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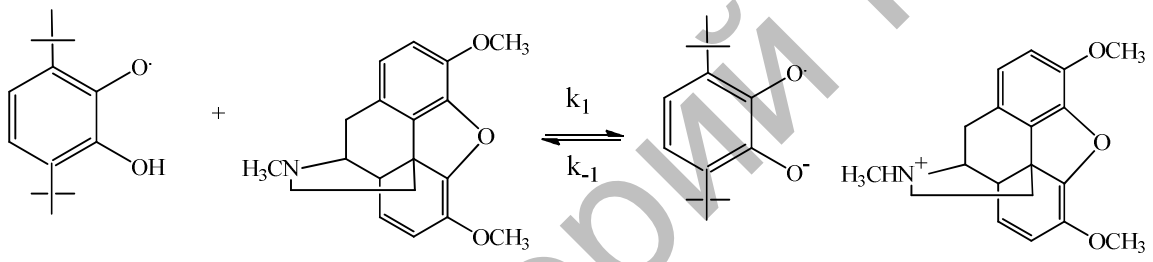
EPR-spectroscopic and quantum-chemical investigations of the fast protolytic reactions of several alkaloids

Kinetic and thermodynamic experimental parameters for the reactions of protonation of alkaloids by spin probe 3,6-di-tert-butyl-2-oxyphenoxyl obtained by ESR spectroscopy in a toluene solution are presented. Values of various physico-chemical data obtained by quantum chemical calculations in the «Gaussian-2009» for some alkaloids, such as ionization potential, electron affinity and proton affinity have been calculated.

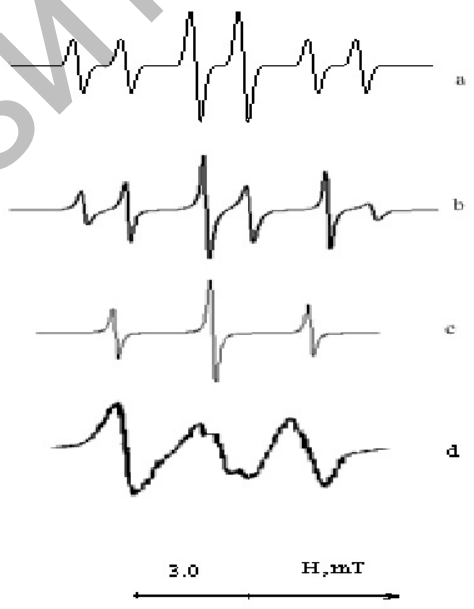
Key words: EPR-spectroscopy, spin probe, 3,6-di-tert.butyl-2-oxyphenoxyl, proton transfer reactions, quantum-chemical investigations, kinetic basicity, alkaloids.

The usage of stable semiquinone free radical 3,6-di-tert.butyl-2-oxyphenoxyl (I) as acid spin probe (XH) allows to investigate the kinetic basicity of many alkaloids (Y) in liquid organic mediums by EPR-spectroscopy method. For example, the fast acid-base protolytic interaction between I and thebaine in toluene solution may be presented with the following working scheme [1]:



(1)

Here k_1 and k_{-1} are the elementary rate constants of direct and reverse protonation reactions in studied system.



Temperature, K: *a* — 310; *b* — 270; *c* — 250; *d* — 230

Figure 1. The dynamic EPR-spectra of toluene solution of protolytic acid-base system I – tebaine at different temperatures

