COMPARISON OF THE CAPACITY OF NITROGEN, OXYGEN, SULFUR, AND SELENIUM ATOMS TO EXIST IN ONIUM STATES. QUANTUM-CHEMICAL INVESTIGATION OF ISOMERIC MODEL SYSTEMS WITH TWO HETEROATOMS*

L. I. Belen'kii, I. D. Nesterov, and N. D. Chuvylkin

HF, B3LYP, and MP2 calculations with the 6-31+G(d) basis set with correction to the energy of zero-point vibrations were carried out to determine the energy characteristics of model molecules containing two heteroatoms in the sp^3- and sp^2-hybrid states; different combinations of N, O, S, and Se atoms were studied. The stability of the onium states of the nitrogen atom was found to be greater than for its chalcogen analogs and the relative stability of onium states of the chalcogen analogs was found to depend on the hybridization of these atoms. Analysis of these results permitted us to construct a stability series of onium derivatives and to interpret the positional selectivity in electrophilic substitution reactions of five-membered heterocyclic compounds with one heteroatom.

The quantitative study of the differences in the reactivity (substrate selectivity) and positional selectivity (α:β ratio) in the electrophilic substitution of pyrrole, furan, and thiophene was undertaken many years ago [1]. There is no correlation between the series of substrate and positional selectivity. While the reactivity decreases in the order: pyrrole >> furan > thiophene, the α:β ratio does not increase in this order, as might have been expected, but in the series pyrrole < thiophene < furan.

Previously, one of us presented a hypothesis to explain the lack of accord of these series for substrate and positional selectivity [2, 3]. The essence of this hypothesis is that the formation of β-substituted compounds traversing σ-complexes **B**, in which only the heteroatom and one of the α-carbon atoms participate in charge delocalization, should depend more on the capacity of elements X to exist in the onium state than formation of α-substituted compounds since charge delocalization in cation **A** in the latter case is achieved with the participation of all the ring atoms except for the geminal carbon atom (Scheme 1). This approach permitted us to qualitatively interpret the available data on α:β ratios both for five-membered heterocycles with one heteroatom and the corresponding benzo-fused systems. Indeed, the positional selectivity drops with increasing stability of the onium states in the order $O^+ < S^+ < N^+$.

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* To J. Stradins, an outstanding and tireless scientist, with our deep respect and sincere affection.
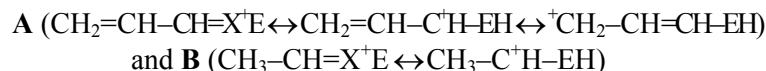

On the other hand, the quantitative data on the stability of onium states of elements at the time of the onset of our work were, unfortunately, clearly insufficient (see, for example, the work of Olah et al. [4]), while the series $O^+ < Se^+ \leq S^+ < N^+$, which also includes data for selenium, was based on purely qualitative estimates [5-7], going back to the pioneering work of Meerwein [8]. Thus, we undertook a quantum-chemical investigation of the protonation of monocyclic and the corresponding benzo-fused five-membered heteroaromatic systems with one heteroatom. The first calculations carried out using the semiempirical CNDO/2 method [9] gave differences in the energies of cations formed upon the protonation of α- and β-positions ($\Delta E_{\alpha\text{-}\beta}$), which were in accord with the available experimental data on the order of change of positional selectivity: furan > thiophene > pyrrole. However, the position of selenium in this series predicted by these calculations between thiophene and pyrrole was not in accord with our findings [10] showing that the α:β ratio drops in the series furan > selenophene > thiophene > pyrrole.

