Theoretical Studies of Aromatic Substitution. Part I. Pyrrole and its Protonated Species

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The MINDO/2 method has been applied to pyrrole and its α-, β-, and *N*-protonated forms. The geometries of the various species have been varied so that the energy of each may approach a minimum. It is found that there are substantial geometrical changes on protonation, and that these changes differ for the different cations. The sequence of reactivity is found to be α > β > N, in accordance with experimental findings. The calculations on pyrrole are compared with the results of other all valence electron calculations.

WITH the advent of semiempirical all-valence electron calculations it has become possible to calculate properties of many systems of interest to the organic chemist. The Extended Hückel[1] and CNDO/2[2] methods have been used to calculate a variety of molecular quantities; whilst they both perform quite well in predicting small energy changes within a molecule, they do not give good

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[1] R. Hoffmann, *J. Chem. Phys.*, 1963, **39**, 1397.

[2] J. A. Pople and D. L. Beveridge, ' Approximate Molecular Orbital Theory,' McGraw–Hill, New York, 1970.

total energies. Dewar has parametrised the EMZDO method of Dixon [3] to give good agreement with experimental heats of formation, calling the method MINDO [4] (modified intermediate neglect of differential overlap). Early faults with the method have now been largely removed, and the second version of this scheme, MINDO/2 [5,6] is currently proving very successful in the calculation of a diverse range of molecular properties. Thus Dewar has been able to predict the course of Cope rearrangements [7,8] and Hoyland the energy of activation of the methyl radical on ethylene.[9]

For much larger systems the construction of a reaction surface would be extremely tedious, so an alternative approach will be followed here, namely that of calculating the energies of reaction intermediates. The energy in this case will be a minimum with respect to all variables, rather than a minimum with respect to all but one variable, and a maximum with respect to that remaining variable.

Of course it is much simpler to calculate just one point on the energy *versus* reaction co-ordinate curve, and the values of the geometric parameters associated with the minimum energy configuration should be of great value in checking current ideas on the structure of these intermediates.

Aromatic substitution is known to proceed *via* the presence of an intermediate, real or inferred, but the geometries of these intermediates have so far remained a matter for speculation; it is commonly assumed that the two bonds adjacent to the site of substitution tend to the appropriate single bond length, but that the rest of the molecule remains the same as in the original substrate. We have no grounds for this latter assumption, and so we must now be prepared to determine the geometry of a given intermediate by varying the geometric parameters until a minimum energy is found. Now it is possible that the proposed ' intermediate ' structure may also be that of the transition state, so that we must be careful that we are not in fact calculating a point at some arbitrary distance up the reaction co-ordinate *versus* energy curve, say P (Figure), instead of at the top, as we should be in this case.

A study has been made of the pyrrole molecule and its protonation reactions, with a simple proton as electrophile, in order that some appreciation of the effect of geometric effects in substitution may be gleaned, and to test the stability of the reactivity sequence $\alpha > \beta > N$ with respect to such changes.

Methods.—The MINDO/1 programme was obtained from Quantum Chemistry Programme Exchange, and modified to the MINDO/2 parameter scheme. The programme was run on an ICL 1909 computer, using the overlay facility, which enabled matrices of dimension 45 to be used, corresponding to a minimum basis set for about a maximum of 23 atoms.

The minimisation procedure was that described by Fischer and Kollmar.[10] This involves choice of a starting geometry, with subsequent variation of each variable about its original value. The variation of each variable enables a force constant and equilibrium value for that variable to be worked out, which enables one to calculate a new origin. The process is repeated until the desired stability of the energy with respect to co-ordinate variation is reached. However the number of variables involved in systems with no symmetry is still inconveniently large, so it was assumed that all C–H bond lengths were fixed at 1·19 Å (the additional 0·1 Å to the experimental bond length being necessary in the MINDO/2 method), and that the dispositions of these bonds were determined by the external bisection of the internal (ring) angles. This latter constraint was relaxed for the positions adjacent to the heteroatom, as angles differed significantly from the external bisection values. These constraints have recently been applied to other systems successfully.[11]

