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QUANTUM-CHEMICAL STUDY OF "HYDRIDE" MOBILITY IN THE MOLECULES OF CHALCOGENOPYRANS

A. N. Pankratov[1] **and B. I. Drevko**[2]

An approach is proposed for the quantum-chemical investigation of "hydride ion" transfer based on analysis of the similarity of the order of variation in the ionization potentials, enthalpies, and free energies of affinity to the hydride ion, the hydrogen atom, and the proton in the substrate molecules and also the derivatives of their cations, radicals, and ions to the experimentally established "hydride" series. It was established that the experimental "hydride" mobility series of six chalcogenopyrans based on "semicyclic" 1,5-diketones agrees with the quantum-chemically calculated ionization potentials of the molecules and with the affinity of the respective radicals to the hydrogen atom participating in the transfer. It was found that direct removal of a hydride ion and initial deprotonation of the substrates followed by the removal of two electrons are unlikely. "Hydride" shift mechanisms, in which the first stage is transfer of an electron or hydrogen atom from the chalcogenopyran molecules, are feasible.

Keywords: chalcogenopyrans, "hydride" transfer, quantum-chemical investigation, reaction mechanisms, ionization potential, hydrogen atom affinity, hydride ion affinity, proton affinity.

Reactions including stages that can formally be represented as hydride-ion transfer are of great significance in chemistry [1]. Examples include the transformations of 1,5-dicarbonyl compounds and chalcogenopyrans in a mixture of chalcogenopyrylium salts and chalcogenocyclohexanes or chalcogenopyrylium salts and other reduced products [2]. The following mechanisms of "hydride" transfer have been discussed for a wide range of chemical compounds [1]:

1. Direct abstraction of a hydride ion ($-H^-$).
2. Successive ejection of an electron, a proton, and another electron ($-e^-$, $-H^+$, $-e^-$).
3. Removal of an electron and a hydrogen atom ($-e^-$, $-H^\cdot$).
4. Transfer of a hydrogen atom and an electron ($-H^\cdot$, $-e^-$).
5. Deprotonation followed by the transfer of two electrons ($-H^+$, $-e^-$, $-e^-$).

The mechanism of the "minus electron, minus electron, minus proton" type ($-e^-$, $-e^-$, $-H^+$) should not be realized since the formation of the dication-radical is unlikely.

However, in our opinion, there also exists a mechanism not examined in the present paper, involving initial protonation of the heterocycle and a final stage with release of H_2 [3] or another electrically neutral molecule [4]. The possible protonation of a heterocycle at a chalcogen atom was demonstrated conclusively in the papers of Lambert and others [5].

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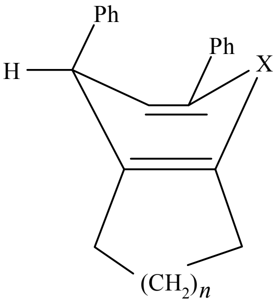
[1] N. G. Chernyshevskii Saratov State University, Saratov 410012, Russia; e-mail: PankratovAN@chem.sgu.ru. [2] Saratov Military Institute of Radiation, Chemical and Biological Protection, Saratov 410037, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1305-1311, September, 2005. Original article submitted January 28, 2004.

Detailed analysis of the "hydride" transfer mechanisms is difficult even by modern experimental methods, such as pulsed NMR. This is due to rapid occurrence of the respective reaction stages. The effectiveness of future experimental investigations can be improved by quantum-chemical analysis based on authentic experimental data.

The reactivity of pyrans and thio- and selenopyrans is determined to a considerable degree by the ability of the molecules to eject a "hydride" ion [2]. The name of the latter is placed in quotation marks because the transfer of a hydride ion as such is rarely encountered in organic chemistry.

Chalcogenopyrans **1-6**, synthesized on the basis of "semicyclic" 1,5-diketones, are interesting as potential biologically active compounds [2, 6].

Subjects of investigation: chalcogenopyrans based on "semicyclic" 1,5-diketones



1–6

1, **4** X = O; **2**, **5** X = S; **3**, **6** X = Se; **1-3** *n* = 1, **4–6** *n* = 2

The aim of the present work was to develop a methodology for the quantum-chemical investigation of "hydride" mobility in molecules and to test the approach named above for the case of the removal of a "hydride" ion from molecules **1-6**.