Scheme 1
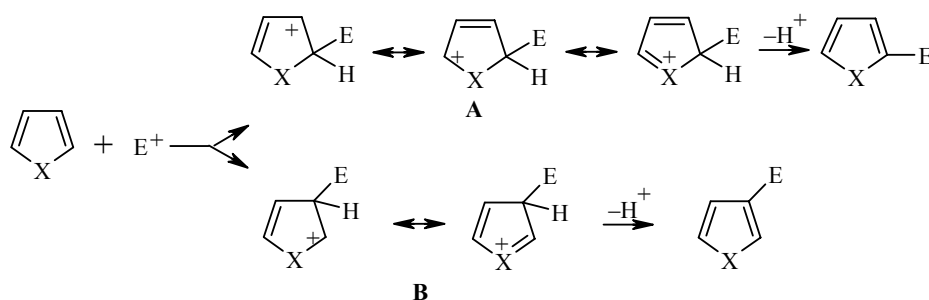
Taking account of this result and previously published data on the change in relative activity for five-membered heterocycles with one heteroatom in the series pyrrole >> furan > selenophene > thiophene [1], we carried out quantum-chemical calculations with the 6-31G basis set in the framework of MP2 perturbation theory and the B3LYP density functional with geometry optimized in the Hartree-Fok approximation in the same basis [11]. The results of these calculations were correlated with the above-mentioned observed drop in positional selectivity in the series, which corresponds to the change in relative stability of onium states of elements ($O^+ < Se^+ \leq S^+ < N^+$) and reflects the predominant role of the heteroatoms in stabilizing the σ-complexes formed upon β-substitution.

In previous work [12], we used the HF, B3LYP, and MP2 methods with the 6-31+G(d) basis set with a correction to the energy of zero-point vibrations for quantum-chemical calculations of the energy characteristics of pyrrole, furan, thiophene, and selenophene, which are the simplest derivatives of N, O, S, and Se with sp^3- and sp^2-hybridized carbon atoms and heteroatoms and also the products of the addition of a proton to these molecules as well as the products of the addition of other electrophiles such as Me^+, SiH_3^+, and BH_3, which may be seen as models of the σ-complexes (see Scheme 1) of types

A $(CH_2=CH–CH=X^+E \leftrightarrow CH_2=CH–C^+H–EH \leftrightarrow {}^+CH_2–CH=CH–EH)$
and **B** $(CH_3–CH=X^+E \leftrightarrow CH_3–C^+H–EH)$

The affinity of nitrogen-containing systems to electrophiles was shown to be much greater than for their chalcogen analogs. The relative stability of the onium states of the chalcogen analogs depends both on the hybridization of the heteroatoms and the nature of the electrophiles. Analysis of these results permitted us to construct stability series for onium compounds and interpret the positional selectivity in the electrophilic substitution of five-membered heteroaromatic compounds with one heteroatom.

METHOD AND DISCUSSION

The accumulation of experimental results and the data of precise quantum-chemical calculations, including our findings, indicate that the sequence of Group VI elements in the series given above may change depending on the nature of the substituents at the onium atom and the hybridization of this atom. In the present work, we examined such effects on model structures, including very simple structures as well as structures reflecting special features of five-membered heteroaromatic compounds with one heteroatom. For this purpose, we carried out quantum-chemical calculations of the required energy characteristics of the selected structures with full optimization of their geometrical parameters using HF, B3LYP, and MP2 methods with the 6-31+G(d) basis set with corrections to the energy of zero-point vibrations with Gaussian 98 program package [13]. With this in mind, we should not be overly concerned that the methods used when applied to the models examined do not always give similar numerical results (these differences are clearly seen in the tables), but rather concentrate on a qualitative analysis of the trends and patterns revealed by these methods.

The total energies of monotypic cations (or complexes) containing different heteroatoms in similar positions (for examples, NH_4^+ and H_3O^+) clearly cannot be compared directly to evaluate the tendency of an atom to be in a state, in which it formally has a complete positive charge. However, we may compare the energies of the monotypic formation of such complexes (for example, the proton affinity (PA) of simple compounds such as NH_3, H_2O, H_2S, and H_2Se). This comparison shows the extent, to which the schematically presented complexation formation is advantageous or disadvantageous for a given element relative to other atoms. In this case, we should bear in mind that one particular complex may be formed in different pathways (see, for example, Scheme 2) and this may lead to several sets of formation energies, to the incongruent results of comparisons within different sets and to equivocal results even for an individually selected series of monotypic cations with different heteroatoms.

