lamp hbox DKB(U)-9 were used as UV radiation sources in a stationary photoreactor. An aqueous solution of paracetamol with a concentration of 0.05 mM and a volume of 90 ml was prepared for irradiation. The control exposure time was 0, 1, 2, 4, 8, 16, 32, 64 and 128 min. Samples were collected to record absorption, fluorescence, and fluorescence excitation spectra during the irradiation process.

2.2. Chromatographic analysis of paracetamol transformation products

Chromatographic analysis was performed at the UrFU Collective Use Center in the laboratory „Complex research and expert evaluation of organic materials“. The composition of the samples was studied using „Agilent 1290 Infinity II“ liquid chromatograph coupled to „Agilent 6545 Q-TOF LC/MS“ quadrupole time-of-flight mass spectrometer on a reversed phase column „Zorbax Eclipse Plus C18“ with the size of $2.1\,\mathrm{mm} \times 100\,\mathrm{mm} \times 1.8\,\mu\mathrm{m}$ (Agilent, p/n 959758-902), additionally protected by a pre-column with dimensions $2.1\,\mathrm{mm} \times 5\,\mathrm{mm} \times 1.8\,\mu\mathrm{m}$. An aqueous solution of 20 mM ammonium formate with the addition of 0.1% (by volume) formic acid (component A) and methanol (component B) were used as components of the mobile phase. Chromatographic separation was carried out in a gradient mode using an initial isocratic step with 5% (volume) methanol content for 1 h, and then the methanol content in the mobile phase was linearly changed from 5 to 30% (volume) for 10 h, the final composition was maintained in for 1 h, after which the methanol content was increased to 85% (volume) for 1 h and this composition was maintained for 3 h. The total analysis time was 15 h. The flow rate of the mobile phase is 0.25 ml/min. The temperature of the column thermostat was set to 30 °C.

The mass spectrometer operated with an ionization source by electrospray in the mode of ionization of positively or negatively charged ions (gallic acid). Nitrogen was used as the drying gas, supplied at a rate of $8-10$ l/min at a temperature of $320-350\,^{\circ}\mathrm{C}$. Temperature of the superheating gas $400\,^{\circ}C$ when supplied at a rate of 12 l/min. The voltage on the fragmenter is 90 V, the voltage on the capillary is 3500 V. The mass spectra were recorded in the range of m/z $70-1700$ in the MS mode and m/z $30-600$ in the MS/MS mode. The measurement error of m/z is less than 5 ppm. MS/MS spectra were obtained as a result of collision-induced dissociation (CID) with nitrogen molecules at collision energy values in the range $10-20$ eV. The device was adjusted and the accuracy of the mass determination was corrected automatically in real time using standard calibration solutions recommended by the device manufacturer.

2.3. Quantum chemical calculations

Quantum-chemical calculations performed using the semi-empirical method of intermediate neglect of differential overlap (INDO) with original parametrization [18]. The method was implemented in the software package developed by the photonics department of the Siberian Physical and Technical Institute, Tomsk State University. This software package is oriented to the study of spectral luminescent properties of polyatomic molecules and photochemical processes in them using various classes of chemical compounds [18]. The package programs calculate the electronic spectra of singlet and triplet excited states, the

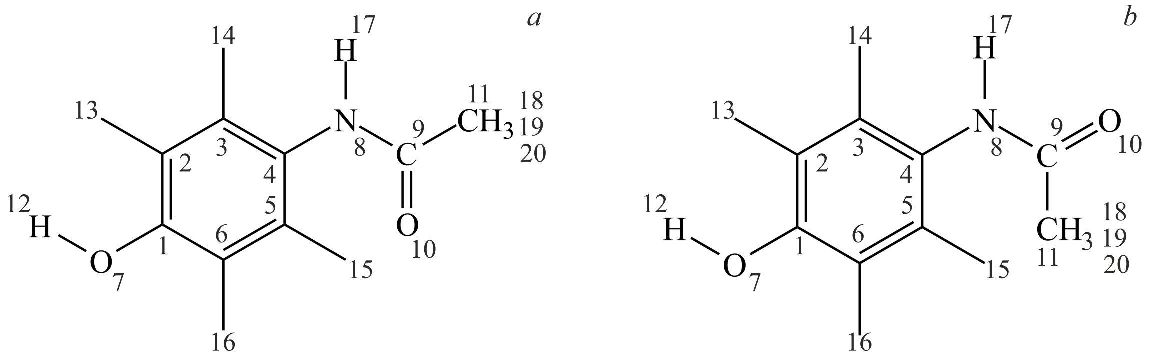


Figure 1. Structural formulas and atomic numbering of paracetamol.

spectra of induced absorption and fluorescence, the physicochemical properties of molecules, the distribution of electron density on atoms and chemical bonds, the dipole moment in the ground and excited states, as well as the proton acceptor ability of a molecule in the ground and excited states by the method of molecular electrostatic potential (MESP)) [19,20]. The ChemDraw Ultra program was used to create a model of the geometry of the molecule. Austin Model 1 geometry optimization method (Austin Model № 1 or AM1) [21–24] was defined using Chem3D Ultra and Hyper Chem programs.

2.4. Quantum chemical approach to the study of photolysis of organic molecules

Phototransformation of a polyatomic molecule causes, in particular, the breaking of individual chemical bonds. The quantum chemical approach to studying the possibility of bond breaking is described in detail in Ref. [25], and it was successfully applied to molecular systems of varying complexity, for example, in Ref. [26–28]. The essence of the method is as follows. At the first stage, changes in the population (strength) of the bonds of the core of the molecule in various electronically excited states are analyzed and the states with the most significant strength changes are selected. In this case, the electronically excited state with the a decrease of the strength of the chemical bond, should be localized on it. It should be noted that fragmentation of a molecule in this way involves the destruction of the σ-core of the molecule, and therefore the state in which rupture is possible should be $\pi\sigma^*$-, $\sigma\pi^*$- or $\sigma\sigma^*$-types.