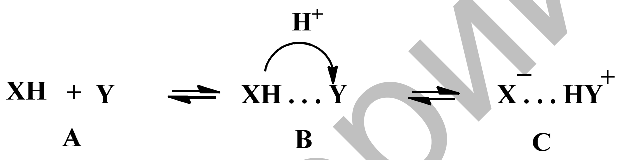
The EPR spectra of spin probe I present as triplet of doublet with hyperfine splitting (hfs) constants equal a_H = 0.392 mT for 2 magnetic equivalent benzene ring protons and a_H = 0.162 mT for hydroxyl proton (see fig. 1*a*). Figure 1*c* illustrates proton lost process for spin probe I and formed semiquinone anion-radical has EPR spectra as simple triplet with hfs equal a_H = 0.162 mT. The figure 1*b* shows the alternating linewidth effect in EPR spectra of acid-base system I – tebaine, connected with kinetic of the fast reversible proton transfer reaction (1) [2]. This effect described by modified theory of F.Bloch for spin relaxation in chemical systems and may be used for determination of the rate constants k_1 and k_{-1} of protolytic reaction (1). On the table 1 physicochemical experimental data for protonation reactions of alkaloids (1), obtained by EPR spectroscopic method are presented.

Table 1

Kinetic and thermodynamic parameters of the fast proton transfer reactions between I and several alkaloids

Base	Solvent	K_e (293) l/mol	$-\Delta H \pm 3{,}0$ kJ/mol	k_1 (293 K) l/mol·c	$E_1 \pm 6{,}0$ kJ/mol	k_{-1} (293 K) c^{-1}	$E_1 \pm 3{,}0$ kJ/mol
Triethylamine	Toluene	9.7	37.7	$7.7 \cdot 10^8$	10.5	$8.7 \cdot 10^7$	48.2
Thebaine	Toluene	1.8	25.3	$5.4 \cdot 10^8$	16.8	$3.0 \cdot 10^8$	42.2
Pseudoephedrine	Toluene	11.3	8.2	$1.8 \cdot 10^9$	28.0	$1.5 \cdot 10^8$	36.2
Triethylamine	THF	6.6	28.0	$3.6 \cdot 10^8$	18.4	$5.5 \cdot 10^7$	46.0
Atropine	THF	9.6	33.0	$7.5 \cdot 10^8$	2.5	$3.7 \cdot 10^7$	85.5
Quinine	THF	26.3	26.7	$1.7 \cdot 10^8$	32.2	$6.3 \cdot 10^6$	58.9

As is generally known, the intermolecular proton transfer (IPT) reaction in acid-base system with hydrogen bonds run in accordance with the scheme:



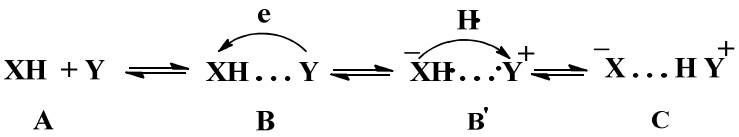
(2)

Here are: B — intermolecular molecular complex with hydrogen bond (MCHB) and C — reactions product, salt or ion pair — ionic complex with hydrogen bond (ICHB). It should be noticed that presented on figure 1 EPR spectra show the molecular dynamic A ⇌ C (see schemes 1 and 2) [3].

Comparison of the experimental values of equilibrium constants (K_e) and enthalpies (ΔH) for protolytic reaction (1) of triethylamine an thebaine, presented in table 1, demonstrate the dependence of these physicochemical parameters from ionization constants of investigated bases [4]. Relatively low strength of ionic pare (ICHB) of 3,6-di-tert.butylsemiquinone anion-radical with thebainium cation bring to loosening this salt by molecules of solvent tetrahydrofurane (THF). The strong solvation decrease rates of acid-base reaction (1) in THF medium, but THF — molecules cannot separate the contact ionic pare of semiquinone anion-radical with triethylammomium cation.

The superposition of EPR spectra on figure 1*d* shows that thebaine form 2 types ionic pare with spin probe I at low temperatures in toluene medium. Simple triplet with hfs constant from 2 magnetic equivalent protons a_H = 0.335 mT belongs to ionic pare with the fast intramolecular transition of ammonium cation between oxygen atoms of 3,6-di-tert.butylsemiquinone anion-radical. This EPR spectra is similar to spectra presented on figure 1*c*. The next low-temperature EPR spectra is doublet of doublet with hfs constants a_H = 0.30 and a_H = 0.37 mT. The disappearance of the magnetic equivalence of 2 benzenes ring protons of 3,6-di-tert.butylsemiquinone anion-radical indicates on absence of fast tautomerism in this ionic pare with specific structural geometry.

