SHORT COMMUNICATIONS

A STUDY OF THE REACTIVITY OF FURAN, PYRROLE, THIOPHEN, AND RELATED COMPOUNDS USING A HMO DELOCALIZED MODEL

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Several quantum-mechanical quantities which relate to accounting for chemical reactivity in conjugated molecules have been proposed in LCAO-MO treatments. These are quantities such as π-electron density, self-polarizability, free valence, localization energy, frontier electron density, superdelocalizability, atom stabilization energy, etc. Such procedures, however, do not account for the nature of the reagent and fail to reproduce the changes in relative reactivity of various positions of attack. An attempt was therefore recently made by Chalvet et al. to develop a unified theoretical treatment of the transition state in the reactions of unsaturated molecules, which was shown to encompass both the Wheland and the delocalized models of the transition state.1-3 In the framework of the simple Hückel method, the attacking species is represented as a single orbital containing none, one, or two electrons depending on whether the reagent is an electrophile, radical, or nucleophile.

Let us consider the following cases:

(a) The molecule and the reagent X before reaction, i.e. without any bonding between them. The computed HMO energy of this supersystem is $E_0^\pi$.

(b) The molecule being attacked by reagent X at a position labelled $\alpha$. The π-delocalization extends to reagent X which is now bonded to the attacked position by a weak π-bond ($k \approx +0.4$). The HMO energy of the system is now $E_\alpha^\pi$.

(c) We suppose that the molecule is attacked at another position labelled $\beta$. Similarly, the HMO energy of the system is $E_\beta^\pi$.

Let us compute the quantity

$$\Delta E^\pi = (E_\alpha^\pi - E_0^\pi) - (E_\beta^\pi - E_0^\pi) = E_\alpha^\pi - E_\beta^\pi$$

which may have the significance of a difference of stabilization energies. Chalvet’s theory assesses that position $\alpha$ will be more reactive than $\beta$ if $\Delta E^\pi > 0$ that is, if $E_\alpha^\pi > E_\beta^\pi$.

Since the value of parameter $h_X$ characterizing reagent X is unknown at first, we must calculate $\Delta E^\pi$ for several values of $h_X$. Subsequent inspection of the curve $\Delta E^\pi$ against $h_X$ will enable us to determine which value of $h_X$ accounts for the experimental features.

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In the present work, we investigate the reactivities against bromination of some heterocyclic rings. The electrophilic reagent Br⁺ is assigned an orbital containing no π-electron. As usual, the Coulomb integral $\alpha_X$ associated to centre X is expressed in the units of the standard $\alpha_C$ and $\beta_{CC}$ of benzene so that

$$\alpha_X = \alpha_C + h_X \beta_{CC} \quad \text{and} \quad \beta_{CX} = k_X \beta_{CC}$$

The values of parameters $h$ and $k$ are standard ones (see for example ref.4); $h_Y$ and $k_{CY}$ respectively are: for O, 2·3, 0·7; N, 1·5, 1·0; S, 1·0, 0·7; Br⁺, varied, 0·4.

Results

(i) *Furan, thiophen, and pyrrole.*—These three fundamental five-membered rings are well known to be halogenated exclusively at position $\alpha$.⁵ This experimental

![Graphs](image)

Fig. 1.—The variation of the relative energies for electrophilic attack on:
(a) furan, thiophen, and pyrrole;
(b) 2-furoic acid, 2-thenoic acid, and pyrrole-2-carboxylic acid;
(c) indole, benzo[b]thiophen, and benzofuran.

feature is well accounted for by the curves in Figure 1(a) showing the variation of $\Delta E^\pi$ against $h_X$. It may be seen that $\Delta E^\pi > 0$ for $h_X > -0·9$ which indicates that


bromination occurs at position \( \alpha \). This first set of curves therefore indicates that
\( \kappa_{\text{Br}^+} > -0.9 \).

(ii) In the same way, we investigated the behaviour against bromination of the
three corresponding 2-carboxylic acids. 2-Furoic and 2-thenoic acids are reported
by Linda and Marino to be attacked by \( \text{Br}^+ \) in acetic acid solution and in the dark
exclusively at position 5 while pyrrole-2-carboxylic acid gives a mixture of 4- and
5-bromo- and 4,5-dibromo derivatives.6 Figure 2(a) shows that the theory correctly
predicts this behaviour if we take \( \kappa_{\text{Br}^+} \simeq 0.15 \).

(iii) Finally, it is known5 that indole and benzo[b]thiophen are attacked by
\( \text{Br}^+ \) at position \( \beta \) while position \( \alpha \) is more reactive in benzofuran. This particular
behaviour of benzofuran is nicely accounted for by the present theory: Figure 1(c)
undoubtedly indicates that position \( \alpha \) is attacked in benzofuran for \( \kappa_X > -0.9 \)
while position \( \beta \) would always be substituted in indole and benzo[b]thiophen.

We may conclude that there is a general agreement between our theoretical
predictions and the experimental determination of the sites of bromination. A
convenient approximate value for \( \kappa_{\text{Br}^+} \) in acetic acid solution and in the dark appears
to be \( +0.15 \). It should however be noticed that this value necessarily depends on
the parametrization used for heteroatoms. But the order of magnitude of \( \kappa_{\text{Br}^+} \) is
probably correct. \( \text{Br}^+ \) may thus be called a soft electrophile.

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