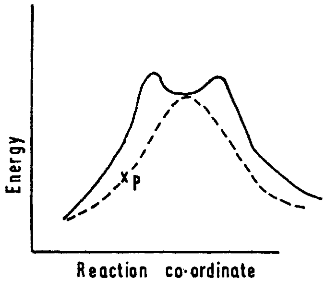

FIGURE —— Profile with intermediate and - - - - profile with transition states and intermediate all equivalent

The results obtained are not, therefore, true minima; they are variously estimated to be between 0·5 and 1·5 kcal above the true minima, these differences in energy reflecting only small deviations in geometry from those given.

RESULTS

The results are best presented as a series of diagrams with the bond distances and angles written in the appropriate places [structures (1) to (7)]; the energies are recorded in Table 1. Structure (3) represents one of the possible structures of Bak.[12] $\widehat{HCH} = 109° 30'$ throughout in the cation calculations.

The calculations on pyrrole itself may be presented more fully, in view of the excellent agreement with the experimental heat of formation, corrected to a gas-phase value.

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[3] R. N. Dixon, *Mol. Phys.*, 1967, **12**, 83.

[4] N. C. Baird and M. J. S. Dewar, *J. Chem. Phys.*, 1969, **50**, 1262.

[5] M. J. S. Dewar and E. Hasselbach, *J. Amer. Chem. Soc.*, 1970, **92**, 590.

[6] N. Bodor, M. J. S. Dewar, A. J. Harget, and E. Hasselbach, *J. Amer. Chem. Soc.*, 1970, **92**, 3854.

[7] A. Brown, M. J. S. Dewar, and W. W. Schoeller, *J. Amer. Chem. Soc.*, 1970, **92**, 5516.

[8] M. J. S. Dewar and W. W. Schoeller, *J. Amer. Chem. Soc.*, 1971, **93**, 1481.

[9] R. Hoyland, *Theor. Chim. Acta*, 1971, **22**, 229.

[10] H. Fischer and H. Kollmar, *Theor. Chim. Acta*, 1969, **13**, 213.

[11] C. S. Cheung, M. A. Cooper, and S. L. Manatt, *Tetrahedron*, 1971, **27**, 689.

[12] B. Bak, D. Christensen, L. Hansen, and J. Rastrup-Andersen, *J. Chem. Phys.*, 1956, **24**, 720.

Thus Table 2 lists the molecular orbital energies and symmetries according to the present work and that of Clementi,[13] and Table 3 lists charge densities according to the present work in comparison with the results of various other calculational procedures. Table 4 gives the dipole moments calculated by the MINDO/2 and the CNDO/2 [14] methods.

TABLE 1

Heats of formation of pyrrole and its cations

Molecule	Heat of formation (kcal mol^{-1})	Estimated correction *
Pyrrole (1)	+28·36	−0·5
Pyrrole (2)	+52·21	
α-Cation (4)	+190·39	−0·5
β-Cation (5)	+194·39	−1·0
N-Cation (6)	+201·36	−1·0 to −1·5
Benzenium cation (7)	+195—196	

* Increasing or decreasing all C–H bonds by 0·01 Å changes the energy by *ca.* 0·2 kcal. Other angular variations are expected to contribute only slightly, since the total energy does not vary rapidly as angles are varied, but does depend strongly on bond lengths.