The next stage involves determining the type of potential curves of the selected electronically excited states depending on the length of the bond, presumably capable of breaking. The potential curves of excited electronic states are constructed by summing the calculated energy of the excited state localized on the chemical bond being investigated for breaking, at each step of changing its length, and the energy of the potential curve of the ground state, using the Morse potential for the ground state energy:

$$V(R) = D_0(e^{-2\alpha X} - 2e^{-\alpha X}),$$

where D_0 is the bond energy, $X = \Delta R/R_0$, R_0 and ΔR is the the equilibrium bond length and its variation, respectively, α is the characteristic of the Morse curve, depending on the reduced mass of bond atoms, the frequency of valence vibrations of the bond and the energy of its rupture. The shape of the curve of the excited electronic state determines the possibility of breakage of the studied bond: the binding potential curve has a minimum, which corresponds to the stable state of the molecule when the electronic excitation is delocalized throughout the molecule. The absence of a minimum on the potential curve (repulsion curve, photodissociative curve) corresponds to the breaking of a chemical bond in the considered electronically excited state. At close energies of the binding and repulsive states, a transition of the molecule to the repulsion curve is possible, which indicates the localization of the absorbed energy on the studied bond, leading to its breakage.

To determine the orbital nature of the excited state in which the studied bond is broken, one of the complex's programs allows calculating the rate constants of nonradiative transition processes from the potential curve of the state exciting photolysis to the potential repulsion curve of the singlet (k_{IC}) or triplet state of the bond being broken (k_{ST}). A comparison of the rate constants of the internal and singlet-triplet conversion processes (k_{IC} and k_{ST}) allows determining the orbital nature of the state in which this bond is broken. It is more likely that the breakage of the test bond occurs in a singlet state at $k_{\mathrm{IC}} > k_{\mathrm{ST}}$, in the opposite case it occurs in a triplet state.

3. Results and discussion

3.1. Choosing the geometry of the paracetamol molecule

The correct choice of the geometry of the studied molecule is of great importance in the calculation. A structural feature of the paracetamol molecule is the possibility of the existence of a large number of its isomers caused by the presence of single bonds in the structure of the molecule. Fig. 1 shows the structure of the isomers of the studied molecule.

The authors of Ref. [15] studied the spatial geometry of a molecule in solution by double NMR spectroscopy and found that the paracetamol molecule exists as a type 1 isomer in a solution of dimethyl sulfamide D-6 (Fig. 1, *a*). The conclusion of the authors of Ref. [15] about the existence of a type 1 isomer in paracetamol solution does not give confidence that paracetamol exists in the same geometry in an aqueous solution. The optimization of the structural parameters of the molecule performed by us gave the type 2 isomer as the main one (Fig. 1, *b*). Optimization of the structural parameters of a polyatomic molecule inspires great confidence in the correct choice of geometry, however, the need to compare the properties of isomers of types 1 and 2 requires the calculation of spectra in the same geometry. Therefore, both isomers were calculated with a geometry based on the averaged structural parameters [23]. The $COCH_3$ group is rotated by 45° relative to the N_8-C_9 bond in the average geometry to eliminate steric stresses between the phenyl and $COCH_3$-fragments. The use of two geometric parameter systems (optimized and averaged) when compared with the experiment showed the similarity of the results regardless of the chosen parameter system, the type of isomer, and demonstrated a satisfactory description of the experimental spectrum [24], although each of the geometries shows some deviations from the experiment that do not fundamentally differ. Both isomers, regardless of the chosen system of geometric parameters, have a non-planar structure, which makes it difficult to determine the orbital nature of electronically excited states.

3.2. Photolysis of paracetamol in water

3.2.1. Experimental study of paracetamol photolysis

The results of the experimental study are shown in Fig. 2. The effect of UV radiation causes chemical changes in the molecules absorbing it. The molecule undergoes photodegradation after light absorption, as a result of which it is possible to break chemical bonds and form various photoproducts consisting of fragments of the initial compound. The changes occurring in the irradiated solution are reflected in the absorption spectra (Fig. 2, *a, b*), fluorescence (Fig. 2, *c, d,f*) and fluorescence excitation (Fig. 2, *e, g*). A decrease of the intensity of bands in the range of 194 and 250 nm is observed in the absorption spectra under the impact of radiation from the KrCl excilamp (222 nm), which indicates photodegradation of the initial substance (Fig. 2, *a*). A shift of the absorption band from 250 to 235 nm was detected under the action of UV radiation from the lamp OUFb-04 (Fig. 2, *b*). The changes observed in the spectra show that the phototransformation mechanism depends on the radiation source. The absorption increases at a maximum of 245 nm during the exposure to a KrCl excilamp for up to 8 min, and a decrease of the intensity of the band is observed with the increase of the exposure time, which is the result of the transformation of the initial compound with subsequent degradation (Fig. 2, *a*). A band in the form of an inflection is observed in the 280 nm region, the absorption intensity of which increases during irradiation with a KrCl excilamp, which indicates the accumulation of a photoproduct (Fig. 2, *a*). A band appears in the absorption spectrum in the region of 235 nm after 128 min of irradiation with OUFb-04 lamp , and a wide absorption band appears in the region of 380 nm during irradiation (Fig. 2, *b*). These bands were not observed in the initial spectra, therefore, various photoproducts formed in the solution after irradiation.

The analysis of the fluorescence and fluorescence excitation spectra also confirms the formation of photoproducts of various nature when irradiated with KrCl (Fig. 2, *c–e*) and OUFb-04 lamps (Fig. 2, *f, g*). The formation of a photoproduct fluorescing in the 430 nm region was recorded in the spectra (Fig. 2, *c, d*). This emission band is formed by a photoproduct of paracetamol absorbing in 320 nm region according to the fluorescence excitation spectrum (Fig. 2, *e*). The fluorescence intensity in 430 nm region first increases and then decreases during the irradiation process, indicating degradation of the resulting photoproduct. Simultaneously with the decrease of the fluorescence intensity in 430 nm region, an increase is observed in 450–500 nm region, which is associated with the accumulation of the secondary product of paracetamol transformation (Fig. 2, *c, d*). The formation and accumulation of a photoproduct fluorescing in the region of 370–380 nm was recorded during the irradiation with OUFb-04 lamp (Fig. 2, *f*). The radiation in this region is formed by a photoproduct of paracetamol absorbing in 300 nm region according to the fluorescence excitation spectrum (Fig. 2, *g*).