Scheme 2

X = NH, O, S, Se
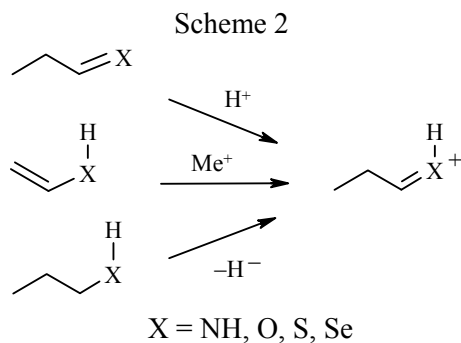
To avoid this problem, we may compare not the formation energies of different cations, but rather the total energies of isomers of some particular cation with more than one heteroatom where only one of the heteroatoms is at a cationic site. By altering positions of the heteroatoms, we may determine to what extent the position of a given structural type at a particular cationic site is energetically favored for each of the heteroatoms examined. We initially used precisely this approach.

Table 1 gives the differences in total energy $\Delta E_{I,II}^+ = E_I^+ - E_{II}^+$, corresponding to pairs of two types of isomers $X{=}CH(CH_2)_2CH{=}YH^+$ and $Y{=}CH(CH_2)_2CH{=}XH^+$, $HX{-}CH_2(CH_2)_2CH_2{-}YH_2^+$ and $HY{-}CH_2(CH_2)_2CH_2{-}XH_2^+$, or $HXCH_2(CH_2)_2CH{=}YH^+$ and $HYCH_2(CH_2)_2CH{=}XH^+$, containing two different heteroatoms and differing in their arrangement (if the value of $\Delta E_{I,II}$ is negative, the first isomer in the given pair is energetically favored). These model structures were selected, on one hand, for the purpose of simplicity and, on the other, in accord with the requirement that the heteroatoms be isolated. Thus, the conformations of all the structures (subsequently, with optimized geometry) were initially selected close to W-shaped and we did not investigate the conformational preferences of these structures. The hydrogen atoms at the double bonds were in *anti* arrangement everywhere possible.

Having obtained the expected results for structures, in which both heteroatoms are sp^2-hybridized, indicating a significant energy preference for the cations with a nitrogen atom in the onium state in comparison with compounds of the other elements examined (Table 1), we gave special attention to the chalcogen derivatives. For chalcogens, the experimentally determined series $O^+ < Se^+ \leq S^+$ [5-8] is in accord with the calculation results only when both heteroatoms are in identical states (either sp^2- or sp^3-hybridized) but not when they differ in hybridization, to which the series $Se^+ < S^+ < O^+$ corresponds. This finding may be attributed to the circumstance that a shift in the sites of the heteroatoms in model structures of the type $HXCH_2(CH_2)_2CH=YH^+$ and $HYCH_2(CH_2)_2CH=XH^+$ leads not only to loss or gain of formal charge by the heteroatoms, but also to a change in their hybridization, which also makes a significant contribution to the difference in energies of both isomeric cations and isomeric neutral carbonyl, thiocarbonyl, and selenocarbonyl compounds (see Tables 1 and 2).

TABLE 1. Differences in Total Energies $\Delta E^+_{I,II} = E^+_I - E^+_{II}$ of Isomers of Types I and II Calculated with the 6-31-G(d) Basis Set without ($\Delta E^+_{I,II}{}^1$) and with ($\Delta E^+_{I,II}{}^2$) Corrections to the Energy of Zero-point Vibrations