The calculations were performed by the semiempirical PM3 method [7, 8] using MOPAC software [9, 10] with full optimization of the geometry (the Broyden–Fletcher–Goldfarb–Shanno procedure [11]) and the fast minimization algorithm of Thiel [12]. Preliminary optimization was realized by molecular mechanics (the MMX procedure) [13] using PCMODEL software [13]. A condition was set during the quantum-chemical calculations so that the norm of the gradient did not exceed 0.084 kJ/(mol·Å). In certain cases sufficient

TABLE 1. The Correlation between the "Hydride" Transfer Stages and the Reactivity Indices Describing Them

Mechanism	Transfer stage	Required to analyze	
		Index	System
1	$BH \rightarrow B^{+} + H^{-}$	HIA	B^{+}
2	$BH \rightarrow BH^{\cdot+} + \bar{e}$	IP	BH
	$BH^{\cdot+} \rightarrow B^{\cdot} + H^{+}$	PA	$B^{\cdot}$
	$B^{\cdot} \rightarrow B^{+} + \bar{e}$	IP	$B^{\cdot}$
3	$BH \rightarrow BH^{\cdot+} + \bar{e}$	IP	BH
	$BH^{\cdot+} \rightarrow B^{+} + H^{\cdot}$	HAA	B^{+}
4	$BH \rightarrow B^{\cdot} + H^{\cdot}$	HAA	$B^{\cdot}$
	$B^{\cdot} \rightarrow B^{+} + \bar{e}$	IP	$B^{\cdot}$
5	$BH \rightarrow B^{-} + H^{+}$	PA	B^{-}
	$B^{-} \rightarrow B^{\cdot} + \bar{e}$	IP	B^{-}
	$B^{\cdot} \rightarrow B^{+} + \bar{e}$	IP	$B^{\cdot}$

decrease in the gradient norm was achieved with rejection of the Thiel fast minimization (the key word NOTHIEL in the MOPAC package was used) and also with optimization by the Davidon–Fletcher–Powell method (key word DFP) [11] and in a combination of approaches symbolized by the key words NOTHIEL and DFP.

The formalism of the restricted Hartree–Fock method (RHF) was used for molecules with closed electron shells. The calculations for the radical-cations and radicals were realized by the unrestricted Hartree–Fock method (UHF) [10].

The molecular systems investigated in the present work are fairly large, and semiempirical methods of quantum chemistry are no less acceptable for solution of the problem than the *ab initio* or DFT methods. We established the accuracy of reproduction of the most important thermodynamic and molecular characteristics [14-38] and the electronegativity, inductive, and mesomeric parameters of the atomic groups [35, 39, 40] in series of compounds of various classes with various functional groups by the MNDO, AM1, and PM3 methods. In addition the relativization principle operates [41]; it is quite correct to compare the values of the quantum-chemical indices in a series of compounds of similar structure. Here, of the named schemes only PM3 [7, 8] has a set of parameters for selenium [8], and we therefore chose the PM3 method.

Such a characteristic of the proton-accepting ability of substances as the proton affinity is well known [42-45]:

$$\mathrm{PA} = E(\mathrm{B}^-) + E(\mathrm{H}^+) - E(\mathrm{BH}),$$

This represents the enthalpy of the removal of a proton in the gas phase ($E = \Delta\Delta H_f$):

$$\mathrm{BH} \rightarrow \mathrm{B}^- + \mathrm{H}^+.$$

By analogy we introduce the following quantities – the hydrogen atom affinity (HAA) and the hydride ion affinity (HIA):

$$\mathrm{HAA} = E(\mathrm{B}) + E(\mathrm{H}) - E(\mathrm{BH}),$$

$$\mathrm{HIA} = E(\mathrm{B}^+) + E(\mathrm{H}^-) - E(\mathrm{BH}).$$

During study of the mechanisms stage by stage it is possible to show which reactivity indices of which molecular systems – the participants of the individual stages of the reactions – must be analyzed (Table 1, IP is the Koopmans ionization potential [46]). Here the affinity values (PA, HAA, HIA) must be expressed as the enthalpy and free energies of the respective processes ($E = \Delta\Delta H_f$, $\Delta\Delta G_f$).

For example, if the experimental values (thermodynamic, kinetic, etc.) characterizing the "hydride" mobility in a series structurally similar compounds (e.g., heterocycles differing in the heteroatom) correlate with the ionization potentials of the initial compounds BH, mechanisms 2 and 3 can be realized on the condition that the first stage is limiting. If the experimental values agree with the hydrogen atom affinity of the substrate BH, then mechanism 4 may be realized, and if they agree with the proton affinity mechanism 5 may be realized. (In both cases the first stage is limiting.) If the experimental data correlate with the hydride ion affinity of BH, mechanism 1 is probable.

It was established as a result of the investigations [47, 48], in which the "heteroaromatic cation–chalcogenopyran" equilibrium was examined, and the construction of comparative reactivity series that thiopyrans are more liable to eliminate a "hydride ion" than the oxygen and selenium analogs.