A photolysis of an aqueous solution of paracetamol was studied in Ref. [16] by liquid chromatography in combination with mass spectroscopy. The solution was irradiated with light with $\lambda = 254$ nm in the absence and presence of oxygen in the solution. The authors of Ref. [16] identified the main products of photolysis, analyzed the kinetics and mechanisms of their formation, and obtained absorption spectra of photoproducts. Ultraviolet irradiation of an aqueous solution of 0.265 mM paracetamol for 3 h resulted in a shift of maxima from 245 to 240 nm and a change of the intensity of bands in the absorption spectrum, as well as the appearance of absorption in the region of $\lambda_{\max} = 380$ nm, which is not present in the spectrum of the unirradiated solution. Regardless of the presence of oxygen in the solution, photo rearrangement is the predominant photoreaction pathway, which produces the paracetamol isomer 2-amino-5-hydroxyacetophenone. 2-amino-5-hydroxyacetophenone passes into the final product peroxyester after prolonged irradiation and saturation of the irradiated solution with oxygen. The formation of para-aminophenol was observed as a secondary competitive pathway in photoreaction.

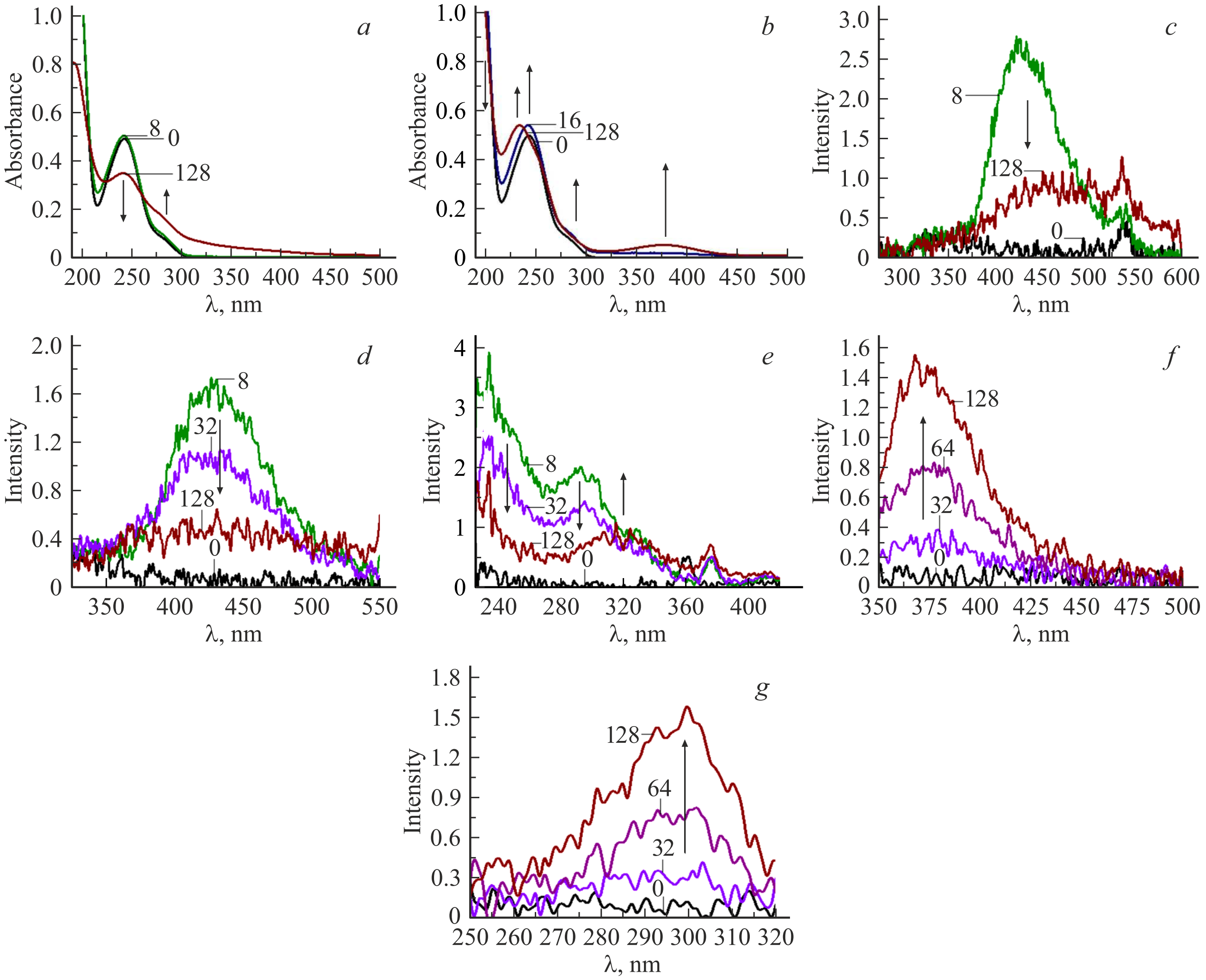


Figure 2. Changes of absorption spectra (a, b), fluorescence (c, d, f) and fluorescence excitation (e, g) of paracetamol in water after exposure to UV radiation, the numbers indicate the irradiation time (min): (a, c, d, e) irradiation with a KrCl excilamp, (b, f, g) irradiation with an antibacterial lamp OUFb-04; with the excitation wavelength of $\lambda_{\text{exc}} = 245$ (c), 280 (d), 300 nm (f); with emission wavelength of $\lambda_{\text{em}} = 430$ (e), 370 nm (g). The figures in the figures correspond to the exposure time (min).

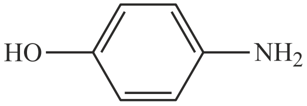
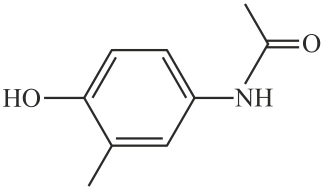
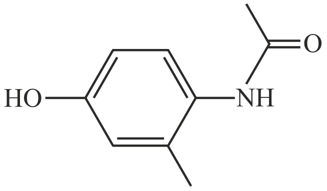
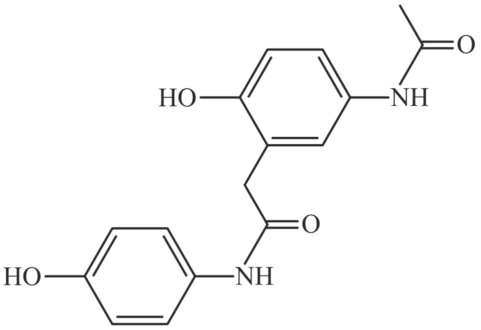
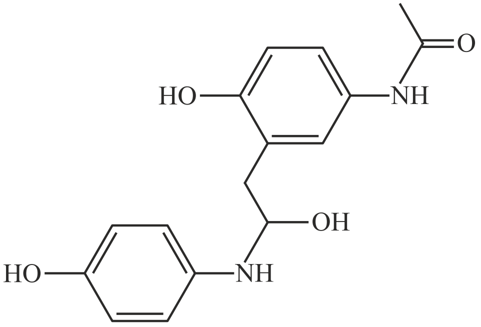
3.2.2. Chromatographic study of paracetamol photolysis