Cation	Izomer type	Method	$\Delta E^+_{I,II}{}^1$, kcal/mol	$\Delta E^+_{I,II}{}^2$, kcal/mol	Preference
$O=CH(CH_2)_2CH=NH_2^+$	I	HF	-41.2	-40.6	
$HN=CH(CH_2)_2CH=OH^+$	II	B3LYP	-38.7	-38.0	$N^+ > O^+$
		MP2	-42.0	-41.2	
$S=CH(CH_2)_2CH=NH_2^+$	I	HF	-34.0	-31.4	
$HN=CH(CH_2)_2CH=SH^+$	II	B3LYP	-30.8	-28.4	$N^+ > S^+$
		MP2	-34.2	-31.7	
$Se=CH(CH_2)_2CH=NH_2^+$	I	HF	-33.7	-30.4	
$HN=CH(CH_2)_2CH=SeH^+$	II	B3LYP	-29.5	-26.7	$N^+ > Se^+$
		MP2	-34.8	—	
$O=CH(CH_2)_2CH=SH^+$	I	HF	-6.7	-8.6	
$S=CH(CH_2)_2CH=OH^+$	II	B3LYP	-5.5	-7.0	$S^+ > O^+$
		MP2	-6.6	-8.1	
$O=CH(CH_2)_2CH=SeH^+$	I	HF	-7.6	-10.6	
$Se=CH(CH_2)_2CH=OH^+$	II	B3LYP	-4.4	-6.8	$Se^+ > O^+$
		MP2	-5.5	—	
$S=CH(CH_2)_2CH=SeH^+$	I	HF	2.8	2.2	
$Se=CH(CH_2)_2CH=SH^+$	II	B3LYP	5.3	5.4	$Se^+ < S^+$
		MP2	4.0	—	
$HOCH_2(CH_2)_2CH_2SH_2^+$	I	HF	-1.5	-2.4	
$HSCH_2(CH_2)_2CH_2OH_2^+$	II	B3LYP	-4.1	-5.2	$S^+ > O^+$
		MP2	-3.0	-4.1	
$HOCH_2(CH_2)_2CH_2SeH_2^+$	I	HF	-3.3	-4.9	
$HSeCH_2(CH_2)_2CH_2OH_2^+$	II	B3LYP	-7.2	-8.8	$Se^+ > O^+$
		MP2	-4.1	—	
$HSCH_2(CH_2)_2CH_2SeH_2^+$	I	HF	-1.8	-2.4	
$HSeCH_2(CH_2)_2CH_2SH_2^+$	II	B3LYP	-3.1	-3.6	$Se^+ > S^+$
		MP2	-1.0	—	
$HOCH_2(CH_2)_2CH=SH^+$	I	HF	6.3	6.3	
$HSCH_2(CH_2)_2CH=OH^+$	II	B3LYP	4.5	4.1	$S^+ < O^+$
		MP2	1.4	1.1	
$HOCH_2(CH_2)_2CH=SeH^+$	I	HF	9.1	8.9	
$HSeCH_2(CH_2)_2CH=OH^+$	II	B3LYP	5.4	5.0	$Se^+ < O^+$
		MP2	4.1	—	
$HSCH_2(CH_2)_2CH=SeH^+$	I	HF	2.6	2.6	
$HSeCH_2(CH_2)_2CH=SH^+$	II	B3LYP	1.2	1.2	$Se^+ < S^+$
		MP2	2.6	—	

In this regard, we note that the much greater shift of the electron density of the C=O bond to the heteroatom than in their sulfur and selenium analogs is due to the high electronegativity of the oxygen atom in carbonyl compounds. Furthermore, for example, the bis(methoxy)methylcarbenium ion stabilized by two methoxy groups exists according to *ab initio* calculations as well as X-ray photoelectron spectroscopy (XPS) as a stable carbenium ion with negative charge on the oxygen compounds. On the other hand, in the case of the bis(methylthio)methylcarbenium ion, there is delocalization of the positive charge by the carbon atom and heteroatoms [14].

This is supported by the results of our quantum-chemical calculations of the charges on the atoms and interatomic distances in model structures $CH_2=X$ and $CH_2=XH^+$ (Table 3). The heteroatom in the formaldehyde molecule bears much more negative charge in comparison with the analogous sulfur and selenium analogs. On the other hand, the carbonyl carbon atom in formaldehyde bears close-to-zero negative charge or even a slight positive charge, while the corresponding atoms in thioformaldehyde and selenoformaldehyde bear negative charge. In the protonated molecules, the oxygen atom, as previously, bears negative charge, while the sulfur and selenium atoms acquire positive charge. The marked increase in the C–O bond length upon protonation may be seen as a manifestation of an increased contribution of the carbocation form $CH_2–C^+–OH$. This effect is much less pronounced for the sulfur and selenium analogs.