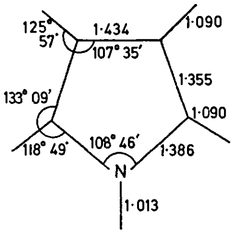
TABLE 2

Molecular orbital energies and symmetries for pyrrole

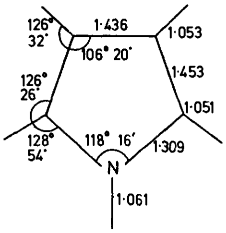
Irreducible representation of group C_{2v}	Orbital energies (eV) MINDO/2	Clementi
*A*2 (π)	−8·84	−10·47
*B*1 (π)	−9·55	−11·48
*A*1 (σ)	−10·82	−15·57
*B*2 (σ)	−11·25	−16·26
*B*2 (σ)	−11·77	−16·86
*A*1 (σ)	−11·99	−17·48
*B*1 (π)	−13·68	−17·05
*A*1 (σ)	−17·32	−21·00
*B*2 (σ)	−18·18	−21·52
*A*1 (σ)	−18·79	−22·28
*B*2 (σ)	−26·42	−27·93
*A*1 (σ)	−28·80	−29·58
*A*1 (σ)	−40·45	−35·74

DISCUSSION

The geometry calculated for pyrrole (1) is very close to one of the possible structures consistent with the microwave spectrum [12] (3); this geometry also gives a heat of formation which agrees with experiment, allowance having been made for the difference between the gas-phase value here calculated and the solution value quoted in the tables,[16] namely +19·48 kcal mol^{-1} (a difference of *ca.* 8 kcal between the two quantities is seen to be the normal state of affairs for a wide range of molecules). In view of this we must reject the geometry



(1)



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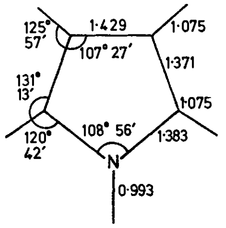

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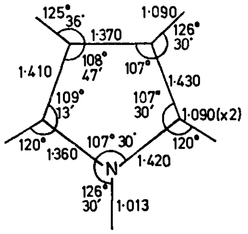

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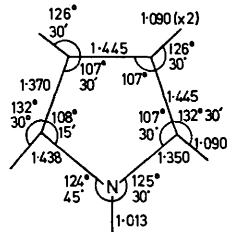

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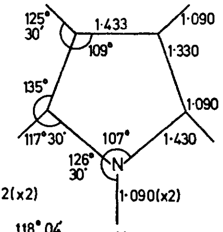

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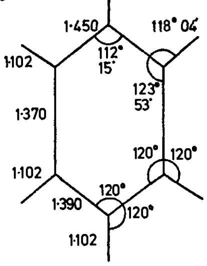

(7)

TABLE 3

Charge density distribution for pyrrole

Atom *	MINDO/2	CNDO/2 [14]	CNDO/2 † [a]	CNDO/2 † [b]	EHT [15]	Clementi [13]
N σ π	5·3687 {3·6582 1·7105	5·2182 {3·5629 1·6553	5·2492 {3·5888 1·6604	5·0875 {3·4367 1·6508		5·4102 {3·7513 1·6589
C1(4) σ π	3·8175 {2·7743 1·0432	3·9225 {2·8377 1·0848	3·9189 {2·8427 1·0762	3·9432 {2·8631 1·0801	3·90 {2·82 1·08	4·1062 {3·1611 1·0953
C2(3) σ π	4·0380 {2·9364 1·1016	4·0880 {3·0026 1·0854	4·0349 {2·9413 1·0936	4·0392 {2·9447 1·0945	4·16 {3·03 1·13	4·2564 {3·0310 1·0752
H1(4)	1·0283	0·9832	0·9963	1·0127		0·7962
H2(3)	1·0179	0·9726	0·9939	1·0094		0·8084
H5	0·8280	0·8449	0·8629	0·9039		0·6610

* C1 α to nitrogen, C2 β to nitrogen, H5 bonded to nitrogen. † Original parametrisation. Hydrogen exponent 1·2; carbon exponent 1·625; nitrogen exponent 1·950.

[a] Charge distribution after 'deorthogonalisation.' [b] Charge distribution in ZDO basis.

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[13] E. Clementi, H. Clementi, and D. R. Davis, *J. Chem. Phys.*, 1967, **46**, 4725.