4-aminophenol and 2-amino-5-hydroxyacetophenone were detected as two end products during chromatographic study of an aqueous solution of paracetamol irradiated with OUFb-04 lamp (128 min) (Fig. 3). The compounds found in the paracetamol sample after irradiation are listed in Table 1. Losses of the hydroxyl group and molecules of ammonia, water, and CO are observed in the structure of compound 1 (Table. 1), which makes it possible to attribute the structure of 4-aminophenol to this compound. Based on the presence of signals of ions with m/z 148, 124 and 107 in the spectrum of compound 2, it can be assumed that there is a methyl group in the benzene ring of the photoproduct of paracetamol. Compounds 3–5 were also detected after prolonged irradiation with OUFb-04 lamp (Table 1). Compound 3 may contain an acetyl group in the benzene ring, while compounds 4 and 5 appear to be dimers of paracetamol. Irradiation (128 min) with KrCl excilamp resulted in the presence of signals of ions with m/z 148, 124, and 107 in the spectrum of the compound of 2-amino-5-hydroxyacetophenone. It is possible to make an assumption about the presence of a methyl group in the benzene ring in the structure of the photoproduct. The long-wavelength absorption band of 2-amino-5-hydroxyacetophenone in the spectrum is in the range of 304 nm according to Ref. [16].

3.2.3. Quantum chemical study of paracetamol photolysis

We considered the excitation of the molecule in the region of the short-wavelength absorption band ($\lambda_{\max} \sim 194$ nm)

Table 1. Compounds found in the paracetamol sample after irradiation

№	$[M+H]^+$, theory	Time of retention, min	Gross formula	Probable structure
1	110.06	1.10	C_6H_7NO	
2	166.086	8.81	$C_9H_{11}NO_2$	 или 
3	194.0812	12.97	$C_{10}H_{11}NO_3$	–
4	303.133	7.72, 9.92	$C_{16}H_{18}N_2O_4$	
5	301.118	8.90,9.57,11.00	$C_{16}H_{16}N_2O_3$	

in the theoretical study of the possibility of bond breaking in the paracetamol molecule. It should be noted that our chosen radiation with $\lambda \sim 200$ nm will ensure the excitation in all the underlying regions of the absorption spectrum, including excitation with light with $\lambda = 254$ nm due to the high rate of the internal conversion process. It is assumed that in case of paracetamol single bonds with $C_4{-}N_8$, $N_8{-}C_9$, and $C_9{-}C_{11}$ can be broken (Fig. 1) as less strong. When constructing the Morse potential of the paracetamol molecule, the energy of breakage of bonds $C_4{-}N_8$ and $N_8{-}C_9$, $C_9{-}C_{11}$, C–C (phenyl), according to Ref. [29], were assumed to be equal to 33 780, 34 650, 40 330 cm^{-1} for the listed bonds, respectively. The equilibrium bond lengths indicated above are taken from the geometry of the optimized complex of paracetamol isomer 2 with water and are equal, respectively to 1.44, 1.45, 1.55, 1.40 Å. The frequencies of valence vibrations of the studied bonds, according to Ref. [30], accepted as equal: $\omega\,(C{-}N) = 1300\,\mathrm{cm}^{-1}$, $\omega\,(C_9{-}C_{11}) = 1450\,\mathrm{cm}^{-1}$, $\omega\,(C{-}C)_{\mathrm{phenyl}} = 1600\,\mathrm{cm}^{-1}$.

3.2.4. Quantum chemical study of potential curves of excited states of paracetamol

The results of calculating the potential curves of excited states of the paracetamol fragment of NH-$COCH_3$ studied for bond breakage showed that the singlet and triplet electron-excited states localized on each of these single bonds are characterized by a disintegration curve. At the same time, the potential curves of the electronic state exciting photolysis ($\lambda = 194$ nm) and states not localized on each of the presumably breaking bonds have a minimum, corresponding to the stable state of the molecule. The type of potential excitation and breakage curves is similar

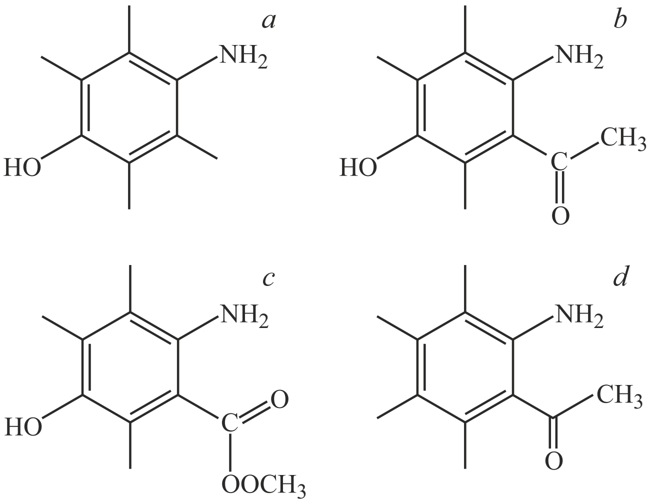


Figure 3. Structural formulas of paracetamol photoproducts: (*a*) para-aminophenol, (*b*) 2-amino-5-hydroxyacetophenone, (*c*) peroxyester, (*d*) 2-amino-acetophenone.

