Molecular Electrostatic Potentials. Mechanistic Aspects of Electrophilic Attack on Furan

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Summary On the basis of its calculated electrostatic potential, we suggest that electrophilic attack on furan proceeds through the shifting of a hydrogen out of the molecule plane, producing an approximately tetrahedral carbon.

As part of an investigation of the electrostatic potentials in the regions around molecules of organic and biochemical interest, we have computed the potential for the furan molecule, using a 'deorthogonalized'[1] CNDO/2 molecular wave function. The electrostatic potential has previously been used successfully in analysing the protonations of a number of molecules.†[2–6]

Furan readily undergoes substitution by electrophiles;[7,8] thus, its reactive sites should be indicated by regions of negative potential. It has been found experimentally that electrophilic attack occurs preferentially on an α-carbon.[7,8]

The electrostatic potential of furan in its normal planar state was found to be positive everywhere except for a negative region above, below, and to the outside of the oxygen. This region has a minimum of −58·3 kcal/mol, located in the molecular plane. No negative potentials were found by any of the carbons. This contrasts with recent results for thiophen,[5] for which regions of negative potential were found near the sulphur, and also above and below the entire aromatic ring.

Table. *Summary of calculated results*

Structure[a,b]	CNDO/2 energy (eV)	Potential minima[c] (kcal/mol)
Planar $\angle_{\alpha\text{-H}} = 125·3°$; $\angle_{\beta\text{-H}} = 126·5°$	−1353·5	−58·3 at (0·00, 6·00, 0·00)
α-H bent $\angle_{\alpha\text{-H}} = 109·6°$; $\angle_{\beta\text{-H}} = 126·5°$	−1352·0	−61·2 at (0·00, 6·00, 0·00). −18·0 at (4·50, 3·22, 1·50).
β-H bent $\angle_{\alpha\text{-H}} = 125·3°$; $\angle_{\beta\text{-H}} = 110·2°$	−1351·6	−56·1 at (0·00, 6·00, 0·00). −18·2 at (2·87, −2·01, 1·50).

[a] The bond lengths and angles for planar furan were taken from V. Schomaker and L. Pauling, *J. Amer. Chem. Soc.*, 1959, **61**, 1769. A C–H bond length of 1·075 Å was used for all three structures.

[b] The angles given in the Table are between the indicated hydrogen, the carbon to which it is attached, and either neighbour of the carbon.

[c] The co-ordinates (*x*, *y*, *z*) of the minima are given in atomic units (1 a.u. = 0·5292 Å), and are relative to an origin at the midpoint of the β-C–β-C bond. The aromatic ring is in the *x*,*y* plane, and the co-ordinates of the atoms are: oxygen, (0·0000, 4·0100, 0·0000); α-carbon, (2·1254, 2·4397, 0·0000); β-carbon, (1·3795, 0·0000, 0·0000).

We investigated the possibility that electrophilic substitution on furan proceeds through a preliminary stage in which either (I) an α-hydrogen or (II) a β-hydrogen moves out of the molecular plane, producing a nearly tetrahedral carbon having one position unoccupied. The results are striking. In both instances, a very significant negative potential developed along the fourth tetrahedral direction, suggesting that it is a likely path of electrophilic attack. In case (I), this region of negative potential is a continuation of that previously mentioned, by the oxygen. The original potential minimum remains nearly the same as in planar furan (Table), but a new minimum of −18·0 kcal/mol has appeared in the fourth tetrahedral direction, at a distance of 1·54 Å from the carbon. In case (II), the new region of negative potential is separated by a positive barrier from that by the oxygen. Otherwise, however, the two sets of results are remarkably similar. Now a minimum of −18·2 kcal/mol is found, again at a distance of 1·54 Å from the β-carbon in the fourth tetrahedral direction.

For none of the structures investigated were negative potentials found which would indicate that electrophilic substitution on furan may occur through the formation of an intermediate π-complex. The fact that such a mechanism was suggested in the case of thiophen[5] does not necessarily imply any inconsistency since, despite important similarities between furan and thiophen, there are also considerable differences in their chemical properties.[7,8] Furthermore, the consequences of shifting hydrogens out of the molecular plane of thiophen have not been investigated.

The present results suggest that electrophilic attack on furan is preceded by the movement of a hydrogen out of the molecular plane, thereby allowing the development of a path of negative potential leading to the particular carbon atom. This path is approximately equally attractive toward the electrophile whether it is an α- or β-carbon that is involved. However, since the negative potential by the α-carbon is part of a large negative region extending over to the oxygen [with a deep minimum near the latter (Table)], an electrophile approaching *via* this very attractive region by the oxygen can fairly readily move over to the presumed path of attack on the α-carbon; there is no intervening barrier of positive potential. An analogous move from the oxygen to the path of attack on the β-carbon *is* impeded by a positive barrier. Thus, β-substitution will presumably occur primarily when the initial approach is to the β-carbon, whereas α-substitution can apparently result from an initial approach to either the α-carbon or the oxygen, and can therefore be expected to occur with considerably greater frequency.

This conclusion, in full accord with experimental observations,[7,8] could not have been reached on the basis of the calculated CNDO/2 atomic charges. These invariably predicted the α-carbons to be positive, both in planar furan and in the two non-planar forms, while the β-carbons were usually found to have negative charges.‡

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† The effectiveness of the electrostatic potential in predicting protonation sites despite not dealing directly with the attacking proton is discussed in ref. 6.

‡ See also ref. 9.

This investigation has been concerned primarily with the mechanism of approach of an electrophile, rather than the nature of any intermediate that may be formed. However, the proposed mechanism is certainly consistent with an intermediate containing a tetrahedral carbon atom. Such intermediates have frequently been postulated for electrophilic aromatic substitutions, and some supporting evidence has been found in specific cases.[9–16]

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