[14] D. T. Clark, *Tetrahedron*, 1968, **24**, 4689.

[15] W. Adam, A. Grimison, and G. Rodriguez, *Tetrahedron*, 1967, **23**, 2513.

[16] D. R. Stull, E. F. Westrum, jun., and G. C. Sinke, 'The Chemical Thermodynamics of Organic Compounds,' Wiley, London, 1969.

proposed by Cumper[17] (2), which gives a heat of formation some 20 kcal too large. This geometry has however been recently quoted in the literature.[18]

TABLE 4

Dipole moments (Debye)

MINDO/2	1·71
CNDO/2[14]	1·53
Experiment[18]	1·84 ± 0·08

The large heats of formation calculated for the cations are suitable only for the gas phase; the presence of a counter ion should considerably reduce these values and give figures more appropriate to the liquid phase. For closely similar solvation energies the stability sequence should not be altered, so that the data herein collected may be compared with experimental solution data. We have therefore the stability sequence α- > β- > N-cation. (that is the α-cation is more stable than the β-cation, *etc.*). Whipple and Chiang[19] have studied the proton magnetic resonance spectra of pyrrole and some derivatives of pyrrole in sulphuric acid solutions, and they found that the α-protonated form predominated over the β-protonated form. This enhanced basicity of the α-position is exhibited also in kinetic data; Bean[20] has measured rates of proton exchange in dioxan–D_2O solutions, and finds that the α-position exchanges faster than the β-position. Thus the calculated reactivity sequence is seen to agree with the experimental situation; the calculations by Hermann[21] using the CNDO/2 and Extended Hückel methods give the same conclusions, but only by gross assumptions concerning the geometries of the intermediates, which introduce a certain amount of fortuitousness into the results.

With benzene as the prototype aromatic molecule it is of interest to compare the heat of formation of the benzenium cation $C_6H_7^+$ with those for the pyrrole cations to see if activation or deactivation is predicted. Although the energy of the benzenium cation is not fully minimised the final value is certainly above both the α and β cationic forms. Using the heat of formation of benzene we find that the energy difference between benzene and its intermediate is greater than that between pyrrole and its α- and β-Wheland intermediates; enhanced reactivity over benzene is thus expected, as long as the intermediates resemble the transition states closely. The MINDO/2 method is, therefore, seen to predict both orientation and activation correctly. The geometry changes ' observed ' on protonation seem to be significant, so that unless due regard is taken of possible changes in geometry during substitution wholly erroneous conclusions may be drawn.

Finally some comments on the pyrrole calculation herein reported compared with the results of other calculations. The symmetry properties of the MO's enable one to discover that the sequence of occupied orbitals in the MINDO/2 scheme differ from those calculated by Clementi[13] using *ab initio* techniques in only two places, the *B*1 orbital at −13·68 eV lying below the *A*1 orbital at −11·99 eV, instead of the *B*1 lying above the *A*1. In both cases the lowest occupied π orbital is seen to be embedded in the σ orbitals. The first ionisation potential may be estimated from Koopman's theorem as 8·84 eV, which compares with the photoionisation value of 8·20 eV[22] and the electron impact value of 8·97[23] eV. The charge density distribution calculated by the MINDO/2 method strictly applies to that for an orthogonal basis set (the ZDO approximation). However transformation back to the real Slater orbital basis set does not substantially change the numbers involved. A CNDO/2 calculation effected by the present author (see Table 3) shows the small differences in the numbers involved in transforming from an orthogonal to a non-orthogonal basis set. Significant differences in the carbon–hydrogen bond polarity are observed however in the CNDO/2 and *ab initio* calculations.[14] (The CNDO/2 programme was kindly supplied by Dr. B. J. Duke). The MINDO/2 calculation of the dipole moment yields the best accord with experiment yet found. Finally all calculations herein reported show the π-electron donating and σ-electron accepting character of the nitrogen in pyrrole, as mentioned by Clementi.

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