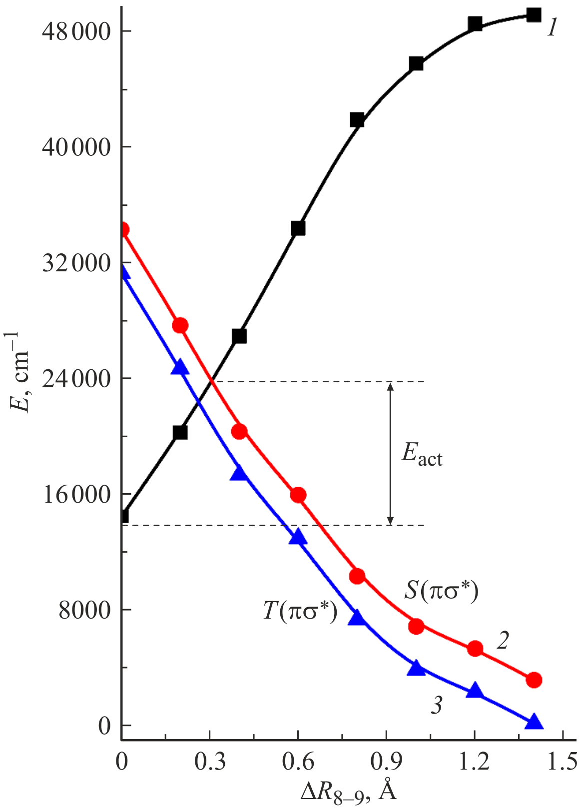


Figure 4. Potential curves of electronically excited states of the paracetamol-water complex: *1* — photolysis-stimulating states; *2* — singlet photodissociative state of bond $N_8{-}C_9$; *3* — triplet photodissociative state of bond $N_8{-}C_9$; E_{act} — activation energy.

for all studied bonds. For this reason, Fig. 4 shows the corresponding potential curves only for the bond $N_8{-}C_9$.

The estimation of the rate constants of the transition of a molecule from a potential excitation curve to photodissociative curves of singlet or triplet states of bond $N_8{-}C_9$ showed a greater efficiency of the internal conversion process in the singlet state system ($k_{IC} = 10^{12}\,s^{-1}$) compared with the singlet-triplet system ($k_{ST} = 10^9\,s^{-1}$), which indicates a break in $N_8{-}C_9$ bond mainly in the singlet photodissociative state. A similar conclusion was made by the authors of Ref. [16]. We determined the sequence of breaking of the studied bonds during the photolysis of paracetamol by using the values of the activation energy and the change in the population (strength) of the bond in the transition state of the molecule compared with the population of the bond in the ground state (Table 2, Fig. 4).

Table 2. Activation energy and population of single bonds of paracetamol in the transition state

Characteristics of bond	Bond			
	$C_4{-}N_8$	$N_8{-}C_9$	$C_9{-}C_{11}$	$O_7{-}H_{12}$
Energy of activation, cm^{-1}	11150	9050	17800	18100
population (strength) bond in S_0-state, *e*	0.781	0.719	0.559	0.575
population (strength) of bond, *e*	0.085	0.057	0.028	0.124

3.2.5. Quantum chemical investigation of paracetamol photoproducts

It follows from the data in Table 2 that the lowest activation energy during the transition to the photodissociative curve is characteristic of the $N_8{-}C_9$ bond with a decrease of the bond population by more than 10 times. According to the chosen criterion, we conclude that it is more likely to expect a break of bond $N_8{-}C_9$. Under the conditions of an aqueous solution, as a result of breakage of $N_8{-}C_9$ bond, it is realistic to assume the formation of para-aminophenol. Experimental data confirm this assumption: para-aminophenol is the first photoproduct that appears on the chromatogram in terms of formation time. $C_4{-}N_8$ bond is the next bond with the most effective disintegration, which is likely to lead to the formation of phenol. One of the products of photolysis is 2-amino-5-hydroxyacetophenone molecule, which is formed by phototransformation of the Frieze, consisting in breakage of N–C bond and migration of the acetyl group to the ortho position of the phenyl ring. 2-amino-5-hydroxyacetophenone s formed both in the absence of oxygen in solution and in its presence according to experimental data from Ref. [16].

We calculated and compared the results of calculation of the electronic absorption spectra with the experimental absorption spectra of photoproducts to ensure that the identification of photoproducts is correct. The comparison results are presented in Table 3. The calculations

Table 3. Calculated and experimental absorption spectra of paracetamol photoproducts

Photo product	Absorption spectrum				
	Calculation				Experiment [16]
	State	E_i, cm^{-1}	λ_i, nm	f	$\lambda_{\max}$, nm
para-aminophenol (secondary photoproduct)	S_1 $(\pi\pi^*)$	33460	299	0.096	$\sim$ 295
	S_2 $(\pi\pi^*)$	36980	270.5	0.195	271
	S_6 $(\pi\pi^*)$	47980	212	0.729	219
	S_7 $(\pi\pi^*)$	47770	209	0.530	
2-amino-5-hydroxy-acetophenone (main photoproduct)	S_1 $(n\pi^*)$	31490	318	0.0	
	S_2 $(\pi\pi^*)$	32860	304	0.200	308
	S_3 $(\pi\pi^*)$	37530	267	0.002	
	S_4 $(\pi\pi^*)$	41490	241	0.054	248
	S_6 $(\pi\pi^*)$	43980	227	0.838	227
	S_8 $(\pi\pi^*)$	46460	215	0.112	
	S_{10} $(\pi\pi^*)$	49340	203	0.434	
ortho-aminoacetophenone (intermediate photoproduct)	S_1 $(n\pi^*)$	28320	353	0.0	362
	S_2 $(\pi\pi^*)$	31990	312	0.141	
	S_3 $(\pi\pi^*)$	38630	259	0.030	$\sim$ 260 inflection
	S_5 $(\pi\pi^*)$	44900	223	0.515	227
	S_8 $(\pi\pi^*)$	46490	215	0.460	
	S_{10} $(\pi\pi^*)$	50080	200	0.473	
peroxyester	S_1 $(\pi\pi^*)$	32220	310	0.130	295
	S_2 $(n\pi^*)$	34040	294	0.0	
	S_3 $(\pi\pi^*)$	38720	258	0.146	250
	S_7 $(\pi\pi^*)$	45480	220	0.824	
	S_{10} $(\pi\pi^*)$	49950	200	0.311	
	S_{13} $(\pi\pi^*)$	53110	188	0.450	

describe the absorption spectra of the main and secondary photoproducts of an argon-saturated solution and a photoproduct occurring in oxygen-saturated solutions (peroxyester) well, but are less adequate for describing an intermediate photoproduct (ortho-aminoacetophenone), in the absorption spectrum of which there is an absorption band with $\lambda \sim 362.4$ nm. According to the calculation (Table 3), the long-wavelength band of the absorption spectrum of ortho-aminoacetophenone is formed by two electronic transitions, the first of which belongs to $n\pi^*$-type of oxygen atom of the carbonyl group and is forbidden. The intensity of the long-wavelength band of this photoproduct forms an electronic transition to the state $S_2(\pi\pi^*)$, forming an absorption band in the region of $\lambda = 312$ nm, far from the absorption spectrum band of the photoproduct at $\lambda \sim 362.4$ nm. The theoretically determined possibility of breaking single bonds in the paracetamol molecule, the correspondence of the results of calculating the absorption spectra of three paracetamol photoproducts identified experimentally, indicates the reality of the phototransformation process of the paracetamol molecule in water under UV irradiation, described in Ref. [16].

