

SHORT COMMUNICATIONS

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

By C. DECORET* and B. TINLAND*

[Manuscript received May 19, 1971]

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^π .

(b) The molecule being attacked by reagent X at a position labelled α . 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_α^π .

(c) We suppose that the molecule is attacked at another position labelled β . Similarly, the HMO energy of the system is E_β^π .

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 α will be more reactive than β 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 ΔE^π for several values of h_X . Subsequent inspection of the curve ΔE^π against h_X will enable us to determine which value of h_X accounts for the experimental features.

* Section de Recherches de Mécanique Ondulatoire Appliquée, Université de Lyon I, 69 Villeurbanne, France.

¹ Bertran, J., Chalvet, O., Daudel, R., McKillop, T. F. W., and Schmid, G. H., *Tetrahedron*, 1970, **26**, 239.

² Chalvet, O., Daudel, R., and McKillop, T. F. W., *Tetrahedron*, 1970, **26**, 349.

³ Chalvet, O., Daudel, R., Schmid, G. H., and Rigaudy, J., *Tetrahedron*, 1970, **26**, 365.

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 α_X associated to centre X is expressed in the units of the standard α_C and β_{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 α .⁵ This experimental

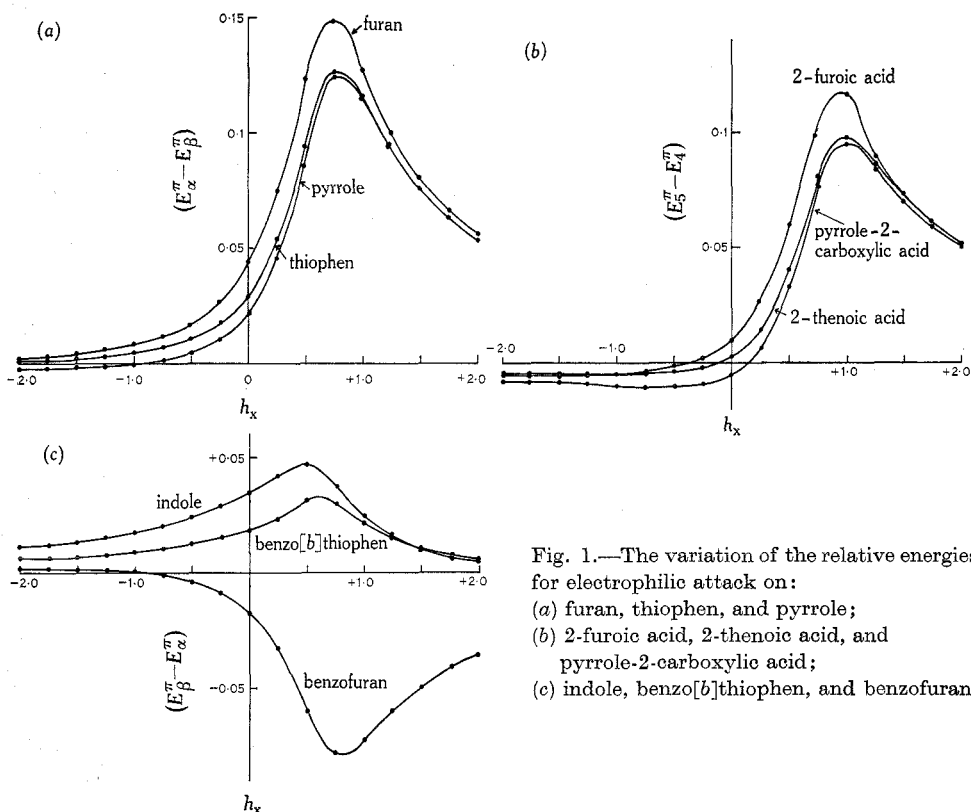


Fig. 1.—The variation of the relative energies for electrophilic attack on:
(a) furan, thiophen, and pyrrole;
(b) 2-furoic acid, 2-thenoic acid, and pyrrole-2-carboxylic acid;
(c) indole, benzo[b]thiophen, and benzofuran.

feature is well accounted for by the curves in Figure 1(a) showing the variation of $\Delta E''$ against h_X . It may be seen that $\Delta E'' > 0$ for $h_X > -0.9$ which indicates that

⁴ Streitwieser, A., "Molecular Orbital Theory for Organic Chemists." (John Wiley: New York 1962.)

⁵ Katritzky, A. R., and Lagowski, J. M., "Principes de la Chimie des Composés Hétérocycliques." (Gauthiers-Villars: Paris 1968.)

bromination occurs at position α . This first set of curves therefore indicates that $h_{\text{Br}^+} > -0.9$.

(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 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 $h_{\text{Br}^+} \simeq +0.15$.

(iii) Finally, it is known⁵ that indole and benzo[b]thiophen are attacked by Br^+ at position β while position α 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 α is attacked in benzofuran for $h_{\text{X}} > -0.9$ while position β 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 h_{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 h_{Br^+} is probably correct. Br^+ may thus be called a soft electrophile.

Acknowledgments

The calculations were carried out on the CDC 3600 computer of the CNRS at Orsay. A grant of computer time from the CNRS is gratefully acknowledged.

⁶ Linda, P., and Marino, G., *J. chem. Soc. (B)*, 1968, 392.