NEW METHOD FOR ALLOWANCE FOR THE ACTIVITY OF THE NUCLEOPHILE IN CALCULATIONS OF THE REACTIVITIES OF HETEROAROMATIC COMPOUNDS

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A new method for allowance for the activity of the nucleophile in calculations of the reactivities of heteroaromatic compounds that is based on the special application of the valence molecular orbital (VMO) theory in the form of Dewar reactivity numbers is proposed. It is shown that there is a correspondence between the proposed method and the general VMO theory. The 5-azacinnoline molecule was calculated by both methods. According to the calculations, the 6-C atom should be the most active in reactions with hard bases, whereas the 4-C atom should be the most active in reactions with soft bases. A qualitative correspondence between the proposed method and the DMTS (delocalization model of the transition state) method is also demonstrated in the case of the quinolinium cation.

An important problem in quantum-mechanical calculations of the reactivities of heteroaromatic compounds is the necessity for allowance for the change in the reactivity of the substrate as the activity of the reagent changes. Two such methods* – the general valence molecular orbital (VMO) theory (the Klopman method) [1] and the DMTS (delocalization model of the transition state) method [2] – are presently known. Calculations by these methods are laborious and require the use of a computer.

In addition, there is a simple and, at the same time, effective method for the estimation of the reactivities of the aromatic compounds with the application of the special VMO theory – the Dewar method [3]. In the determination of the localization energies by this method there is no need to make cumbersome calculations, since the coefficients of the AO for the boundary MO are found by simple rules. During a study of electrophilic substitution reactions in heterocycles it was found that the β value in the Dewar formula is not a constant equal to the resonance integral but rather depends on the electrophile used and decreases as the activity of the latter increases [4]. It is logical to assume that as applied to nucleophilic substitution reactions, the calculation of the change in the localization energy with variations in β will correspond to a change in the reactivity of the substrate as a function of the nature of the nucleophile. The Dewar formula can then be represented as $\Delta E_{(\pi)} = 2\beta_X(C_{0,r} + C_{0,s}) - \beta\sum_i h_i(C_{0,i})^2$, where β_X is a measure of the activity of the nucleophile and takes on values ranging from zero to β, and $C_{0,r}$, $C_{0,s}$, and $C_{0,i}$ are the coefficients of the AO for the lower vacant MO (LVMO) for the r and s atoms adjacent to the reaction center and for the i atoms with parameters h_i (the coulombic factor in $\alpha_i = \alpha + h_i\beta$).

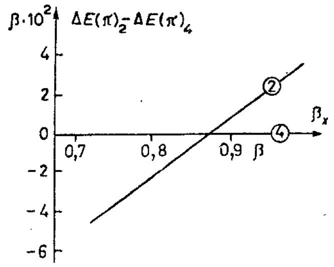

Fig. 1. Calculations of the reactivity of the quinolinium cation by the Dewar method: $\Delta E_{(\pi)}$ is the localization energy of the anion, and β_X is a parameter that characterizes the activity of the nucleophile.

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*More complex computational methods are presently not applicable to many-atom systems and not found in the literature.

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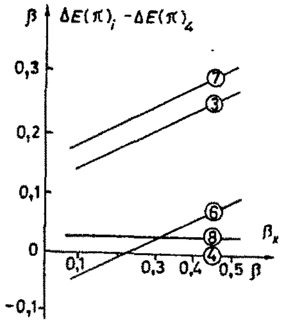

Fig. 2

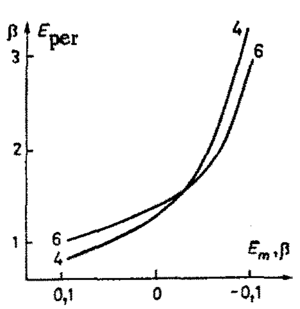

Fig. 3

Fig. 2. Calculation of the reactivity of 5-azacinnoline by the Dewar method: $\Delta E_{(\pi)}$ is the localization energy of the anion [relative to $\Delta E_{(\pi),4}$], and β_X is a parameter that characterizes the activity of the nucleophile.