A study of the spectral luminescent properties of an aqueous solution of paracetamol showed that the molecule forms a complex with an H-bond of 1 : 1 composition between a water molecule and an oxygen atom of the carbonyl group in an aqueous solution [24]. Table 3 shows the calculated and experimental electron absorption spectra of the complex with water of the studied molecule, a comparison of which shows satisfactory agreement with

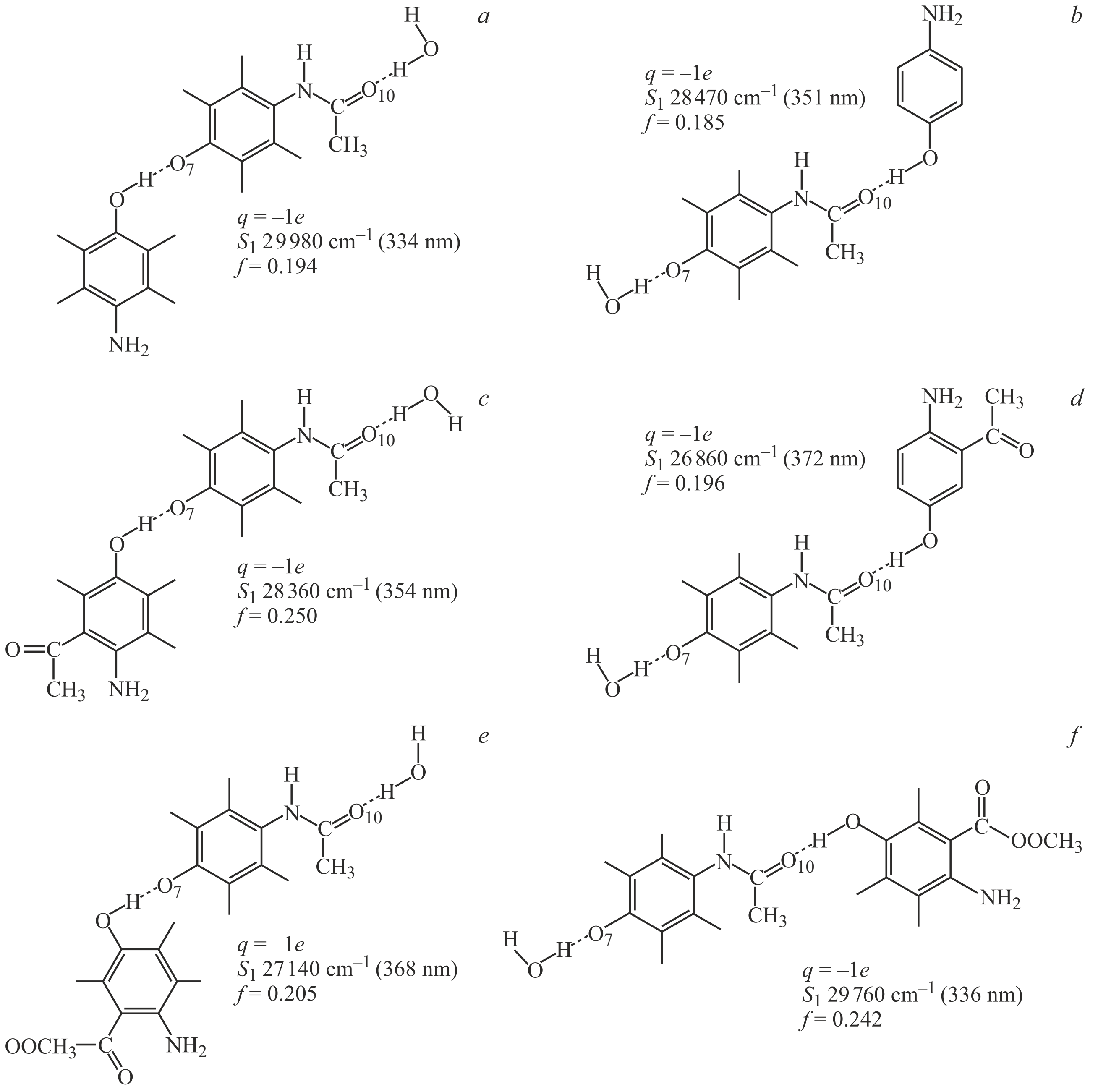


Figure 5. Structures of paracetamol anion complexes with its photoproducts: H-bond of O_7 atom of the paracetamol anion with para-aminophenol (*a*), 2-amino-5-hydroxyacetophenone (*c*), peroxyester (*e*); H-bond of O_{10} atom of the paracetamol anion with para-aminophenone (*b*), 2-amino-5-hydroxyacetophenone (*d*), peroxyesterone (*f*). q is the effective charge, f is the oscillator strength of the electronic transition.

the calculation of the experiment [24] in both energy and intensity. The absorption spectrum of an aqueous solution of paracetamol is formed by three absorption bands with $\lambda_{\max} = 280$, 245 and 194 nm, the oscillator strength of which is 0.02, 0.26 and 0.72, respectively.