But our EPR-investigations showed that for formation of salt C base Y have to the appropriate ionization potential (IP). For example: the stable paramagnetic H-acid semiquinone radical 3,6-di-tert.butyl-2-oxyphenoxyl (I) form only MCHB with very strong proton-acceptor as hexametapol. The ionic pair C or ICHB generates by addition of donors of electron: alkaline metals, amines to I — hexametapol mixture. On the basis of available data and acid-base theory of M.I.Usanovitch the next alternative scheme of the proton transfer reaction may be suggested [5–7]:



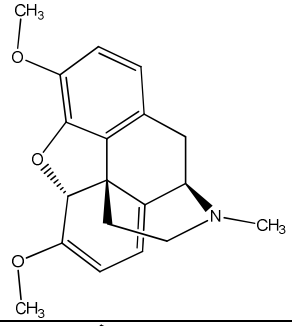
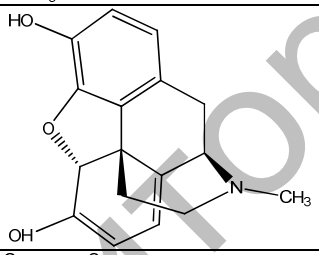
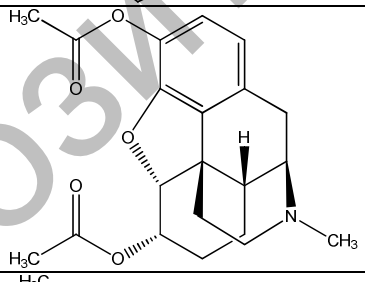
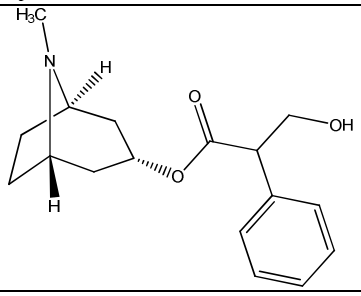
(3)

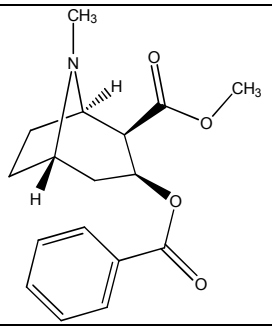
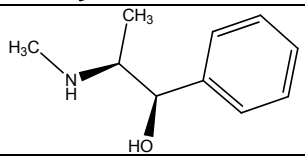
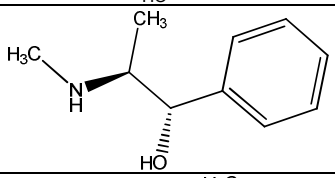
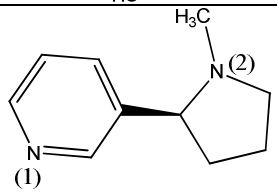
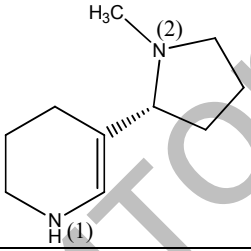
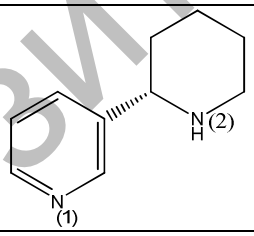
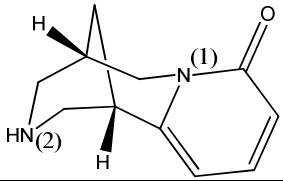
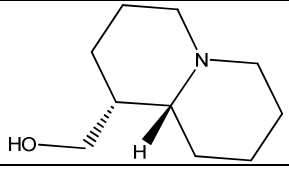
In accordance with this scheme (3) the quantum transfer of electron from bases molecule to acid provokes fast decoupling and transfer of hydrogen atom and formation of ICHB C.