TABLE 2. Differences in the Total Energy $\Delta E_{I,II} = E_I - E_{II}$ of Isomer Types I and II Calculated with the 6-31+G(d) Basis Set without ($\Delta E^+_{I,II}{}^1$) and with ($\Delta E^+_{I,II}{}^2$) Corrections to the Energy of Zero-point Vibrations

Compound	Type of isomers	Method	$\Delta E_{I,II}{}^1$, kcal/mol	$\Delta E_{I,II}{}^2$, kcal/mol	Advantage
$HOCH_2(CH_2)_2CH=S$	I	HF	13.8	15.8	I < II
$HSCH_2(CH_2)_2CH=O$	II	B3LYP	11.3	13.1	
		MP2	8.9	10.8	
$HOCH_2(CH_2)_2CH=Se$	I	HF	16.2	19.0	I < II
$HSeCH_2(CH_2)_2CH=O$	II	B3LYP	13.1	15.5	
		MP2	10.7	—	
$HSCH_2(CH_2)_2CH=Se$	I	HF	2.5	3.2	I > II
$HSeCH_2(CH_2)_2CH=S$	II	B3LYP	1.8	2.6	
		MP2	1.8	—	
$O=CH(CH_2)_2CH=SH^+$	I	HF	-6.7	-8.6	$S^+ > O^+$
$S=CH(CH_2)_2CH=OH^+$	II	B3LYP	-5.5	-7.0	
		MP2	-6.6	-8.1	

TABLE 3. Calculated with the 6-31+G(d) Basis Set Charges on Atoms Z and Interatomic Distances d in Model Structures $CH_2=X$ and $CH_2=XH^+$

X	Method	$CH_2=X$			$CH_2=XH^+$		
		Z_X, e	Z_C, e	d_{XC}, Å	Z_X, e	Z_C, e	d_{XC}, Å
NH	HF	-0.52	-0.18	1.25	-0.61	-0.03	1.26
	B3LYP	-0.43	-0.24	1.27	-0.46	-0.09	1.28
	MP2	-0.52	-0.19	1.28	-0.62	-0.03	1.28
O	HF	-0.39	0.08	1.19	-0.40	0.16	1.23
	B3LYP	-0.30	-0.01	1.21	-0.25	0.06	1.25
	MP2	-0.41	0.08	1.22	-0.41	0.16	1.26
S	HF	-0.13	-0.32	1.60	0.38	-0.24	1.62
	B3LYP	-0.07	-0.37	1.62	0.44	-0.30	1.63
	MP2	-0.14	-0.31	1.62	0.37	-0.24	1.62
Se	HF	-0.11	-0.35	1.72	0.33	-0.23	1.73
	B3LYP	-0.05	-0.38	1.74	0.41	-0.27	1.75
	MP2	-0.11	-0.34	1.75	0.33	-0.22	1.74

Thus, in this approach, it is fruitful to compare compounds of different types according to a comparative analysis of the model structures containing sp^2-hybridized oxygen, sulfur, and selenium atoms given in Tables 1 and 2. In this case, we should select specific model structures, in which the states of the heteroatoms differ only in the absence or presence of formal charge on these atoms in the vicinity of the necessary number of substituents. This circumstance diminishes the range of suitable objects for study and requires the use of structures more suitable for the present purposes and, thus, more cumbersome structures, which might be presented as correct models for further investigation. However, even some of these apparently simple models, for which we carried out calculations, are, in fact, rather complicated relative to available computer capacities. Thus, for technical reasons, we were unable to obtain corrections to the energy of zero-point vibrations using the MP2/6-31+G(d) basis for the selenium-containing models.

On the other hand, those differences in isomer-containing energies presented in Table 1 may be attributed to the relative stability of the onium states (models with the same heteroatom hybridization), i.e., in essence, we may consider these values as the differences in the energy of protonation of the corresponding ambient neutral bases at different heteroatoms. However, with this assumption, it is undoubtedly simpler to calculate and compare the energies of protonation of much smaller molecules with one heteroatom as in our previous work [12] despite the necessity of calculating the energies of the neutral precursors.

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