Analyzing the energy of singlet states forming a long-wavelength absorption band in the spectra of paracetamol and its photoproducts, the identification of which is beyond doubt, it should be noted that the longest wavelength band belongs to the molecule of 2-amino-5-hydroxy-acetotophenone ($\lambda \sim 312$ nm), formed in a solution saturated with argon as a result of irradiation. An analysis of the nature of the bands in the spectrum of an aqueous solution of paracetamol in Ref. [24] showed that the phenolic fragment of the molecule is the main one in the formation of electronic transitions of paracetamol, forming the absorption spectrum in the range of up to 50 000 cm^{-1} (200 nm): it is responsible for absorption in all areas of the electronic

Table 4. Calculated and experimental spectra of absorption of complexes with water of isomer 2 of paracetamol and its anion

Calculation				Experiment [24]	
State	E_{si}, cm^{-1}	λ, nm	f	λ, nm	f
paracetamol+H_2O					
S_1 ($\pi\pi^*$)	35490	282	0.058	280	0.02
S_2 ($n\pi^*$)	36250	276	0.001		
S_3 ($\pi\pi^*$)	42170	237	0.041	245	0.26
S_4 ($\pi\pi^*$)	44500	224	0.045	194	0.72
S_8 ($\pi\pi^*$)	46380	216	0.751		
S_{10} ($\pi\pi^*$)	48980	204	0.501		
paracetamol anion $(q = -1e) + 2H_2O$					
S_1 ($\pi\pi^*$)	30950	323	0.180		
S_2 ($\pi\pi^*$)	35900	279	0.237		
S_3 ($n\pi^*$) O_7	37470	271	0.009		
S_4 ($n\pi^*$) O_{10}	37870	264	0.004	No data available	
S_{11} ($\pi\pi^*$)	46310	216	0.373		
S_{12} ($\pi\pi^*$)	47930	209	0.579		

spectrum. It is known that the hydroxyl bond breaks when irradiated with UV light in phenol with the separation of a proton and the formation of a phenol anion. We studied previously this process in phenol, its substituted compounds and their complexes with water [26–28]. The calculation of the strength of O–H bond of paracetamol showed that the substitution of $NH{-}COCH_3$ fragment of phenol does not change the population of this bond ($P_{\text{O-H}} = 0.576\,e$), therefore, the breakage of the hydroxyl bond in paracetamol and the formation of its anion can be assumed.

Calculated and experimental electron absorption spectra of the complex of the studied molecule are provided in Table 4, a comparison of which shows a satisfactory agreement between the calculation and the experiment data [24] in terms of both energy and intensity. The absorption spectrum of an aqueous solution of paracetamol is formed by three absorption bands with $\lambda_{\max} = 280$, 245 and 194 nm, the oscillator strength of which is 0.02, 0.26 and 0.72, respectively. A study of the spectral luminescent properties of an aqueous solution of paracetamol showed that the molecule forms a complex with an H-bond of 1 : 1 composition between a water molecule and an oxygen atom of the carbonyl group in an aqueous solution [24].

Calculation of the absorption spectrum of the paracetamol anion (Table 4) gives an electronic transition $S_0 \rightarrow S_1$, forming a long-wavelength absorption band of the anion with $\lambda \sim 323$ nm, i.e. the absorption band of the anion turns out to be the longest wavelength among the considered photoproducts. It should be added that the anion of paracetamol is much more active than its neutral form. According to MESP calculations, two acceptor centers active for intermolecular interaction in the ground state increase the interaction energy to −692 kJ/mol (atom O_{10}) and −1120 kJ/mol (atom O_7) compared to the neutral molecule of paracetamol (−370 kJ/mol for atom O_{10} and −110 kJ/mol for atom O_7).

Table 5. Calculated and experimental absorption spectra of the complex with the H-bond of the paracetamol anion and 2-amino-5-hydroxyacephenone

Calculation				Experiment
State	E_i, cm^{-1}	λ_i, nm	f	λ_i, nm
S_1 ($\pi\pi^*$)	26860	372	0.196	380
S_2 ($\pi\pi^*$)	28540	350	0.178	
S_3 ($n\pi^*$)	28990	345	0.0	
S_4 ($\pi\pi^*$)	31410	318	0.129	$\sim$ 290–320
S_{10} ($\pi\pi^*$)	36960	271	0.230	250
S_{20} ($\pi\pi^*$)	44710	224	0.806	$\sim$ 190
S_{29} ($\pi\pi^*$)	50460	198	0.578	

As a result of UV irradiation of an aqueous solution of paracetamol, its decomposition products are present simultaneously with neutral and charged forms of paracetamol. This creates conditions for the formation of complexes with the H-bond of photoproduct molecules with the paracetamol anion as the most active particle with the lowest transition energy, which forms absorption in the long-wavelength region of the spectrum. Therefore, we assumed the possibility of the formation of complexes of the paracetamol anion with the identified photoproducts (para-aminophenol, hbox2-amino-5-hydroxyacetophenone and peroxyester) and calculated the absorption spectra of these complexes (Fig. 5). When constructing the complexes, the possibility of forming an H-bond of photoproducts with the O_7 and O_{10} atoms of the paracetamol anion (with each separately) was taken into account. Fig. 5 shows the structures of the calculated complexes, the energy, and the strength of the transition oscillator $S_0 \rightarrow S_1$, which forms a long-wavelength band of the absorption spectrum.

A comparison of the obtained results of calculating the absorption spectra showed that the complex, the first electronic transition of which forms the absorption band of the irradiated solution with $\lambda = 380$ nm, can be a complex with an H-bond at the atom O_{10} of the paracetamol anion with its main photoproduct 2-amino-5-hydroxyacetophenone (fig. 5, *d*). Table 5 shows the full calculated spectrum of this complex in comparison with the experimental spectrum of an irradiated aqueous solution of paracetamol (Fig. 2, *b*). There is a satisfactory correspondence between the calculation and the experiment.

Analyzing the calculation results, it is possible to say that the mechanism of photoresistance of the considered bonds is pre-dissociation, since the energy of breakage of these bonds is much higher in the equilibrium state than the energy of the photolysis excitation source.

Conclusions

1. The absorption spectra of paracetamol complexes with water and its anion, as well as chromatographically identified photoproducts of paracetamol formed upon excitation by UV radiation from an OUFb-04 bactericidal lamp (radiation range from 180 to 275 nm) and radiation from a KrCl (222 nm) excilamp, have been calculated using quantum chemistry methods.
2. The results of quantum chemical calculations confirm the probability of breaking all three single bonds of the molecule under UV irradiation of an aqueous solution of paracetamol. The identification of three photoproducts formed as a result of the breakage of single bonds of $CNHCOCH_3$ fragment has been confirmed by calculations. It is determined that bonds break in a singlet electronically excited state.
3. To identify the molecular structure responsible for the appearance of the absorption band in the region of $\lambda_{\max} = 380$ nm in a UV-irradiated aqueous solution of paracetamol, the absorption spectra of the putative complexes of the paracetamol anion with its photoproducts were calculated. The calculation results suggest that such a structure may be a complex with an H-oxygen bond of the carboxylic group of the paracetamol anion with the main photoproduct of its disintegration — 2-amino-5-hydroxyacetophenone.