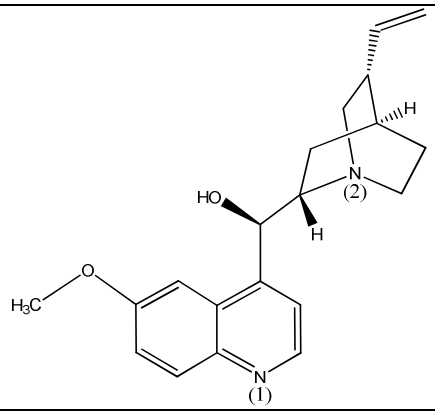
The values of different physicochemical data, obtained by quantum chemical calculations with programs packet of «Gaussian-2009» are presented in table 2 [8–10].

Table 2

The physicochemical data of several alkaloids obtained by quantum chemical calculation with UHF 3–21G method

Alkaloids	Molecular structure	Ionization potential, eV	Electron affinity, eV	Proton affinity, eV
1	2	3	4	5
Thebaine		5,8430	1,5280	11,0949
Morphine		5,9673	2,4389	11,3813
Heroin		5,8720	1,3767	10,9469
Atropine		5,8614	1,9745	10,9958

1	2	3	4	5
Cocaine		5,9850	0,9391	10,7010
Ephedrine		6,0997	2,6516	11,1359
Pseudoephe-drine		6,0465	2,6368	11,1135
Nicotine		6,0730	2,2490	10,9033 (N1) 10,7764 (N2)
Tetrahydro-nicotine		5,4015	3,5282	10,6665 (N1) 11,3851 (N2)
Anabasine		6,4674	2,1728	10,7980 (N1) 10,6864 (N2)
Cytisine		6,3451	1,4274	8,7136 (N1) 10,4824 (N2)
Lupinin		5,3819	5,2183	11,2183

1	2	3	4	5
Quinine		5,9042	0,9696	11,2935 (N1) 11,5659 (N2)

If the experimental values of ionization potentials for alkaline metals are equal 3–5 eV and for small molecules of water 12.6 eV, ammonia 10.0 eV, then the calculated values of adiabatic IP for contained in table 2 big molecules of alkaloids change in range 5–6 eV [4]. It is very interesting that narcotic molecules of morphine and heroin have appropriate equal values of adiabatic IP as a molecule of thebaine. Analogous effect be observed for narcotic cocaine and similar molecules of atropine.

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Кейбір алкалоидтардағы протондану реакцияларын ЭПР-спектроскопиялық және кванттықхимиялық зерттеу

Толуол ерітінділеріндегі ЭПР-спектроскопия әдісі арқылы алынған спиндік зонд 3,6-ди-үш. бутил-2-оксифеноксилмен алкалоидтардың протондану реакцияларының кинетикалық және термодинамикалық тәжірибелік өлшемдері көрсетілген. Кейбір алкалоидтар үшін инондану потенциалы, электронға жақындығы және протонға жағындығы тәрізді әр түрлі физика-химиялық қасиеттерінің кванттықхимиялық мәндері «Gaussian-2009» бағдарламасында есептелді.

А.С.Масалимов, Э.М.Ергалиева, С.Н.Никольский, Е.А.Ральченко, А.А.Тур

ЭПР-спектроскопические и квантово-химические исследования быстрых протолитических реакций некоторых алкалоидов

Представлены кинетические и термодинамические экспериментальные параметры для реакций протонирования алкалоидов спиновым зондом 3,6-ди-трет-бутил-2-оксифеноксилом, полученные методом ЭПР-спектроскопии в растворе толуола. Для некоторых алкалоидов квантовохимически рассчитаны значения различных физико-химических данных, такие как потенциал ионизации, сродство к электрону и сродство к протону, полученные в программе «Gaussian-2009».

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