TABLE 2. The Affinity and Ionization Energies

Com-pound	HIA/4.184, kJ/mol*		HAA/4.184, kJ/mol*[2]		HAA/4.184, kJ/mol*[3]		PA/4.184, kJ/mol*[4]		PA/4.184, kJ/mol*[5]		IP/4.184, kJ/mol*[6]		
	$\Delta\Delta H_f$	$\Delta\Delta G_f$	$\Delta\Delta H_f$	$\Delta\Delta G_f$	$\Delta\Delta H_f$	$\Delta\Delta G_f$	$\Delta\Delta H_f$	$\Delta\Delta G_f$	$\Delta\Delta H_f$	$\Delta\Delta G_f$	BH	$B^{\cdot}$	B^{-}
1	191.81	186.29	31.33	24.89	52.06	43.65	339.95	330.77	187.83	179.43	198.67	178.75	54.93
2	197.01	191.43	41.77	35.39	51.42	42.49	330.28	320.95	192.54	183.63	191.48	181.01	61.37
3	205.41	199.92	41.63	36.33	54.24	45.63	328.85	319.56	186.82	179.21	198.67	185.78	66.49
4	192.54	187.03	32.33	25.90	53.54	45.00	341.89	332.88	189.69	181.06	198.72	178.40	56.02
5	198.60	192.78	43.16	36.17	52.24	43.34	331.66	322.97	193.16	183.91	192.42	181.42	62.68
6	207.98	201.62	45.09	37.80	56.31	47.59	331.14	322.07	189.78	180.95	198.90	185.76	66.99

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* Hydride ion affinity of B^+ cations: HIA = $E(B^+) + E(H^-) - E(BH)$, where $E = \Delta\Delta H_f, \Delta\Delta G_f$.

*[2] Hydrogen atom affinity of B^+ cations: HAA = $E(B^+) + E(H^{\cdot}) - E(BH^{\cdot+})$, where $E = \Delta\Delta H_f, \Delta\Delta G_f$.

*[3] Hydrogen atom affinity of $B^{\cdot}$ radicals: HAA = $E(B^{\cdot}) + E(H^{\cdot}) - E(BH)$, where $E = \Delta\Delta H_f, \Delta\Delta G_f$.

*[4] Proton affinity of B^- anions: PA = $E(B^-) + E(H^+) - E(BH)$, where $E = \Delta\Delta H_f, \Delta\Delta G_f$.

*[5] Proton affinity of $B^{\cdot}$ radicals: PA = $E(B^{\cdot}) + E(H^+) - E(BH^{\cdot+})$, where $E = \Delta\Delta H_f, \Delta\Delta G_f$.

*[6] The ionization potentials (IP) of the molecular systems (BH, $B^{\cdot}$, B^-).

By the PM3 method we calculated the energy characteristics of molecules **1-6** and derivatives from their cations, radical-cations, radicals, and anions. The standard free energy of formation ΔG_f was calculated by the equation:

$$\Delta G_f = \Delta H_f - T\Delta S_f,$$

and the standard entropies of formation ΔS_f by the equation:

$$\Delta S_f = S - \sum_i S_i\,,$$

where S represents the standard entropies of the substances and S_f represents the entropies of the elements comprising the molecule in their standard states [50, 51], obtained with allowance for the diatomic nature of the hydrogen, oxygen, and sulfur molecules; $T = 298.15$ K.

The contributions from the individual degrees of freedom of translational, rotational, and vibrational movement to the entropy were calculated in the rigid molecule approximation (the barriers to rotation and inversion significantly exceed kT) without allowance for the anharmonicity of the vibrations. The contributions from the translational motion were calculated without quantum-chemical calculations, and the contributions from rotational motion were calculated from data on the equilibrium internuclear distances obtained in the course of the quantum-chemical calculations. Finally, the contributions from the vibrational components of the entropy were estimated on the basis of the frequencies of the normal vibrations calculated by the quantum-chemical method. In order to calculate the frequencies after geometry optimization the second derivatives of the total energy with respect to natural coordinates (the force constants) were first calculated [52]. During calculation of the rotational contributions to the thermodynamic functions the symmetry was taken as equal to 1.

Table 2 gives the calculated values of the hydride ion, hydrogen atom, and proton affinities and also the ionization potentials of the named molecular systems. The results of the calculations show that the experimental "hydride" mobility series S > O ≈ Se [47-49] does not contradict the ionization potentials (IP) of molecules **1-6** or the hydrogen atom affinity (HAA) of the radicals formed by removal of the hydrogen atom at position 4 of the heterocycle from the initial systems **1-6**.

We will compare this with the data in Table 1. The IP index describes the removal of an electron from the substrate molecule BH – the first stage of mechanisms 2 and 3. The abstraction of a hydrogen atom from the initial BH molecule, which corresponds to the value of the HAA, is the first stage of mechanism 4. If the first stage is rate-determining, the correlation of the experimental results with the calculated ionization potentials presupposes the realization of mechanism 2 or 3, while correlation with the hydrogen atom affinity of the radicals $B^{\cdot}$ means the realization of mechanism 4.

Thus, according to the quantum-chemical calculations, mechanisms 1 and 5 are rejected. Mechanisms 2-4 can be realized on the condition that the first stage of the reaction is limiting in each case.

The obtained results make it possible to concentrate the attention of research workers toward substantiating the really possible mechanisms of "hydride" transfer in the chemistry of chalcogenopyrans.

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