Funding

The results were obtained as part of the Russian Science Foundation project №24-19-20031.

Conflict of interest

The authors declare that they have no conflict of interest, financial and other conflicts.

References

[1] G.G. Graham, K.F. Scott. Am. J. Ther., **12** (1), 46 (2005). DOI: 10.1097/00045391-200501000-00008

[2] S.S. Ayoub. Temperature, **8** (4), 351 (2021). DOI: 10.1080/23328940.2021.1886392

[3] G.W. Przybyła, K.A. Szychowski, J. Gmiński. Clin. Exp. Pharmacol. Physiol., **48** (1), 3 (2021). DOI: 10.1111/1440-1681.13392

[4] M. Yan, Y. Huo, S. Yin, H. Hu. Redox Biol., **17**, 274 (2018). DOI: 10.1016/j.redox.2018.04.019

[5] O.V. Ryzhkova. *Differentsial'naya diagnostika khronicheskih gepatitov: uchebnoe posobie* (IGMU, Irkutsk, 2020) (in Russian).

[6] S. Fatima, N. Asif, R. Ahmad, T. Fatma. Environ. Sci. Pollut. Res. Int., **27** (28), 35208 (2020). DOI: 10.1007/s11356-020-09802-0

[7] C. Nnodum, K.A. Yusuf. IJSRM., **10**, 56 (2022). DOI: 10.18535/ijsrm/v10i5.c1

[8] Å. Wennmalm, B. Gunnarsson. Drug Inf. J., **39** (3), 291 (2005). DOI: 10.1177/009286150503900307

[9] S. Wu, L. Zhang, J. Chen. Appl. Microbiol. Biotechnol., **96** (4), 875 (2012). DOI: 10.1007/s00253-012-4414-4

[10] F.J. Chacón, M.L. Cayuela, M.A. Sánchez-Monedero. Environ. Pollut., **307**, 119546 (2022). DOI: 10.1016/j.envpol.2022.119546

[11] W.J. Lee, P.S. Goh, W.J. Lau, A.F. Ismail. Arab. J. Sci. Eng., **45**, 7109 (2020). DOI: 10.1007/s13369-020-04446-1

[12] Y. Vieira, J.E. Spode, G.L. Dotto, J. Georgin, D.S. Franco, G.S. dos Reis, É.C. Lima. Environ. Chem. Lett., **22** (5), 2343 (2024). DOI: 10.1007/s10311-024-01751-1

[13] A.G. Al-Kaf, K.M. Naji, Q.Y.M. Abdullah, W.H. Ali Edrees. Chron. Pharm. Sci., **1** (6), 341 (2017).

[14] M. Chen, J. Liu, Y. Bi, S. Rehman, Z. Dang, P. Wu. J. Hazard. Mater., **388**, 122078 (2020). DOI: 10.1016/j.jhazmat.2020.122078

[15] I.A. Khodov, R.S. Kumeev, M.Yu. Nikiforov, V.A. Golubev, T.A. Alper. Izv. vuzov. Khimiya i khimicheskaya tekhnologiya, **3**, 106 (2013).

[16] M. Martignas, E. Oliveros, M.-T. Maurette, C. Claparols. Photochem. Photobiol. Sci., **12**, 527 (2013). DOI: 10.1039/c2pp25341k

[17] N.P. Bezlepkina, E.N. Bocharnikova, O.N. Tchaikovskaya, G.V. Mayer, V.I. Solomonov, A.S. Makarova, A.V. Spirina, S.A. Chaikovsky. J. Fluoresc. (2024). DOI: 10.1007/s10895-024-03640-w

[18] V.Ya. Artuykhov, A.I. Galeeva. Izv. vuzov. Fizika (in Russian). **29** (11), 96 (1986).

[19] V.Ya. Artuykhov. J. Struct. Chem., **19**, 364 (1978). DOI: 10.1007/BF 0075 3260

[20] E. Scroco, J. Tomasi. Adv. Quantum. Chem., **11**, 115 (1978).

[21] V.A. Blatov. *Semiempirical computational methods of quantum chemistry: a textbook* (Publishing house „University Group", Samara, 2005) (in Russian).

[22] M.J. Dewar, R.C. Dougherty. *The PMO Theory of Organic Chemistry* (Springer, US, 2012).

[23] Kitaygorodsky, P.M. Zorky, V.K. Belsky. *Stroenie organicheskogo veshchestva* (*dannye strukturnykh issledovanij* 1929−1970 *gg.*) (Nauka, M., 1980) (in Russian).

[24] O.N. Tchaikovsky, O.K. Bazyl, E.N. Bocharnikova, N.P. Bezlepkina, G.V. Mayer. Izv. vuzov. Physics, **67** (12), (2024) (in Russian).

[25] G.V. Mayer, O.K. Bazyl, V.Ya. Artyukhov. Opt. and spectr., **72** (6), 1471 (1992).

[26] O.K. Bazyl, V.Ya. Artyukhov, G.V. Mayer, I.V. Sokolova. KhVE, **35** (1), 33 (2001).

[27] V.A. Svetlichny, O.N. Tchaikovsky, O.K. Bazyl, R.T. Kuznetsova, I.V. Sokolova, T.N. Kopylova, Yu.P. Meshalkin. KhVE, **35** (4), 288 (2001).

[28] O.K. Bazyl, E.N. Bocharnikova, O.N. Tchaikovsky, G.V. Mayer. Izv. vuzov. Fizika, **64** (11), 14 (2021) (in Russian).

[29] L.V. Gurvich, G.V. Karachevtsev, V.N. Kondratiev, Yu.A. Lebedev, V.A. Medvedev, V.K. Potapov, Yu.S. Khodeev. *Energiya razryva khimicheskih svyazej. Potentsialy ionizacii i srodstva k elektronu* (Nauka, M., 1974) (in Russian).
[30] L. Bellami. *Infrakrasnyye spektry slozhnykh molekul* (Izdatel'stvo inostrannoy literatury, M., 1957)(in Russian).

Translated by A.Akhtyamov