Fig. 3. Calculation of the reactivity of 5-azacinnoline by the Klopman method: E_{per} is the perturbation energy during attack on the 4-C or 6-C atom, and E_m is a measure of the hardness of the base (it increases from the right to the left).

To verify this assumption we calculated the change in the localization energy in the case of nucleophilic attack at the 2-C and 4-C atoms of the quinolinium cation as β_X changes. It follows from the calculated data presented in Fig. 1 that attack at the 2-C atom is energetically more favorable for hard bases – for low β_X values – whereas attack at the 4-C atom is more favorable for soft bases – for larger β_X values. The results of the calculation by the proposed method are in agreement with the calculations by the DMTS method [2], as well as with the experimental data: the attack by hard bases – O-anions – is directed at the 2-C atom, and attack by soft bases [5] – carbanions – is directed at the 4-C atom of the quinolinium cation.

We also used the improved Dewar method for the calculation of the change in the reactivity of 5-azacinnoline in nucleophilic substitution reactions involving the hydrogen atom as a function of the activity of the nucleophile. It follows from Fig. 2 [$\Delta E_{(\pi)}$ for the 4-C atom was selected as the standard] that the 6-C atom is most reactive in the hard-base region, whereas the 4-C atom is most reactive in the soft-base region. The same relationship was previously observed [7] for reactions controlled by the charge and the boundary electron density.

A similar result is obtained in the calculation of the change in the reactivity of 5-azacinnoline as a function of the activity of the nucleophile with the use of the general VMO theory. The upper occupied MO (UOMO) energy (E_m)* is a measure of the strength of the nucleophile (the hardiness of the base) in this method [1], and the perturbation energy during attack on this position is a measure of the reactivity of any position in the substrate molecule:

$$E_{per,\,i} = \sum^{vac} \frac{2(C_{n,i})^2}{E_m - E_{n+1}} \beta^2.$$

The results of the calculation, which are presented in Fig. 3, are in complete agreement with the calculations by the proposed method: attack at the 6-C atom is energetically more favorable in the hard-base region, while attack at the 4-C atom is more favorable in the soft-base region.

This agreement between the two methods is not accidental, since the starting physical models for the calculation of the reactivities of the heterocycles by the two methods correspond to one another. This assertion can be explained. In the case of a reaction with a strong base the transition state of the reaction is reached rapidly and is structuraly closer to the starting state; the coulombic interaction between the reagents is large, as a result of which the reaction is controlled by the charge distribution in the reagent molecules – in the Klopman method this corresponds to a low-lying UOMO of the nucleophile with small E_m values. At the same time, in the Dewar method this corresponds to slight perturbation of the π-electron system of the

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*In addition to other factors, the charge of the reagent enters into calculations of E_m by the method of the general VMO theory [1].

substrate when the carbon atom undergoing attack has not yet taken on sp^3 hybridization and has not gone out of conjugation with the adjacent atoms of the ring; this is described by small β_X values. In the reaction with a soft base the orbital interaction takes on its maximum value, as a result of which the reaction is controlled by the boundary electron density – in the Klopman method this corresponds to a high-lying UOMO of the nucleophile with large E_m values. In the Dewar method this interaction corresponds to pronounced perturbation of the π-electron system of the substrate, when the conjugation of the carbon atom undergoing attack with the adjacent atoms is disrupted in view of its conversion to the sp^3 state; this is described by larger β_X values.

Thus we have demonstrated the correspondence between our proposed method for allowance for the activity of the nucleophile, which is based on the special application of the VMO theory in the form of Dewar reactivity numbers, and the method for allowance for the activity of the nucleophile on the basis of the general VMO theory – the Klopman method. A qualitative correspondence between the proposed method and the DMTS model was also demonstrated in the case of reactions of the quinolinium cation.

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